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Scientific Abstracts



FISPGHAN Member Societies:



Thursday, October 6, 2016

**CONCURRENT SESSION I
10:00 AM**

GLOBAL HEALTH

1 DIFFERENTIAL METABOLIC PROFILES IN CHILDREN WITH SEVERE WASTING AND EDEMATOUS MALNUTRITION IN MALAWI

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Context: Mortality rates in children with severe acute malnutrition (SAM) remain high despite standardized rehabilitation protocols. Two forms of SAM are distinguished: marasmus and kwashiorkor. Marasmus is characterized by severe wasting, whereas kwashiorkor presents with nutritional edema and is characterized by more profound metabolic disturbances, including hypoalbumenia and a fatty liver. However, it is unknown if there are differences in the metabolic profiles between children with marasmus and kwashiorkor and whether these differences could indicate the need for distinct clinical treatment plans for each form of SAM.

Objective: We aimed to 1) identify metabolic pathways which change due to nutritional rehabilitation and 2) determine if children with marasmus demonstrate different metabolic profiles from children with kwashiorkor.

Design: We studied 40 children with SAM (18 marasmus and 22 kwashiorkor) aged between 6 to 60 months, who were treated at Queen Elizabeth Central Hospital in Blantyre, Malawi. Using the Biocrates p180 kit for targeted metabolomics, we obtained measurements for 149 metabolites in serum at admission and prior to discharge after nutritional rehabilitation. Metabolites include 32 amino acids and biogenic amines, 14 acylcarnitines, 15 sphingolipids, 87 glycerophospholipids, and others.

Results: At admission, 8 amino acids, including 4 essential ones, differed between marasmus and kwashiorkor; these were all lower in children with kwashiorkor. However, with nutritional recovery, 17/21 amino acids were significantly increased and only tryptophan continued to be lower in kwashiorkor. Nutritional recovery increased only 4/12 biogenic amines which are related to cell cycle progression and oxidative stress. Again, kwashiorkor tended to have lower values; both kynurenine and total dimethylarginine continued to be lower in kwashiorkor compared to marasmus after nutritional rehabilitation. Sphingolipids were not altered by nutritional recovery and also did not differ between groups. At admission, most acylcarnitines (9 out of 14) were lower in kwashiorkor patients compared to those with marasmus, and 3 continued to be lower after nutritional recovery. Acylcarnitines were of particular interest as they relate to beta oxidation, energy metabolism, fatty acid transport and mitochondrial damage.

Conclusions: Many but not all metabolites increased following nutritional recovery, pointing to a restoration in metabolic homeostasis. At admission, metabolites levels that differ between the two forms of SAM are systematically lower in children with kwashiorkor. In particular, lower levels of acylcarnitines in kwashiorkor patients point to potentially impaired beta oxidation of fatty acids, which can be a source of energy during malnutrition. Our results suggest that specific metabolic disruptions may underlie the different clinical manifestation of marasmus and kwashiorkor and could be the basis for differential targeted treatments.

2 ACTIVATION OF CALCIUM-SENSING RECEPTOR IN THE GUT INHIBITS ENTEROTOXIN-INDUCED SECRETION AND BACTERIA-INDUCED INFLAMMATION IN RODENTS AND REDUCES INFECTIOUS DIARRHEAS IN CHILDREN

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Introduction: Treatment of infectious diarrhea remains a challenge globally, particularly in infants, young children, and immune-compromised patients. Children with infectious diarrhea who become dehydrated are normally treated with oral or intravenous rehydration. Although rehydration can replace the loss of fluid, it neither stops ongoing intestinal secretion nor does it reduce underlying gut inflammation. Therefore, there has been continuous effort to search for new cost-effective ways to safely stop diarrhea. The extracellular calcium-sensing receptor (CaSR) is a unique Class C G protein-coupled receptor that uses nutrients such as calcium, polyamines and aromatic amino acid as its ligands. Recent studies indicate that CaSR is highly expressed in the gut, and when activated by selective nutrients or specific chemical agonists, exhibits unusual pro-absorptive, anti-secretory, and anti-inflammatory properties. We therefore hypothesized in the present study that activating CaSR in the gut reduces secretory and inflammatory diarrheas.

Methods: To test this hypothesis, three models of diarrhea were induced in 4-6 week-old Sprague-Dawley rats and/or C57BL/6 mice (CaSR wild-type and knockout), and the effects of CaSR agonists calcium, spermine, tryptophan, and R568 were examined. These included 1) cholera toxin model of secretory diarrhea; 2) citrobacter model of infectious diarrhea; and 3) dextran sodium sulfate (DSS) model of inflammatory diarrhea. To further prove the concept, antidiarrheal effect of calcium, primary ligand of CaSR, was also assessed on patients with viral, bacterial, and/or parasitic enterocolitis.

Results: Mice receiving cholera toxin gavage developed secretory diarrhea; the latter was inhibited by R568 i.p. in wild-type but not in CaSR null mice. Similarly, mice receiving *C. rodentum* gavage or DSS treatment developed inflammatory diarrhea, which was significantly more severe in knockout mice than the wild-type controls. Increasing dietary calcium reduced the severity of diarrhea in wild-type mice; such an effect was not seen in CaSR mice. In rats, activation of CaSR by dietary calcium significantly delayed the onset, reduced the severity, and accelerated the recovery of DSS-induced colitis; so did dietary spermine and dietary tryptophan. Finally, five patients with infectious enterocolitis who developed severe diarrhea and hypocalcemia were selected to receive calcium replacement therapy. As calcium therapy continued and hypocalcemia improved, stool output decreased; when serum calcium levels normalized, diarrhea stopped.

Conclusion: These results suggest that targeting intestinal CaSR with nutrients, alone or in combination, may represent a new cost-effective method to stop diarrhea and treat inflammation in children. Clearly, randomized controlled trials are warranted.

3 ROTAVIRUS IMMUNIZATION: GLOBAL COVERAGE AND LOCAL BARRIERS FOR IMPLEMENTATION

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Background: Since 2006 two effective and safe vaccines against rotavirus (RV) infection (Rotarix™ and RotaTeq®) have been recommended by WHO worldwide. In 2012, FISPUGHAN identified the spreading of RV immunization (RVI) as a top priority for the control of diarrheal illness in childhood.

Aims: FISPUGHAN Working Group (WG) on acute diarrhea aimed at estimating the current RVI coverage and identifying the major barriers to local implementation in all countries of the world.

Methods: A survey was distributed to national experts in infectious diseases and vaccinations between March 2015 and April 2016. The survey provided information on the inclusion of RVI in the National Immunization Plan, presence of RVI programs, costs and perception of local barriers to implementation.

Results: Among the 76 countries contacted, 44 provided a survey eligible for analysis (response rate 58%). RVI is recommended in 23/44 countries (52.3%) participating in the survey. Although five countries have recommended RVI since 2006, most (13/44, 29.5%) included RVI in National Immunization Schedule between 2012 and 2014. The costs of vaccination are covered by the government (38.6%), by the GAVI Alliance (9%) or public and private insurances (6.8%) in some countries. However, in most cases, those costs are charged to families (43.1%). The limited perception of RV severity by families (50%) and elevated costs (45.4%) are the major barriers for large-scale implementation of RVI program. Surprisingly, only 6 countries (13.6%) reported the timing of first administration within 6 weeks as a major barrier.

Conclusion: After approximately 30 years since the introduction of RVI, the implementation of this major life-saving intervention is still unacceptably low and remains a major target for reaching the Millennium Developmental goal.. To sustain and implement RVI, FISPUGHAN could promote education for families/caregivers and physicians focused on the risk of RV diarrhea and efficacy of immunization.

4 THE EFFECT OF TWO PROBIOTIC STRAINS BB-12® and LGG® ON DIARRHEA IN CHILDREN WITH SEVERE ACUTE MALNUTRITION IN UGANDA

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Globally, undernutrition is the cause of approximately 3.1 million child deaths annually. Diarrhea is a major cause of morbidity and mortality in undernourished children. Probiotics seem to reduce duration of diarrhea in children, but results have mainly been obtained in well-nourished children in high-income countries. We aimed at investigating the effect of probiotics on diarrhea in children with severe acute malnutrition (SAM) during in- and outpatient treatment in a low-income country.

A randomized, double-blind, placebo-controlled study was carried out in 400 children admitted with SAM. Children received one sachet daily with a mixture of BB-12® and LGG® (10 billion colony-forming units/sachet, 50:50) or placebo during hospitalization and subsequent outpatient treatment for 8 – 12 weeks. The primary outcome was number of days with diarrhea during inpatient treatment. Secondary outcomes included number of days with diarrhea during outpatient treatment, diarrhea incidence and severity, pneumonia incidence, duration and severity, days with fever or vomiting, weight gain and recovery. All outcomes were analyzed separately for in- and outpatient treatment. Diarrhea data was collected using a stool diary in which caregivers noted every time their child passed stool and categorized the stool consistency according to a 4-point photo scale.

There was no difference in number of days with diarrhea during inpatient treatment for the probiotic vs. the placebo group (adjusted difference +0.2 days, 95% CI -0.8 to 1.2 days, $p=0.69$). However, during outpatient treatment the number of days with diarrhea was reduced in the probiotic group compared to the placebo group by 26% (adjusted difference -2.2 days, 95% CI -3.5 to 0.3, $p=0.025$). There was no significant effect of probiotics on diarrhea incidence or severity, pneumonia outcomes, fever, vomiting, weight gain or recovery. Although not significant, some outcomes related to infections occurred less frequently in the probiotic group during outpatient treatment (diarrhea incidence odds ratio (OR) 0.7 (0.4 to 1.2), $p=0.17$, pneumonia incidence OR 0.5 (0.2 to 1.3), $p=0.17$, fever -0.5 days (-1.3 to 0.2 days), $p=0.16$). Mortality was 13% ($n=26$) in the probiotic and 10% ($n=20$) in the placebo group ($p=0.24$).

LGG® and BB-12® did not reduce diarrhea during inpatient treatment of children with SAM, but reduced the number of days with diarrhea during outpatient treatment. This result is in line with a study testing a mixture of pro- and prebiotics in children with SAM which reported no effect of the intervention during inpatient treatment but a trend towards reduced mortality during outpatient treatment. Probiotics may have a future role in outpatient treatment of children with SAM.

5 ENVIRONMENTAL ENTERIC DYSFUNCTION IS ASSOCIATED WITH POOR LINEAR GROWTH AND CAN BE IDENTIFIED BY HOST FECAL mRNAs

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Background and Objective: Environmental enteric dysfunction (EED) can be assessed by the lactulose:mannitol (L:M) test. Our objective was to determine if selected host fecal transcripts were correlated with EED, and whether transcripts and clinical characteristics could be used to predict EED in rural African children.

Methods: Demographic and sanitation characteristics, along with L:M testing and host fecal transcript analyses from 798 asymptomatic Malawian children aged 12-61 months were compared to linear growth over the subsequent 3 months. Fecal host mRNA analysis included quantification of expression of 18 transcripts associated with L:M. Permeability was categorized as normal ($L:M \leq 0.15$), moderate ($0.15 < L:M < 0.45$) and severe ($L:M \geq 0.45$), and random forest predictive models were created.

Results: L:M was inversely correlated with linear growth over the subsequent 3 months ($r = -0.32, p < 0.001$) and severe EED was associated with stunting ($p < 0.0001$). Age < 24 months, weight-for-height Z-score < 0 , domesticated animals in the child's sleep environment, lack of a pit latrine or clean water source, and a recent history of diarrhea were associated with severe EED. A random forest model using CD53, HLA-DRA, MUC12 and TNF was 84% sensitive for severe EED and 83% sensitive for no EED.

Conclusion: Selected host fecal transcripts can be used in a random forest model as a non-invasive biomarker for categories of EED in rural African children.

6 ASSESSING THE IMPACT OF MATERNAL EXPOSURE TO DROUGHT ON CHILD GROWTH

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Early childhood adversity that impacts the growth of mothers in their childhood may negatively influence the growth outcomes of their young offspring. Famine studies in Holland and China have shown the impact of epigenetics. A study in Malawi investigates this phenomenon in the context of three meteorological droughts (1981, 1987, and 1992 respectively) and women residing in rural and peri-urban Mangochi district. A hypothesis is tested that there was a difference in mean LAZ, mean WAZ, and mean birthweight between children born to drought exposed mothers and children born to non-exposed mothers.

Being a natural experiment, women were already pre-selected into groups of those exposed and not exposed to three different droughts (1981, 1987, and 1992 respectively) by virtue of their date of birth (DOB). This retrospective cohort study used children's neonatal size measurements taken during a randomized controlled trial (iLiNS-DYAD-M). Their mean birthweight, mean LAZ, and mean WAZ were the outcomes ($n=1403$ includes 12 twins) while their mothers' environmental experience of drought was the exposure ($n=1391$). Some of the covariates were child sex and the maternal variables of education, height, BMI, marital status, sole head of household, "at risk" during pregnancy, and primiparity at "at risk" ages.

LAZ, WAZ and birthweight were positively associated with mother's exposure to the drought of 1987 even with covariate analysis ($p < 0.01$) except for the birthweight which no longer showed statistically significant results. The droughts of 1981 and 1992 as independent variables were not associated with the study outcomes at any level of significance ($\alpha 0.01; 0.05; 0.1$) even when covariates were added to the models. The covariates that were associated with LAZ and WAZ in the 1987 drought model were maternal height, being both a mother and head of household, and being an older or younger "at-risk" mother who was primiparous. Only maternal height had a positive association ($p < 0.01$). Older mothers (age > 35 yr) or younger mothers (age > 18 yr) deemed "at-risk" during pregnancy were more likely to have children with a relatively lower LAZ and WAZ than mothers who were not at risk as did mothers who were heads of household.

The 1987 drought appears to be different to the other droughts in that there were some noteworthy associations. It has been historically noted as being moderate while the 1992 one was the worst of the three; however, major drought relief efforts were implemented and offset much of the impact. In terms of the puzzling positive association observed with the 1987 drought and LAZ or WAZ, epigenetics may have played a role as reported in studies on the Great China Famine and the Dutch Famine. In sum, the present study may provide additional evidence for the reversal of the negative intergenerational impact of early childhood adversity.

Thursday, October 6, 2016

POSTER SESSION I 12:00 – 2:00 PM

* Poster of Distinction

CELIAC AND OTHER LUMINAL DISORDERS

23 EOSINOPHILIC ESOPHAGITIS IN CHILDREN: A RETROSPECTIVE COHORT STUDY

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Short title: Pediatric Eosinophilic Esophagitis.

Keywords: children, eosinophilic esophagitis, and intervention.

Background: Eosinophilic esophagitis (EoE) is a chronic allergy/immune-mediated disease with significant morbidity. It is characterized by dense eosinophilic infiltration of esophageal epithelium. EoE is increasingly recognized in children with high prevalence in patients with atopic disease.

Objective: To report our experience in children with EoE.

Methods: We conducted a retrospective cohort study using prospectively collected data in children (0-18 years) with an eosinophilic esophageal disorder between July 2014 and October 2015. Clinical characteristics including personal and family history for allergy, peripheral eosinophilia and IgE levels, endoscopic and histologic findings, treatment details, and outcomes were studied.

Results: A total of 31 children were diagnosed with EoE during the short study period (mean age: 7.6 years; 24 males and 7 females). Presenting symptoms varied with age; 12 had atopic condition. On endoscopy, 29/31 had abnormal appearing esophageal mucosa. Linear furrowing and mild erythema were the most common endoscopic findings. The treatment included topical steroids and/or dietary therapy.

Conclusion: Our experience indicates that the diagnosis of eosinophilic esophagitis in children is on the rise, presenting symptoms vary with age and has a common pathophysiological background with allergy as reported in previous studies. Identifying causative allergen and monitoring response to treatment remains problematic. Treatment options include topical steroids or avoidance of food allergen. Dietary therapy, though safe, lacks strict compliance.

24 ASSESSMENT OF RELIABILITY OF PLASMA CITRULLINE AND I-FABP AS NON-INVASIVE MARKERS OF ENTEROPATHY: A STUDY IN A HUMAN MODEL

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Background/Aim: There is a need for non-invasive biomarker of enteropathy both for diagnosis and monitoring of enteropathic diseases such as celiac disease. Assessment of plasma citrulline and plasma levels of intestinal fatty acid binding protein (I-FABP) have been proposed, but their reliability is yet not confirmed. For confirmation of reliability of these markers, we used a model [patients with hematological malignancies receiving myeloablative therapy for hematopoietic stem-cell transplantation (HSCT)] where changes occur cyclically in rapidly dividing cells with myeloablative therapy.

Patients and Methods: Seventy adult patients with hematological malignancies receiving myeloablative therapy for HSCTs were recruited. Plasma samples were collected at different time-points i.e., before and after transplantation on HSCT days -7, -5, -1, 0, +7, +15 and +28. Levels of plasma citrulline (by HPLC), I-FABP (by commercially available ELISA) and total leukocytes counts were measured at each point of time.

Results and discussion: Concentration of citrulline in plasma decreased significantly and consistently below the baseline at day+7 ($p < 0.001$), and its level rose gradually at day +15 and day+28. The concentration of I-FABP fluctuated between day +7 and day+15 and then it rose at day +28. The decrease in level of plasma citrulline followed similar pattern as observed by total leucocytes count in peripheral blood.

Conclusions: The data suggests that plasma concentration of citrulline follows pattern of cyclical changes in enterocyte mass as induced by myeloablative therapy. Therefore, an assessment of plasma level of citrulline may prove to be a reliable marker of enterocyte mass.

25 PERSISTENT BASAL CELL HYPERPLASIA IN INACTIVE EOSINOPHILIC ESOPHAGITIS: IS INACTIVE REALLY INACTIVE?

Bridget C. Godwin¹, Hiroshi Nakagawa², Kelly Whelan², Ben Wilkins¹, Alain J. Benitez¹, Maureen DeMarshall², Gary Falk², Jonathan Spergel¹, Amanda B. Muir¹, ¹The Children's Hospital of Philadelphia, Philadelphia, PA, USA, ²University of Pennsylvania, Philadelphia, PA, USA

Background and Aims: Eosinophilic esophagitis (EoE) is a chronic, antigen and immune-mediated esophageal disease characterized by symptoms such as dysphagia and food impaction. Histologic changes in active EoE include a peak eosinophil count of \geq eosinophils per high-power field (eos/hpf) and basal cell hyperplasia (BCH) in esophageal mucosa. According to current diagnostic criteria, EoE transitions from active disease to inactive disease when the peak eosinophil count drops below 15 eos/hpf, typically following therapeutic intervention. We aimed to evaluate BCH in EoE patients with inactive disease in relation to eosinophil count as well as patient-reported symptoms within 30 days prior to biopsy.

Methods: Pediatric and adult histology from an IRB-approved patient repository of esophageal biopsies was reviewed by a pathologist specializing in gastroenterology. Specimens were scored for eosinophils and BCH. These data were then correlated with clinical data obtained at time of endoscopy through the same IRB-approved study, specifically presence of symptoms within 30 days of endoscopy. 304 pediatric and 137 adult specimens were scored from a total of 204 pediatric and 107 adult patients. Patient age ranged from 1-66 years, with 75% of patients being male. Of the specimens reviewed and included for analysis, 52 were from non-EoE patients, 221 from patients with inactive EoE, and 74 from patients with active EoE. 94 patients were excluded from analysis given unclear diagnosis or status at time of endoscopy.

Results: Scoring revealed the presence of BCH (defined as basal cells that reached $>20\%$ of epithelial height) in 5.8% ($n=52$) of non-EoE patients, 24.9% ($n=221$) of inactive EoE patients, and 97.3% ($n=74$) of active EoE patients. Average BCH score was significantly higher in patients with inactive EoE than in non-EoE ($p=0.0024$). Eosinophil count in inactive EoE was significantly higher with persistent BCH ($n=55$, average eos/hpf 6.9 ± 0.62) than without ($n=166$, average eos/hpf 2.2 ± 0.25) ($p < 0.0001$). In the inactive EoE cohort, symptoms such as heartburn, dysphagia and regurgitation were more prevalent in patients with BCH (53.7%, $n=67$) than patients without BCH (30.4%, $n=87$) ($p=0.0007$).

Conclusions: BCH persists in patients with EoE that is clinically defined as inactive. Persistent BCH correlates with patient symptoms and eosinophil burden in inactive EoE patients. These findings suggest that BCH may be used to evaluate symptoms in patients with inactive EoE. Although current clinical EoE guidelines define inactive EoE disease as <15 eos/hpf present on esophageal biopsies, our data suggest that a lower eosinophil count than 15 may be necessary to truly define inactive disease. Further studies regarding basal cell hyperplasia and its role in inflammation and barrier defect will further characterize the importance of re-defining inactive disease.

26 CAESAREAN SECTION AND COW'S MILK PROTEIN ALLERGY (CMA): IS IT A RISK FACTOR IN ARGENTINE INFANTS?

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Introduction: CMA is a continually growing disorder. Several studies suggest that babies delivered via vaginal canal acquire the mother's vaginal microbiota, which may help protect them and promote a healthy immune system' however, babies born via Caesarean section acquire bacteria from the hospital environment that may increase the risk of food allergies and other problems.

Aim: To evaluate Caesarean section as a risk factor to develop different forms of CMA presentation.

Methods: All children from 2010-2014 who were referred to the Pediatric Gastroenterology Section at Pirovano Hospital with a diagnosis of CMA were included. Treatment was provided depending on the treating physician. Medical records were used to recruit by sex, age, birth weight, gestational age, clinical presentation of CMA and type of delivery.

Results: 238 patients were included. Mean age 0.60 months \pm SD 0.97 (range 0-48-0.72). Females 50.8%. Mean gestational age: 38.38 weeks \pm SD 1.72 (range 32-42). Mean birth weight: 3.149 gr \pm SD 595.19 (range 2.936-4.355). Clinical presentation: rectal bleeding (RB) 44.5%, reflux (GER) 19.3%, immediate reactions (IMM) 14.3%, enteropathy (ENT) 11.8% and colic (COL) 10.1%. Type of delivery: Caesarean 56.3%, vaginal 43.7%. No statistical significant differences were found between type of delivery and clinical presentation ($p=0.70$), type of delivery and sex ($p=0.28$) and sex and clinical presentation ($p=0.62$) (Chi square Test). A positive risk correlation was found between IMM and Caesarean section (OR 1.45 95% CI, 0.69-3.04) and between GER and COL and Caesarean section (OR 1.26 95% CI, 0.65-2.43 and OR 1.33 95% CI 0.55-3.17 respectively).

Conclusions: Caesarean section was found to be a risk factor for developing not only IMM but also delaying the reactions (GER and COL) of CMA.

***27 ANTI-TISSUE TRANSGLUTAMINASE NORMALIZATION POST DIAGNOSIS IN CHILDREN WITH CELIAC DISEASE.**

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Introduction: Celiac disease (CD) is a common autoimmune enteropathy to gluten, leading to intestinal inflammation, villous atrophy, and malabsorption. CD screening involves anti-tissue transglutaminase (atTG) IgA levels, followed by intestinal biopsy for confirmation. A gluten-free diet (GFD) is required to alleviate symptoms, normalize atTG, and heal the intestinal mucosa in CD patients. CD monitoring includes following atTG titers post diagnosis. Limited pediatric studies exist examining the trend of atTG normalization, with no studies examining predictors of atTG over time in children with CD. We aimed to evaluate time to normalization of atTG in children post CD diagnosis, and to assess for independent predictors impacting this time.

Methods: A retrospective chart review was completed to evaluate atTG normalization time in pediatric CD patients diagnosed from 2007 to 2014 in the Stollery Pediatric Celiac Clinic (Edmonton, Alberta, Canada). The following clinical predictors were assessed for impact on time to normalization: initial atTG, Marsh score at diagnosis, GFD compliance (GFDC), age at diagnosis, gender, ethnicity, medical comorbidities, and family history of CD. Kaplan-Meier survival analysis was completed to assess time to atTG normalization, followed by Cox hazard regression to assess for independent predictors of atTG normalization time.

Results: 487 of 616 patients reviewed met inclusion criteria. Mean age was 9.3 years at diagnosis, with 64% females. Patients were followed from 6 months to 6 years. 80.5% of patients normalized atTG levels within the study time period. Median time to normalization was 407 days for all patients (95% CI [361-453]), and 364 days for GFD compliant patients (95% CI, [335-393]). Type 1 diabetes mellitus (T1DM) patients took significantly longer to normalize at 1204 days (95% CI, [199-2209], $p < 0.001$). Ethnicity was associated with longer time to normalization, with South Asians (SA) taking 809 days (95% CI, [262-1356], $p = 0.001$); however, the validity was poor due to wide differences in censoring between ethnicities (Caucasian 18.2%, SA 35.2%). T1DM (HR 0.363 [0.238-0.553], $p < 0.001$) and higher baseline atTG (HR 0.999 [0.999-1], $p < 0.001$) were significant predictors of longer time to atTG normalization on Cox hazard regression. Conversely, GFDC was a significant predictor of earlier normalization (OR 13.91 [7.859-24.621], $p < 0.001$). The remaining variables assessed were not significant.

Conclusions: There is wide variation of rate and time to atTG normalization in children with CD. GFDC and lower atTG at diagnosis are predictors of earlier normalization. Patients with T1DM are less likely to normalize atTG levels, and have longer time to normalization. There may be an association between SA ethnicity and longer duration to normalization, but the validity of this finding is poor due to wide differences in censoring. Overall, there is a need for closer attention and education for these higher-risk populations.

28 IS CANDIDA DETECTED IN DUODENAL BRUSHINGS CLINICALLY SIGNIFICANT?

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Background: Recent studies support a role of small intestinal fungal overgrowth (SIFO) in adults with IBS disease symptoms, immunocompromised or not. Commensal candida density has been reported to be < 100 cfu/mL. We aimed to find the clinical significance of Candida detected by duodenal brushings in children undergoing diagnostic endoscopy, and assess histology, candida staining, and mucosal disaccharidases to look for evidence of pathology.

Methodology: Out of a total of 111/1900 studies had had Candida overgrowth (> 1000 cfu/mL cfus) had their mucosal histology, associated diagnostic findings, and disaccharidase activity assessed in comparison with those without Candida. A subset of duodenal biopsy samples were examined microscopically with hematoxylin and eosin (H&E) and special periodic acid shift with diastase (PASD) staining. Statistical analyses between SIFO and 2500 sequential disaccharidases were done using IBM SPSS.

Results: One hundred eleven patients (age: 0 to 20+ years; female 61) had fungal overgrowth with differential counts ranging from 1 to 300×10^3 CFU/mL. Most of the fungal species were Candida but one had *Trichosporon asahii* overgrowth. Combined fungal and bacterial overgrowth ($> 10^4$) was present in 57 patients. 12 (12/111) patients had abnormal histology of which 3 (3/12) had focal villous blunting without any other known cause. 2 of these 3 samples revealed increased intraepithelial lymphocytes. 3 samples exhibited chronic duodenitis and one had Crohn's disease. An examination of 30 patients with a PASD stain revealed no evidence of candida hyphae. Of these 33/111 patients with fungal overgrowth had normal disaccharidase activity, compared with 1454/2489 entire population ($p < 0.000$), 17/111 had generalized depression compared with 124/2489 ($p < 0.000$), 35/111 had lactase deficiency compared with 1045/2849 population ($p < 0.05$).

Conclusion: Duodenal brushing sample was found to be suitable to detect fungal over growth at a threshold level of 1000 CFU/mL. Fungal overgrowth was caused by different Candida species. A significant number of patients with fungal overgrowth were found to have generalized depressed activities of all the disaccharidases and many of them have lactase deficiencies separate from generalized depression of disaccharidases compared with population rates. However, direct staining using PASD in a subgroup of 30 did not show evidence of invasion/hyphae. Further studies are warranted to evaluate the association of fungal overgrowth and disaccharidase deficiencies and IBS symptoms.

29 INCREASED INTESTINAL MAST CELLS IN CHILDREN WITH CHRONIC ABDOMINAL PAIN

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Mast cells are immune cells that secrete vasoactive mediators (histamine, tryptase) and are usually associated with anaphylactic responses. Increased numbers of mast cells have been found in both adults and pediatric patients with chronic abdominal pain. Mast cell activity has been recently linked with enteric nerve proliferation due to neuronal growth factors but its role in functional abdominal pain is unclear. There is currently limited research on determining the characteristics of pediatric patients with abdominal pain and increased intestinal mast cell counts, risk factors and outcomes to treatment.

Objective: To determine if there are any generalizable characteristics for pediatric ($< 18y$) patients experiencing recurrent abdominal pain with increased gastrointestinal mast cell counts in order to better determine disease risks and outcomes from therapy.

Methods: We performed a retrospective study of all children and adolescents with abdominal pain who had staining to assess mast cell (MC) burden ($n=42$). MC specific stains (CD117) were requested in cases of refractory abdominal pain, with a history of headaches, flushing or hives. Non-parametric data on these patients was then gathered by chart review. Characteristics such as age, race, weight, allergy history, and location

of residency were collected. Also treatment data and symptom reporting was collected for all subjects. We then ran statistical analyses to determine if any factors seemed to be a determinant of the presence of increased mast cell counts in intestinal biopsies, their anatomic location, and the prevalence of allergic disorders and response to treatment.

Results: From our sample population, 83% (n=35) of patients met biopsy criteria for increased mast cell presence (>20 MC/hpf) in at least one biopsy sample. Of these patients, 90.5 percent were white and 9.5 percent were black. There was a female predominance within the group at 64 percent. A large proportion of these patients were underweight (36%) and this was statistically significant in patients with colonic involvement (*p*-value 0.02). Of those patients who received allergy testing, 60 percent had positive results. 71% of positive patients were treated with either an H₁ or H₂ blocker, mast cell stabilizer, or leukotriene inhibitor and 68% of these had symptom improvement.

Conclusion: The presence of clinical symptoms of mast cell activation in children and adolescents with chronic abdominal pain appears to be a significant indication for performing mast cell staining on biopsy. While typical hematologic markers for mast cell activation do not seem to correlate to increased GI mast cell presence, allergy testing may be indicated in those with positive biopsy results. Existing treatment options appear to have a substantial effect on symptom improvement but standardization of treatment strategies could enhance treatment outcomes and this might be an area for new drug development.

30 WHERE DID ALL OF THE INFANT SPITTERS GO? DIAGNOSES OF INFANT GERD, REGURGITATION, VOMITING AND COLIC IN GENERAL PEDIATRIC PRACTICE

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Infant gastroesophageal reflux (GER) is a common physiologic process that is frequently not distinguished from true infant gastroesophageal reflux disease (GERD). Non-adherence to clinical guidelines leads to over-diagnosis of gastroesophageal reflux disease, misdiagnosis of other conditions, over prescribing unnecessary medications and unnecessary medical testing. We conducted a retrospective electronic medical record review across the Nemours Children's Health System's general pediatrics practices over a 6 month period between 10/01/2015-3/31/2016 comprising 120 providers, 6249 unique infants and 21,823 total visits among infants 6 months of age or less. Among 919 unique infants with 1372 encounters over the time period, primary care practitioners recorded the following ICD-10 diagnoses: regurgitation (6.9%, 94 diagnoses/1,372 total encounters); GERD (55.8%, 766 diagnoses/1372 total encounters), other vomiting (5.5%, 75 diagnoses/1,372 total encounters); and colic (7.4%, 102 diagnoses/1372 total encounters). Proton pump inhibitor (PPI) medications were prescribed in 5.7% (52/919 unique infants) and H₂ receptor antagonist (H₂RA) were prescribed in 0.5% (5/919 unique infants). Among 18 upper GI radiology tests and 42 pyloric ultrasounds, 94.4% and 50.0% were respectively ordered for a diagnosis of GERD only. Infants were frequently given a diagnosis of GERD over regurgitation or colic, and PPI medications were prescribed for infants inconsistent with guidelines. We propose these findings indicate a gap between actual decision making and the widely disseminated AAP Clinical Report and the NASPGHAN Consensus Guidelines. An intervention to ensure clinicians are educated around best practices and that the knowledge is retained over time is discussed. We will explore the impact of promoting knowledge retention on decision making related to diagnosis, prescription of medications and request for medical testing.

*31 THE L2-IL5(OXA) MOUSE: A NOVEL MODEL OF CHRONIC FIBROSTENOTIC EOSINOPHILIC ESOPHAGITIS

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Background: Dysphagia, stricture and food impactions are common symptomatic consequences for eosinophilic esophagitis (EoE) patients. However, to date limited understanding of the pathophysiologic mechanisms of remodeling in EoE exists. We hypothesized that a hypersensitivity reaction with prolonged and localized eosinophilic inflammation in mice would lead to esophageal remodeling similar to that observed in EoE patients.

Methods: Transgenic mice overexpressing the eosinophilopoietin IL-5, selectively in the esophageal epithelium (L2-IL5), were sensitized and challenged with oxazolone 9 times/29 days (chronic: L2-IL5-OXA-C) and compared to a previously published EoE model where mice are challenged 3 times/8 days (acute: L2-IL5-OXA-A). Treatment with Dexamethasone (Dex: 200ug/ms i.p.) 3 times/week was used as a therapeutic intervention. H&E stained esophagi were evaluated using a histological score (index of epithelial inflammation [eosinophil & chronic inflammatory infiltrate], epithelial remodeling [basal zone hyperplasia (BZH), dilated intracellular spaces, hyperkeratosis], internal esophageal layer fibrosis and intramuscular inflammation. Immunohistochemistry was performed evaluating fibrosis (Massons Trichrome) and proliferation/BZH (Ki67). Esophageal tissues were processed for Taqman mRNA analysis, and immune cell infiltrates were characterized by flow cytometry.

Results: Significant esophageal histopathological alterations were observed in the L2-IL5-OXA-C mice compared to L2-IL5-OXA-A counterparts, including eosinophilia (6 vs. 3.8, *P* 0.01) microabscesses (1 vs. 0.75, *p*=0.1) and basal zone hyperplasia (BZH) (2.8 vs. 2, *p*<0.001). Increases in dilated intercellular spaces (DIS) (3.2 vs. 0.5, *p*<0.001) and internal esophageal layer fibrosis (IELF) (5.6 vs. 1, *p*<0.001) were observed in L2-IL5-OXA-C mice compared to L2-IL5-OXA-A. The overall histological score was significantly higher in L2-OXA-C mice (22.6 vs. 11.8, *p*<0.001). L2-IL5-OXA-C mice had increased Trichrome staining and expression of fibrotic remodeling genes including COL1A1 (3-fold, *p*<0.05) and COL4A1 (7-fold, *p*<0.05), while barrier dysfunction was indicated by decreased CLDN1 expression. Flow cytometry confirmed a significant increase in esophageal eosinophilia in L2-IL5-OXA-C mice compared to L2-IL5-OXA-A (14.5x10⁵ vs. 1.15x10⁵, *p*<0.05). Treatment with dexamethasone significantly attenuated histopathologic indices (3.8 vs. 22.6, Dex vs. Saline, *p*<0.001), including eosinophilia, DIS and fibrosis. Of note, Ki67 immunohistochemistry indicated a significant decrease in BZH (15 vs. 66 cells/hpf, *p*<0.001). Eosinophilic chemokines CCL11 (80%) and CCL24 (93%) were decreased and tight junction molecules CLDN1 (5-fold, *p*<0.05) and CLDN7 (15-fold, *p*<0.001) were increased indicating restored barrier.

Conclusion: Collectively, these studies identify the L2-IL5OXA mouse as a novel preclinical model to study the epithelial barrier dysfunction, fibrosis and remodeling associated with chronic EoE.

32 EOSINOPHILIC ESOPHAGITIS OCCURRING IN CHILDREN WITH CYSTIC FIBROSIS: A CASE SERIES

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Background and Aims: Pediatric patients with cystic fibrosis (CF) and pediatric patients with eosinophilic esophagitis (EoE) can both present with feeding problems which can complicate clinical care. This study evaluated the association of eosinophilic esophagitis (EoE) and CF occurring in a single pediatric cystic fibrosis (CF) center.

Methods: Patients with EoE and CF from our center were identified from the electronic medical record and from the Cystic Fibrosis Foundation Patient Registry. Specific endoscopic and biopsy findings of EoE as well as clinical findings and treatment modalities were evaluated in these patients.

Results: Five patients with CF and EoE were identified (1.8% of all patients) over a 13-year time period. The average age at the time of EoE diagnosis was 5.9 years (range 1 to 16 years). Younger patients presented with feeding problems; older patients presented with dysphagia. All patients were treated with proton pump inhibitor therapy, and four patients received oral fluticasone therapy. Two patients received a gastrostomy for elemental formula therapy. Most patients had a documented history of food allergies.

Conclusions: EoE can occur in pediatric patients with CF, and the prevalence potentially may be higher than the general population. Patients with CF and associated feeding problems may need further evaluation for EoE.

33 A 34-YEAR REVIEW OF HERPES SIMPLEX ESOPHAGITIS IN CHILDREN: DOES HERPES LEAD TO EOSINOPHILIC ESOPHAGITIS OR VICE VERSA?

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Background: Herpes simplex virus (HSV) has long been recognized as a common cause of infectious esophagitis. While the majority of cases occur in immunocompromised hosts, cases have been reported in the immunocompetent individuals. Therefore, an immunodeficiency work-up is not indicated after diagnosis of HSV esophagitis in an otherwise healthy individual. To date, 9 cases have been reported of concomitant HSV esophagitis and eosinophilic esophagitis (EoE) suggesting a causal relationship between these two entities. Most reports of HSV esophagitis in immunocompetent children are prior to publication of diagnostic guidelines for EoE and do not report follow-up endoscopies. The aim of this study is to review all patients diagnosed with HSV esophagitis at our institution and identify co-morbid conditions before and after diagnosis.

Methods: We conducted an IRB-approved retrospective review of HSV esophagitis diagnosed at a single large academic institution between 1/1982 and 3/2016. Pathology records were queried for the inclusion of "herpes" and/or "HSV". Records including biopsies from the upper gastrointestinal tract were reviewed to identify patients diagnosed with HSV esophagitis by microscopic examination or viral culture. Medical records of these patients were retrieved for additional clinical information including presentation, treatment, and outcomes.

Results: Sixteen patients with HSV esophagitis were identified. Five cases were immunosuppressed at diagnosis. Of the 11 immunocompetent patients, 3 (27.3%) had an underlying genetic syndrome, 3 (27.3%) had no significant past medical history and no follow-up after symptom resolution. Of the 5 remaining patients (45.6%), 1 had a history of EoE prior to HSV infection. Three patients experienced symptom recurrence after initial improvement following HSV treatment and on follow-up endoscopy within 6 months of infection were diagnosed with EoE. All of these patients had co-morbid atopic conditions. One patient had symptom recurrence and a follow-up EGD showed 15-16 eos/hpf in the single obtained esophageal biopsy while on proton-pump inhibitor therapy. At last follow-up in 2003 (3 years after HSV infection), this patient continued to be symptomatic.

Conclusions: Our 34-year retrospective review supports prior studies that while immunocompromised patients are at highest risk of HSV esophagitis, this diagnosis should be considered in all patients with acute onset dysphagia/odynophagia. Among the immunocompetent patients, EoE was a frequent co-morbidity, with the majority diagnosed within 6 months of HSV infection. On biopsy specimens at the time of active HSV esophagitis, the number of eosinophils in the squamous mucosa was not high enough to suspect the diagnosis of EoE. Therefore, clinical follow-up with endoscopy may be necessary for children with atopic conditions presenting with HSV esophagitis. Further investigation is needed to clarify the relationship between EoE and HSV esophagitis.

ID	Age at HSV Diagnosis	Sex	PMH	Immuno-suppressed	Symptoms	Symptom Duration	HSV Diagnosis	Treatment	Follow-up EGD
1	17.6	M	-	No	Dysphagia, chest pain	7 days	Culture	Acyclovir, PPI	-
2	11.5	M	-	No	Dysphagia, emesis, chest pain, fever	8 days	Culture	Acyclovir	-
3	15.4	M	Pyloric stenosis as infant	No	Odynophagia, chest pain	2 days	Immunohistochemistry	Acyclovir	-
4	3.2	M	-	No	Odynophagia, chest pain, weight loss, fever	5 days	Culture	PPI	2 m: 15-16 eos/hpf
5	13.4	M	Allergies	No	Odynophagia, chest pain, weight loss	3 days	Culture	Acyclovir, PPI	2 m: EoE (OSH): >30 eos/hpf
6	8.3	M	Allergies, asthma	No	Odynophagia, weight loss, fever	5 days	Culture/ Immunohistochemistry	Acyclovir, PPI	2 m: EoE: 20-70 eos/hpf
7	11.5	M	Allergies, asthma	No	Dysphagia, emesis, fever	6 days	Culture	Acyclovir, PPI	5 m: EoE: 35->200 eos/hpf
8	16.2	M	EoE, asthma	No	Dysphagia, emesis, chest pain	8 days	Culture	Acyclovir	Continued EoE
9	4.6	M	Cornelia de Lange, Failure to thrive	No	UGIB, fever	1 day	Immunohistochemistry	Acyclovir, PPI	4 m: stricture
10	15.8	F	VACTERL association	No	Odynophagia, fever	5 days	Culture	Acyclovir, PPI	-
11	4.6	M	Angelman's syndrome, Arnold Chiari	No	UGIB, fever	2 days	Culture/ Immunohistochemistry	Valganciclovir	-
12	24.8	F	Ewing sarcoma on chemotherapy	Yes	Dysphagia	N/A	Tzank cells	N/A	2 m: active HSV esophagitis
13	13.75	F	Ewing sarcoma, s/p BMT	Yes	Emesis, UGIB	N/A	Viral cytopathic morphology	Acyclovir	1 m: normal
14	18.6	F	Aplastic anemia s/p BMT	Yes	Emesis	N/A	Culture	Acyclovir	1 m: normal
15	14.9	M	Li-Fraumeni, ALL s/p BMT, GVHD	Yes	UGIB, fever	1 day	Culture/ Immunohistochemistry	Acyclovir	1 m: active esophagitis (HSV negative)
16	7.4	F	AML on chemotherapy	Yes	Dysphagia, emesis	2 weeks	Culture/ Immunohistochemistry	Acyclovir	5 m: normal

N/A: data not available

PPI: proton-pump inhibitor; OSH: outside hospital; UGIB: upper gastrointestinal bleed; BMT: bone marrow transplant; ALL: acute lymphoblastic leukemia; GVHD: graft-versus-host disease

34 NOVEL INSIGHT INTO SALMONELLA TYPHI PATHOGENESIS FROM EX-VIVO HUMAN TISSUE MODELS

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Introduction: Typhoid fever is a common worldwide illness, transmitted by the ingestion of food or water contaminated with the feces of an infected person, which contain the bacterium *Salmonella Typhi*.

The World Health Organization estimates that 22 million cases of typhoid fever occur annually, resulting in ~200,000 deaths. In common with other enteropathogens, *S. Typhi* has developed means of breaching the mucosal epithelial barrier by usurping signaling mechanisms within host cells. At present, much remains to be uncovered concerning the host responses to *S. Typhi* infection. Available vaccines are moderately protective. Current therapeutic strategies include antibiotic treatment; however the frequency of antibiotic-resistant serovars is increasing worldwide. Additionally, in some individuals chronic *S. Typhi* colonization of the gall bladder culminates in gall bladder cancer, therefore highlighting the significant short- and long-term consequences of infection. Given the adverse consequences of *S. Typhi* infection there is a critical need to understand the mechanisms of the disease process and the host immune response for the development of efficacious and cost-effective vaccines.

Materials and Methods: Terminal ileum biopsies were collected from donors for direct infection. Whole biopsy infections were conducted using micro-snapwell mounting of tissue followed by addition of *S. enterica* serovar Typhi 2a to the apical surface. Prior to infection, Typhi was grown in Luria Bertoni broth under static or shaking conditions. Upon infection, changes in trans-epithelial electrical resistance (TEER), cytokine release, gene expression, and cellular localization were assessed.

Results and Conclusions: Use of whole biopsy (WB) model identified specific contributions of the epithelium in response to Typhi infection as assessed by RNA-sequencing, qPCR, and cytokine secretion. Consideration for bacterial inoculum preparation revealed that Typhi grown under static conditions express the Vi antigen, as well as, SPI-1 and SPI-2 effector proteins. Therefore, static or shaking inoculums were applied on the *ex-vivo* tissue model. Differences in cellular association of bacteria were assessed using immunofluorescence and transmission electron microscopy. To identify how the gut mucosa responds to infection, apical and basolateral culture supernatants were collected for cytokine production analysis. Some of the key pro-inflammatory molecules, such as IL-8 and IL-6 appeared decreased in *Salmonella*-infected tissues, in line with our RNA-seq data showing *Salmonella*-induced immune suppression. Together, our data characterizes key aspects of terminal ileum response to Typhi infection addressing a critical gap in our current understanding of Typhoid fever pathogenesis.

*35 PROSPECTIVE STUDY FOR THE DEVELOPMENT OF A MACHINE LEARNING ALGORITHM AS A DIAGNOSTIC TOOL FOR EOSINOPHILIC ESOPHAGITIS

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Background: Eosinophilic esophagitis (EoE), an allergic inflammatory disease, requires expensive, repeated, and invasive esophagogastroduodenoscopies (EGDs) and esophageal biopsies for diagnosis and treatment, resulting in substantial physical, psychological, and financial impact. Previous EoE biomarker research found targets that are weakly predictive when studied independently. Using multivariate machine learning algorithms to combine biomarker and clinical data (features) into one model, we trained a support vector machine (SVM) algorithm to develop a powerful and statistically supported diagnostic tool. A previous study utilizing large retrospective and simulated datasets evaluated which machine learning algorithms and biomarkers performed best, identifying the feature set for this prospective study with a predicted specificity of approximately 0.99.

Methods: Patients presenting to pediatric gastroenterology with known or suspected EoE and planned EGDs and biopsies were enrolled. Diagnoses and survey symptomology, standard-of-care complete blood count (CBC), allergen-specific immunoglobulin E (IgE), and pathological biopsy data were collected. Eotaxin-3 and eosinophil-derived neurotoxin (EDN) levels in patients' serum were determined through commercially available ELISAs. SVM was trained with some patients to learn to diagnose EoE, as defined by biopsy, and tested with others to assess whether the model was correct. Accuracy, sensitivity, and specificity were calculated using leave-one-out cross-validation (LOOCV): with n patients, SVM was trained with $n-1$ patients and tested with one patient left out. This procedure was repeated for each patient, and the results were averaged. Then, different combinations of features were temporarily removed from the model, which was re-trained, and the feature set producing the maximum LOOCV accuracy was used for the final model.

Results: Thirty patients were enrolled; seven patients undergoing treatment or missing data were excluded, resulting in a dataset of 23 patients (7 EoE, 16 control). The final model incorporated eotaxin-3 and EDN ELISAs, 18 survey questions, IgE averaged across all allergens, 15 CBC results, and 8 symptoms, with LOOCV accuracy, sensitivity, and specificity equal to 1: all patients were correctly diagnosed with only non-invasive data. Statistical significance was assessed with an approximate permutation test ($n=10,000$). For accuracy, sensitivity, and specificity respectively, the approximated p values were 0.0000, 0.0005, and 0.0011.

Conclusions: Algorithms utilizing non-invasively obtained data successfully diagnose EoE, potentially alleviating the substantial diagnostic burden on patients and cost of care. Additional enrollment and future studies would provide further validation and refinement of the model, as well as establish a method for non-invasive, quantitative monitoring of EoE patients.

36 ESOPHAGOGASTRODUODENOSCOPY AND IMPEDANCE MONITORING IN PATIENTS UNDERGOING LARYNGOTRACHEAL RECONSTRUCTION

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Introduction: Although there is controversy surrounding the use of impedance testing affecting outcomes of children undergoing laryngotracheal reconstruction (LTR), we propose routine gastroesophageal reflux disease (GERD) screening allows for treatments that significantly improve outcomes in children undergoing LTR.

Laryngoscopic findings of GE reflux include erythema, edema, nodularity, ulceration, granuloma and cobblestoning. Evidence suggests a connection between GERD and the development of subglottic stenosis, and studies in animal models has shown that gastric juices negatively effect mucosal healing after subglottic injury. We have developed a multidisciplinary aerodigestive team and any children undergoing LTR will have a preoperative diagnostic evaluation with esophagogastroduodenoscopy (EGD) and impedance testing.

This study's primary objective was to determine if the EGD and impedance testing results impact treatment decisions in patients undergoing preoperative LTR evaluation.

Methods: An observational case series with retrospective electronic medical record review was conducted at The Children's Hospital of Philadelphia analyzing existing patients' preoperative LTR evaluation data from January 2008 through June 2014.

The primary endpoint was to determine the utility of EGD and esophageal impedance monitoring leading to changes in medical management such as adjustment of medication doses, avoidance of potential food allergens or surgical interventions prior to LTR.

Results: Seventy-four subjects were included in the study; 29 (39%) were female and 45 (61%) were male. The subjects had a median of 2.8 years. Sixty (81%) subjects had subglottic stenosis and 63 (85%) had a tracheostomy tube. Sixty-one (82%) subjects reported GERD symptoms and 7 (9%) reported none. Twenty-two (30%) had a previous fundoplication.

Of the 74 subjects, 64 (86%) on gross appearance had normal EGD results, 4 (5%) had esophagitis and 7 (9%) had gastritis. Fifty-nine patients (80%) had normal esophageal biopsies. Impedance testing revealed that 13 (18%) had an abnormal acid:non-acid ratio.

EGD and impedance study results lead to change in treatment in 24 (32%) subjects. Eighteen (75%) subjects had a new medication added. Of the 18 subjects that had a new medication added, 1 (5.6%) was prescribed an H₂ blocker, 15 (83.3%) were prescribed proton pump inhibitors, 2 (11.1%) were prescribed erythromycin, 1 (5.6%) was prescribed bethanechol and 1 (5.6%) was prescribed Biaxin. Two subjects had multiple medications added. Seven (29.2%) had their current GI medication increased. One (4.2%) subject had tube feedings changed to post-pyloric feeding. No subjects had their medications discontinued.

Conclusion: Abnormal EGD and impedance results lead to a treatment change in 32% of patients in this study population. Fundoplication may not be protective in all centers and no subjects with normal EGD and/or impedance results had medications withdrawn.

37 PROTEIN-LOSING ENTEROPATHY: REDEFINING THE ANATOMY AND PATHOPHYSIOLOGY AND PROVIDING NOVEL THERAPY

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Objective: To review the outcome of liver lymphatic and intestinal lymphatic embolization in patients with PLE, in whom leak of the intestinal or liver lymph was demonstrated.

Methods: This is a retrospective review of medical records and imaging of 5 consecutive patients (M/F 3/2, mean age 14.8 y) with PLE. Three patients presented after Fontan surgery and two patients post-thoracic duct (TD) ligation for chylothorax. Lymphatic imaging included heavy weighted T2 MRI and DCMRL, intranodal lymphangiogram (IL) and liver lymphangiogram. Abnormal lymphatics were percutaneously accessed and embolized with Lipiodol or n-BCA glue.

Results: In 3 patients after Fontan surgery, liver lymphangiography demonstrated leak of liver lymph into the duodenum. Embolization of liver lymphatics with lipiodol in the first 2/3 patients was performed with temporary increase in albumin and improvement of symptoms in one

patient, however complicated by duodenal bleeding. Embolization of the liver lymphatics with n-BCA in 1 patient resulted in temporary normalization of the serum albumin level and resolution of symptoms without complications. In 2 patients post-TD ligation lymphatic leak into intestine was demonstrated on DCRM and IL. Embolization of the intestinal lymphatics in these patients resulted in normalization of albumin level and resolution of the symptoms with no complications.

Conclusions: In this study, we demonstrated development of abnormal liver or intestinal flow with leakage of the lymph in duodenum in patients with PLE post Fontan surgery and TD ligations. Embolization of these abnormal lymphatics with the goal of stopping the lymph loss in intestine is a promising new treatment for this disease.

38 DELAYED DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS IN YOUNG CHILDREN

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Eosinophilic esophagitis (EoE) is an emerging disorder of children and adults. Its natural history is largely unknown. Although the prevalence of this disorder is increasing, the number of patients diagnosed in early childhood remains low, and there is a paucity of clinical and epidemiologic data regarding young children with this disease. We have identified a cohort of 27 children diagnosed with EoE aged 6 years and younger. The mean age of onset of gastrointestinal symptoms was 10.9 months, with 46% of children reporting "symptoms since birth." The most common symptoms included vomiting (63%), failure to thrive (41%), choking/gagging (33%), abdominal pain (30%) and feeding difficulty (22%). On average, these patients initially presented to the pediatric gastroenterologist at 25.9 months, at which time 67% were diagnosed with gastroesophageal reflux disease. Forty-seven percent had a known food allergy, and 37% had atopic dermatitis. Upper endoscopies (esophagogastroduodenoscopy/EGD) and biopsies were performed on average at 38.5 months of age. Biopsy results revealed a mean eosinophil count of 36 eos/hpf in the mid-esophagus, and 55 eos/hpf distally. The mean interval between onset of symptoms and EoE diagnosis was 25 months. Thus, even though young children with EoE have early onset of symptoms, there still remains a significant delay before EGD, definitive diagnosis, and most importantly, the initiation of treatment. Pediatric gastroenterologists should have a high index of suspicion for EoE in young atopic children presenting with nonspecific upper gastrointestinal symptoms and should consider performing an EGD more promptly to assess for this disease.

39 FOOD IMPACTION IN PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, inflammatory esophageal disease, characterized by eosinophilic inflammation and esophageal dysfunction. Upper gastrointestinal (GI) symptoms in EoE are age-dependent. Adults and adolescents typically experience dysphagia and esophageal food impaction (EFI), while the occurrence of EFI in younger children is less common and poorly investigated. There is limited information regarding the natural history of EFI in adolescents.

Objectives: 1) To characterize a cohort of pediatric EoE patients who experienced EFI as the presenting symptom of the disease.

2) To describe the management of EFI patients presenting to the emergency room.

Methods: A retrospective chart review was performed of pediatric EoE patients diagnosed at 18 years or younger. Patients who presented with EFI leading to EoE diagnosis were compared to controls who did not present with dysphagia or a history of EFI, and the management of the EFIs was examined. Controls were age-matched to EFI patients at the time of EoE diagnosis. Patients with achalasia, esophageal atresia, or tracheo-esophageal fistula were excluded.

Results: 32 children with EoE that experienced EFI, and 26 age-matched controls were identified. In 81% of EFIs the impacted food was meat. Clinical characteristics are presented in Table 1, and EFI management is shown in Figure 1. Average age at EoE diagnosis in the EFI group was 13.9 ± 3.0 years (6.7-17.8 years) and was 13.5 ± 3.0 years (6.7 – 17.8 years) in the controls. 29/32 patients presenting with EFI were male vs. 13/26 controls (90.6% vs. 50%, $p=0.001$). Endoscopy results were obtained in 28/32 patients following the EFI: 42% underwent an endoscopy within 30 days post-EFI (0-252 days, mean 75.8 ± 82.9 days). No EFI patient had a stricture on endoscopy, 3 had esophageal narrowing, and 1 had a Schatzki ring.

32 patients presented with EFI. 7 passed spontaneously, and 25 presented to the ER for further management. In the ER, 7 received glucagon or nitroglycerin, 12 underwent upper endoscopy, and 6 passed without intervention. Three failed management with muscle relaxant and went on to have an upper endoscopy. 15 upper endoscopies were done in total, and 4/15 revealed no further EFI. 10/25 (40%) EFIs presenting to the ER resolved spontaneously.

Conclusions:

- Food impaction resolved spontaneously in 40% of the children visiting the ER. This finding could have implications for the clinical management of food impaction in an emergency setting.
- Patients that present with EFI leading to an EoE diagnosis are likely to be male. Clinical characteristics of pediatric patients presenting with and without EFI are similar to previously published data in the adult population.

40 LONG-TERM CLINICAL OUTCOMES IN PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Background: Pediatric Eosinophilic Esophagitis (EoE) is a chronic, waxing and waning disease which can present with symptoms that include abdominal pain and dysphagia. A previous study demonstrated that pediatric EoE patients are at risk for adverse quality of life and long-term clinical outcomes. The Pediatric Eosinophilic Esophagitis Symptom Score v2.0 (PEESS)—a validated symptom metric—consists of items designed to measure the frequency and severity of patient- and proxy-identified EoE symptoms. Long-term outcomes of pediatric EoE have not yet been evaluated using this instrument, nor have differences between the long-term symptoms of patients with abdominal pain predominant EoE (EoE-AP) and dysphagia predominant EoE (EoE-D). Aims: Using the PEESS, 1) investigate changes in clinical outcomes of pediatric EoE over time; 2) compare the long-term outcomes of EoE-AP and EoE-D patients.

Methods: Of the 210 EoE patients contacted, 100 (48%) participated. Parent proxy-reported symptoms were collected using the PEES. Item response theory was used to obtain measures of frequency and severity of symptoms for all 100 patients. Change in frequency and severity of symptoms over time was investigated via regression analysis. Differential item functioning (DIF) analysis was employed to compare differences in symptoms between EoE-AP and EoE-D patient groups.

Results: For the full cohort of 100 patients [mean age: 14.3 ± 5.1 years, mean time since diagnosis: 4.1 ± 2.3 years, 79% male], on average, the measure of symptom frequency decreased over time ($b1 = -0.145, p = 0.035$). Severity of symptoms remained stable over time ($b1 = 0.002, p = 0.98$). 14 patients reported no symptoms. Of the 100 patients, 45 were classified as having EoE-AP, 36 as EoE-D, and 19 as other-symptom predominant. Results of the DIF analysis show that, in terms of frequency of symptoms, EoE-AP patients were more likely to report stomach pain ($t = -3.59, p < 0.001$) and nausea ($t = -2.09, p = 0.041$) than EoE-D patients, who were more likely to report difficulty swallowing ($t = 3.13, p = 0.003$) and needing to drink a lot to help swallow food ($t = 2.67, p = 0.010$). On the severity scale, EoE-AP patients were more likely to report severe stomach aches ($t = -2.34, p = 0.025$), while EoE-D patients reported greater severity in needing to drink a lot to help swallow food ($t = 2.22, p = 0.036$).

Conclusion: In this long-term follow-up study, not all EoE pediatric patients reported persistent symptoms. Across all EoE subgroups, frequency of symptoms subsided over time, while severity remained constant. Stomach pain and nausea were more prevalent in EoE-AP patients, and difficulty swallowing was more frequently reported by EoE-D patients. Stomach pain was more severe in EoE-AP patients, while the need to drink a lot to swallow was more severe in EoE-D patients. Further study is needed to better understand the impact of treatment regimens on these two clinical EoE disease phenotypes and their outcomes.

41 *HELICOBACTER PYLORI* ELICIT IMMUNE RESPONSE IN PEDIATRIC MONOCYTE DERIVED DENDRITIC CELLS AND T CELLS IS INDEPENDENT OF VIRULENCE FACTOR CAG A

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Background and aims: *H. pylori* infection in children causes increased T regulatory cell responses, which down-regulate T cell-mediated inflammation. The CagA virulence factor is the main immunodominant protein in *H. pylori* strains. Previous reports in mice and adults suggest a role of this oncoprotein in the suppression of DC maturation in a manner dependent of IL-10. In this study, we sought to evaluate the effect of the CagA protein from *H. pylori* on pediatric monocyte-derived DCs (MoDCs) and T cell response.

Methods: Mononuclear cells were isolated from peripheral blood of non-infected pediatric donors ($n=10$ for DC, $n=5$ for T cell studies) by gradient centrifugation. CD14+ and CD4+ naïve T cells were purified by MACS. CD14+ cells were cultured for 5 days in presence of IL-4 and GM-CSF to generate pediatric MoDCs. Then we analyzed MoDC for maturation/activation markers (HLA-DR, CD86, CD83) by FACS and cytokine secretion after a 48h exposure with *H. pylori* strains 26695 (western isolate), 26695 Δ CagA and Hpk5 (eastern isolate) at MOI of 10. In addition we analyzed Treg cell generation (CD4CD25Foxp3+) and cytokine secretion in 3 days DC:T cell co-culture previously stimulated with the same three strains of *H. pylori* for 2 hrs.

Results: *H. pylori* exposed MoDC, regardless of CagA status showed a suppressive phenotype characterized by low levels of expression of CD83, CD86 and HLA-DR. Moreover high levels of IL-23 and IL-10 but not IL-12 were observed in *H. pylori* exposed DC irrespective of CagA virulence factor. In co-culture experiments, generation of inducible Tregs (CD4CD25Foxp3+) occurred in low percentages in response to *H. pylori* exposed DCs. Cytokine secretion profiles in T cells was characterized by the expression of high levels of IFN- γ and IL-10 but not IL-17 and IL-13 regardless of CagA status.

Conclusion: *H. pylori* induces a suppressive phenotype in pediatric MoDC with secretion of high levels of IL-10 regardless of CagA status of the strains. Further T cell differentiation from pediatric T naïve cells is also not determined by the presence of CagA and is characterized by a mixed Th1 and Treg profile.

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42 *NUTRITIONAL STATUS AND FEEDING BEHAVIORS OF CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE OR EOSINOPHILIC ESOPHAGITIS*

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Background: Gastroesophageal reflux disease (GERD) and eosinophilic esophagitis (EoE) have been associated with malnutrition and feeding dysfunction. The aim of this study was to compare the frequency of nutritional deficiencies and feeding dysfunction in children with GERD and EoE.

Methods: A prospective study enrolling children aged 1-17 with GERD or EoE was performed. Children were excluded with a dual diagnosis of GERD and EoE or other comorbidities associated with nutrition and feeding. Assessments included height, weight, 3-day food diary, and serum levels of ferritin, 25-OH vitamin D, parathyroid hormone (PTH), and prealbumin. Feeding dysfunction was characterized by the Behavioral Pediatric Feeding Assessment Scale (BPFAS), a validated measure of feeding dysfunction. It consists of measures of child behaviors as well as parental feelings and strategies used to cope with these behaviors. Comparative means and frequencies were analyzed using Student's t-tests, Chi-square, or Fisher exact tests. Spearman's rank correlation coefficient was used to determine associations with BPFAS scores. Hedges' g was calculated to compare BPFAS scores with those of a historical group of healthy controls.

Results: Participants were divided into a nutrition cohort (GERD $n=47$, EoE $n=65$) and a feeding cohort (GERD $n=44$, EoE $n=73$) based on inclusion/exclusion criteria. The mean weight-for-length (WFL) z-score of children younger than 36.5 months of age with GERD was -1.11 and EoE was -1.12 ($p=0.92$). The BMI Z-score for children older than 36.5 months of age with GERD was 0.10 and EoE was 0.23 ($p=0.16$). Both GERD and EoE children had normal intake of calories, carbohydrates, proteins, fats, and iron but Vitamin D intake less than the daily recommended intake. Both GERD and EoE children had normal mean ferritin (30 vs. 34 ng/mL), prealbumin (21 vs. 20 mg/dL), PTH (40 vs. 38 pg/mL), and Vitamin D (30 vs. 31 ng/mL) with no significant differences between GERD and EoE groups ($p = 0.45, 0.35, 0.68, \text{ and } 0.69$ respectively). Thirty-two participants with EoE (49%) were on dietary elimination therapy. No significant differences in WFL z-score, BMI z-

score, ferritin, prealbumin, PTH and vitamin D ($p=0.22, 0.13, 0.20, 0.69, 0.97,$ and 0.64 respectively) were found when comparing children on and off dietary elimination therapy. There was no significant difference in BPFAS scores between GERD and EoE children with total BPFAS frequency scores of 81.5 for GERD and 76 for EoE ($p=0.14$) and problem scores of 8.4 for GERD and 9.7 for EoE ($p=0.88$). Both frequency and problem scores were higher than those of historical healthy controls (Hedges' g of 0.99 and 1.2 respectively).

Conclusion: A highly selected group of children with esophagitis are without nutritional complications. There may be benefit to providing anticipatory guidance to minimize mealtime challenges, monitoring for improvement, and referral to a feeding therapist if necessary.

43 STOOL CYTOMEGALOVIRUS POLYMERASE CHAIN REACTION FOR THE DIAGNOSIS OF CYTOMEGALOVIRUS CAUSING GASTROINTESTINAL DISEASE IN IMMUNOCOMPROMISED CHILDREN

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Background: Cytomegalovirus causing gastrointestinal disease (i.e., CMV-GI disease) is a complication in immunocompromised patients which can lead to significant morbidity and mortality but can also be treatable. The current gold standard diagnostic investigation requires histopathology of mucosal biopsy demonstrating intranuclear/intracytoplasmic inclusion body. However, endoscopy and mucosal biopsy are considered invasive. Recently, studies on noninvasive markers such as stool or plasma CMV polymerase chain reaction (PCR) have been proposed to aid in the diagnosis of CMV-GI disease. Few reports on stool CMV PCR in immunocompromised adults showed promising results, and diagnostic values of plasma CMV PCR in CMV-GI disease demonstrate diverse findings. We evaluated the values of stool CMV PCR in the diagnosis of CMV-GI disease.

Objective: To determine the sensitivity, specificity and accuracy of stool CMV PCR, using histopathology as a gold standard, in the diagnosis of CMV-GI disease among immunocompromised children.

Study design: Cross-sectional diagnostic study.

Methods: We enrolled immunocompromised individuals (e.g., post-transplantation, receiving chemotherapy or high-dose corticosteroids) aged < 20 years presented with gastrointestinal symptoms (e.g., prolonged diarrhea >10 days, lower or upper GI bleeding) at a tertiary care and teaching hospital from January 2015 to March 2016. We excluded children with uncorrectable coagulopathy, suspected surgical condition, or who received ganciclovir for ≥ 7 days. Stool samples were analyzed for quantitative CMV PCR by Abbott Real-time amplification with the limit of detection at 20 copies per mL. All underwent esophagogastroduodenoscopy and colonoscopy with tissue biopsies to evaluate histopathology for CMV.

Results: We had performed stool CMV PCR in 31 patients but two could not undergo endoscopy. Therefore, 29 patients were analyzed. Most were female (55%) with a median age of 75 months (IQR: 33,152). Post-liver transplantation (34%) was the most common underlying condition. Prolonged diarrhea > 10 days (37%) and lower GI bleeding (34%) were two most common presenting symptoms. Two stool samples showed inhibitors and were precluded from the final analysis. Among 27 patients, we found CMV-GI disease in 7 patients (26%). The sensitivity, specificity and accuracy of stool CMV PCR were 71, 85, 82% respectively. Moreover, plasma CMV PCR was performed in all study children, which likely due to our institution's practice in immunocompromised patients. The sensitivity, specificity and accuracy of plasma CMV PCR were 100, 86, 90% respectively (by using the cutoff value of 150 copies per mL). We found a significant correlation between stool and plasma CMV PCR ($p<.001$).

Conclusion: Stool CMV PCR may be used as a non-invasive tool for aiding in the diagnosis of CMV-GI disease. Plasma CMV PCR demonstrates significant correlation with stool CMV PCR and represents high diagnostic values.

*44 FOUR FOOD ELIMINATION DIET IS EFFECTIVE TREATMENT OF EOSINOPHILIC ESOPHAGITIS: A PROSPECTIVE MULTICENTER PEDIATRIC STUDY

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Background and aims: Eosinophilic esophagitis (EoE) is a chronic immune-mediated disorder of the esophagus that is triggered by food antigen. Empiric six food elimination diet (SFED) is effective in inducing remission in children and adults and is recommended diet therapy for treatment of EoE. Milk, wheat, egg and soy were the four most common food triggers identified in children treated with SFED. Our hypothesis is that four food elimination diet (4-FED) excluding milk, wheat, egg and soy should induce histological, endoscopic, and clinical remission in a majority of children with EoE.

Methods: Children meeting the consensus guidelines for diagnosis of EoE were enrolled in this prospective multicenter study and empirically eliminated milk, wheat, egg and soy from their diet and after 8 weeks underwent upper endoscopy with biopsies to establish histologic remission. Histologic remission was defined as esophageal peak eosinophil count of <15 eosinophils per high power field (eos/hpf). Secondary endpoints were identification of specific food triggers.

Results: Eighty children (68% male, 9 years, 84% white, 90% atopic) were treated with 4-FED and histologic remission was demonstrated in 51 (64%) children with decrease in esophageal eosinophil count from 61 ± 34 eos/hpf to 5 ± 4 eos/hpf ($p<0.0001$) after treatment. One or more symptoms resolved in 78% of responders. Exudates improved in 96% ($p<0.0001$), edema in 67%, ($p<0.0001$), and furrows in 57% ($p<0.0001$). Milk (85%), wheat (32%), egg (31%), and soy (17%) were triggers identified. A single food trigger was identified in 59%, two foods in 20% and three foods in 5%.

Conclusion: Empiric 4-FED by inducing remission in a majority of children with EoE is an effective dietary modality to treat EoE in children. It compares favorably with SFED.

*45 CORRELATION BETWEEN INTESTINAL DISACCHARIDASES AND MICROBIOME IN CHILDREN WITH AUTISM

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Autism is a neurodevelopmental disorder; however, many children with autism have gastrointestinal (GI) problems including constipation, diarrhea and abdominal pain that might affect behavior. GI problems have been associated with carbohydrate malabsorption (decreased lactase activity) or dysbiosis, alteration of the indigenous microbiota. Prior analysis of stool, colon, ileal and duodenal bacteria has revealed microbial dysbiosis, overgrowth of microorganisms, or depleted microbial diversity in autistic individuals relative to non-autistic populations.

Aims: To correlate disaccharidase activity (DA) and the duodenal mucosal microbiome of children with and without autism to determine if altering substrate availability in children with carbohydrate malabsorption affects the microbiome.

Methods: Activity of lactase, sucrase, maltase, and palatinase were evaluated in biopsies from 21 autistic subjects and 19 neurotypical subjects (controls) undergoing diagnostic upper endoscopy. Enzymes activity was evaluated using enzymatic assays. DNA was isolated from the duodenal biopsies, 16S rRNA was amplified via PCR; pyrosequencing was followed by computational analysis.

Results: There was no difference in DA between the two groups. In autistic group 17 out of 21 subjects and in controls 18 out of 19 subjects were lactase deficient. In samples from autistic subjects, the relative abundance of genus *Bacteroides*, *Faecalibacterium*, and *Clostridium* showed a statistically significant positive correlation with lactase activity. The duodenal microbiome in neurotypical children was different than in children with autism. None of the three groups of bacteria were observed to be correlated with disaccharidase activity in control samples, which instead showed strong positive correlations between lactase activity and the relative abundance of the genera *Porphyromonas*, *Barnesiella*, *Gemella*, and *Leptotrichia*. Correlation between activity of intestinal disaccharidases and abundance of microbiota was also found at the species level.

Conclusion: There are differences at the genus and species level in the duodenal microbiota in children with autism that could be influenced by maldigestion of lactose or nutritional differences in food consumption.

46 INCIDENCE COW'S MILK ALLERGY IN A HOSPITAL IN BUENOS AIRES

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Introduction: The increase in food allergies in children is a worldwide concern. Studies on prevalence, incidence and the natural history of cow's milk allergy (CMA) are difficult to compare because of the deficiencies and inconsistencies in their designs. In the different series published, an incidence of 1% decreases to 0.3% when open challenges (the gold standard) are used for diagnosis. That is why it is important to determine incidence by considering all immunological mechanisms involved.

Objective: To estimate the incidence of CMA in a hospital in Buenos Aires from June 1, 2015 until January 31, 2016.

Material and Methods: A prospective study was conducted in a population of an affiliated community hospital in Buenos Aires. Data were collected using electronic medical records. CMA incidence was calculated taking into account the proportion of children with CMA detected on the annual number of births.

The diagnosis was established according to clinical practice guidelines (DRACMA).

All patients with suspected CMA underwent skin prick test, patch test and open challenges to confirm the diagnosis.

Monthly monitoring of patients was performed, recruiting those who had suspected CMA.

Results: 768 infants were included from June 1, 2015 to January 31, 2016.

Of the 768 infants analyzed in our cohort, 51% were male, and 60% were born by Caesarean section.

13 patients with clinical suspicion of CMA showed an incidence of 1.7% (95% CI, 0.9 to 3), when open challenges were performed; 8 cases were confirmed, showing a cumulative incidence of CMA of 1% (IC 95 from 0.4 to 2% CI).

Conclusion: Conducting open challenges can confirm the presumptive diagnosis of CMA.

The systematic application of this test in patients with suspected non IgE-mediated CMA can reduce overdiagnosis and improve patients' quality of life.

Although these preliminary results are similar to those seen in other countries, this is the first study done in a Latin American Country.

47 RACIAL AND GENDER DIFFERENCES IN SYMPTOMS AT PRESENTATION IN EOSINOPHILIC ESOPHAGITIS: A SYSTEMATIC REVIEW

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Background and Aims: Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease characterized by esophageal inflammation and dysfunction. To ensure a timely diagnosis of EoE in children, it is important for clinicians to be aware of common symptoms at presentation and potential differences across patient groups. This systematic review (SR) was designed to evaluate the literature on symptom patterns and progression of EoE in children.

Methods: Electronic databases (MEDLINE, Embase, Cochrane) and recent congresses were searched in February 2016 for studies describing the natural history of EoE in children.

Results: Of 1145 articles identified, 14 met the inclusion criteria. Data were available for 1830 patients who presented at centres in the US, Europe or Australia in 1982-2012. The mean age at diagnosis was 6 years. However, the average duration of symptoms prior to diagnosis was 1.2-3.5 yrs. The most commonly reported symptoms at presentation were dysphagia (57-61% of patients), emesis (17-60%), abdominal pain (16-55%) and food impaction (7-22%). Evidence from three studies suggests that symptoms may differ by ethnicity, age and sex. Failure to thrive (44-52% vs. 9-22%, both $p < 0.05$), emesis (63% vs. 37%, $p = 0.005$) and emesis/acid reflux (90% vs. 52%, $p < 0.01$) were more common in African American (AA) than in Caucasian (Ca) children, while abdominal pain (27-29% vs. 40-57%, both $p < 0.05$) and food impaction

(10% vs. 26%, $p=0.003$) were less common. Eczema was also more frequent in AA children than in Ca children (57% vs. 9%, both $p<0.05$), while only one of two studies found asthma more common in AA compared with Ca children (51% vs. 32%, $p=0.05$). Additionally, symptom onset in AA children occurred at a younger age than in Ca children (3.7 vs. 9.1 years, $p<0.01$). Food impaction, dysphagia and heartburn were associated with age ≥ 8 yrs, while emesis, growth failure and food refusal were associated with age < 8 yrs (all $p<0.05$). Food impaction was more common in males (25 vs. 11%, $p=0.016$) whereas abdominal pain was more common in females (58% vs. 35%, $p<0.001$). After a mean follow-up of 7 years, 34% of adult patients still had difficulty swallowing. Resolution of symptoms was also rare, with the findings from one large study revealing that only 11/565 (2%) participants experienced complete resolution after a mean follow-up of 5.2 yrs. A second study found that untreated children experienced worsening of symptoms over a mean follow-up of 6 years. Conclusions: Symptoms of EoE differ by ethnicity and age. Emesis and failure to thrive may be more common in AA than Ca children, and age at presentation may be lower in AA children. Inflammatory manifestations, such as emesis and growth failure, may be more common in younger children, while fibrotic manifestations, such as dysphagia and food impaction, may be more common in older children.

48 THE CLINICAL UTILITY OF FECAL CALPROTECTIN IN ROUTINE PAEDIATRIC PRACTICE: A REGIONAL RETROSPECTIVE COHORT STUDY

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The clinical utility of fecal calprotectin in routine pediatric practice: a regional retrospective cohort study.

Background: Fecal calprotectin (FC) is elevated in children with inflammatory bowel disease (IBD). There is little information available regarding the use of FC in other pediatric gastrointestinal (GI) conditions.

Objectives: To determine the patient outcome of all clinical cases where FC was requested in routine pediatric practice by any pediatric specialist in a regional cohort of children. To evaluate the utility of a negative FC result when used in routine clinical pediatric practice.

Method: Using a retrospective study design, all FC samples taken over a 6-year period between 2005 and 2010 in children < 17 years old were obtained. All case notes were reviewed. Patients were followed up for a minimum of 5 years. FC was measured using the PhiCal Test (Calpro). Exclusion criteria were (1) known chronic GI disease; (2) age < 1 yr and ≥ 17 yrs; (3) insufficient FC sample; (4) second or subsequent FC in the same diagnostic cycle; (5) FC taken following endoscopy.

Results: 728 patients were included (62% male, median age 8.2 (IQR 4.7-11.8) years with median follow-up 7.8 (range 5.3-11.2) years). 7% (49/728) were diagnosed with IBD, 18% (131/728) had non-IBD GI inflammation, 75% (548/728) had no GI inflammation (see table for diagnostic categories). Median FC was 1110ug/g (IQR 550-1630) for patients with IBD, 110ug/g (IQR 30-360) for non-IBD GI inflammation, and 30ug/g (IQR 20-70) for no GI inflammation. 6 of 49 (12%) IBD patients had FC < 200 ; 3 with perianal disease (minimal luminal). 1.4% (10/728) of patients with initial FC < 200 ug/g developed IBD in a subsequent diagnostic cycle during a follow-up period of 14-124 months. The repeat FC ($n=9$) at the time of IBD diagnosis was > 200 ug/g in 70% (5/7); the other 2 patients had perianal disease with minimal luminal inflammation. 3.8% (28/728) of patients without a diagnosis of IBD had a FC > 500 ug/g; none developed IBD during follow-up but 75% (21/28) were diagnosed with non-IBD GI inflammation.

Conclusions: In routine pediatric clinical practice via a large regional cohort, FC < 200 ug/g rules out GI inflammation in 86% of symptomatic cases, which should help decrease endoscopy rates in this group. A minority (37%) of cases of GI inflammation are IBD, but the likelihood of IBD rapidly rises with higher FC values as FC results are higher in IBD than other causes of GI inflammation. Our study shows that an FC of > 500 identifies mainly GI inflammation (non-IBD and incident IBD), but also a few cases without any evidence of GI inflammation even when followed up for a minimum of 5 years. Serial FC estimation is therefore important for patients with ongoing symptoms due to the possibility of either IBD or non-IBD GI inflammation in evolution.

49 ADRENAL INSUFFICIENCY SCREENING IN EOSINOPHILIC ESOPHAGITIS: CURRENT PRACTICE AND FUTURE IMPLICATIONS

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Background: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated condition of the esophagus. Topical corticosteroids (TCS), mainly fluticasone propionate and budesonide, are used for treatment of EoE. Recent literature has raised concerns about the possible association between chronic TCS use and risk of adrenal insufficiency (AI), a potentially life-threatening condition.

Aim: To assess practice patterns for AI screening of EoE patients on long term TCS.

Methods: A prospective study was performed to assess the practice patterns of gastroenterologists using a self-administered online survey. An email was sent to physicians ($n=6$) in various eosinophilic diseases consortia including, Consortium of Eosinophilic GI Diseases Research (CEGIR), The International Gastrointestinal Eosinophil ResearcherS (TIGERS), physician members of American Partnership For Eosinophilic Diseases (APFED) and Pediatric GI bulletin board listserv ($n=2567$), with a link to an online survey. The study was IRB approved, voluntary and no remuneration was given. Study participants were divided into 2 groups based on whether they are members of different EoE consortia (C Consortia group, NC Non-consortia group). One survey was sent to an individual regardless of if they were a member of more than one consortium; i.e. only unique surveys were analyzed. Chi-square and Student's t-test were used for statistical comparison.

Results: One hundred fifty-one respondents started the survey of which 140 completed it. Twenty-one of 140 were from C group and 119 were from NC group. Overall, 14/140 (10%) respondents screen for AI. C group was statistically more likely to screen for AI as compared to NC group [9/21 (43%) vs. 5/119 (4%); $P 0.0001$]. The majority of respondents [10/14 (71%)] use a morning cortisol level as the initial screening test. 6/14 (43%) respondents reported abnormal initial screening in $> 25\%$ of patients. Referral to endocrinologist was made if initial screen is abnormal by 43% of respondents, whereas 28% repeat the screening test and 21% perform low dose ACTH stimulation test. Overall, 9/14 (64%) respondents reported one or more confirmed cases of AI. Of those who do not currently screen for AI, 25/126 (20%) plan to screen for AI in the next 6 to 12 months, mainly due to recent literature.

Conclusions: C group members are more likely to screen for AI, possibly due to their expertise. While there is consistency in initial screening, there is considerable variability in follow-up testing. Even though an unexpectedly high number of respondents reported confirmed cases of AI, this is based on a small sample size of a selective group. However, 90% of respondents currently do not screen for AI, implying that AI may be

an under-recognized condition in this patient population. Since 20% of respondents who currently do not screen report plans to change their practice pattern in next year, there is an urgent need for additional studies and formal AI evaluation guidelines for EoE patients on TCS.

50 CLINICAL SYMPTOMS AND MODIFIED BARIUM SWALLOW (MBS) SCORE IN EVALUATION OF PEDIATRIC PATIENTS WITH DYSPHAGIA AND ASPIRATION (DA)

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Background: Dysphagia with aspiration (DA) is a common symptom in patients presenting for multidisciplinary gastroenterology, pulmonology, and ENT diagnostics at Phoenix Children Hospital's Aerodigestive Clinic (ADC). DA is associated with chronic respiratory or gastrointestinal symptoms, chronic thickener use, constipation, and enteral tube dependency. MBS is routinely used to evaluate dysphagia severity and guide thickener treatment of DA patients and for re-evaluation after feeding therapy or other medical and surgical intervention. Previous ADC patients with deep interarytenoid notch (DIN) given injection laryngoplasty had improved symptoms despite post-intervention MBS scores worsening, and vice versa. We initiated a Quality Improvement (QI) project to determine if MBS severity is reflective of clinical symptoms of DA, aimed at changing dysphagia monitoring protocols in DA patients.

Methods: A clinical questionnaire of DA symptoms was developed and administered over 3 months to patients aged 1-3 years who had an MBS within 6 months of their initial ADC visit, standard of care for DA. 17 symptoms (12 gastrointestinal symptoms and 5 pulmonary symptoms) were given a numerical score 0-4 based on parent recall of frequency. MBS was scored 1-10 based on the thickness of liquid recommended for aspiration prevention (1 being thin and 10 being pudding consistency). Individual symptoms and symptom sets (total questionnaire score, GI symptom score, pulmonary score) were compared to MBS scores using linear regression model.

Results: 30 families of patients aged 1-3 were surveyed with median MBS score of 6 and range from 0 to 8. 18 patients had an MBS score above 6. 23 patients had more than one MBS evaluation performed before their initial presentation to the ADC, ranging from 2 to 4 previous evaluations. Median questionnaire score was 18 (range of 4 to 53). All 30 patients presented with at least 1 GI symptom and 29 patients presented with at least 1 pulmonary symptom. 8 patients had DIN. All analysis showed NO significant correlation between individual symptom or symptom sets and MBS score, with the highest R2 value for individual symptoms being 0.05.

Conclusions: Among ADC patients with symptomatic DA, MBS severity score did not correlate with severity and specificity of symptoms, questioning the use of MBS as a repetitive tool for diagnosing severity of persistent DA and for assessing response to laryngeal cleft surgical interventions and thickener wean therapy. In our patient population the use of repetitive MBS is challenged by these findings. Our team is developing a combined clinical and radiologic tool for long-term management aimed at minimizing radiation exposure while promoting best clinical outcomes.

51 INNATE IMMUNE RESPONSES TO ROTAVIRUS VACCINES AND A RECOMBINANT ATTENUATED SALMONELLA VACCINE IN CACO-2 CELLS, IN VITRO M CELLS, AND EX VIVO HUMAN COLONIC MUCOSA

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Two currently licensed rotavirus vaccines, Rotarix and RotaTeq, are efficacious and safe in protecting children from rotavirus gastroenteritis. However, innate immune responses of human intestinal epithelia to rotavirus vaccination remain little known. Furthermore, live attenuated Salmonella strains have been developed as carriers of recombinant attenuated *Salmonella* vaccines (RASV) expressing heterologous antigens. This study aimed to investigate innate immune responses to rotavirus vaccines and the intracellular non-replicating *S. Typhimurium* Δ speG mutant comprising plasmid encoding rotavirus VP4 and VP6 as a RASV in 5-d-old Caco-2 cells, *in vitro* M cells by coculturing Caco-2 cells and Raji B lymphocytes, and *ex vivo* human colonic mucosa using surgical explants established in polarized *in vitro* organ culture (pIVOC). Non-polarized 4-d-old Caco-2 cells, polarized 20-d-old Caco-2 cells, and *in vitro* M cells were treated with Rotarix, RotaTeq, *Salmonella Typhimurium* Δ speG, RASV, or none for 18 h, and human colonic mucosa *ex vivo* were treated with Rotarix, RotaTeq, or none for 5 h. The mRNA and protein expression levels of interleukins (IL-8 and/or IL-4, IL-6, IL-15) and hBD-2 were quantified using qRT-PCR and ELISA, respectively; the expression levels of untreated controls and treated groups were compared using the Student's t-test in cell lines and Mann-Whitney test in pIVOC. In 5-d non-polarized Caco-2 cells, Rotarix and RotaTeq significantly increased the protein and mRNA expression levels of IL-4, IL-6, IL-8, and IL-15 (all $p < 0.05$, Table 1), but not hBD-2, whereas Δ speG and RASV significantly increased both expression levels of IL-4, IL-6, IL-8 and hBD-2 (all $p < 0.05$), but not IL-15. In 20-d polarized Caco-2 cells and *in vitro* M cells, the mRNA expression levels of IL-4, IL-6 and IL-8 were significantly upregulated in the Rotarix-treated Caco-2 cells, whereas those of IL-6 and IL-8 were significantly upregulated in the Rotarix-treated *in vitro* M cells. In addition, hBD-2 expression was non-significantly downregulated in the Rotarix-treated Caco-2 cells and *in vitro* M cells compared to untreated controls. RASV significantly induced higher apical secretion of hBD-2 from *in vitro* M cells than its vector Δ speG. In pIVOC, Rotarix, but not RotaTeq, significantly suppressed hBD-2 mRNA expression of human colonic mucosa compared to untreated controls (1.00 [0.06-2.64] vs. 0.09 [0.05-0.19] fold change, $p = 0.041$). No significant regulation of IL-6, IL-8, and IL-15 was found.

In conclusion, rotavirus vaccines can induce human innate responses in non-polarized Caco-2 cells, polarized Caco-2 cells, and *in vitro* M cells, particularly expression of IL-6 and IL-8. We successfully demonstrated hBD-2 suppression in *ex vivo* human colonic mucosa and a similar tendency in *in vitro* M cells after rotavirus vaccination for the first time. Our establishment of *in vitro* M cells and pIVOC can be developed as a platform to study novel oral vaccines.

4d non-polarized Caco-2 cells (*p<0.05 compared to NT control, n=3)						
ELISA (mean±SE)	NT control	Rotarix	RotaTeq	$\Delta speG$	RASV	IL-1 β
IL-4 (pg/mL)	49.6 ± 0.5	75.6 ± 3.7*	66.6 ± 1.1*	74.1 ± 1.4*	74.2 ± 2.4*	56.0 ± 0.01*
IL-6 (pg/mL)	10.5 ± 5.1	47.0 ± 4.1*	55.9 ± 5.1*	248.8 ± 4.5	246.7 ± 5.4*	70.6 ± 4.4*
IL-8 (pg/mL)	17.5 ± 4.1	61.2 ± 1.4*	58.3 ± 2.9*	181.8 ± 2.8	188.8 ± 14.4*	252.8 ± 12.6*
IL-15 (pg/mL)	31.6 ± 5.6	53.1 ± 0.8*	54.7 ± 2.8*	50.4 ± 1.9*	46.8 ± 2.3	47.0 ± 1.6
hBD-2 (pg/mL)	25.9 ± 3.6	28.6 ± 1.2	22.9 ± 2.8	781.6 ± 71.	807.9 ± 11.2*	455.4 ± 45.8*
qRT-PCR	NT control	Rotarix	RotaTeq	$\Delta speG$	RASV	IL-1 β
IL-4 (fold change)	1.0 ± 0.1	4.9 ± 0.7*	4.3 ± 0.3*	4.6 ± 0.3*	5.4 ± 0.4*	2.6 ± 0.2*
IL-6 (fold change)	1.0 ± 0.2	3.2 ± 0.4*	2.6 ± 0.2*	6.3 ± 1.0*	5.9 ± 0.6*	2.8 ± 0.3*
IL-8 (fold change)	1.0 ± 0.1	1.9 ± 0.3*	3.3 ± 0.4*	10.6 ± 1.6*	10.4 ± 1.6*	3.8 ± 0.4*
IL-15 (fold change)	1.0 ± 0.1	1.3 ± 0.2*	1.4 ± 0.1*	1.2 ± 0.3	1.0 ± 0.1	1.4 ± 0.2*
hBD-2 (fold change)	1.0 ± 0.1	1.1 ± 0.1	0.8 ± 0.1	10.8 ± 1.6*	10.6 ± 1.8*	4.5 ± 0.5*
20d polarized Caco-2 cells (*p<0.05 compared to NT control, n=3)						
ELISA	NT control	Rotarix	RotaTeq	$\Delta speG$	RASV	IL-1 β
IL-8 (pg/mL) basolatera	0 ± 0	1.7 ± 1.4	0 ± 0	12.8 ± 2.9*	20.5 ± 3.9*	13.3 ± 3.2*
hBD-2 (pg/mL) apical	0 ± 0	0 ± 0	3.3 ± 2.9	17.2 ± 14.9	11.4 ± 9.8	13.1 ± 7.9
IL-8 (pg/mL) cell	0 ± 0	0 ± 0	0 ± 0	31.0 ± 5.2*	30.0 ± 1.6*	0 ± 0
hBD-2 (pg/mL) cell	0 ± 0	6.4 ± 3.3	2.1 ± 1.8	0 ± 0	0 ± 0	79.8 ± 9.5*
qRT-PCR	NT control	Rotarix	RotaTeq	$\Delta speG$	RASV	IL-1 β
IL-4 (fold change)	1.0 ± 0.6	5.3 ± 1.2*	-	-	0.7 ± 0.2	-
IL-6 (fold change)	1.0 ± 0.2	6.7 ± 1.5*	-	-	3.9 ± 0.5*	-
IL-8 (fold change)	1.0 ± 0.2	2.6 ± 0.1*	-	-	6.0 ± 0.5*	-
IL-15 (fold change)	1.0 ± 0.1	1.5 ± 0.2	-	-	1.4 ± 0.2	-
hBD-2 (fold change)	1.0 ± 0.2	0.6 ± 0.1	-	-	249.9 ± 66.4*	-
20d <i>in vitro</i> M cells (*p<0.05 compared to NT control; †compared to $\Delta speG$, n=3)						
ELISA	NT control	Rotarix	RotaTeq	$\Delta speG$	RASV	IL-1 β
IL-8 (pg/mL) basolatera	0 ± 0	16.2 ± 3.4*	11.4 ± 3.3*	23.2 ± 1.8*	32.3 ± 7.0*	49.8 ± 4.9*
hBD-2 (pg/mL) apical	0 ± 0	0 ± 0	0 ± 0	0 ± 0	10.3 ± 8.9†	61.7 ± 18.7*
IL-8 (pg/mL) cell	11.0 ± 4.0	15.0 ± 3.8	21.0 ± 4.0	13.0 ± 4.9	14.0 ± 6.1	37.0 ± 6.7*
hBD-2 (pg/mL) cell	14.4 ± 10.2	0 ± 0	2.3 ± 2.0	5.3 ± 4.6	7.9 ± 6.9	53.7 ± 5.9*
qRT-PCR	NT control	Rotarix	RotaTeq	$\Delta speG$	RASV	IL-1 β
IL-4 (fold change)	0.8 ± 0.4	3.4 ± 2.0	-	-	0.8 ± 0.4	-
IL-6 (fold change)	1.0 ± 0.1	5.5 ± 1.0*	-	-	3.9 ± 0.2*	-
IL-8 (fold change)	0.8 ± 0.1	2.9 ± 0.3*	-	-	6.9 ± 2.6	-
IL-15 (fold change)	1.1 ± 0.0	2.2 ± 0.5	-	-	1.3 ± 0.2	-
hBD-2 (fold change)	1.2 ± 0.4	0.5 ± 0.1	-	-	202.5 ± 67.5*	-
Human colonic mucosa in pIVOC (*p<0.05 compared to NT control, n=6)						
RT-PCR	NT control	Rotarix	RotaTeq			
hBD-2 (median, range)	1.00 (0.06-2.64)	0.09 (0.05-0.19)	0.56 (0.16-2.9)			
IL-6 (median, range)	1.00 (0.07-6.19)	0.75 (0.02-4.99)	0.66 (0.03-2.46)			
IL-8 (median, range)	1.00 (0.05-4.13)	0.64 (0.04-2.57)	0.90 (0.07-1.97)			
IL-15 (median, range)	1.00 (0.17-2.64)	0.09 (0.05-0.50)	0.56 (0.16-2.90)			

*52 NOVEL INSIGHT INTO SALMONELLA TYPHI PATHOGENESIS FROM HUMAN-DERIVED TERMINAL ILEUM ORGANOIDs
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Introduction: *Salmonella enterica* serovar *Typhi* is the causative agent of Typhoid fever, from which an estimated 22 million cases occur annually resulting in 200,000 deaths. In some areas of the globe, the incidence of Typhoid fever is as high as 500 cases out of every 100,000 children. At present, little is understood about host response to Typhi infection. As such, no long-term preventive vaccine therapy is available. Current therapeutics include antibiotic treatment, however antibiotic resistant serovars are increasing worldwide. Furthermore, chronic Typhi colonization of the gall bladder is sufficient to cause gall bladder cancer, therefore demonstrating significant health risks upon both long- and short-term infection. To design alternative therapeutic strategies, there is immediate need to understand Typhi infection and pathogenesis. Materials and Methods. Terminal ileum biopsies were collected from donors for generation of organoid culture. Culture conditions were optimized to maintain terminal ileum epithelial stem cells; cells were then seeded onto transwell inserts for generation of monolayers.

Monolayers were infected with *Salmonella enterica* serovar Typhi 2a to the apical surface. Upon infection, changes in trans-epithelial electrical resistance (TEER), cytokine release, gene expression, and cellular localization were assessed.

Results and Conclusions: Terminal ileum derived organoids give rise to a diversity of epithelial cells, including goblet, paneth and M cells, which are grown as a monolayer *in vitro*. Use of the epithelial monolayer model identified specific contributions of the epithelium in response to Typhi infection as assessed by qPCR, immunofluorescence and cytokine secretion. Differences in cellular association of bacteria were assessed using IF and TEM. To identify how epithelium responds to infection, apical and basolateral culture supernatants were collected for ELISA analysis. ELISA analysis demonstrated differences in IL-8, IL-1 β and IL-12p70 cytokine production, with significant levels of basolateral cytokine secretion. Finally, infection decreased TEER at 120m post infection. Together, our data characterizes key aspects of terminal ileum response to Typhi infection addressing a critical gap in our current understanding of Typhoid fever pathogenesis.

53 LONGITUDINAL EVALUATION OF NON-INVASIVE BIOMARKERS FOR EOSINOPHILIC ESOPHAGITIS

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Background: The diagnosis and management of eosinophilic esophagitis (EoE) often requires multiple endoscopies. Serum biomarkers can be elevated in EoE patients, but their clinical utility is not well established.

Goals: To evaluate serum biomarkers in EoE subjects compared to controls and followed longitudinally in response to treatment.

Methods: We conducted a prospective cohort study of children and adults undergoing esophagogastroduodenoscopy (EGD) for suspected EoE. After completing a course of proton pump inhibitor therapy, esophageal mucosal biopsies were obtained, as well as serum analysis of absolute eosinophil count (AEC), eotaxin-3, eosinophil derived neurotoxin (EDN), eosinophil cationic protein (ECP) and interleukin-5 (IL-5). Subjects with normal endoscopic and histologic findings constituted controls. Those meeting criteria for EoE underwent repeat EGD and biomarker measurements following treatment with topical steroids for 8 weeks.

Results: AEC (263.50 cu/mm vs. 102 cu/mm, $p < 0.001$), ECP (26.98 ng/mL vs. 5.20 ng/mL, $p < 0.001$) and EDN (31.70 ng/mL vs. 14.18 ng/mL, $p = 0.004$) levels were significantly elevated in EoE subjects compared to controls and correlated with esophageal eosinophilia. The level of AEC (odds ratio [OR], 1.79; 95% confidence interval [CI], 1.28-2.64) and ECP (OR, 1.61; 95% CI, 1.23-2.36) were associated with a diagnosis of EoE. Only AEC significantly predicted esophageal eosinophilia following topical steroid therapy in EoE subjects ($p = 0.006$).

Conclusion: AEC, ECP, and EDN were higher in EoE subjects compared to controls and correlated with degree of esophageal eosinophilia. Furthermore, AEC predicted post-treatment eosinophilia, suggesting a potential role in monitoring EoE disease activity.

54 COLLECTION OF STOOL ON FECAL OCCULT BLOOD CARDS IS EFFECTIVE FOR FECAL MICROBIOME BUT NOT MECONIUM MICROBIOME STUDIES IN CHILDREN

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Background: Fecal occult blood cards (FOBC) that can be mailed and require small amounts of stool may be an effective solution for collecting fecal samples from children for large scale microbiome studies; however, the quality of sequencing resulting from this is unknown.

Aims: To compare 16s rRNA sequencing results from stool, and also meconium, stored on a FOBC vs. in an eppendorf tube (ET) under different conditions.

Methods: 8 stool samples from children in diapers aged 1 month-2 years and 3 meconium samples were collected and stored as follows: 1) ≤ 2 days at room temperature (RT) in an ET 2) 7 days at -80°C in an ET 3) 3-5 days at RT on a FOBC 4) 7 days at RT on a FOBC and 5) 7 days at -80°C on a FOBC. DNA was extracted and each specimen/condition was sequenced with replicates on the Illumina MiSeq. Overall microbiome structure and taxa distributions were compared between collection method. Alpha diversity (observed, Shannon, Simpson) was compared pairwise between different storage conditions. The Adonis method was used to determine whether the 5 different conditions used for storing the samples were different based on unweighted unifrac distances.

Results: Overall microbiome structure differed between individual stool specimens as expected ($p < 10^{-5}$), but there was no significant difference between the storage method ($p = 0.18$). However there was a significant difference between storage methods for meconium ($p = 0.039$). For alpha diversity, when compared to a goal standard of stool in an ET at RT for < 2 days, there was no difference in diversity for FOBCs at 7 days at RT or 7 days at -80°C . Stool stored on FOBCs did tend to have an increase in Firmicutes and a decrease in Proteobacteria compared with ETs.

Conclusion: In stool collected from diapers from young children, there was no significant difference in alpha and beta diversity from stool collected and stored on FOBCs compared with fresh or frozen stool in ETs. There was a significant difference in microbiome structure between storage conditions for meconium however. Collection of stool and mailing on fecal occult blood cards may be a low-cost, effective method for large scale population based microbiome studies in children, but not for meconium.

55 ESOPHAGITIS IN INFANTS AND TODDLERS WITH FEEDING DIFFICULTIES: PREVALENCE AND ASSOCIATED CLINICAL CHARACTERISTICS

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Background: In infants and young children with feeding difficulties, esophagogastroduodenoscopy (EGD) is increasingly performed to look for reflux or eosinophilic esophagitis, but few studies have examined the prevalence of esophagitis and associated risk factors in this population. Identification of risk factors associated with esophagitis could help physicians decide which patients should undergo EGD.

Aim: Among young children with feeding difficulties who underwent EGD, to determine the prevalence of esophagitis and compare the clinical characteristics of children with and without esophagitis.

Methods: We retrospectively reviewed electronic medical records of children who met the following inclusion criteria: initial outpatient gastroenterology visit at Boston Children's Hospital between January 2014 and December 2015 with an ICD-9 diagnostic billing code for feeding difficulties or dysphagia, and 0 to 36 months old at the time of their first EGD. We excluded subjects with pre-existing enteropathies or

congenital GI anomalies. We recorded demographic and clinical data using a data abstraction form. We compared characteristics of children with and without histologic esophagitis using chi-square and t-tests.

Results: Of 171 subjects, 56% were <1 year old. Of 38 (22% of 171) subjects with histologic esophagitis, 37 had eosinophilic and 1 had neutrophilic inflammation. Gross and histologic findings were not well-correlated; 72% of subjects with esophagitis had grossly normal mucosa. Of the 22 subjects (13% of 171) with a history of food allergy, 64% had esophagitis. Food allergy history was present in 8 of 134 (6%) subjects without esophagitis, 10 of 25 (40%) subjects with <20 eosinophils/hpf, and 4 of 12 (33%) subjects with >20 eosinophils/hpf ($p<0.0001$). Subjects with and without esophagitis did not differ in presenting symptom rates of gastroesophageal reflux or vomiting (63% vs. 65%, $p=0.80$), food refusal (37% vs. 41%, $p=0.68$), and choking or gagging with food (37% vs. 45%, $p=0.36$). Subjects with esophagitis had lower rates of fussiness as a presenting symptom (5% vs. 20%, $p=0.03$) but only 2 of 29 children who presented with fussiness had esophagitis. Subjects with and without esophagitis did not differ in history of past or current proton pump inhibitor (71% vs. 76%, $p=0.57$) or elemental formula use (32% vs. 19%, $p=0.11$).

Conclusion: Almost 1 in 4 infants and toddlers under 3 years old who presented with feeding difficulties had esophagitis, usually with increased eosinophils. Among the small number of subjects with food allergy, 64% had esophagitis. These data suggest that clinicians should consider EGD to look for esophagitis in infants and toddlers with feeding difficulties and a history of food allergy.

56 PRESCHOOLERS WITH ALLERGIC DISEASES HAVE AN INCREASED RISK OF IRRITABLE BOWEL SYNDROME WHEN REACHING SCHOOL AGE

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Objectives: To systematically investigate the risk of subsequent irritable bowel syndrome (IBS) in children with antecedent allergic diseases in a population-based case-control study in Taiwan.

Methods: We evaluated 11,242 children (age range: 7-18 years) with IBS and 44,968 age and sex-matched control subjects who had been examined between 2000 and 2008. IBS odds ratios (ORs) were calculated for children with antecedent allergic diseases, including allergic conjunctivitis (AC), allergic rhinitis (AR), asthma, atopic dermatitis (AD), urticaria, and food allergy (FA).

Results: Children with antecedent allergic diseases had a greater risk of IBS than did control subjects ($p<0.001$). Among the 6 evaluated diseases, the highest adjusted OR (aOR) of 1.78 was observed with AR (95% confidence interval [CI], 1.69-1.87), and the lowest aOR of 1.40 was observed with AD (95% CI, 1.2-1.62). With 2 or more allergic diseases, the aORs increased to 2.06 (95% CI, 1.932-1.9) for all subjects, 2.07 (95% CI, 1.88-2.28) for girls, and 2.18 (95% CI, 2.02-2.35) for children ≥ 12 years old. The highest aOR of 2.94 (95% CI, 1.35-6.40) was noted when food allergy concurrent with asthma.

Conclusions: Preschoolers with a history of allergic disease had an increased risk of subsequent IBS development upon reaching school age. This risk increased in the presence of concurrent allergic disease and a higher clinical allergy burden.

57 CHARACTERIZATION OF DYSPHAGIA PREDOMINANT EOSINOPHILIC ESOPHAGITIS (EoE-D), WITH AND WITHOUT FOOD IMPACTION: 101 ADOLESCENTS

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EoE in children is associated with many symptoms. Consensus-2011 statement classifies patients into four groups based on predominant symptom; EoE-D, abdominal pain (AP), GERD and failure to thrive. Previously, we showed the features and outcome of EoE-D with and without food impaction (FI) in a small group of 36 patients.¹ This study compares a larger group.

Aim: Compare clinical features, endoscopy+ biopsy, and outcomes of 101 EoE-D patients presenting with and without FI.

Methods: In this retrospective study, patients with EoE-D seen between January 2001 and August 2015 were stratified into Group I, with FI and Group II, without FI. Physical findings, CBC, esophagram, EGD+ biopsies of the duodenum, antrum, distal and mid-esophagus were captured. Diagnosis of EoE was made as per the consensus guidelines. Treatments included topical or oral steroids, dietary modification, \pm PPIs, as per our EoE Clinic protocol. Symptom score for dysphagia, nausea, vomiting, regurgitation, early satiety and heartburn were scored: absent -0, mild -1, and severe -2 except dysphagia had a score up to 3 with FI. Esophageal EGD findings were scored at diagnosis and follow-up.

Results: Patients; Gr I- 30, Gr II- 71, mean age 10.9 and 10.4 yrs. ($p=0.27$). Clinical features, X-ray, EGD + biopsy findings are given in Tables 1. All patients with FI required endoscopic removal, and strictures, if present, were dilated later. Follow-up: Gr I; mean 1.7 yrs. (range 1/12-8 yrs) and in Gr II 1.1 yrs (1/12-7yrs). Treatments included; fluticasone, diet or combination, \pm PPI. Symptom improvement; Gr I mean dysphagia score improved from 3 to 1.25 ($p<.001$) and Gr II- 1.21 to 0.71 ($p<.001$) and mean composite score from 3.3 to 1.45 ($p<.001$) and 2.49 to 1.48 ($p<.001$). EGD: Gr I, 15/30 (50%) and Gr II 45/71(63.4%) had a follow-up, at 8-12 weeks. Cumulative EGD score improved from 1.8 to 1.7 in Gr I ($p=.70$) and from 1.6 to 1.5 in Gr II ($p=0.08$); peak eos. count in Gr. I was 53.2 at diagnosis and 37.5 after treatment ($p=.04$), and in Gr. II 47.6 and 29.8 ($p=.001$). Mean eos. count in Gr. I was 42 before treatment and 27.5 after ($p=.03$), and in Gr. II 39.3 and 22.1 ($p<.001$). Patients with strictures (8); it stayed open after dilation while the small caliber esophagus was recalcitrant. 1/30 (3.3%) patients in Gr I had recurrence of FI and none in Gr II developed FI. There were no perforations.

Conclusion: There were no significant differences in the clinical features and endoscopic findings and outcome of dysphagia of the two groups. With treatment there was a significant improvement in the eosinophil count in Group II (without FI) and not in Gr I. Strictures opened up and remained open, while small caliber esophagus was recalcitrant. 1/30 (3.3%) patient in Gr I had recurrence of FI and none in Gr II developed FI. More prospective studies with long-term follow-up are needed to validate this data.

Reference:1. Gunasekaran T. Characterization of Dysphagia Associated EoE in Children with and witho

Presenting Symptoms, Esophagram, EGD and Biopsy findings at Diagnosis:

	Gr I Food Impaction (n=30)		Gr II No Food Impaction (n=71)		P value
	n	%	n	%	
Demographics					
Male	25	83.3	59	83.1	1
Mean age	10.9		10.4		0.27
Presenting Symptoms					
Dysphagia	30	100	71	100	0.66
Associated allergies	8	26.7	9	12.7	0.09
Regurgitation	1	3.3	6	8.5	0.35
Nausea	0		5	7	0.14
Vomiting	2	6.7	13	18.3	0.13
Heartburn	3	10	11	15.5	0.47
GI bleeding	1	3.3	0		0.12
Constipation	0		8	11.3	0.06
Number of patients who had Esophagram*					
	12	40	35	49.3	0.39
*Gr I Abnormal: 2 stricture, 1 small caliber esophagus, 1 spasm. Gr II Abnormal: 2 stricture, 1 Spasm, 3 esophageal reflux, 2 abnormal swallowing, 3 mucosal irregularity, 1 Esophageal tear					
EGD Findings					
Edema	16	53.3	24	33.8	0.07
Rings	3	10	7	9.9	0.98
Exudates	10	33.3	28	39.4	0.54
Furrows	22	73.3	37	52.1	0.05
Stricture	3	10	5	7.04	0.61
Biopsy at diagnosis					
Peak eosinophil count (mean)	53 (37.5)		47.6 (29.8)		
Eosinophilic microabscess	5	16.7	16	22.5	0.51
Basal cell hyperplasia	11	36.7	23	32.4	0.68
Spongiosis	5	16.7	8	11.3	0.46
Papillomatosis	5	16.7	9	12.7	0.60

58 FACTORS ASSOCIATED WITH MORTALITY IN PEDIATRIC GASTROINTESTINAL HEMORRHAGE; A MULTICENTER DATABASE ANALYSIS

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Background: The risk factors associated with mortality in children with gastrointestinal hemorrhage (GIH) are poorly understood. This is presumably related to the rarity of fatal outcomes limiting the feasibility of prospective studies. GIH in children frequently complicates multisystem chronic illness. The Pediatric Health Information System (PHIS) database collects admission, diagnostic, and treatment data among 44 children's hospitals across the United States (U.S.) and affords an insight on the demographic and clinical characteristics that are associated with mortality in children with GIH.

Methods: The study is a retrospective multi-institutional database analysis. PHIS was interrogated through combined discharge diagnosis (ICD 9, ICD 10), procedure codes (CPT) and pharmacology therapeutic codes (CTC) for children diagnosed with GIH from 2011 to 2015 at the time of admission or complicating their inpatient course. Demographics, co-morbidities, inpatient course including pharmacotherapy and procedures were analyzed using the generalized linear mixed model framework. The R statistical package was used for analysis.

Results: During the period studied, 61,629 children were diagnosed with GIH through ER (43,254) 24-hour observation unit (3198), ambulatory surgery unit (257) and inpatient service (14,200). Mortality was 0.5% overall (M:F 1.1:1), mean age (SD) was 8.4 (7.4) years for mortality cases, and 6.8 (7.3) years for non-mortality cases. No difference was noted across racial definitions. Median inpatient length of stay in children with GIH who died was 18.5 days (range: 1 to 687 days), compared with 1 day for non-mortalities (range: 1 to 376 days). After adjustment for potential confounding factors, mortality was significantly associated with urban/rural residence ($p=0.007$), being higher in children reported to live in rural zip codes (OR 1.65 95% CI, 1.21-2.26), and when GIH was not reported at the time of admission compared to complicating

inpatient course (OR 1.84 95% CI, 1.47-2.30, P value <0.0001). Mortality was higher in chronic liver disease (CLD) (OR 3.36 95% CI, 2.31-4.88 $p < 0.0001$) although chronic complex disease was present in nearly all mortality cases (97%). Treatment with proton pump inhibitor therapy (79%), H₂ receptor antagonists (43%), erythromycin (9%) and octreotide/vasopressin (18%) was not ubiquitous to all mortalities; octreotide use highly associated with CLD diagnosis ($\chi^2(1) = 2010.1, p < 0.0001$).

Conclusions: This study represents the largest cohort of patients diagnosed with GIH and underscores important differences in children who succumb after the diagnosis of GIH compared to survivors. Early intervention and rapid access to specialized care appears to be important. The occurrence of GIH in children with chronic disease, especially liver disease, appears especially ominous and demands greater vigilance and greater adherence to standard pharmacologic interventions including acid suppression.

59 ESOPHAGEAL EOSINOPHILIA IN PEDIATRIC PATIENTS WITH CELIAC DISEASE RESOLVES ON A GLUTEN-FREE DIET

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Background: Celiac disease (CD) is an autoimmune disease that has a prevalence of 1% in the general population in the United States.

Esophageal eosinophilia due to gastroesophageal reflux disease (GERD) and Eosinophilic Esophagitis (EoE) have been found to be more prevalent in patients with CD than the general population, but the relationship appears to be coincidental. In this case series, we sought to characterize our patients who have CD and EoE and evaluate their response to gluten-free diet (GFD).

Methods: We searched our clinical databases for the diagnosis codes for CD and EoE and then extracted patients who had both diagnosis codes diagnosed between 2012 and 2015. A total of 13 patients were identified. We then reviewed their laboratory data for positive celiac serologies and histology records to confirm the diagnosis of CD based on published diagnostic criteria (villous blunting and increased intraepithelial lymphocytes). We also reviewed the esophageal histology to confirm the diagnosis of EoE based on the 2011 NASPGHAN consensus guidelines (presence of >15 eos/hpf, basal layer hyperplasia and elongated papilla). We collected patient demographics and clinical data.

Results: A total of 13 patients were identified to have co-existent CD and EoE (ages 1-15 years, mean 8.5 years, 77% females, and 69% Caucasians, 31% with asthma). 11/13 patients were treated with GFD + PPI and 2/13 were treated with GFD only as their initial therapy. A repeat endoscopy was performed 4-9 months after the initial endoscopy. The esophageal eosinophilia resolved or improved in 9/13 (69%) patients on the GFD ± PPIs and 3/13 (23%) patients were placed on a dairy-free diet and 1/13 (8%) was placed on SFED, which eventually resolved the eosinophilia. The average peak eosinophil count on initial endoscopy was 43 eos/hpf (range 25-80), post-GFD ± PPIs was 7 eos/hpf (range 0-15) in the responders and 33 eos/hpf (range 25-40) in the non-responders. After adding dairy-free diet (n=3) and SFED (n=1) the peak eosinophil count decreased to an average of 2.5 eos/hpf (range 0-5).

Conclusion: We present a case series of 13 patients with CD who were found to have esophageal eosinophilia. The majority of patients (69%) responded to GFD ± PPI's, which may indicate that these patients have GERD, EoE due to wheat, or that the esophageal eosinophilia is directly related to the CD. The rest of the patients responded to other dietary eliminations (dairy, SFED), which indicates that they likely had EoE. From this series, we propose a therapeutic algorithm to manage esophageal eosinophilia in patients with CD.

60 RAPID FECAL CALPROTECTIN IN PRETERM INFANTS AT HIGH RISK FOR NECROTIZING ENTEROCOLITIS

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Introduction: Necrotizing enterocolitis (NEC) in preterm infants of very low birth weight imposes high morbidity and mortality. Fecal calprotectin may serve as a viable non-invasive screening test to detect early signs of NEC, predicting low-grade mucosal inflammation prior to overt signs and symptoms of NEC. However, this likelihood has not been explored, as the traditional send-out ELISA calprotectin assay has limited clinical utility due to the time to result. Unlike the ELISA test, the Quantum Blue assay has a rapid turn-around of 15 minutes with the potential for point-of-care use with results possibly in advance of symptoms. As an exploratory pilot study, we aim to examine normative calprotectin values as measured by the Quantum Blue assay in a high-risk cohort.

Methods: We are conducting a longitudinal cohort analysis of patients admitted to the Lucile Packard Children's Hospital Neonatal Intensive Care Unit (NICU). The list of all infants admitted to the NICU is reviewed daily, and patients with a birth weight of <1,500 grams are enrolled. Infants with known bowel pathology are excluded from the study. Stools are collected once daily for 30 days or until postmenstrual age of 32 weeks, whichever is longer. Collected stool samples are tested using Quantum Blue® Calprotectin High Range Rapid Test. Recruitment, testing, and analysis are ongoing.

Results: Thirty-five patients have been enrolled to date. Two were excluded due to early death, leaving samples from 33 patients for data analysis. Of those 33 patients, the majority are male (n=21, 63.6%) and were delivered via c-section (n=26, 78.8%). Mean birth weight is 999.5±307.5g at mean gestational age 28.4 ± .7 weeks. Preliminary data show two distinct groups in our cohort: first sample in the first week of life with low calprotectin level (<200 mcg/g) versus high calprotectin level (≥200 mcg/g). Descriptive statistics show that maternal indication for preterm birth (i.e., preeclampsia or eclampsia) is significantly correlated with an elevated calprotectin level in the first week of life. Of note, history of maternal chorioamnionitis is not correlated with higher first calprotectin levels. No patient within this cohort has developed NEC, but further enrollment may prove that this subset of patients with higher initial calprotectin values may be more at risk. Additional analysis is required to determine indicators of increasing calprotectin levels after the first week of life and whether these states may be predictive of NEC.

Conclusion: In a cohort of premature, at-risk infants for NEC, there exists a subgroup of infants with high perinatal calprotectin levels in the first week of life correlating with maternal causes for preterm birth. Validation is necessary to determine whether maternal causes for preterm birth as a predictor of NEC is detectable by high calprotectin levels. A rapid calprotectin assay has the potential for point-of-care use in this population.

61 DIFFERENTIAL GASTRIC CYTOKINE RESPONSES AND LEWIS ANTIGEN MATURATION DETERMINE H. PYLORI COLONIZATION BETWEEN CHILDREN AND ADULTS: AN IN VITRO STUDY

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Background: The prevalence and disease severity of *H. pylori* infection increased from childhood to adulthood. The gastric Lewis antigens served as receptors contribute to the *H. pylori* colonization. Different inflammatory severity and colonization density were demonstrated on gastric epithelium between children and adults with persistent *H. pylori* infection. However, acute gastric cytokine responses and Lewis antigens maturations after *H. pylori* infection are unclear. This study aimed to validate the differences of cytokine responses, Lewis b antigen (Leb) expression, and colonization density between youth and adult primary gastric epithelium cell after *H. pylori* infection.

Methods: We applied a gHuman stomach fetal epithelium (HSFE) cells and human gastric epithelial immortalized gGES-1 cells to mimic child and adult primary gastric epithelial cells. Each group was challenged with *H. pylori* at various time periods. The *H. pylori* colonization density and Lewis antigens expression intensity were measured by flow cytometry. Cytokine expressions, including IL-6 and IL-8, were measured by ELISA.

Results: After *H. pylori* challenge, the colonization intensity was significantly higher in GES-1 than in HSFE cells. An earlier achieve full density of colonization in GES-1 but the colonization density slowly increased by a time-dependent manner in HSFE cells. *H. pylori* infection induced Lewis b antigen (Leb) expression in both GES-1 and HSFE cells. The features of Leb increment were compatible with colonization density in both cells. *H. pylori*-induced IL-6 and IL-8 expressions were significantly higher in HSFE cells than in GES-1 cells, respectively.

Conclusions: Leb antigen-mediated gastric *H. pylori* colonization is an acquisition age-dependent process. The gastric IL-6 and IL-8 responses are different between children and adults after *H. pylori* infection.

62 CLINICORADIOLOGICAL RISK FACTORS FOR PEDIATRIC STRANGULATED SMALL BOWEL OBSTRUCTION

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Background: Diagnosing intestinal strangulation complicating a small bowel obstruction (SBO) remains a considerable challenge in children. Our goal was to evaluate the clinicoradiological parameters to predict the presence of strangulated intestine.

Methods: Medical records were reviewed for 226 pediatric patients operated for acute small bowel obstruction over a 15-year period. The clinical, radiologic findings and operation results were examined. Regression analysis was applied to identify parameters that would predict strangulated SBO.

Results: Of 226 patients with SBO, 65 patients had intestinal strangulation. In multivariable analysis, four clinical variables corrected with intestinal strangulation and were given one point each towards the clinical score: severe continuous abdominal pain, tachycardia, WBC count >14,500/mm³, and abdominal distention. The area under the receiver operating characteristic curve was 0.77 (CI, 0.69-0.84), with the optimal cutoff of 2. With score < 2, strangulation rate was 16.5 % (95% CI, 0.11-0.23) vs. 74% (95% CI, 0.59-0.85) with score ≥ 2, ($p < 0.001$). In patients with clinical score ≥ 2 combined with the presence of ascites on ultrasound or with the wall thickness and reduced wall contrast enhancement on abdominal computed tomography (CT) had the strong evidence of intestinal strangulation (LR 13.5, 95 % CI, 0.6-0.82, $p < 0.001$; LR infinite, 95 % CI, 0.58-0.91, $p < 0.001$).

Conclusions: By combining two more clinical parameter including severe continuous abdominal pain, tachycardia, leukocytosis, and abdominal distention with ascites on US or wall thickness and reduced wall contrast enhancement on CT allowed identification of strangulated SBO.

63 PREDICTIVE RISK FACTORS OF RECURRENT ILEOCOLIC INTUSSUSCEPTION AFTER SUCCESSFUL REDUCTION IN CHILDREN

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Background: The intussusception recurs in approximately 10 percent of children after successful nonoperative reduction. Multiple recurrences of intussusception may occur in those with idiopathic intussusception and is not necessarily an indication for surgery.

Study Objectives: The main objective was to determine the clinical and sonographic findings that could be used to predict recurrences of ileocolic intussusceptions in children that had been successfully reduced by enema.

Methods: A retrospective search was performed on 83 children with successful enema reduction of ileocolic intussusception, 3 months to 7 years of age, during a 3.2-year period from January 2013 through April 2016. The clinical, laboratory records and sonographic findings were compared between the recurrence of intussusception group (ROI) and the non-recurrence group (NROI).

Results: Nineteen children (22.9%) of recurrence of intussusception were identified. In 16 cases of 19 ROI, and 26 of 64 NROI, the thickening of terminal ileum closest to ileocolic valve was obtained just after successful enema reduction. Statistical significances were found in terminal ileal wall thickening (median, 9.4 vs. 7.95 mm; $p = 0.0133$), in contrast, not in age (median, 24.5 vs. 19.5 months; $p = 0.204$), gender (male, 68.8% vs. 53.8%, $p = 0.867$), irritability (median, 0.1 vs. 0.7 day; $p = 0.074$), currant jelly stool (median, 0.1 vs. 0.1 day; $p = 1.0$), or C-reactive protein (median, 0.69 vs. 1.83 mg/dL; $p = 0.908$).

Conclusion: Recurrence is associated with the thickening of terminal ileal wall but not clinical or laboratory findings. Given the small numbers of cases, further studies should be considered. We recommend a premeditated measurement of terminal ileal wall after successful reduction of ileocolic intussusception.

ENDOSCOPY

79 SMART APPS: REDUCING PRE-PROCEDURAL ANXIETY IN PEDIATRIC GASTROENTEROLOGY ENDOSCOPY PATIENTS

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Background: Anxiety is easily provoked in children undergoing invasive medical procedures including endoscopy. Two prior studies have documented the effectiveness of psychological preparation prior to endoscopy for reduction of anxiety in children. Technology now permits the common place use of hand-held devices (smart phones and tablets) as entertainment by parents and patients during medical appointments. We hypothesized that smart applications (apps) on these devices could be used as possible relaxation and distraction tools to reduce pre-procedural anxiety in children.

Objective(s): a) Compare pre-procedural anxiety in pediatric patients undergoing endoscopy within two groups: Intervention group (play with apps) vs.. control group (no apps). b) Identify areas of greatest anxiety for patients and parents during outpatient endoscopy.

Methods: Prospective randomized control study with patients between the ages of 8-18 yrs undergoing outpatient endoscopy. Patients enrolled on day of procedure and randomized into two groups intervention or control. Patients with prior endoscopy, anxiety disorder, on anxiolytics,

history of cardiac/metabolic diseases, neurologically impaired/unable to complete questionnaire or who previously received psychological therapies (CBT) were excluded. Intervention group had access to an electronic tablet preloaded with smart applications- (fruit ninja, Koi pond and balloon animals) and were allowed to play with app for ≥ 10 minutes prior to procedure. Anxiety measured upon arrival and just prior to procedure; anxiety was measured with vital signs (BP, HR, and RR) and a State Trait Anxiety Inventory for Children (STAI-C). Post endoscopy questionnaire completed by patient and parents.

Results: 46 patients enrolled, with one dropout. Total of 45 patients: 22 in control group vs. 23 in intervention group. After smart app use for a minimum of ≥ 10 minutes, those in the intervention group had significantly lower mean post-intervention systolic BP (SBP) than the control group ($p 0.017$). There was also decrease in other surrogates of anxiety (DBP, HR and STAIC) except for RR, albeit not statistically significant. Majority of the patients and their parents in the intervention group found pre procedural use of the app beneficial (55% and 72% respectively). Post-procedure survey of patients and parents revealed IV placement and waiting for procedure as the two most common causes of pre-procedural anxiety.

Conclusions: Smart applications (apps) significantly reduced pre-procedural anxiety as measured by SBP in children undergoing endoscopy. Other surrogates for anxiety (DBP, HR, and STAI-C) also trended downward with smart app use, albeit not statistically significant. IV placement was the key driver of anxiety for patients. Parents reported waiting while child was in the procedure and observing child undergo anesthesia as major causes of anxiety for them during the procedure.

***80 HOW OFTEN WILL CHILDREN WITH GASTROESOPHAGEAL REFLUX DOCUMENTED BY pH MONITORING STUDIES SHOW EVIDENCE OF ESOPHAGITIS?**

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Purpose: Diagnosis of gastroesophageal reflux disease (GERD) in children is challenging, as there is no defined gold standard. GERD is suspected by either the presence of acid reflux documented during esophageal pH monitoring and/or by esophagitis documented by endoscopy. There are two methods of esophageal pH monitoring including 24-hour-pH-multichannel-intraluminal-impedance measurement (pH-MII) or Bravo pH monitoring. It is unclear how often children with GERD will have both pathological reflux detected esophageal pH monitoring, and histopathological changes of mucosal injury seen on esophageal endoscopy.

Methods: We retrospectively examined clinical characteristics of pediatric patients with suspected GERD evaluated at our institution between January 2009 and July 2014. Subjects on anti-reflux medications or with known esophagitis, secondary to conditions other than GERD, were excluded.

Results: There were a total of 220 patient charts reviewed, of which 134 met inclusion criteria. All of the patients had an endoscopy and a 24-48 hour pH monitoring study. The breakdown of results and clinical features is seen in Table 1. Only a minority (24/86) of subjects with GERD had both an abnormal endoscopy and pH study, while the majority (41/86) had an abnormal pH study only. Also, we found that 21/86 only had an abnormal endoscopy, however of these subjects, 5/21 were newly diagnosed with eosinophilic esophagitis.

Impression: Children with GERD documented by Bravo/Impedance studies did not have significant changes of esophagitis detected on endoscopy. These two methods of detecting GERD are independent of each other and do not yield consistent results. Further studies must be done to establish a standard of care in diagnosing GERD.

FIGURE 1

	Normal pH Normal EE	Abnormal pH Abnormal EE	Abnormal pH Normal EE	Normal pH Abnormal EE
Subjects (N=134)	35.8%(48)	17.9% (24)	30.6% (41)	15.7% (21)
Age (years)	9.8	10.0	7.1	11.0
Gender -Male	35.4% (17/48)	70.8% (17/24)	48.8% (20/41)	50% (10/20)
BMI	18.7	19.1	20.3	20.0

EE: Endoscopic evaluation

pH: 24-48 hour reflux monitoring

81 COMPLICATIONS OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PEDIATRIC PATIENTS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Objectives: Endoscopic Retrograde Cholangiopancreatography (ERCP) is increasingly utilized in pediatrics. We hypothesize that ERCP has been applied with acceptable complication rates in children reported in the literature during the past two decades.

Methods: A systematic literature search of MEDLINE, Embase, and Web of Science from January 1995 to January 2016 was conducted for observational studies published in English. Studies reporting ERCP complications in patients <21 years of age without history of liver transplant or cholecystectomy were included. A summary estimate of the proportion of children who experienced any complications following ERCP was derived using a random effects meta-analysis.

Results: Thirty-two studies involving 2612 children and 3566 procedures were included. Subjects' ages ranged from 3 days to 21 years. Procedures were performed for biliary (54%), pancreatic (38%), and other (8%) non-specific indications; 56% of ERCPs were interventional. Procedural complications included post-ERCP pancreatitis in 166 (4.7%), bleeding in 22 (0.6%) and infections in 27 (0.8%). Pooled complication rate was 6% (95% CI, 4%-8%). Pooled estimate of post-ERCP pancreatitis was 3% (95% CI, 2%-5%), and other complications were 1% (95% CI, 2%-5%). In the subset of articles reporting diagnostic ERCPs performed in neonates with cholestasis the pooled complication rate was 3% (95% CI, 1%-7%). Available data limited the ability to report on differences between pediatric-trained and other endoscopists.

Conclusions: Complications associated with pediatric including neonatal ERCP range widely in severity and are reported inconsistently. Our review suggests 6% of children undergoing ERCP have complications, comparable with rates reported in adults undergoing ERCP. Societal

guidelines should be established for defining and reporting timing, and severity of adverse events. Further studies using systematic and standardized methodologies are needed to determine the frequency and risk factors for ERCP related complications.

82 OVER THE SCOPE CLIPS FOR TREATMENT OF ACUTE GI BLEEDING IN CHILDREN IS SAFE AND EFFECTIVE

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Introduction: Through the scope (TTS) clips have been used successfully in both adult and pediatric populations to provide mechanical tamponade in cases of gastrointestinal bleeding. Positioning and placement of the TTS clips can be challenging in certain parts of the GI tract. The safety and effectiveness of Over The Scope Clip (OTSC) in gastrointestinal bleeding has been demonstrated in adult studies; however, there are no pediatric reports demonstrating their use or effectiveness. This report is the first to detail the clinical safety and effectiveness of OTSC in the pediatric population

Methods: A bleeding registry was queried for patients where OTSC were utilized in an attempt to achieve hemostasis. Charts for these cases were then reviewed retrospectively. Data collected included age, weight, indications, rates of technical success, need for re-intervention, and complications from the procedure. All lesions were classified utilizing the Forrest classification. Technical success was defined as successful clip positioning and deployment on first attempt. Immediate hemostasis was defined as achieving hemostasis without need for utilization of other modalities during the same endoscopic session. Need for re-intervention was defined as any need for re-intervention during the follow-up period.

Results: 11 cases of OTSC utilization for hemostasis were identified in 10 unique patients and were included for analyses. Procedures were performed between 11/2014 and 5/2016. The median age at intervention was 14.7 years (range 3.9– 6.8 years). The median weight was 39 kg (range 17.4–85.8 kg). Table 1 summarizes patient and procedural characteristics. Technical success and immediate hemostasis was achieved in all cases and there were no complications. Both patients with anastomotic ulcerations required further interventions. The first (Patient 9) received additional iron infusions which were slowly spaced out following the procedure and his Hgb has remained normal with no further interventions for 163 days. The second (Patient 10) required a second endoscopy to treat additional anastomotic ulcer sites. At repeat endoscopy, the initially placed OTSC remained in place and there was no evidence of ongoing bleeding from this site. A separate site was treated during that session. This patient continues to require transfusions after her second procedure.

Conclusions: We report the first series demonstrating the safety and short-term effectiveness of the OTSC in the pediatric population for acute gastrointestinal bleeding throughout the GI tract. In our experience, it is extremely effective for non-anatomic ulcers and polypectomy bleeds even when other hemostatic techniques have failed. OTSC may be less effective in the setting of anastomotic ulcerations, reaffirming the refractory nature of this type of GI bleed although further work is needed to clarify long-term benefits.

Patient	Age (Yrs)	Sex	Weight (kg)	Site	Diagnosis	Forrest Classification	Previous interventions	# (Type of OTSC Used)	Technical Success	Immediate Hemostasis	Length of F/U (days)	Need for reintervention
1	16.8	F	59.4	Stomach (angular incisura)	Ulcer	Forrest 2a	TTS during same session	1 (11/6 A)	Y	Y	121	N
2	10	M	30.6	Stomach (angular incisura)	Ulcer	Forrest 1b	None	1 (12/6 T)	Y	Y	331	N
3	11.1	F	61.1	Stomach (body)	Post-polypectomy	Forrest 2a	None	1 (12/6 T)	Y	Y	175	N
4	15.9	M	81	Duodenum (D1)	Ulcer	Forrest 2a	None	1 (12/6 GC)	Y	Y	439	N
5	15.8	M	85.8	Duodenum (D1)	Ulcer	Forrest 2c	None	1 (12/6 T)	Y	Y	17	N
6	12.4	M	38.2	Duodenum (major papilla)	Post-sphincterotomy	Forrest 1a	Epi injection, TTS clip during same session	1 (12/6 T)	Y	Y	395	N
7	16.8	M	48.6	Colon (Sigmoid)	Ulcer	Forrest 2a	TTS placement during prior session	2 (12/6 T separate lesions)	Y	Y	370	N
8	3.9	F	17.4	Colon (Sigmoid)	Post-polypectomy	Forrest 1b	TTS during same session	1 (12/6 T)	Y	Y	2	N
9	9.2	M	25	Ileocolonic anastomosis	Anastomotic ulcer	Forrest 2a	Medical therapy for iron def anemia	1 (12/6 T)	Y	Y	371	continued need for iron infusions
10a	14.7	F	38	Ileocolonic anastomosis	Anastomotic ulcer	Forrest 2c	Multiple endoscopic interventions during prior sessions	1 (11/6 A)	Y	Y	547	continued need for chronic transfusions, repeat OTSC placement at different site
10b	15.2	F	39	Ileocolonic anastomosis	Anastomotic ulcer	Forrest 2c	Multiple endoscopic interventions during prior sessions	1 (11/6 A)	Y	Y	351	continued need for chronic transfusions

83 TEN YEAR EXPERIENCE WITH LARGE POLYP REMOVAL (≥15 mm) IN PEDIATRIC PATIENTS

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Introduction: Limited pediatric data is available regarding the removal of large intestinal polyps in children. We evaluated the techniques used to remove polyps ≥15 mm in consecutive pediatric patients from 2006-2015.

Methods: We performed a retrospective single center study using a pathology database paired with endoscopic documentation software from 2001 to 2015.

Polyp removal technique was divided into surgical sub-divisions (rigid anoscopy, laparoscopic, open and other) or endoscopic (snare, snare with pre-clip, snare with post-clip, snare with post-cautery, and other). Polyp type, size (with and without stalk), location and adverse events were recorded. SPSS 23 was used to calculate means, interquartile ratios and differences between groups. Institutional Review Board approval was obtained for this analysis.

Results: Of 648 polyp related procedures (585 unique patients) identified, 113 procedures yielded at least one polyp ≥15 mm from 105 unique patients. Polyp size in this group was 2.18 cm and IQR (1.68-2.5) with a maximum of 5.5 cm and 2.35 and IQR (1.7-2.5) when stalk size was included. There were 11 small intestinal polyps, 83 left-sided colon polyps, 18 right-sided polyps and one colon NOS. 20 patients had more than one large polyp removed at the same session. 86% (88 of 102) were juvenile polyps while polyposis syndromes (1 FAP, 15 JPC, 14 Peutz-Jeghers) accounted for only 26.5% of the patients. Additionally, there was one tubulovillous adenoma, but no advanced malignancies. PJS polyps were larger than JPC ($p=.036$) polyps.

The mean age at time of removal was 6.5 years (range 6 months to 17 years). There was no difference between patient age and size of polyp ($p=.373$). A total of 93 patients had some form of endoscopic snare cautery, standard snare ($n=72$) compared to snare with other techniques ($n=21$) including hemostatic clip placement, "piecemeal" or bipolar cautery. 19 patients had surgical therapy, including 10 bowel resections and 6 ligations of rectal polyps. There was a difference between size of polyps removed endoscopically vs. surgery ($p=.028$). Significant adverse events ($n=4$) included one equipment failure that led to repeat procedure, 2 patients had repeat endoscopies due to size or atypical location, and one patient had bradycardia that resolved with medication.

Conclusion: Large polyp removal in pediatric patients is safe and the majority are removed endoscopically with snare cautery. Surgical intervention was typically for intussusception or obstruction requiring bowel resection with polyp removal.

***84 QUALITY INDICATORS IN PEDIATRIC COLONOSCOPY: AN AUSTRALIAN TERTIARY CENTER EXPERIENCE**

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Introduction: Quality indicators for colonoscopy in adults are mainly driven by colorectal cancer screening, and include cecal intubation and adenoma detection rates. Cecal intubation rates of >90% is recommended in adults by most societies and colleges internationally. In contrast, colorectal cancer is rare in children so colonoscopy is predominantly diagnostic. Common indicators for pediatric colonoscopy include investigating for inflammatory bowel disease (IBD), diarrhoea or abdominal pain. In these conditions, ileal intubation is strongly recommended as it optimizes diagnostic yield. There is, however, a paucity of data on quality indicators for pediatric colonoscopy, and it remains unclear whether high rates of cecal and ileal intubation is achievable in pediatrics.

Aims: This study was undertaken to audit all colonoscopies performed in a tertiary pediatric center to examine for the clinical indications for procedure, completion rates to cecum and ileum, and rate of significant findings.

Methods: Retrospective review of all colonoscopies from November 2011 to the end of October 2015 was performed. The ORMIS theatre management database was used to identify patients having colonoscopy using ICD-10 codes 32090 (colonoscopy) and 32087 (colonoscopy ± polypectomy). Patients having intentional flexible sigmoidoscopy were excluded from further analysis although incorrectly coded patients who proceeded to total colonoscopy were included. Patient demographics, indication for procedure, presence of trainee, quality of bowel preparation, extent of colonoscopy and confirmation of location, reasons for incomplete procedure, diagnostic findings, and complications were noted.

Results: 652 patients were identified as having had or intended to have total colonoscopy after exclusion of incorrectly coded patients. Median age of patients was 13.0 (range 0.4-18.2) years, with 53% male. The most common indications for colonoscopy were IBD review (57.9%, 378/652), rectal bleeding (10%, 68/652), abdominal pain (10%, 68/652), and diarrhea (8.6%, 56/652). All patients had procedures under general anesthesia. Trainees performed 69.8% (452/652) of procedures. Quality of bowel preparation was mentioned in 62.9% (410/652), of which 21.9% (90/410) were considered inadequate. Cecal intubation rate was 96.3% (628/652) and ileal intubation 92.4% (603/652). Photographs and/or biopsies were used to confirm extent of procedure in 99.2% of patients. Factors predicting success of ileal intubation include quality of bowel preparation and patient age. Normal histology was noted in 61.8% (403/652) of colonoscopies. 37 (5.6%) patients had polypectomy; most were juvenile polyps (54%, 20/37). No perforations occurred but three patients had hematoma, which were managed expectantly.

Conclusion: High rates (≥90%) of cecal and ileal intubation are achievable in pediatric colonoscopy. Ileal intubation should be considered a quality indicator in diagnostic colonoscopy in pediatrics.

85 RESULTS OF THE ESPGHAN ENDOSCOPY TRAINING SURVEY

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Objectives: Endoscopy training is an essential part of pediatric gastroenterology, hepatology and nutrition (PGHN) fellowship as specified in the ESPGHAN training syllabus. The aim of this study was to evaluate the endoscopy training among fellows and young professionals in PGHN. The recently published ESPGHAN syllabus suggests a minimum of 100 esophagogastroduodenoscopies (EGDs) and 50 colonoscopies for certification (D'Antiga *et al.*, 2014).

Methods: 84 PGHN fellows participated in an electronic survey called by ESPGHAN between February 2014 and September 2015. The survey comprised 32 questions on general information, number of endoscopies performed, specific endoscopic procedures, supervision and certification, and endoscopy training.

Results: Among 84 participants 28 (33%) have already finished their training and 42 (50%) are still in training. 53 fellows (63%) reported to be enrolled in an official PGHN fellowship program leading to a subspecialty certification. 32 (38%) devote their entire time to PGHN training and 34 (40%) between 50 and 99% of their time. 66 PGHN fellows (79%) are trained in endoscopy during their fellowship. Of all fellows, 29 (35%) are trained by an adult gastroenterologist and 6 (7%) by surgeons. 30 (36%) follow the ESPGHAN syllabus. Concerning the numbers of endoscopic procedures, PGHN fellows have completed 207 EGDs, 67 colonoscopies, 11 polypectomies, 10 variceal bandings and 20 PEG changes/ insertions on average. The terminal ileum is intubated in 29% most of the time (>90%). 63 fellows (75%) enjoy continuous supervision, 65 fellows (77%) keep an endoscopy logbook, and 28 (33%) have formal assessments (paper or online) during and 47 (56%) at the end of their training.

During their training 54 fellows (64%) have attended basic skills endoscopy courses and 43 fellows (51%) have completed endoscopy simulator trainings. 79 fellows (94%) wish participation in future ESPGHAN endoscopy summer schools and 75 fellows (89%) would like to attend basic endoscopy skills courses. Fellows feel that their upper GI endoscopy training will allow practicing as consultant in 86% and their colonoscopy training in 67%. 59 fellows (70%) would like ESPGHAN to be responsible for the accreditation of endoscopy centers.

Conclusions: This survey shows that endoscopy training differs among fellows in Europe regarding accomplished procedures, the training program including supervision and certification, and specific endoscopy courses. Only 36% have followed the ESPGHAN training syllabus and only 86%, respectively 67%, feel skilled enough to perform EGDs and colonoscopies when practicing as a consultant. We encourage all European GI centers to follow the ESPGHAN training syllabus to harmonize endoscopy training during PGHN fellowship throughout Europe, eventually leading to better endoscopy skills of young consultants.

86 EFFICIENCY OF MACROGOL 3350 WITH ELECTROLYTES AND ASCORBATE IN AMBULATORY PREPARATION OF COLONOSCOPY IN CHILDREN OVER 2 YEARS OF AGE

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Introduction: Inadequate colonic cleansing is frequent in pediatric patients undergoing colonoscopy and is the main reason to admit the patient to hospital for bowel preparation. Hospital admission significantly increases the cost of the procedure and causes family discomfort. The aim of the study was to assess the effectiveness of a regime of outpatient bowel preparation with macrogol 3350 in patients older than 2 years.

Material and methods: 390 children, 2 to 14 years old (mean age 8.6 years) were given macrogol 3350 with electrolytes and ascorbate for bowel preparation the day before colonoscopy with a weight-adjusted dose of 2 g per kg. If the child failed to take the medication at home, hospital admission was arranged in order to administrate the bowel preparation by a nasogastric tube (NGT). Efficacy in colon preparation, side effects and the need for admission to complete the bowel preparation were assessed.

Results: 345 children (88%) completed the bowel preparation at home. In 295 (76%) colonic cleansing was adequate, in 44 (11%) it was incomplete but allowed us to explore the entire colon and in 5 (1%) colonic preparation was inadequate and colonoscopy was cancelled. 47 (12%) children failed to complete bowel preparation at home and were admitted to hospital (16 for vomiting and 31 for inability to drink the medication): in 26 (7%) children bowel preparation through NGT was successful, 15 (4%) children vomited the medication given by NGT and in 5 (1%) patients, NGT administration of the bowel preparation had to be stopped due to intense abdominal cramping. In total, 39 (10%) children reported cramping abdominal pain and 21 (5%) children reported vomiting. Overall, colonic cleansing at home was successful in 87% of children.

Conclusions: Outpatient bowel preparation with macrogol 3350 (2 g per kg) is successful in most cases and ensures adequate colonic cleansing resulting in a significant reduction of costs and family discomfort.

87 EXPERIENCE WITH SELF EXPANDING FULLY COVERED METAL BILIARY STENTS: CASE SERIES

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Background: Endoscopic retrograde cholangiopancreatography (ERCP) is used for a variety of biliary and pancreatic indications in pediatric patients including biliary strictures, common bile duct stones, biliary leaks, pancreatic duct strictures and others. Biliary stent placement is often used for biliary strictures and other obstructive lesions to maintain bile flow. Multiple plastic stents are used commonly in pediatric patients but may not be effective in some cases due to migration or obstruction of the stents. Self-expanding metal stents (SEMS) have been used more recently by adult gastroenterologists, for both malignant and benign lesions but their use and placement in adolescents and children has not been well described by pediatric endoscopists. **Case Presentation:** We present a series of two adolescents and one young adult with complex medical needs who had biliary SEMS placed for different indications. Patient 1 is a 15-year-old, 53-kg adolescent who had liver transplant for CF related liver disease and refractory post transplant anastomotic stricture that did not resolve with two rounds of multiple plastic stenting. He had improvement in bile duct diameter and GGT after 10 mm x 8 cm SEM placement (Wallflex, covered metal biliary stent, Boston Scientific, Boston, MA) for 7 weeks which was sustained at 3.5 months after placement. Patient 2 is 18-year-old, 7- kg adolescent with autoimmune hepatitis who had liver biopsy complicated by gallbladder perforation bile peritonitis. She had persistent bile leak after partial cholecystectomy, which was technically difficult because of surrounding inflammation, and did not resolve with sphincterotomy and multiple plastic stents placed across the cystic duct. Bile leak resolved with covered SEM placement 8 mm x 8 cm across the cystic duct for 6 weeks and she has had no symptoms of bile leak recurrence 4 months after last stent removed. Patient 3 is a 24-year-old, 36-kg young woman with Rett syndrome and multiple pulmonary and neurologic comorbidities who had obstructive choledocholithiasis 2 years after cholecystectomy. She continued to have multiple biliary stones and signs of obstructive choledocholithiasis after multiple ERCs with balloon sweeps, sphincterotomy and multiple plastic stenting so 10 mm 6.0 cm SEM was placed with resolution of biliary obstruction after 8 weeks. In all cases, the stents were well tolerated and no adverse events were encountered. Removal was performed endoscopically using a raptor forcep (US Endoscopy, Mentor, OH) without difficulty.

Conclusion: SEMs may be considered by pediatric endoscopists for patients with benign obstructive lesions or perforations of the common bile duct who are not responding to plastic stents. Additional research is needed, however, for more comprehensive evaluation of the efficacy and potential adverse events in pediatric patients undergoing SEM therapy.

88 SAFETY AND EFFICACY OF THE ADVANCEMENT (PUSH) TECHNIQUE IN THE TREATMENT OF ESOPHAGEAL FOOD IMPACTION IN CHILDREN

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Background: Esophageal food impaction is one of the conditions that often requires immediate attention including urgent endoscopy. Adult-based guidelines support the use of the extraction (pull) technique but allow the consideration of the advancement (push) technique with caution due to the high probability of esophageal pathology and risk of perforation. The NASPGHAN guidelines mention the use of gentle advancement for disimpaction but elaborate that the use of this technique in children has not been studied.

Hypothesis: The push technique is safe and effective in the treatment of pediatric esophageal food impactions.

Methods: This was a retrospective cohort study of all pediatric patients presenting with esophageal food impactions to a pediatric tertiary care center from 2003 to 2016. Procedures were identified using billing records.

Results: Two hundred and forty-two procedures were identified based billing codes for esophageal foreign body removal. Forty procedures were for treatment of esophageal food impaction in a total of 24 patients (range: 1-4 procedures per patient). The most common underlying diagnoses were eosinophilic esophagitis (42%) and history of tracheoesophageal fistula (38%). The cohort had a median age of 8.5 years and median weight of 35.2 kg. Initial endoscopic disimpaction methods include 21 push technique and 19 pull technique attempts with success rates of 62% and 68% respectively ($p=0.67$). Unsuccessful attempts using one technique were successfully accomplished using the other technique. All patients were discharged within 24 hours of the procedure, except for one patient who was transferred from another hospital with an esophageal perforation secondary to a failed disimpaction. The perforation was managed conservatively. No procedure-related complications were reported at our center. The two groups of patients (managed by the two disimpaction techniques) did not differ in age, weight, gender, presenting symptoms, type of anesthesia used or underlying diagnoses except that patients with known fixed esophageal strictures (n=4) were managed using the pull technique only.

Conclusion: This study shows that the push technique is as safe and effective as the pull technique in managing esophageal food impactions in pediatric patients in the absence of known fixed esophageal strictures.

89 THE IMPACT OF AN INTERACTIVE COMPUTER APPLICATION ON THE QUALITY OF COLONOSCOPY PREPARATION, PATIENT SATISFACTION AND OUTPATIENT AMBULATORY CENTER EFFICIENCY

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Background: Colonoscopies can be a source of anxiety for patients and their families. From a grant provided by NASPGHAN, we developed software (an "app") that familiarizes patients with the procedure, answers commonly-asked questions, informs patients of when and where to report for their colonoscopy and guides patients through the colonoscopy prep process, providing real-time instructions about which medications to take, when to take them and how they should be prepared.

Methods: 46 patients aged 5-18 were randomized to receive either written or software prep instructions. Prep quality was measured with the Boston Scoring Scale. The number of calls to the gastroenterology service were recorded. Patient arrival time was recorded on the day of their procedure. A questionnaire was given to patients on the day of the colonoscopy.

Results: App users had superior mean Boston scores of 9.80 versus controls' 7.96 ($p=0.014$). Although not statistically significant, 10/20 (50%) app users had improved knowledge of the colonoscopy versus 8/22 (36.4%) controls ($p=0.37$). App users made fewer phone calls to the GI service than controls (6 vs. 2), although this difference also did not reach statistical significance ($p=0.27$). There was no difference between arrival times at the endoscopy suite between app users and controls ($p=0.56$).

Conclusion: App users had significantly better quality preps than control subjects. While results showed a trend towards app patients feeling better informed and knowledgeable about the colonoscopy prep, and requiring less physician guidance, these results were not statistically significant. App and control subjects arrived at the endoscopy suite at nearly the same time. We anticipate that future studies with greater numbers of subjects will reach statistical significance for these measures.

90 SAFETY AND EFFICACY OF ENDOSCOPIC ASSISTED PUSH GASTROSTOMY USING GASTROPEXY TECHNIQUE COMPARED TO PERCUTANEOUS GASTROSTOMY TUBE PLACEMENT

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Background: Most pediatric gastroenterologists use the pull technique for percutaneous endoscopic gastrostomy tube placement (PEG).

Gastropepy is a new technique for endoscopic gastrostomy tube placement. T-fasteners are placed through the skin into the stomach, attaching the stomach to the abdominal wall, visualized directly by endoscopy. Serial dilators are used to create a gastrostomy tract, allowing a low profile gastrostomy (GT) or gastrojejunostomy tube (GJT) to be placed. There are no published studies that compare the gastropepy procedure outcomes to the standard PEG procedure in pediatrics.

Objective: To study the safety and outcomes following gastropepy vs. PEG.

Methods: Gastropepy and PEG patient charts were compared for immediate complications (perforation, bleeding, and infection), pain and long term complications (feeding problems, pain, tube dislodgement, infection, bleeding, granulation, readmission, and death) in the three months following procedure.

Inclusion criteria: Pediatric patients requiring gastrostomy placement for enteral nutrition. Subjects were from 0-17 years of age that underwent a procedure in 2014 to 2015.

Results: 13 subjects who underwent gastropepy were between the ages of 1-16 years (avg. 6.6 years), 6 males, with average weight of 23 kg. Fourteen subjects who underwent PEG placement ranged from 0.16-9.5 years of age (avg. 1.5 years), 7 males, with average weight 7.2 kg. There were no immediate short-term complications in either group. Long-term complications were assigned a score according to the severity values, ranging from 0 to 7. The average complication score for both groups was 3, with a median and mode of 2. The procedure length averaged 26 minutes (min) in the gastropepy group compared to 10 min in the PEG group. Average anesthesia time was similar- 53 min in gastropepy group versus 47 min in PEG. Pain treatment for mild, moderate and severe pain was similar in both groups except Toradol that was only used by the gastropepy group. Pain treatment was shorter in the gastropepy group (avg. 1.7 days) vs. PEG group (avg. 3.5 days). Time to start clears was <24 hours in 11/12 subjects for the gastropepy group and in 10/11 subjects for the PEG group. Time to start feeds was <36 hours in 8/11 subjects for the gastropepy group and 12/14 subjects for the PEG group.

Discussion: Our results show that the gastropepy technique is a safe and effective alternative for placement of GT and GJT. The major advantage is that patients who underwent gastropepy did not require a second procedure compared to PEG patients for low profile tube conversion or subsequent placement of a GJT. Disadvantages include longer procedure time for the gastropepy group likely due to the learning curve and differences between operators, but the last 5 procedures averaged 17 minutes.

91 ESOPHAGEAL ENDOSCOPIC DILATION IN CHILDREN: EXPERIENCE OF A TUNISIAN PEDIATRIC ENDOSCOPY UNIT

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Background: The endoscopic treatment of esophageal stenosis seems to be the most frequently used strategy in children. Improvement in endoscopes and techniques have led to the increase in the number of patients who are conservatively treated with endoscopic dilation rather than surgical treatment. This is a report of our experience with esophageal dilation, its indications, methods and results in children.

Methods: Retrospective study of children admitted in our pediatric endoscopy unit for esophageal dilation between November 2007 and March 2016.

Results: 39 admissions were registered. There were 24 males and 15 females with a mean age of 4 years. Esophageal atresia anastomotic stenosis ($n=2$, 25.6%) and post-corrosive esophagitis ($n=0$, 25.6%) are the most frequent types of cicatricial esophageal stenosis. The other indications were peptic stenosis ($n=$, 15.3%), achalasia ($n=$, 12, 82%), congenital stenosis ($n=$, 7.6%), herpetic esophagitis ($n=$, 2.5%) and unidentified causes ($n=$, 5.1%). The average number of sessions to achieve adequate dilation was 4 per patient with extremes from 1 to 13. Different dilators were used: in 86 cases (54%) we used the balloon dilators, whereas in 37 (23.2%), the Savary-Giliard bougie. Balloon followed by Savary-Giliard bougie dilation had been used in 25 cases (15.7%). In 11 sessions, the dilation method had not been mentioned. Dilation was successful in all cases except one.

Conclusion: The conservative treatment of esophageal stenosis rather than surgery is a well-known strategy for children. Young patients can be treated effectively and safely only by endoscopic dilation.

92 RELIABILITY ASSESSMENT OF ENDOSCOPIC DISEASE SEVERITY USING CENTRAL VIDEO REVIEW OF COLONOSCOPIES IN PAEDIATRIC PATIENTS WITH CROHN'S DISEASE: DATA FROM THE CANADIAN CHILDREN INFLAMMATORY BOWEL DISEASE NETWORK.

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Objectives: Reliable and consistent endoscopic assessment of mucosal disease severity is important in the evaluation of patients with inflammatory bowel disease (IBD). There are a number of scoring tools available for use in the endoscopic assessment of Crohn's disease, however none have been formally evaluated in pediatric patients. To reduce variability in the assessment of endoscopic severity, centralised review of video colonoscopies has been increasingly implemented in adult clinical trials, where excellent inter-rater reliability has been noted in the hands of IBD experts. To date, similar assessments have not been performed in pediatric IBD. We undertook to assess inter-rater reliability for the Simple Endoscopic Score (SES-CD) and Crohn's disease Endoscopic index of Severity (CDEIS), using videos of colonoscopies performed in pediatric patients from the Canadian Children IBD Network.

Methods: Video recordings of colonoscopies obtained from pediatric patients with Crohn's disease undergoing endoscopic assessment at Network sites were utilised for the analysis. 3 central readers reviewed the videos independently, and were blinded to clinical information. Colonoscopies were assessed using data encompassing the commonly employed scoring tools for Crohn's disease (SES-CD and CDEIS), assessing the total score and individual items across each anatomical segment. A global assessment of endoscopic lesion severity (GELS) was also recorded using a visual analogue scale. Inter-rater agreement was measured using Intraclass correlation coefficients (ICCs) with 95% confidence intervals. Correlation between scoring tools was measured using Pearson's test of correlation (r).

Results: The ICC for inter-rater reliability for SES-CD was 0.94 (95% CI, 0.84–0.98), for CDEIS was 0.83 (95% CI, 0.58–0.93), and for GELS was 0.90 (95% CI, 0.74–0.96). There was very good correlation between the SES-CD score and CDEIS ($r = 0.81, p < 0.001$). The correlation between GELS and each scoring tool was also very good, with SES-CD and CDEIS demonstrating $r = 0.77 (p < 0.001)$ and $r = 0.81 (p < 0.001)$ respectively. The most common sources of disagreement between readers were estimation of the degree of ulcerated surface and evaluation of the depth of ulceration. Disagreement was most notable in the transverse colon (ICC 0.48 and 0.46 for ulcer surface and ulcer depth respectively).

Conclusion: Centralized video review of colonoscopy is a feasible way to assess endoscopic severity in pediatric Crohn's disease. Assessment of the existing scoring tools (SES-CD and CDEIS) using video recordings showed excellent inter-rater reliability in the hands of IBD physicians familiar with the tools. These scores also correlated well with GELS, demonstrating some measure of validity for these tools in pediatric Crohn's disease. Ongoing assessments are planned in order to explore the variability in scoring and relationship to GELS across different disease phenotypes.

93 DIAGNOSTIC YIELD OF ESOPHAGOGASTRODUODENOSCOPY IN CHILDREN PRESENTING WITH FAILURE TO THRIVE AND FEEDING DISORDER

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Background: Esophagogastroduodenoscopy (EGD) is commonly performed in infants and children with failure to thrive (FTT) or feeding disorder (FD). There have been no studies looking at the efficacy of performing EGDs in these populations.

Aim: To determine the diagnostic yield of EGD in children diagnosed with FTT or FD and to document the association between the presence of FTT, FD, other presenting symptoms, and key past medical history and family history with pathological findings on endoscopy.

Methods: We performed a retrospective cross-sectional cohort study in children <5 years of age who were undergoing EGD for evaluation of FTT or FD at the Children's Hospital of Wisconsin between December 2010 and June 2014. We documented symptoms present prior to EGD including history of atopy, food allergies, family history of atopy/food allergies, specific progression of feeding skills, and family history of eosinophilic esophagitis. We also looked at the association between the presence of FTT, FD, and other symptoms, and pathological findings on endoscopy.

Results: A total of 350 children met criteria for the study. Their mean age at time of EGD was 2.12 years (SD 1.247). The mean z-scores for weight, weight-for-length z-score (<2 y) and BMI Z-score (>2 y) were -0.97 (SD 1.466), -0.59 (SD 1.442) and -0.47 (SD 1.406) respectively. Ninety-eight children (28%) had FTT alone, 160 children (45.7%) had FD alone, while 90 children (25.7%) had both FTT and FD. EGDs were diagnostic in 40.8% of FTT alone, 25.6% FDD alone, and 38.9% FTT and FD combined. In the entire cohort, the diagnostic yield of EGD was 33.1%. The top diagnoses revealed by the EGD in FTT alone were abnormal pancreatic stimulation test (ABST) in 10.2%, celiac disease 8.2%, and eosinophilic esophagitis 5.1%. Other important diagnoses in this subgroup included *H. pylori* infection 2%, autoimmune enteropathy 1%, IPEX 1%, and antral web 1%. The top diagnoses in FD alone were reflux esophagitis 10.6%, eosinophilic esophagitis 6.9%, and ABST 1.3%. The top diagnoses in children with both FTT and FD were reflux esophagitis 13.3%, eosinophilic esophagitis 8.9%, and ABST 5.6%.

Chi square analysis showed that the presence of diarrhea and food allergies increased the diagnostic yield. EGDs were diagnostic when diarrhea was a presenting symptom in 50.9% vs. 30.3% in the absence of diarrhea ($p = 0.003$) and food allergies occurred in 35.4% of diagnostic EGDs vs. 25.4% of non-diagnostic EGDs ($p = 0.023$). Other historical features were not associated with significant differences in diagnostic yield.

Conclusions: There appears to be benefit in using EGDs in the evaluation of FTT and FD. The presence of diarrhea or food allergies may be associated with increased diagnostic yield.

94 AN INNOVATIVE APPROACH: IMPLEMENTATION OF AN ASYNCHRONOUS PILOT PEDIATRIC GASTROENTEROLOGY E-CONSULT PROGRAM

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Electronic consultation (e-consults) have emerged as a promising approach to enhance provider communication and have demonstrated feasibility and facilitated timely specialty advice in a variety of settings. E-consults are alternatives to traditional outpatient pediatric gastroenterology visits in which a patient physically presents to the office for an in-person visit. In the adult literature, studies have demonstrated that e-consults provide responsive high-quality care, reduce total costs of care as well as high rates of satisfaction among both providers and patients. Nevertheless, information about e-consults in pediatrics is limited. We sought to establish an e-consult program in pediatric gastroenterology and assess preliminary results. At Mass General Hospital for Children (MGHfC), a tertiary pediatric center, e-consults in outpatient pediatric gastroenterology enable primary care providers (PCP) to submit patient-specific clinical questions to a specialist. At MGHfC, a tertiary pediatric center, e-consults in outpatient pediatric gastroenterology enable PCP's to submit patient-specific clinical questions to a specialist. MGHfC is part of the Partners Healthcare network, an integrated healthcare network and is part of several accountable care organization (ACO) contracts with a shared electronic medical record system. Structured e-consults are sent to a pediatric gastroenterologist who reviews the electronic data and imaging as appropriate and then provides detailed clinical recommendations to the referring doctor. The pediatric gastroenterologist is reimbursed a flat fee through the ACO. To assess the results of this pilot project, medical records were individually reviewed by a pediatrician. From July 2015 to November 2015 we implemented e-consult referrals by MGHfC PCPs. PCPs received recommendations within 48 hours of their referral request. The patients referred for e-consult ranged from 2 months to 5 years of age. The reasons for referral included abdominal pain, reflux, poor weight gain, abnormal liver function tests and acholic stools. Recommendations included reassurance, indications for further testing as well as medication and formula changes. Only one was referred for a traditional consult. No clinical adverse events related to the e-consult were detected. Although we currently have limited roll-out in our pilot, we anticipate being able to report on over 60 e-consults by October 2016. Even with our initial implementation, we were able to demonstrate feasibility of a pediatric gastroenterology e-consult pilot program within a large ACO. An e-consult program allows efficient, high-quality recommendations to PCPs for a variety of referral questions. This potentially results in significant cost savings by avoiding a traditional in-person visit. As a pilot study, our next steps aim to expand this to other pediatric subspecialties as well as look at provider satisfaction and cost analysis of our program.

***95 CARBON DIOXIDE INSUFFLATION VERSUS AIR INSUFFLATION FOR COLONOSCOPY IN DEEPLY SEDATED PEDIATRIC PATIENTS: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND, CONTROLLED TRIAL**

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Background and Aims: Several studies in adults have reported reduced abdominal pain after colonoscopy with carbon dioxide (CO₂) insufflation in lightly sedated and deeply sedated patients. This study was designed to investigate the efficacy and safety of CO₂ insufflation in deeply sedated children undergoing colonoscopy.

Methods: This was a prospective, randomized, double-blind clinical trial. We recruited 100 consecutive pediatric patients who underwent colonoscopy for various indications. Patients were randomly assigned to either CO₂ or air insufflation. Deep sedation was achieved with a combination of propofol, sevoflurane and nitrous oxide. Post-interventional pain levels were registered on a 10-point visual analog rating scale. Abdominal circumferences and end tidal CO₂ (ETCO₂) levels were measured. Complications during and after the procedure were recorded. **Results:** There were no significant differences in pain scores between the two groups at immediately, 1 hour, 2 hours, 3 hours, 4 hours, at discharge, 24 hours and 72 hours after colonoscopy. We performed a subgroup analysis on patients with chronic abdominal pain undergoing colonoscopy and found no statistically significant difference in pain scores between air and CO₂ insufflation in this patient population. We also analyzed the factors related to pain scores and found that duration of the procedure was significantly associated with pain immediately after the procedure ($p= 0.01$) and previous abdominal surgery significantly associated with pain at discharge ($p= 0.02$). The mean highest ETCO₂ values measured during the procedure was statistically different, being higher in the CO₂ group than in the air group (CO₂: 54.4 ± 8.21 Hg vs. air: 48.9 ± 6.36 Hg, $p= 0.0003$). No clinical signs of impaired ventilation or other adverse events were observed. The mean increase in abdominal circumference was greater with air than with CO₂, however, this was not statistically significant (air: $+ 1.32$ cm vs. CO₂ $- 1.26$ cm, $p= 0.17$). The procedure times including time to cecum and duration of colonoscopy, and time to discharge after the procedure were not statistically different between the two groups [time to cecum (min) air 12.8 ± 7.3 vs. CO₂ 12.9 ± 7.8 , $p= 0.89$; duration of colonoscopy (min) air 28.1 ± 13.6 vs. CO₂ 28.8 ± 14.4 , $p= 0.9$; time to discharge after the procedure (min) air 137.2 ± 35.6 vs. CO₂ 126.6 ± 37.4 , $p= 0.06$]. We didn't observe any statistically significant difference between the two groups in pain medications received and adverse events during recovery, and post-procedural events following discharge.

Conclusions: CO₂ insufflation during colonoscopy may not of benefit in reducing the post-procedural abdominal pain associated with the procedure. Duration of the procedure and previous abdominal surgery were identified as key predictors of pain after colonoscopy.

96 OUTCOME OF BAND LIGATION IN ESOPHAGEAL VARICES OF BANGLADESHI CHILDREN: A TERTIARY CENTRE EXPERIENCE

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Background: Band ligation is the main endoscopic treatment for esophageal varices. In our country, few studies are available in adults, and none are available absent in children.

Objective: To see the outcome of band ligation of esophageal varices in extra-hepatic and hepatic cases of portal hypertension.

Materials and Methods: The prospective study was done in the Department of Pediatric Gastroenterology, Hepatology & Nutrition, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh on 40 consecutive cases of portal hypertension enrolled from April 2014 to March 2016. Every case was treated with band ligation followed by Tab. Propranolol. Cases were followed up for a minimum period of one year after the band ligation.

Results: Age of the children was 2-12 years with mean age of 7.2 ± 4.3 years and male:female ratio was 1.5:1. Out of 40 children, 32 (80%) were extra-hepatic and 8 (20%) hepatic (chronic liver disease with portal hypertension) causes. Only 1 session required in 50% extra-hepatic cases and multiple (2-3) sessions required in hepatic (100%) cases. Almost same number of band (average 2-3) required in every session of both

cases. Grade-II esophageal varices with red sign were more common in extra-hepatic cases and severity of grading much more (grade-III and IV) in hepatic cases. Gastric varices were more common in hepatic (50%) cases than extra-hepatic (12.5%) cases. Recurrence of bleeding occurred in all hepatic (100%) cases and half (50%) of the extra-hepatic cases. Early re-bleeding was more common in hepatic (75%) cases and late re-bleeding in extra-hepatic cases (87.5%). Minimal side effect like discomfort (25%) and Nausea (25%) were present after the procedure. Conclusion: Extra-hepatic was the most common etiology of portal hypertension in studied children. Fewer sessions were required in extra-hepatic cases than in hepatic cases. Severity of grading, re-bleeding and associated gastric varices were more common in hepatic cases. Band ligation is the treatment of choice for the control of acute variceal bleeding and prevention of re-bleeding with less complications.

97 OUTCOME OF CHILDREN AFTER SURGICAL REPAIR FOR ESOPHAGEAL ATRESIA: A TUNISIAN COHORT

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Aim: To determine the frequency of gastrointestinal and respiratory complications after surgical repair for esophageal atresia.

Methods: A retrospective analysis of the endoscopic files during the last 12 years (from January 2003 to December 2015) revealed that 41 children presenting with esophageal atresia, 23 males and 18 females, mean age 2.8 years (\pm 3.3), underwent upper gastrointestinal (UGI) endoscopy for dysphagia (n=16, 39.1%), cyanosis (n=3, 7.3%), abdominal pain (n=2, 4.8%), food impactions (n=1, 2.4%), UGI bleeding (n=1, 2.4%) and miscellaneous causes (n=18, 44%). Study parameters included dysphagia, gastroesophageal reflux disease, anastomotic stricture, asthma, recurrent respiratory infections.

Results: The mean follow-up was 4.3 years (\pm 1.8). Thirty four children had a type 3 atresia (82.9%) and 7 (17%) had associated congenital malformations (musculoskeletal 3, renal 2, digestive 2). A primary repair was performed in 34 cases (82.3%) with anastomotic tension for 5 of them. Thirty patients (73.1%) had gastrointestinal disorders: gastroesophageal reflux (n=2, 29.2%), anastomotic strictures requiring endoscopic dilatations (n=28; 68.3%), feeding troubles (n=3), food impaction (n=1). Ten children (24.4%) had respiratory complications: asthma (8), recurrent respiratory infections (2).

Conclusion: Morbidity of esophageal atresia after surgical treatment is very high with a high frequency of gastrointestinal complications in this cohort. We recommend an extended specialized follow-up of this population.

98 AMOXICILLIN CLAVULANATE DOES NOT IMPROVE COMPLETION RATE OF CAPSULE ENDOSCOPY IN PATIENTS UNDERGOING ENDOSCOPIC PLACEMENT

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Background: Capsule endoscopy (CE) in pediatrics can be challenging due to difficulty swallowing the capsule, requiring endoscopic placement. Completion of CE is suboptimal with completion rates of less than 85%. Endoscopic placement has been noted to be a risk factor for incomplete CE studies. Previous studies using prokinetic medications in orally ingested CE have not demonstrated consistent results in improving CE completion rates. Amoxicillin-clavulanate is noted to stimulate small intestinal motility in certain patients. We aim to evaluate the impact of the use of amoxicillin-clavulanate on completion rates of CE in patients who had endoscopic placement of the capsule endoscope.

Methods: A retrospective chart review was conducted for patients who received VCE at our center during the years 2009 to 2015. Parameters were assessed to determine predictors of capsule completion, including route of administration, BMI, inpatient status, abdominal surgical history, use of prokinetic agents, indication for CE, concurrent colonoscopy, comorbidities, small bowel transit time (SBTT), completion of CE, and findings. Paired T-test was used to compare groups. This study was approved by the Institutional Review Board at our institution.

Results: A total of 196 patients (46% male) underwent CE from 2009–2015 at our institution. Endoscopic placement of the capsule was performed in 72 patients and 124 patients orally ingested the capsule. Twenty-seven of 72 (37.5%) patients received prokinetic medications (amoxicillin-clavulanate [78%], erythromycin [18%], or metoclopramide [4%]) following endoscopic placement of capsule. Eighteen of the 27 patients (67%) who received prokinetic agents had successful completion of CE. Of the 45 patients who did not receive prokinetic agents following endoscopic placement, 32 patients had successful completion of CE (71%). There was no significant difference in rate of completion between patients receiving amoxicillin-clavulanate and those who did not. There was no significant difference in completion of CE between patients receiving prokinetics overall and those who did not. There was no significant difference in mean SBTT in patients who received prokinetics and in those who did not ($p=0.8$). When comparing predictors of CE completion in patients who did or did not receive prokinetics, there was no statistical significance in BMI ($p=0.3$), concurrent colonoscopy ($p=0.4$), history of abdominal surgery ($p=0.2$), inpatient status ($p=0.2$), or presence of comorbidities ($p=0.07$).

Conclusions: The use of amoxicillin-clavulanate does not significantly increase the rate of CE completion or decrease SBTT in patients undergoing endoscopic placement of capsules. Inpatient status, BMI, abdominal surgical history, concurrent colonoscopy, and comorbidities cannot be used as predictors of CE completion. Further investigation into specific populations of patients who may benefit from promotility agents in CE is warranted.

99 THE INCREASING PREVALENCE OF GASTROESOPHAGEAL REFLUX DISEASE IN CHILDREN

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Objective: The prevalence of gastroesophageal reflux disease (GERD) is increasing especially in the developed countries. The etiology of the disease in most cases is unknown. The hallmark of GERD is erosive esophagitis. The aim of this study was to evaluate the prevalence and the trend of the severity of erosive esophagitis in the country where life style during the past 25 years has changed greatly.

Methods: Retrospectively we investigated 2090 children (0 to 18 years of age) with erosive esophagitis. The diagnosis was made after upper endoscopy performed at Vilnius University Children's Hospital during the years 2000 to 2015. Esophagitis was diagnosed when erosive lesions were seen on endoscopy. Modified Savary-Miller scale was used to grade erosive esophagitis.¹ Children with combination of the esophagus or immunodeficiency were excluded. The same five physicians performed all endoscopies.

Results: During 2000–2008 years the total number of upper endoscopies was similar, but from 2010 the total number increased (Table 1). The prevalence of erosive esophagitis during 2000–2015 years was increasing, except 2015. The biggest prevalence was in the 13–18 years' group.

The severity of erosive esophagitis didn't change during 2000-2015 years. The prevalence of erosive esophagitis was slightly more frequent among boys.

Conclusions: 1) The prevalence of erosive esophagitis during 2000–2015 years was increasing, except 2015 2) The severity of erosive esophagitis was mostly grade 1 and didn't change during 2000-2015 years.

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Table 1. Data of severity of erosive esophagitis during 2000-2015 years.

Year	2000		2004		2008		2010		2012		2014		2015	
Endoscopies total n.	1271		1414		1124		1986		1893		2195		2163	
Esophagitis n (%)	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	27	2.1	119	8.4	131	11.6	381	19.2	415	21.9	599	27.3	418	19.3
Endoscopic classification														
1°	21	77.8	107	89.9	115	87.8	337	88.4	379	91.3	544	90.8	394	94.2
2° (a;b)	4	10.8	8	7.6	9	6.8	30	7.8	13	3.1	13	2.1	11	2.63
3°	2	7.4	3	2.5	5	3.8	14	3.67	19	4.6	42	7.1	13	3.11
4°					1	0.8			4	0.96				
5°			1	0.8	1	0.8								
Age (n/%)							n	%	n	%	n	%	n	%
0-6 yr.							55	14.5	27	6.5	91	15.2	77	18.4
7-12 yr.							105	27.7	111	26.7	175	29.2	111	26.6
13-18 yr.							219	57.7	277	66.7	333	55.6	230	55
Girls							137	36	132	31.8	230	38.4	182	43.5
Boys							244	64	283	68.1	369	61.6	236	56.4

100 ENDOSCOPIC FINDING WITH CLINICAL MANIFESTATIONS HELICOBACTER PYLORI INFECTION IN CHILDREN WITH RECURRENT ABDOMINAL PAIN AT DR. HASAN SADIKIN GENERAL HOSPITAL BANDUNG, INDONESIA.

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Background: Prevalence of recurrent abdominal pain (RAP) 10-30%; RAP is abdominal pain that occurs three times or more within 3 months that can interfere with daily activities for children with functional or organic causes. Organic causes include infection with *Helicobacter pylori* (*H. pylori*). The aim of this study was to assess the characteristic endoscopic findings with clinical manifestations of *H. pylori* infection. Method: A cross-sectional study was conducted on 30 patients with complaints RAP children who came to Dr. Hasan Sadikin General Hospital Bandung during the period April 2015 to January 2016 and doing endoscopic procedure with biopsy for histology finding.

Results: 30 children with RAP, comprising 14 (47%) boys and 16 (63%) girls, median age 12 years; the clinical manifestations are RAP 14 (47%) found most, endoscopic findings 23 (77%), erosion and ulcers 4 (14%). Positive *H. pylori* infection was seen in 90% of subjects. Duration of RAP is highest at 3-6 months. Symptom make the clinical manifestation 13 (43.3%).

Conclusion: Clinical manifestation *H. pylori* in children with recurrent abdominal pain show that increase at endoscopic finding worse.

Keywords: Endoscopy, infection of *H. pylori*, recurrent abdominal pain

*101 ROLE OF VIDEO CAPSULE ENDOSCOPY IN PATIENTS WITH BIALLELIC MISMATCH REPAIR DEFICIENCY SYNDROME: REPORT FROM THE INTERNATIONAL CONSORTIUM

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Background: Biallelic mismatch repair deficiency (BMMRD) is caused by biallelic mutations in mismatch repair genes and manifests features of gastrointestinal (GI) polyposis, early-onset brain, hematological, and GI cancers. The International BMMRD Consortium and the European Consortium Care for CMMRD recommend video capsule endoscopy (VCE) starting at 8 and 10 years of age, respectively. The small bowel phenotype is not well described and the utility of VCE remains unstudied.

Objectives: To evaluate the usefulness and clinical impact of VCE for small bowel polyp and cancer surveillance in BMMRD patients.

Methods: Patients from 11 countries were included in the International BMMRD Consortium dataset after identification of mutations and/or immunohistochemical confirmation. Treating physicians were contacted and VCE report data extracted using a standardized template.

Results: @ Fifty-eight patients (37 kindreds) were identified. Mutations included MLH1 (n=4), MSH2 (n=5), MSH6 (n=14), and PMS2 (n=35). In total, 38 VCEs were completed on 17 patients. Median age of first VCE was 14 years (range: 4-31). The number of VCEs performed on each patient ranged from 1 to 7. Polyps were identified in 24 VCEs (63%) on 10 patients. First polyp was detected at the median age of 14 (range: 4-17). Twelve VCEs prompted further investigations, including 5 laparotomies and 2 double balloon enteroscopies. Five patients in the consortium, including 3 siblings, had small bowel adenocarcinomas (SBC) with a median age of diagnosis of 13 (range: 11-33). VCE detected the cancer in 1 patient as it revealed multiple polyps which led to intraoperative enteroscopies revealing a duodenal cancer. Cancers were detected by other imaging modalities in the remaining 4 cases. Three patients with a history of small bowel cancers underwent VCE; polyps were identified in 10 of 12 VCEs. Ten VCEs (28%) were incomplete due to slow bowel transit secondary to previous GI surgery; none required capsule removal.

Conclusions: Small bowel polyps were identified in nearly two-thirds of the surveillance VCEs. Polyps were common in patients with previous small bowel cancer; therefore, a higher index of suspicion is needed for these patients. The rate of incomplete VCE study was high, especially in

patients with a history of previous abdominal surgery, which may suggest a risk of capsule retention. VCE can detect polyps in the BMMRD population. A larger sample size is needed to assess the accuracy of concurrent evaluation using other modalities and thereby, to build an evidenced-based small bowel surveillance protocol for patients with BMMRD syndrome.

GLOBAL HEALTH

104 A LACTOBACILLUS GG AND MICRONUTRIENT CONTAINING MIXTURE IS EFFECTIVE IN PREVENTING NOSOCOMIAL INFECTION IN CHILDREN: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

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Background: Nosocomial infections are a major public health issue and preventive strategies using probiotics and micronutrients are being evaluated.

Aim: To investigate the efficacy of a mixture of Lactobacillus GG (LGG) and micronutrients in preventing nosocomial infections in children.

Methods: A randomized, double-blind, placebo-controlled trial was conducted in hospitalized children. Children (6 months to 5 years of age) received LGG (6x10⁹CFU/day) with vitamins B and C and zinc or placebo, for 15 days, starting on the first day of hospitalization. The incidence of gastrointestinal and respiratory nosocomial infections after discharge was determined by follow-up telephone call at 7 days. The incidence of infections in the long term was evaluated through a telephone call after three months from the discharge. Written informed consent was obtained from the parent of each child included in the study. This trial was registered at Clinical Trial.gov (NCT02558192).

Results: Ninety children were enrolled and completed the follow-up. 18/90 children had a nosocomial infection (20%), of which 4/45 children (9%) were in the treatment group and 14/45 (31%) were in the placebo group ($p=0.016$). Specifically, 2/45 (4%) children in the treatment group vs. 11/45 (24%) children in the placebo group ($p=0.007$) presented with diarrhea. No difference was observed in the incidence of respiratory tract infections between the two groups. The duration of hospitalization was significantly shorter in the treatment group (3.9 days \pm 1.7 vs. 1.2 \pm 4.9 days; $p=0.003$). During the follow-up period, a total of 11/45 (24.4%) children in the treatment group had at least one episode of infection compared to 22/45 (48.9%) children in the placebo group ($p=0.016$). The main effect was observed in the incidence of gastrointestinal infections (5/45 vs. 14/45, $p=0.02$).

Conclusions. A mixture containing LGG and micronutrients is effective in reducing the incidence of nosocomial infections, mainly gastrointestinal infections and the protective effect is sustained over time. This study supports the hypothesis that the administration of LGG and micronutrients may provide a valid strategy to prevent hospital-acquired infections.

105 PREVALENCE OF SYMPTOMS ASSOCIATED WITH SLEEP-DISORDERED BREATHING AMONG PATIENTS SEEN IN A PEDIATRIC GASTROENTEROLOGY CLINIC

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Background: Sleep-disordered breathing (SDB) in children is associated with daytime functional decrements in cognitive performance and behavioral regulation. As recently published data has shown a relationship between obstructive sleep apnea (OSA), a manifestation of sleep disordered breathing and the severity of non-alcoholic fatty liver disease, we sought to identify the prevalence of symptoms of sleep-disordered breathing among patients seen in the pediatric gastroenterology clinics.

Methods: IRB retrospective chart review of children seen in both urban and suburban Johns Hopkins Pediatric Gastroenterology Clinics between 7/2015-4/2016. Data collected included: anthropometry, labs, relevant clinical information in addition to sleep questionnaire results. The Sleep-Related Breathing Disorder Questionnaire is a validated measure for SDB extracted from the Pediatric Sleep Questionnaire developed by Chervin *et al.* Questionnaire scores $>$ (or equal to) 0.33 are considered positive and suggestive of high risk for a pediatric sleep-related breathing disorder. Statistical analyses including Mann-Whitney and Chi-Square were used where appropriate.

Results: A total of 104 children were eligible for participation in the study. The majority of diagnoses at presentation were constipation, abdominal pain or reflux. Median population age was 8.4 \pm 5.1 years, 50% of the population was male. Ethnicity was 62% Caucasian/23% African American/7% Hispanic/8% other. Median BMI Z-score was 1.23 \pm 1.41. 17/104 children 16.4% of the population had abnormal questionnaire results. There was no difference in mean age, or sex distribution across groups stratified by ethnicity or sleep questionnaire scores. Surprisingly, there was no difference in BMI z-score across sleep questionnaire groups. There was a higher prevalence of sleep disordered breathing among African American (30%) vs. Caucasian children (11%) $p=0.029$ and a trend toward significance among children with constipation $p=0.06$.

Conclusion: A significant number of children seen in the GI clinic had evidence of sleep-disordered breathing on assessment without relation to weight status. Further evaluation is warranted re: impact upon long-term disease management.

106 LONGITUDINAL PROFILE OF NEUTRAL HUMAN MILK OLIGOSACCHARIDE FROM THREE URBAN POPULATIONS: THE GLOBAL EXPLORATION OF HUMAN MILK (GEHM) STUDY

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Background: Breastfeeding is recommended as the optimal method of infant feeding. Human milk oligosaccharide (HMO) is a major component of human milk, but its composition varies between mothers, and this variation has been reported to influence infant health outcomes, including diarrhea, allergy, and growth or malnutrition. The HMO composition of milk varies with maternal FUT2 ("secretor") and FUT3 (Lewis) genetics and the relative abundance of type 1 and non-type 1 precursor molecules. To define the conserved and variable patterns in HMO composition over lactation, we compared 12 neutral HMOs in milk collected at standardized times from 375 urban mothers with term deliveries representing different ancestry groups, and examined the potential impact of maternal clinical and demographic factors.

Methods: We analyzed the HMO composition of milk from 120 white and African-American mothers in Cincinnati, Ohio; 135 mothers in Mexico City, Mexico of mestizo ancestry; and 120 Chinese mothers in Shanghai, China. Samples and data were collected at 2, 4, 13 and 26 weeks of life following a standardized protocol. A total of milk 956 samples were analyzed by LC-MS. Maternal and infant clinical factors included birth weight, gestational age, delivery mode, maternal race/ethnicity, maternal prepregnancy BMI, and pregnancy weight gain. Statistical modeling of HMOs was conducted using generalized estimating equations (GEE) to compare the cohorts accounting for maternal and infant characteristics and repeated samples per mother.

Results: Neutral HMOs were higher in Cincinnati milk compared to the other cohorts ($p < 0.001$) and decreased over the first 6 months of lactation in all three cohorts ($p < 0.001$). The cohorts differed in the abundance of individual HMOs and in the percent classified into three milk oligosaccharide types: 1) secretor and Lewis positive mothers, whose milk included all HMOs; 2) secretor positive but Lewis negative mothers, whose milk lacked $\alpha 1,4$ -linked fucosylated HMOs; and 3) secretor negative mothers, whose milk lacked $\alpha 1,2$ -linked fucosylated HMOs. Cincinnati milk had more type 1 and Lewis HMOs; Mexican milk had more non-type 1 and secretor HMOs. The HMOs of Cincinnati white mothers had significantly more Lewis HMOs ($p < 0.001$) than African-American mothers or mothers from other sites. In all cohorts, type 1 and secretor HMOs decreased over lactation. In contrast, non-type 1 HMOs and Lewis HMOs remained consistent or increased over lactation in all cohorts. Maternal and infant clinical factors were not associated with HMO composition.

Conclusions: Neutral HMOs vary between populations due to genetic differences and the importance of type 1/non-type 1 chains. Nevertheless, HMO composition changes over lactation in a pattern that is consistent across populations. These systematic differences in HMOs could influence infant gut health and development, and requires functional studies.

107 ASSOCIATION OF EOSINOPHILIC ESOPHAGITIS AND ASTHMA

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Introduction: Asthma is a chronic disease of the airways and it is the most common chronic disease of childhood. Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder characterized by eosinophilia in the esophageal mucosa that causes feeding difficulties, regurgitation, vomiting, abdominal pain, dysphagia, and food impaction. EoE and asthma, as well as other atopic diseases, are frequently associated and have a number of similarities in their pathogenesis.

Objective: This project will help to estimate the prevalence of bronchial asthma in patients with EoE, and to estimate the association between severe eosinophilic esophagitis and severe asthma.

Methods: This is a cross-sectional study. The interview will include a question to identify which patients also have a diagnosis of bronchial asthma. Those patients with bronchial asthma will be assessed using the AAP Asthma Severity Scale and a history of bronchial asthma medications will also be obtained. For those patients who have both bronchial asthma and EoE, a comparison analysis will estimate the association between severe EoE and severe asthma, using the Prevalence Ratio and its corresponding 95% Confidence Interval.

Results: 30 patients with EoE participated in our study, with a male predominance 63% ($n=19$). Age distribution was more prevalent in the 6-10-years' group ($n=14$). Half of the patients evaluated were asthmatic, 43% had mild intermittent asthmatic and 7% were persistent asthmatics. Almost all patients were diagnosed with asthma (4 years old) previous to EoE diagnosis (9 years old); average time frame between asthma and EoE diagnosis was almost 5 years. There was no relation between the total eosinophil count in the tissue biopsy and the presence of asthma, and there was no correlation between the severity of both conditions that can be attributable to the eosinophil count in the esophageal biopsy.

108 IODINE NUTRITION DURING PREGNANCY AND RELATED NEONATAL PHYSICAL DEVELOPMENT IN SHANGHAI

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Objective: To monitor iodine nutrition of women during late pregnancy in Shanghai a Coastal Area in China, and to examine the correlation between maternal urine iodine concentration and newborn physical development.

Method: We used the prospective cohort study data from the women during late pregnancy (28-34 week) who accepted the follow-up intervention in the Department of Clinical Nutrition in Shanghai Xinhua Hospital affiliated to Shanghai Jiao Tong University School of Medicine between December 2014 and February 2015. All participants collected a spot urine sample three times every two weeks. Study participants completed a iodine-related food frequency method and 24-hour food diary and that was administered twice at 28°C34 weeks of gestation. TSH in neonatal heel blood was analyzed 72 h after birth.

Results: 151 women were recruited into the study. Data from the study showed all pregnant women ($n=151$) had a median UI concentration of $100.0 \mu\text{g/L}$ (25th-75th percentiles: $64.7\sim 155.6 \mu\text{g/L}$). In sequence, urinary iodine levels of $150 \mu\text{g/L}$, $249 \mu\text{g/L}$ were defined as the cut-off points iodine insufficient, adequate, more than adequate; all subjects were divided into three subgroups, 76.8% ($n=116$), 19.2% ($n=29$) and 4.0% ($n=6$), respectively.

Subgroup analysis showed that the iodine insufficient group ($n=116$) compared with the adequate iodine group ($n=29$), their birth weight, length and placental weight were [$(3295 \pm 370) \text{ g}$ vs. $(3397 \pm 504) \text{ g}$, $p=0.311$], [$50.0 (2.0) \text{ cm}$ vs. $50.0 (2.5) \text{ cm}$, $p=0.316$] and [$(636 \pm 89) \text{ g}$ vs. $(658 \pm 104) \text{ g}$, $p=0.268$] respectively, and there were no significant difference between the two subgroups. In addition, analysis of the head circumference of newborns [$34.5 (1.0) \text{ cm}$ vs. $34.5 (1.0) \text{ cm}$, $p=0.316$] and TSH in neonatal heel blood [$(4.0 \pm 1.9) \text{ g}$ vs. $(3.9 \pm 2.1) \text{ mIU/L}$, $p=0.895$], no significant difference between the two subgroups (Table 1).

Conclusion: According to WHO standards, the rate of iodine deficiency ($\text{UI} < 150 \mu\text{g/L}$) in pregnant women in Shanghai in late pregnancy is 76.8%. The results of the study suggested that there was no significant difference between the status of iodine nutrition during pregnancy and fetal development. Therefore, the standard was applicable to Chinese pregnant women. There is a need to have more multi-center studies confirmed.

109 THE APPLICATION AND EPIDEMIOLOGICAL RESEARCH OF XTAG GASTROINTESTINAL PATHOGEN PANEL MULTIPLEX PCR IN THE DIAGNOSIS OF CHILDREN PERSISTENT AND CHRONIC DIARRHEA

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Objective: To Investigate the application value of xTAG gastrointestinal pathogen panel (xTAG GPP) multiplex PCR in the early diagnosis of children with persistent and chronic diarrhea, and to understand the epidemiology of intestinal diarrhea pathogens.

Methods: One hundred and ninety-nine specimens were collected in Nanjing Children's Hospital, Nanjing Medical University, from October 1, 2014 to September 30, 2015. The xTAG GPP Multiplex PCR Assay was compared with the traditional methods (culture, rapid enzyme immunoassay chromatography, microscopic examination) and modding the statistical analysis.

Results: The positive rate of 199 patients with diarrhea specimens was 72.86% (145/199) the proportion of girls and boys was 1:1.39; the average age was 13 months. The virus detection rate was 48.7%; Rotavirus A was the most common organism detected (34.6%), concentrated in winter, and prevalent in children. Norovirus GI/GII was second, at 20.6%. The positive rate of bacteria was 40.2%, and *Campylobacter* (22.11%, 44/199) was most frequently detected. With *C. difficile* toxins A/B and *Salmonella* detected 44 and 17 samples, respectively. Infections with *Shigella* occurred 4 times, *E. coli* O157 was only detected once. There were three samples with parasitic (1.51%), two samples were positive for *Entamoeba histolytica*, one for *Cryptosporidium*. Adenovirus 40/41, STEC, ETEC, *Giardia*, *Yersinia enterocolitica* and *Vibrio cholera* were not detected. All of them did not have obvious distribution followed by season and population. Totally 86 (43.2%) infected specimens with single pathogen were detected. There were 57 co-infections (28.64% of samples) of viruses and/or bacteria and/or parasites. Co-infections involved 29 double infections (23.62%) samples, 9 triple infections (4.52%) and 2 quadruple infections (0.5%). Norovirus GI/GII was found to have the highest involvement in co-infections 30 (15.08%).

Conclusions: xTAG GPP multiplex PCR is simple, sensitive, specific and can be used as a quick way to diagnose children's persistent and chronic diarrhea. Diarrhea pathogen has significant characteristics according to season and population.

Keywords: Persistent diarrhea; Chronic diarrhea; Nucleic acid amplification techniques; Viruses; Bacteria; Parasites

Table 1. Summary of results of XTAG GPP for the detection of enteric pathogens in the stool samples collected from patients with persistent and chronic diarrhea.

Class	Target	No. (%)
Virus	Adenovirus 40/41	0
	Rotavirus A	69(34.67%)
	Norovirus GI/GII	41(20.60%)
Bacteria	<i>Salmonella</i>	17(8.54%)
	<i>Campylobacter</i>	44 (22.11%)
	<i>Shigella</i>	4 (2.01%)
	<i>Clostridiumdifficile</i> Toxin A/B	30 (15.08%)
	ETEC	0
	<i>Escherichiacoli</i> O157	2 (1.01%)
	STEC	0
	<i>Yersinia enterocolitica</i>	0
	<i>Vibrio cholerae</i>	0
Parasite	<i>Giardia</i>	0
	<i>Entamoeba histolytica</i>	2 (1.01%)
	<i>Cryptosporidium</i>	1 (0.50%)

110 SiO₂ NANOPARTICLES MODIFIED WITH SELF-ASSEMBLED MONOLAYER: TOXICOLOGY STUDIES IN A MOUSE MODEL

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Background: Nanoparticles (NPs) are studied for their potential applications in bioassay, diagnosis, and therapy in recent decades. For example, nanogold and gold-shell NPs have been applied in drug delivery and photothermal therapy, respectively. However, little research focuses on NPs of non-gold materials *in vivo*. In this study, SiO₂ NPs modified with self-assembled monolayer is utilized in an animal model. The aim of this study is to investigate the toxicity of SiO₂ NPs in mice by bio-safety experiment and LD50 toxicity test.

Material and methods: The modified NP has a size of 150 nm. LD50 toxicity test is determined by serial doses (0, 1, 2, 2.5, 5, 10, 100, 200 and 300 mg/kg body weight) of SiO₂ NPs. Male BALB/c mice received SiO₂ NPs by a single dose of tail intravenous injection and were sacrificed 14 days later.

Results / Body Weight: The body weight was not significantly different in each group after 14 days. Serum Biochemistry: BUN was significantly decreased at all concentration groups to control, except the 2.5 mg/kg group. GPT, CPK were mostly higher than control. GOT, CRE and T-BIL were mostly lower than control; TP and ALB were similar to control. However, those serum levels were within normal limits. Histopathologic Analysis: Liver, brain, heart, lung, kidney and spleen were examined under microscopy with no histopathologic lesions seen.

Conclusion: All mice survived until sacrificed. Various organs were found to have no nanoparticles-related pathological reactions. SiO₂ nanoparticles caused no apparent toxicity under the present experimental conditions.

111 *GENDER DISPARITY AMONG PEDIATRIC GASTROENTEROLOGISTS IN NORTH AMERICA AND AUTHORSHIPS IN MAIN PEDIATRIC JOURNALS*

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Background: Authorship in peer-reviewed medical journals is a marker for success in academic medicine.

Objective: To determine the representation of female physicians in the field of pediatric gastroenterology and authorships of original research in common journals for pediatric gastroenterologists.

Subjects: Members of North America Society of Pediatric Gastroenterology, Nutrition, and Hepatology (NASPGHAN) who were practicing in North America were included in the study and classified by gender. All first and senior authors of pediatric gastroenterology original research published in the years 2005, 2009, and 2013 in main pediatric journals with pediatric gastroenterology publications were also classified by gender.

Results: Members of NASPGHAN practicing in North America increased from 1,016 in 2005 to 1,484 in 2009 and 1,670 in 2013. We evaluated 3033 original research articles. A total of 273 articles met the criteria of 1) pediatric gastroenterology theme; 2) first author, senior author or both female; and 3) based in North America. There were no significant differences in the proportion of female first authors over the years ($p>0.05$). There are significantly fewer female senior authors compared to the proportion of pediatric gastroenterologists in North America in 2013.

Conclusions: The proportion of female pediatric gastroenterologists is increasing in North America. The proportion of female senior authors is significantly lower than the proportion of practicing pediatric gastroenterologists in 2013.

112 *FEEDING DIFFICULTIES OF PATIENTS WITH FOOD ALLERGIES IN A PEDIATRIC GASTROENTEROLOGY REFERENCE CENTER*

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Introduction: Food allergy (FA) is an immune response to a food antigen: IgE mediated, non-IgE, or mixed. Patients with FA may have eating disorders; however, studies that assess this relationship are limited. The purpose of this study was to describe the types and distribution of feeding difficulties in patients with a FA in the Gastroenterology, Hepatology, and Nutrition Reference Center (Gastronutriped) in Bogota, Colombia.

Methodology: A retrospective study was performed, which involved patients ages 0–18 who were diagnosed with FA and feeding difficulties, attended at Gastronutriped from 2013 to 2015. Patients with genetic syndromes, malformations of the gastrointestinal tract, autism spectrum disorders, and hypoxic encephalopathies were excluded. The data was extracted from medical records. The analysis was made using Stata 13. The description of continuous variables was performed with mean or median, with their respective measure of dispersion (standard deviation or interquartile range), according to their distribution. Discrete variables were expressed as proportions. For the comparison of the variables of interest, the Fischer exact test was applied, and a value of $p<0.05$ was considered significant.

Results: From a total of 644 patients, 109 (16.92%) were diagnosed with FA. Of these, 40 (36.69%) had an eating behavior disorder (EBD), and the most frequent manifestation was alteration of the appetite. In patients with FA and EBD, a mixed mechanism FA prevailed (62.5%), the most frequent clinical expression was eosinophilic esophagitis (37.5%), and selective appetite was the most common symptom. In patients with FA without EBD, the group with IgE-mediated FA was dominant (52.17%). Mixed mechanism FA was associated with increased prevalence of eating disorders ($p<0.009$). Feeding difficulties were more frequently found in males (22, 55%) and infants (31, 77.5%), with an average age of 13.3 months. More than half of the patients with FA and EBD (55%) exhibited a normal nutritional status. Risk factors for eating disorders were found: prior hospitalization (52.5%), use of catheters, nasogastric or orogastric feeding (15%), and history of prematurity (5%).

Conclusions: Feeding difficulties occur in parallel or as a result of FA. They seem to be more associated with the mixed mechanism, and within it, with eosinophilic esophagitis. In these particular patients, selective appetite predominated. However, the limited numbers of patients in our study seems to call for wider studies. For this approach, an interdisciplinary system is needed, because of the great impact that both phenomena have on the family and on the psychosocial level.

113 *ACIDIC HUMAN MILK OLIGOSACCHARIDES VARY ACROSS CHINESE, MEXICAN, AND AMERICAN POPULATIONS AND OVER LACTATION*

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Background: Human milk oligosaccharides (HMOs) inhibit pathogens, promote colonization through a prebiotic effect, and inhibit inflammation of the intestinal mucosa. The content of HMOs varies qualitatively and quantitatively among individuals and over the course of lactation.

Objective: To compare the acidic HMOs composition of milk from mothers in Cincinnati, OH, Shanghai, China, and Mexico City, Mexico over the course of early lactation.

Methods: Cohort- 120 mothers, 760 milk samples per site as part of the Global Exploration of Human Milk (GEHM) study. Eligibility required healthy, singleton, term delivery and > 5% of feedings from breast milk for at least 3 months. Milk samples were collected between 9AM-1PM at 2, 4, 13 and 26 wks postpartum using Medela Symphony breast pumps, and represented the contents of one breast that was not used for feeding within two hours of pumping. Analysis - defatted, deproteinated, reduced, and filtered samples were analyzed by LC-MS.

Oligosaccharides were separated on a Hypercarb graphitized column with gradient of acetonitrile/0.02% aq ammonium acetate and detected by electrospray mass spectrometry with a positive target of [M-H]⁺ and [M-2H]²⁺ ions.

Results: Total oligosaccharides decreased over lactation, from 5.8 (week 2) to 2.8 g/L (week 26, $p<0.001$). However, the most rapid decline in HMOs occurred in the acidic oligosaccharide fraction, from 2.4 (week 2) to 0.4 (week 26, $p<0.001$). Milk from Shanghai was significantly lower than the other two sites in total HMOs (at month 1: 4.1 vs. 5.1 g/L, $p<0.001$). The most abundant individual acidic HMOs across the populations were 3'-sialyllactose (3'SL), 6'-sialyllactose (6'SL), and disialyllacto-N-tetraose (DSLNT). Comparing populations, 3'SL was higher ($p<0.001$),

6'SL was lower ($p<0.001$), and DSLNT was lower ($p<0.001$) in Mexican than Cincinnati or Shanghai mothers. The concentrations of 6'SL and DSLNT declined, whereas 3'SL did not decline, over the first 26 weeks of lactation.

Conclusions: Concentrations of different HMOs differ among populations, and change over the course of lactation. The biological ramifications of these differences warrant closer investigation.

114 INCIDENCE AND CHARACTERISTICS OF ANORECTAL MALFORMATIONS IN HISPANIC CHILDREN ON THE USA-MEXICO BORDER

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Background: Anorectal Malformations (ARMs) are widely known as the range of congenital malformations involving the gastrointestinal, urogenital, and/or the gynecological anatomy. These affect male and females with a slightly greater predominance in males and occur in approximately 1:5000 live births. ARMs are classified as: high (anorectal agenesis and rectal atresia), intermediate (agenesis anomalies), and low (perineal and vulvar malformations). ARMs can be isolated or associated with other syndromes. Review of the current literature suggests that there is poor characterizations of ARMs in the Hispanic population.

Objective: Determine the incidence of ARMs in Hispanic children over a 3-year period and to describe the characteristics of these malformations.

Methods: We performed an IRB-approved chart review of all patients with ARMs at the Pediatric Surgery outpatient clinic from January 2012 to December 2015. Demographic data, type of malformations, associated syndromes, and long-term complications were recorded. An incidence rate was also calculated. Patients older than 4 years of age and non-Hispanic patients with ARMs were excluded.

Results: A total of 57 patients' charts were reviewed and 24 patients were included in the study. Using the US Census Bureau birth data for El Paso County, the incidence rate for ARMs was approximately 1:1428 births. Our cohort included 16 males and 8 females. Twenty-one patients had major ARMs which included: imperforated anus (n=20), Perianal fistulas (n=6), cloacal malformation (n=4), and rectourinary fistulas (n=5). Only 3 patients had minor ARMs that included: bowel atresia, ectopic anus, and anorectal stenosis. The most common post-surgical complication was poor wound healing (22.7%). There were 14 patients that had multiple ARMs: 12 patients had 2 ARMs, 1 patient had 3 ARMs and 1 patient had 6 ARMs. In patients with major ARMs, 72.7% were isolated cases and 6 cases (27.2%) were associated with a syndrome. The most common associated syndromes were VACTERL, Down's syndrome, DiGeorge syndrome, Chromosome 9 deletion and Trisomy 16 mosaicism. Patients with minor ARMs had an associated syndrome in 66% of the cases. Constipation was the most common long term complication for ARMs (43%), followed by fecal incontinence (14%), and persistent rectal bleeding (8%).

Conclusion: Based on our study, we are able to demonstrate an increased incidence of ARMs in Hispanic children born on the US-Mexico border. The most frequently found ARMs in our population were imperforated anus, perianal fistulas, and cloaca malformation. The vast majority of ARMs were isolated defects. Constipation and fecal incontinence were the most common long term complications. Additional studies are needed to determine the reason for the increase incidence of ARM in this population.

115 LEVELS OF AND INTERRELATIONS BETWEEN MAJOR HUMAN MILK OLIGOSACCHARIDES IN BREAST MILK FROM THE LIFE COHORT

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Background/Aim: Human milk oligosaccharides (HMOs) are among the most abundant components of human milk, however the majority of these oligosaccharides is not digestible by the infant. HMOs can act as prebiotics for the infant's microbiota and contribute to the beneficial effects of human milk. Depending on the mother's genotype, types and abundance of HMOs vary, with most decreasing in concentration as lactation progresses. Besides genotype dependence, not much is known about the regulation of HMO synthesis. We quantified some of the major HMOs in breast milk to better understand their interrelations and their regulation to eventually study their relations with clinical health measures in infants.

Methods: Milk samples at 3 months of lactation were obtained from 156 volunteers who participated in the 'LIFE' cohort in Leipzig, Germany. Using a validated UHPLC based method, 10 different HMOs were quantified in each sample.

Results: Most milk samples contained detectable amounts of the 10 measured HMO, except for A-tetrasaccharide, for which 64.5% of samples had levels below the limit of detection (4.9 mg/kg) and 68% had levels below the limit of quantification (LOQ) of 20 mg/kg. For Lacto-N-neofucosylpentaose, 32% of samples were below LOQ (12 mg/kg). Average values for the 156 samples are listed in order of increased concentration (mg/kg): Lacto-N-neofucosylpentaose (LNnFP; 17), A-tetrasaccharide (PI; 46), lacto-N-fucosylpentaose-V (LNFP-V; 70), 3'-sialyllactose (3'SL; 144), Lacto-N-Neotetraose (LNnT; 148), 6'-sialyl-lactose (6'SL; 167), lacto-N-fucosylpentaose-I (LNFP-I; 528), Lacto-N-Tetraose (LNT; 607), 3-fucosyllactose (3-FL; 1044), and 2'-fucosyllactose (2'FL; 1882). Of the 156 samples, 20 contained hardly any of the usually abundant 2'-FL, indicating inability to synthesise α -1,2- fucosylated oligosaccharides. Synthesis of α -1,2- fucosylated oligosaccharides is performed by fucosyltransferase-2 (FUT2), individuals who are unable to secrete this enzyme are known as "FUT2 non-secretors". We observed that 2'FL levels were strongly correlated with LNFP-I as expected from their FUT2 dependence. Interestingly, 2'FL and LNFP-I also showed a positive correlation with LNnT, but not with LNT, one of the main acceptors substrates of FUT2, and an inverse correlation with 3-FL, which is fucosylated but via different linkage.

Conclusion: HMO levels in milk samples from a German cohort (LIFE) show similar levels as found in the literature. Of the included 156 subjects, 12.8% were non-secretors. When FUT2 is functional (secretor mothers), high levels of 2'FL and LNFP-I are produced, while when FUT2 enzyme is dysfunctional (non-secretor mothers), other fucosyltransferases like FUT3 lead to the synthesis of higher levels of 3-FL.

116 CLINICAL PRACTICE GUIDE FOR THE DIAGNOSIS AND COMPREHENSIVE CARE OF CHILDREN WITH FUNCTIONAL CONSTIPATION

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Introduction: The present guide is the result of the implementation of the “Rapid Adaptation of Clinical Practice Guides” (RACPG), a strategy with no precedents. Chronic functional constipation is a frequent clinical situation in pediatric consultations and represents up to 25% of consultations with pediatric gastroenterologists.

General objective: To adapt a guide on chronic functional constipation in children from 0 to 18 years of age to unify the diagnosis and treatment of this pathology in our hospital.

Specific objectives: a) to implement recommendations based on the best clinical evidence for chronic functional constipation diagnosis and treatment; b) to provide direction in order to unify its management; c) to improve the quality of life of pediatric patients with this pathology; and d) to reduce costs for the current health system.

Methodology: With the counsel of trained personnel and the oversight of a Trials Search Coordinator from Cochrane Collaboration in Colombia, a systematic, highly sensitive search was conducted to identify Clinical Practice Guides (CPG) on chronic functional constipation diagnosis and treatment in children. The Developer Group (group of experts) with the methodologist reviewed the guides identified by the theme and with the MeSH words “children”, “idiopathic constipation”, “functional constipation”, and “guideline”, arriving at a selection of 27 documents. Titles that did not fulfill specific theme expectations were excluded, and the quality of each document was analyzed. Finally, a publication and its update was chosen because its characteristics coincided with the approaches of the group of experts, and the methodological requirements of AGREE II were applied.

Results: With the selected guide from 2010 and its update in 2012, researchers proceeded to its adaptation following an established order: the guidelines to follow for those older and younger than 1 year were given, the critical points were established in terms of anamnesis, physical examination, pharmacological disimpaction treatment and non-pharmacological treatment. When points of discussion, un contemplated topics, or inapplicable concepts for our context were found, consensus was reached based on the experiences and publications of Developer Group members, and resolved with the best evidence.

Discussion: With this adaptation, a quality, up-to-date, and methodologically sound Clinical Practice Guide has been achieved that will resolve difficulties by unifying criteria for the management of this pathology. It is obvious that the implementation of Clinical Practice Guidelines is indispensable for rational management, but the high cost and the time that must be spent are insurmountable obstacles on some occasions and in most low-income countries. In these circumstances, the RACPG becomes a valid and timely strategy to lower costs, save time, and optimize resources

117 IMPACT OF PROBIOTICS ON CONSTIPATION AND INTESTINAL MICROFLORA IN CHILDREN WITH FUNCTIONAL CONSTIPATION

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Aim: To evaluate the effect of probiotics on the symptoms and intestinal microflora in pediatric patients with functional constipation.

Methods: A prospective, randomized controlled trial of probiotics in children (aged 6 months -10 years old) with functional constipation was performed. The enrolled patients were randomized into group A received magnesium oxide and probiotics (*Clostridium butyricum Miyairi*); group B received only magnesium oxide. Each patient was assigned the evaluation of constipation symptoms every day for 12 weeks and collection of fecal samples for detection of microflora at enrollment, 4 weeks, and 12 weeks.

The severity of constipation was quantified by scoring of constipation symptoms (ROME III criteria), and the reduction in scores was used to assess the therapeutic effect. Using real-time PCR, microflora (*Clostridium butyricum Miyairi*, *Bacteroides fragilis*, *Bifidobacterium longum*, *Clostridium difficile*, and *Lactobacillus casei*) was quantified from fecal DNA samples. Fecal samples of 40 healthy children were enrolled as control. An independent samples t-test for evaluation of differences between different group subjects was performed. A $p < 0.05$ is considered significant.

Results: A total of 81 participants [(A group, 41 cases (mean age: 3.7 ± 1.5 yrs, M/F17/24); B group, 40 cases (mean age: 4.0 ± 1.8 yrs, M/F 19/21)] were included in the study. After 4-week and 12-week treatment, the average increase of defecation frequency was significant in both groups [A: 1.6 (baseline), 4.5 (4 weeks), 5.9 (12 weeks); B: 2.4 (baseline), 3.6 (4 weeks), 4.9 (12 weeks)], while the increase was more significant in A group ($p < 0.05$). The mean scores of constipation symptoms were 7.0 ± 1.7 (baseline), 3.5 ± 2.1 (4 weeks), 1.7 ± 1.3 (12 weeks) in A group; and 6.5 ± 1.7 (baseline), 4.8 ± 1.9 (4 weeks), 2.6 ± 1.3 (12 weeks) in B group. Reduction of scores was significant in both groups, with more significant found in A group ($p < 0.05$). Comparing to the controls, the expressions of fecal *Clostridium difficile* and *Lactobacillus casei* was higher and lower in both groups, while no significant differences in the expressions of fecal *Clostridium butyricum Miyairi* and *Bacteroides fragilis* in both groups. After 12-week treatment, significant increase in the expressions of fecal *Clostridium butyricum Miyairi* was found in A group. Otherwise, significant reduction in the expressions of fecal *Clostridium difficile* was found in both groups ($p < 0.05$), while more significant reduction was found in A group. No significant increase in the expressions of fecal *Bifidobacterium longum* was found in both groups.

Conclusion: Probiotics help to reduce constipation symptoms in pediatric patients with functional constipation. Probiotics supplementation may increase intestinal probiotic microflora and decrease intestinal harmful microflora in children with constipation.

118 THE RELATIONSHIP BETWEEN ACTIVITY ENERGY EXPENDITURE AND BODY COMPOSITION IN SCHOOL-AGE CHILDREN

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Aims: To assess the association between activity energy expenditure (AEE) and body composition in school-age children.

Methods: A total of 62 school-age children (8–10 yr) from Shanghai were enrolled in the study. Body composition was evaluated by bioelectrical impedance analysis (BIA). Activity energy expenditure (AEE) was estimated with a FitMate metabolic system (Cosmed, Rome, Italy).

Results: There were no differences in total AEE (kcal) between obese and lean children (boys: $t=-1.422$, $p=0.165$; girls: $t=1.351$, $p=0.203$). The boys who were obese or overweight tend to have lower weight-adjusted AEE (kcal/kg/min) ($t=2.043$, $p=0.051$) and higher AEE (kcal/min) than lean boys ($t=-2.910$, $p=0.007$); while the girls who were obese or overweight tend to have lower weight-adjusted AEE (kcal/kg/min) ($t=3.244$, $p=0.003$) and higher AEE(kcal/min) ($t=-0.676$, $p=0.504$) than lean girls.

After controlling for age and gender, AEE(kcal/min) was significantly positively correlated ($p<0.05$) with degree of obesity, FAT%, FM, FFM, FFMI in boys, while no statistical significance association was found between AEE(kcal/min) and the body composition ($p>0.05$) in girls. There were negative correlation between weight-adjusted AEE (kcal/kg/min) and BMI, degree of obesity, FAT%, FM, FFM, FMI both in boys and girls ($p<0.05$). In addition, no statistical significance association was found between weight-adjusted AEE (kcal/kg/min) and FFMI in boys($r=0.347$, $p=0.056$).

Conclusion: The hypothesis that obesity reduces AEE in children is partially supported. There are complex interactions among body size, body composition, and metabolic activity in children.

Keywords: Obesity; children; energy expenditure; metabolism

*119 A COMBINED PACKAGE OF MICRONUTRIENTS AND ALBENDAZOLE DOES NOT IMPROVE ENVIRONMENTAL ENTERIC DYSFUNCTION OR STUNTING IN RURAL MALAWIAN CHILDREN

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Background: Environmental enteric dysfunction (EED) and linear growth stunting affect many rural agrarian children in the developing world and contribute to the persistently high rates of stunting that are observed worldwide. Effective interventions to improve EED are lacking.

Objective: We tested whether a package of interventions that included a single dose of albendazole, 14 days of zinc, and daily multiple micronutrient powder would decrease EED and stunting over 12–24 weeks in a cohort of rural Malawian children 12–23 months old.

Methods: This was a randomized, double-blind, placebo-controlled clinical trial with the primary outcomes being improvements in EED, as measured by the urinary lactulose-mannitol ratio from dual-sugar absorption testing, and linear growth. Outcomes were evaluated after 12 and 24 weeks of intervention, and compared to a placebo group.

Results: A total of 254 children were enrolled. After 12 weeks of study, children in the intervention group had an increase in their L:M ratio of 0.071 units, while children in the placebo group had an increase of 0.073 units ($p=0.87$). There was also no significant difference in L:M ratios at 24 weeks (increase of 0.088 units in the intervention group vs. increase of 0.080 units in the placebo group, $p=0.19$). Relative changes in length and weight also did not differ between the two groups.

Conclusion: The combined usage of a dose of albendazole, a course of zinc, and a daily multiple micronutrient powder did not decrease EED or stunting during the course of this study. Alternative interventions to improve these diseases should be investigated further.

120 AN ASSESSMENT OF THE ALVARADO SCORING SYSTEM IN THE DIAGNOSIS OF ACUTE APPENDICITIS AMONG THE PEDIATRIC PATIENTS AT A TERTIARY CARE MEDICAL CENTER

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Objectives: To review the demographics and clinical course of admitted patients, determine the Alvarado score of the surgically-confirmed cases and correlate the findings with histopathology results, correlate the Alvarado score and the results of the ancillary procedures, describe the alternative diagnoses of the patients initially considered to have an acute appendicitis and determine the negative appendectomy rate among patients who underwent operation.

Design: Retrospective, descriptive study.

Setting: St. Luke's Medical Center, Quezon City, a tertiary, private institution.

Participants: Eighty-two admitted pediatric patients from the emergency department assessed from January 1, 2012 to June 30, 2013 using the Alvarado score and suspected to have acute appendicitis were included in the study. Patients with imaging-confirmed diagnosis of appendicitis on arrival to the emergency department, those who were already treated conservatively with medications, patients with incomplete documentation, and those who were discharged against medical advice were excluded.

Main Outcome Measure: Histopathology findings among post-appendectomy patients and alternative diagnoses among those who were not operated on.

Results: There was a significant difference in the number of patients with scores 1–4, 5–6, and 7–10, with and without appendicitis, thus a significant correlation between the Alvarado score and the diagnosis of acute appendicitis existed. Among patients with acute appendicitis, there is an increasing trend of making accurate diagnosis with an increasing score group. Conversely, an opposite trend is observed among those without acute appendicitis. The negative appendectomy rate of this study was 10.6%.

Conclusion: The Alvarado scoring system is a helpful practical non-invasive diagnostic procedure that is simple, fast, cheap, safe, and reliable. It categorizes patients for discharge and for admission for further evaluation and management. Patients with score 7–10 should be admitted and undergo appendectomy to avoid complications. Patients with score 5–6 should also be admitted for close observation, who may require further studies to accurately make a diagnosis. Score 1–4 can be discharged with a general advice to seek medical attention as indicated.

Keywords: Acute appendicitis, Alvarado score

121 SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF TREATMENTS FOR ACUTE DIARRHOEA AND GASTROENTERITIS IN CHILDREN.

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Background: Acute diarrhea and acute gastroenteritis (ADG) are common among children in low- and middle-income countries (LMIC) and high-income countries (HIC). Treatments for reducing the duration of ADG, in addition to oral rehydration, have been compared to placebo/standard treatment in randomized control trials (RCTs). They have shown some effect in reducing diarrhea against placebo/no-treatment (PLC/NT). Systematic reviews have synthesized some of these results showing that most of them are better than placebo. No summary of all the evidence is available to date. Our aim was to determine the comparative effectiveness of all available interventions for ADG in children and to describe the source and characteristics of the evidence across the world.

Methods: We conducted a systematic review of RCTs comparing zinc, vitamin A, probiotics (*LGG*, *S. boulardii*, and other strains), prebiotics, symbiotics, racecadotril, smectite, loperamide, fermented, diluted and lactose-free formula/milk, or its combinations, against them or standard treatment/placebo for reducing ADG treatment in children. Protocol registered at PROSPERO (CRD42015023778). We searched Medline, Embase, CINAHL, CENTRAL, Global-Health, LILACS, and grey literature. Review was performed in duplicate. We described the setting, types of comparisons, and results of effectiveness with descriptive statistics. We performed a Bayesian random-effects network meta-analysis to determine the comparative effectiveness, and the effect estimates were calculated along with their credible intervals (95% CI). A ranking was performed to determine the best interventions. Quality of evidence was assessed with the GRADE approach.

Results: We screened 2898 studies; 156 proved eligible. In LMIC countries were performed 113 studies (72.4%). In total 124 studies (18,190 patients) measured diarrhea duration. Most of the trials compared a single intervention vs. placebo/no-treatment being the most common probiotics, zinc, and lactose-free (70.2%). Except for vitamin A, micronutrient mixtures, diluted milk and prebiotics, all the interventions were better than PLC/NT. Differences among the effective interventions ranged from a reduction of 14.92 to 38.4 hours, less than PLC/NT. Symbiotics (Mean Difference in hours: -29.10[-40.92; -17.19]) and *S. boulardii*+Zinc (-38.45 [-53.97; -22.70]) were the best-ranked interventions. Loperamide was the least safe. The GRADE quality of Evidence was Low and Very Low in most of the cases. Evidence of effectiveness of symbiotics was the one with the highest quality of evidence.

Conclusions: Evidence about treatments for reducing ADG duration comes mostly from comparisons: intervention vs. PLC/NT, and from LMICs. There is scant evidence directly comparing the interventions among them. Almost all the interventions were better than PLC/NT. However, differences among the interventions are small.

122 EPIDEMIOLOGY OF KAWASAKI DISEASE AND HENOC-SCHÖLEIN PURPURA: 14-YEAR SINGLE-CENTER EXPERIENCE

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Background: Kawasaki disease (KD) and Henoch-Schönlein purpura (HSP) are the two most common vasculitis in children. Although many nationwide epidemiology researches were performed, there was no study of regional epidemiology in certain areas in Korea. The purpose of this study was to evaluate the epidemiology of Kawasaki disease and Henoch-Schönlein purpura in the National Health Insurance Service (NHIS) Ilsan hospital, Goyang, Korea.

Methods: We retrospectively reviewed medical records of patients who were diagnosed with Kawasaki disease and Henoch-Schönlein purpura from March 2000 to February 2014 at the NHIS Ilsan Hospital in Goyang, Korea.

Result : The total cases of KD and HSP were 1202 and 623 patients over 14 years. The male-to-female ratio was 1.36:1 and 0.98:1, and mean age was 39.5±29.7 months and 100.5±54.1 months respectively. The annual numbers of KD patients changed from 45 in 2000 to 121 in 2013. The annual numbers of HSP patients were 35 in 2000 and the same in 2013. The monthly number for KD was slightly higher in summer (July) and winter (December), but the monthly number of HSP was lower in summer (August). The proportion of patients with KD among total inpatients and outpatients was 1.86% and 0.05%, and HSP was 0.45% and 0.06%, on average. Each inpatient and outpatient average annual growth rate of KD and HSP was 5% and 9% vs. -5% and -1%.

Conclusion: The number of Kawasaki disease patients and the proportion of the total number of patients in our institution was increasing, but the number and proportion of Henoch-Schönlein purpura patients has been gradually reduced. And, our epidemiology study of vasculitis in children is similar to that reported in previous nationwide studies in Korea.

123 EFFECTS ON FATTY ACID METABOLISM OF A NEW POWDERED HUMAN MILK FORTIFIER CONTAINING MEDIUM-CHAIN TRIACYLGLYCEROLS AND DOCOSAHEXAENOIC ACID IN PRETERM INFANTS

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Background and Aims: In preterm infants, fortification of human milk (HM) with essential fatty acids (FA) is critical to support the high demands of growth. FA metabolism was investigated in preterm infants fed HM supplemented with a new fortifier (nHMF) that provided an additional intake of 0.76 g of medium-chain FA (MCFA), 58 mg of linoleic acid, 25 mg of alpha-linolenic acid (ALA), and 10 mg of docosahexaenoic acid (DHA) per kg/day to comply with the latest recommendations.

Methods: 153 preterm infants (birth weight ≤1500 g or gestational age ≤32 weeks) were randomized to receive HM fortified with nHMF or a lipid-free HMF. FA profile in plasma phospholipids, triacylglycerols (TAG), and red blood cell phosphatidylcholine and phosphatidylethanolamine (RBC-PE) were analyzed in a subgroup of 40 infants before and after 21 days of feeding.

Results: Increased intake of MCFA in the nHMF group raised the levels of *de novo* synthesized palmitic acid and monounsaturated FA, possibly due to a larger available pool of acetyl-CoA resulting from dietary FA oxidation. ALA fortification in the nHMF group improved its incorporation in plasma TAG and the synthesis of eicosapentaenoic and docosapentaenoic acid. Similarly, additional DHA intake resulted in an increased DHA content in RBC-PE, which was not associated with a lower arachidonic acid content in this compartment as observed in plasma TAG and phospholipids. Numerous significant differences in FA levels were observed in RBC-PE (Table), a good indicator of FA metabolism and accretion.

Conclusions: HM fortification with nHMF efficiently supports FA anabolism and DHA accretion.

TABLE. FA profile (in g/100g of FA) of RBC-PE in preterm infants receiving HM fortified with

nHMF or a control HM fortifier (cHMF)						
	Baseline		After 21 days		Estimate ¹	pvalue
	cHMF	nHMF	cHMF	nHMF		
16:00	15.3	16.37	16.47	15.71	-0.123	0.04
16:1 n-7	0.34	0.36	0.39	0.41	-0.039	0.699
16:1 n-9	0.31	0.34	0.36	0.38	-0.061	0.588
18:00	6.69	6.56	6.84	6.64	-0.019	0.735
18:1 n-7	1.25	1.15	1.29	1.4	0.114	0.013
18:1 n-9	15.49	14.65	14.31	14.67	0.029	0.243
18:2 n-6 (LA)	2.66	2.85	2.97	3.3	0.013	0.779
18:3 n-3 (ALA)	0.2	0.25	0.25	0.29	-0.139	0.414
20:00	0.09	0.09	0.09	0.1	0.059	0.723
20:1 n-7	0.06	0.06	0.08	0.09	-0.011	0.958
20:1 n-9	0.5	0.43	0.56	0.6	0.174	0.003
20:3 n-6 (DGLA)	1.76	1.56	1.8	1.84	0.099	0.031
20:3 n-9	1.33	1.22	1.58	1.95	0.247	0.011
20:4 n-6 (ARA)	20.78	21.13	20.54	19.65	-0.024	0.374
20:5 n-3 (EPA)	0.79	0.71	0.68	0.95	0.301	<0.001
22:00	0.03	0.03	0.04	0.05	-0.25	0.193
22:1 n-9	0.07	0.05	0.07	0.07	0.352	0.008
22:4 n-6	4.75	4.77	4.78	4.48	-0.036	0.349
22:5 n-3 (DPA)	1.46	1.31	1.48	1.65	0.117	0.019
22:5 n-6 (DPA)	0.97	0.9	1	0.95	0.047	0.327
22:6 n-3 (DHA)	5.64	5.76	5.14	5.61	0.092	0.016
24:00:00	0.05	0.04	0.04	0.04	-0.201	0.351
24:1 n-9	0.05	0.04	0.03	0.03	0.172	0.577

¹Difference between groups (nHMF-cHMF) in change from baseline to 21 days (log scale).

124 COW'S MILK PROTEIN ALLERGY IN INFANTS (CMPA). ENVIRONMENTAL FACTORS AS FACILITATORS OF DEVELOPMENT OF ALLERGY

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Background: It is suggested that the neonatal intestinal microbiota is highly variable in its composition and depends on factors such as gestational age, mode of delivery, type of feeding, and environmental exposure. Intestinal microbiota has an important role in the postnatal development of the immune system and imbalances may lead to food allergies.

Aims: To analyze the association between the diagnosis of CMPA and the factors that could alter the intestinal microbiota in relation to perinatal record, personal history, environmental and/or pathological history.

Material and Methods: A retrospective descriptive study; 376 medical records of out-patient children, younger than 1 year, divided into two groups were analyzed:

Group 1: Children diagnosed with CMPA, confirmed by controlled oral food challenge.

Group 2: Children without CMPA.

We analyzed mode of delivery, history of hospitalization, feeding, treatment with antibiotics (ATB) and episodes of gastroenteritis, before diagnosis of allergy in group 1, and during the first year of life in group 2.

Chi-square test and Mann-Whitney tests were used. It was considered significant, at $p < 0.05$.

Results: Group 1: Children with CMPA n=182 Male: 54.4%

Group 2: Children without CMPA n=194 Male: 47.9%

	Group 1	Group 2	Chi Square	Df	Significance
Caesarean Delivery	53.30%	30.90%	19.320	1	$p < 0.001$
Breastfeeding	56.60%	96.90%	91.913	2	$p < 0.001$
History of Hospitalization	18.1%	16%	0.308	1	$p = 0.579$
ATB	15.9%	33%	14.673	1	$p < 0.001$
Gastroenteritis	23.1%	24.7%	0.143	1	$p = 0.705$

Children with CMPA were fed exclusively with breastfeeding 44%, with formula 43.4% and with breastfeeding and formula 12.6%. Children without CMPA: 62.9%, 3.1% and 34% respectively ($p < 0.001$).

Caesarean delivery increased the risk of CMPA, Odds ratio: 2,549 (95% CI 1.672- 3.884).

Conclusions: In this studied population, birth by Caesarean increased the risk of CMPA more than twice. Breastfeeding and vaginal delivery were protective factors.

The history of hospitalization, of treatment with ATB and episodes of gastroenteritis during the first year of life did not increase the allergy risk.

125 BRAZILIAN PAEDIATRICIANS' APPROACH TO CHILDREN WITH GASTROESOPHAGEAL REFLUX SYMPTOMS

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Gastroesophageal Reflux (GER) is usually present in pediatric daily practice, with difficult management in some situations, which may involve pediatric gastroenterologist consultations. GER consists in the passage of gastric contents into the oesophagus that may occur as a physiologic process several times per day even in healthy infants and children. At 4 months old, up to 67% of the infants present regurgitation. However, only 2 to 3.3% are considered as Gastroesophageal Reflux Disease (GERD) and need intervention. Based on evidence of excessive GERD diagnosis and treatment, NASPGHAN and ESPGHAN jointly published a Pediatric Gastroesophageal Reflux Clinical Practice Guidelines in 2009 to provide a common resource for evaluation and management of infants and children with GER and GERD. This protocol remains as a reference nowadays all over the world. Quitadamo *et al* (2014) interviewed 567 European pediatricians to evaluate this guidelines implementation and observed that the majority was unaware of this protocol, frequently prescribing proton pump inhibitors (PPIs) despite a lack of efficacy for the symptoms being treated.

Objective: The aim of this study was to evaluate the current approach of Brazilian general pediatricians to children with GER symptoms, according to the NASPGHAN-ESPGHAN protocol.

Methods: Three hundred ninety randomly identified Brazilian general pediatricians were invited to ask a case report –structured questionnaire during 37th Brazilian Congress of Paediatrics in October, 2015. The Portuguese version of the European’s twelve multiple choice case reports-like issues questionnaire, concerning the approach to infants, children and adolescents with symptoms suggestive of GER were presented to the pediatricians.

Results: None of the 390 interviewed pediatricians showed complete adherence (100%) to the guidelines. No difference in guidelines’ compliance was observed among the five regions of the country ($p=0.774$). Eleven percent of the respondents reported that usually request specific tests (upper gastrointestinal endoscopy and pH monitoring) and only 18.6% consider the child’s age to establish diagnostic approach. Twenty-nine percent prescribe PPIs irrespective of child age; the majority of the pediatricians (59.5%) prescribe PPIs in infants with unexplained crying and/or distressed behaviour and 37.4% guide empiric trial of PPIs for all age children.

Conclusion: Although the 2009 NASPGHAN-ESPGHAN Guidelines recommendations are disseminated all over the world and are the reference for GER/GERD management, Brazilian pediatricians’ practice generally diverges from this document. PPI prescription is high despite a lack of efficacy on the symptoms being treated.

126 WITHDRAWN

127 EFFECTS OF MATERNAL NUTRITION ON QUANTITY AND NUTRITIONAL QUALITY OF BREAST MILK: SYSTEMATIC REVIEW

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Background and Objectives: Breastfeeding is considered infant nutrition’s gold standard. However, the composition of breast milk varies according to the stage of lactation, time of day and between mothers. The role of maternal nutrition in breast milk quantity and content is of great importance to understand because of its potential for intervention. Consequently, we systematically reviewed the literature on the effects of diet, supplement use, and nutrient status on nutritional quality and quantity of breast milk.

Methods: Eight electronic databases were searched (up to February 2015) for interventional and observational studies that reported associations between nutrient blood levels, food or nutrient intake, dietary patterns, or dietary supplement use during pre-pregnancy (up to 6 months before conception), pregnancy, or lactation with nutritional quality or quantity of breast milk. Study selection was performed by two independent investigators.

Results: We identified 6198 unique references and retrieved full-texts for 814 articles, of which 370 met all selection criteria. Many of the included studies focused on breast milk levels of fatty acids (93 studies), vitamin A or carotenoids (63 studies), B vitamins (50 studies), zinc (44 studies), iron (31 studies), and calcium (22 studies). Overall, high-quality research on the effect of nutrition on breast milk production is scarce, and evidence for effects on energy content or macronutrient composition is inconsistent. However, there is strong evidence for effects of intake of omega-3 polyunsaturated fatty acids on its concentrations in breast milk. For micronutrients, there is moderate to strong evidence that dietary intake and blood levels of iodine, selenium, vitamin A, certain B vitamins (e.g., thiamine, riboflavin, choline, vitamin B12), vitamin C, vitamin D, and vitamin K are associated with their respective levels in breast milk. Evidence for an effect of maternal nutrition on breast milk iron, zinc, and vitamin E is inconclusive; and evidence for chromium, fluoride, sodium, potassium and other minerals is scarce. The current evidence supports no effect of dietary intake or blood levels of calcium, magnesium, or copper on their concentration in breast milk.

Conclusions: The literature to date suggests an effect of maternal nutrition on breast milk quality. Breast milk levels of several nutrients that are important for infant growth and development, such as polyunsaturated fatty acids, iodine, selenium and vitamins A, B, C and D, depend on adequate maternal nutrition, whereas concentrations of calcium, magnesium and copper in breast milk are not affected by maternal nutrition. More research is needed on the effects of maternal nutrition on breast milk content of iron, fluoride, potassium, zinc, chromium, sodium, and vitamin E and on breast milk quantity.

128 IMPACT OF MEDICAL AND NUTRITIONAL MANAGEMENT IN PATIENTS WITH FOOD ALLERGIES IN A GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION REFERENCE CENTER OF COLOMBIA (2008 - 2014)

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Introduction: In the Colombian pediatric population, as has as well been reported in the literature worldwide, an increase in food allergy (FA) has been observed. In our experience, a significant proportion of these patients have been diagnosed as having some degree of compromise of their nutritional status. Therefore, early diagnosis and an appropriate interdisciplinary approach would favor the window of opportunity for growth.

Objective: To evaluate the impact of medical-nutritional treatment on the growth of patients diagnosed with FA in the first two years of life in a gastroenterology, hepatology, and nutrition reference unit between 2008 and 2014.

Materials and Methods: Retrospective cohort study. Patients aged 0 to 2 years old, who had been diagnosed with FA and who had completed medical-nutritional treatment, were included. The data were extracted from medical records. A descriptive analysis was made. Nominal and

ordinal categorical variables were summarized with distributions of absolute and relative frequencies. For continuous variables, measures of central tendency and dispersion measures were used. The assumption of normality was validated using the Shapiro-Wilks test (quantitative variables). To determine differences between groups, Student's t-test was used. $p < 0.05$ was considered statistically significant in a single queue. Nutritional status was defined by anthropometric indicators using WHO Anthro software. The frequency of each WAZ, HEZ, and WHZ indicator was estimated at the beginning of the treatment and at the food challenge. To determine the changes in physical growth parameters, Student's t-test was used for related data, prior to assessment of equal variances. $p < 0.05$ in a single queue was considered statistically significant at.

Results: The sample consisted of 50 patients. There were increases in median weight (460 g; RIC 340-608 g), in length (1.9 cm; RIC 1.6 to 2.5 cm), and in head circumference (0.7 cm; RIC 0.5 - 0.7 cm) for each consultation attended by the patients. The WAZ media was -1.15 (95% CI, -1.50, -1.80) at the start of treatment and -0.39 (95% CI, -0.65, -0.12) at completion, with $p < 0.0001$. The HAZ was -1.60 (95% CI, -1.99, -1.21) when starting treatment and -0.98 (95% CI, -1.32, 0.65) at the end thereof, with 0.001 p. WHZ was 0.06 (95% CI -0.29, 0.43) at the beginning and 0.11 (95% CI, -0.17, 0.41) after the treatment, with no significant difference.

Conclusions: In patients with FA, statistically significant differences for WAZ and HAZ indicators before and after the medical-nutritional treatment were found. The negative effect on weight and height of some children with FA could improve with a proper approach between pediatric nutrition and gastroenterology.

129 PRESCRIPTION TENDENCY OF GASTRIC ACID SUPPRESSANTS IN HOSPITALIZED CHILDREN IN A UNIVERSITY HOSPITAL

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Background: There is over-prescription of proton-pump inhibitors (PPIs) and H₂-blocker receptors (H₂B) in the inpatient pediatric population. Acid suppressive therapy in hospitalized children has been associated with adverse events such as acute gastroenteritis and pneumonia, resulting in increased days of hospital stay, and augmented costs to the healthcare system. Furthermore, there are no international guidelines regarding the appropriate PPI and H₂B use in hospitalized pediatric patients.

Methods: Retrospective cross-sectional study. Patients between 1 and 15 years old, who were hospitalized between January 1st, 2013 and December 31, 2013, and received PPIs and/or H₂B, were included. Demographic information, the drug used, its indication, dose, administration route and length of therapy were abstracted by retrospective chart review. Guidelines for the appropriate use of PPIs and H₂B in pediatric inpatient population were proposed, based on the current guidelines available for adults. The collected prescription indications were evaluated by use of the proposed guidelines, in order to determine whether an indication was appropriate or not.

Results: 67 patients were included (mean age 6.9 years, SD 4.6, 55.2% male). 24 patients (38.5%) met the proposed criteria for prescription of gastric acid suppressants in hospitalized children. Intravenous ranitidine was used in 66 (98.5%) patients. The most frequent correct indications were gastroesophageal reflux disease in 8 (12%) and prevention of bleeding associated with stress in 8 (12%). The mean length of stay and length of acid suppressive therapy were 5.1 and 4.8 days, respectively. The most common unaccepted, but prophylactic indication was their use in vomiting and acute gastroenteritis.

Conclusions: PPIs and H₂B prescription patterns do not meet the proposed indications for pediatric inpatients, resulting in over-prescription in the pediatric inpatient section of a university hospital.

130 HYPOVITAMINOSIS D IN PEDIATRIC AND PREGNANT POPULATIONS IN A UNIVERSITY HOSPITAL

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Introduction: Vitamin D deficit is a public and global health problem. In Colombia and Latinamerica, there are few reports available on the prevalence of hypovitaminosis D in neonatal and pregnant populations. Although in equatorial countries it is assumed that constant UVB exposure potentially prevents vitamin D deficiency, a prevalence of hipovitaminosis D of 9%-83 % and 30-96% has been reported for pregnant women and newborns, respectively. We prospectively evaluated hipovitaminosis D prevalence in newborns and their mothers.

Methods: A prevalence study was conducted. Pregnant women who underwent labor in Hospital Universitario Fundación Santa Fe de Bogotá (HU-FSFB), Bogotá, Colombia, from October 2015 to January 2016 were included. Maternal and cord blood samples were obtained during labor. Peripheral blood samples were obtained from newborns with low vitamin D levels demonstrated on umbilical cord blood samples.

Quantitative determination of 25-hydroxvitamin D levels was performed by use of the chemiluminescent microparticle immunoassay, Architect 25 OH Vitamin D assay®. Vitamin D status was classified as sufficiency if 25 OH vitamin D levels ≥ 30 ng/mL, as insufficiency if < 30 ng/mL or ≥ 20 , and as deficiency if < 20 ng/mL.

Results: 85 pregnant women and 86 newborns were evaluated (1 twin pregnancy). 60 (69.7%) mothers and 74 (86%) newborns were found to have vitamin D deficit. The prevalence of vitamin D deficiency was 24 (27.9%) and 30 (34.8%), of insufficiency it was 36 (41.8%) and 44 (51.2%), and of sufficiency it was 26 (30.2%) and 12 (13.9%), for mothers and newborns, respectively. Peripheral confirmation was performed in 45 newborns: medium value of 17,6 ng/mL (± 5.42 SD). 32 (71.1 %) demonstrated deficiency (initial classification: deficiency 17 (53.1%), insufficiency 15 (46.9%) and 13 (28,9%) demonstrated insufficiency (initial classification: deficiency 1 (7,7%), insufficiency 12 (92.3%).

Conclusion: Vitamin D deficiency is a highly prevalent condition in both maternal and newborn populations. Studies to assess its prevalence in other areas the risk factors should be performed. Routine measurement of vitamin D levels and its appropriate substitution during pregnancy and the neonatal period are encouraged. Cuantification of Vitamin D levels in umbilical cord blood samples is a sensitive but unspecific test to identify hypovitaminosis D.

HEPATOLOGY

148 LONG-TERM (MORE THAN 10 YEARS) OUTCOME OF LIVER TRANSPLANTED CHILDREN

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Liver transplantation (LT) is an effective treatment for a variety of irreversible liver diseases for which there is no other satisfactory therapy, as well as for cases in which late diagnosis precludes other therapeutic options. The progress of surgical techniques and the monitoring of the complications had improved the long-term survival of patient with end-stage liver disease. Nevertheless, the long-term outcome of patients receiving liver transplantation during the pediatric age is not yet well described.

Aim: The aim of this study is analyse the long-term outcome of liver transplanted children having survived 10 years or more from liver transplantation.

Methods: The medical records of 108 patients younger than 18 years of age undergoing liver transplantation for end-stage liver disease from March 31, 1986 to December 31, 2005 were reviewed retrospectively. Actuarial patient and graft survival rates were determined at 10 and 20 years. The etiology of the liver disease and incidence of post-transplantation complications were determined.

Results: A total of 106 patients underwent 116 LTs. Seven (6.6%) out of the 106 patients died, but only 1 after 10 years of follow-up. Therefore, 99 (93.40%) patients are alive >10 years post liver transplantation, of whom 53 (53.53%) survived for 20 years or more. The male sex represented 51.51% of the cohort. Biliary atresia 32 (32.32%) and tyrosinemia 26 (26.26%) were the most common causes (58.58%) of end-stage liver disease in our population. The median recipient age was 3.58 years. All grafts (55.14% reduced livers, 44.85% whole organs) were from deceased donors. The median age of donor was 31 years. Four patients (4.04%) required retransplantation after ten years. On average, 0.6 late acute rejections (after 1 year post-transplant) per patient were registered. Overall, 23.23% of patients showed signs of chronic hepatitis at liver biopsy between 10 and 30 years of follow-up, and 18.18% presented liver cirrhosis. One patient developed cirrhosis due to chronic hepatitis E virus infection. Epstein Barr virus primary infection was seen in 16 patients. One patient developed post-transplant lymphoproliferative disease. At last follow-up, the mean alanine aminotransferases was 31 U/L (12-982) and bilirubin at 14.8 $\mu\text{mol/L}$ (4-765). The synthetic liver function was normal in all patients. Portal thrombosis was the only vascular complication seen in 6 patients (6.06%). The renal function was normal with glomerular filtration rate above 120 cc/min/1.73cm³. For metabolic screening, the median of BMI is 24.32 and only 1 patient developed type 2 diabetes.

Conclusion: Patient and graft survival, as well as liver function, are excellent in the long-term follow-up of liver transplanted children. The most frequent complication in the studied period is the development of chronic hepatitis (supposedly secondary to immune-mediated hepatocyte rejection).

149 MARKERS OF SLEEP-DISORDERED BREATHING AND METABOLIC RISK FACTORS IN PEDIATRIC NON-ALCOHOLIC FATTY LIVER DISEASE

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Objective: To determine whether markers of sleep-disordered breathing, other than obstructive sleep apnea, are associated with markers of liver injury and metabolic risk factors in pediatric non-alcoholic fatty liver disease (NAFLD).

Methods: Retrospective chart review of pediatric patients with NAFLD followed at the Hospital for Sick Children. Children ages 2-18 with NAFLD were included. Demographic, clinical, laboratory and polysomnography data were collected. Subjects were divided into groups based on: a) obstructive apnea hypopnea index (OAH) \geq or $<$ 5 events/h; b) Desaturation index (DI) \geq 6 or $<$ 6 events/h and 3) Arousal Index (AI) \geq 14 vs. $<$ 14 events/h. Markers of liver disease severity were compared between groups using Mann-Whitney or Student's t-test, as appropriate.

Results: Thirty children (70% male) were included in the study. Mean age (\pm SD) was 13 \pm 4 years and mean BMI z score 2.4 \pm 0.9. There was no difference in serum levels of ALT (91 vs. 112 U/L, p=0.52), AST (8.2 vs. 16.4 U/L, p=0.64), alkaline phosphatase (ALP, 28.3 vs. 33.6 U/L, p=0.84) and GGT (6.6 vs. 8.4 U/L, p=0.73) between those with a low and a high OAH. In addition, there was no difference between the groups in BMI z score (2.2 vs. 2.7, p=0.18); HbA1c (5.6% vs. 5.5%, p=0.50); fasting glucose (5.1 vs. 5.0 mmol/L, p=0.77), insulin (111 vs. 132 pmol/L, p=0.40), triglyceride (TG, 1.4 vs. 1.6 mmol/L, p=0.66), LDL cholesterol (2.3 vs. 2.9 mmol/L, p=0.19), HDL cholesterol (mean 1.1 vs. 1.2 mmol/L, p=0.36), and total cholesterol (mean 4.1 vs. 4.8 mmol/L, p=0.16). When dividing the cohort using the DI threshold, there was no difference between the groups in ALT (23 vs. 16 U/L, p=0.27), AST (63 vs. 43 U/L, p=0.24), ALP (206 vs. 215 U/L, p=0.85), and GGT (43 vs. 39 U/L, p=0.67). Further, there was no difference in BMI z score (2.2 vs. 2.9, p=0.06); HbA1c (mean 5.6 vs. 5.4%, p=0.60); fasting glucose (5.2 vs. 4.9 mmol/L, p=0.47), insulin (117.3 vs. 110.1 pmol/L, p=0.79), TG (1.4 vs. 1.5 mmol/L, p=0.88), LDL (2.3 vs. 2.8 mmol/L, p=0.23), HDL (1.2 vs. 1.1 mmol/L, p=0.55) and total cholesterol levels (4.1 vs. 4.6 mmol/L, p=0.33). Finally, we determined if there was a relationship between AI and the above parameters. Again, there were no differences in ALT (94 vs. 103 U/L, p=0.80), AST (54 vs. 58 U/L, p=0.80), ALP (236 vs. 186 U/L, p=0.25), and GGT (47.1 vs. 38.1 U/L, p=0.40), nor in any metabolic parameters: BMI z score (2.2 vs. 2.6, p=0.29), HbA1c (5.5 vs. 5.5%, p=0.94), fasting glucose (5.2 vs. 4.9 mmol/L, p=0.45), insulin (113 vs. 122 pmol/L, p=0.68), TG (1.6 vs. 1.4 mmol/L, p=0.42), LDL (2.4 vs. 2.7 mmol/L, p=0.48), HDL (1.1 vs. 1.2 mmol/L, p=0.57), and total cholesterol levels (4.2 vs. 3.5 mmol/L, p=0.55).

Conclusion: This study did not find associations between markers of sleep-disordered breathing and evidence of liver injury or metabolic factors in children with NAFLD. Further studies to assess the impact of sleep-disordered breathing on NAFLD are needed.

150 OUTCOME OF NON-PHARMACOLOGICAL MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE IN HISPANIC VS. NON-HISPANIC CHILDREN

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a slowly progressive disorder of fat accumulation within hepatocytes with gradual development of inflammation, focal necrosis, and in many cases, fibrosis. It is the most common liver disease in the United States, particularly in those who are of Hispanic descent, male gender, and/or obese.

The pathophysiology of NAFLD is poorly understood but is much more prevalent in obese individuals. A number of events may precipitate the injury associated with this disorder. Insulin resistance is often described as the "first hit" or injury that predisposes and individual to NAFLD.

This can lead to alterations in hepatic fat metabolism and accumulation of lipid droplets within the hepatocytes. Oxidative stress or a 'second hit' is required to develop inflammation and fibrosis, and diet, environment, drugs, and toxins are believed to be a source of this stress.

Purpose: To determine the outcome of NAFLD using non-pharmacological management including lifestyle modification involving daily exercise and dietary modification in Hispanic versus non-Hispanic children.

Methods: A retrospective study of individuals younger than 19 years. Information regarding gender, ethnicity, age at diagnosis, BMI, family history of liver disease, and other comorbidities were collected.

Data collected included BMI percentile, Z-score for weight, ALT, AST, GGT, liver biopsies, and liver ultrasounds, which were obtained at the time of diagnosis and after 6-9 months of lifestyle modification. The patients were divided into two groups: Hispanic and non-Hispanic. Outcome was improvement of BMI Z-scores, AST and ALT at the end of 9 months.

Results: A total of 42 patients with NAFLD were included to date in the study; of which 30 were Hispanic. All patients were evaluated by the same hepatologist and received the same counseling regarding lifestyle modification. Median age at diagnosis was 10 and 11.6 years respectively. Median ALT level at time of diagnosis was 121 unit/liter in the Hispanic group and 225 unit/liter in the non-Hispanic. After 9 months of non-pharmacologic management; 66% of patients in the non-Hispanic group had a normal ALT level, and 16% showed improvement without normal ALT levels. On the other hand in the Hispanic group, only 7% of patients had normal ALT at the end of 9 months, 33% had improvement of ALT, while 50% had worsening of the ALT. ($p = 0.001$). Table 1.

Conclusion: Nonpharmacologic management with lifestyle modification resulted in limited improvement in Hispanic patients with NAFLD, in comparison to non-Hispanic patients. While compliance may play a major role in patient outcome, differences in outcome in Hispanic and non-Hispanic children may suggest some other underlying genetic modifiers. Also, the low rates of improvement in children with intensive lifestyle modification suggests a strong need for other therapeutic strategies for management of this disease.

Table -1 Results of non-pharmacological management in patients with NAFLD

	Hispanic n=30	Non-Hispanic n=12
Median age of diagnosis	10	11.6
Male	26 (86%)	5 (100%)
Normal ALT at after Management	5 (17%)	8 (66%)
Improved ALT at after Management	10 (33%)	2 (16%)
Worsening of ALT after Management	15 (50%)	2 (16%)
Worsening of BMI Z score after Management	11 (36%)	2 (16%)

151 CARBOHYDRATE-RESTRICTED DIET LOWERS HEPATIC TRIGLYCERIDE IN OBESE ADOLESCENTS WITH METABOLIC SYNDROME AND NON-ALCOHOLIC FATTY LIVER DISEASE

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Background: Non-alcoholic fatty liver disease (NAFLD) has become the most common cause of chronic liver disease in children. Obesity, insulin resistance and metabolic syndrome (Met-S) are strongly associated with NAFLD. The pathophysiology of NAFLD indicates that the presence of excess triglycerides (TG) in liver is an absolute requirement for disease progression to occur. TG is derived primarily from peripheral lipolysis as well as lipid synthesis from carbohydrate (CHO) precursors in liver. While decreasing adiposity is the mainstay of therapy, data in adults have shown that dietary carbohydrate restriction is more effective in reducing hepatic TG content than calorie restriction. To date, the effectiveness of carbohydrate restriction on pediatric NAFLD has not been studied.

Objective: The aim of this study is to determine whether a 6-month dietary carbohydrate-restriction is superior to calorie-restriction in reducing hepatic TG content in children with biopsy proven NAFLD and Met-S.

Methods: Nineteen subjects with Met-S and NAFLD (14 male and 5 female) ages 11-17 years were enrolled and randomized to either a carbohydrate-restricted diet (20% carbohydrates, 35% protein and 45% fat) or calorie-restricted diet (50% carbohydrate, 15-20% protein and 30-35% fat) for 6 months. Hepatic proton magnetic resonance spectroscopy (1H-MRS) and serologic testing were obtained at baseline, after 2 months and after 6 months of dietary intervention.

Results: There was no difference between the carbohydrate-restricted and calorie-restricted group in BMI z-score change from baseline to 2 months or 6 months post-intervention. Hepatic TG decreased significantly more in carbohydrate-restricted subjects (mean \pm SD, $-26.80 \pm 17.60\%$, $-31.61 \pm 25.95\%$ at 2 months and 6 months, respectively) than in calorie-restricted subjects ($3.80 \pm 20.18\%$, $19.38 \pm 28.01\%$). The plasma alanine aminotransferase (ALT) level was also significantly reduced in carbohydrate-restricted subjects compared to calorie-restricted subjects ($p < 0.05$ at 2 months and $p = 0.004$ at 6 months).

Conclusions: This preliminary study shows that a carbohydrate-restricted diet effectively reduces hepatic TG and ALT in obese adolescents with NAFLD and Met-S.

152 NEONATAL LIVER FAILURE DUE TO HERPES SIMPLEX VIRUS INFECTION: A TERTIARY LIVER CENTRE EXPERIENCE

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Introduction: Neonatal liver failure (NLF) though rare is a life-threatening condition. Liver transplants (LTx) have made a substantial improvement to the mortality and morbidity rates in this group of patients. Infections contribute to a sizeable cause of NLF and Herpes simplex (HSV) infection is the commonest viral infection.

Aim: To report the incidence of NLF due to HSV and their outcome at a national pediatric liver transplant centre 1991-2014.

Methods: Retrospective analysis of liver unit data and medical notes of neonates admitted with acute liver failure. NALF was defined as age < 28 days, admitted with acute liver failure (PT > 15 or INR > 2 not correctable by Vitamin K) between 1991 to 2014. The primary outcome measure in NLF was survival without transplantation, death or transplantation.

Results: 133 neonates with NLF were identified between 1991-2014. All babies were transferred from other hospitals. The other etiologies included Galactosemia (n=29, 21.8%), neonatal haemochromatosis (n=26, 19.5%), mitochondrial causes (n=10, 7%), HLH (n=4, 3%), metabolic conditions (n=8, 6%) and infections (n=25, 18.7%). In 31 babies (16.5%), the cause was indeterminate. The infectious group was predominated by the viruses (n=21), Herpes simplex group being the most common (n=16, 12%). Of the 16 babies with HSV neonatal failure, 7 were girls

and 9 boys. All babies were term except two being premature at 34 and 36 weeks. History of genital lesions was present in only two mothers. The median age of presentation was 9 days (2-21 days). All babies presented with signs of sepsis and only 4 babies had vesicles on clinical examination. Surface swabs were positive in 9 and blood PCR in 12 babies. HSV was type 1 in 7 babies and type 2 in 6. 3 babies did not have the type documented. The median Prothrombin time was 45 secs (18-120). All 10 babies required multi-organ support in form of ventilation, inotropes and renal replacement therapy and of these only 4 survived. The total survivors in this cohort were 6, 5 -medical treatment and one-transplant. 10 babies died (2 on the waiting list for liver transplant, 2 after LTx and 6 on medical management). All babies who died, including the ones after LTx, were receiving multi-organ support. The two neonates transplanted at 12 days (weight 3.5 kg) and 20 days (wt 3.4 kg) died at 3 days and 43 days respectively. The only neonate surviving after LTx was transplanted at 15 days of age, weighing 2.5 kg. One baby was listed for transplant but suspended due to multi-organ failure (MOF) but then went on to improve with medical support and eventually recovered without a LTx.

Conclusion: Herpes simplex virus infection is a common cause of NLF. Early referral, early start of acyclovir and prompt management of intensive care should be instituted in these children as progression to multi-organ failure is rapid. LTx can be offered to a select sub-group of children with isolated liver failure who recovered from MOF.

153 PEDIATRIC LIVING-RELATED LIVER TRANSPLANTATION-EXPERIENCE IN CENTRAL TAIWAN

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Background: Pediatric living-related liver transplantation (LRLT) is widely accepted as treatment for children with endstage liver disease and acute liver failure. The pediatric LRLT program was started in 2006 in Taichung Veterans General Hospital, the only LTx medical center in central Taiwan. We aimed to review the outcome and complications of LRLT of our program.

Method: We reviewed children who received LRLT between January 2006 and December 2014. Charts were reviewed including patient characteristics, transplantation indication, operation method and the graft selection. The main outcomes were 5-year survival of patients, and graft and the complications after LRLT.

Result: Within the study period, twenty-five children (12 boys and 13 girls) received LRLT. The age was between 5 months to 17 years old. The median age was 1 year, 5 months. There were 8 patients under one year of age (32%). For patient with biliary atresia (17, 68%), the main indication for LRLT was advanced cirrhosis with portal hypertension, with or without GI bleeding. Recurrent cholangitis also contributed to transplantation. The other etiologies (8, 32%) included acute fulminant hepatitis (3), Wilson's disease (1), autoimmune hepatitis (1), Alagille's syndrome (1), Budd-Chiari syndrome (1) and idiopathic liver cirrhosis (1). The donor liver segment was chosen according to the size of recipient (left lateral segment: 12; left lobe: 11; right lobe: 2). Five patients expired during follow-up (20%). The causes of mortality included H1N1 infection, PTLN, recurrent autoimmune hepatitis, sepsis and subdural hemorrhage each. No re-transplantation was performed after LRLT. Five-year patient and graft survival rate were both 79.5% calculated by Kaplan-Meier survival analysis. For patients under one year of age, the 5-year survival rate was 85.7% (7/8). For patients older than one year, the 5-year survival rate was 76.5% (13/17). Operative complications included hepatic vein stenosis (1), portal hypertension (3), biliary complication (7). Infection was defined as patient with fever response to antibiotic treatment or positive bacterial culture. Seventeen patients (68%) had at least one episode of infection after LRLT. Seven patients (28%) had acute rejection (early or late). *De novo* HBV infection occurred in 3 patients after LRLT. ABO incompatibility LRLT was done in a 10-month-old female with biliary atresia who survived for more than 7 years to the present.

Conclusion: Biliary atresia is the most common underlying disease in our series in children who need LTx. The survival rate of patients less than one year of age had relatively good outcome compared to older ages in our study. Complications and mortality might occur after LTx that need careful management for the best results. ABO incompatibility LTx remains a choice of pediatric LRLT as needed.

154 TENDER HEPATOMEGALY AND ABNORMAL PATTERN OF HEPATIC STEATOSIS IN NON-COMPLIANT ADOLESCENTS WITH POORLY CONTROLLED TYPE 1 DIABETES MELLITUS

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Background: Glycogenic hepatopathy (GH) is an under-diagnosed condition in adolescents with poorly controlled Type 1 diabetes mellitus (T1DM). Though Mauriac syndrome has been described as a complication of T1DM and characterized by growth retardation, delayed puberty, and cushingoid facies, most patients do not present with these classic features. In this study we describe clinical-pathologic characteristics, which are unique and specific to this condition in adolescents with poorly controlled T1DM.

Methods: Patients with known DM1 who were found to have hepatomegaly or elevated liver function tests were referred to hepatology services at a single, tertiary care institution over a period of 18 months. Initial evaluation included screening for common liver disorders, imaging and liver biopsy. Patient characteristics including age at diagnosis of diabetes, HbA1C levels, age at diagnosis of liver dysfunction or hepatomegaly, glycemic control and compliance were noted.

Results: Of the 19 patients with Type 1 diabetes mellitus and hepatic involvement, there was a female predominance (15:4), with median age of 15 (11-19) years and normal BMI at presentation. Median age at diagnosis of diabetes mellitus was 9 (1-16) years. Hepatomegaly was noted in 18/20 and was the reason for referral; with 2/20 being referred for elevated LFTs. Half (9/18) had developed acute tender liver enlargement requiring an unscheduled visit to the clinic or Emergency room. The median age at liver presentation was 15 (11-19) years. Patients with hepatic involvement demonstrated poor glycemic control with a median HbA1C of 12.4 (7.6-14.2) % and reported non-compliance with insulin regimen. Liver enzymes varied widely, ranging from 21-1461 IU/l (AST) and 17-564 IU/l (ALT) at the time of diagnosis of hepatomegaly, which was confirmed in all patients by imaging. Interestingly, hepatomegaly showed a dramatic decrease with resolution of abdominal pain with improvement in blood sugar even in the absence of a detectable change in HbA1C. Ten patients had a liver biopsy, which showed abnormal presence and pattern of steatosis with perisinusoidal deposition of fat, which was unusual and distinct from fatty liver seen in metabolic syndrome. Though glycogen deposition was also seen, it did not show any distinct characteristics.

Conclusion: Poorly controlled T1DM in non-compliant adolescents can lead to liver dysfunction presenting with acute onset of tender hepatomegaly and elevated LFTs, which improve with glycemic control. Presence of perisinusoidal fat in the liver likely represents an as-yet unidentified mechanism of development of hepatic dysfunction in T1DM requiring further investigation.

155 LIVER INTERVENTIONAL RADIOLOGY IN CHILDREN: A 20 YEAR EXPERIENCE

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Background: Diagnostic and therapeutic management of liver disease, and in particular in recipients of liver transplants, includes the use of interventional radiology procedures. Although challenging, the use of this technique in children is an emerging field and provides a large number of possibilities for diagnosis and/or therapeutics of liver disease.

Aim: The authors report the interventional radiology experience in children and the changes in type of procedures performed over two decades in an adult facility care associated with a liver transplantation centre.

Methods: Descriptive analysis of interventional radiology procedures performed in a twenty-year period (October 1995 to December 2015) in children (<18 years) with liver disease. All patients were admitted.

Demographic features, weight, type of procedure, previous liver transplantation (LT), time since LT, success of the procedures, complications and mortality were recorded and analyzed. The variation of the type of procedures performed over time in four periods (1995-2000; 2001-2005; 2006-2010; 2011-2015) was also assessed.

Results: 101 procedures were performed in 59 patients (median 1 procedure/ patient (1-5)); 51% (30) males; median age: 9 years (7M-16Y); median weight: 28 Kg (4,6-70); Type of procedure: 31 abdominal selective angiography (SAA); 11 cavography, 31 percutaneous colangiography (PCT), 10 direct portography (DP), 8 TIPS placement; 10 combined procedures (8 SAA + cavography; 1 DP + PCT; 1 SAA + DP).

81 patients (80%) had previous LT. Median time between LT and procedure was 185 days (1-3369 days). In 75% procedures, there was therapeutic intervention.

There were complications in 17% (17) of procedures: 2 major complications: hypovolemic shock (2); 15 minor: fever (4), gastrointestinal bleeding (3), endotoxemia (2), small hematoma (2), cholangitis (1), catheter fracture (1), local pain (1), biliary leak (1). No patient died from a procedure. Intervention was successful in 64% (65). In the period 1995 to 2000, 19 procedures were performed (10 PCT; 4 cavography; 3 SAA; 2 DP); from 2001 to 2005, there were 14 procedures (8 SAA; 2 PCT; 2 DP; 1 cavography; 1 SAA + cavography); in the period 2006-2010, 28 procedures were performed (9 SAA; 9 PCT; 4 SAA + cavography; 4 cavography; 1 DP + PCT; 1 DP) and from 2011 to 2015, there were 40 procedures (11 SAA; 10 PCT; 3 ASA + cavography; 5 DP; 2 cavography; 8 TIPS placement; 1 ASA + DP).

Discussion: The great majority of interventional radiology procedures were performed in children previously submitted to LT. We highlight the high rate of therapeutic interventional procedures in this series, such as the low prevalence of major complications. The number of procedures has been growing over the years, and the types of procedures have also been changing, currently including complex procedures such as TIPS placement.

156 LONG TERM DEVELOPMENTAL OUTCOME OF INFANTS (<5 kg) PRESENTING WITH ACUTE LIVER FAILURE

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Introduction: Acute liver failure in neonates is rare, but carries a high mortality. Neonatal liver failure can be defined as failure of the synthetic function of liver within 4 weeks of birth. Acute liver failure in neonates differs from children with regard to aetiology and outcome. Early diagnosis and referral to a pediatric liver centre is recommended as liver transplantation is the only definitive treatment when supportive or a disease-specific treatment fails. Very little is known about the developmental outcome in these children. We studied the long-term developmental outcome in neonates weighing less than 5 kg presenting to a national tertiary liver unit with acute liver failure.

Methods: Retrospective review of case notes was undertaken and PEDS (Parents' Evaluation of Developmental Status) Parent questionnaire was sent out to parents of eligible patients. PEDS questionnaire elicits parents' concerns regarding cognitive, language, self-help, personal-social, and motor skills.

Results: Eligible number of patients (<8yrs at the time of sending out questionnaires) were 25. Age on admission with acute liver failure ranged from 1 to 210 days. Aetiologies included GAL (galactosaemia), NNH (neonatal haemochromatosis), ALF due to HSV and undetermined causes. Questionnaire response received in 13 (52%). Gross and fine motor concerns were expressed in 23%. Expressive language concerns were present in 30%. Social/emotional and school concerns were present in 38%. Conclusion: Results from this study have provided quantitative information regarding developmental outcome in this cohort of patients.

157 TRANSIENT ELASTOGRAPHY MEASUREMENT OF LIVER AND SPLEEN STIFFNESS IN CHILDREN WITH BILIARY ATRESIA AS A NON-INVASIVE MARKER OF PORTAL HYPERTENSION

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Background: Children with biliary atresia (BA) have an increased risk of developing gastrointestinal (GI) varices secondary to portal hypertension (PHT). The diagnosis of PHT in children is often made by endoscopy, an invasive procedure to directly visualize any GI varices. Liver and spleen stiffness measurements have been suggested as non-invasive predictors of liver fibrosis.

Aim: Assess the feasibility and prognostic value of spleen stiffness measurements (SSM) and liver stiffness measurements (LSM) by transient elastography (TE; Fibroscan) in respect to PHT in children with BA.

Methods: A total of 76 patients (41M) with BA underwent TE (64 had both LSM and SSM, 12 had only LSM) during a hospital visit. All patients had undergone a Kasai portoenterostomy and had their native liver and no ascites. Upper and lower surveillance GI endoscopies were performed in 34 patients, while 6 had emergency endoscopies due to acute GI bleeding.

Results: SSM by Fibroscan was feasible in 64 of 76 patients, while LSM was feasible in all 77. Median platelet count (PLT), haemoglobin (Hb), INR, albumin, bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), spleen size, Clinical Prediction Rule (CPR) were 163x10⁹/L, 116g/L, 1.13, 40.1g/L, 40.9 µmol/L, 124IU/L, 118IU/L,

584IU/L, 315IU/L, 13.5cm and 216, respectively. LSM had a significantly higher success rate than SSM (88.4% vs. 72%, $p=0.02$). SSM was not recorded in 12 out of 22 patients with normal spleen size. LSM and SSM were significantly higher in patients with any varices (31.6 and 47.7 vs. 16.6 and 14.6kPa, $p=0.003$ and <0.001 , respectively), with cut-off points of 21.1kPa and 22.5kPa giving AUC of 0.74 ($p=0.003$) and 0.95 ($p<0.001$) respectively; clinically significant varices (38.2 and 45.5 vs. 21.1 and 29.4kPa, $p=0.006$ and 0.01, respectively), with cut-off points of 28.4kPa and 37.9kPa giving AUC of 0.76 ($p=0.001$) and 0.73 ($p=0.006$) respectively; active or a history of variceal haemorrhage (50.7 and 51.9 vs. 20.1 and 30.1kPa, $p=0.002$ and 0.005) with a cut-off point of 31.8kPa and 25.7kPa giving AUC of 0.82 ($p=0.004$) and 0.71 ($p=0.04$) respectively; and a CPR below the cut-off point of 116 (33.1 and 50.1 vs. 18.8 and 22.8kPa, $p=0.002$ and <0.001 , respectively) with cut-off points of 23.3 kPa and 29.1kPa giving AUC of 0.72 ($p=0.001$) and 0.86 ($p<0.001$).

Conclusions: SSM and LSM by TE can be useful in the management of children with BA. Only 3 children, with GI bleeding, had SSM of 75 kPa suggesting a more reliable application in BA children. Both measurements have a predictive role in the diagnosis of PHT and presence of varices.

158 PERIPHERAL BLOOD MACROPHAGE ACTIVATION PATTERNS IN CHILDHOOD CHRONIC LIVER DISEASES

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Background: Macrophage polarization is an essential component of innate immunity and orchestrates host pro-inflammatory (M1), pro-TH2 inflammation (M2a), immune regulatory (M2b), and tissue remodeling (M2c) signals upon incoming pathogens and toxic injuries. Differential patterns of M1/M2 macrophage activation have been implicated in the pathogenesis of hepatitis and liver fibrosis. The purpose of this study was to investigate the circulating macrophage populations and their specific M1/M2 polarization profiles in children with chronic liver diseases.

Methods: Thirteen patients, aged 1 to 15 years old, with chronic liver diseases (7 non-alcoholic steatohepatitis, 2 Wilson's disease, 2 biliary atresia, 1 choledochal cyst with post-operative cholangitis, 1 idiopathic chronic hepatitis) were enrolled in the study. Twenty-three school-aged children, admitted for growth hormone study, were assigned as the control group. Clinical symptoms, laboratory and image findings were recorded. Peripheral blood macrophage populations and polarization-related surface markers were evaluated by the flow-cytometry.

Results: Percentage of circulating macrophage-like populations (PM-2K+ CD14+) and macrophages (PM-2K+ CD14-) were higher in pediatric patients with chronic liver disease than the control (11.5% vs. 5.1%, $p=0.09$ and 4.5% vs. 0.1%, $p<0.01$). Both the peripheral blood macrophage-like cells and macrophages showed suppressed M1 markers (CCR7+ CD86+, 17.4% vs. 64.3% and 6.9% vs. 29.6%; both $p<0.01$). Contrarily, bias towards M2 polarization was found in the macrophage-like populations (M2a: CCR7- CXCR1+, 11.1% vs. 0.3%; M2b: CCR7- CD86+, 25.8% vs. 4.1%; M2c: CCR7- CCR2+, 15.2% vs. 2.5%; all $p<0.01$) but not in the circulating matured macrophages (M2a 3.3% vs. 1.6%, $p=0.23$; M2b 6.4% vs. 6.4%, $p=0.99$; M2c 10.3% vs. 5.8%, $p=0.21$). Interestingly, nearly abolished M1 activation was observed in the circulating macrophages of patients with non-alcoholic steatohepatitis (0.1~1.7%) and biliary atresia (0 and 0.5%).

Conclusions: Differential activation patterns of circulating macrophage populations were found in children with chronic liver diseases. Increased peripheral blood macrophages but low M1 expressions might imply depletion of pro-inflammatory innate immunity. However, lack of significant M2 polarization indicates a potential role of inadequate immune tolerance in the development of chronic liver disorder.

159 SPONTANEOUS PERFORATION OF BILE DUCT: A STUDY FROM A TERTIARY CARE HOSPITAL IN PAKISTAN

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Spontaneous perforation of bile duct (SPBD) is a rare and often misdiagnosed entity. Despite being rare, it is still the second only to biliary atresia as the most common surgical cause of jaundice in infants. We describe 22 clinical presentations, treatments and outcomes in cases, which posed several diagnostic and management difficulties.

Patients & Methods: Over a 20-month period, 22 patients were seen with SPBD. Clinical presentation, biochemical abnormalities, imaging details and management as data were recorded prospectively.

Results: Of these 22 patients, there were 12 males and 10 females age ranging in age from 1.5 months – 36 months. Presentation, biochemical parameters and imaging result are shown in the table. All 22(100%) had abdominal distension and ascites. 15 (68.2%) had jaundice at time of presentation, 6 (27.3%) had vomiting, 6 (27.3%) were febrile, 6 (27.3%) had abdominal pain, 5 (22.7%) had clear history of passing acholic stools, while 3 each (13.6%) had bilateral inguinal hernia and peritonitis. Choledochal cyst was seen in 7 (31.8%) and acquired biliary atresia in 1(4.5%). Elevated liver enzymes (ALT and AST) were present in 16 patients (72.7%) and 5 (22.7%) had bilirubin above 3 mg/dl. Coagulopathy was seen in 8 (36.6%) patients. Abdominal USG showed presence of ascites in all 22 (100%), hydrocele in 2 (9.0%), inguinal hernia in 1 (4.5%), choledochal cyst in 7(31.8%) and atretic gallbladder signifying acquired biliary atresia in one (4.5%) patient. HIDA scan was diagnostic in all 17 (77.27%) in which it was performed. MRCP was done in 3 (13.6%) patients. Most patients were managed with intravenous antibiotics, percutaneous drainage and t-tube insertion while patients with choledochal cysts required cholecystectomy with Roux-en-y choledochjejunostomy. Two patients(9.09%) died from surgical complications.

Conclusion: Spontaneous Perforation of Bile Duct should be suspected as an important cause of neonatal biliary ascites or peritonitis. Timely recognition and intervention is associated with favorable outcome.

160 NUTRITIONAL STATUS DYNAMICS ASSESSMENT IN CHILDREN WITH CHRONIC HEPATITIS C DURING THE COMBINATION ANTIVIRAL THERAPY

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Background: Combination therapy (pegylated interferon + ribavirin) is the most effective treatment method of chronic hepatitis C in children now. It is known that one of the side effects of antiviral therapy is the reduction of appetite in infants which results in body weight decrease. The aim of the research is to assess the nutritional status of children receiving a course of combination antiviral therapy (pegylated interferon + ribavirin) in children with chronic hepatitis C.

Materials and Methods: Ninety-four children (46 girls and 48 boys in age from 3 to 17 years, mean age 10 years) with chronic hepatitis C received antiviral therapy (pegylated interferon 60 g / m² - 1 time per week + ribavirin - 15 mg / kg / day daily). The assessment of nutritional status included measurement of body weight, height, calculation of body mass index (BMI) and BMI Z-score. Body composition was examined

by impedance analysis, amounts of fat and lean body mass were measured. The assessment study was conducted before the start of therapy and after its termination.

Results: The therapy yields an average decrease in body weight by 3.9 kg (from 0.8 to 13 kg) in 80 children (85%). The median BMI z-score of the surveyed children before the start of antiviral treatment was 0.28 [-0.36- + 1.57] and after its termination -0.49 [-1.53-0.11], $p= 0.001$. The initial value of fat body mass and lean body mass were 5.0 [3.3-10.2] and 14.3 kg [11, 6-23.1] kg, after completing the course of treatment of 5.4 [3.0-9.4] kg and 13, 8 [11,8-21,9] kg, $p= 0.28$ and 0.01 respectively.

Conclusion: Combination antiviral therapy in children with chronic hepatitis C is accompanied by reduction of absolute amount of lean body mass and BMI Z-score reduction and thus requires timely administration of nutritional support.

161 DEATH IS RARE AND PROGRESSION TO TRANSPLANT IS SLOW, DESPITE A BURDEN OF PORTAL HYPERTENSION, IN LONGITUDINAL OUTCOMES OF ALPHA-1-ANTITRYPSIN DEFICIENCY FROM THE CHILDREN COHORT

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Background: The Childhood Liver Disease Research Network (ChiLDReN) is a longitudinal study of pediatric liver diseases, including subjects with alpha-1-antitrypsin deficiency (AAT), aiming to document the natural history in North America, identify predictors of clinical outcomes and identify disease modifiers.

Objective: Summarize and identify predictors of clinical outcomes, including portal hypertension (PHT), liver transplantation and death, in AAT subjects with native liver.

Methods: PIZZ and PISZ subjects, 0-25y, have enrolled since November 2007 at 14 North American tertiary care centers, with liver disease as defined by having one of: neonatal cholestasis, chronically elevated AST, ALT or GGT (>1.25xULN), chronic hepatomegaly, clinical findings or complications of PHT or cirrhosis, impaired liver synthetic function, or liver biopsy abnormalities other than globular inclusions. Baseline visits recorded data from medical records, history, physical exam, laboratory, imaging and other information obtained as part of routine clinical care, that were updated at prospective annual visits. PHT was defined as: (1) history of a complication of PHT (variceal hemorrhage, ascites, or hepatopulmonary syndrome) or (2) clinical findings consistent with PHT (splenomegaly [spleen > 2 cm below the costal margin] or thrombocytopenia [platelet count < 150,000]). PHT was "absent" if none of the criteria were met. Available clinical studies (ultrasounds, endoscopies, etc.) were examined to confirm the PHT assignment. Kaplan-Meier methods and Cox regression were used to analyze time to event and correlated longitudinal dichotomous outcomes. 71 subjects with liver transplant prior to enrollment are not included in this analysis. Results: 301 subjects enrolled with native liver (60% male). 223 (74%) entered the cohort without PHT, and approximately 3% of these developed PHT per year (Table 1). 27 of 301 had liver transplants during 790 person-years of follow-up. 25 of the 27 subjects transplanted entered the cohort with PHT. One death was reported following transplant. Physical exam and laboratory measures associated with future development of PHT included changes in weight, height, head circumference, INR, total bilirubin, AST, and GGTP ($p<0.05$), although small numbers of events has so far prohibited the development of a predictive algorithm with useful specificity. Significantly lower height Z-scores, mid arm circumference, and triceps skinfold thickness were seen after development of PHT compared to those without PHT ($p<0.05$).

Conclusions: Children and young adult AAT patients at tertiary care centers have a significant burden of PHT, affecting growth parameters, but progress slowly to liver transplant. Death is very rare in the transplant era. PHT almost always precedes transplant by several years. The specificity of predicting clinical outcomes will require more study. There is likely an important role for unidentified genetic and environmental modifiers.

Outcome		Baseline	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
Age (Years)	N	301	197	147	115	79	60	41	23	3
	Median (IQR)	4.67 (7.85)	6.02 (7.32)	6.71 (7.23)	7.86 (7.38)	8.12 (7.01)	9.04 (5.37)	10.79 (5.16)	10.72 (4.83)	13.91 (6.56)
PHT	Cumulative n	78	84	89	94	98	100	100	100	100
	KM estimate (95% CI)	0.74 (0.69,0.79)	0.71 (0.66,0.77)	0.69 (0.63,0.74)	0.65 (0.59,0.71)	0.62 (0.55,0.68)	0.59 (0.52,0.67)	0.59 (0.52,0.67)	0.59 (0.52,0.67)	0.59 (0.52,0.67)
	Person-Years (Time on study)	0	164.5	295	392.5	462.7	508.9	542.5	558.4	560.3
Transplanted	Cumulative n	0	10	18	21	23	25	26	26	27
	KM estimate (95% CI)	1	0.96 (0.93,0.98)	0.91 (0.88,0.95)	0.89 (0.85,0.94)	0.88 (0.83,0.93)	0.85 (0.79,0.91)	0.84 (0.77,0.90)	0.84 (0.77,0.90)	0.56 (0.11,1.01)
	Person-Years (Time on study)	0	223.7	403	537.1	639.5	710.8	759.9	785.5	789.6

162 THE ROLE OF TRANSIENT ELASTOGRAPHY IN THE ASSESSMENT OF CYSTIC FIBROSIS-ASSOCIATED LIVER DISEASE

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Background: Cystic Fibrosis-associated liver disease (CFLD) occurs in 30% of patients, and 10% develop advanced fibrosis. CFLD manifests by age 18 in 90% of cases and is the third most common cause of mortality in CF patients. CFLD diagnosis and monitoring are challenging as specific tests for detection have not been developed and existing investigations do not correlate well with presence or severity of disease. The Aspartate Aminotransferase Platelet Ratio Index (APRI) is one tool that has been validated as a surrogate marker of hepatic fibrosis in other chronic liver disease.

Transient Elastography (TE) is a novel, rapid, non-invasive method for assessing liver stiffness (LS). Studies suggest it may be valuable in the assessment of liver fibrosis in pediatric patients with liver disease, though its role in detecting CFLD has only begun to be explored. The purpose of this study was to assess the utility of APRI and TE in identifying liver fibrosis in pediatric CF patients.

Methods: Patients 2-18 years were recruited from the British Columbia Children's Hospital Cystic Fibrosis clinic. Patients were determined to have CFLD using standard criteria. Where the original basis for CFLD diagnosis was unclear from chart review, patients maintained on ursodeoxycholic acid were included in the CFLD group. Charts were reviewed for demographic and clinical data. Each patient underwent TE by a trained operator.

Results: Of the 55 patients that were included in the study (50.9% male, mean age 11.6 (3.8) years) 49% were homozygous for $\Delta F508$ gene and 22 patients had CFLD. All mean liver enzymes were higher in the CFLD group, significantly ALT ($p=0.031$) and ALP ($p=0.030$). Mean LS as determined by TE was higher in the CFLD group (5.92 vs. 4.54; $P 0.0147$). APRI was higher in the CFLD group but not significantly different (0.396 vs. 0.324, $p=0.119$). Linear regression showed a mild positive association between TE and APRI (Slope 0.058 +/- 0.01, CI 0.038-0.79, $R^2 0.386$).

Discussion: CFLD is one of the leading causes of morbidity in CF, but limitations of existing tests hamper diagnosis and monitoring. Liver stiffness scores were higher in CFLD patients and correlate with APRI values, suggesting that TE may have clinical applications for identifying and following patients with this condition. Further studies are needed to determine the role of TE in CFLD.

163 LIVER SIZE AND GALLBLADDER ABNORMALITIES IN PATIENTS WITH EXTRAHEPATIC PORTAL VEIN OBSTRUCTION

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Background: The extrahepatic portal vein obstruction (EHPVO) is a vascular disorder characterized by an obstruction of the extrahepatic portal vein, with or without involvement of the intrahepatic portal vein or splenic vein or superior mesenteric vein. In many studies, EHPVO is reported as a major cause of portal hypertension in pediatric patients. An abdominal ultrasonography allows evaluation of liver size and gallbladder abnormalities. Modifications in blood flow resulting from EHPVO have been associated with the decreased liver size, and this phenomenon could be related with an increased incidence of gallbladder varices and gallstones.

Objectives: The aim of the present study was to assess the changes in liver size and gallbladder ultrasonographic findings in patients with extrahepatic portal vein obstruction, and study the correlation between the presence of gallstones and reduced liver size.

Methods: The study included 82 patients with EHPVO followed at university hospital. Ultrasonography was done using a Toshiba Power Vision 6000 with sectorial (3,75MHz) and linear (5MHz) transducers. References of normal liver size were based on tables established by Konus et al.

The presence of gallstones, biliary sludge and gallbladder wall thickening (greater than 2.5mm) were investigated. Statistical analysis was performed using Chi-square and a 5% significance level was adopted.

Results: The average age at the moment of ultrasonographic evaluation was 14.5 years, with a median of 13.4 years; 65% (n=53) of subjects were male and 35% (n=29) female. Reduction in liver size was observed in 41.5% (n=34). The prevalence of gallbladder ultrasonographic findings was 73% (n=60) – gallbladder wall thickening/gallbladder varices being the most common finding (58.5% - n=48), followed by gallstone (14.5% - n=12), however 8 patients had both. In 4 cases, gallbladder was not assessed through ultrasonography due to previous cholecystectomy. No examination showed the presence of biliary sludge. In the group of patients with gallstones (n=12), 50% (n=6) presented reduced liver size and the same number had a normal liver size – no statistically significant difference was observed ($p > 0.05$). In the other hand, occurrence of gallbladder wall thickening / gallbladder varices were observed in 27 out of 34 patients with reduced liver size, establishing a statistically significant association ($p < 0.05$).

Conclusions: In the present study, we observed a reduced liver size in almost half of patients with EHPVO, as well as a higher frequency of biliary lithiasis when compared with the general pediatric population. An association between reduced liver size and gallbladder wall thickening/gallbladder varices, but not with cholelithiasis, was observed. It is likely that the pathogenesis of gallstones is not related to decreased blood flow, which should be the main factor involved in liver reduction.

164 LONG-TERM BENEFIT OF SEBELIPASE ALFA OVER 52 WEEKS IN CHILDREN AND ADULTS WITH LYSOSOMAL ACID LIPASE DEFICIENCY (ARISE TRIAL)

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Background: Lysosomal acid lipase deficiency (LAL-D) is a progressive multisystem disease that is an underappreciated cause of cirrhosis, severe dyslipidemia, and early-onset atherosclerosis.

Methods: Affected children and adults (n=66; median age 13 y, range 4–58 y) were randomized to placebo (PBO) or sebelipase alfa (SA) 1 mg/kg every other wk (qow) for 20 wk in the phase 3 trial (ARISE; NCT01757184). After 20 wks, ALT normalization (the primary endpoint) was achieved in 31% of the SA group and 7% of the PBO group ($p=0.0271$). Multiple secondary efficacy endpoints were also met. After the double-blind period, 65 participants entered an ongoing open-label extension in which they all received SA. We report efficacy at 52 weeks of SA exposure for all subjects, representing 1693 infusions of 1 mg/kg qow and 13 infusions of 3 mg/kg qow. Safety analysis results from the open-label period involves subjects with between 86 and 152 weeks of SA exposure (week 22 to January 26, 2016).

Results: After 52 weeks of SA exposure, 47% (29/62) achieved ALT normalization and 56% (33/59) achieved AST normalization, with 73% of subjects reaching ALT $\leq 1.5 \times$ ULN and 85% of subjects reaching AST $\leq 1.5 \times$ ULN. Upon crossing over to SA, the PBO group exhibited marked and sustained improvements in ALT and AST mirroring those seen in the SA group during the double-blind phase, whereas those in the SA/SA group sustained the improvements they had achieved in the first 20 weeks. Mean baseline values for LDL-C (199.2 mg/dL), non-HDL-C (230.0 mg/dL), and triglycerides (153.9 mg/dL) decreased by -30%, -29%, and -23%, respectively, after 52 wk of SA exposure; mean HDL-C (baseline 32.5 mg/dL) increased by 24%. Liver fat and volume were reduced by 25% and 13%, respectively. Most adverse events (AEs) in the open-label period were mild to moderate in severity. Similar to the profile seen during the double-blind portion, patients most commonly experienced headache, nasopharyngitis, cough, and pyrexia. Four subjects had serious AEs of which 1 was treatment-related (an infusion-associated reaction). Twelve subjects (19%) experienced infusion-associated reactions, which were mild or moderate in severity in all but 1 subject. There were no discontinuations due to an AE. Six (9%) of the 66 subjects had at least 1 positive anti-drug antibody (ADA) sample; of these, 2 developed neutralizing antibodies. The safety profile for ADA-positive subjects was consistent with that of the overall study population. Conclusion: SA was well tolerated and the long-term safety profile was similar to the profile seen during the double-blind portion. Long-term treatment with SA produced early and rapid improvements in markers of liver injury and lipid abnormalities which were sustained: reductions in serum aminotransferases, increasing proportion of patients achieving ALT/AST normalization, sustained improvement in lipid levels, and reduction of liver fat and volume through 52 weeks of SA treatment.

165 A COMPARISON OF THE EFFECTS OF THYMOQUINONE, SILYMARIN AND N-ACETYLCYSTEINE ON LIVER INJURY INDUCED BY CARBON TETRACHLORIDE

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Objective: Although liver diseases, some of them having high morbidity and mortality rates, are common, treatment methods and drugs used to stop the process are limited. Different studies reported that thymoquinone, silymarin, and N-acetylcysteine had a positive effect on hepatic pathologies. In this study, thymoquinone, silymarin, and N-acetylcysteine were administered to the rats with hepatic injury induced by carbon tetrachloride (CCl₄) and the effects of these agents were investigated.

Methods: A total of 50 male Wistar albino rats, 8-12 weeks old, were randomly allocated into 5 groups, consisting of 10 rats each, as follows: Group I (CCl₄), group II (thymoquinone and CCl₄), group III (silymarin and CCl₄), group IV (N-acetylcysteine and CCl₄), group V (control group). CCl₄ (1.5 mL/kg, as a mixture of CCl₄: olive oil, 1:2, intraperitoneally) was administered twice-weekly, thymoquinone (10 mg/kg, intraperitoneally), silymarin (100 mg/kg, every day, intraperitoneally), and N-acetylcysteine (10 mg/kg, every day, intraperitoneally) daily during four weeks. Blood and liver analyses were performed. The results were evaluated as statistically via Kruskal Wallis and Duncan's tests. P value < 0.05 was considered statistically significant.

Results: The mean weight of rats included in the study was 225.6 g (range: 167- 350 g). During the study, nine rats died (four in group II, one in group IV, two in group III, and two in group I). Two rats in control group were excluded from the study. Thymoquinone, silymarin, and N-acetylcysteine improved the levels of alanine aminotransferase, tumor necrosis factor- α , transforming growth factor- β platelet-derived growth factor- BB, and interleukin-6 which were increased by CCl₄ ($p < 0.05$). N-acetylcysteine and silymarin significantly increased liver reduced glutathione levels which were decreased by CCl₄ ($p < 0.05$). Thymoquinone, silymarin, and N-acetylcysteine improved blood total oxidant status ($p < 0.05$). In the histopathological and immunohistochemical examination of liver tissue, three agents decreased necrotic cell count and

inflammatory cell count, and mitosis ($p < 0.05$), but not fibrosis score ($p > 0.05$). Statistically significant decreasing in α -SMA stained hepatic stellate cell count was seen with only thymoquinone ($p < 0.05$). Blood and liver test results are seen in Table as a median values.

Conclusions: Thymoquinone, silymarin, and N-acetylcysteine have the potential importance for the treatment in diseases causing liver injury.

Groups	Blood analyses (median value)					
	Alanine aminotransferase (U/L)	Tumor necrosis factor- α (ng/L)	Transforming growth factor- β (pg/mL)	Platelet-derived growth factor- BB (pg/mL)	Interleukin-6 (pg/mL)	Total oxidant status (mmol/mL)
I	365 ^a	492 ^a	194.18 ^a	159.09 ^a	218.15 ^a	15.28 ^a
II	67	155 ^c	86.37 ^b	91.14 ^b	70.77 ^c	2.67 ^c
III	173	242.5 ^b	59.65 ^b	55.32 ^c	98.22 ^b	5.32 ^{b,c}
IV	85	193.5 ^b	60.88 ^b	59.34 ^c	81.38 ^c	6.47 ^b
V	30	237.5 ^b	45.49 ^b	84.46 ^{b,c}	103.18 ^b	5.64 ^{b,c}

(Different letters indicate significant differences between the groups, $p < 0.05$)

Groups	Liver analyses (median value)					
	Reduced glutathione level (μ mol/mL)	Necrotic cell count	Inflammation score	Fibrosis score	Mitosis count	α -SMA stained hepatic stellate cell count
I	4.37 ^d	5 ^a	105.5 ^a	1.5 ^a	29 ^a	190.5 ^a
II	5.65 ^{c,d}	2 ^{c,d}	53.5 ^b	1 ^a	0.5 ^c	101.5 ^{b,c}
III	7.75 ^b	2 ^b	54 ^b	1.5 ^a	4.5 ^b	182 ^{a,b}
IV	5.4 ^{b,c}	2 ^{b,c}	50 ^b	2 ^a	2 ^{b,c}	148 ^{a,b}
V	8.96 ^a	0 ^d	40 ^b	0 ^b	0 ^c	21.5 ^c

(Different letters indicate significant differences between the groups, $p < 0.05$)

***166 SPLICING ANALYSIS USING INDUCED PLURIPOTENT STEM CELL-DERIVED HEPATOCYTE-LIKE CELLS GENERATED FROM A PATIENT WITH PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS TYPE 2**

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Background: The bile salt export pump (BSEP) is a key molecule that transports bile acid into the biliary canaliculi in humans. Progressive familial intrahepatic cholestasis type 2 (PFIC2) is mainly characterized by BSEP deficiency, which is followed by intrahepatic cholestasis. Because the expression of BSEP gene is only observed in hepatocytes among human somatic cells, the spliced form of BSEP mRNA cannot be analyzed using other types of cells. It is difficult to obtain biopsy samples of the liver, although blood cells and dermal fibroblasts are often used to analyze genomic DNA. Recently, patient-specific induced pluripotent stem cells (iPSCs) and their derivatives are expected to become a novel disease model. Therefore, to analyze the spliced form of BSEP mRNA, we attempted to obtain hepatocytes derived from PFIC2 patient-specific iPSCs.

Methods: One healthy donor and a PFIC2 patient participated in the present study. A patient was diagnosed with PFIC2 based on the presence of compound heterozygous mutations in BSEP gene (c.-24C>A and c.2417G>A) and liver histology results. The iPSCs were generated from blood cells obtained from the participants (Control-iPSCs and PFIC2-iPSCs) by using a Sendai virus vector expressing Yamanaka factors. The iPSCs were then differentiated into hepatocyte-like cells (HLCs). Total RNA was extracted from the iPSCs and HLCs. The sequence of BSEP mRNA was analyzed using the cDNA synthesized from total RNA.

Results: We successfully obtained iPSCs from blood cells. These iPSCs were positive for OCT4 and expressed markers specific to human embryonic stem cells. The HLCs were obtained on day 25 after hepatocyte differentiation. Immunostaining analysis for HLCs indicated bile canaliculi between the cells were observed by electron microscopy. The HLCs were positive for albumin and abundantly secrete albumin into the culture medium. To examine whether the BSEP mutation in the 5' f-UTR (c.-24C>A) would cause aberrant splicing in the HLCs derived from PFIC2-iPSCs (PFIC2-HLCs), direct sequence analysis of BSEP cDNA was performed. The exon 2 sequence of BSEP cDNA was heterozygously eliminated in the PFIC2-HLCs.

Conclusion: We could analyze the spliced form of BSEP mRNA using PFIC2 patient-specific iPSC derived hepatocyte-like cells.

167 HISTAMINE CORRELATES WITH LIVER FIBROSIS IN BILIARY ATRESIA

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Background and Aims: Biliary atresia is a severe neonatal cholestasis disease that is caused by obstruction of extra bile ducts. Liver fibrosis progresses dramatically in biliary atresia, and the underlying molecular mechanism is largely unknown.

Methods: Amino acids and biogenic amines were quantified by targeted metabolomic methods in livers of 52 infants with biliary atresia and 16 infants with neonatal hepatitis syndrome. Normal adjacent nontumor liver tissues from 5 hepatoblastoma infants were used as controls.

Orthogonal partial least-squares discriminant analysis was used to identify the differences between biliary atresia, neonatal hepatitis syndrome, and control tissues. Histamine metabolism enzymes and receptors were analyzed by immunohistochemistry and Western blot.

Results: The orthogonal partial least-squares discriminant analysis clearly separated biliary atresia from neonatal hepatitis syndrome and the controls using amino acid and biogenic amine profiles. Histamine was significantly increased in the livers of biliary atresia infants and was positively correlated with the severity of fibrosis. This finding was supported by the elevated L-histidine decarboxylase and reduced monoamine oxidase type B expressions in the biliary atresia infants with severe fibrosis. Furthermore, histamine receptor H1 was observed in the cholangiocytes of biliary atresia livers.

Conclusions: Histamine was positively correlated with fibrosis and may be a potential target to prevent liver fibrosis in biliary atresia.

168 *STERILE CEREBROSPINAL FLUID ASCITES: A RARE COMPLICATION AFTER VENTRICULOPERITONEAL SHUNTING*

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Sterile cerebrospinal fluid ascites is a rare complication following ventriculoperitoneal shunt placement and should be considered in shunted patients who present with ascites. While the exact etiology is unknown, suggested mechanisms include insufficient absorption due to pathology within the peritoneum, possibly related to the silicone tubing. Treatment for sterile ventriculoperitoneal shunt-associated ascites involves diversion of the draining cerebrospinal fluid, typically by converting to a ventriculoatrial shunt. We describe a patient with a ventriculoperitoneal shunt found to have sterile ascites which responded to cerebrospinal fluid re-direction.

A 20-year-old male with cerebral palsy, seizure disorder, Dandy Walker syndrome, and hydrocephalus status post ventriculoperitoneal shunt placement at birth with revision at 14 years of life secondary to shunt malfunction presented with a four-month history of progressive abdominal distension. He had no history of shunt infection or abdominal surgery. Results of routine blood tests were notable for anemia with a hemoglobin of 10.5 mg/dL, hypoalbuminemia with an albumin of 2.0 g/dL, and an elevated erythrocyte sedimentation rate of 39 mm/h. A pre-albumin was also found to be low, and his hypoalbuminemia was attributed to poor nutritional intake. Additional markers of synthetic hepatic function were normal. An abdominal ultrasound showed a large amount of ascitic fluid with a coarse echotexture of the liver but patent hepatic vessels with normal directional flow. Abdominal computed tomography showed extensive ascites but normal appearing liver. Paracentesis revealed clear fluid, 41 leukocytes per cubic millimeter (86 percent lymphocytes) and a protein level of 2.7 g/dL; cytologic examination showed no malignant cells. The serum-ascites albumin gradient was less than 1.1 g/dL. No organisms grew in cultures of ascitic fluid, and the CSF-specific transferrin beta-2 was negative. Laparoscopy revealed a grossly erythematous peritoneum and a normal appearing liver. Liver biopsy showed minimal ductular reactivity with no evidence of hepatitis or fibrosis, and a peritoneal biopsy revealed fibrosis and chronic inflammation. The ventriculoperitoneal shunt was externalized and later internalized to a ventriculoatrial shunt with resolution of abdominal distension. Repeat abdominal ultrasound six weeks later showed improved ascites without evidence of re-accumulation.

While silicone and its constituents do not cause specific immune responses, silicone shunts can degrade over time and elicit a nonspecific inflammatory reaction. It is quite possible that an inflammatory reaction to the silicone tubing used in the creation of our patient's ventriculoperitoneal shunt was a cause of his sterile ascites. Additionally, the sensitivity of transferrin beta-2 to detect CSF in ascitic fluid may be lower than its reported ability in other fluids.

169 *AGE, FIBROSIS AND SUCCESS OF KASAI HEPATOPORTOENTEROSTOMY IN BILIARY ATRESIA: IS THERE A CORRELATION?*

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Background: Biliary atresia (BA) is a progressive cholestatic liver disease associated with development of biliary cirrhosis. It is unclear why infants with biliary atresia who undergo Kasai Hepatportoenterostomy (KHPE) later (after 90-120 days) are less likely to benefit. One possible hypothesis is that older infants have advanced fibrosis which impairs the success of KHPE. To test this, we analyzed infants with BA who underwent percutaneous liver biopsy as part of their diagnostic evaluation at Texas Children's hospital. We examined the correlation of degree of fibrosis at needle liver with age of the infant, secondly the degree of fibrosis with success of KHPE.

Methods: Charts of infants with subsequent diagnosis of BA born between 2011 and 2014 were reviewed. Patients who underwent needle liver biopsy as part of their diagnostic evaluation were included. Infants with BA who had liver biopsy at a referral hospital or a wedge biopsy at our institution were excluded. Demographic data for all patients and age at which conjugated bilirubin normalized in patients who received KHPE were obtained. We defined successful KHPE as conjugated bilirubin of < 0.2 mg/dL at 3 months post KHPE. For each patient trichrome stained slides were de-identified and two pathologists blindly scored the degree of fibrosis. Stage of fibrosis was defined by Batts and Ludwig four tier system in patients with an adequate sample (≥ 7 portal tracts). The Pearson correlation coefficient was calculated using STATA13, and Student's t-test was used to compare mean fibrosis.

Results: Twenty-five infants subsequently diagnosed with BA underwent needle liver biopsy at a median age of 72 days (15-158 d). One subject was excluded due to inadequate tissue sample. 18/24 infants were female (75%) and 2(8%) had syndromic features. 14/24 (58%) had KHPE following needle biopsy (median age at KHPE 59.5 days (22d-96d) and at liver needle biopsy 53.5 days (15-93 d). The average fibrosis in the KHPE group was 3.25 (range 2-4). 7/14 (50%) had successful KPE with average fibrosis score of 3.5 (2.5-4). The degree of fibrosis was similar in infants with successful and unsuccessful KHPE ($p = 0.15$) 10/24 (42%) did not undergo KHPE, median age 117.5 days (71-158 d) with average fibrosis score of 3.5 (range 2-4). The inter-rater agreement, kappa statistic for pathologists was 0.25 ($p = 0.008$). There was no correlation between age and degree of fibrosis with correlation coefficient, $r = 0.12$ (CI -0.28 to +0.49, $p = 0.5$).

Discussion: First our study demonstrates that extensive liver fibrosis is found in all ages in BA and fibrosis is not correlated with age of infant in BA. Second, the success of the KHPE is not related to degree of fibrosis. Infants with successful and unsuccessful KHPE had similar average fibrosis scores on percutaneous liver biopsy. Our findings suggest that patients should not be denied KHPE based on fibrosis when predicting whether or not an infant would benefit from KHPE.

170 *UGT1A1 GENOTYPES AND UNCONJUGATED HYPERBILIRUBINEMIA PHENOTYPES IN POST-NEONATAL CHINESE CHILDREN: A QUANTITATIVE CORRELATION AND FUNCTIONAL ANALYSIS*

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Background: Uridine-diphosphoglucuronosyltransferase 1 family, polypeptide A1 (UGT1A1) is the key enzyme that catalyzes the glucuronidation of bilirubin. Previous reports on UGT1A1 sequencing among Mainland Chinese children with hyperbilirubinemia focused on either newborns, or small number of cases. Full spectrum of quantitative genotype-phenotype correlation data on post-neonatal children were lacking. Earlier functional research mainly focused on A(TA)7TAA variant which is more prevalent among Caucasians, and little attention has been given to G71R, and Y486D that commonly occurs in yellow-skinned East Asians.

Objectives: To quantitatively correlate UGT1A1 genotypes to all post-neonatal phenotypes of unconjugated hyperbilirubinemia (UCH) among Chinese children, and to functionally analyze the effect of G71R+Y486D combined variant.

Methods: Aims of this study were to quantitatively analyze the UGT1A1 genotype-phenotype correlation among Chinese children with unconjugated hyperbilirubinemia, to elucidate the clinical significance of complex UGT1A1 genotypes that occurred in a single patient (multiple SNPs, SNP plus mutation, and multiple mutations), and to expand UGT1A1 variant spectrum by discovering novel mutations or variants. We retrospectively reviewed UCH patients, used Chi-square and single/multiple logistic regression analyses for the quantitative genotype-phenotype correlation. Recombinant wild-type, G71R, Y486D, and G71R+Y486D variants of UGT1A1 proteins were used to determine enzyme activity towards various substrates.

Results: 74 cases including 21 PUCH (Prolonged Unconjugated Hyperbilirubinemia), 30 GS (Gilbert Syndrome), 22 CNS-II (Crigler Najjar Syndrome type II), and 1 CNS-I phenotypes were analyzed. Total of 21 variants, including 7 novel variants were found. In the multiple regression model that all other variants were controlled, heterozygous A(TA)7TAA, G71R/P364L, and Y486D/other mutations were significantly associated with increased risk of GS, PUCH, and CNS-II, respectively. Total allele number is significantly associated with GS and CNS-II, with each increase in total allele number, the odds ratio (OR) of having GS and CNS-II increased by 1.46 and 4.47 fold, respectively. UGT1A1 gene variants reduced the enzyme activity, the enzyme activity of G71R variant is 57% that of the wild-type. Y486D, and G71R+Y486D variant have the lowest enzyme activity with 29%, and 28% that of wild-type. Affinities of G71R, Y486D, and G71R+Y486D towards bilirubin and acetaminophen were lower than the wild-type.

Conclusion: We detected 7 novel variants, and quantitatively calculated risks of having specific phenotypes using genetic data. G71R, Y486D, and G71R+Y486D variants affected recombinant UGT1A1 enzyme activities towards various substrates.

171 EFFECT OF AGE IN THE PRESENTATION AND OUTCOME OF CHOLEDOCHAL CYST AMONG FILIPINO INFANTS AND CHILDREN

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Background: Choledochal cyst is a rare hepatobiliary congenital anomaly with age-associated clinical manifestations. While this has been reported in other countries, the different features and outcome of choledochal cyst in infants as compared to older children had not been investigated locally. Knowledge of these differences is important for early recognition and prompt treatment of the disease to prevent adverse outcomes.

Objective: To compare the clinical, biochemical, anatomical and histological features and outcome of infants and children diagnosed with childhood choledochal cyst.

Study Design: Retrospective cohort.

Methods: From 2004–13, the medical records of 100 choledochal cyst patients from a tertiary hospital were reviewed and classified into the infant group (n 32, 53% girls) or classic pediatric group (n=68, 74% girls) based on the age at presentation.

Results: Jaundice, acholic stools and clinical (all $p < 0.001$) and histological ($p = 0.467$) evidence of cirrhosis were more common in the infant group; while abdominal pain and vomiting (both $p < 0.001$) were predominant in the classic pediatric group. Median total bilirubin (10.9 mg/dl vs. 2.8), AST (156 IU/L vs. 82), ALT (101 IU/L vs. 72) were significantly higher, albumin (26 g/L vs. 32) lower and prothrombin time (1.35 sec. off vs. 0) more deranged in the infant group. Todani type 1a was the commonest choledochal cyst type in both groups. Preoperative morbidities of sepsis and upper gastrointestinal bleeding (both $p = 0.001$) were more frequent in the infant group while choledocholithiasis ($p = 0.033$) was prevalent in the classic pediatric group. Seventy-two patients underwent choledochal cyst excision (47% of infant; 84% of classic pediatric group) while 9 had drainage procedure only. No surgery was done on 9 with Caroli's disease, 7 with cirrhosis and 3 with septicemia. Over a median follow-up of 5 months, 59% of the classic pediatric groups are alive without liver disease while 66% of the infant group died or required liver transplant.

Conclusion: Infants diagnosed with choledochal cyst have a more severe clinical, biochemical and histological features with poorer outcomes as compared to the older group.

172 IMPACT OF THE TIMELY DETECTION PROGRAM IN ITS TERTIARY CARE-LEVEL PHASE OF BILIARY ATRESIA BY MEANS OF THE VISUAL COLORIMETRIC STOOL CARD

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Introduction. Biliary atresia (BA) is responsible for 50% of indications for liver transplantation in pediatric population and should always be considered as probable diagnosis at any infant who remains jaundiced at 2 weeks of age and needs to be evaluated for cholestasis. Timely detection can be carried out by the Visual Colorimetric Stool Card (VCSC), in that it allows to identify different grades of hypoacholia or acholia, for which it has been described as convenient, simple, and cost-effective.

Objectives: To determine the impact of the BA timely detection program through the VCSC in its tertiary care-level phase.

Materials and Methods: Descriptive study, comprising the period from January 2013 to December 2015, including patients admitted with a diagnosis of cholestatic syndrome. Demographic, clinical, and medical consultation characteristics were registered, as well as age at surgical bile-duct exploration, the Kasai-type surgical procedure, and its reference by the timely detection program through VCSC.

Results: Seventy six patients were included, with a median age at admission of 72 days (range, 28–30 days), feminine gender 38.1%. BA was diagnosed in 19 patients (25%), feminine gender predominated (52.6%), with a median age at admission of 120 days. In six cases (31.5%), the

mothers of the patients had knowledge of the VCSC. Only four patients were admitted (5.26%) through the timely detection program by VCSC, two of these with BA, who were submitted to Kasai-type surgical derivation at an age of <60 days.
Conclusions. No positive impact has been reported in terms of diagnostic and therapeutic opportunity after implementation of the BA timely detection program through the VCSC. There should be greater emphasis placed on the BA timely detection program.

173 EPIDEMIOLOGICAL DATA FROM ASYMPTOMATIC PATIENTS WITH PERSISTENT HYPERTRANSAMINASEMIA

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Introduction: The measurement of serum transaminase levels has become part of the routine biochemical evaluation in many countries. An investigation of unexpected hypertransaminasemia is important for differentiating muscular and hepatic disease; to institute timely and specific treatment for progressive, but still asymptomatic, treatable liver conditions.

Purpose of the present study was to analyze the epidemiological data of asymptomatic patients with persistent hypertransaminasemia.

Material and Methods: The study population consisted 42 patients (12 females and 30 males) mean age 5.3 years (2 months - 15.5 years) who were examined in pediatric gastroenterology outpatient clinic during the last 5 years because of persistent asymptomatic hypertransaminasemia. The medical files of all patients were reviewed and data (body weight, height, age, sex, duration of hypertransaminasemia, & investigations made) were recorded. The investigations made were: full blood count, CRP, thyroid hormones and extended hormonal investigations when considered, bilirubine, gGT, LFT, BUN, Creatinine, CPK, Aldolase, Fe, Ferritin, antibodies for hepatotropic infection agents, celiac antibodies, Immunoglobulins, antibodies for autoimmune hepatitis, blood gazes, a1AT, Ceruloplasmine, Cu (blood/urine), a-FP, aminograms, lipid profile, sweet test and liver ultrasound.

Results: Definite diagnosis was made in 15/42 (35.7%) of patients. Three patients, (7%) had celiac disease without other manifestations and the hypertransaminasemia recovered 2-7 months after gluten free diet. In one girl, a 1AT deficiency was detected. Muscular dystrophy was diagnosed in four children (boys) 9.5%. One boy had persistent CMV infection without other manifestations and two boys had chronic active HBV infection. One girl, infant, was diagnosed with biliary atresia. Glycogen storage disease type IX was diagnosed in one toddler (boy).

Autoimmune hepatitis type I was found in one adolescent (girl) and Wilson's disease in one adolescent boy and they are under treatment. Non-alcoholic fatty liver disease was suspected in one adolescent boy. In 8 patients elevation only of AST was observed and Macro-AST condition was suspected but has not been identified yet. One girl with Down syndrome had elevated auto antibodies for autoimmune hepatitis but biopsy was normal and has not fulfill the criteria for that diagnosis. In one patient elevation of muscular enzymes has been observed but genetic test were negative and definite diagnosis no made yet. In 7 patients hypertransaminasemia resolved spontaneously during the follow-up without to have diagnosis. Two patients continues to have transaminasemia without diagnosis and 7 patients were lost from the follow-up.

Conclusions: Persistent asymptomatic transaminasemia in children should be stepwise investigated. Several treatable conditions could be the etiological factor for its appearance.

174 INFECTIONS CAUSE SIGNIFICANT MORBIDITY IN CHILDREN WITH ACUTE VARICEAL BLEEDING

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Background and Aim: The morbidity and mortality associated with acute variceal bleeding (AVB) in children have been poorly characterized. Because death from the first bleed seems to be unusual, the need for primary prophylaxis in children is unclear and depends largely on the extent of the associated morbidity, including infection. We aimed to measure the morbidity associated with AVB in children caused by infections.

Methods: Retrospective study of AVB episodes between May 2000 and May 2015. We included children with liver disease or portal vein thrombosis who presented with acute upper gastrointestinal bleeding requiring volume support and/or red cell transfusion if endoscopy confirmed the presence of varices.

Results: We identified 70 episodes of AVB in 57 children (median age 6 y, 52% female). 47 (67%) episodes were the patient's first AVB. 33 (58%) patients had cirrhotic portal hypertension, 17 (30%) had portal vein thrombosis, 6 (11%) Caroli disease/Congenital Hepatic Fibrosis and 1 Nodular Regenerative Hyperplasia. Median admission values for platelets were 79 (7-407) $\times 10^9/l$, total bilirubin 14 (1-503) $\mu\text{mol/l}$, PELD score -1.4 (n=53, range -6.7 to +43.5), MELD score 9 (n=13, range 6-19). Management included octreotide in 62 (89%) and antibiotics within 24h in 38 (54%). Endoscopy showed predominantly grade III (33 (47%)) and IV (21 (30%)) esophageal varices. Endoscopic therapy was performed in 55 (79%). Post-AVB morbidity was identified in 39 (55%) episodes and in 29 (61%) of first AVB. Infection occurred in 19 episodes (27%), and in 15 (32%) of first AVB. Seven patients had bacteremia/occult bacteremia, 3 sepsis, 9 localized infections (1 aspiration pneumonia, 1 cholangitis, 1 liver abscess, 2 respiratory infections, 2 viral enteritis, 2 urinary infections). Incidence of infection did not change between eras 2000-04, 2005-09 and 2010-15. Median time to diagnosis of infection after AVB was 2 days (range 0-30). 13 (68%) patients had prophylactic antibiotics. Comparing the two groups, one with episodes of infection (inf+) and other with no infections (inf-), median length of stay was longer in inf+ (22 days (range 5-220)) compared to inf- (6 days (2-209)) Inf + were more frequently admitted in CCU (9 (47%) vs. 5 (10%)). One patient died in each group (inf+ 5% and inf- 2%). Infection was associated with severity of liver disease (PELD, Odds ratio 1.06, 95% CI 1-1.12, $p=0.04$) but not with age ($p=0.07$) or cause of portal hypertension (cirrhotic vs. non cirrhotic, $p=0.5$).

Conclusion: AVB in children is associated with low mortality but significant morbidity, especially due to infections. Future studies are needed to examine the effectiveness of prophylactic antibiotics on admission and of primary prophylactic treatment of varices in reducing overall morbidity and infection rate.

175 THROMBOPHILIA PROFILE IN PEDIATRIC PATIENTS WITH CIRRHOSIS AND LIVER FAILURE FROM THE PEDIATRICS HOSPITAL AT THE WESTERN NATIONAL MEDICAL CENTER

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Introduction: The liver plays a central role in the hemostatic system. The coagulation system in patients with cirrhosis is in a state of rebalance between antihemostatic and prohemostatic factors. The observation of inherited thrombophilia (protein C deficiency, protein S deficiency,

antithrombin III deficiency, mutation of factor V Leiden, gene mutation of prothrombin G20210A, polymorphism of methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C, and polymorphism of angiotensin converting enzyme (ACE-1) increase the risk of thrombosis of the portal vein in patients with cirrhosis. It is suggested that hypercoagulability may play a role in thrombosis of the hepatic artery after liver transplantation.

Objective: To characterize the profile of thrombophilia of pediatric patients with cirrhosis and liver failure at the Hospital of Pediatrics, Western National Medical Center.

Material and Methods: A study was conducted in pediatric patients, carriers of cirrhosis and liver failure at the Hospital of Pediatrics.

Anticoagulant activity protein (protein C, protein S and antithrombin III) and factor VIII were determined by clotting assay. Mutations of thrombophilia panel, including factor V Leiden mutation, prothrombin gene mutation G20210AA, MTHFR C677T and A1298C polymorphisms, and polymorphism of angiotensin converting enzyme ACE-1 were determined by the technique of polymerase chain reaction.

Results: There were 25 children, 13 males, 12 females. The average age was 50.76 ± 46.96 (4-189) months. The main cause of cirrhosis was biliary tract atresia (72%). Distribution based on the Child-Pugh stadium was the following: stage A 24%, stage B 48%, and stage C 28%. It was identified protein C deficiency in 14 patients (56%), protein S deficiency in 3 patients (12%), antithrombin III deficiency in 9 patients (36%).

Factor VIII elevated in 92% of the population was documented. The mutations were made only to 23 patients; the main identified mutation was polymorphism deletion ACE-1 in 8 patients (34.7%), the MTHFR C677T polymorphism was the second cause with 21.7%, MTHFR A1298C polymorphism in 8.6%, compound heterozygote of MTHFR C677T / A1298C in 17.3%.

Conclusions: It is considered that the deficiency of anticoagulant proteins and elevation of factor VIII is acquired secondary to chronic liver disease itself. The highest frequency of submission of ACE-1 may be due to the association of ACE-1 in metabolic processes of the liver and liver fibrogenesis participation.

***176 EFFECTIVE GENERATION OF INDUCED PLURIPOTENT STEM CELLS FROM SMALL VOLUME PERIPHERAL BLOOD SAMPLES FOR IN VITRO MODELING OF PEDIATRIC LIVER DISEASES**

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Background: Induced pluripotent stem cells (iPSC) proved to be suitable for *in vitro* modeling of liver diseases. Although iPSCs can be generated by reprogramming almost any somatic cell, skin fibroblasts are still the most widely used. Unfortunately, the need for skin biopsies complicates the feasibility of large studies with iPSCs in children.

Aim: To define reprogramming and culture conditions allowing an effective, reproducible generation of high quality iPSCs from small volume peripheral blood samples.

Methods: Peripheral blood mononuclear cells (PBMC) were isolated from blood samples, and expanded *in vitro* for 9 days in a conditioned medium to enrich the erythroblast population. Reprogramming was achieved using a Sendai virus carrying the four Yamanaka's factors. By day 14 post-transduction, iPSC colonies were identified through fluorescence live staining with anti-TRA-1-60 antibodies. Individual populations were seeded on vitronectin and expanded in Essential 8 medium, in physiological oxygen (4%) conditions. After 8 passages and the elimination of thermosensitive Sendai virus through 2 cycles at 39 C, the cells were analyzed for the expression of pluripotency-associated markers by real-time PCR, fluorescence immunostaining and flow cytometry. iPSCs were then differentiated to hepatocyte-like cells following a well-validated protocol (Si-Tayeb K, Hepatology 2010), with some modifications. iPSC-derived hepatocytes were assessed for the expression of markers and functions typical of mature hepatocytes, as we previously described (Paganelli M., *Hepatology* 2013).

Results: PBMC were obtained from 1.5 mL of peripheral blood drawn from 4 different subjects (0.5, 12, 16 and 37 years of age, respectively). Transduction with the Sendai virus led to the generation of 6.3 ± 5.6 TRA-1-60-positive colonies for each subject ($0.22 \pm 0.19\%$ reprogramming efficiency). One population per subject was expanded under strict feeder-free and xeno-free culture conditions. Pluripotency markers (NANOG, OCT3/4, SOX2) were upregulated in all selected iPSC populations as compared to skin fibroblasts, and the expression was similar to H9 embryonic stem cells (p ns). Sox2, Nanog, Oct3/4, Tra-1-81 and SSEA were all strongly expressed in iPSCs at immunofluorescence. Single cell analysis by flow cytometry showed 86.1% (66.2-90.3 IQR) of triple-positive (SSEA4/TRA-1-81/Nanog) cells. Differentiation to hepatocyte-like cells was achieved with all tested populations (Cyp3A4 activity: 3.1 ± 0.5 fold increase v. undifferentiated iPSCs; urea synthesis: 3.2 ± 0.3 mg/dl/million cells).

Conclusions: The methods described above allow generating high-quality iPSCs from only 1.5 mL of peripheral blood in less than 6 weeks, facilitating the use of iPSC technology for disease modeling in newborns, infants and children. Furthermore, the use of a non-integrating virus and the respect of strict feeder-free and xeno-free conditions allow a much faster scale-up for any future therapeutic applications.

177 ETIOLOGY AND PROGNOSTIC FACTORS OF CHILDHOOD ACUTE LIVER FAILURE IN A CENTER IN MEXICO CITY.

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Acute liver failure (ALF) is a rapidly progressive, potentially fatal clinical syndrome occurring in previously healthy children. PALF is defined as biochemical evidence of liver injury and coagulopathy not correctable by vitamin K with International Normalized Ratio (INR) ≥ 1.5 in the presence of hepatic encephalopathy (HE) or INR ≥ 2.0 regardless of presence or absence of HE.

The majority of studies on ALF were conducted in Europe, EUA and Japan. The etiology and prognosis in those countries are different from Mexico. Prognoses features are suggested in pediatric patients from develop countries but not in developing.

Aim: To determine the causes of ALF and the possible prognosis markers in a center in Mexico city.

Design: Retrospective case and controls study. One hundred pediatric patients with ALF were included from January 2001 to January 2016.

Medical records were reviewed for demographic, laboratory and clinical data.

Results: 100 children (51 female), median age 60.6 months, range 192-1 month. 66 (66%) patients recovered spontaneously, 34 (34%) patients died without transplantation. Specific causes of ALF could be identified as infectious diseases 48% the most frequent Hepatitis A virus infection, immunologic diseases 10%, metabolic diseases 7%, toxic liver injury (paracetamol) 2% and indeterminate 33%. Conjugated

hyperbilirubinemia, low albumin, high ammonia, and prolonged INR were associated with worse outcome. Hepatic encephalopathy results in a bad prognosis factor.

Conclusion: In developing countries Hepatitis A virus is the most common known cause of ALF. Conjugated hyperbilirubinemia, albumin levels, ammonia and severe coagulopathy may be prognostic value to predict outcome.

178 INITIAL TREATMENT OF AUTOIMMUNE HEPATITIS IN CHILDREN: NEORAL CYCLOSPORINE VERSUS PREDNISONE PLUS AZATHIOPRINE

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Prednisone (PRED) plus azathioprine (AZA) is the conventional treatment for autoimmune hepatitis (AIH). The adverse effects related to steroids result in low tolerance and poor adherence.

Aim: To evaluate the outcome, and adverse effects in patients with AIH comparing one group receiving PRED plus AZA (G1) with a second group receiving Cyclosporine (CsA) (G2) as initial treatment, followed by low dose of PRED plus AZA after remission, in both groups.

Patients and Methods: This prospective randomized study consisted of consecutive patients < 18 years old with definite or probable diagnosis of AIH using the IAHG criteria. In children presenting with liver failure (LF) persisting after one week of treatment, were placed on a triple immunosuppressive regimen (TIT), adding PRED-AZA or CsA depending on which initial group they were assigned to. Patients who recovered from LF were switched back to their initial treatment scheme.

Results: Fifty patients were enrolled, G1:26, G2:24. Clinical and laboratory features were similar in both groups. Thirteen (26%) patients presented with LF (8 received TIT). All children recovered liver function, G1: 4,7 ± 4,8 weeks, G2: 5,8 ± 2,3 weeks ($p < 0.4$). Liver biopsies were performed in 37/50 patients (71%), no difference in inflammation or fibrosis was observed. Median time of follow-up was 32 months. The outcome was favorable in both groups, although remission was achieved earlier in G1 ($p < 0.0081$). The adverse effects observed during initial treatment until achieving remission (excluding those who received TIT) were: Cushingoid syndrome, more frequently observed in G1 ($p < 0.001$) and gingival hypertrophy ($p < 0.001$) more commonly observed in G2. There was significant increase of the body mass index (BMI) in all patients since initial treatment until remission achievement ($p < 0.001$), however it was more important in G1. At one year of follow-up, 18 children presented mild cushingoid features, nine from each initial treatment group. Only two children were overweight in this period (BMI > 25), one from each group. No differences in height were found. Infectious events and adherence to treatment were similar in both groups.

Conclusion: Both therapeutic schemes were effective and safe. Remission was achieved earlier in G1. All patients presenting with LF recovered. Adverse effects were mild and transient in both groups. Significant BMI increase was observed during the initial period of treatment to remission, mainly in G1. In the maintenance period, despite receiving low doses of steroids, all patients showed a tendency to increase BMI.

179 DIAGNOSTIC DETERMINATION SYSTEM FOR HIGH-RISK SCREENING FOR INBORN ERRORS OF BILE ACID SYNTHESIS: RESULTS AND RECENT TREND

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Background: Some patients with cholestasis of unknown cause may have inborn errors of bile acid synthesis (IEBAS), leading to abnormalities of bile acid biosynthesis. Although many types of bile acid synthesis defects have been reported as this disorder, no detailed information on its incidence and other aspects in East Asia has been available. To elucidate the current status of IEBAS, we have conducted a high-risk screening using a diagnostic determination system over the past 21 years, between July 1996 and May 2016.

Methods: The target patients included children with hepatic disorders of which the cause could not be identified by conventional liver function testing or hepatitis virus testing, patients with liver cirrhosis of unknown etiology, sibling cases, and patients with cholestasis who exhibited serum levels of direct bilirubin (D-Bil) ≥ 2.0 mg/dL. Urine samples were sent to the Bile Acid Institute located in Tokyo, via refrigerated delivery service. From 2013, impregnated filter paper with sufficient urine volume (dried urine spots) were also start to be available. Urinary bile acids were analyzed via gas chromatography-mass spectrometry (GC-MS/MS) or liquid chromatography-tandem mass spectrometry (LC-MS/MS).

Results: Out of a total of 1,000 samples, 15 were differentially diagnosed with IEBAS, including 5 cases of 3 β -hydroxy- Δ^5 -C₂₇-steroid dehydrogenase/isomerase deficiency (2 in Japan, 2 in China, 1 in Thailand), 4 cases of 3-oxo- Δ^4 -steroid 5 β -reductase deficiency (3 in Japan, 1 in Taiwan), 5 cases of oxysterol 7 α -hydroxylase deficiency (1 in Japan, 1 in Korea, 3 in Taiwan), 1 case of bile acid-CoA amino acid N-acyltransferase deficiency (speculated in Thailand). In Japanese cases, 2 cases of both 3 β -hydroxy- Δ^5 -C₂₇-steroid dehydrogenase/isomerase deficiency and 3-oxo- Δ^4 -steroid 5 β -reductase deficiency were effectively treated with oral bile acid therapy. The third case of 3-oxo- Δ^4 -steroid 5 β -reductase deficiency had spontaneous remission without oral therapy. The Japanese cases of oxysterol 7 α -hydroxylase deficiency underwent successful liver transplantation.

Conclusions: Fifteen patients were identified with IEBAS in East Asia over the past 21 years. IEBAS is a rare, hereditary disease; therefore, increased cost and large amount of labor are required to make a definitive diagnosis via genetic analysis. The diagnostic determination system with urinalysis is considered useful for diagnosis and treatment planning, and furthermore, it contributes to improved treatment efficacy for IEBAS.

*180 HEPATOCELLULAR INJURY IS MEDIATED THROUGH CASPASE 1/11 AND IL-1 RECEPTOR IN STEATOTIC LIVER UNDERGOING ISCHEMIA REPERFUSION INJURY

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Background: A steatotic liver is increasingly vulnerable to ischemia reperfusion injury (IRI), which is commonly encountered during hepatic resection, shock, myocardial infarction and liver transplantation. After IRI, the steatotic liver develops exacerbated cell death and hepatocellular dysfunction but the underlying mechanisms leading to this response are incompletely defined. Caspases are endoproteases, which provide critical regulatory connections between cell death and inflammation and Caspase 1 is driven by the Inflammasome which are key signaling platforms that detect sterile stressors (DAMPs), releasing the highly pro-inflammatory cytokines interleukin 1 β (IL-1 β). Though an area of intense study, there is lack of literature on the role of Caspase 1 and the Inflammasome in steatotic liver injury.

Aim: To delineate the involvement of Inflammasome and Caspase 1 in mediation of exacerbated hepatocellular injury in steatotic liver undergoing IRI.

Methods: Male C57BL6/Wild-Type (WT) and Caspase 1/11 double KO and IL-1 receptor KO mice were fed a high-fat diet (HFD) for 12 weeks. Hepatic steatosis was determined by oil red O (ORO) staining. These mice were subjected to 40 minutes of ischemia followed by 2-24 hours of reperfusion. Hepatocellular injury was assessed by propidium iodide (PI) staining, histopathologic cell death scoring and serum ALT. Pro-inflammatory cytokines were measured by 20-Plex Luminex assay, and levels of Caspase 1, IL-1 β and NLRP3 were quantified by RT-PCR. **Results:** Mice fed a HFD diet showed significant increase in body weight (42 ± 1.2 , vs. 24.6 ± 0.6 grams; $p < 0.0001$) and presence of hepatic steatosis by ORO stain. Significant increase in pro-inflammatory cytokines (IFN γ , IL-1 α , IL-1 β , IL-6 and IL-17) was seen in HFD fed mice undergoing IRI, suggesting a pro-inflammatory milieu in HFD IRI. RT-PCR demonstrated significant increase in levels of Caspase 1, IL-1 β , and NLRP3 levels in HFD IRI at 2 hours of reperfusion. In addition, genetic deletion of Caspase 1/11 and IL-1R demonstrated significant reduction in serum ALT (WT IRI 935.6 ± 80 vs. Caspase 1/11 KO 435 ± 134.5 IU/l, $p < 0.01$ and IL-1 receptor KO 331.8 ± 96 IU/l, $p < 0.003$). Histopathologic cell death score for WT HFD IRI was 22.7 ± 2.4 vs. Caspase 1/11 KO 5.6 ± 1.38 , $p < 0.0002$, IL-1R: 7.3 ± 2.2 , $p < 0.0008$. In contrast, HFD fed AIM2 KO and AIM2/NALP3 double KO mice did not show any protection from liver injury and had high serum ALT. **Conclusion:** Steatotic liver undergoing IRI is associated with elevation of the highly pro-inflammatory cytokine IL-1 β , and shows protection from cell death in HFD fed Caspase 1/11 and IL-1R KO mice. On the contrary, no protection from cell death was seen in HFD fed AIM2/NALP3 KO mice suggesting a novel mechanism of injury in a steatotic liver involving Caspase 1 but independent of AIM2/NALP3.

181 FACTORS PREDICTIVE OF AN OBSTRUCTIVE PATHOLOGY AMONG FILIPINO INFANTS WITH NEONATAL CHOLESTASIS

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Background: It is important to determine the etiology of jaundice in infants to avoid delay in management. There is presently no local study that has identified the features of infants predictive of an obstructive type of neonatal cholestasis.

Objective: To determine factors predictive of obstructive neonatal cholestasis among Filipino infants and to describe their outcome.

Methodology: The study is a retrospective and prospective cohort done at a local tertiary hospital. Jaundiced infants within the first 8 weeks of life who underwent percutaneous liver biopsy were included. Excluded were those with cholestasis secondary to metabolic or infective cause. Retrospective chart review (2009-2012) and prospective recruitment of patients (2013) were done. Factors investigated were the following: clinical (sex, family history of idiopathic neonatal hepatitis, maternal age at birth, order of birth, low birth weight, prematurity, type of feeding at onset of cholestasis, age at onset of cholestasis [< 15 or > 15 days old], persistently pale yellow/acholic stools, high-grade hepatomegaly and splenomegaly), biochemical (total bilirubin > 10 mg/dL, direct bilirubin > 7 mg/dL, aspartate serum transaminase > 300 IU/L, alkaline phosphatase > 200 IU/L, prothrombin time > 4 seconds off from control and GGT > 300 IU/L), and ultrasonographic factors (normal, hepato- and/ or splenomegaly, contracted/absent gall bladder, ascites, and liver parenchymal liver disease). A final diagnosis of non-obstructive or obstructive neonatal cholestasis was made using histology and/ or operative cholangiogram as gold standard. Outcome was assessed on the 6th and 12th month from diagnosis as alive (well or with liver disease) or died. Crude odds ratio for obstructive jaundice was computed. Multiple logistic regression on significant variables was done ($p < 0.05$). Minimal computed sample size is 222.

Results: 263 patients were included: 161 with non-obstructive and 102 with obstructive cause (95 with biliary atresia; 7 with sclerosing cholangitis). Mean age at first consult was higher in those with obstruction [3.95 (SD 3.06) months vs. 2.59 (SD 1.55), $p < 0.001$]. On univariate analysis, obstruction was associated with females, pale yellow/acholic stools, high-grade hepatomegaly and splenomegaly on palpation, GGT > 300 IU/L, and hepatomegaly on ultrasound. On logistic regression (Table 1), females (OR: 2.3), no family history of idiopathic neonatal hepatitis (OR: 1/0.25 or 4) and pale yellow/acholic stools (OR: 13) were predictive of obstruction. 85% of patients with non-obstructive cause are alive and well while 80% of patients with obstruction have died.

Conclusion/Recommendation: Among jaundiced infants, females, no family history of idiopathic neonatal hepatitis and pale yellow/acholic stools are predictive of obstruction. These infants had poor outcome. Prompt referral to a specialist is needed for any jaundiced infant with abnormal stool color.

Table 1. Logistic regression analysis of possible factors predictive of an obstructive neonatal cholestasis in 263 Filipino infants

Factors	Obstructive neonatal cholestasis n/n _{total} (%)	Non-obstructive neonatal cholestasis n/n _{total} (%)	<i>p</i> value	Crude odds ratio	Logistic regression <i>p</i> value	Logistic regression odds ratio (95% Confidence Interval)
Female Sex	45/102 (44.12%)	49/161 (30.43%)	0.026	1.804	0.05	2.32 (1.02, 5.30)
Family history of neonatal idiopathic hepatitis	6/74 (8.11%)	24/102 (23.53%)	<0.001	0.287	0.02	0.25 (0.08, 0.81)
Persistently pale yellow to acholic stools	89/101 (88.12%)	49/131 (37.40%)	<0.001	12.412	<0.001	12.99 (5.21, 32.38)
High-grade hepatomegaly	52/88 (59.09%)	38/130 (29.23%)	<0.001	3.50	0.10	1.98 (0.86, 4.58)
Splenomegaly	53/89 (59.55%)	54/134 (40.30%)	0.006	2.181	0.27	1.60 (0.70, 3.70)
Normal ultrasound	24/89 (26.97%)	59/139 (42.45%)	0.024	0.501	0.94	0.97 (0.40, 2.35)
Hepatomegaly on ultrasound	25/89 (28.09%)	20/139 (14.39%)	0.016	2.324	0.07	2.45 (0.92, 6.53)

n = no. of subjects with the parameter; n_{total}= total no. of subjects included

182 ACUTE LIVER FAILURE OF AUTOIMMUNE ETIOLOGY IN CHILDREN AND ADOLESCENTS OF A PEDIATRIC INSTITUTION IN BRAZIL

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Introduction: Autoimmune hepatitis (AIH) is a rare entity of liver chronic disease. The clinical spectrum is wide, may be acute, acute severe (fulminant), insidious or asymptomatic. An acute severe (fulminant) presentation, characterized by the development of hepatic encephalopathy within 26 weeks of the discovery of the disease, rarely has been described in children in South America. Corticosteroid therapy can be life-saving, but its use in the fulminant presentation of AIH (AIH-FHF) remains controversial.

Aim: To describe features of children diagnosed as having AIH-FHF and to describe the outcome of patients treated with immunosuppressive drugs.

Methods: Retrospective analysis of a collected database identified children and adolescents presented with AIH-FHF from 2000 to 2015 and followed up at the Liver Department of the Children's Institute of the University of São Paulo. AIH was diagnosed based on positive autoantibodies, raised immunoglobulin G, and histology when available. FHF were based in biochemical evidence of acute liver injury without previously recognized liver disease, with prothrombin time (PT) >15 sec or international normalized ratio (INR) > 1.5 not corrected by vitamin K, with clinical hepatic encephalopathy, or a PT > 20 sec or INR > 2.0 regardless of encephalopathy.

Results: 13 patients were identified with AIH-FHF being 12 (92.3%) patients classified as AIH type 2, one (7.7%) with AIH type 1. The average age was 30.5 months (range 12-171 m), 10 (76.9%) female. Since the onset of symptoms till the diagnosis the average time was 30 days (range 4-45 days). Among the 13 patients 10 (76.9%) were treated with methylprednisolone pulse therapy of whom 3 (30.0%) required liver transplantation, while all 3 (23%) untreated patients required LT. Untreated patients with methylprednisolone (n=3) demonstrated 39.6 (mean) PELD scores during the initial presentation. Among treated patients, no difference in PELD scores were observed between responders and failures (42.7 x 39). Despite 6 (46%) patients undergoing LT, death occurred to 50% of them. The total survival rate in AIH-FHF in our study was 61.5%.

Conclusion: The most important strategy for AIH-FHF is to diagnose and consider treatment with corticosteroids. Liver transplantation should be considered before the occurrence of complications that can occur in acute liver failure influencing morbidity of the patients.

183 OBJECTIVE MEASUREMENT OF EFFECT OF LIFE STYLE MODIFICATION THROUGH A MULTIDISCIPLINARY APPROACH ON NON-ALCOHOLIC FATTY LIVER DISEASE: A RETROSPECTIVE STUDY

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children. NAFLD can progress to advanced liver disease. The most common etiology of NAFLD is related to obesity. Currently there is no specific treatment for NAFLD/NASH but evidence supports a role for dietary modification and exercise. A multidisciplinary approach has been reported to stabilize mean BMI and improving aminotransferase levels at 1 year follow-up in obese children with NAFLD.

There have been no studies in Oklahoma exploring the efficacy of lifestyle measures and multidisciplinary approach for NAFLD.

Aim: The purpose of this retrospective chart review is to objectively measure the effect of lifestyle modification through multidisciplinary approach on NAFLD in children followed in the Pediatric Hepatology Clinic at OU Childrens Physicians. We will also investigate for association of a type I axis disorder and rate of improvement.

Methods: This is a retrospective chart review involving obese children (BMI ≥ 95th percentile) with NAFLD, 2-18 years old, seen in Pediatric Hepatology Clinic at OU Childrens Physicians. It will include all visits between June 2014 to June 2015 and August 2015 to Aug 2016. Data is

being collected for age, ethnicity, weight, height, BMI, BP, triglycerides, cholesterol, HDL, transaminases, GGT, alkaline phosphatase and insulin levels at all the visits. In addition, time interval for first follow-up, number of visits in one year and associated behavioral disorders is also being recorded.

Prior to August 2015, families were provided instructions for healthy lifestyle and dietary habits without any set guidelines in place. A written protocol for dietary and behavioral modification "Healthy Lifestyle Screening" was implemented in August 2015. "Healthy Lifestyle Screening" form was completed by the patient's family at every visit to record compliance and progress. After August 2015, frequency of follow-up visits was also increased. A visit with a dietician and psychologist was also implemented with every follow-up after August 2015. In our study, we will compare data one year before and after the implementation of protocol.

Results are being analyzed statistically in the following age groups: 2-5 years old, 6-13 years old, and 14-18 years old. Descriptive statistics will be computed for all demographic and clinical variables for all study subjects. The time period of June 2014- June 2015 and Aug 2015-Aug 2016 will define the retrospective control group and the current treatment groups, respectively. Comparisons of data between these groups will be made using appropriate statistics tests.

Results: Total number of subjects in control group is 38, and 36 have been enrolled in current treatment group until now. Preliminary data collection has revealed a predominance of male gender (72%) in children with NAFLD at our center and 50% of subjects are Hispanic. Chart review is ongoing and final results are still pending.

184 THE DISTANT OUTCOME OF HEPATITIS C VIRUS INFECTION IN CHILDREN

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Background: The long-term natural history of hepatitis C virus (HCV) infection in children is not well known. With recent developments in HCV treatment, understanding natural histories of HCV infection are likely to become more important.

Patients and Method: We conducted a retrospective cohort review of the medical records of patients newly diagnosed with HCV infection and referred to Saitama Children's Medical Center from April 1990 to March 2016. Only children with documented positive HCV-RNA and a minimum of 6 months follow-up records were included. Children ≥ 18 years at the time of diagnosis and those with incomplete medical records were excluded from the analysis. We defined the day of infection as the date of birth for those who were vertically infected and the date of first blood transfusion for those infected via a transfusion.

Results: A total of 34 children (23 boys and 11 girls) were enrolled. The median age at diagnosis was 7.7 years (0.6-17.9 years) and the median follow-up period was 9.8 years (1.9-19.8 years). All children were asymptomatic with no occurrence of liver cirrhosis and hepatoma. The routes of infection were vertically acquired (VAC) in 7 (20.5%) and transfusion acquired (TAC) in 27 (79.4%) children. Moreover, before 2000, the number of children with VAC was 1 (3.6%) and with TAC was 27 (96.4%); after 2000, the number of children with VAC was 6 (100%) and no children with TAC were noted. The genotype was identified for 22 children: 1 (4.5%) with genotype 1a, 16 (72.2%) with genotype 1b, 3 (13.6%) with genotype 2a, and 2 (9.0%) with genotype 2b. 9 children received treatment for HCV infection and all of them were treated with interferon alone. Following treatment, a sustained viral response (SVR) was achieved in 3 children, no sustained viral response (NVR) in 3 children, 1 child relapsed, and 2 children discontinued treatment because of side effects. Natural clearance of HCV-RNA was observed in 7 (20.5%) with a median age of 8.4 years (4.1-15.1 years). The median period for natural clearance was 4.9 years (3.3 - 6.5 years) from the time of initial infection. A liver biopsy was performed in 19 children at a median of 7.8 years (1.2-12.7 years) since the initial infection. Fibrosis staging was scored using METAVIR scoring and all children had mild fibrosis (F0-2). There was no noteworthy association between fibrosis and genotype, period of infection, or amount of HCV-RNA.

Conclusion: In this study, all were asymptomatic, HCV progression was gradual, and neither liver cirrhosis nor hepatoma developed. When applying treatment guidelines of HCV infections, it is important to refer to the natural history in children. We think that treatment for HCV infections in children should be conducted with caution considering unknown or distant side effects of the drugs because it is possible that the treatment will not be required. We are accumulating similar cases from a multicenter database in Japan and the results are awaited.

185 LABORATORY AND HISTOLOGICAL FEATURES OF EARLY BILIARY ATRESIA

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Introduction: While the natural history of biliary atresia (BA) has been generally well-characterized, there is little information about the disease's early period, i.e., in the first 30 days of life. In this report, we describe early laboratory and histological findings in infants with BA.

Methods: Subjects were included if they were born between 2007-2014 and diagnosed with BA at our institution. For each subject, first aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (AP), gamma-glutamyl transferase (GGT), conjugated bilirubin (Bc), and unconjugated bilirubin (Bu) results were collected from the electronic medical record. In addition, for subjects receiving a liver biopsy before 30 days of life, liver and bile duct remnant tissue were analyzed. Bc ratios were calculated as $(Bc/[Bc+Bu])$, and Spearman's rank correlation coefficients (rs) were calculated to correlate laboratory results with age. Hematoxylin and eosin staining, cytokeratin 19 immunohistochemistry, and trichrome staining were used to study tissue samples.

Results: There were 65 subjects who fulfilled inclusion criteria, of which 43 were females (66%) and five had syndromic features (8%). The median age of first serum laboratory testing was 63 days (range 1-163 days). AST and ALT had a strong positive correlation with age (rs 0.77 and rs 0.79, respectively), and were within the laboratory upper limits of normal when tested before 20-30 days of life. AP and the Bc ratio had a weaker positive correlation with age, whereas GGT and Bu did not correlate with age. Bc always exceeded the laboratory reference interval, and Bc ratios were above 0.20 in all infants except one who was tested at five days of life. Six infants underwent liver biopsy before 30 days of life. All six infants showed signs of extrahepatic obstruction, including bile plugging, duct proliferation, and portal fibrosis. All six infants also had bile duct remnants lacking epithelial-lined lumens and replaced with fibrous tissue.

Conclusion: Early BA is characterized by normal AST and ALT levels despite histological findings of obstructive biliary disease. In addition, similar to later periods, early BA has elevated Bc levels, almost all Bc ratios exceeding 0.20, and evidence of bile duct obliteration. Clinicians should be aware of these results when evaluating young infants with cholestasis, to identify BA earlier, accelerate treatments, and potentially improve overall outcomes.

186 SYNCHRONIZED APOPTOSIS AND MITOCHONDRIAL DAMAGE OF HEPATOCYTES SEEN IN PATIENTS HAVING LIVER FAILURE
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Background: Organ failure including hepatic one can occur in patients having metabolic / mitochondrial diseases. Some show microsteatosis with no evidence of inflammation in liver biopsy specimen. The real mechanism for liver failure is still obscure partly because of the high hurdle of hemorrhagic diathesis due to lowered protein synthesis to perform biopsies. We seldom see evidence of apoptosis in most clinical samples though experimental models show massive cell death via necrosis and apoptosis. Cytochrome C, released from mitochondria, are sensitive marker for apoptosis. We examined liver specimens and sera obtained from children having hepatic dysfunction including organ failures. Methods: We included 10 patients with acute encephalopathy, 3 with hemophagocytic syndrome, 2 with Reye syndrome, one having Pearson disease, and one with hepatic failure due to hepatitis B virus. Serum specimens for cytochrome C obtained at various timings. Cytochrome C was measured by electrochemiluminescence immunoassay. Sixteen specimens from the liver, one from the heart, and one from the brain were obtained in acute clinical stages or at autopsy. TdT uridine nick endlabelling (TUNEL) was applied for detecting apoptosis. Immuno-staining for cytochrome C in addition to conventional histological staining and electron microscopy was also applied for examination. Results: Serum cytochrome C elevated in acute stages and showed correlation with ALT increase and Ca²⁺ decrease. Histologically marked accumulation of small fatty droplets and diffuse synchronized apoptosis signals in the livers of acute encephalopathy, Reye syndrome, and acute hepatic failure. This feature disappeared shortly, e.g., 2 weeks later. Their mitochondria were swollen, but not so prominent as Pearson's disease. Simultaneously, granular patterns of cytochrome C localized to mitochondria were lost. One with acute encephalopathy recovered by using cyclosporine A.

Conclusions: Apoptosis can occur in such cells as the liver, brain, or muscles simultaneously and diffusely. Serum cytochrome C reflect apoptosis in tissue damages. Apoptotic change and mitochondrial malfunction occur in the same cells simultaneously. To rescue mitochondria from apoptosis should be considered to treat organ failures. Cyclosporin A, which suppresses apoptotic process by blocking formation of mitochondrial permeability transition, was proved effective.

187 CONTROLLED ATTENUATION PARAMETER VALUES IN HEALTHY THAI CHILDREN

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Background: The prevalence of non-alcoholic fatty liver disease (NAFLD) in children is increasing worldwide. The gold standard for diagnosis of NAFLD is liver biopsy which is prone to several complications. The controlled attenuation parameter (CAP) is an attractive method of assessing hepatic steatosis due to its noninvasiveness, simplicity, reproducibility, and high accuracy.

Aims: To determine the normal range of CAP values in healthy Thai children and to identify the association of demographic, anthropometric parameters and body fat percentage with CAP values.

Methods: Children attending an elementary school in Bangkok were enrolled. Subjects with current or a history of liver disease were excluded. Overweight and obesity were defined according to the 2007 WHO child growth references. Body fat percentage was measured with bioelectrical impedance analysis using a body composition analyzer (Tanita®, BC-418). A FibroScan® 502 machine equipped with an M probe (Echosens, Paris, France) was used to capture CAP values.

Results: The mean age of the 531 recruited children (282 boys and 249 girls) was 8.8 years. In all 25% of these children were overweight and 18.3% obese. Boys had significantly higher body mass index (BMI) and body fat percentage than girls (18.9 ± 3.9 vs. 17.6 ± 3.3 kg/m², $p < 0.001$ and 22.3 ± 11.6 vs. 20.0 ± 7.6 percent, $P < 0.01$, respectively). The mean CAP value was 181.2 ± 32.9 dB/m (5th -95th percentiles 130.0-235.4 dB/m). Boys had significantly higher CAP values than girls (185.6 ± 33.7 vs. 176.3 ± 31.2 dB/m, $p = 0.001$). The univariate analyses with CAP as a dependent variable revealed that gender, age, weight, height, BMI, and body fat percentage were significantly associated with the CAP values (all $p < 0.01$). In a multivariate linear regression analysis, only BMI ($\beta = 0.409$, $p < 0.001$) and body fat percentage ($\beta = 0.372$, $P < 0.001$) were independently associated with CAP values.

Conclusion: Normal range of CAP values in children was determined. Body mass index and body fat percentage were associated with the CAP values of the studied children.

188 THE TYPES OF LIVER PATHOLOGIC FINDINGS OF NON-ALCOHOLIC STEATOHEPATITIS IN KOREAN CHILDREN: SINGLE-CENTER STUDY

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Background: Histologically, non-alcoholic steatohepatitis (NASH) is divided into 2 groups, adult type (Type I) and pediatric-type (Type II). Severe steatosis, inflammatory cell infiltration in acinar zone 1 are histological features of Type II; on the other hand, weak steatosis, inflammatory cell infiltration in acinar zone 3 are features of Type I. We studied whether liver pathologic findings from children with NASH truly shows only children's type, not adult type.

Method: Liver biopsies were performed in 41 children of NAFLD of 7-15 years old in NASH was diagnosed in 35. We investigated the types of their pathologic finding, and whether there are any correlating factors of clinical and anthropometric data (height percentile, BMI percentile, obesity index, systolic blood pressure percentile, diastolic percentile) toward the trend for a specific pathologic typing.

Result: In 35 children, 19 patients (54%) were type I, 16 (46%) were type II. Type II was more numerous in ages 7, 9 and 15 years old, and the other age group showed more of type I. Among the clinical and anthropometric data, children with high BMI (>95 percentile) were noted in 81.25% of type II; hematocrit, albumin, and systolic blood pressure (SBP) percentile were significantly higher in type II (p value: 0.01, 0.005, 0.018, respectively). However, there was no correlation between NASH type and hypertension severity ($p = .310$). Other clinical variables did not show statistically significant difference between the two types.

Conclusions: Not only pediatric-type NASH but also adult-type NASH was found in children. It might be meaningless that NASH in children would show children's pathologic findings.

Keywords: Non-Alcoholic Steatohepatitis (NASH), Children, Liver biopsy, Pathologic finding

189 FEASIBILITY AND USEFULNESS OF SIMULTANEOUS MEASUREMENT OF LIVER STIFFNESS AND HEPATIC FAT DEPOSITION BY FIBROSCAN IN CHILDREN

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Backgrounds and Aims: The aim of our study was to determine the usefulness and feasibility of transient elastography (FibroScan®) assessing liver stiffness and hepatic fat deposition without biopsy in children.

Methods: Obese children (Obese group BMI-SDS above 90th percentile) and non-obese children without liver disease (Control group) were examined for liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) simultaneously using Fibroscan®. The correlation between FibroScan results and clinical and biochemical data were analyzed with Pearson's correlation coefficient.

Results: A total of 244 patients (11.7 y ± 3.6 y, mean±SD) including obese group (n=71, 12.6 y ± 3.1 y) and the control group (n=173, 11.4 y ± 3.8 y) were included. The CAP of obese group (290.5 ± 56.7 dB/m) showed significantly higher value than control group (185.5 ± 45.9dB/m) ($p < 0.0001$). The LSM of obese group (5.6 ± 2.3 kPa) also showed the higher value than control group (4.0 ± 1.0 kPa) ($p < 0.0001$). In the obese group, the LSM correlated to CAP ($\rho = 0.548$), age ($\rho = 0.407$), AST ($\rho = 0.714$), ALT ($\rho = 0.735$), and APRI ($\rho = 0.761$), and the CAP correlated to age ($\rho = 0.415$), AST ($\rho = 0.442$), ALT ($\rho = 0.457$), and APRI ($\rho = 0.420$), and BMI-SDS ($\rho = 0.532$). On the other hand, in the control group, there is no correlation between FibroScan results and laboratory data.

Conclusions: Fibroscan® is a non-invasive tool to assess the liver stiffness and hepatic fat deposition simultaneously thus useful as a screening tool for nonalcoholic fatty liver disease especially in obese children.

*190 SPECTRUM OF HEPATITIS IN DENGUE FEVER: DO ASPARATE AMINOTRANSFERASE LEVELS HELP IN GRADING SEVERITY OF DENGUE?

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Introduction: Dengue fever is a major health problem in many Southeast Asian countries. There is a paucity of data regarding the spectrum of dengue hepatitis in children.

Objective: We studied the profile of liver involvement in children with dengue fever and compared liver function tests in three categories of WHO dengue case classification.

Methods: Study design: Prospective study; Period: October 2013 to December 2014; serologically confirmed dengue patients were grouped into three categories: Group 1 - dengue without warning signs; Group 2 - dengue with warning signs (abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing hematocrit with decreasing platelets) and severe dengue (dengue with severe plasma leakage, severe bleeding or organ failure). Biochemical and clinical profile of hepatic involvement was studied. The comparison between groups for key outcome parameters has been done using standard normal deviation test (Z test); SPSS software has been used.

Results: One hundred and sixty two children with dengue fever (M:F – 2.37) were included in the study. Median age was 12 years (range 6 m–18 yrs). Hepatitis was observed in 151 (93.2%) patients. On comparing the various liver function tests (LFT) parameters among three groups, the difference in average serum bilirubin levels and Asparate Aminotransferase (AST) were significant in each group ($p < 0.05$). However, there was no difference in the average values of ALT and serum albumin levels among group 1 and 2 [$p = 0.06$ and 0.16 respectively]. Eight cases presented with Acute Liver Failure. Their median AST was 4817 (range 220–26,957); median alanine aminotransferase (ALT) was 2386 (range 176–11,100); median INR was 2.57 (range 1.6–4.2) and their median serum bilirubin was 2.95 (range 0.6 – 9.0). An AST of >3 times normal had a 61% PPV of falling in group 2 (Dengue with warning signs).

Conclusion: Some degree of hepatitis is very common in dengue infection with rise in AST being more than ALT irrespective of the severity of dengue. Of all liver function parameters, S. bilirubin and AST levels correlates best with severity of dengue infection. The new WHO classification of dengue correlates well with the degree of liver involvement. Severity of hepatitis correlates well with the severity of dengue and can help in triaging of dengue patients well. An AST value of >3 times the normal should warn the patient of the need for probable admission.

191 PRIMARY LIVER TRANSPLANT VERSUS TRANSPLANT POST KASAI IN BILIARY ATRESIA: WHICH IS BETTER?

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Introduction: Biliary atresia (BA) is the most common surgical cause of neonatal cholestasis. Kasai portoenterostomy, if done earlier, is successful. Most Kasai portoenterostomy patients eventually need liver transplant. Primary liver transplant for patients with BA is offered when there is delayed presentation or if features of significant liver dysfunction/cirrhosis is present at diagnosis.

Aim: To review experience of living related liver transplantation (LDLT) for BA, and to compare the outcome (Medical/surgical complications and survival) in patients who underwent LT with/without prior Kasai portoenterostomy (PE).

Methods: Prospectively collected data of living related donor liver transplantation in children from mid September 2004 to March 2016 were analyzed. The cases were divided into two groups: Group A - BA with previous Kasai PE; Group B: BA without previous Kasai PE. The short- and long-term complications and survival were compared in both the groups.

Results: 190 LDLTs were performed during this period. There were total 68 BA patients of which 43 were post-Kasai. Children in the Group A - 43 (63%), mean age (40.6 months (5-15, 6 months)) with M:F ratio of 23:20 and mean weight 13.18 Kg (4.2-41 Kg) and Mean Pediatric End-Stage Liver Disease (PELD) scores of 18(7-37). 13(30%) patients in this group were less than 1 year. In Group B 25 (37%), mean weight was 7.84 Kg (4.8-10.9) and mean age 14.6 months (4-65 months), 15 (60%) were less than 1 year and mean PELD 22.8 (11-37). In comparison to Group B, patients in group A had significantly more vascular complications and perforation (8(19%) biliary, 9 (24%) perforation, 11 (26%) vascular complications (2 Hepatic Artery Thrombosis HAT, 9 Portal vein thrombosis PVT) ($p < 0.005$). In group B, 2 had HAT and 2 (10%) had biliary leak with no perforation. Mean duration of stay was 29 days in Group A and 21 days in group B. Three died in Group A and 4 in Group B with overall survival of 93% and 84% respectively over a mean follow-up period of 3.76 years.

Conclusions: A previous Kasai-PE increases post-LT surgical complications such as portal vein thrombosis, bowel perforations and reexploration. Survival in <1 year is significantly lower than >1 year. Post kasai patients seemed to have better survival than primary transplant group but there was no statistically significant difference in K+/K- <1 year group. Post-operative surgical complications were seen more in patients who underwent transplant after Kasai procedure.

INFLAMMATORY BOWEL DISEASE

217 THE ASSOCIATION BETWEEN PEDIATRIC-ONSET INFLAMMATORY BOWEL DISEASE AND BONE MINERAL DENSITY IN ADULTHOOD

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Background: Inflammatory bowel disease (IBD) is known to pose a risk for low bone mineral density (BMD) in both children and adults. We aimed to evaluate the impact of pediatric-onset IBD on BMD in adulthood.

Methods: Records of patients diagnosed with pediatric IBD were retrospectively reviewed. Patients who had documentation of dual energy X-ray absorptiometry (DXA) scans after the age of peak bone mass accrual (females-18 years, males- 20 years) were included. BMD was expressed as Z-score and defined as the lower between lumbar and femoral-neck BMD for each patient.

Results: 61 patients with pediatric-onset IBD were included. Median age at diagnosis was 15.3 years (IQR 14-16.5). Median age at first DXA scan in adulthood was 21.9 years (IQR 20.2-27.3). Mean BMD Z-score was -1.12 (\pm 1.04). Overall, 44.3% (n=27) had osteopenia (BMD Z-score \leq -1), and 8.2% (n=5) had osteoporosis (BMD Z-score \leq -2.5). This deviation from normal distribution of BMD was statistically significant ($p < 0.001$). Bone status showed no correlation with age, disease severity, height z-score and vitamin D status at diagnosis, type of IBD or duration of disease. Significant correlation ($r=0.306$, $p=0.05$), was identified between low weight Z-score at diagnosis and abnormal bone status in adulthood. Thirty-six patients had at least 2 DXA scans during follow-up. During a median interval of 3.6 years there was no significant change in BMD between first and last measurement.

Conclusions: Osteopenia and osteoporosis are frequent in adult IBD patients with pediatric-onset disease. BMD does not significantly change over time in these patients.

218 IMPACT OF AN IBD CAMP UPON DISEASE-SPECIFIC KNOWLEDGE AND QUALITY OF LIFE IN CHILDREN AND ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction and Aims: Residential camps for children and adolescents with Inflammatory Bowel Disease (IBD) appear to have numerous benefits, including enhancing peer support. This study evaluated the impact of a four-day camp for children with IBD in New Zealand, with particular focus upon disease-specific knowledge and quality of life.

Methods: Prior to New Zealand's first dedicated camp for children with IBD in January 2015, all campers were contacted and asked to participate in an evaluation of outcomes arising from the camp. Campers were asked to complete questionnaires regarding background disease status and demographic information, disease-specific knowledge (IBD-KID) and quality of life (IMPACT). Assessments were completed before the camp and then again one month and six months after the camp. The camp was based around adventure-based experiences and did not include specific IBD-related educational activities.

Results: Thirty-nine of 44 campers provided baseline information. The responders comprised 21 boys. Thirty-five were diagnosed with Crohn's disease and 4 with ulcerative colitis or IBD-unclassified. Median age of the campers was 14 years. At baseline, the average IBD-KID scores were 10.67 (\pm 4), and median IMPACT scores were 133 (interquartile range 114.75-149.25). Mean IBD-KID scores increased from baseline at both 1 and 6 months (p 0.03 and p 0.04 respectively). One month after the camp, 58.1% of campers had improved disease knowledge while 64.3% had scores above baseline at 6 months. Similarly, 50% of children had improved QOL scores at 1 month. Although average QOL scores did not increase after 1 or 6 months, body image subscores ($p=0.015$) were increased at 6 months.

Conclusions: Children and adolescents with IBD attending this residential camp demonstrated enhanced disease-specific knowledge following the camp. These improvements in knowledge were maintained during the six months following the camp. These results demonstrate a further benefit of residential camps for these children and adolescents.

219 COMPARISON OF GENOTYPE AND PHENOTYPE BETWEEN CAUCASIAN AND HISPANIC CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Background: Inflammatory bowel disease (IBD) is a chronic inflammation of intestinal tract caused by an interplay of genetics, environment and microbiome. Most of the studies in inflammatory bowel disease including large genetics studies for susceptibility and large clinic trials for drugs used in IBD were conducted in areas where minority population were underrepresented. Incidence of IBD in Hispanics is rising as this population is becoming the fastest growing minority population in US. NOD 2 mutations are associated in Crohn's disease in Caucasians but significance of this genetic variation in Hispanic population in United States is not known.

We hypothesize that differences exist between Hispanic and Caucasians children with inflammatory bowel disease, specifically disease presentation, clinical course and genetics.

Method: We conducted a multicenter study (Children's Hospital Los Angeles and University of Chicago) on Hispanic and Caucasian children with IBD to describe phenotypic and genotypic differences (NOD2 polymorphism). We also analyzed the frequency of NOD 2 mutation in control samples. DNA extraction was done using buccal swabs and SNP polymorphism using quantitative PCR technique for two common CD-associated NOD2 mutations rs2066844 (R702W), rs2066845 (G908R).

Results: Total of 232 IBD patients were analyzed (African American- 29, Hispanic 43, Caucasian 135, other 15). Total of 100 controls were analyzed (African American- 6, Caucasian 9, Hispanic 82, and Other 3). Refer to *Table 1* for details. Significantly higher number of males with Crohn's disease (CD) was seen in Hispanic (84%) as compared to females (15%), but the Caucasian population had equal distribution. No difference was seen in ulcerative colitis (UC) between males and females in these populations. UC was more common in Hispanics. CD was more common in Caucasians. In both Caucasian and Hispanic population age of diagnosis was highest in >10-17 years in CD and UC. Disease location in Crohn's disease in Caucasian was mostly ileocolonic (60%, 23% in Hispanic). In Hispanics, disease location was mostly colonic (54%, 17%) in Caucasians). Caucasians had more non-structuring non-penetrating type disease. Perianal disease was higher in Hispanic population compared to Caucasian. We also analyzed NOD 2 polymorphism R702W and G908R in CD and overall IBD patients and no difference in genotype frequencies was seen in Hispanic IBD patients and Hispanic controls (*p* value not significant).

Conclusion: There are significant difference in phenotypes between hispanic and Caucasian population, NOD 2 polymorphisms which are known susceptibility genes playing a role in IBD in Caucasians is not significant in Hispanic population. Thus, role of diet, environmental factors and socioeconomic factors as well as other susceptibility genes may play a role in Hispanic IBD etiology and progression.

220 BASELINE WALL THICKNESS IS LOWER IN MUCOSA-HEALED SEGMENTS 1 YEAR AFTER INFLIXIMAB IN PEDIATRIC CROHN'S DISEASE PATIENTS

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Backgrounds: Magnetic resonance enterography (MRE) has emerged as a valuable tool in diagnosing and monitoring treatment responses in Crohn's disease. We aimed to quantitatively investigate the therapeutic response to combined immunosuppression treatment by magnetic resonance enterography (MRE) in active luminal Crohn's disease in the pediatric population.

Methods: Pediatric patients with moderate-to-severe luminal Crohn's disease who received scheduled infliximab and azathioprine were included in this preliminary study. Ileocolonoscopy and MRE were performed at baseline and at 1 year, and Simple Endoscopic Score for Crohn's disease (SES-CD) and Magnetic Resonance Index of Activity (MaRIA) scores were calculated. The correlation between SES-CD and MaRIA scores were investigated with analysis per-person and per-segment.

Results: A total 167 segments from 17 patients were evaluated by both ileocolonoscopy and MRE. SES-CD and MaRIA scores showed significant correlations on both per-person analysis ($\rho=0.699$, $P<0.001$), and per-segment analysis ($\rho=0.596$, $P<0.001$). Analysis according to ileocolonic location of each segment revealed that correlation strength was strongest in the right colon ($\rho=0.653$, $P<0.001$), while the correlation in the rectum was statistically insignificant ($\rho=0.29$, $P=0.096$). Comparative analysis of MaRIA components revealed a significantly thinner bowel wall thickness at baseline in endoscopically healed segments (50/65) compared to unhealed segments (15/65) (median 4.3 vs. 7.2 mm, $P=0.036$).

Conclusion: Therapeutic response to combined immunosuppression at 1 year assessed by MRE correlates with ileocolonoscopy in pediatric patients with Crohn's disease. Bowel wall thickness of the involved segments at baseline may affect treatment response to combined immunosuppression.

221 ASSESSMENT OF IMPACT III WELL-BEING DOMAIN SCORES IN ADALIMUMAB-TREATED PAEDIATRIC PATIENTS WITH CROHN'S DISEASE

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Background: We assessed the impact of adalimumab (ADA) treatment on the well-being domain from the recently restructured IMPACT III questionnaire in patients (pts) enrolled in the IMAGINE 1 trial. The effect of ADA on emotional and social functioning domains has been reported previously.¹

Methods: In IMAGINE 1, 6-17 years old pts with moderate to severe CD (baseline [BL] PCDAI >30) who failed or were intolerant to conventional therapy received ADA for 52 weeks (wks).² Escalation to blinded weekly (EW) ADA was allowed after wk 12 for pts with disease flare/non-response followed by open-label (OL) EW ADA for continued flare/non-response. Pts ≥ 10 yr at BL received the IMPACT III questionnaire; each individual question has five Likert response options (0-4); scores are then linearly transformed to a range of 0 to 100 for ease of data interpretation, with higher scores representing better HRQoL. Changes from BL in the well-being domain score and in individual IMPACT III questions at wks 12, 26, and 52 were reported. Prior infliximab exposure was used for subgroup analyses. Last observation carried forward (LOCF) was used for missing data (post-BL), pts who discontinued, or who moved to OL EW ADA.

Results: A total of 172 pts were analyzed: 55% were males, median PCDAI was 40, median CRP 1.2 mg/dL, and mean IMPACT III well-being score 46 at BL. 75 pts had prior exposure to infliximab. Mean well-being domain scores at BL for infliximab-naïve and experienced pts were 49 and 44, respectively. Statistically significant improvements in well-being domain and individual questions scores were observed from week 12 and maintained to week 52 (Table). Overall well-being domain score at wks 12, 26, and 52 was 69, 68, and 68, respectively. Numerically higher changes from BL in well-being domain scores were seen in infliximab-naïve pts compared with infliximab-experienced pts at wks 12, 26, and 52 (26, 27, and 25 vs. 18, 16, and 16, respectively).

Conclusions: ADA treatment was associated with significant improvements in HRQoL in children with CD. Increases in well-being domain scores and individual question scores were maintained up to week 52 regardless of prior infliximab exposure.

1. Grant *et al.* Poster presentation at the 2016 European Crohn's and Colitis Organisation Congress. [Abstract # A-1340]. Amsterdam, Netherlands March 16-19, 2016; 2. Hyams *et al.* *Gastroenterol.* 2012;143:365.

	Mean baseline score	Mean change from baseline		
		Week 12	Week 26	Week 52
Well-being domain	46	22***	22***	21***
How much has your stomach been hurting you in the past two weeks?	41	26***	25***	25***
How often has your IBD prevented you from eating what you want in the past 2 weeks?	45	20***	22***	22***
How often have you been worrying about having a flare-up (increase of symptoms) in the last 2 weeks?	48	22***	21***	20**
How much energy did you have during the past 2 weeks?	43	23***	23***	22***
How often did you have to miss out on certain things (hobbies, play, parties) because of your IBD in the past 2 weeks?	49	24***	25***	23***
How often have you been bothered by diarrhea in the past 2 weeks?	41	24***	23***	21***
Did you have fun during the past 2 weeks?	59	17***	16***	15***
How often did you feel sick to your stomach in the past 2 weeks?	47	23***	23***	21***
How did you feel during the past 2 weeks?	43	26***	23***	21***
How tired have you felt in the past 2 weeks?	37	25***	24***	23***
Does your IBD get in the way of playing sports the way you would like to?	43	17***	20***	21***
In the past 2 weeks how often were you able to go to school?	62	21***	19***	19***

***p<0.0001 for mean change from baseline to weeks 12, 26, or 52 was based on a one sample t-test.

***222 CLINICAL CHARACTERISTICS AND LONG-TERM SURGICAL RISK OF PEDIATRIC CROHN'S DISEASE: A SINGLE-CENTER EXPERIENCE**

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Background and Aims: Although pediatric Crohn's disease (CD) has a different phenotype and clinical course to adult CD, its clinical features and surgical risks are poorly defined, especially in Asian countries. The aim of this study was to investigate the clinical features and long-term surgical prognosis of pediatric CD in a Korean population.

Methods: We retrospectively analyzed 600 patients who were younger than 18 years of age at CD diagnosis between 1987 and 2013. Patient characteristics at CD diagnosis and clinical courses were analyzed.

Results: The male-to-female ratio was 2.4:1 and the median age at CD diagnosis was 14 years (range, 6 months to 17 years). A positive first-degree family history of inflammatory bowel disease was present in 30 patients (5%). Seventy patients (11.7%) showed a growth delay. The cumulative probabilities of perianal fistula at 1, 5, and 10 years after diagnosis were 50.1%, 54.7%, and 57.4%, respectively. The cumulative probabilities of anti-tumor necrosis factor treatment at 1, 5, 10, and 20 years after diagnosis were 10.9%, 26.6%, 42.3%, and 77.4%, respectively. The cumulative probabilities of intestinal resection at 1, 5, 10, and 20 years after diagnosis were 4.8 %, 17.5%, 33.1%, and 63.7 %, respectively. In multivariate analysis, complicated behavior at diagnosis was associated with an increased risk of intestinal resection.

Conclusions: Our study is the largest Asian pediatric study which applied the Paris classification to patients. The prevalence of perianal fistula at diagnosis was higher than other western studies. Biologics and immunomodulators had no impact on the surgery rate.

223 CELLULAR DISTRIBUTION OF INNATE LYMPHOID CELLS ON THE PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Introduction: Innate lymphoid cells (ILCs) are effectors of innate immunity and regulators of tissue modeling. ILC subpopulations have a cytokine expression pattern which resembles that of the helper T cell subsets TH1, TH2, TH17 and TH22. ILCs have been classified into distinct groups based on their cytokine secretion. ILC1 produce IFN- γ , ILC2 secrete IL-5 and IL-13, and ILC3 produce IL-22 and IL-17. Recent studies have discovered the heterogeneity of ILCs in the gastrointestinal tract. It is not known well about the distribution of ILCs in the pediatric inflammatory bowel disease.

Methods: In an ongoing study, intestinal mucosal tissue samples were obtained from inflammatory bowel disease patients and control aged between 7 and 19 years, undergoing endoscopy for assessment of disease activity or diagnosis. After cell preparation, cell-surface fluorescence

intensity was assessed by flow cytometric analysis for sorting ILC subpopulation. ILC related cytokines were also assessed with conjugated antibody by fluorescein isothiocyanate. Clinical manifestation including disease activity and pathologic finding were reviewed. We compared normal mucosal tissues with inflamed mucosal tissue.

Result: Biopsy samples were collected from 13 inflammatory bowel disease patients (11 Crohn's disease and 2 ulcerative colitis) and 3 controls. Total 26 intestinal tissues were obtained and subdivided into 3 groups, disease cecum (n=7), normal cecum (n=10), small intestine (n=9). ILC1 and ILC3 were major population of intestinal mucosal tissue in this study sample and ILC2 were detected as a small proportion of ILC. The proportion of the ILC 1 was significantly increased in disease cecum than normal cecum ($p<0.05$). Total ILC population was decreased in diseases cecum than normal cecum. Discordance between surface marker and cytokine expression were observed.

Conclusion: The proportion of the ILC1 subset was higher in inflamed intestinal mucosa. ILC1 subsets which produce IFN-g may contribute to the pathogenesis of gut mucosal inflammation. Our results further support the general importance of ILC in the pathogenesis of inflammatory bowel disease.

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224 ASSESSMENT OF PREPAREDNESS FOR TRANSITION FROM PEDIATRIC TO ADULT CARE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Objectives: Many pediatric patients with Inflammatory Bowel Disease are not well prepared for transition to adult care. While tools such as the Transition Readiness Assessment Questionnaire are available, no tool has been developed specifically for transition of care in IBD. In our study, we surveyed IBD patients to assess preparedness for transition from pediatric to adult care. We then developed a questionnaire specifically for IBD transition. We hypothesized there would be disparity based on age, race and/or socioeconomic/payor status.

Methods: A survey was given to patients 13-19 years with previously diagnosed Crohn's disease or ulcerative colitis, seen at Advocate Children's Hospital Park Ridge between January 2016 and March 2016. 18 questions were divided into 4 categories (Medications, Knowledge, Independence, Feelings about transition). A total of 34 surveys were collected. Age, ethnicity, insurance type, medications, procedures and physician global assessment were taken from patient charts. Scores were determined based on number of correctly answered questions, which were assumed to indicate greater readiness to transition. Cronbach's alpha was used to evaluate internal structure of the survey, looking at total and subscale analysis. Patient variables were then correlated with total score and subscores.

Results: One question was dropped from analysis as it did not contribute useful variance. Total scale using the remaining questions had good reliability with Cronbach's alpha of 0.66. Each subscale of questions also had good reliability (Meds 0.68, Knowledge 0.61, Independence 0.7). Only age was mildly correlated with total score (r 0.31, t (32) 1.85, one-tailed $p=0.037$). No patient variables were significantly associated with Meds subscore. Knowledge subscore was significantly higher in Crohn's (mean 7.6, sd 2.6) than UC (mean 5.1, sd 2.7, t (18.6) 2.56, $p=0.019$). Independence subscore was significantly higher with age (r 0.54, $p<.001$) and higher in non-white (mean 15.7, sd 3.5) compared to white pts (mean 11.0, sd 2.8, t (6.4) 3.04, p .02). These effects remained significant in a linear regression that included both as predictors (p .001 for each).

Conclusion: We developed a survey tool that demonstrated good interitem reliability in total and within three planned subscales. As expected, older age was correlated with overall readiness for transition scores; older patients were also more independent in managing their disease. While there was no discrepancy found based on socioeconomic/payor status, we found discrepancy based on disease type and ethnicity. Patients with Crohn's were more knowledgeable about their disease compared to UC, and non-white patients were more independent in management of disease compared to white patients. Future studies will be necessary to better understand these discrepancies and to identify any additional correlations. While we did not include the number of years since diagnosis, we expect this to also impact scores.

225 EVALUATION OF A NOVEL EDUCATIONAL TOOL IN ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE: THE NEAT STUDY

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Objectives: Approximately 65-88% of adolescents are nonadherent to treatment regimens. In pediatric Inflammatory Bowel Disease (IBD) medication nonadherence rates are 50-88% across medications. Improving education in patients with chronic diseases has been shown to improve coping and to improve adherence to treatment in adults with IBD. Therapeutic patient education (TPE) has been used in patients with chronic diseases to train patients in the skills of self-managing or adapting treatment to their particular chronic disease, and in coping processes and skills.

Methods: In this pilot, mixed-methods study we sought to evaluate the feasibility and effect of TPE with a new guide-The IBD Pocket Guide on medication adherence, IBD knowledge and transition readiness in adolescents aged 11-18 years. Medication adherence was monitored using a MedMinder® Pill Dispensing system. Participants who were <90% adherent during a 4 week run-in phase were randomized to either a usual care group or an educational intervention (EI) group. Participants were followed for an additional 4 weeks after intervention.

Results: Trends were found in the EI to suggest improved medication adherence as well as improved IBD knowledge. Patients in the EI group had significantly improved knowledge of osteoporosis ($p=0.0476$). Qualitative data showed that participants did not like the use of the large pillbox, but did perceive that they had improved knowledge after the educational intervention. Families and patients found the IBD Pocket Guide to be useful and informative as a succinct guide to IBD.

Conclusion: Therapeutic patient education may be beneficial for improving patient medication adherence and IBD knowledge. Future studies guided by these pilot results will recruit a larger number of patients to test for the anticipated differences between groups.

*226 INTERNATIONAL VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE COHORT STUDY (NEOPICS): RESULTS FROM THE FIRST FIVE YEARS OF STUDYING VEOIBD

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Background: The incidence and prevalence of Inflammatory Bowel Disease (IBD) is rapidly increasing worldwide, particularly in infants and very young children. Very Early Onset (VEO) and infantile IBD often present and manifest uniquely: disease location, severity, (non) response to conventional therapy, and outcomes can be very different than what is seen in older-onset patients. Even within VEOIBD, there can be great heterogeneity in phenotype. Much still remains unknown about the causes, disease progression, and outcomes for VEOIBD patients – including how to best optimize existing and potential therapies. These differences within and in comparison to older cohorts may be best explained by regarding VEOIBD as many different diseases, each influenced strongly by various genetic pathways or monogenic causes.

Objective: The interNational Early Onset Paediatric IBD Cohort Study (NEOPICS) is a SickKids' based initiative that brings together international pediatric gastroenterologists and academic scientists to identify and investigate the causes, and develop new treatments and cures for VEOIBD (www.neopics.org).

Methods: VEOIBD patients are consented by their local pediatric gastroenterologist, with de-identified data and family biological samples shipped to NEOPICS. Whole exome sequencing on Illumina Hi-Seq is done for all participants. Based on the individual's phenotype/genotype, additional genetic, functional, and/or microbial assays may be performed to validate and further examine candidate mutations. All clinically significant results are reported to the clinician and validated in a CLIA-certified lab.

Results: To date, 535 VEOIBD patients (59.0% male, age 3.8 ± 0.2 yr, 93.5% with colonic distribution) have participated in NEOPICS along with 315 relatives (263 trios) from 26 countries. With our collaborators, over 50 genes have been recognized as monogenic causes of VEOIBD. In NEOPICS, 26 clear genetic diagnoses have been made in patients from Canada, United States, Chile, Uruguay, China, Australia, New Zealand, Sweden, Israel, Ireland, Spain, Romania, and others. Seven new genes have been discovered including TTC7A, PLVAP, TRIM22, and NHE3, with 18 additional genes/pathways examined, and 36 organoids generated for further assays and future drug trialing. Four patients had successful bone marrow transplant with more now awaiting transplant; others have been advised against specific therapies due to genetic profile and predicted risks.

Discussion: VEOIBD are more likely genetic driven diseases, including monogenic causes, that vary widely in presentation and will require precision based medicine to identify and treat appropriately. There are also many young patients with no clear, disease-causing genetic or functional pathway despite complex disease. NEOPICS has had great success to date and a strong, international collaboration will be vital to continue to identify and investigate the causes, and develop new treatments and cures.

227 LESS COLONIC BUT MORE UPPER GASTROINTESTINAL AND PERIANAL INVOLVEMENT IN JAPANESE CHILDREN WITH CROHN'S DISEASE: RESULTS OF JAPAN PEDIATRIC INFLAMMATORY BOWEL DISEASE REGISTRY

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Background: There is a few nationwide registry report from Asia for pediatric inflammatory bowel disease (IBD). This study aimed to reveal the characteristics of Japanese children with IBD, and compare them to that of Europe.

Methods: This is a prospective web-based registry study of newly diagnosed Japanese children with IBD. The Paris classification was used to categorize the feature of subjects. The results were compared to those of published EUKIDS data.

Results: Between November 2012 and December 2015, 265 IBD children were registered from 20 institutions. After the exclusion of 22 cases for incomplete workup, 91 Crohn's disease (CD), 146 ulcerative colitis (UC), and 6 IBD-unclassified, were analyzed. For the age at diagnosis, 20.9%, 21.9% and 83.3% of CD, UC and IBD-U were categorized as A1a (<10 y), respectively. For the CD location, L1 (ileocecal), L2 (colonic), L3 (ileal and colonic), and L4 (upper intestinal) were 18.7%, 13.2%, 64.8%, and 54.9%, respectively. For the disease extent of UC, 76% had E4 (pancolitis) and 6.8% had E1 (proctitis). For the CD behavior, B1 (non-stricturing/non-penetrating), B2 (stricturing), B3 (penetrating), and B2B3 were 83.5%, 11.0%, 3.3%, and 2.2%, respectively. The comparison between two registries revealed less L2 (13.2% vs. 27.3%, $p < 0.05$) and more L4a (47.3% vs. 29.6%, $p < 0.05$) involvement as well as higher prevalence of perianal modifier in Japanese children (34.1% vs. 9.4%, $p < 0.01$).

Conclusions: This study revealed similar results in age of diagnosis for CD/UC and disease extent of UC. However, there were less colonic but more upper gastrointestinal and perianal disease in Japanese CD.

228 THE PREVALENCE OF FUNCTIONAL ABDOMINAL PAIN DISORDERS IN PEDIATRIC PATIENTS WITH ESTABLISHED INFLAMMATORY BOWEL DISEASE

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Background: Patients with inflammatory bowel diseases (IBD) may have overlapping functional abdominal pain disorders (FAPDs) as a cause of underlying GI symptoms. The relationship between FAPDs and IBD has been well described in adults. However, there is a dearth of information on this overlap in children.

Objectives: 1) Describe the prevalence of FAPDs in pediatric patients with IBD in remission; 2) Describe the psychological profile of this group of children; 3) Assess the impact of the overlap of FAPDs and IBD on the child's quality of life.

Methods: This is a cross-sectional prospective study. Inclusion criteria: English speaking patients 8-18 years of age who were previously diagnosed with IBD. Disease activity was determined based on physician's global assessment, laboratory studies, and sPCDAI or PUCAI scoring. Children completed age appropriate validated questionnaires during GI clinic or infusion center visits including questionnaires to

diagnose FAPDs (functional dyspepsia, irritable bowel syndrome (IBS), functional abdominal pain, abdominal migraine) according to the Rome III criteria (QPGS-III); Children Depression Inventory (CDI-2); State-Trait-Anxiety-Inventory for Children (STAIC-C2); and Pediatric Quality of Life-GI (Peds QoL-GI).

Results: 128 subjects were recruited; 81 (63%) fully completed the questionnaires. Those with incomplete questionnaires were excluded from the analysis. There were 36 females and 45 males with a mean age of 14.4 ± 2.6 years (62 with Crohn's disease [CD], 19 with ulcerative colitis [UC]). Seventy one patients (87.6%) were classified as being in remission. The prevalence of FAPDs in IBD patients in remission was 25.9% (17 CD, 4 UC; 95% CI, 20.6% - 79.4%), 14 females & 7 males with FAPD vs. 19 females and 31 males without FAPD (p 0.0375). Children with FAPDs had IBS 13.6% (63.6% IBS-diarrhea predominant and 9.1% IBS-constipation predominant, 27.3% could not be further subcategorized), abdominal migraine 11.1%, functional abdominal pain 1.2%. Children with IBD and remission with and without FAPDs met criteria for anxiety 14.3% vs. 2% (p 0.0640) and depression 23.8% vs. 2% (p 0.0057) respectively. The average Peds QoL-GI score of children with IBD in remission with FAPDs was 71 vs. 86.5 (higher means better quality of life) in those without FAPDs (p 0.0077).

Conclusions: We found a high prevalence of FAPDs among children with IBD in remission. The prevalence found in our study is higher than the values found in the only two other published pediatric studies. This is the first study to systematically assess all FAPDs using the Rome III criteria and to demonstrate that this group of children has worse anxiety, depression and quality of life than children with IBD without FAPDs. The identification of the subgroup of patients that are predisposed to developing FAPDs may allow implementing early intervention strategies that could prevent or improve anxiety, depressive symptoms and poor quality of life.

	IBD In Remission	IBD Remission No FAPD	IBD Remission Any FAPD diagnosis	P
	n = 71	n = 50	n = 21	
Age Range, years	8 to 18	8 to 18	10 to 18	N/A
Mean age, years	14.49 \pm 2.68	14.14 \pm 2.86	15 \pm 2.01	0.0872
Gender, n (%)				0.0375
Females,	33 (46.5%)	19 (38%)	14 (66.7%)	
Males	38 (53.5%)	31 (62%)	7 (33.3%)	
Type of IBD, n (%)				0.7626
Crohn's Disease	55 (77.5%)	38 (76%)	17 (81%)	
Ulcerative Colitis	16 (22.5%)	12 (24%)	4 (19%)	

***229 UNCOVERING TRIPARTITE MOTIF CONTAINING 22 BINDING PARTNERS AND THEIR ROLES IN INFLAMMATORY BOWEL DISEASE.**

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Background: The severe multi-systemic phenotype of very early onset inflammatory bowel disease (VEOIBD) is often difficult to treat with conventional therapies. Although monogenic mutations of known genes have been identified, the majority of VEOIBD patients do not present with any known defect. Our recently published whole exome sequencing (WES) of VEOIBD patients and their parents identified autosomal recessive variants in the antiviral E3 ubiquitin ligase TRIM22, identifying and characterizing TRIM22's novel role in NOD2 signalling regulation through its direct interaction and ubiquitination of NOD2. The mutant forms of TRIM22 found within the patients exhibited aberrant NOD2 antiviral and pro-inflammatory signalling. TRIM22's implication in both antiviral and inflammatory pathways, and roles TRIM proteins play in proliferation and apoptosis, inspires confidence in its critical role in VEOIBD patients. However, the complete range of pathways influenced by TRIM22 remains a mystery. We hypothesize that TRIM22 lies at a crossroad of multiple cellular pathways related to inflammatory disease phenotypes. We propose to validate TRIM22 binding partners and uncover novel pathways with clinical implications in patients with severe VEOIBD.

Method: BioID, a method by which the protein of interest is fused with a promiscuous biotin ligase (BirA*), was used to identify candidate binding partners of TRIM22. Proximal proteins were biotinylated by the TRIM22-BirA* fusion and were identified by biotin affinity capture and mass spectrometry. Co-immunoprecipitation (co-IP) and immunofluorescent co-localization were used to validate these potential binding partners of TRIM22.

Results: Co-IP demonstrates TRIM22 interaction with histone deacetylase 1 (HDAC1), a component of the Mi-2/nucleosome remodeling and deacetylase (NuRD) complex involved in cell growth and apoptosis. TRIM22 may associate with interferon regulatory factor 8 (IRF8) based on co-IP with supporting immunofluorescent co-localization in the cytoplasm near the nucleus. Co-IP suggests TRIM22 may also interact with nuclear pore scaffold Nup153, a protein involved in host-virus interaction and selective nuclear entry of proteins and mRNAs.

Conclusion: Candidate TRIM22 binding partners revealed by BioID include multiple proteins of the Mi-2/NuRD complex, genes linked with primary immune deficiency including cyclin T1 and its associated kinase (CDK9), locations of host-virus interaction, regulators of NOD2 signal regulation (e.g., PML), and genes within known inflammatory bowel disease loci. This research is currently validating these BioID-derived associations while confirming co-IP of TRIM22 with HDAC1, IRF8, and Nup153. Our patient WES database can be interrogated for novel disease causing mutations within TRIM22 pathways unveiled by these interactions, providing the potential for future therapies for phenotypes typically unresponsive to current treatments.

230 ASSESSMENT OF PEDIATRIC GASTROENTEROLOGISTS' PERCEPTIONS AND PRACTICES REGARDING VENOUS THROMBOEMBOLISM PROPHYLAXIS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Background: The risk of venous thromboembolism (VTE) is increased in children with Inflammatory Bowel Disease (IBD). This complication can have significant medical consequences and can lead to major morbidity and sometimes, mortality. While adult IBD guidelines recommend VTE prophylaxis in IBD patients, there are no similar guidelines for pediatrics and practice regarding prevention of VTE in pediatric IBD is variable. In this study, we sought to assess the opinions of pediatric gastroenterologists regarding VTE risk and prophylaxis practices in pediatric IBD patients.

Methods: An electronic survey of 21 questions regarding pediatric gastroenterologists' knowledge of VTE and prophylaxis practices in IBD patients was created using REDCap, a secure web application for survey and data management. The survey was distributed to members of NASPGHAN via e-mail in three instances over a three-month period. Survey participants' responses were collected in REDCap database and analyzed by Fisher's exact test and Chi-square test.

Results: Survey response rate was 9.3%. 92% of participants agree that pediatric IBD patients have an increased risk of VTE, but only 1/3 of respondents reported providing prophylaxis to their IBD patients. The most common setting for providing prophylaxis was in hospitalized patients with an IBD flare; mechanical and pharmacologic methods were used with equal frequency. For those practitioners who do not initiate VTE prophylaxis, the most commonly cited reason was lack of pediatric literature, with risk of bleeding, lack of education, and patient resistance reported as additional concerns. Thrombophilia evaluation was also addressed and most respondents did not feel that hematologic investigation was required.

Conclusions: Our findings demonstrate that pediatric gastroenterologists are aware that pediatric patients with IBD have an increased risk of VTE. However, despite this recognition, most practitioners are reluctant to start VTE prophylaxis for a number of reasons, with the primary reason reported as lack of literature. Despite limited response rate, these results bring forth important concerns among pediatric gastroenterology practitioners that prevent them from providing potentially life-saving VTE prophylaxis to children with IBD. This study also highlights the need for further investigation so that we can better understand the nature of VTE in pediatric IBD, guide pediatric gastroenterologists as they care for their pediatric IBD patients, and ultimately improve patient outcomes in pediatric IBD.

**231 CANNABINOID RECEPTOR 2 ACTIVATION AMELIORATES INFLAMMATION IN MURINE MODEL OF CROHN'S DISEASE*

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Background: Expanding marijuana legalization has generated vast interest in its therapeutic use in human disease. Limited scientific evidence suggests that marijuana use may have a positive symptomatic effect on inflammatory bowel disease (IBD) patients due to its analgesic and anti-inflammatory effects. However, our lack of understanding of how cannabinoids impact disease outcomes has prompted us to investigate the roles of cannabinoid 1 (CB1) and cannabinoid 2 (CB2) receptors in preclinical chronic IBD models. The CB1 receptor is preferentially associated with central nervous system functions while the CB2 receptor is found primarily on immune cells, including CD4 T cells, key regulators of intestinal inflammation. Furthermore, IBD is associated with upregulation of CB2 receptor in the inflamed intestines. Nevertheless, there remains a significant gap in our knowledge of how activation of CB1 and CB2 receptors will affect intestinal inflammation.

Methods: TNFΔARE mice express elevated TNF protein leading to Crohn's-like spontaneous ileitis and discontinuous transmural inflammation. In our study, wild-type (WT) and inflamed TNFΔARE mice were treated for two weeks with either CB1 agonist WIN55,212-2 or CB2 agonist Gp1a, and the ileitis was evaluated by PCR, flow cytometry, and blinded scoring by a pathologist. We also quantified intestinal endocannabinoids by HPLC, measured CB2 expression on regulatory T cells, and evaluated regulatory T cell suppressive function upon CB2 receptor activation.

Results: The endocannabinoid anandamide was induced in ilea of TNFΔARE mice (27 pmol/g) relative to WT (18.8 pmol/g; $p < 0.05$). In addition, CB1 receptor expression increased 3-fold ($p < 0.0001$) while CB2 receptor expression increased 19-fold ($p < 0.01$) in TNFΔARE as compared to WT mice. Unexpectedly, CB1 activation with WIN55,212-2 exacerbated intestinal inflammation and demonstrated increased expression of pro-inflammatory Th1 cells in the ileal lamina propria ($p < 0.01$). In contrast, CB2 activation with Gp1a significantly decreased intestinal inflammation as demonstrated by reduced Th1 infiltration ($p < 0.01$) and improved histologic scoring ($p < 0.05$). Additionally, CB2 receptor expression is preferentially increased on regulatory T cells versus T effector cells, up to 2-fold in WT ($p < 0.05$) and up to 11-fold in TNFΔARE mice ($p < 0.001$). Moreover, CB2 receptor agonism led to a decrease of 7% in T effector cell proliferation due to improved suppressive function of regulatory T cells ($p < 0.01$). Lastly, CB2 receptor agonism increased concentration of anti-inflammatory cytokine IL-10 (vehicle 123 pg/mg, Gp1a 253 pg/mg; $p < 0.05$).

Conclusion: While CB1 receptor activation aggravates intestinal inflammation, CB2 receptor agonism attenuates murine ileitis through improvement in regulatory T cell suppressive function. Based on these findings, we would caution against the use of marijuana to treat IBD symptoms pending more comprehensive investigation in human disease.

232 AZATHIOPRINE IN PREVENTION OF ENDOSCOPIC RECURRENCE IN CHILDREN WITH CROHN'S DISEASE AFTER ILEOCECAL RESECTION

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Objective: Ileocecal resection (ICR) is frequent type of surgery in patients with Crohn's disease (CD). Cumulative risk of surgery is growing with disease duration, so patients with CD, diagnosed in young age, have high risk to undergo intestinal surgery. The aim of this study was to evaluate endoscopic recurrence in children with CD, six months after ICR and also try to find potential risk factors.

Methods: In this study we prospectively observed children after ICR treated with azathioprine (AZA) in monotherapy or in combination with aminosalicylates, endoscopy was performed in follow-up 6 month after ICR and was described by Rutgeerts score.

Results: Twenty one patients fulfilled inclusion criteria and finished 6 month follow-up. Eight patients had endoscopic recurrence (Rutgeerts score ≥ 2). Only potential risk factor found, was lower concentration of serum albumin at the time of surgery that was associated with higher endoscopic recurrence rate at 6 months ($p = 0.042$).

Conclusion: Endoscopic recurrence rate in children after ICR in our study is similar as in studies on adult patients. Albumin at the time of surgery could be potential predictor of disease recurrence. Supported by grants VZ FNM 64203/6001, GAUK 136215 and GAUK 246216.

233 QUALITY OF LIFE IN PEDIATRIC PATIENTS RECEIVING EXCLUSIVE ENTERAL NUTRITION IS EQUIVALENT TO CORTICOSTEROID THERAPY IN PATIENTS WITH ACTIVE INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease (IBD) is a chronic illness that can affect a child's physical, social and psychological well-being. Studies have shown that active IBD is associated with lower quality of life (QOL) scores in children. Exclusive enteral nutrition (EEN) and corticosteroids (CS) are effective treatment options for induction of remission in pediatric Crohn's disease (CD), while CS is effective for induction of remission in ulcerative colitis (UC). EEN involves the use of a nutritional formula, via nasogastric (NG) tube or taken by mouth for 8 continuous weeks, however it is often poorly utilized due to perceived increased treatment burden for patients. Two studies have shown that QOL in children receiving EEN is significantly better at the end of therapy compared to baseline. However, no studies have assessed the effects of EEN therapy on QOL longitudinally during treatment, or against other IBD treatment options. The objective of this study was to compare longitudinal QOL scores in pediatric CD and UC patients receiving an 8-week course of EEN versus CS therapy.

Methods: This prospective cohort study involved patients 5-18 years old with IBD, followed up at McMaster Children's Hospital (Hamilton, Ontario, CANADA). Patients were included if they received EEN (Peptamen® 1.5) or CS therapy for induction of remission of moderate to severe CD or UC. All patients received 8 weeks of treatment. QOL was assessed using the KIDSCREEN-10 index. Clinical outcomes were assessed using the Pediatric UC Activity Index (PUCAI), or the modified Pediatric CD Activity Index (PCDAI). QOL and disease activity indices were assessed weekly during the 8-week induction therapy, and after 4 weeks of completion of therapy.

Results: Twenty-six patients were enrolled in the study. Fourteen patients received induction therapy with EEN (14 CD, 0 UC) and 12 with CS (4 CD, 8 UC). Among patients receiving EEN, 12 received therapy via NG tube, 2 refused NG tube insertion and received Ensure® orally. In CD patients, as PCDAI decreased, QOL significantly increased ($r = -0.43$; $p < 0.001$). Similar trends were seen in UC patients; results did not reach statistical significance ($r = -0.25$; $p = 0.245$). Importantly, there was no significant difference in QOL between patients receiving EEN versus CS at each week of treatment, at 4 weeks post treatment, or overall (mean difference in QOL score 1.71; $p = 0.092$, 95% CI, 0.28-3.71).

Conclusion: Pediatric IBD patients receiving treatment for induction of remission experienced no difference in QOL on EEN therapy versus CS therapy. QOL in pediatric IBD is correlated with improvements in disease activity, not method of therapy used for induction of remission. Physicians and families should consider the benefits of EEN therapy and its superior side-effect profile when choosing therapy for induction of remission.

234 IS EARLY ONSET A RISK FACTOR IN THE OUTCOME OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE?

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Introduction: Very early onset Inflammatory Bowel Disease (VEO-IBD) represents an exclusive form of IBD which is diagnosed in children younger than 5 years of age. It has been associated with increased disease severity, aggressive progression and poor responsiveness to most conventional therapies.

Aim: To evaluate if children with VEO-IBD show a different behavior after 5 years-follow-up compared to those pediatric patients with late onset.

Materials and Methods: Retrospective and transverse study in pediatric patients with IBD diagnosed from 1996 to 2010 at one reference center in Argentina. Diagnosis was established according to clinical presentation, laboratory, endoscopy, radiology and histology criteria. The variables considered were: median age, sex and location at diagnosis; severity, treatment requirements during follow-up and autoimmune diseases (AI) association. They were divided into 2 groups according to age in G1: younger than 5 years old and G2: older than 5 years of age.

Results: 147 IBD children (G1 50/147 and G2 97/147) were followed at a Pediatric Gastroenterology Unit. After 5 years follow-up or more: G1: n 29; 18/29 ulcerative colitis (UC) (62%), 7/29 (24%) Crohn's disease (CD) and 4/29 (14 %) Unclassified IBD (U-IBD). G2: n 88 UC: 52 (59%), CD: 31 (35%) and U-IBD: 5 (6%). Median age at diagnosis was G1: 2.8 years (SD: 1.3) and G2 8.3 years (DS: 5.2). Growth failure was seen in 3/29 in children in G1 vs. 24/88 in G2 ($p = 0.0605$). All of them were treated with mesalazine. Patients with moderate disease, received immunomodulators as maintenance therapy. In G1 2/29 (7%) received biological therapy (anti TNF α) vs. G2 10/88 (11%) ($p = 0.4729$). In G1 3/29 patients required colectomy due to failure to immunosuppressive medications vs. 6/88 in G2, 4 required ileocolonic resection due to stenotic or fistulizing behavior and two proctocolectomy. In G1 13/29 (45%) presented AI diseases (Celiac disease, AI hepatitis, sclerosing colangitis, rheumatoid arthritis) vs. 19/88 (21.5%) in G2 ($p = 0.0362$). In G1: 1/29 required liver transplantation due to cirrhotic evolution and in G2: 2/88 under azathioprine treatment developed myeloid leukemia and another presented a non-Hodgkin lymphoma.

Conclusion: According to this cohort, early onset did not represent a major risk factor, at least in the first five years of follow-up. The differences observed to previous published data may be due to genetics and /or local environmental characteristics in Latin America. More studies are necessary to shed light on the complex mechanisms involved in IBD outcome in childhood.

235 LONG-TERM EFFICACY AND SAFETY OF LOW DOSE THIOPURINE-ALLOPURINOL COMBINATION THERAPY (TP/AP) IN PEDIATRIC INFLAMMATORY BOWEL DISEASE (PIBD)

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PIBD patients are routinely treated with thiopurine drugs for maintenance therapy. In some, metabolic hypermethylation precludes successful therapy by promoting preferential production of inactive 6-methylmercaptopurine (6MMP) over active thioguanine nucleotides (6TG). This metabolism can be reversed by switching to a regimen of low dose thiopurine and concomitant allopurinol (Sparrow Alim Pharm Ther 2005). There have, however, been few studies in the pediatric population that address the long-term efficacy and safety of this approach.

Objective: To evaluate the efficacy and safety of low-dose TP/AP combination therapy in PIBD patients.

Methods: A retrospective single center chart review of all children who had thiopurine metabolite testing (Prometheus Labs) between 2005-2015 was performed to identify all who received TP/AP. Metabolite changes after TP/AP, and clinical efficacy as evidenced by ongoing or recurrent

corticosteroid use, IBD-related surgery, or escalation in therapy (methotrexate or anti-TNF) were determined. Leukopenia, elevated AST or ALT, serious infection and malignancy were also recorded.

Results: 424 children had metabolite testing after initiating treatment with either 6-mercaptopurine or azathioprine monotherapy. Of these, 38 (9%) were switched to TP/AP. Incomplete records in 10 left 28 evaluable subjects (11 male, mean age 14±4 yrs, 17 CD, 11 UC), including 1 who began TP/AP shortly after a bowel resection. Mean duration of TP/AP was 30.9±25.2 mos. Prior to TP/AP, 6MMP levels were 8723±6305 pmole/8X108RBC, with 18 (64%) subjects having 6MMP levels above the potentially toxic level of 5700 pmole/8X108RBC (range 6091-23555 pmole/8X108RBC). Baseline 6TG was less than the therapeutic target range of 230-400 pmole/8X108RBC in 17 (61%). After TP/AP, 6MMP was below the limits of detection in 25 (89%), while 6TG levels were >230 in 21 (75%, mean 339±184 pmole/8X108RBC). Overall, 14/28 (50%) subjects were successfully maintained on TP/AP without additional steroids, biologics or surgery for a mean 27 mos (range 5-67mos). By contrast, 5 were steroid dependent, 3 were switched to methotrexate (after 3, 39, 79 mos of TP/AP), 5 to Remicade (after 3, 3, 17, 19, 27 mos of TP/AP) and 1 required surgery 2 mos after starting TP/AP. No child discontinued therapy due to hepatotoxicity. Therapy was briefly held in 3 due to leucopenia, but ANC remained >1500 and/or WBC >5. No serious infections occurred. One patient was diagnosed with a pseudopapillary pancreatic tumor 1 mos after TP/AP and underwent a Whipple procedure within 5 mos.

Conclusion: TP/AP was well tolerated up to a maximum follow-up of 85 mos, and effectively rescued 50% of children who had previously not responded to thiopurine monotherapy. TP/AP may be a safe and effective option for children whose families are hesitant to initiate alternative immunomodulatory or biologic therapy.

236 CONCOMITANT USE OF METHOTREXATE RESULTS IN HIGHER 14-WEEK INFLIXIMAB TROUGH LEVELS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Inflammatory bowel disease (IBD) is a chronic inflammatory disorder that often has an unpredictable clinical course. Methotrexate and Infliximab (IFX) are effective therapies for IBD and can be used individually as monotherapy or in combination (concomitant therapy.) The goal of this study was to compare pediatric patients with IBD on IFX monotherapy to patients on concomitant therapy with IFX and Methotrexate specifically with regard to 14-week IFX trough and antibody to infliximab (ATI) levels. The secondary objective was to compare the groups with regards to change in the pediatric Crohn's disease activity index score (PCDAI), mean corpuscular volume (MCV) and C-reactive protein (CRP) over the first 14 weeks of therapy. The study's aim was to show that concomitant therapy with IFX and Methotrexate resulted in higher IFX trough levels and prevented the development of immunogenicity with antidrug antibodies.

This was a retrospective chart review of all patients with a diagnosis of Crohn's disease, ulcerative colitis and IBD-unspecified who received IFX between 2010 and 2015 at a single tertiary care center. Inclusion criteria were patients previously naïve to biologic therapy who were started on IFX and had IFX trough and ATI levels checked at 14 weeks of therapy. The excluded patients were those started on methotrexate after starting IFX, patients on a thiopurine or patients who did not follow standard IFX induction dosing. Included patients were divided into two groups: those on monotherapy with IFX and those on concomitant therapy. Both groups had week 14 IFX trough and ATI levels assessed and also were evaluated for change in PCDAI score, CRP and MCV from week 0 to week 14 of therapy.

32 patients met inclusion criteria: 10 patients on concomitant therapy and 22 patients on monotherapy. Demographics including disease scores at the start of therapy were similar between the two groups with the exception of sex; 100% of the patients in the monotherapy group were male while only 45% of patients in the concomitant therapy group were male. IFX trough levels at week 14 of therapy were significantly higher in the concomitant therapy group as compared to the monotherapy group (10.3 +/- 5.6 versus 5.9 +/- 3.7 $p=0.0119$). There was a trend towards significance when ATI levels were grouped as positive or negative (10 vs. 36% $p=0.12$) but overall the difference still lacked significance. There was no significant difference in the change in PCDAI score, CRP or MCV from week 0 to week 14 when the groups were compared. This is the first pediatric study examining the effects of concomitant IFX therapy with methotrexate on 14-week IFX trough and antibody to IFX levels compared to IFX monotherapy alone. This study shows that the use of concomitant methotrexate promoted higher IFX trough levels after the completion of induction dosing. There was no significant difference in ATI levels between the two groups which may be secondary to small sample size.

237 POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH VEDOLIZUMAB

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Background: Vedolizumab is a gut-specific $\alpha 4\beta 7$ integrin inhibitor with efficacy in Ulcerative Colitis (UC) and Crohn's disease (CD). Vedolizumab affects leukocyte adhesion in the gut, a process important for wound healing, thus raising concern for postoperative complications in patients treated with vedolizumab prior to surgery. As there is minimal data on postoperative complication risk in patients treated with vedolizumab, the aim of this study was to examine the rate of postoperative complications in a cohort of patients treated with vedolizumab who required surgery at our institution.

Methods: By surveying the electronic medical record, we identified a cohort of patients with CD or UC who were treated with vedolizumab at Boston Children's Hospital from 2014-2016 and were followed for at least 3 months. Data on demographics, operations, concurrent medications, disease phenotype, and response to vedolizumab was extracted from the record. The specific postoperative complications were described.

Results: At our institution, 31 patients (mean age 17.2 years±3.7 years SD, range 9-24 years) with CD (n=21) and UC (n=10) have been treated with vedolizumab for refractory disease. 30/31 patients had failed 1 TNF α inhibitor and 21/31 had failed at least 2 TNF inhibitors prior to vedolizumab administration. 13/31 patients required surgery following initiation of vedolizumab. The operations included diverting ileostomy (n=6), laparoscopic proctocolectomy with ileoanal J-pouch and diverting ileostomy (n=6), and ileocecal resection (n=1). 8/13 (61%) patients had a postoperative complication, including 5 complications associated with poor wound healing or infection (intra-abdominal abscess [n=1], mucocutaneous separation at the ileostomy [n=3], stoma-related small bowel obstruction requiring ostomy takedown [n=1]) and 3 other complications (seizure [n=1] and readmission for pain and dehydration [n=2]).

Conclusion: Patients who receive vedolizumab often have refractory disease and are likely to require surgery. This study highlights the high postoperative complication rate in patients treated with vedolizumab who require surgery at our institution. Large multicenter studies are required to further examine the risk of postoperative complications in patients treated with vedolizumab.

238 INCIDENCE OF DENTAL CARIES AMONG A PEDIATRIC POPULATION DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE
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Introduction: Inflammatory Bowel Disease (IBD) can manifest itself in the oral cavity. The DMDF measures the average number of Decayed, Missing and Filled teeth and the World Health Organization (WHO) set 1.50 as the target to 2020, in Portugal.

Aim: To characterize the state of oral health in patients diagnosed with Inflammatory Bowel Disease (IBD) at pediatric age and compare it with a same-age healthy sample at a school in the same district.

Methods: Observational descriptive study, with survey application and direct evaluation of the oral cavity, based on the DMFD index of patients diagnosed with IBD at pediatric age (cases) from a tertiary hospital. The control group was healthy children and adolescents from a school. The oral cavity was photographed. The statistical analysis used the Chi-square test.

Results: From a database of 72 patients with IBD at pediatric age, 55 phone calls were answered: 5 people weren't in the country and 50 agreed to an appointment at the hospital to participate in the study. One IBD patient missed the appointment and 49 IBD patients completed the protocol: 34 affected by Crohn's disease, 14 cases of ulcerative colitis (UC) and 1 indeterminate case. In the control group, the authors sent the parents of 50 children and adolescents a written consent and 26 completed the protocol. The DMFD average, in the IBD sample, was 3.22 versus 5.19 in the control group, $p=0.036$. The IBD patients had a mean age \pm standard deviation of 17.49 ± 4.94 years and the control group average age \pm standard deviation was 17.42 ± 0.50 years, $p=0.981$. Regarding the number of cavities present at the time of evaluation; the case group had an average of 2.37, and the control group 2.92, $p=0.340$. In Crohn's disease, the DMFD was 3.35, while the UC value was 2.86, $p=0.627$. The recurring presence of ulcers in IBD group occurred in 20.4% people. 75.52% subjects in the IBD group used immunosuppressants; UC patients didn't use them. The DMFD average proved to be higher when the diagnosis preceded 7 years of age (permanent teeth age formation) in the IBD group. The number of brushings, meals and cleanings weren't negligent in the patient population. 46.9% of patients only see the dentist when feeling pain. In the control population, there was also a good level of care and dental hygiene, with longer gaps between trips to the dentist than that observed in the patient population. Sweetened foods were regularly consumed by 79.5% of IBD patients, while in healthy population it occurred in 50% of individuals.

Conclusions: The prevalence of decayed teeth in the IBD group, according to the DMDF index, was significantly lower than the healthy sample one, even if the control population healthcare was better and candy consumption in the diseased population was higher. There were no significant differences between the types of IBD and cariogenic index of the individual. The IBD diagnosis before 7 years old may be important to prevent tooth decay, perhaps for the special care of young children with IBD.

239 DIFFERENTIATION OF CROHN'S DISEASE AND ULCERATIVE COLITIS IN CHILDREN BASED ON THE SERUM CYTOKINE PROFILE

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Background and Aims: Cytokines have been directly implicated in the pathogenesis of inflammatory bowel diseases (IBDs) such as Crohn's disease (CD) and ulcerative colitis (UC). In recent genetic and immunological studies, they appear to play a crucial role in controlling intestinal inflammation and the associated clinical symptoms of IBD. However, the changing cytokine production patterns in pediatric IBDs has not yet been well established. The aim of this study was to investigate the expression of the cytokine profile in pediatric IBDs and to differentiate between CD and UC based on the serum cytokine profile.

Methods: Seventy-three children (48 boys and 25 girls) aged from 5.8 to 17.3 years were enrolled in this study. This group included 20 patients with CD (CD group), 20 with UC (UC group), and 33 with non-IBDs (control group). Diagnosis of CD and UC was based on case histories and clinical, laboratory, endoscopic, and histological data. The control group included healthy subjects as well as patients with functional constipation and irritable bowel syndrome. Disease activity in patients with IBDs was assessed using the Pediatric CD Activity Index (PCDAI) or the Pediatric UC Activity Index (PUCAI).

A total of 27 cytokines, chemokines, and growth factors (IL-1 β , IL-1ra, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-17, Eotaxin, FGF-basic, G-CSF, GM-CSF, IFN- γ , IP-10, MCP-1, MIP-1a, MIP-1 β , PDGF, RANTES, TNF- α , and VEGF) were determined in the blood sera using a double-beam laser automatic analyzer (BioPlex Protein Assay System; BioRad, USA).

Results: Cytokine distribution in the sera is presented in Table 1. Three cytokines (IL-1 β , PDGF, and RANTES) were excluded as levels were out of range. The levels of IL-6, and G-CSF were significantly increased in the CD and UC groups when compared with those in the control group. Furthermore, the levels of IL-15, MCP-1, and MIP-1a were significantly increased in the CD group when compared with the UC group. Multivariate logistic regression analysis revealed that three cytokines, MCP-1, TNF- α , and Eotaxin as good biomarker potential for differentiating between CD and UC using the serum cytokine profile.

Conclusion: There is potential for differentiation between patients with CD and UC using serological methods for adaptable cytokine measurement.

Serum Cytokines(pg/ml)	CD	UC	Control	Kruskal-Wallis	CD vs UC	CD vs Ctrl	UC vs Ctrl
Eotaxin	90.4(17.5-353)	129(41-368.8)	45.9(0-253.3)	**			***
FGF-basic	48.8(7.5-183.8)	27.9(0-99.6)	0(0-151.9)	***		***	*
G-CSF	20.3(7.3-67.6)	27.3(6.7-88.9)	11.5(3-25.8)	***		***	***
GM-CSF	46.2(15.6-111.6)	45.4(9.2-111.3)	27.7(0-117.1)	*		*	*
IFN- γ	157.7(54.4-545.3)	147.2(34.7-518.7)	127.8(26.9-471.5)				
IL-10	58.9(4.7-157.4)	28.1(0.3-188)	13.6(0.3-59.2)	***		***	*
IL-12	11.4(2.1-39.6)	8.7(1.9-56.2)	6.2(0.3-14.5)	**		*	*
IL-13	21.2(3.3-38.5)	13.5(1.4-25.2)	9(1.7-25.3)	***		***	*
IL-15	4.6(0-17.1)	0.9(0-26.7)	0(0-10.2)	***	*	***	*
IL-17	88.9(27.9-293.4)	96.1(8.9-187.8)	82.8(15.5-307.5)				
IL-1ra	192.9(55.7-940.6)	203.7(59-773.6)	129.2(25-804.2)				*
IL-2	8.7(2.6-32.8)	8.1(0.6-28.1)	5.3(0-25.8)	*		*	
IL-4	5(3.1-8.3)	4.6(1.8-7.3)	3.4(0.3-7.1)	**		***	
IL-5	1.9(0.5-8.7)	2.1(0.1-7.5)	1.7(0.1-10)				
IL-6	23.8(2.4-178.4)	13.7(2.5-36.2)	4.9(0-17.6)	***		***	***
IL-7	22.5(8.1-54)	18.3(2.7-33.6)	9.1(1.4-32.3)	***		***	*
IL-8	34.3(8.4-8699.7)	40.1(5.1-88.5)	14.3(0-151.6)	**		**	*
IL-9	60.6(36-101.3)	49.5(19.6-87.1)	40.7(6.2-177)	*		*	
IP-10	1024.2(225.5-13563.7)	956.4(483.6-18933.4)	564(163.9-3503.1)	***		*	***
MCP-1	29.9(6.3-320.6)	16.3(1-113.1)	18.8(1.4-79.7)	**	**	*	
MIP-1 α	19.9(6.9-50.1)	8.9(0-54.9)	4(0-25.3)	***	**	***	
MIP-1 β	134.2(49.9-1150.5)	125.6(19.6-420.5)	100(15.9-323.5)			*	
TNF- α	60.3(0-2607.9)	29.5(0-96.9)	13.6(0-130.4)	*		**	
VEGF	391.5(14.9-1041.9)	195.2(19.2-996.9)	117.8(4.5-329.3)	***		***	*

*: P<0.05, **: P<0.01, ***: P<0.001 (Kruskal-Wallis rank sum test)

*: P<0.05, **: P<0.01, ***: P<0.001 (Mann-whitney U test)

240 CHARACTERIZATION OF THE INTESTINAL MICROBIOME OF VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE

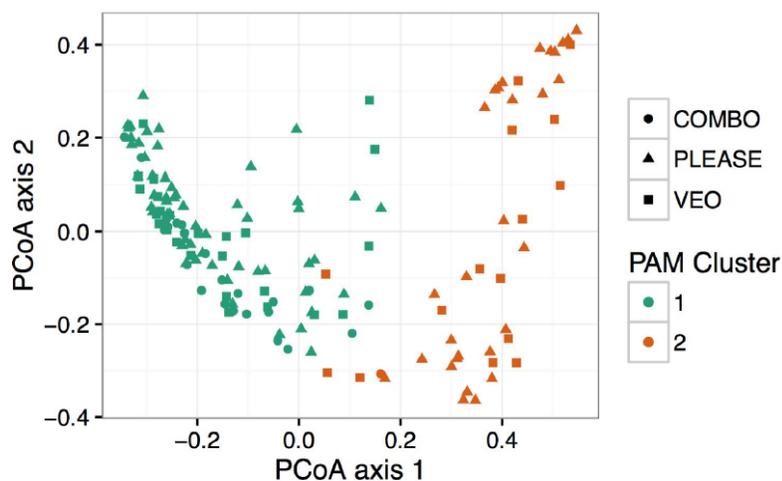
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Inflammatory bowel disease (IBD) is a multigenic and environmentally triggered disease resulting in a dysregulated immune response to commensal or pathogenic microbes in the intestinal tract. Very early onset (VEO-IBD), IBD diagnosed <5 years of age, can present with a more aggressive phenotype and there appears to be a more prominent genetic contribution to the disease compared to older patients. However, the rapidly increasing incidence and prevalence of VEO-IBD points to an environmental and gut microbiome influence in disease development as well. Using shotgun metagenomic sequencing, we previously analyzed the gut microbiome of a prospective pediatric Crohn's disease cohort initiating therapy.¹ Here, we aim to characterize the intestinal microbiome of patients with VEO-IBD who have had whole exome sequencing (WES) performed, and to compare the results to the previously analyzed cohort of older pediatric patients with IBD. Stool samples were collected from subjects diagnosed with VEO-IBD who underwent WES. Genomic DNA was prepared from whole stool and sequenced using the Illumina HiSeq paired-end method. Reads were aligned to the human genome to identify human DNA in the sequencing results. Taxonomy was assigned using MetaPhlan2 and confirmed by One CodeX, which identifies clade-specific marker genes from bacterial, fungal, archaeal, and viral sources. Samples were compared to post-therapy samples from older-onset IBD patients. Among the samples obtained, 35 stool samples from VEO-IBD patients were analyzed and were compared to 80 older-onset IBD patients and 24 healthy controls from prior studies.^{1,2} Samples were compared by the percentage of shared species (Jaccard distance), and clustering was performed by the method of partitioning around medoids. Two clusters were detected in the combined dataset. One cluster was near to healthy controls (Figure 1, cluster 1). The second cluster was more distant from the healthy controls, and had lower diversity and altered bacterial composition (Figure 1, cluster 2). The VEO-IBD patients in cluster 2 were diagnosed in the first 3 years of life and had increased disease severity as compared to cluster 1. This distinction was seen in older-onset IBD as well. In addition, percentage of human DNA detected in the stool sample was greater in cluster 2, similar to the older-onset IBD cohort.

Two clusters were detected in the microbiome composition of patients with VEO-IBD, reflecting our previous findings in older-onset IBD. The two clusters were associated with clinical features of disease severity. Further studies are ongoing to include a larger cohort of VEO-IBD. In addition, analyses are being performed to associate the microbiome composition with host genomic data and clinical characteristics in the VEO-IBD cohort.

1. Lewis JD *et al. Cell Host Microbe* 2015;18(4):489-500; 2. Wu GD *et al. Science*. 2011;334(6052):105-8.

Table: Dysbiotic Cluster in Pediatric IBD



241 THERAPEUTIC DRUG MONITORING IS A NEW TOOL FOR IMPROVING THE CARE OF PATIENTS TREATED WITH ANTI-TNF ALPHA : DOES THIS APPLY TO CHILDREN WITH INFLAMMATORY BOWEL DISEASE?

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Introduction: Infliximab (IFX) was proven effective in the induction and maintenance of remission in IBD in both children and adults. However, there is a significant number of individual who lose clinical response to the medication. Monitoring of serum IFX drug level was shown to correlate with clinical response, and mucosal healing. Few studies demonstrate similar benefits in children, some suggesting that perhaps the target serum level of antiTNF in children should be higher than in adults.

Objective: To review our experience with therapeutic drug monitoring (TDM) in children with inflammatory bowel disease (IBD) treated with IFX. The primary objective was to assess the serum levels of IFX in children aged 5-18 years during the maintenance period. The secondary objectives were to correlate the levels with clinical response and to assess the proportion of patients in which a proactive dose adjustment approach had been taken.

Methods: This was a single-center retrospective cohort study. Patients were included if they had at least one serum level of IFX between June 2014 and November 2015, and had a follow-up of at least 3 months after the levels were drawn. We collected all trough levels drawn during maintenance phase. All levels were analyzed using the progenika promotor-IFX ELISA technique. We collected biochemical markers drawn a maximum of two weeks prior to the IFX level. We also collected clinical assessments at the time of IFX infusion as reported by the patient. This outcome was graded on a three-point scale (well, moderately well and unwell). The physician global assessment was also recorded if it was done within 4 weeks of the IFX level.

Results: During the study period a total of 301 children were receiving IFX. Among them, 188 children had at least one IFX serum level. From the first 102 patients (59.8% boys; 232 IFX levels) evaluated we excluded the 45 serum levels drawn during induction. IFX was started with a mean interval of 19 weeks from diagnosis (Range 0–130.6 weeks) at a dose of 5 to 10mg/Kg/dose depending on disease severity. Twenty seven percent were on combination therapy with the majority on methotrexate (65.3%). The 84 patients in maintenance phase had a total of 187 serum IFX levels drawn. The median trough IFX level was 6.6 ug/mL for children with UC and 3.61 for children with CD (Range 0.01–14.4) taken at a median dose interval of 7 weeks. Serum IFX levels were comparable between males and females. Levels were subtherapeutic in 43% and suprathereapeutic in 33%. Clinical status as reported by patients did not correlate with IFX levels.

Conclusion: Despite dose adjustments, nearly 50% of serum IFX levels were sub-therapeutic, although the majority of the patients reported feeling well. TDM of IFX is therefore mandatory in the treatment of IBD and patient self-reported clinical status is not an indicator of adequate levels.

242 CLINICAL OUTCOMES IN PAEDIATRIC ULCERATIVE COLITIS: A SINGLE-CENTRE COHORT STUDY.

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Objectives and study: The disease course of children with ulcerative colitis (UC) can vary substantially, and published data on clinical outcomes remains scarce. We describe the outcomes of children and adolescents with UC or unclassified inflammatory colitis (IBD-U) based on induction treatment and requirement for subsequent medical and surgical treatment interventions focusing on the first 18 months upon diagnosis.

Methods: We retrospectively identified all patients aged 2 to 18 years diagnosed with UC or IBD-U in our centre between September 2006 and February 2014, with a minimum follow-up of 18 months. For all patients we recorded the type of induction treatment (i.e., steroids or 5-Aminosalicylic acid (5-ASA)) received within 3 months from diagnosis; maintenance therapy at 6, 12 and 18 months follow-up; commencement dates of second-line therapy such as Azathioprine (AZA), 6-mercaptopurine (6MP); and requirement for third-line therapy (i.e., biologics) and surgical intervention (i.e. colectomy). Patients were stratified into 3 different groups based on their requirements for escalation therapy over an 18-month period: mild disease course maintained on 5-ASA alone (Group 1); moderately severe disease course requiring escalation to AZA or 6-MP (Group 2) and severe disease course requiring biologics (IFX) and/or colectomy (Group 3).

Results: 93 patients were included in our study with a mean follow-up duration of 59.2 months +/- SD 33.4 months (median 49.7 months, range 18-195 months). 58/93 (62.3%) were diagnosed with UC and 35/93 (37.6%) with IBDU colitis. The mean age at diagnosis was 11.7 years (+/-

SD 3.12 years, range 2.2 - 17 years). 77/93 (82.8%) required induction of remission with steroid therapy, while only 16 patients (17.2%) were started on 5-ASA as induction treatment upon diagnosis. During 18 months follow-up, 38/93 (40.9%) patients were stratified into Group 1, 38/93 (40.9%) into Group 2, and 17 patients (18.2%) into Group 3. Within Group 3, 15/17 (88.2%) patients progressed to IFX therapy, out of which 12/15 (80%) required IFX as part of their treatment for acute severe colitis (ASC) (80%) and 3/15 (20%) received IFX as maintenance treatment for chronic active colitis (CAC). 6/12 (50%) patients experiencing ASC were found to progress from IFX to colectomy. Conclusion: Our study provides important insight into disease behaviour and outcome in children diagnosed with UC and UC-like IBDU. The data indicates that only a relatively small proportion (18%) of patients with UC and IBDU- colitis experience an aggressive phenotype, characterised by a rapid progression to treatment with IFX and/ or requirement for colectomy within 18 months from diagnosis. Importantly, in our cohort, 50% of patients receiving IFX for ASC failed to respond to medical therapy and required colectomy. Future work has to focus on identifying reliable disease prognostic biomarkers, which allow early detection of at risk patients and preventative treatments.

243 CREATING A PROCESS TO OBTAIN HEPATITIS B SEROLOGY AMONG PATIENTS TREATED WITH INFLIXIMAB AT A LARGE URBAN CHILDREN'S HOSPITAL

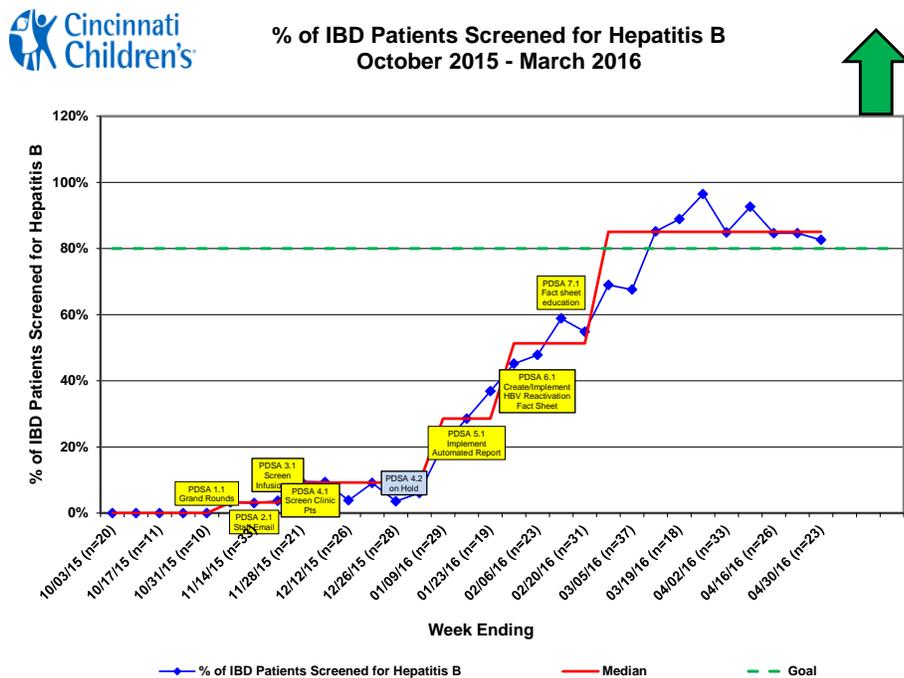
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Background: Hepatitis B infection is a significant public health challenge despite improvements in vaccination efforts, especially in the setting of today's heroin epidemic. A particularly vulnerable population includes patients treated with chronic immunosuppressive therapy, including patients on infliximab for inflammatory bowel disease (IBD) or rheumatic disease. The risk of reactivation of hepatitis B while on immunosuppressive therapy is considerable with reports of up to a 25% mortality rate. Patients on these medications should be screened with hepatitis B surface antibodies (anti-HBs) for evidence of immunity in addition to hepatitis B surface antigen (HBsAg) and hepatitis B core antibodies (anti-HBc) for evidence of acute or chronic infection. Our aim was to develop a process to reliably complete hepatitis B screenings on patients receiving infliximab within the gastroenterology (GI) and rheumatology divisions at Cincinnati Children's Hospital and Medical Center (CCHMC).

Methods: Providers from GI and rheumatology at CCHMC recognized common barriers to obtaining hepatitis B serology. Eligible patients included all GI and rheumatology patients receiving infliximab between October 2015 and March 2016. Using quality improvement methodology and the "Plan-Do-Study-Act" (PDSA) approach, several interventions were designed which centered around: education of clinic providers and nurses, pre-visit planning resulting in ordering of serology, and the development of physician "talking points" for patients.

Results: While 48% of the IBD patient population had previously been screened for anti-HBs, no patients from either division had a complete set of hepatitis B serology prior to the intervention. A total of seven PDSA cycles were performed during the 32-week intervention period (see Figure 1) which resulted in an increase in patients screened from 0% to 85%. By March 2016, a total of 270 patients (220 GI, 50 rheumatology) had up-to-date hepatitis B serology. Appropriate ordering of the hepatitis B serology and "talking points" for the provider had the greatest impact on successful screening.

Conclusion: We were able to develop a method to obtain hepatitis B serology on at-risk patients on infliximab within two subspecialty divisions within a large children's hospital. Next steps will be to develop a process to reliably provide vaccines for patients who are seronegative, expand this process to all patients who are identified as immunocompromised within GI and rheumatology, and then expand this process to other divisions at CCHMC.



244 IS THERE A CORRELATION BETWEEN ANTI-TUMOR NECROSIS FACTOR TROUGH LEVELS AND THE OCCURRENCE OF PARADOXICAL CUTANEOUS AND ARTICULAR MANIFESTATIONS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE (IBD)?

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Background: Anti-tumour necrosis factor (TNF) agents have dramatically improved the prognosis of IBD and are widely used in adult and pediatric IBD patients. However, despite their good safety profile, use of these agents may lead to paradoxical manifestations involving skin or joints. Pathogenesis of such side effects is poorly understood and may involve anti-TNF pharmacokinetics.

Objective: The aim of our study was to look for an association between the use of anti-TNF agents trough levels and the occurrence of adverse events like skin reactions or joint pain.

Materials and Method: Pediatric IBD patients treated with anti TNF agent (Infliximab or adalimumab) for maintenance therapy were included in a cross-sectional prospective monocentric study. At inclusion, patients had a dosage of anti-TNF trough levels and/or antibodies measurement and were assessed for paradoxical manifestations: skin manifestations, joint pain, fatigue. Clinical remission was assessed with the PUCAI and PCDAI score for UC and CD. Skin problems as rash, xerosis and pruritus were evaluated during the clinical examination. Side effects such as fatigue and arthralgia were measured with a visual analogic score (VAS).

Results: 117 pediatric patients with a diagnosis of IBD (102 with Crohn's disease and 17 with ulcerative colitis) were included in the study. Skin manifestations (such as eczema, cheilites, acne) were observed in 55/117 patients (47%). Eczema was the most commonly described skin manifestation (n=37, 31%), followed by acne (n=12; 10%) and folliculitis (n=8; 6%). The strongest association factor for skin manifestations was Crohn's disease, in nearly 85% of afflicted patients. In addition, 7/117 (0.05%) of patients developed arthritis during anti-TNF alpha treatment. Any correlation was found between TNF trough level and the appearance of skins and joint manifestations ($p= 0.01$, $p= 0.1$, respectively).

Conclusions: Anti-TNF alfa therapy is frequently associated with newly onset skin reactions, most commonly in patient affected by Crohn's disease. However ,no correlation was found between high TNF trough level and the occurrence of dermatological and articular manifestations.

245 IMMUNIZATION RATES FOR PPSV23 (PNEUMOVAX) IN IMMUNOCOMPROMIZED PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: ROOM FOR IMPROVEMENT

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Background: Protection against vaccine preventable diseases in immunocompromised patients is important as these patients have impaired host defenses. These patients also have greater exposure to pathogens due to frequent contact with medical environments which leads to an overall increased risk or severity of vaccine-preventable infection. However, vaccination rates are frequently suboptimal as clinicians have insufficient or inaccurate information concerning recommended immunization schedules of such patients. Specialty clinicians may also lack the infrastructure needed to administer vaccines to their at-risk patient populations. PPSV23 has been shown to decrease severe pneumococcal infections. Advisory Committee on Immunization Practices (ACIP) recommends it for children greater than or equal to 2yrs of age with chronic inflammatory illnesses prior to starting or while on immunosuppressive therapy.

Objective(s): 1) determine rate of immunization for PPSV23 in our IBD patients receiving immunosuppressive therapy with Infliximab (IFX) in the Cleveland Clinic Pediatric Gastroenterology (GI) department; 2) if rate determined to be suboptimal, increase rate of immunization for PPSV23 by >10% in this patient population.

Methods: A quality improvement project was devised to sequentially review the charts of patients that received IFX over a 2 month period to assess baseline PPSV23 Immunization rates. ACIP recommendations for PPSV23 immunization in immunocompromised patients were subsequently presented at pediatric GI grand rounds in addition to chart review results. Immunization rates were then determined at 2 months and 8 months following the educational intervention in the cohort of pediatric GI patients with IBD receiving IFX.

Results: Table 1.

PPSV23 counseling and immunization rates in pediatric patients receiving IFX vs. Influenza vaccination rates

Baseline PPSV23 rates (n=155)	Counseled-3.2%	Received-7.0%
Post Intervention PPSV23 rates (N-155)at 2 months:	Counseled 14.1%	Received 9.6%.
Post Intervention PPSV23 rates (N-155) at 8 months:	Counseled 30.3%	Received 16.7%
Influenza vaccine rates(N-155)for same time period:		Received 84%

Conclusions: 1) Suboptimal immunization rates for PPSV23 were identified in pediatric IBD patients receiving IFX. 2) Single educational intervention resulted in an increase in PPSV23 immunization rates from 7.0% at baseline to 16.7 % at 8 months. While it is difficult to comprehensively address all patient needs in this complex sub-set of pediatric patients, it is important for pediatric subspecialists to be aware of the ACIP recommendations on immunization of immunocompromised patients and work to improve the immunization rates. In our institution, a sustained effort with multiple iterations of the PDSA cycle to get the immunization rates for PPSV23 at par with the immunization rates for Influenza is planned.

246 ACTIVE LOCALIZED ILEO-CECAL CROHN'S DISEASE IS ASSOCIATED WITH EARLY STRICTURING AND POOR MEDICAL OUTCOMES IN CHILDREN.

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Background: Localized ileo-cecal (IC) disease is a specific CD phenotype whose prevalence and natural history in pediatric age is not well characterized. The aims of this study were to evaluate and compare the natural history and the outcomes of medical therapy in IC CD children at diagnosis with pediatric patients showing different CD localizations.

Methods: We reviewed charts of children diagnosed with CD at our referral center from January 2005 to December 2014. Only patients with luminal CD and with a minimum follow-up of 6 months were included in the study. Demographic characteristics, disease localization, behaviour at diagnosis and during the follow-up, induction therapy and need for treatment escalation, including immunosuppressants (IM), biologics, endoscopic/surgical therapies, were collected. Patients were then divided into Group 1 (IC CD children) and Group 2 (remaining luminal CD patients).

Results: Seventy- four CD children were identified, of whom 23 (31%) had a localized IC CD (median age: 17 yrs) and 51 (69%) had other luminal localizations (median age: 15.9 yrs). Among the 51 children of group 2 CD localization was: L1 (n=11, 21.6%), L2 (n=10, 19.6%), L3 (n=28, 54.9%) and L4 (n=11, 19.6%). Median follow-up was 49.5 months (range: 6-154). Median age at diagnosis was not significantly different between the two groups (12.8 yrs vs. 10.5 yrs; $p=0.1$), as well as induction therapy ($p=0.1$). Eight out of 23 children of group 1 presented with stricturing behaviour at diagnosis versus none of Group 2 ($p<0.001$); 16 out of 23 patients (69.5%) developed a stricture during disease course versus 3/51 (5.8%) of group 2 ($p<0.001$). Twenty out of 23 (87%) patients with IC CD started an IM [Azathioprine (AZA):17 (85%); methotrexate (MTX): 3 (15%)] versus 21 out of 51 children of Group 2 [(AZA: 19 (90.4%); MTX: 2 (9.6%)] ($p<0.001$). A higher number of patients of Group 1 needed to switch to another IM when compared with Group 2 [10/20 (50%) vs. 4/21 (19%); $p=0.05$]. More children with IC disease started biologics with a trend towards statistical significance [7/23 (30.4%) vs. 7/51 (13.7%); $p=0.08$]. Nine out of 23 (39.1%) children of Group 1 underwent surgery or endoscopic dilation compared with 2 out 51 (3.9%) patients of group 2 ($p<0.001$). Seven out of 9 patients (77.7%) of group 1 had a sustained remission after surgical procedure with a median follow-up of 28 months (range 7-42 months). Conclusion: Patients with localized IC CD show a more severe disease, including early stricturing and need for therapy escalation. Our data suggest that IC CD should receive a top-down strategy and that early elective surgery as a first line treatment should be evaluated in future studies.

247 MONITORING AND TREATMENT OF VITAMIN D LEVELS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE.

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Background and Aims: Vitamin D is an essential micronutrient in regulating calcium absorption and overall bone mineralization. Recent studies have also demonstrated that vitamin D plays a role in the maturation and maintenance of normal immune function. Patients with inflammatory bowel disease (IBD), often struggle to maintain micronutrient sufficiency. Assessment of vitamin D status in children with IBD is an area of active interest due to growing data demonstrating the potential role played by vitamin D in immune homeostasis. However, physician practice remains highly variable with respect to identification and treatment of patients with vitamin D deficiency. The aim of this study is to identify variation in the monitoring and treatment of vitamin D status in pediatric patients with IBD at a single tertiary care center.

Methods: We conducted a retrospective chart review of all pediatric IBD patients with 25-OH vitamin D levels drawn between January 2014 and December 2014. Vitamin D deficiency was defined as a serum 25-OH vitamin D level less than 32 ng/mL. Initial and follow-up Vitamin D levels were recorded. Concurrent serologic labs, as well as the presence or absences of Vitamin D supplementation was also collected. Data was collected from patients enrolled and not enrolled in the Improved Care Now network.

Results: We identified a total of 500 patients for inclusion in the study; 65.6% were enrolled in the Improved Care Now (ICN) network. 63.6% of IBD patients were deficient in vitamin D with a mean level of 23.8 ng/mL (SD 5.9). There was no difference in the prevalence of vitamin D deficiency rates between those patients enrolled in ICN and those not enrolled; nor was there a difference in rates of subsequent supplementation (in vitamin D deficient patients) between the two groups. Initial vitamin D levels were checked most frequently in January. In those with vitamin D levels less than 32 ng/mL, 61.6% were not prescribed supplementation. In those who were prescribed supplementation, 14.5% received 50,000 IU weekly for an average of 7 weeks. The mean change in vitamin D levels for those supplemented with 50,000 IU weekly was 13.9 ng/mL (SD 10.9) as compared to a mean change of 5.5 ng/mL (SD 7.6) in patients supplemented with lower doses ($p<0.0001$). Mean duration between vitamin D levels was 215 days (SD 153). Supplementation with high dose (50,000 units) vitamin D was a significant explanatory variable with respect to variation in change to vitamin D levels even after controlling for gender, ethnicity, CRP, and BMI.

Conclusion: Vitamin D deficiency is highly prevalent in the pediatric IBD population. Treatment rates for Vitamin D deficiency are poor despite good responses in those treated with high dose supplements.

248 ENTERIC VIROME AND BACTERIAL COMMUNITY IN CHILDREN WITH ULCERATIVE COLITIS AND CROHN DISEASE

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Purpose: Pediatric inflammatory bowel disease (IBD) is believed to be caused by a combination of genetic, environmental, and autoimmune factors. Recent evidence supports contribution of the enteric microbiome. Intestinal dysbiosis has been reported in children with IBD. We examined the enteric virome and bacterial community composition of children with Crohn disease (CD) or ulcerative colitis (UC) to test the hypothesis that unique patterns of viral organisms and/or presence of bacterial pathogens contribute to the pathogenesis of IBD in these patients.

Methods: Fecal samples from children diagnosed with CD or UC and similar aged children with no known intestinal disease were processed to determine individual viromes. In the six weeks prior to collection, 2 IBD patients had self-reported non-infectious diarrhea, all other patients denied diarrheal symptoms. Five (3 IBD, 2 control) patients were on prebiotics at time of sample collection; no IBD patients received antibiotics during the four weeks prior to collection, one control received antibiotics five days prior to collection. Classification of IBD disease extent varied: CD: 4 ileocolonic, 1 ileal, 2 colonic; UC: 2 right colon, 3 pancolitis. Following collection, for virome analysis fecal suspensions were centrifuged, filtered and treated with a mixture of DNase and RNase enzymes. Viral sequences were identified through translated protein sequence similarity search (BLASTx) to annotated viral proteins available in GenBank's databases. The twenty most common phages in each sample were selected and the number of sequence reads compared in CD, UC and healthy controls. DNA was extracted from fecal samples using cetyltrimethylammonium bromide, prior to amplification and sequencing of the V4 region of the 16S rRNA gene. Quality filtering, chimera-checking and data analyses were performed in QiiME. IRB approval was obtained prior to initiation of this study.

Results: Samples were obtained from 24 children (7 CD, 5 UC; 12 control). Mean age was 12.2 years; 54% were male, and mean BMI was 19.4. Virome analyses focused on bacterial viruses. No differences were found in phage content between the groups (UC, Crohn's, and control). Bacterial community analysis is ongoing and will be related to patient health status.

Conclusions: Increasing focus has been placed on the enteric biome in IBD. While other investigators have identified unique viral patterns in adults with IBD, our study does not support prior studies and is unable to replicate this finding in pediatric patients. This study is limited by a small sample size and heterogeneity among IBD patients in terms of treatment and disease severity and location.

***249 FECAL CALPROTECTIN IS A VALUABLE SCREENING TOOL IN A LARGE NORTH AMERICAN PEDIATRIC GASTROENTEROLOGY CENTER**

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Background: Fecal calprotectin (FC) is a valuable non-invasive screening tool for the detection of lower gastrointestinal (GI) pathology, including inflammatory bowel disease (IBD). Most studies (especially in children) in this respect originate from Europe with potentially differing medical practice from the United States (US).

Objectives: To determine the negative predictive value of FC for lower GI pathology within a large pediatric gastroenterology center of the US.

Methods: This retrospective study was conducted at Texas Children's Hospital, assessing colonoscopies between January 2009 and December 2015, where a FC was obtained within 1 month of that colonoscopy. Only cases without established GI diagnoses (i.e. diagnostic endoscopy) prior to the index colonoscopy were selected. C-reactive protein (CRP), rectal bleed (both self-reported and fecal occult blood results), indication for colonoscopy, colonoscopy findings (macroscopic and microscopic), treatment change within a month after colonoscopy, and final diagnoses were recorded. Three laboratories performed the FC test. Normal values by laboratories were: $\leq 50 \mu\text{g/g}$ (ARUP Laboratories, Salt Lake City, UT), $\leq 120 \mu\text{g/g}$ (LabCorp, Burlington, NC), and $\leq 162.9 \mu\text{g/g}$ (Quest Diagnostics, San Juan Capistrano, CA). We also examined a combination of FC with both CRP and rectal bleed (triple screen).

Results: 194 out of 3742 colonoscopies (5.2%) met inclusion criteria. Of those, 115 patients (59.3%) had normal colonoscopies. Of the 69 patients diagnosed with a lower GI disease, 47 (24.2% of total) were diagnosed with IBD. When using lab-specific reference ranges for FC, 84 (43.3%) cases had a normal FC (median 42.3 $\mu\text{g/g}$). Lab-specific reference FC screening would have missed 10 out of 79 (12.6%) abnormal colonoscopies and 3 of the 47 (6.4%) IBD cases. Using a FC cutoff of 50 $\mu\text{g/g}$ would have missed none of the IBD cases, and only 4 of 79 (5.1%) of abnormal colonoscopies. The triple screen (all negative: lab-specific FC, CRP, rectal bleed) would have missed none of the IBD cases and only 2 (2.7%) of the abnormal colonoscopies, which had final diagnoses of pinworms and eosinophilic esophagitis. Therefore, none of the triple screen negative cases would have required a colonoscopy to establish the conclusive GI diagnosis. Table 1 summarizes the predictive values of the screens utilized in our study.

Conclusions: This work confirms the outstanding negative predictive value of FC as a screening tool for lower GI pathology, especially IBD in a US-based tertiary care pediatric practice. Combination of FC with CRP and rectal bleeding can further its clinical utility. This triple screening method could have prevented 48.9% (45 of 92) of normal colonoscopies within our cohort. We propose that the judicious use of FC may help avoid a large number of unnecessary colonoscopies in children.

	Sensitivity	Specificity	NPV
Calprotectin ($\leq 50 \mu\text{g/g}$)			
Predicting abnormal colonoscopy	0.94	0.37	0.89
Predicting IBD	1.00	0.32	1.00
Calprotectin (lab-specific normal values)			
Predicting abnormal colonoscopy	0.85	0.65	0.86
Predicting IBD	0.94	0.56	0.97
Both Negative: Calprotectin & rectal bleeding			
Predicting abnormal colonoscopy	0.93	0.49	0.90
Predicting IBD	0.96	0.40	0.97
Both Negative: Calprotectin & CRP			
Predicting abnormal colonoscopy	0.91	0.59	0.89
Predicting IBD	0.98	0.50	0.98
Triple Screen Negative (FC, CRP, rectal bleeding)			
Predicting abnormal colonoscopy	0.97	0.49	0.96
Predicting IBD	1.00	0.39	1.00

250 CLINICAL MANIFESTATIONS OF THIOPURINE S-METHYLTRANSFERASE VARIANTS IN KOREAN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Azathioprine (AZA) is used to maintain clinical remission in inflammatory bowel disease (IBD). Thiopurine S-methyltransferase (TPMT) is the key enzyme in the metabolic pathway of thiopurine compounds and its activity is largely influenced by polymorphisms of the TPMT gene. This study evaluated the clinical manifestations of TPMT variants in Korean pediatric IBD patients.

Methods: A total of 293 IBD patients who required AZA to maintain remission were genotyped for TPMT. There were 209 Crohn's disease patients and 84 ulcerative colitis patients ranging in age from 3 to 21 years. We carried out a complete sequencing analysis to screen all TPMT variants in pediatric patients and assessed the clinical manifestations including adverse drug reactions (ADR), WBC counts and optimal AZA dose in TPMT variants.

Results: TPMT variants were detected in 12 among 293 patients (4.1%). TPMT*3C was found in 9 patients (3.1%): 8 patients (2.7%) with TPMT*1/*3C and one (0.3%) with TPMT*3C/*3C. Rare TPMT variants including TPMT*6 and TPMT*16 were detected in three patients (1.0%). The patient with *3C/*3C mutation had prominent leukopenia and required low dose of AZA, 0.18 mg/kg/day to maintain an optimal therapeutic range of 6-thioguanine nucleotide (6-TGN). Three of eight patients with *1/*3C mutation had ADR such as leukopenia, rash and hair loss and one of two patients with *1/*6 mutation had nausea. However, one patient with *1/*16 mutation did not present any ADR.

Conclusions: TPMT*3C was the most frequent TPMT variant and TPMT*6 was the second most common. Although TPMT genotype could not completely explain the thiopurine-induced ADR, it could be helpful to examine TPMT genotypes before administering AZA. The results of our study will be useful for future clinical studies on TPMT pharmacogenetics and dosage adjustment in the Asian IBD population.

251 MUCOSAL MICROBIOTA PROFILE IN NEWLY-DIAGNOSED CROHN'S DISEASE; DATA FROM A MIDDLE EASTERN PEDIATRIC POPULATION

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Background and objective: Most reports on the the microbiome in Crohn's disease (CD) are from Western populations.

Objective: To evaluate the gut microbiota in a population of children from Saudi Arabia.

Patients and Methods: All children were Saudi nationals from 0.5 to 17 years of age at presentation. The diagnosis of CD was confirmed according to standard criteria. Controls were children who had a normal colonoscopy and no infection. Colonic mucosal samples (25 CD and 11 controls) were immediately frozen in -800 C. Samples were shipped in dry ice to MR DNA, Shallowater, TX, USA where Amplicon pyrosequencing (bTEFAP®) was performed using 16 S primers. Bioinformatic analysis was performed to assess microbial diversity as well as genera and species associated with CD.

Results: There was a significantly reduced bacterial alpha diversity in CD mucosa (Shannon index $p=0.010$). There were significant species reduction of certain bacterial genera (*ruminiclostridium*; $p=0.00001$) and species (*eubacterium siraeum*; $p=0.00001$, $q=0.003$, *Dialister* spp; $p=0.000031$, $q=0.0058$) in CD. This pattern parallels previous findings on CD in Western microbiota. Overall, we found the mucosal microbiota profile similar between Western and this Middle East population in both health and disease, suggesting a minor effect of ethnicity and lifestyle.

252 UNDERSTANDING THE PATHOGENIC ROLE OF TETRATRICOPEPTIDE REPEAT DOMAIN 7A IN CAUSING VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE THROUGH ITS BINDING PARTNER, E3 UBIQUITIN LIGASE UBR5

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Background: Inflammatory bowel disease (IBD) is on the rise in infants as well as children and the genetic factors show a more prominent role in causing the disease for very early onset IBD patients. Patients with mutations in the Tetratricopeptide Repeat Domain 7A (TTC7A) result in an untreatable IBD and the majority die before 2 years of age. TTC7A mutation(s) produce spectrum of intestinal diseases such as apoptotic enterocolitis to multiple intestinal atresia with combined immunodeficiency. Pathological feature of these patients show disrupted apicobasal polarity. TTC7A's role in cellular function is unknown and can be elucidated through identifying its binding partners to reveal its pathway of action. Recent data have shown that TTC7A is part of an evolutionarily conserved complex where it acts as a scaffolding protein by recruiting PI4KIIIa to the plasma membrane and through EFR3B, PI4KIIIa is involved in generating PI4P. PI4P's levels at the plasma membrane have been implicated in cell survival and the maintenance of cell polarity. Mass spectrometry results from our lab has shown E3 ubiquitin ligase UBR5 as one of the potential interactors of TTC7A. Previous research with UBR5 has shown to interact with β -catenin to up-regulate Wnt signaling. I hypothesize that UBR5 binds to PI4KIIIa-TTC7A-EFR3B to form a molecular complex to maintain the apicobasal polarity. Mutation(s) in the TTC7A results in a defective TTC7A protein, disrupting the complex and consequently losing the apicobasal polarity of the cellular tissue.

Methods: The HEK 293T cells were co-transfected with appropriate plasmid and were then harvested and lysed. Co-immunoprecipitation (co-IP) was performed with the lysates to pull down either the UBR5, TTC7A or PI4KIIIa, followed by Western blot analysis.

Results: My preliminary results have shown the interaction between the UBR5 and TTC7A wild-type and the mutants (E71K, A832T and Q526X) through co-IP and Western blot analysis. Another set of preliminary results show an interaction between PI4KIIIa and UBR5.

Conclusion/Future directions: Overall, this work aims to elucidate the pathogenic role of TTC7A in disrupting apicobasal polarity through its interaction with the binding partners. Once the interactions are confirmed between the UBR5, PI4KIIIa and TTC7A variants through additional co-IP experiments, functional studies will be done to understand the pathogenesis of TTC7A. This will be done by knocking out TTC7A using shRNA. The Western blot will also be used to test for apicobasal polarity markers to find out if UBR5-TTC7A mutant interaction has an impact on apicobasal polarity. Immunofluorescence studies will be performed to find the localization of UBR5 and TTC7A variants within the cell. We hope that further understanding the role of TTC7A and its binding partners will lead to the discovery of novel therapies for patients with these mutations as well as other IBD patients.

253 A RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF FECAL MICROBIAL TRANSPLANTATION FOR PEDIATRIC ULCERATIVE COLITIS (PEDIFETCH TRIAL)

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Purpose: Previous studies have demonstrated therapeutic benefit of fecal microbial transplant (FMT) in ulcerative colitis (UC). This is one of the first randomized, placebo-controlled trials of FMT in pediatric UC and inflammatory bowel disease unclassified (IBD-U). We are testing the hypothesis that retention enemas containing live, fecal bacteria from unrelated, healthy human donors can improve disease activity.

Methods: Patients 6-17 yo with active UC or IBD-U, and stable pre-existing medications, were randomized to biweekly normal saline (placebo) or fresh-frozen stool (intervention) enemas over 6 weeks. Clinical response was assessed through the Pediatric UC Activity Index (PUCAI).

Mucosal inflammation was measured through serial fecal calprotectin and blood samples. Microbial profiling was conducted on donor and patient stools via 16s rRNA sequencing.

Results: Recruitment opened November 2015 and is ongoing. 19 patients were approached. 5 enrolled, 10 requested participation but did not meet eligibility criteria, and 4 declined participation. 2 patients (P001/P004) were randomized to intervention, and 1 patient (P002) to placebo. P001 stopped treatment after 8 enemas due to disease flare at week 4; fecal calprotectin showed improvement (1024 $\mu\text{g/g}$ baseline; 578 $\mu\text{g/g}$ week 3). P004 showed improvement in fecal calprotectin (3462 $\mu\text{g/g}$ baseline; 744 $\mu\text{g/g}$ week 3), and CRP (3.1 mg/L baseline; 0.4 mg/L week 6). P002 showed improvement in PUCAI score (15 baseline; 0, week 6), and fecal calprotectin (607 $\mu\text{g/g}$ baseline; 38 $\mu\text{g/g}$ week 6); at week 10, PUCAI score (30) and fecal calprotectin (1234 $\mu\text{g/g}$) increased. Results for 2 additional patients are pending. α -diversity increased over treatment in the placebo arm, and in 1 patient from the intervention arm (Shannon-index, difference from baseline: 0.82; 0.21; -0.29). Bacterial taxonomy from the placebo arm showed decreased abundance of *Bifidobacteria*, *Clostridium* (*Firmicutes*), and increase of *Faecalibacteria*. The intervention arm showed similar decreased abundance of *Bifidobacteria*, but also a decrease in *Faecalibacteria*, and increase in *Clostridium*

(*Firmicutes*). Mean α -diversity of healthy donor stools was lower than study patients at baseline (Shannon-index: 3.24 donor stool; 3.585 patient stool). Taxonomy of healthy donors showed enrichment of *Ruminococcus*, *Blautia*, and *Faecalibacteria*. Patients in the intervention arm did not increase abundance of these genera with treatment.

Conclusions: Preliminary results demonstrate significant patient interest in FMT for UC/IBD-U. Two patients in the intervention arm showed improvement in disease activity, with one withdrawing due to a disease flare despite improvement in mucosal healing. Bacterial profiling shows variability in α -diversity and taxonomic richness at baseline, and over the course of treatment in placebo, and intervention arms. Ongoing recruitment and data collection will further delineate the therapeutic role of FMT in pediatric UC and IBD-U.

254 ASSESSING READINESS FOR TRANSITION IN ADOLESCENTS AND YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE

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More than 30 percent of youth 10 to 17 years of age have a chronic illness. Previous research has linked poorly managed transfer to adult care of patients, including inflammatory bowel disease (IBD) patients, to treatment nonadherence, loss to follow-up, increased disease severity, emergency hospitalizations and excessive stress for patients, families, and providers. Numerous medical organizations have highlighted the need for adolescents and young adults (AYAs) to receive coordinated care from an interdisciplinary team to provide individualized planning and skill development for transition readiness. In order to understand the level of progress toward medical self-management in adolescence and young adulthood in a clinic for inflammatory bowel disease, 25 youth between the ages of 15 and 21 completed the Transition Readiness Assessment Questionnaire (TRAQ) as a part of routine comprehensive care. Eight patients completed the TRAQ more than one time to assess change in transition readiness throughout the course of intervention. The TRAQ is a reliable and valid 20-item self-report measure which assesses healthcare self-management skills in AYAs.

Preliminary results indicated that IBD patients completing the TRAQ for the first time, with a mean age of 17 years, typically scored in the range indicating some learning ("I am currently learning to do this") about adult medical self-management responsibilities (M 3.50, SD 0.86). Patients indicated relative strength in talking with providers (M 4.68, SD 0.80), but relative weakness with appointment-keeping responsibilities (M 2.89, SD 1.13). Overall, higher scores were related to older age, being female, and having private insurance. Results also appear to indicate that, over time, patients move toward readiness, indicating benefit in routine assessment and the interventions to help them move forward. Implications of these findings, limitations, and future directions for transition readiness education and intervention for youth with IBDs will be discussed.

255 FLAXSEED IN A LOW-FAT DIET EXACERBATES CITROBACTER RODENTIUM-INDUCED COLITIS IN MICE

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Background: Flaxseed is a rich source of α -linolenic acid, fiber, and lignans, and has been shown to protect against colorectal cancer. However, the role of flaxseed as a dietary supplement for use in the management of inflammatory bowel disease is controversial.

Objective: To test the impact of flaxseed in a murine model of infectious colitis.

Methods: Three-week-old C57BL/6 mice just post-weaning were separated into four diet groups and fed either a high-fat diet (36% kcal from fat; HF) or low-fat diet (12% kcal from fat; LF) or isocaloric high or low-fat diets supplemented with 7% w/w whole ground flaxseed (36% kcal from fat with flax; HF Flx) or (12% kcal from fat with flax; LF Flx). After 4 weeks of feeding, mice in each diet group were either infected with 10^8 CFU of *Citrobacter rodentium* or sham infected by oral gavage (n=8-10). Weights were monitored and stools collected during the course of infection. Mice were sacrificed 10-14 days post infection. Distal colons were examined for mucosal inflammation, epithelial cell proliferation, and pathogen colonization. Impact of flaxseed ingestion on levels of liver and intestinal tissue polyunsaturated fatty acids (PUFA), gut microbial diversity, and cecal pH and short-chain fatty acids were measured. Statistical analyses were performed by ANOVA with Tukey's multiple comparison test.

Results: LF Flx fed mice lost weight and HF Flx fed mice showed impaired weight gain after infection with *C. rodentium*, despite significant increases in liver and intestinal n-3 PUFAs. LF diet protected against *C. rodentium*-induced colonic crypt epithelial cell hyperplasia compared to HF diet (mean crypt length \pm SEM; 162 ± 11 μ m, vs. 219 ± 16 μ m, $p < 0.01$), decreased pro-inflammatory cytokine levels (TNF α , IL18, and IFN γ), and promoted more rapid clearance of the enteropathogen. By contrast, the LF Flx diet exacerbated colitis compared to the LF diet, with increases in epithelial cell hyperplasia (mean crypt length \pm SEM; 231 ± 16 μ m, vs. 162 ± 11 μ m, $p < 0.01$), infection-induced expression of IL17 α and IL22, and persistence of *C. rodentium* colonization. Relative to the LF diet, the LF Flx diet increased γ -proteobacteria and decreased Akkermansia muciniphila independent of infection. The negative effects of flaxseed in the LF Flx diet were apparent despite the fact that flax promoted an increase in microbial diversity, cecal short-chain fatty acids, and a decrease in cecal pH.

Conclusions: These data indicate that whole ground flaxseed exacerbates colitis in the setting of a low-fat diet and did not improve inflammation in a high-fat diet. The results serve to explain divergent effects of whole flaxseed supplementation in previous evaluations. These data also show that a low-fat diet lowers intestinal inflammation in response to *C. rodentium* and promotes rapid clearance of the enteropathogen from stool and colon tissues.

256 GM-CSF ANTIBODIES AND PERIPHERAL TREG CELLS AS POTENTIAL MARKERS OF THERAPEUTIC RESPONSE IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Introduction: The majority of adults with IBD respond to first line medications for remission. However, pediatric IBD is often associated with a more severe presentation, where aminosalicylates or steroids are ineffective in inducing remission, requiring more potent medications like biologics, with subsequent increase in cost and potential adverse effects. This study aims to measure non-invasive biomarkers, specifically GM-

CSF antibodies and peripheral Treg cells, during induction of remission in pediatric IBD. Hypothesis: GM-CSF antibodies are present in high titer in more severe IBD in association with reduced intestinal GM-CSF bioactivity and increased intestinal permeability. Foxp3+ Treg cells are present in low titer in peripheral blood of patients with severe IBD, indicating a primary immune dysregulation, in which an inherently reduced Treg cell population is incapable of downregulating the immune response.

Methods: Blood collected before treatment was analyzed for GM-CSF antibodies by ELISA and peripheral Tregs by flow cytometry. Patients were followed prospectively to assess response to first-line medications versus step-up to biologics. GM-CSF antibodies, peripheral Tregs, and fecal calprotectin were monitored in patients during remission. PCDAI and PUCAI were scored to assess clinical improvement. We enrolled 28 patients with IBD of which 18 completed the study with pre- and post- treatment samples. Wilcoxon Rank Sum tests were used to compare baseline values between groups and Paired Signed-Rank tests used to compare pre- and post-treatment values. A two-sided p-value of 0.05 was considered significant.

Results: Median GM-CSF antibodies were higher (0.50 vs. 0.37) and Tregs lower (5.23 vs. 6.71) in the biologic cohort but no significant difference was found between initial GM-CSF antibody and Treg levels of patients requiring first-line versus biologics for remission ($p=0.75$ and $p=0.62$ respectively). In the biologic cohort, 37.5% showed decrease in GM-CSF antibodies and 75% showed increase in Tregs after treatment but the % change was not significant ($p=0.42$ and $p=0.37$, respectively). There was a trend toward higher GM-CSF antibodies in the CD versus UC group (0.81 vs. 0.31, $p=0.073$). Activity indices showed significant improvement in the biologic cohort only in UC ($p=0.04$).

Conclusions: Two new biomarkers may add value to the existing non-invasive biomarkers to guide management strategies in IBD and monitor response to therapy. No individual biomarker was able to reliably predict need for biologics in this study. Further studies are needed to develop a predictive model using a combination of biomarkers that may help identify the most effective treatment in pediatric IBD to reduce hospitalizations, healthcare cost and increase the chance of a steroid-free remission.

257 BUILDING A CLINICAL AND RESEARCH DATABASE FOR CHILDREN WITH INFLAMMATORY BOWEL DISEASE (PEDI DATA): A STEP-BY-STEP PROCESS

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Background: Quality of care is important for children with Inflammatory Bowel disease (IBD). Recently various quality indicators have been identified by scientific societies to assist and guide the management of IBD patients. But the monitoring of these indicators implies a systematic process of data collection and update. Many hospitals use paper based medical records or electronic medical record not designed for collecting and updating these indicators. Some initiatives like ImproveCareNow (ICN) project in the United States have demonstrated a benefit of a quality improvement (QI) process in the follow-up of children with IBD. In 2012, we initiated a process of creating a database to prospectively follow our large cohort of children with IBD.

Objective: The aim of the present work is to share the various steps toward building the database, the usability and the clinical and research usefulness.

Methods: Sainte Justine Hospital is a tertiary hospital in Quebec. The gastroenterology unit comprises 10 senior physicians, 6 fellows, and 1 nurse dedicated to IBD patients. Each year, 90-100 new cases of IBD are diagnosed in our unit. The active cohort comprises approximately 500 patients. PediData is a prospective database that was built from scratch following various steps following of the plan-do-study-act (PDSA) cycle: (1) literature review, (2) focus group (3) choice of the software (4) drafting of the first version of the software (5) diffusion (6) validation (5) evaluation of usefulness.

Results: We chose Filemaker Pro software version 14 because of its usability and functionality on multiple platforms: Windows, Mac, tablets. The final version of PediData includes different sections organized in tabs: administrative, imaging, treatment, follow-up, lab results. This database is hosted internally in a server in our hospital and access is granted by a private password for each user (physician, nurse, dieticians). From January 2013 to December 2015, there was a total of 287 new cases of IBD (154 male; 183 Crohn's disease, 60 ulcerative colitis, 44 indeterminate colitis). The database enabled us to identify the following baseline quality indicators: rate of children treated with corticosteroid/enteral nutrition (at diagnosis), anemia, transfusion, hospitalization, emergency visits, remission etc. Medication logs and lab results logs were two useful functionalities that enhanced the usefulness of the database. With PediData search fields, we are able to easily identify children with specific characteristics for research purpose.

Conclusions: PediData gives a synoptic view of each patient and the whole IBD cohort. We have noticed a usability of the database with ease of data recording. PediData is part of a quality improvement process established in our hospital and will be a useful tool to track changes in quality indicators. The PediData structure could be easily shared with other centers.

258 INTERDISCIPLINARY QUALITY IMPROVEMENT APPROACH TO IMPLEMENTATION OF SCREENING, EVALUATION AND FOLLOW-UP FOR DEPRESSION IN YOUTH WITH INFLAMMATORY BOWEL DISEASE AND DIABETES

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Background: Adolescence is a high-risk period for behavioral health concerns and suboptimal self-management of chronic disease. Symptoms of depression have been shown to negatively impact disease management and health outcomes in chronic illness, including inflammatory bowel disease (IBD) and type 1 diabetes.¹⁻³ Guidelines from the U.S. Preventive Services Task Force and professional organizations call for routine screening for depression in adolescents with systems to ensure accurate diagnosis, effective treatment, and appropriate follow-up.⁴ However, gaps exist and untreated depression leads to decreased adherence to therapy and adverse health outcomes.

Methods: Using a quality improvement approach, we aimed to create, implement and test a process for depression screening, assessment, and follow-up for youth (age > 12 years) with IBD and diabetes in a large pediatric specialty center. Our interdisciplinary team included GI and endocrine physicians, social workers (SW), psychologists and our IBD center coordinator. Depression was assessed with a validated measure, the Patient Health Questionnaire (PHQ)-9.5. A PHQ-9 score of >10, suggestive of moderate to severe symptoms, or a positive response to the suicidal ideation (SI) item triggered a real-time assessment by a psychology fellow or social worker. When needed, behavioral health services were established with the psychology fellow or support provided in identification of outside services with phone follow-up to identify and

address barriers. For the initial implementation, patients were screened during one half-day clinic session per week. Resource utilization was tracked to inform expansion.

Results: Thirty-three patients were screened with diagnoses of Crohn's disease (n=5), ulcerative colitis (n=7), IBD unclassified (n=1) and diabetes (n=20). See Table 1 for demographics. Within IBD, 2 patients (15%) had moderate to severe disease on physician global assessment at the time of screening. Eight out of 13 were on treatments with biologics, representing underlying moderate to severe disease. Nine patients required same-day assessment for positive score on the PHQ; 6 diabetes (30%) and 3 IBD (23%). One patient endorsed SI with a PHQ <10. All ten received same-day assessments with a clear plan for follow-up. Patients with positive screens required 45 minutes of psychologist or SW time for assessment, referral, communication with the medical team, and documentation. Clinic flow was not disrupted.

Conclusions: Implementation of depression screening into routine pediatric specialty care is feasible using an interdisciplinary team and quality improvement framework. Integrating processes to address the identified behavioral health needs is essential to reduce barriers to adherence and improve health outcomes for youth with IBD and diabetes. Next steps include expansion to screen all youth in our centers and assessment of other patient reported outcomes.

Demographics		IBD (n=13)	Diabetes (n = 20)
Age Mean (SD)		16.8 (1.99)	15.7 (1.89)
Female Gender		9 (69%)	13 (65%)
Ethnicity	Hispanic	-	4 (20%)
	Asian or Pacific Islander	1 (7.5%)	4 (20%)
	White, Non-Hispanic	8 (62%)	8 (40%)
	Other	1 (7.5%)	1 (5%)
	Mixed	3 (23%)	3 (15%)
Insurance	Private	9 (69%)	12 (60%)
	Public	4 (31%)	8 (40%)
Screening Scores		IBD (n = 13)	Diabetes (n = 20)
Patient Health Questionnaire (PHQ)-9 Mean (SD)		9.23 (6.41)	6.05 (6.25)
Scores leading to same day assessment	PHQ > 10	6 (30%)	3 (23%)
	+ Suicidal Ideation (SI)	2 (10%)	4 (31%)

259 *CONCEPTUALIZING SUMMER CAMP AS A PSYCHOSOCIAL INTERVENTION: SIGNIFICANT IMPROVEMENT IN EMOTIONAL FUNCTION AND HEALTH-RELATED QUALITY OF LIFE AFTER PARTICIPATION IN A SUMMER CAMP FOR YOUTH WITH IBD*
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Background: Summer camp has long been conceived as a possible psychosocial intervention for pediatric patients with chronic illness. While research has explored the efficacy of these experiences among patients with a wide range of pediatric diagnoses (including hematology/oncology, HIV/AIDS, burn-victims, diabetes, and Celiac disease), research that has explored the significance of summer camp for pediatric patients with IBD is scarce. This research aimed to explore the psychosocial implications of participation in a summer camp specifically for youth with IBD.

Methods: Researchers completed a prospective, longitudinal, single cohort study. Participants were recruited from a cohort of patients registered to attend an overnight summer camp for children and adolescents with IBD. Questionnaires were completed online 2 weeks prior to camp participation and 2 weeks thereafter. Study measures assessed psychosocial function, health-related quality of life, post-traumatic growth, social connectedness, and loneliness. All measures were validated with sound psychometric properties.

Results: Twenty-eight participants and their parents completed all study measures. Fifty-nine percent of participants were male and mean participant age was 13.5 years. Sixty-eight percent of participants had a prior Crohn's disease diagnosis. At baseline, prior camp participants reported significantly less avoidance of IBD-related thoughts and significantly greater emotional function than participants with no prior experience. At post-camp assessment, there was a significant reduction in psychosocial symptoms following participation in camp (t (27) 2.6, p= .02, d= .50). Post-camp total health-related quality of life was significantly greater than the total health-related quality of life reported prior to camp (t (27) -2.4, p= .02). Campers also reported significant improvements in individual health-related quality of life subscale measures including emotional function, school function, and general psychosocial health. All improvements reflected a moderate effect size. Campers reported significantly greater personal strength related to their IBD diagnosis after camp participation than prior to it (Z = -2.1, p= .04).

Conclusion: Camp can, and should, be conceptualized as a successful psychosocial intervention that provides pediatric patients with an unprecedented opportunity to surround themselves by peers with shared experiences. This environment appears to act as an exposure, reducing the pediatric patient's need to avoid reminders of illness and subsequently increasing their emotional function, health-related quality of life, and sense of personal resilience. Physicians and caregivers should strongly consider the importance of camp participation and the potential psychosocial gains that it may afford, particularly for patients who are at risk for poor psychosocial function or who have limited exposure to/experience with other pediatric IBD patients.

260 *INTRAVENOUS IRON SUCROSE FOR ANEMIA ASSOCIATED WITH PEDIATRIC INFLAMMATORY BOWEL DISEASE*
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Background: Anemia is a common extra-intestinal manifestation in children with inflammatory bowel disease (IBD). Oral iron therapy is widely used and patients tend to have poor compliance due to side effects, especially the gastrointestinal ones. Intravenous iron therapy was shown to be safe and efficacious in adult patients with IBD, but has not been well studied in children. We use Intravenous Iron Sucrose (IVIS) at our institution for iron deficiency anemia (IDA). We hypothesized that IVIS is safe and efficacious in children with IBD as it is in adults. Therefore, we conducted a retrospective review investigating the safety and efficacy of IVIS in for IDA in pediatric IBD.

Methods: We reviewed the inpatient and outpatient medical records at our institution of all IBD patients 21 years of age or less who received IVIS between July 1,2009 and October31,2014. The diagnosis of anemia was based on blood hemoglobin (Hgb) level below the normal range for age and sex. IDA was identified based upon serum iron studies and red cell mean corpuscular volume. Each IVIS administration was evaluated for safety (any adverse reaction). Efficacy was defined as a ≥ 2 g/dL increase in Hgb level at 4, 8 or 12 weeks following the initiation of the IVIS course (a course might consist of one or more infusions). Normally distributed data are reported as mean \pm standard deviation (SD) and non-normally distributed as median with interquartile range (IQR).

Results: We identified 88 patients with IBD (Crohn’s disease, n=52; ulcerative colitis, n=33; and IBD-undetermined, n=3) who underwent IVIS infusions during our study period. The female to male ratio was 1.1:1. The median age at the time of infusion was 15 years (IQR 12 –17 years, range 1-21 years). The majority (n=67) of patients received one course of IVIS, 14 patients received two, 3 received three, 3 received four, and 1 received five. 121 courses of IVIS were evaluated. The median number of infusions per course was 3 (IQR 2 –3, range 1 - 14 infusions). The median dose per course was 365 mg (IQR 200 –600; 7.0 mg/kg, IQR 4.0 –12.2). No patient developed anaphylaxis. Minor adverse reactions occurred in 6 patients; none required discontinuation of the IVIS infusion. Out of the 121 IVIS courses, 40 were excluded from the efficacy evaluation due to a recent blood transfusion, incomplete clinical data, or non-IDA. Overall 58% (47/81 courses) resulted in the goal therapeutic increase in Hgb (24 courses by 4 weeks; 15, 8 weeks; 8, 12 weeks). There was a significant rise in Hgb for all 81 courses from a mean of 9.1 (SD 1.45) to 11.8 g/dL (SD 1.77; $p < 0.0001$, paired t-test).

Conclusion: IVIS is safe as only a few mild adverse events were observed. Furthermore, IVIS appears to be an efficacious treatment for IDA in pediatric IBD patients. The observed rise in hemoglobin was significant for all evaluated IVIS courses, with the majority achieving the goal Hgb.

261 UTILITY OF FECAL CALPROTECTIN IN THE ROUTINE EVALUATION OF CHRONIC GASTROINTESTINAL COMPLAINTS IN CHILDREN IN THE PRIMARY CARE SETTING

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Background: Evaluation of chronic gastrointestinal symptoms in children and differentiating between organic and non organic causes can often be a diagnostic challenge. Fecal calprotectin is now a well-recognized non invasive marker of Inflammatory Bowel Disease (IBD). It is routinely used in the evaluation of chronic gastrointestinal complaints to screen patients for possible IBD and further evaluation with endoscopy. However, only limited data is available regarding the utility of routine fecal calprotectin testing for evaluation of chronic GI symptoms in the primary care setting.

Methods: Charts of all patients between the ages 0-21 who had a fecal calprotectin between the years 2010–2014 were identified through an electronic pull from the Kaiser NW Permanente database. The age at time of testing and calprotectin values were also obtained. Each chart was then individually reviewed to identify the primary indication for testing and the outcome in the subsequent 12 months from the time of testing.

Results: Between 2010–2014, there were a total of 822 patients in the age group 0-21 who had a fecal calprotectin test without a known diagnosis of IBD and at least a year follow-up. Abdominal pain was the primary indication in 532 patients. Other primary indications included diarrhea (115), blood in stool (95), poor weight gain/ weight loss (44), nausea and vomiting (16) and anemia (4). Other miscellaneous causes include rectal pain (5), fistula (2), GERD (4), constipation (2), canker sores (2) and allergies (1). 689/822 (84%) patients had normal fecal calprotectin values of < 162.9 ug/gm (Quest Laboratories). In the subsequent 12 months, 14 underwent endoscopies and biopsies were normal; 12 received other diagnoses including EoE, celiac disease, polyp and *H. pylori*; 663/822 patients did not receive a diagnosis of IBD and no concerning symptoms or red flags were documented in subsequent visits that could indicate presence of missed IBD.

133/822 (16%) patients had elevated fecal calprotectin (> 162.9 ug/gm); 42/133(31%) received diagnosis of IBD with histologic confirmation, 18/133 received other diagnoses including *Clostridium difficile* infection, Celiac disease, *E. Coli*, Salmonella, giardiasis, *H. pylori*, Cystic Fibrosis, milk protein sensitivity, Henoch Schonlein Purpura and polyps. 5/133 had normal endoscopies and biopsies. 39/133 had repeat fecal calprotectin tested in the next 12 months that returned to normal; the remaining 29/133 patients had resolution of symptoms in the next 12 months. Mean calprotectin values for the IBD vs. non IBD groups were 1206 ± 106.5 vs. 74.53 ± 5.9 ($p < .0001$). Sensitivity and specificity analyses were done (Table 1).

Conclusion: Based on this cohort, fecal calprotectin has 100% sensitivity in detection of IBD. Thus it is an excellent tool in the primary care setting to exclude IBD and avoid unnecessary referrals and endoscopies.

Table 1

		95% CI
Sensitivity	100%	89-100%
Specificity	88%	85-90%

262 PREVALENCE OF DUODENAL PATHOLOGY IN PEDIATRIC CROHN'S DISEASE

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Introduction: The duodenum is a major site of drug absorption for perorally administered (PO) medications. Recently published data from our group suggest decreased expression of proteins and enzymes important to drug disposition (e.g. CYP3A4) in inflamed vs. non-inflamed duodenum of children with CD. The prevalence of duodenitis in children with Crohn’s disease (CD) is reportedly higher than the estimated 28% in the adult CD population; however, existing pediatric studies are limited by small sample size. Accurate information regarding the prevalence

of duodenal disease in children with CD is important, as many of these patients are treated with PO drugs (e.g., prednisone, azathioprine), which are susceptible to first-pass metabolism in the duodenum.

Objective: The aim of this descriptive study was to determine the prevalence of duodenal pathology in pediatric CD.

Methods: Retrospective data from a clinical database at The Children's Mercy Hospital (CMH) was reviewed to assess prevalence of duodenitis in patients with CD who received care at CMH between January 2002 and April 2010 (n=577). In an independent cohort (n=32), prevalence of duodenal pathology was prospectively assessed in children with CD who underwent endoscopy at CMH between September 2014 and April 2016.

Results: Of the patients treated for CD in 2002-2010, 313 were specifically evaluated for duodenitis. Of these, 222 (71%) were diagnosed with duodenitis. In the prospective CD cohort, duodenal pathology was confirmed by gross endoscopy, histopathology, and/or imaging in 15 of 32 children (47%).

Conclusions: The prevalence of duodenal pathology in children with CD is higher than what has been previously reported in adults. Duodenal disease may be an important factor to consider in pediatric CD phenotypes. Studies are ongoing to investigate duodenal pathology as a source of variability in disease outcomes and treatment response in children taking PO medications for the treatment of CD.

***263 MUCOSAL MICROBIOME RESPONSES IN PEDIATRIC ULCERATIVE COLITIS DURING IMMUNOTHERAPY AND FECAL MICROBIOTA TRANSPLANTATION**

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Background: Disturbed gut microbiome-mucosa interactions are thought to be critical in the pathogenesis of inflammatory bowel diseases (IBD: Crohn's disease (CD) and ulcerative colitis (UC)). IBD is a precancerous condition linking microbiome-related-inflammation with enterocyte/epithelial proliferation.

Objectives: We aimed to examine an unprecedented compendium of specimens from pediatric UC patients with respect to microbiome-mucosa interactions based on high-throughput methodologies.

Methods: Serial rectosigmoid biopsy samples were collected from 3 pediatric UC patients suffering from pancolitis at diagnosis (treatment naïve [TN]), during remission under immunotherapy (IT), and following fecal microbiota transplantation (FMT) without IT. Microbiome composition was evaluated by 454 based 16S rRNA pyrosequencing. Log-transformed bacterial abundances were paralleled with RNA-sequencing based mucosal gene expression changes between the IT and FMT specimens.

Results: Between diagnosis (TN) and immunotherapy induced remission (IT), increase of abundance occurred in *Bacteriodes vulgatus* (average 0 to 14.83%), and *Faecalibacterium prausnitzii* (0.08 to 5.56%) among others, while *Ralstonia pickettii* decreased the most (8.51 to 0.02%) (Table 1). Log-transformation augmented the significance of these changes. Following the FMT series, *Enterorhabdus spp.* and *Roseburia spp.* increased in abundance among others (Table 1). Log-transformed abundance changes of these species, however, had the largest number of significant (Pearson correlation $p \leq 0.048$) mucosal gene suppression correlations. Twenty-eight percent (28%) of the genes responsive to FMT correlated with the abundance shifts of both bacterial species. The 289 common, *Enterorhabdus spp.* and *Roseburia spp.* responsive genes were significantly enriched in functional roles related to nucleotide binding and cell cycle control. The mucosal gene and microbiome changes secondary to FMT associated with decreased epithelial mitosis/proliferation in the UC patients.

Conclusions: Our findings suggest that microbiome-based treatment strategies may provide added benefit for pediatric UC patients by modulating the precancerous nature of the disease through the suppression of epithelial proliferation.

Species	TN (%)	IT (%)	Change after IT (%)	p (paired T-test)	p (paired T-test of log abundance)
<i>Ruminococcaceae spp.</i>	0.0000	0.7860	0.7860	0.0117	0.0003
<i>Burkholderia pyrrocinia</i>	0.4870	0.0000	-0.4870	0.0842	0.0044
<i>Erysipelotrichaceae spp.</i>	0.0000	2.3700	2.3700	0.1961	0.0056
<i>Alicyclophilus acidovorax avenae_subsp.avenae</i>	0.1443	0.0000	-0.1443	0.1108	0.0062
<i>Coprococcus clostridium sp. ss2/1</i>	0.0000	0.3397	0.3397	0.1232	0.0067
<i>Dorea formicigenerans</i>	0.0000	0.4445	0.4445	0.1179	0.0069
<i>Bacteroides vulgatus</i>	0.0000	14.8266	14.8266	0.2050	0.0116
<i>Bacteroides spp.</i>	0.0000	5.9410	5.9410	0.2013	0.0205
<i>Anaerostipes spp.</i>	0.0000	1.0171	1.0171	0.3451	0.0228
<i>Ralstonia spp.</i>	3.4888	0.0030	-3.4858	0.2505	0.0265
<i>Ralstonia pickettii</i>	8.5086	0.0212	-8.4873	0.1426	0.0380
<i>Acidovorax spp.</i>	7.3407	0.0372	-7.3035	0.2377	0.0616
<i>Clostridium innocuum</i>	0.0000	5.8976	5.8976	0.4093	0.0672
<i>Faecalibacterium prausnitzii</i>	0.0755	5.5643	5.4888	0.1755	0.0860
<i>Roseburia spp.</i>	0.3883	2.2735	1.8852	0.0715	0.1550
<i>Dorea spp.</i>	0.0324	0.1946	0.1622	0.2352	0.1596
<i>Acinetobacter junii</i>	1.9457	0.2902	-1.6555	0.1808	0.1921

Species level mucosal microbiome changes upon immunotherapy in the pediatric ulcerative colitis patients. Black bold highlights the top 5 species with increased abundance and bold grey highlights the top 5 species with decreased abundance following immunotherapy induced clinical remission. Significance level for statistical analysis was relaxed to $p < 0.2$. TN: treatment naïve, IT: immunotherapy

Species	IT (%)	FMT (%)	Change after FMT (%)	p (paired T-test)	p (paired T-test of log abundance)
<i>Bacteroides plebeius</i>	0.0000	14.0937	14.0937	0.1716	0.0117
<i>Clostridium innocuum</i>	5.8976	0.0112	-5.8865	0.4092	0.0216
<i>Sarcina spp.</i>	0.0000	0.0311	0.0311	0.1461	0.0240
<i>Anaerosporebacter spp.</i>	0.0000	0.2034	0.2034	0.3090	0.0320
<i>Ruminococcus gnavus</i>	0.0212	0.1536	0.1324	0.3280	0.0396
<i>Ruminococcus spp.</i>	0.5138	1.6514	1.1376	0.1725	0.0963
<i>Enterohabdu</i> s spp.	0.0558	0.3633	0.3075	0.0532	0.1373
<i>Roseburia human gut metagenome</i>	0.0781	0.1198	0.0417	0.1484	0.1812

Species level mucosal microbiome changes upon FMT in the pediatric ulcerative colitis patients. Black bold highlights the top species with increased abundance and bold grey highlights the top species with decreased abundance following immunotherapy induced clinical remission. Significance level for statistical analysis was relaxed to $p < 0.2$. Underline highlights the two species with the largest number of significant ($p < 0.048$) FMT induced mucosal gene expression correlations. IT: immunotherapy, FMT: fecal microbiota transplantation

264 IMPACT OF INITIAL TREATMENT STRATEGY ON SECONDARY LOSS OF RESPONSE TO INFLIXIMAB IN PEDIATRIC CROHN'S DISEASE

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Introduction and Aims: The use of infliximab has significantly improved the management of Crohn's disease refractory to conventional therapies. Unfortunately, a number of children, after an initial response, develop a secondary loss of response (LOR). Whether the choices of the initial treatment agents have an effect on the subsequent outcome with regards to LOR to infliximab is not known. We studied the effect of initial treatment strategies on secondary LOR to infliximab.

Methods: In this single-center retrospective study we reviewed the medical records of children with Crohn's disease who had received scheduled maintenance infliximab therapy for at least 12 months. We compared children who developed LOR with those who did not, with regards to the different therapeutic modalities that they received before developing LOR.

LOR was defined as clinical relapse while on maintenance therapy requiring dose intensification or switching over to adalimumab therapy.

Results: 73 children (median age at diagnosis - 11 (2 – 16) years, 41 boys) who had received a median duration of 33 (13-110) months of infliximab therapy were enrolled. LOR was seen in 25 (34.2%) children after a median duration of 18 (8-48) months of therapy.

Children with LOR were compared with those who did not develop LOR. The disease clinical phenotype (age, disease location and behavior) and PCDAI at induction with infliximab was similar between both groups.

On comparing the treatment regimens between the two groups, there was no statistical difference in LOR rates between children in whom EEN [3/13 (23.07%)] or steroids [21/53 (39.6%)], $p = 0.34$ was used as an induction agent. In 7 children with fistulizing Crohn's disease, infliximab was used as an induction agent at the time of diagnosis. On comparison of maintenance agents, LOR rates between those on thiopurines [12/43 (28%)] and methotrexate [13/30 (43.3%)], $p = 0.14$ were similar. Majority of the children were on a concomitant immunomodulator [65/73 (89%)] while on infliximab. The median time – lag between diagnosis and induction with infliximab was significantly longer in children with LOR as compared to those who did not have a LOR [28 (4-90) months vs. 12.5 (1 – 121) months, $p = 0.004$]

Conclusion: Early use of infliximab in pediatric Crohn's disease leads to a decrease in secondary LOR.

265 THE HETEROGENEOUS PRESENTATION OF PANCREATITIS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Introduction: Pancreatitis is a known extraintestinal manifestation of inflammatory bowel disease (IBD), but the association between pancreatitis and IBD in the pediatric population is not well-defined.

Aim: To describe the characteristics and disease course of children with IBD who develop pancreatitis.

Methods: A retrospective chart review of all IBD patients up to the age of 21 years admitted to The Children's Hospital of Philadelphia for the diagnosis of pancreatitis between January 2011 and April 2016 was performed. Demographics, date of diagnosis, disease activity, medication and surgical history were recorded.

Results: there were 40 hospitalizations for the indication of pancreatitis among 26 children with IBD (16 with Crohn's disease, 5 with ulcerative colitis, and 5 with indeterminate colitis). Among the 16 children with Crohn's disease 11 (68.8%) were known to have disease in the duodenum. The mean age +/- SD at the first episode of pancreatitis was 14.5 +/- 3.5 years. Pancreatitis was the presenting symptom for 7/26 (26.9%) newly-diagnosed patients. The median lag-time between initial diagnosis of IBD and the first episode of pancreatitis was 0.6 (interquartile range 0.1, 2.4) years. Median Pediatric Crohn's disease Activity Index and Pediatric Ulcerative Colitis Activity Index scores were 17.5 (interquartile range 10.0, 25.0) and 22.5 (interquartile range 10.0, 45.0), respectively. Stool calprotectin was obtained within 3 months of a pancreatitis episode on 19 occasions and found to be elevated (>250 µg/g) in 13 cases (68.4%) with a median calprotectin of 453.0 (interquartile range 150.0, 1,250.0). IBD medications, including 5-aminosalicylates, methotrexate, sulfasalazine, and thiopurines, were identified as the likely cause of pancreatitis in 9/26 (34.6%) children and were discontinued. Recurrent pancreatitis occurred in 6 patients. No hereditary causes of recurrent pancreatitis were discovered on genetic testing among these patients, although 1 patient was later diagnosed with autoimmune pancreatitis and another was found to have pancreatic divisum. Two patients were found to have imaging findings consistent with chronic pancreatitis. Neither pancreatic necrosis nor pseudocyst formation was seen in this cohort.

Conclusion: Pancreatitis, an extraintestinal manifestation of IBD, can be the presenting symptom or occur early in the disease course. It may coincide with active disease in some patients with IBD. Future genomic discoveries may provide important insight regarding the association between pancreatitis and pediatric IBD.

***266 BISPHENOL-A AT ENVIRONMENTAL DOSES INCREASES INTESTINAL PERMEABILITY AND INDUCES INFLAMMATION**

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Bisphenol-A (BPA), an obesogen endocrine disruptor, main plastic component, has a pro-inflammatory effect on adipose tissue and on immune system and is responsible for low-grade systemic inflammation associated with overweight and obesity. Humans are chronically exposed to BPA mainly via oral contact, through contaminated food and beverages. Considering that the prevalence of inflammatory bowel diseases (IBD) is rapidly increasing in the world and that the gut is the first point of contact for BPA, its effect on the intestinal barrier function can be suggested. We hypothesize that BPA acting during the maturation of intestinal barrier function against foreign agents, might be responsible for alteration in epithelial gut monolayer function and for the impairment of mucosal immune system and tolerance. Thus, the aim of this study was to investigate the BPA role, at low environmental doses, in the development of intestinal inflammatory diseases. To evaluate the effect of BPA on human intestinal barrier, human colon adenocarcinoma derived cells (Caco-2 cells) were grown in monolayers and challenged with 1nM BPA during differentiation (20 days). The trans-epithelial electrical resistance (TEER) was used as index of monolayer integrity, with paracellular solute flux measurement to monitor the permeability. The redistribution of tight junction (TJ) proteins was analyzed in cells cultured on coverslips and the examination was performed using a confocal laser microscopy (Zeiss 510 Meta Confocal Laser Scanning Microscope). Immune-precipitation and immune-blot analyses were employed to investigate the intracellular pathways. A panel of 27 different cytokines, chemokines and growth factors was determined in the culture supernatants using BIOPLEX multiplex Human assay kit (Bio-Rad, Hercules, CA, USA). At day 17 of differentiation, a significant TEER reduction ($p < 0.01$) was reported in cells upon BPA incubation compared to control cells. An alteration in TJ redistribution was confirmed at confocal microscopy observation, supporting the increased permeability of enterocyte monolayer. Moreover, activation of NF κ B inflammatory pathway and a significant increase in Interleukin-7 (IL-7) and Monocyte Chemoattractant Protein-1 (MCP-1/CCL2) secretion was observed upon BPA treatment. In conclusion, at environmental low doses, BPA may induce alteration in gut barrier permeability via trans-epithelial and para-cellular flux variation, with deregulation of the TJ integrity and barrier function. These effects can be responsible for enhanced translocation of pathogenic molecules from the gut lumen to extra-intestinal sites, increasing the risk of impaired tolerance to food antigens and colonic inflammation in adult life. The BPA direct contact may cause activation of inflammatory pathways, with subsequently production of pro-inflammatory cytokines and probably inappropriate immune response in lamina propria.

267 METHOTREXATE INDUCTION AND MAINTENANCE OF REMISSION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Methotrexate (MTX) is an immunomodulator commonly used for the treatment of pediatric inflammatory bowel disease (IBD). However, while randomized controlled trials (RCTs) have demonstrated treatment efficacy for adult patients, there are currently no RCTs that assess the treatment efficacy of methotrexate within the pediatric IBD patient population. This systematic review and meta-analysis attempted to assess the efficacy of MTX therapy among the existing pediatric literature.

Methods: A systematic literature search was performed using MEDLINE and the Cochrane library from inception until March 2016. Abstracts from GI conferences were also searched. Synonyms for 'pediatric', 'methotrexate' and 'IBD' were utilized as both free text and MESH search terms. The studies included contained clinical remission (CR) rates for MTX treatment of pediatric IBD patients 18yrs old, as mono- or combination therapy. Case studies with less than 10 patients were excluded. Quality assessment was performed with the Newcastle-Ottawa Scale. Meta-analysis calculated pooled CR rates and distinguished between patient subgroups. A random-effects meta-analysis with forest plots was performed using R. X² test and $p < 10$ level significance was used to assess for heterogeneity.

Results: Fourteen (11 monotherapy, 1 combination therapy, 2 both; n=886 patients) observational studies were eligible out of 200 studies. No interventional studies were identified. The pooled CR rate for IBD patients on monotherapy within 12 months was 54.3% (95% CI, 45.2%-63.2%), with a moderate risk of heterogeneity ($p = 0.08$; I² = 44%). When ulcerative colitis (UC) was excluded, the achieved pooled CR rate for Crohn's disease (CD) was higher and very consistent among studies CR: 56.9% (95% CI, 50.1-63.5%), ($p = 0.46$; I² = 0%). The CR decreased to 35.4% (95% CI, 30.5-40.1%), ($p = 0.41$; I² = 0%) for maintenance therapy at 12 months since induction. Two studies assessed treatment efficacy for maintenance therapy 12 months after achieving CR, and demonstrated similar CR rates (31% and 42%). Sub-analysis could not identify CR differences between MTX administration types, thiopurine exposed vs. naïve (uOR 1.34 (95% CI, 0.72-2.49); $p = 0.35$), thiopurine failure vs. intolerance (pooled OR 1.03 (95% CI, 0.51-2.06); $p = 0.31$). Combination therapy outcomes were only described for 23 patients in 3 studies. One study assessed mucosal healing. Growth-velocity outcomes were described by 3 studies. Two UC studies were identified which showed lower rates for both induction as maintenance of remission.

Conclusion: This meta-analysis demonstrated that, within the published literature over 50% of pediatric IBD patients who are prescribed methotrexate achieved remission. Among pediatric CD patients, CR rates are highly consistent and demonstrate a remission rate of 57% for induction and 35% for 12-month maintenance. Prospective controlled interventional trials should assess treatment efficacy among patient subgroups.

268 VARIABLE LEVELS OF TRANSITION READINESS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS

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Background: IBD patients diagnosed as children will need to transition to adult doctors. The process of transition from pediatric to adult care can be difficult. Poor transition can result in unfavorable outcomes such as increased hospitalizations. A pediatric IBD transition clinic was

established to guide this process. In order to establish areas of need, a validated transition readiness assessment questionnaire (TRAQ) is administered to patients in the transition clinic.

Methods: Patients 17-18 years of age were referred to the transition clinic by their pediatric gastroenterologists. Our transition clinic is a 2-visit process. First, the patient is seen by a pediatric IBD specialist. At visit 2, a few months after, the patient is seen by an adult IBD specialist. The morning prior to the visit, pediatric and adult doctors meet to discuss transitioning patients. After the 2nd visit, the patient's care is transferred to adult IBD. Patients are given the TRAQ to complete at the beginning of their visit. TRAQ version 5 has 20 questions in 5 domains of care: managing medications, appointment keeping, tracking health issues, talking with providers and managing daily activities.

Results: From April 2014 through January 2015, 13 patients were seen in the transition clinic. In response to question 3, 12/13 (92%) patients reported always taking their medicines correctly on their own, while 1/13 (8%) reported learning to take their medicine. Question 9 asks if patients apply for health insurance. 3/13 (23%) patients responded they always apply, 2/13 (15%) are learning to apply, 3/13 (23%) want to learn and 4/13 (30%) reported not knowing how to apply. Question 12 asks if patients fill out the medical history form. 6/13 (46%) patients responded always, 5/13 (38%) have started filling out the form, 1/13 (8%) want to learn how to fill out the form and 1/13 (8%) do not fill out the medical history form. Transition readiness was found to be variable between the different domains, even within one individual. One patient's responses to the 20 questions in the TRAQ included 9 "always", 1 "started", 7 "learning", 1 "want to learn" and 2 "I do not know how".

Overall, for some questions most patients reported high readiness, such as question 3. For other questions, there was much lower readiness and greater variability, such as question 9.

Conclusions: We found that the transition clinic is feasible and sustainable. The administration of TRAQ does not interfere with clinical care. Patients can have different levels of transition readiness. Patients reported high transition readiness in areas of managing daily activities and talking with providers. Transition readiness was lowest in the appointment keeping domain. The lowest median score was for the question "Do you apply for health insurance if you lose your current coverage?" Further study is needed to understand what factors affect different domains of transition readiness in order to improve transition care.

269 CELL DIVISION CYCLE 42 IS REQUIRED FOR GUT STEM CELL REGENERATION AND RESPONSE TO COLITIC INJURY

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Objectives: CDC42 is a small GTPase that controls intestinal epithelial (IEC) apical-basal polarity, growth and intestinal epithelial stem cell (IESC) survival. However, the underlying mechanisms are not clear. Here, we determine the effects of CDC42 signaling upon intestinal epithelial stem cell (IESC) regenerative responses to intestinal injury.

Methods: Cdc42 floxed mice (Cdc42^{fl}), Villin-Cre (VilCre) and Villin-CreER (VilCreER) mice were utilized to generate constitutive or inducible IEC-specific Cdc42 deficient mice. Lgr5-eGFP-IRES-CreER (Lgr5CreER) mice were used to determine the role of Cdc42 in Lgr5 IESCs. Irradiation, DSS challenge, and mouse intact crypt culture were used to evaluate the IESC regenerative activity of Cdc42-deficient IESCs.

Results: Coincident with mislocalization of lysozyme Paneth cells in the intestinal villus, depletion of Cdc42 in IECs led to reduced numbers of Lgr5 IESCs at the crypt base. VilCre;Cdc42 mice exhibited a disrupted villus crypt architecture, characterized by significantly increased crypt \uparrow °cyst \uparrow ± structure, intestinal villus hypertrophy and crypt fissions compared to littermate controls. These morphological aberrations in the small intestine, measured by villus height, villus width and crypt depth, were further progressed in the 4- and 6-month-aged mice compared to 1-month old Cdc42 depleted mice. To evaluate IESC regenerative activity, Cdc42 was inducibly deleted in VilCreER;Cdc42 mice, which were then exposed to either 12 Gy irradiation or 2.5 % DSS administration. Loss of Cdc42 in IECs showed significantly reduced nascent crypts in small bowels following irradiation compared to controls (13.5 ±0.5 versus 0.6 ±0.1 crypts per mm, n = 5, p < 0.01), and increased crypt loss in colon following DSS challenge. Intestinal crypts were isolated from VilCreER;Cdc42 or VilCre;Cdc4 mice, and cultured. Consistently, inducible depletion of Cdc42 in IECs resulted in markedly reduced enteroid crypt budding.

Conclusions: Cdc42 controls intestinal stem cell activity to maintain intestinal villus-crypt architecture. Loss of Cdc42 leads to increased sensitivity to intestinal mucosal injury.

270 DOES STANDARD THERAPY IN PAEDIATRIC CROHN'S DISEASE REALLY PREVENT OUR PATIENTS FROM THE NEED OF EARLY INITIATION OF ANTI-TNF TREATMENT?

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Background: Previous studies have shown the efficacy of exclusive enteral nutrition (EEN) for induction of remission in pediatric Crohn's disease (CD). The recent ECCO-ESPGHAN guidelines recommend the use of EEN (6–8 weeks) combined with early use of immunosuppressant as the optimal therapy in these patients at diagnosis. However, a high rate of relapse after EEN has been reported.

Moreover, the potential effect of this strategy in postponing or avoiding the future need of biological treatment has not been evaluated. Our aim is to determine the proportion of CD patients diagnosed in the last years in our Centres and treated with EEN and thiopurines at diagnosis have required escalation to anti-TNF treatment during their follow-up.

Methods: Data from CD pediatric patients diagnosed between 2007 and 2014 who entered remission with EEN combined with thiopurines were retrospectively collected. The percentage of patients that needed to escalate to anti-TNF therapy (infliximab or adalimumab) after failure of maintenance treatment during their follow-up in our Unit was analysed. The follow-up period was considered until their last visit in our Unit at the time of preparing the abstract or up to the end of the transition programme to an adult IBD Unit.

Results: In total, 110 patients, 70 boys with a mean age at diagnosis 12.2 ± 2.9 years fulfilled the inclusion criteria. In 60 patients (54.9%) anti-TNF treatment was started; 24 received IFX and 36 ADA. The age of initiation of treatment with anti-TNF was 13.2 ± 2.3 years and the time

from diagnosis of 10 months (IQR 4.5-20.5). We did not find any differences between both anti-TNF regimens in terms of age [IFX 13.7 (IQR 11.0-14.8) vs. ADA 13.5 (IQR 11.7-14.9), $p=0.718$] or time from diagnosis [IFX 11.8 (IQR 4.0-20.0) vs. ADA 9.85 (IQR 4.6-24.5), $p=0.375$]. Mean follow-up was 3.6 years (IQR 1.6-5.8).

Conclusion: The use of EEN has proved to be effective for the remission of pediatric CD and may delay somewhat the use of biological treatment. However, in our study 63% of the patients required initiation of anti-TNF treatment. Further studies showing the long-term follow-up of patients treated with standard therapy (EEN and immune-modulators) are needed to know the real effect of this combination in avoiding initiation of biological therapy.

271 PREDICTIVE FACTORS OF RESPONSE TO THE EXCLUSIVE ENTERAL NUTRITION IN NEWLY DIAGNOSED CROHN'S DISEASE CHILDREN

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Background: Exclusive enteral nutrition (EEN) has been shown to be more effective than corticosteroids in achieving mucosal healing in children with Crohn's disease (CD) without having their side effects.

Objectives: The aims of this study were to determine the efficacy of EEN in terms of inducing clinical remission in newly diagnosed CD children; to study the efficacy of this therapeutic approach in improving the degree of intestinal mucosa inflammation and to describe the predictive factors of response to EEN.

Materials and Methods: An observational retrospective and prospective study including newly diagnosed CD patients who received at least 6 weeks of EEN. The degree of mucosal inflammation was assessed by fecal calprotectin (FC). Remission was defined as a wPCDAI < 12.5. Results: Sixty-one patients (38 males) were included; the mean age at diagnosis was 11.5 ± 2.8 years. The median duration of EEN was 7.6 weeks (IQR 6.5-8.2). Fifty-two out of 58 patients who completed the EEN period (89.6 % per-protocol analysis) achieved clinical remission. This percentage fell to 85% in the intention-to-treat analysis. The compliance rate was 95%. The FC levels (mcg/g) descended significantly at the end of EEN period: 665 IQR (503-836) vs. 177 IQR (125-342). As is shown in table 1, exclusive colonic CD (L2 of Paris classification), CRP and FC levels and disease activity were not predictive factors of response. Older patients and those with higher weight Z- score responded better to the EEN.

Conclusions: EEN administered for 6-8 weeks is effective for inducing clinical remission and achieving mucosal healing. The NEE must be used as the first therapeutic option in patients with CD independently of the age at diagnosis, the location of the disease and the value of wPCDAI.

Variable	Univariate analysis OR (CI 95%)	p
A1a vs A1b	2.7 (0.49-15)	0.253
Age (years)	1.3 (1.01-1.75)	0.040
Gender (male)	0.265 (0.04-1.68)	0.146
Time to diagnosis (months)	0.90 (0.82-1.001)	0.052
L2	0.16 (0.02-1.20)	0.076
Weight Z score	2.5 (0.81-8.01)	0.107
Height Z score	1.62 (0.83-3.2)	0.157
BMI z score	2.07 (0.57-7.55)	0.267
CRP	0.98 (0.964-1.011)	0.276
Fecal calprotectin	0.99 (0.99-1.002)	0.583
wPCDAI < 57.5 (Severe)	0.147 (0.016-1.34)	0.090
	Multivariate analysis OR (CI 95%)	
Age (years)	1.4 (1.07-2.04)	0.019
Weight Z score	4.3 (0.97-18.8)	0.054

OR: Odds ratio. A1a: Age at diagnosis <10 years. A1b: Age at diagnosis 10-17 years. wPCDAI: weighted Pediatric Crohn's Disease Activity Index. CRP: C-reactive protein. BMI: body mass index. L2: colonic CD.

272 LONG-TERM FUNCTIONAL OUTCOME OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE DIAGNOSED DURING CHILDHOOD AND ADOLESCENCE

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Background: Inflammatory bowel disease (IBD) is a group of immune system disorders characterized by a chronic course with remissions and relapses. As with any chronic illness, IBD diagnosed early in life has a significant impact on physical, emotional and social development.

Consequently, it is logical to speculate that patients with IBD may not do as well in education levels or employment status attained compared to their peers without IBD. The aim of this study was to assess the functional outcome of adult IBD patients followed in Manitoba whose diagnoses were initially made during childhood in comparison with an age and sex-matched population-based sample of healthy Canadians.

Methods: Adult patients who were initially diagnosed with IBD in childhood or adolescence (diagnosis was made < age of 18 years) and initially seen at the Pediatric Gastroenterology Clinic, the Children's Hospital, Winnipeg, Manitoba, Canada from January 1978 to December 2007 were invited to answer a semi-structured questionnaire regarding their highest level of educational achievement, employment and marital status. Each case was then age- and sex-matched with 5 random healthy adult Canadians from the Canadian Community Health Survey (CCHS 2012). Occupation was coded using Canadian National Occupation Classification (NOS 2011). Conditional binary logistic regression and random-effects ordinal logistic regression models were used for analysis.

Results: There were 397 patients with IBD seen (56% boys, 233 (59%) had Crohn's disease (CD), 141 (35%) had ulcerative colitis (UC), and 23 (6%) had unclassified IBD (IBD-U). The contact details were verified for 124 persons. Of the 124 approached, 12 persons were excluded as they either did not have IBD, had another chronic debilitating disease or did not complete the survey. A total of 112 (88 %) completed the questionnaire, (mean age at diagnosis 12.9 years; range 4.3-17 years, 58 males, 76 with CD). The mean duration of follow-up was 14.3 years; range 3.1-34.5 years. Persons with IBD were more likely to earn more money *per annum* and attain a post-secondary school degree/diploma compared to those without IBD (odds ratio (OR) 1.72, 95% confidence interval (CI), 1.13 - 2.60, $p < 0.01$) (OR 2.73, 95% CI, 1.48 - 5.04, $p < 0.01$) respectively. There was no statistically significant difference between the 2 groups in employment or marital status (OR 0.96, 95% CI 0.58 - 1.58), OR 0.69, 95% CI, 0.44-1.06) respectively.

There was no significant difference between persons with CD compared to those with UC in all measured functional outcomes.

Conclusions: Adults with IBD diagnosed during childhood seem to achieve higher education levels compared to those without IBD. This would be enormously reassuring to children with IBD and their parents.

273 RAPID INFlixIMAB INFUSION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE: A MUTLI-CENTER NORTH AMERICAN EXPERIENCE

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Background: Infliximab (IFX) is a chimeric (part murine, part human) monoclonal antibody against tumor necrosis factor alpha (TNF- α) used to treat inflammatory bowel disease (IBD). Typically IFX is administered via intravenous (IV) infusion over 2-3 hours. Since IFX is a protein-derived medication, infusions can lead to formation of anti-IFX antibodies (ATI) which may lead to infusion reactions (IRs) with subsequent infusions. IRs are reported in as many as 5% of infusions and to occur in 10-20% of patients.^{1,2} While the safety of rapid IFX infusion has been confirmed in several adult studies (1,2), it has been under-evaluated in children. Our aim was to examine the incidence of IRs associated with rapid infusion of IFX and report variation in pre-medication regimens among different centers and their effect on IRs.

Methods: The medical records of consecutive patients (< 21 years) with IBD who were on rapid IFX infusions between January 2014 and April 2016 from 3 North American centers were examined. Variables examined included patient demographics, diagnosis, duration of IFX treatment and duration of infusions, time interval between infusions, reported immediate and delayed infusion reactions, pre-medications for IFX, if any, and presence or absence of concomitant immunomodulators.

Results: A total of 53 patients (mean age 13.6+3.1 years, 29 males, 37 Crohn's disease, 15 ulcerative colitis, and 1 IBD-U) with 365 rapid infusions were included. All had at least the initial 3 induction infusions over 2-3 hours followed by rapid IFX infusions over 60 minutes for the maintenance infusions. The mean dose for IFX was 7 mg (range 4.9-13.8) /kg/infusion. Only 5 patients (9%) had IRs on rapid infusions. The incidence for immediate IRs was 0.03% and delayed IRs was 1%. None of these reactions resulted in discontinuation of IFX. Pre-medications included none (6 (11%) patients), acetaminophen (40 (75%) patients), anti-histamines (11 (20%) patients) and steroids (3 (5.5%) patients). *Thirty three (62%) patients were on concomitant immunomodulators. In a univariate logistic regression analysis, the presence of pre-medication, concomitant immunomodulators and IFX dose did not result in any significant effect on incidence of IRs.

Conclusions: Rapid IFX infusions over 60 minutes are safe and well-tolerated in children with IBD. This strategy may save significant time and health resources for both patients and healthcare providers. The presence of absence of pre-medications did not have any effect on the incidence of IRs. Larger prospective well-designed studies are needed to confirm our conclusions.

*Several patients had more than one medication simultaneously.

References:1. Breaert *Cet al.* Tolerability of shortened infusion times in patients with IBD: a single center cohort study. *Am J Gastroenterol* 2011;106:778; 2) Neef HC *et al.* Meta-analysis: rapid infliximab infusions are safe. *Aliment Pharmacol Ther* 2013;38:365.

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284 PREDICTION OF INFANT COLIC SINCE THE DEFECATION PATTERN AND REGURGITATION: LOGISTIC REGRESSION MODEL

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Aim: Our aim was to develop a predictive model of infant colic since independent variables of the defecation pattern and the frequency of regurgitation.

Patient and methods: One-hundred and fifty consecutive infants attended by colic (Wessel criteria) at five GI outpatient clinics and 101 healthy infants seen for follow-up at two general pediatrics clinics were included. Cases with cow's milk allergy (exclusion/challenge trial), GERD (24-h esophageal pH test), and presence of enteropathogens in the stools (fresh smear and stool culture) were excluded. Independent variables included socio-demographic (parents age, education and employment; marital status; family size), type of diet, defecation pattern (times/day, days/week, stool consistency by Bristol classification, color and smell of feces) and associated GI symptoms (vomiting, abdominal distention, worsening during or after eating and hiccups). Statistics: chi square, OR, CIO5% and binary regression models.

Results: The mean age was 11.7 (\pm 3.9) and 9 (\pm 7.6) weeks for controls and cases respectively ($p= 0.02$); 48.9% were girls. Forty-three (16.8%) were exclusively breast fed; 49 (19.1%) received infant formula; and 164 (64.1%) mother's milk plus infant formula. The independent predictors of colic included in the final regression model were: stool frequency equal to or less than 5 per week (OR: 5.2, CI, 95%: 2.3-11.8); increased stool consistency (1-3 Bristol scale, OR: 3.4, CI, 95%: 1.5-7.5); regurgitation (OR:2.7, CI, 95%: 1.4-5); daily stool frequency equal to or less than 2 per day (OR: 2.3, CI, 95%: 1.1-4.5). Although the color and smell of feces had a significant association with colic, they were not included in the analysis due to their subjective nature. Socio-demographic variables and the type of feeding were not predictive of colic. Hiccups were more frequent in infants with colic but did not enter the model.

Conclusion: Our data point in the direction that defecation pattern plus regurgitation are predictors of colic once other causes of GI discomfort have been ruled out. Although a cross-sectional study does not evaluate causality, the association strength and de confident intervals suggest that in this series infant colic was associated to digestive disorders.

285 ABDOMINAL RADIOGRAPHS: APPROPRIATELY USED IN THE MANAGEMENT OF FUNCTIONAL CONSTIPATION IN CHILDREN?

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Abdominal radiographs (KUB) are frequently used to assess stool burden when managing pediatric constipation, despite evidence that radiographic findings poorly correlate with clinical symptoms or severity of fecal retention and despite recent guidelines which recommend obtaining KUBs only in children in whom fecal impaction is suspected but in whom physical examination is unreliable or not possible.

Aim: This study aims to discern reasons for obtaining KUBs and how they are used in diagnosis and management of pediatric constipation.

Method: 25 pediatric gastroenterologists were surveyed on 71 patients seen for known or suspected functional constipation and evaluation of which included obtaining a KUB. Physicians were given a questionnaire after the visit and asked about their reasons for obtaining a KUB. Plan, usefulness, utilization, and confidence in their plan before and after viewing the KUB. Multiple answers were permitted for each question.

Confidence was rated on a scale from 1-5 (1 unsure, 5 very confident).

Results: Reasons for obtaining KUB:

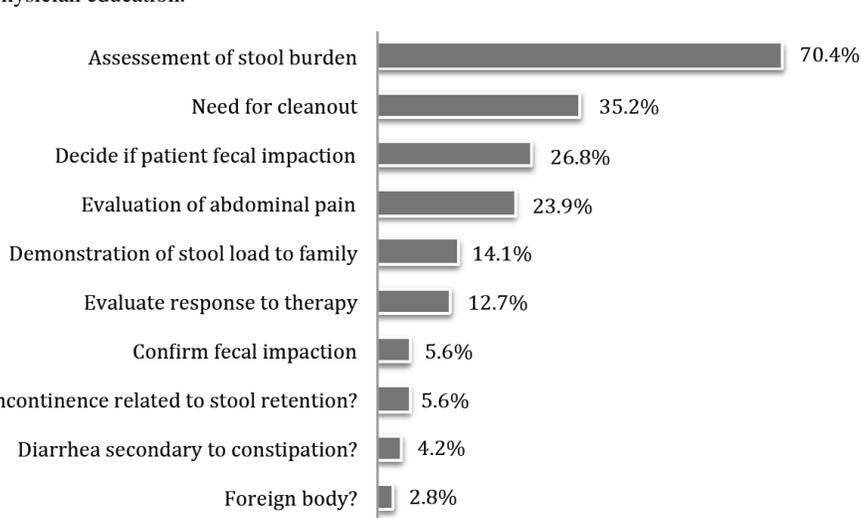
Table 1: Plan of management before and after viewing KUB: 69% of physicians had a treatment plan in mind before obtaining KUB. After viewing the KUB, the plan to do a clean out at home was decreased by 11.2% of physicians, inpatient clean out by 1.4%. Adding an osmotic laxative was increased by 5.6%. No change in the plan whether to add a stimulant laxative. The plan not to make any changes was decreased by 5.7% after obtaining KUB. Decreasing laxatives increased by 2.8%. New plans after viewing KUB included administering an enema (2.8%) or suppository (2.8%). 47.6% implemented or changed their plan based on KUB findings.

Utilization of the KUB: 97.2% of physicians found KUB helpful for their visit. Stool burden on KUB was as expected (39.7%), worse (39.7%) or less (20.6%) than expected. 63.4% used both their personal and the radiologist read of the KUB, whereas 33.8% relied on the radiologist's read alone.

81.7% of physicians report that the KUB was helpful in making a diagnoses: Constipation as reason for abdominal pain (27%), Constipation (22%), demonstration to family (16%), fecal impaction (10%), worsening fecal retention (8.6%), stool retention as reason for incontinence (5%), need for inpatient disimpaction (2%).

Physician confidence: Mean level of confidence in management plan prior to obtaining abdominal radiograph was 2.41 \pm 2.697 and increased at 4.07 \pm 1.751 after viewing KUB.

Conclusion: KUBs are commonly obtained by pediatric gastroenterologists in managing functional constipation. Nearly all find it useful. Most common reason for obtaining a KUB was the assessment of stool burden and the need for a clean out, despite evidence that KUBs poorly correlate with clinical symptoms or severity of fecal retention, contradictory to current guidelines. This discrepancy highlights the need for further physician education.



286 SYMPTOM PRESENTATION AND CLINICAL OUTCOME IN CHILDREN WITH FUNCTIONAL DYSPEPSIA

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Background: A subgroup of children with functional dyspepsia (FD) have gastroparesis (GP). It is unknown if either there are differences in symptoms (including both upper and lower gastrointestinal symptoms) or differences in clinical symptom resolution (outcome) between children with FD who have GP vs. those without GP.

Objective: To determine in children with FD whether the presence or absence of GP may affect either clinical symptoms or clinical symptom resolution (outcome).

Methods: Retrospective chart review of children with FD that completed a four-hour gastric emptying scintigraphy (GES) evaluation at a tertiary care children's hospital. Studies were completed between 2012-2013. Children were excluded if no symptoms were captured in the medical record; an organic etiology (e.g., celiac disease) was subsequently identified; or if they had previously had abdominal surgery. Patient demographics, GES results, symptoms (nausea, abdominal pain, vomiting, early satiety, weight loss/poor weight gain, fatigue, constipation, impairment in activities of daily living) at the time of first presentation and throughout their clinical course were systematically captured. The primary outcome was the severity of gastrointestinal symptoms at the time of the last identified follow-up visit (office visit or telephone encounter) in comparison to baseline. Outcomes were categorized as being: excellent (resolution of all symptoms); good (improvement in majority of symptoms with medication); fair (no improvement in majority symptoms); or poor (worsening in symptoms and/or impairment of activities of daily living). Statistical analyses (Chi-square or Fischer Exact) were completed using IBM SPSS Statistics 23 (Armonk, NY).

Results: 171 children with FD were included of whom 44 (25.7%) had GP. The mean (\pm SD) age at time of the GES was 12.5 ± 3.6 years and 117 (68.4%) were female. Overall, children with FD had the following symptoms: abdominal pain 141 (82.4%); nausea 75 (43.9%), vomiting 70 (40.9%), early satiety 31 (18.1%), weight loss/poor weight gain 50 (29.2%), fatigue 11 (6.4%), constipation 51 (29.8%), diarrhea 19 (11.1%), impaired activities of daily living (e.g., missing school) 32 (18.7%). Other than constipation ($p < 0.05$) (which was more common in those with GP), there were no differences in symptoms between those with GP and without GP. Outcomes: Children with GP did not differ from those without GP with respect to median [25%, 75%] follow-up time (13.0 [5.5-32.0] vs. 7.4 [2.4-21.0] months, respectively). Clinical outcome was able to be determined in 139 (81.3%). Children with FD with GP had worse outcomes vs. those without GP (Table).

Conclusions: Constipation is the only differentiating symptom (more common) in those with FD with GP vs. without GP. Children with FD without GP had better clinical outcomes vs. those with GP.

Table: Symptom Based Outcomes in Children with FD with Gastroparesis (GP) vs. without GP

Outcome	FD with GP (n=39)	FD without GP (n=100)
Excellent	0	4 (4%)
Good	23 (59.0%)	42 (42%)
Fair	12 (30.8%)	53 (53%)
Poor	4 (10.3%)	1 (1%)*

* $P < 0.05$ comparison FD with GP vs. without GP

287 SUGAR CONSUMPTION IN COLOMBIAN CHILDREN WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

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Introduction: Hypothetically intake of certain foods can produce some types of functional gastrointestinal disorders (FGDs) in children.

Objective: To determine the influence of sugar consumption in the occurrence of FGDs in children between 8-18 years of age from a public school in Cali, Colombia.

Methods: Cross-sectional study in children between 8 and 18 years old at a public school in Cali, Colombia. The outcome variable was measured by survey FGDs Rome III Criteria validated in Spanish. In the statistical analysis per occurrence ratio (95% CI) percentages, averages, standard deviations, 2x2 tables, ORs with their respective 95% CI were estimated. For statistical significance Fisher's exact test ($p < 0.05$) was used. To estimate the statistical model analysis of multiple logistic regression.

Results: Data 653 children were analyzed; the mean age was 13.19 years (between 8-18 years), the overweight prevalence was 28.9%. The FGDs prevalence was 19.9% and Functional Constipation (FC) was the most common disorder at 8.27%. There was no association or nutritional status influence in the occurrence of FGDs; however, those students who had excess sugar consumption (greater than 10% of total caloric value (TCV), had a four times greater opportunity to FGDs (95% CI, 2.04 to 7.68; $p = 0.00$). The excess sugar consumption is a confounding factor in the study of the possible association between excess weight and FGDs

288 COULD THE ROME III CRITERIA PREVENT UNNECESSARY COLONOSCOPIES IN CHILDREN AND ADOLESCENTS ADMITTED FOR INVESTIGATION OF ABDOMINAL PAIN?

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Background: Based on Rome III criteria, functional gastrointestinal disorders (FGID) could only be diagnosed when organic disease had been excluded, resulting in some normal colonoscopies. The newly published Rome IV criteria advocate for a positive diagnosis of FGID based on appropriate medical evaluation, allowing the physician to make the diagnosis with "selective or no testing". The objective of our study was to evaluate the diagnostic value of the Rome III criteria among pediatric patients undergoing colonoscopy for abdominal pain.

Methods: Between June 2013 and June 2015, all patients admitted for an elective colonoscopy in our pediatric endoscopy suite were invited to answer the qPGS questionnaire based on Rome III criteria for FGID in children/adolescents. Reason for colonoscopy, most recent complete blood count, result of colonoscopy and biopsies were obtained from the chart. Confirmed functional pain was defined as a normal colonoscopy and having Rome III criteria for « Irritable bowel syndrome », « Functional abdominal pain », « Functional abdominal pain syndrome », « Dyspepsia » or « Abdominal migraine ».

Results: Over the study period, 278 patients admitted for colonoscopy accepted to participate, 183 of which underwent colonoscopy primarily for abdominal pain. One hundred and three of these had a normal colonoscopy and 80 had abnormalities. There were 59% girls and median age was 14.8 years (IQR 25-75 11.4 – 16.3). Among the 103 patients with a normal colonoscopy, 85 (83%) fulfilled Rome III criteria, compared to 51 (64%) of the 80 patients who had an abnormal colonoscopy ($p = 0.01$).

Predictors of normal colonoscopy among patients admitted for abdominal pain, by multivariable logistic regression, were: having Rome III criteria of functional pain (OR 2.9 [CI, 95% 1.15 – 7.32] p 0.02) and a higher mean corpuscular volume (OR 1.16 [CI, 95% 1.08 – 1.24], p < 0.0001). Normal colonoscopy was less likely if colonoscopy had also been ordered for intestinal bleeding (OR 0.25 [CI, 95% 0.1 – 0.62], p 0.003) or positive markers of inflammation (OR 0.31 [CI, 95% 0.10 – 0.90], p 0.03), and if neutrophils (OR 0.72 [CI, 95% 0.59 – 0.89], p 0.002) or monocytes (OR 0.16 [CI, 95% 0.03 – 0.91], p 0.04) were increased.

The diagnostic properties of the QPGS alone to predict normal colonoscopy among patients admitted for abdominal pain without bleeding or inflammation, were: Sensitivity 86%, specificity 45%, positive predictive value 82% and negative predictive value 53%, Youden index 0.32. Adding biological data, we built a score using parameters from the multivariable model: score $-9.96 + 0.53 \times \text{pain} - 0.69 \times \text{bleed} - 0.59 \times \text{inflam} - 0.32 \times \text{neutrophils} - 1.85 \times \text{monocytes} + 0.15 \times \text{MCV}$. Using this score to predict normal colonoscopy showed: Se 56%, Sp 79%, PPV 77%, NPV 58%, Youden index 0.35.

Conclusion: The Rome III criteria alone or associated with CBC were insufficient to predict normal colonoscopies among patients investigated for abdominal pain in a tertiary center.

289 DEGLUTITION DISORDERS IN CEREBRAL PALSY WITH INDICATION FOR GASTROTOSMY

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Introduction: Cerebral palsy refers to a group of disorders in the posture and motor control development, occurring as a result of a non-progressive lesion of the developing central nervous system. Deglutition disorders, oropharyngeal dysphagia, are a very common symptom in this population. The aim of this study was to describe the oral transit time of deglutition in cerebral palsy in individuals with indication for gastrostomy.

Materials and Methods: A cross-sectional clinical study, included 15 individuals with cerebral palsy and indication for gastrostomy, 10 males and 5 females, 13 with oral feeding and 2 with nasal probe, age range 1 until 14 years old, that were followed in two Research Dysphagia Centers in Brazil. The swallowing was analyzed by videofluoroscopic swallowing study. Normal oral transit time of deglutition until 3 seconds was considered normal. It was analyzed by 19 images from oral transit time of deglutition, by a specific software, using puree bolus (13 images) and liquid bolus (6 images).

Results: The middle and standard deviation for oral transit time of deglutition were 10.75 seconds (middle) and 11.76 (SD) to puree and 4.22 seconds (middle) and 1.54 (SD) to liquid.

Conclusions: These results demonstrated that oral transit time of deglutition in children with cerebral palsy with indication for gastrostomy is raised.

290 SOX2, PLP-1 EXPRESSING ENTERIC GLIA IN THE POSTNATAL GUT DIFFERENTIATE INTO NEURONS IN RESPONSE TO LPS

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Objective: Mechanisms mediating adult enteric neurogenesis are largely unknown. Using models of inflammation-associated neurogenesis, and a strategic transgenic model approach we aimed to understand the cell-source.

Design: Dextran sodium sulfate (DSS) and *Citrobacter rodentium* colitis (CC) was induced in adult mice and colonic neurons were quantified. Sox2 GFP and PLP1 GFP mice served to confirm the glial specific expression of Sox2 and PLP1. Then Sox2CreER::YFP and PLP1creER::tdT mice were used for glial cell fate mapping after colitis. The effect of lipopolysaccharide (LPS) on enteric neurogenesis was tested *in vitro* and *in vivo* with or without administration of IAXO, a TLR4 inhibitor. Finally, expression of Sox2 as an indicator of neurogenesis was investigated in colonic neurons from human biopsies from patients with *C. difficile* or ulcerative colitis.

Results: Both DSS and CC led to an increase in colonic neuronal numbers. Following induction of colitis in adult Sox2CreER::YFP mice, YFP, initially expressed by enteric glia becomes expressed by neurons, without evidence of DNA replication suggesting glial cell transdifferentiation. A similar result was observed with the PLP1creER::tdT mouse. PLP1-expressing cells, which co-express S100b but not RET, also give rise to enteric neurons following colitis. These new neurons expressing YFP or tdT are, consistent with neurogenesis arising from glial transdifferentiation and less likely from neuronal progenitors. Systemic delivery of LPS into mice, led to an 18.4% increase in total neuronal density and a 40% increase in the number of double-immunoreactive Sox2+Hu+ neurons compared vehicle treated groups. The effect of LPS was abrogated by co-administration of IAXO. The percentage of Sox2-expressing enteric neurons in normal colon is 1-2% but rises up to 17% in human colitis.

Conclusions: These results suggest that colitis promotes enteric neurogenesis in adult mice and humans through transdifferentiation of Sox2 and PLP1 expressing enteric glia to neurons. This effect is mediated through microbiome-derived LPS via the TLR4 pathway. Further defining adult neurogenesis will improve our understanding of injury-associated dysmotility and identify targets for inducing therapeutic neurogenesis.

291 HEALTHCARE UTILIZATION ASSOCIATED WITH COMORBIDITIES IN CHILDREN WITH ANORECTAL MALFORMATIONS ACROSS THE USA

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Background: A variety of congenital anomalies are associated with anorectal malformations (ARMs) in children. Large population-based studies of the prevalence and healthcare utilization across different comorbidities associated with ARMs have not been performed in the U.S. Our aim was to identify trends in healthcare utilization differentiated by associated comorbidities in children with ARMs.

Method: We used Kids' Inpatient Database (KID) for the years 2006, 2009 and 2012 for data collection. ICD 9 codes (48.40, 48.41, 48.42, 48.43, 48.49, 751.2, and 751.5) were used to identify patients with ARMs.

Results: A total of 2396 children <2 years of age were identified using weighted analysis from the KID database. Congenital anomalies other than ARM were reported in approximately 80% of patients. Hospital length of stay (LOS) and hospital charges were differentiated across multiple congenital anomalies (Table 1). Genetic disorders and Hirschsprung's disease as well as esophageal, heart, renal and vertebral anomalies were associated with significantly longer hospital stays and associated charges (length of stay > 11 days, charges > \$100,000). In

patients with VACTERL associations, the length of hospital stay and related charges were increasing proportionally with the number of VACTERL associations.

Conclusion: The vast majority of children with ARMs have one or more additional congenital anomaly. The management of these complex congenital anomalies is associated with a significant healthcare expenditure. The cost of healthcare management for ARMs is highly correlated with the types of associated comorbidities, in particular for patients with VACTERL syndrome. This data provides useful information for screening of associated anomalies, planning healthcare resource allocation and overall management of children with ARMs.

Table 1

Comorbidities Associated with ARM	% of cohort	Average length of stay (days)	p value	Average charge per hospital stay (\$)	p value
Genetic disorders	14.1	12.7	<0.05	121,058	<0.05
Esophageal anomalies	3	36.9	<0.05	368,415	<0.05
Renal anomalies	15	11.8	<0.05	107,040	<0.05
Heart anomalies	21.2	14.1	<0.05	116,998	<0.05
Vertebral anomalies	4.9	13.3	<0.05	136,063	<0.05
Urogenital anomalies	38.5	7.5	<0.05	62,337	0.931
Hirschsprung's disease	1.3	17.4	0.094	130,744	0.063
Spinal anomalies	6.3	9.7	<0.05	75,857	0.437
Other GI anomalies	35.3	7.2	<0.05	59,329	0.663
VACTERL with 3 associations (including ARM)	6.8	16.1	<0.05	138,636	<0.05
VACTERL with 4 associations (including ARM)	1.7	35.2	0.058	336,908	<0.05
VACTERL with 5 associations (including ARM)	0.1	41.0	0.606	470,027	<0.05
No identified comorbidities	20.5	4.0	<0.05	35,029	<0.05

292 RISK FACTORS FOR FUNCTIONAL CONSTIPATION IN EARLY CHILDHOOD ATTENDING DAYCARE CENTERS

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Our objective was to determine the risk factors associated with the development of functional constipation (FC) in young children attending daycare centers. A cross-sectional survey using a questionnaire based on the Rome III criteria was conducted in children aged 25 to 84 months from 3 randomly selected daycare centers in January 2016. The items in a questionnaire were statistically compared in the constipated and non-constipated groups. A total of 212 children were included and FC was found in 8.5%. Multivariate logistic regression analyses revealed that maternal history of constipation (odds ratio [OR] 4.1, 95% Confidence Interval [CI], 1.2-13.9), history of painful bowel movements before age 1 (OR 10.4, 95% CI, 1.1-101.3), history of painful bowel movements during toilet training (OR 28.9, 95% CI, 1.9-423.8), no or difficult bowel movements at a daycare center (OR 5804.6, 95% CI, 134.4-250718.4), no meat consumption (OR 10.1, 95% CI, 1.2-88.1), and 500 cc or less of water intake per day (OR 9.9, 95% CI, 0.9-99.5) were powerful predictors of FC in young children ($p < 0.05$). Additionally, the constipated group was significantly associated with 2 hours or less of outdoor play activities per day, 6 hours or more of attendance at a daycare center per day, breastfeeding for less than 6 months, 3 meals or less per day, and 3 or fewer servings of fruits and vegetables per day ($p < 0.05$). The findings of this study can guide parents, daycare teachers, and clinicians in prevention, early recognition and early intervention for the risk factors associated with FC in young children.

293 EFFECTS OF FEEDING METHOD ON RATES OF GASTROESOPHAGEAL REFLUX IN CHILDREN RECEIVING GASTROSTOMY TUBE FEEDINGS

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Introduction: Gastroesophageal reflux disease (GERD) is common in children with gastrostomy tubes. Clinicians often alter feeding schedules, rates and formula types to try to reduce reflux burden. However, there is limited data to support this practice in pediatric patients. The aim of this study is to compare rates of gastroesophageal reflux measured using multichannel intraluminal impedance with pH (pH-MII) for different feeding variables in children receiving gastrostomy tube feedings.

Methods: We retrospectively reviewed the pH-MII tracings for all children receiving exclusive enteral nutrition through a gastrostomy tube who underwent pH-MII testing between 2003 and 2014. Patients receiving a combination of daytime bolus and overnight continuous feedings were included in the study. Reflux parameters were compared between the three feeding methods for each subject: no feedings, bolus and continuous. The impact of other feeding variables (caloric density, type of formula and rate of feeds) was also assessed. Means \pm SE were compared using t-tests or analysis of variance (ANOVA). The impact of feeding variables on reflux burden was assessed using linear regression.

Results: Eighteen subjects (mean age 4.5 ± 0.8 years, 14 (78%) female) were included in this analysis. Six (33%) had previously undergone a fundoplication. Nine (50%) patients received a milk-based formula, the remainder received a semi-elemental or elemental formula. Fourteen

(78%) patients were on formula with a caloric density of ≤ 30 calories per ounce and 4 (22%) received a formula with > 30 calories per ounce. Sixteen (89%) subjects were on acid suppressive therapy during their pH-MII study: 15 (83%) on proton pump inhibitors (mean dose 1.7 ± 0.2 mg/kg/day) and 7 (39%) on H2 blockers (mean dose 5.1 ± 1.4 mg/kg/day). 25% of all reflux events were acid events and 75% were non-acid. The mean percentage of study time that pH was < 4 was 4.4 ± 1.9 . Differences in rates of reflux (number of reflux events per hour) during no feed, bolus and continuous feeding periods are shown in Table 1. There was no effect of an elemental formula on the rate of reflux during the study ($p = 0.48$). Similarly, there was no significant impact of caloric density on the rate of reflux ($p = 0.50$). After adjusting for age, BMI, feeding rate and caloric density in multivariate analysis, there were no significant differences in reflux rates between feeding methods in either the fundoplication ($p > 0.05$) or non-fundoplication group ($p > 0.06$).

Conclusions: After multivariate analysis, altering methods of gastrostomy tube feedings in older children does not have a significant impact on reflux burden. Continuous feeds do not offer a significant advantage in reducing reflux rates.

Table 1: Rate of reflux (number of events per hour) by feeding method

	No feeds	Bolus	Continuous	P*
	Mean (SEM)	Mean (SEM)	Mean (SEM)	
Overall (n = 18)	0.68 (0.16)	0.19 (0.05)	0.61 (0.15)	0.02
No fundoplication (n = 12)	0.89 (0.21)	0.27 (0.07)	0.83 (0.20)	0.03
Prior fundoplication (n = 6)	0.24 (0.10)	0.03 (0.02)	0.17 (0.07)	0.16

* p-value calculated using one-way analysis of variance (ANOVA)

294 LOW-DOSE ENDOTOXIN (LPS) EXPOSURE INDUCES M1-SPECIFIC MACROPHAGE INFLAMMATION AND DOWN REGULATES OCCLUDIN IN TERMINAL ILEUM OF NEAR-TERM OVINE FETUSES: RELATION TO HEART RATE VARIABILITY (HRV) AS POTENTIAL PREDICTIVE MARKER OF INCIPIENT NECROTIZING ENTERO

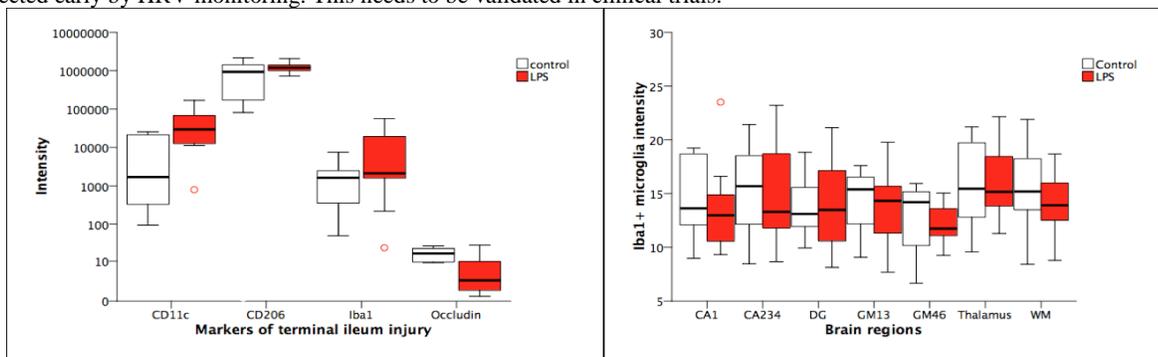
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Introduction: Low-dose endotoxin (LPS) triggers an increase in Iba1 intensity in the terminal ileum in near-term fetal sheep and that increase is correlated to a subset of HRV measures suggesting a potential to detect incipient gut inflammation non-invasively in utero using FHR monitoring to predict NEC. Here we address the questions: 1) are these macrophages of M1 (pro-inflammatory, CD11c) or M2 (anti-inflammatory, CD206) phenotype; 2) does this exposure lead to increase in gut leakiness (occludin) and 3) do HRV measures correlate uniquely to gut's and not another organ's inflammation? We hypothesized that LPS will recruit M1, but not M2 macrophages and a gut M1 macrophages-specific subset of HRV measures will be identified.

Methods: Chronically instrumented fetal sheep were exposed to 400ng LPS or NaCl q.d. for 2 days and sacrificed at 54h. Terminal ileum was studied for M1, M2 and occludin changes and Iba1+ microglia in the brain were quantified. All signals were correlated to the HRV measures determined at selected time points during fetal monitoring (cf. doi: 10.1088/0967-3334/36/10/2089). Results are presented for $p < 0.05$ after adjustment for multiple comparisons.

Results: In the terminal ileum, M1 and Iba1, but not M2, macrophages were increased and occludin signal was diminished vs. controls. In the brain, there was no significant difference between LPS and control animals (Figure 1). We identified unique subsets of HRV measures correlating to changes in M1 macrophages and occludin signal 48h in advance.

Conclusions: Low-dose endotoxin disrupts the integrity of the ileum's epithelial tight junctions and recruits M1 macrophages. Both effects can be detected early by HRV monitoring. This needs to be validated in clinical trials.



***295 BLADDER CONTROL PROBLEMS IN CHILDREN WITH CONSTIPATION: A MULTICENTER STUDY**

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Background: The prevalence of disturbed bladder control in children with constipation and fecal incontinence is not well studied. Chronic constipation and bladder control problems have been reported in children with attention deficit hyperactivity disorder (ADHD).

Aim: We evaluated the prevalence of bladder control problems in children with constipation seen in six large pediatric gastroenterology clinics in the United States and also evaluated the relationship of bowel and bladder control problems with ADHD.

Method: In this prospectively collected data there were 438 children with constipation and fecal incontinence diagnosed using Rome III criteria. 331 (75%) were over 5 years of age (145 female) and included in this study. 62% of children with constipation also had fecal incontinence.

Bladder control problems evaluated included bedwetting and day time urinary incontinence. Bowel problems were categorized as constipation alone or constipation with fecal incontinence. We also collected data regarding established diagnosis of ADHD at the time of evaluation in the GI clinic.

Results: Bedwetting was reported in 33% of the patients, day time urinary incontinence in 34% and 21% had both bedwetting and day time urinary incontinence. Children with combined fecal incontinence and bladder control problems and those with constipation and bladder control problems were significantly younger than children with constipation alone (Table). 38 patients had established diagnosis of ADHD and 61% of these patients had urinary and/or fecal incontinence. The prevalence of bowel and bladder control problem was not significantly different between the ADHD group and those without.

Conclusion: Bladder control problems are common in children seen in pediatric gastroenterology clinic with constipation and fecal incontinence and appropriate screening can help with timely diagnosis and referral to Urology. Defining the clinical phenotype of pediatric patients with bowel and urinary bladder control problems may help identify patients who do not respond to conventional medical management and may be candidates for sacral neuromodulation.

Table. Median age (SD) of 222 children with bowel and bladder control problems, children with fecal and urinary incontinence were significantly younger than children with constipation alone ($p < 0.001$)

	Median (SD) age in yrs.
Constipation with bladder problems (n=45)	8.8 (3.1)
Fecal incontinence and bladder problems (n=105)	7.4 (2.5)
Constipation alone (n=72)	10.6 (3.4)

296 BILIARY DYSKINESIA IN CHILDREN: A SYSTEMATIC REVIEW

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Background and objectives: Cholecystectomy rates for biliary dyskinesia (BD) in children are rising in the USA, but not other countries. In adults, biliary colic is required to diagnose BD. In children there appears to be consensus that chronic or recurrent upper abdominal pain is required for a BD diagnosis. Symptoms of BD and functional dyspepsia, a common functional disorder, overlap. The second criterion for BD diagnosis is an abnormal 1 h gall bladder ejection fraction (GBEF) on a CCK-stimulated HIDA scan, but this test has not been validated or shown to be reliable for BD in children. In adults many factors, including functional dyspepsia, decrease GBEF. The goal of this review was to determine the validity and reliability of criteria used to diagnose BD, and to assess treatment outcomes.

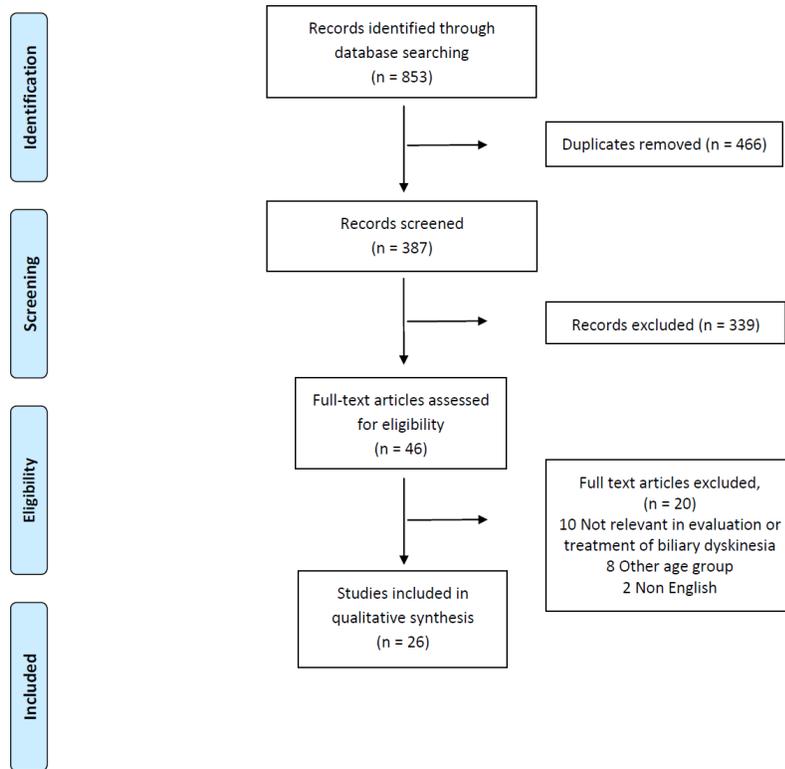
Methods: We performed a systematic review according to PRISMA-P guidelines and searched 7 databases including PUBMED, SCOPUS, EMBASE, OVID, PROQUEST, Web of Science and COCHRANE Libraries. Bibliographies of articles were screened for additional studies.

Results: Our search terms, BD and children, yielded 387 articles. We excluded 94 non-English, 145 adult and 122 irrelevant studies. We reviewed 26 peer-reviewed publications; 24 were retrospective chart reviews. None clearly described symptoms. The role of GBEF was assessed in 24; 20 assessed how gall bladder pathology correlated poorly with GBEF, and had evidence of chronic cholecystitis ranging from 17 to 100%. Most studies accepted GBEF <35% as abnormal. There were vast ranges in cut-offs for GBEF predicting benefit from surgery, from hypokinesia (GBEF < 11%) to hyperkinesia (GBEF > 65). In one paper, CCK-elicited pain was a better predictor of pain relief with cholecystectomy than GBEF. One paper reported no difference in outcome for those with normal vs. abnormal GBEF, and suggested that there was no need for HIDA scans. Twenty papers assessed cholecystectomy outcomes. Predictors of outcome were controversial: symptom duration, GBEF, weight loss, nausea, pain with CCK injection were found to be predictive or not predictive. 14 large series reported high rates of early post-op pain relief (76-100%) and favored cholecystectomy, while 6 studies found recurring or persisting symptoms on long term follow-up in 30-60%. Two studies showed similar outcomes of surgery vs. conservative care (observation alone or proton pump inhibitors). There were no prospective randomized clinical trials comparing medical to surgical care.

Conclusions: There is insufficient and poor quality evidence to recommend biliary imaging or cholecystectomy for children with chronic upper abdominal pain. Our findings support 1) validating a consensus definition for BD that does not overlap with functional dyspepsia, 2) testing validity and reliability of CCK-stimulated HIDA scans in children, 3) innovative studies to examine the comparative effectiveness and safety of cholecystectomy for BD vs. medical management of dyspepsia.



PRISMA 2009 Flow Diagram for Biliary Dyskinesia in Children



297 EFFECTS OF ERADICATION THERAPY ON CHILDREN WITH CHRONIC OR RECURRENT ABDOMINAL PAIN WITH *H. PYLORI* INFECTION

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Introduction: Chronic or recurrent abdominal pain is a common reason for visiting a physician. It is a condition comprising both functional and organic diseases. In children, the majority of cases are functional and the prevalence of organic diseases is not well known. *H.pylori* infection is one of the causes of organic disease such as gastritis or gastric ulcer and can be responsible for abdominal pain. Here we report the effect of eradication therapy on children who were diagnosed with *H.pylori* infection during the investigation of chronic or recurrent abdominal pain. **Case:** From April 2009 to October 2013, 15 patients (11 men, four women; age range, 8-15 years) received *H.pylori* eradication therapy for chronic or recurrent abdominal pain. Upper gastrointestinal endoscopy and drug susceptibility test for *H.pylori* were conducted in all patients before initiating the eradication therapy.

Results: After the completion of the eradication therapy, symptoms disappeared in eight cases, but remained in seven cases (including patients whose symptoms improved temporarily).

Discussion: It is not clear whether nodular gastritis due to *H.pylori* infection causes clinical symptoms such as stomach pain or not. Considering that some patients experience improvement in symptoms by eradication and that *H.pylori* infection is a risk factor for the development of gastric cancer, eradication therapy should be tried in patients with proven *H.pylori* infection. However, follow-up after eradication therapy is necessary as some may not experience any improvement or achieve only a temporal improvement. Because functional diseases may coexist with *H.pylori* infection, psychological approach with careful evaluation of patient's background and other physical symptoms is also important.

298 EFFICACY OF LACTOBACILLUS REUTERI DSM 17938 FOR INFANTILE COLIC: SYSTEMATIC REVIEW WITH NETWORK META-ANALYSIS (NMA).

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Background: Infantile colic represents one of the most frequent gastrointestinal functional disorders (GFDs) in infancy. Evidence shows the negative effect of this GFDs on the quality of life of infants and families. Misbalance of the gut-brain interactions seems to participate on the pathogenesis of this disorder and microbiota seems to play a pivotal role. The objective of this Network-Meta-Analysis (NMA) is to compare the efficacy of *Lactobacillus reuteri* DSM 17938 with other interventions to improve the symptoms associated with infantile colic.

Methods: Randomized clinical trials published between 1960-2015 for treatment of infantile colic were analyzed. Interventions included *Lactobacillus reuteri* DSM 17938, specialized infant formulas, manipulative, massage, acupuncture, herbals, drugs and reassurance/education.

Primary outcome was duration of crying after 21-28 days of treatment. Different databases were searched. Information was analyzed using control group as central axis. A random effect model was used. Hedges' weighted mean difference (WMD) and odds ratio (OR) were calculated and represented by Networking Forrest Plot (NFP). A funnel plot was assembled to identify publication bias. SUCRA analysis was performed to evaluate superiority for each intervention.

Results: 32 RCTs were analyzed, including 2242 patients. Studies with *L. reuteri* DSM 17938 [WMD -51.3h (CI, 95% -72.2 to -30.5h), $p=0.0001$, I² 42%] and some dietetic interventions [WMD -37.4h (CI, 95% -56.1 to -18.7h), $p=0.0001$, I² 49%] showed superiority. The rest of the interventions [some herbals [fennel], reassurance/education, massage, manipulative, drugs [simethicone] and acupuncture] were associated with significant grades of heterogeneity.

Conclusions: *L. reuteri* DSM 17938 followed by some dietetic interventions must be considered as evidence-based recommendations for reducing the symptoms associated with infantile colic.

299 THE PROGNOSTIC VALUE OF MANOMETRY TESTING IN CHILDREN WITH CONSTIPATION TREATED WITH SACRAL NERVE STIMULATION

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Background: Sacral nerve stimulation (SNS) can be effective in the treatment of children with severe constipation unresponsive to other treatment modalities, but prognostic factors of treatment success have not been identified. There is evidence that SNS modulates anorectal and colonic function in adults with defecatory dysfunction. The objective of this study was to evaluate the prognostic value of anorectal manometry (AM) and colonic manometry (CM) testing in children with constipation treated with SNS.

Methods: Using a prospective patient registry, we identified patients up to 21 years old who underwent AM or CM prior to SNS initiation for treatment of severe constipation. Encounters at baseline prior to SNS and at the most recent follow-up visit were reviewed. Successful response to SNS was defined as having ≥ 3 bowel movements and < 1 episode of fecal incontinence per week. We also compared medication usage, antegrade continence enema (ACE) usage, and PedsQL GI Symptom Scale (GSS) at baseline and follow-up. Results of AM and CM testing prior to SNS were reviewed.

Results: We included 21 patients (57% female, median age 13 years at SNS initiation, range 6-19 years). Three patients had a history of anorectal malformation, 2 had Hirschsprung's disease, 1 had a spinal cord abnormality, and the remaining 15 were diagnosed with functional constipation. Seventy-one percent had urinary symptoms and 67% had fecal incontinence at baseline. Twenty underwent AM prior to SNS initiation and 7 underwent CM. Of the 21 patients, 10 (48%) were classified as responders. Of the 11 non-responders, 1 had undergone SNS removal due to lack of response, 1 had undergone subsequent segmental colonic resection, and 2 had undergone SNS removal due to infection. Four of 10 responders were successfully weaned from laxatives and ACE at follow-up compared to none of the non-responders. Baseline AM and CM results and association with SNS response are shown in Table 1. Three patients had repeat AM testing; 1 showed an improvement in rectal sensitivity while the other 2 did not show any meaningful changes. One patient had repeat CM testing, which showed worsened colonic motility. Overall, the median GSS score improved from 50.0 before SNS to 61.1 after SNS (p 0.047).

Conclusion: In this sample of children with constipation treated with SNS, AM and CM findings were not associated with successful or unsuccessful response to SNS. Therefore, abnormal AM or CM should not preclude children with intractable constipation from consideration for SNS treatment. Further studies with larger sample sizes are needed to better understand the role of manometry in the evaluation of children with intractable constipation treated with SNS.

Table 1: Baseline manometry results and evaluation of association with SNS response.

Variable		Responders	Non-responders	p-value
Anorectal manometry				
Normal resting pressure ^{1,†}	Yes	9	6	0.30
	No	1	3	
Normal sensation ^{2,†}	Yes	6	6	0.47
	No	2	0	
RAIR present ¹	Yes	10	9	1.00
	No	0	1	
RAIR complete ¹	Yes	9	7	0.58
	No	1	3	
Normal overall interpretation ¹	Yes	6	5	1.00
	No	4	5	
Colonic manometry				
Postprandial response ^{3,†}	Yes	3	4	N/A
	No	0	0	
Response to bisacodyl ³	Yes	2	4	0.43
	No	1	0	
Urge after bisacodyl ³	Yes	2	4	0.43
	No	1	0	
Stools after bisacodyl ³	Yes	2	4	0.43
	No	1	0	
Overall normal interpretation ³	Yes	2	4	0.43
	No	1	0	
Patient characteristics				
Fecal incontinence ⁴	Yes	6	8	0.66
	No	4	3	
Urinary symptoms ⁴	Yes	5	10	0.06
	No	5	1	
Anorectal malformation ⁴	Yes	1	2	1.00
	No	9	9	

¹ Total number of patients who underwent AM, n=20

² Only determined in patients who underwent AM awake, n=15

³ Total number of patients who underwent CM, n=7

⁴ Total number of patients, n=21

† 1 missing value

300 GASTRIC DYSMOTILITY RATHER THAN GASTROESOPHAGEAL REFLUX PREDICTS PEDIATRIC LUNG TRANSPLANT OUTCOMES

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Background: Gastroesophageal reflux (GER) has been linked to increased risks of acute and chronic rejection following lung transplant in adults. However, little is known about the impact of reflux and gastric dysmotility on pediatric lung transplant survival. The objective of this study is to describe the impact of reflux burden and gastric dysmotility on allograft outcomes in children.

Methods: This is a retrospective study of pediatric patients who underwent combined pH-multichannel intraluminal impedance (pH-MII) testing and, in a subset, gastric emptying scans (GES) within 12 months of lung transplant between December 2004 and March 2015. An abnormal impedance study was defined as > 73 episodes of reflux per 24 hours. An abnormal pH study was defined as pH<4 for >6% of the study period. Abnormal gastric emptying was considered delayed when >60% of the ingested food remained in the stomach after one hour of imaging. Pulmonary outcomes of interest included the rate of acute rejection diagnosed by transbronchial biopsy, and the incidence of chronic lung allograft dysfunction (CLAD) diagnosed by spirometry decline and/or biopsy.

Results: The mean age of 14.3 ± 5.1 years. Combined pH-MII testing was performed at a mean of 4.6±0.4 months after lung transplantation. Three of 30 (10%) patients had an abnormal number of reflux episodes by impedance, 7 (23%) patients had abnormal pH-metry and 5 patients (17%) had abnormal results for both pH-metry and impedance portions. 9 patients underwent fundoplication as a result of pH-MII testing. GES was performed in 19 patients prior to any surgical interventions. The mean gastric residual at 1 hour of testing was 42±6%. Five of 19 (26.3%) had more than 60% residual after one hour of imaging. No statistical difference in reflux parameters was found between patients with normal versus abnormal GES ($p>0.3$). There was no benefit of fundoplication in reducing death or relisting (HR 0.63, 95% CI, 0.18-2.20, $p=0.47$), acute rejection (HR 1.32, 95% CI, 0.26-6.56, $p=0.74$), or CLAD (HR 1.48, 95% CI, 0.49-4.48, $p=0.48$). No associations were seen between gastric emptying status and survival/relisting status (HR 5.56, 95% CI, 0.77-40.11, $P=0.09$), nor with incidence of acute rejection (HR 4.86, 95% CI, 0.43-55.03, $p=0.20$). However, Cox proportional hazard analyses revealed a consistent link between delays in gastric emptying and the development of CLAD after adjusting for reflux burden and fundoplication history (table).

Conclusions: Neither reflux burden or fundoplication status has a significant impact on transplant survival. After adjusting for fundoplication status and reflux burden, gastric dysmotility was a significant predictor of chronic lung allograft dysfunction.

Predictors	Chronic Lung Rejection	
	HR(95%CI)	P value
Model (a)		
Nissen Fundoplication	5.94(1.03-34.43)	0.046
Abnormal Gastric emptying study	31.65(3.20-313.39)	0.003
Model (b)		
Nissen Fundoplication	5.93(1.03-34.25)	0.047
Abnormal pH study	0.94(0.27-3.25)	0.93
Abnormal Gastric emptying study	32.25(3.16-329.01)	0.003
Model (c)		
Nissen Fundoplication	5.34(0.87-32.80)	0.07
Abnormal impedance study	2.17(0.51-9.31)	0.30
Abnormal Gastric emptying study	33.99(3.26-354.76)	0.003
Model (d)		
Nissen Fundoplication	6.03(0.998-36.47)	0.0502
Abnormal reflex testing	1.51(0.42-5.41)	0.53
Abnormal Gastric emptying study	30.83(2.94-323.63)	0.004

301 GASTROGRAFIN FOR THE MANAGEMENT OF FECAL IMPACTION IN CHILDREN WITH CONSTIPATION: A MULTICENTER RETROSPECTIVE CHART REVIEW STUDY

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Background and Aim: Fecal impaction is a common problem in children with functional constipation, and early recognition is important. Evaluation of fecal impaction with careful history taking and physical examination, in conjunction with radiological imaging, is imperative. Conservative treatment with diluted gastrografin enema is an effective initial treatment in patients with meconium ileus or distal intestinal obstruction syndrome. However, there is uncertainty regarding the optimal regimen of disimpaction in children with functional constipation. The aim of this study was to review and assess the use of diluted gastrografin enema for management of fecal impaction.

Methods: A multicenter retrospective chart review was performed in 18 hospitals with a focus on experience of the use of diluted gastrografin enema for management of fecal impaction. Data collected electronically included indication for gastrografin treatment, identification of fecal impaction with X-ray imaging, period up to excretion of fecal impaction, and any complications.

Results: We analyzed data from 15 (83%) hospitals where disimpaction was performed with gastrografin enema. Indications for gastrografin are shown in Table 1. Successful disimpaction was achieved with gastrografin enema (93%). From 1:1 to 1:5 diluted gastrografin enema was effective within 24 hours after the enema solution was administered (87%). There were two side effects about abdominal distention and iodine-induced hypothyroidism.

Conclusions: Our results showed that gastrografin was effective for establishing the extent of impaction and for prompt relief of fecal impaction without any serious complications.

Table 1. Major characteristics of treatment with diluted gastrografin enema (n=15).

	Hospital no. (%)
Indication for gastrografin treatment	
overflow soiling	10 (67)
rectal impaction on abdominal radiography	9 (60)
fecal mass palpable abdominally	6 (40)
straining	5 (33)
"rabbit droppings"	3 (20)
no bowel movement for * days	3 (20)
fecal mass palpable rectally	3 (20)
Feature of gastrografin treatment	
effective	13 (87)
less painful	7 (47)
immediate	7 (47)
possible evaluation of underlying disorders or conditions	7 (47)
safety	5 (33)
possible evaluation of fecal impaction	4 (27)

302 VALUE OF TEMPORARY GASTRIC ELECTRIC STIMULATION TO PREDICT RESPONSE IN PEDIATRIC PATIENTS WITH REFRACTORY GASTROPARESIS

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Introduction: Gastroparesis is not an infrequent condition, with 4.6 per 10,000 pediatric patients being affected. Unfortunately, conventional treatment is not always successful. Gastric electrical stimulation (GES) is emerging as a possible alternative in patients that failed conventional treatment, but with the inconvenience that requires invasive surgery for the permanent placement. Temporary placement of GES allows patients to trail the therapy and determine if symptoms improve before undergoing permanent placement. The goal of this study was to determine if symptom relief from temporary GES correlated with long term relief of symptoms provided by permanent placement of stimulators.

Methods: This was a retrospective chart review, that included fourteen patients followed in the pediatric surgical and GI clinic with gastroparesis, who were determined to potentially benefit from gastric electrical stimulation. Gastric stimulator was placed either nasogastrically or inserted into prior gastric tube stoma. Patients were then tracked for symptomatic improvement of nausea, vomiting, retching, oral intake, and gastric tube residuals. Ten patients underwent permanent gastric stimulator placement after symptom relief with temporary stimulators.

Correlation of relief of symptoms between temporary and permanent placement was determined with follow-up after permanent placement.

Results: Of the fourteen patients with temporary GES, four did not find symptomatic relief from temporary placement of the stimulator and chose not to proceed with permanent stimulator placement. The major symptoms conveyed by the ten patients were nausea and vomiting. After temporary stimulator placement, 10 of the 14 patients (71%) affirmed significant relief of symptoms. After the placement of the permanent stimulator, all ten patients described relief of symptoms consistent with the temporary stimulator. Intermittent nausea and vomiting was noted in five patients that resolved with increase in parameters of the stimulator. Patients who had poor weight gain prior to placement all gained weight over subsequent visits after permanent placement. There was one patient that identified adverse effect of the temporary gastric stimulator placement which was: pain, ulcer formation, and gastric secretion leakage around gastrostomy site.

Conclusions: GES is a meaningful intervention for gastroparesis and has been proven to be a viable treatment. Our study showed that symptom relief after temporary placement could be directly correlated to symptom relief and patient satisfaction after permanent placement in a small cohort of patients. Four patients chose to not proceed with permanent placement of the gastric stimulator after trial of temporary GES. This spared these patients from a surgery and permanent stimulator that would not have improved their symptoms.

303 CAN PROPOFOL BE USED TO ASSESS THE PRESENCE OF THE RECTOANAL INHIBITORY REFLEX DURING ANORECTAL MANOMETRY STUDIES?

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Introduction: Anorectal manometry (ARM) is a valuable adjunct in the evaluation of pediatric patients with defecation disorders. Its main indication is to determine the presence of the rectoanal inhibitory reflex (RAIR) that rules out the possibility of Hirschsprung's disease (HD) or a non-relaxing internal anal sphincter (NR-IAS). RAIR can be difficult to assess in uncooperative young patients and sedation or anesthesia are sometimes used for a better assessment. In limited studies, propofol has been shown to decrease the intra-anal pressure (IAP), but there is no information on its effect on the RAIR. Therefore, the aim of this study was to examine the effect of propofol on the presence of the RAIR and to determine if it could be a good alternative for the performance of ARM in uncooperative patients or patients undergoing other procedures under anesthesia.

Methods: Analysis of ARM parameters in children undergoing manometry testing as part of their evaluation for chronic intractable constipation (CIC) before and after the administration of propofol. All patients had an ARM prior to anesthesia induction with propofol, followed by colonoscopy for catheter placement for a colonic manometry. The ARM catheter was left in place during propofol infusion and the study was repeated. Resting IAP and characteristics of the RAIR were measured and compared before and after propofol infusion.

Results: A total of 27 patients were analyzed (63% male, mean age of 9.2 yrs). Mean propofol dose was 93.5 ± 63.9 mg (2.9 ± 1.3 mg/kg). The mean resting IAP was significantly lower during propofol when compared to baseline (34.2 ± 1.9 vs. 66.9 ± 3.2 mmHg, $p < 0.001$). Time from propofol infusion start to initial IAP drop was 76.9 ± 5.3 sc. Overall, RAIR was successfully elicited during propofol and, there was a shift of the RAIR dose response curve to the left. The percentage of relaxation after balloon distension was significantly higher during propofol with balloon volumes of 10, 20 and 30 cc ($p < 0.05$). There was no difference with balloon volumes of 40, 50 and 60 cc. RAIR was present on 21 patients and absent in 6 before propofol. All that had a RAIR at baseline continued to have a RAIR during propofol. Of the 6 patients with an absent RAIR, 2 had a RAIR during propofol (CIC 2); in the other 4, RAIR was absent before and after propofol (HD 3; NR-IAS 1). The minimum IAP measured during the RAIR for all balloon volumes was significantly lower during propofol ($p < 0.05$). No difference was observed over the latency to relaxation time or the total relaxation time.

Conclusions: Propofol does not affect the presence of the RAIR during an ARM and is a good alternative to exclude HD or a NR-IAS in patients who are uncooperative or are undergoing other procedures under anesthesia. Propofol can not be used to assess baseline IAP as the pressure is significantly reduced with its administration.

304 PSYCHOSOCIAL FACTORS ASSOCIATED TO CHILDREN WITH FUNCTIONAL CONSTIPATION

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Aim: Identify psychosocial factors associated with functional constipation in children treated at the outpatient service of Gastroenterology.

Patient and Methods: Cross-sectional study.

Sample size: 145 children aged 7 to 15 years 11 months divided into 2 groups; 71 children with functional constipation according to the Rome III criteria and 74 without constipation attending primary and secondary school, patients who were on treatment of mood disorder were excluded.

Independent variable: Functional constipation.

Dependent variable: Psychosocial factors. Application of assessment: an assessment tool for psychosocial factors, developed based on the various aspects included in previous studies, adapted to our population, which included two parts was applied; the first part evaluated social factors both patient and parent and the second part consisted of questions aimed at finding symptoms of anxiety and / or depression, using two instruments guaranteed for pediatric population such as the scale of Birleson for Depression children and adolescents with Cronbach's alpha of 0.79 and manifest anxiety scale CMAS-R for children 6 to 19 years with Cronbach's alpha of 0.85.

Statistical analysis: Frequencies, percentages, and t-student.

Results: The mean age in both groups was 10.16 years; there was no difference in gender distribution, 70% were schoolchildren. In the group with functional constipation, clinical characteristics were evaluated at the time of disease progression with a mean of 4.8 years, 55% of our patients had fecal incontinence. When analyzing psychosocial factors in both groups there was no statistical significance in terms of parental age, marital status of parents, parents' time away from home for employment, but showed significant difference maternal education ($p = 0.024$), single-parent family ($p = 0.034$) and stressful family event ($p = 0.019$). As for school-related factors, total hours attending school ($p = 0.000$) and the number of absences in the last year ($p = 0.039$) showed statistically significant difference. The presence of symptoms of depression and anxiety levels in both groups was evaluated, showing no statistically significant difference in the level of depression ($p = 0.156$) but with full anxiety ($p = 0.011$) and sub anxiety scale concern/hypersensitivity ($p = 0.003$).

Conclusion. There are several psychosocial factors associated with functional constipation. As would be expected, children with fecal incontinence have anxiety, but what caught our attention is that the group without constipation also showed high levels of anxiety, which shows that this group of healthy children also have a degree of involvement in the mental sphere. Therefore interdisciplinary management is required with medical and psychological support in both groups.

305 RUMINATION SYNDROME IN INDIAN CHILDREN: OVERLOOKED, UNDER RECOGNIZED AND UNTREATED.

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The rumination syndrome was once thought to occur only in the developmentally delayed. The last decade has proven that this condition is much more frequent than realized and the most commonly affected are normal children and adolescents. Frequently overlooked and under recognized, subjected to unnecessary testing and inappropriate treatment, for a condition which can be diagnosed clinically and managed simply these children represent a fascinating study in functional Gastrointestinal disease. In the first ever systematic exploration of this condition from India, we present a prospective study of children with chronic vomiting where rumination emerged as the predominant cause.

Methods: This was a prospective study where all consecutive children (5 - 18 years) presenting with chronic or recurrent vomiting of at least 2 months duration were enrolled. Clinical history was assessed by a physician-administered questionnaire. All underwent a barium study, gastroscopy, gastric emptying scan, 24 hour pH monitoring, blood work and additional investigations if required.

Results: Fifty children (28 boys, age 12.2 ± 3 years) were enrolled. Duration of symptoms at presentation was 12 months (range 2 - 180 months). Diagnosis was rumination 30, cyclical vomiting 8, functional vomiting 6, intestinal tuberculosis 4, intestinal malrotation 1 and superior mesenteric artery syndrome 1. Children with rumination syndrome had a relapsing and remitting (18, 60%) or a chronically symptomatic course (12, 40%). These children received incorrect diagnoses (26, 87%) or no diagnosis (3, 10%) and extensive investigation before referral. 24 (80%) of these children reported missing a median of 8 weeks (range 2 to 40 weeks) of school in the past year. Before referral, children with rumination were treated with a median of four drugs (range 1 to 9); two underwent surgery for their symptoms while one child was subjected to electroconvulsive therapy. The duration of follow of the whole cohort of fifty children was 14.4 ± 5.2 months. Children with rumination were treated with either counseling alone (7) or counseling with diaphragmatic breathing (23). Overall, resolution was seen in 26 (87%) with a relapse in 8 (27%). Features that differentiated an organic etiology (n 6) from functional causes (CVS, functional vomiting, n 14) were pain abdomen relieved by vomiting (100% vs. 21%, $p = 0.002$), weight loss (83% vs. 7%, $p = 0.002$) and audible borborygmi (83% vs. 14%, $p = 0.007$). A barium meal follow through was the most useful investigation to differentiate between the two.

Conclusion: Rumination syndrome in children has never been reported from India. Due to a lack of awareness of this condition, the diagnosis is delayed, leading to unnecessary testing and incorrect treatment. Therapy in the form of diaphragmatic breathing has a good success rate. The functional vomiting subtype, which is not currently classified in children in the ROME III criteria, was seen in this cohort.

306 HIGH RESOLUTION ANORECTAL MANOMETRY IN CHILDREN WITH FUNCTIONAL CONSTIPATION WITH OR WITHOUT FECAL INCONTINENCE

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Introduction: High resolution anorectal manometry (HRARM) based on a spatio-temporal plot is expected to better study the anal pressures when compared to conventional anorectal manometry. The aim of this preliminary study was to characterize and compare anorectal pressures of children with functional constipation with or without fecal incontinence by HRARM.

Methods: Children with a diagnosis of FC with or without fecal incontinence (FI), according to Rome III criteria, referred to the Department of Translational Medical Science, Section of Pediatrics of the University of Naples "Federico II", were enrolled. After the enrolment, all children underwent HRARM. HRARM was performed using a 24-channel customized water-perfused silicone catheter. Measurements were performed during rest and squeeze. The recto-anal inhibitory reflex (RAIR) and the anal canal length were analyzed. In the absence of normative data of HRARM, we compared our findings with the results of Banasiuk *et al.* (Clinical Gastroenterology and Hepatology 2016) which performed HRARM in children without lower gastrointestinal symptoms.

Results: We enrolled 13 consecutive children, of whom 8 affected by functional constipation without fecal incontinence (FC) (median age: 133 + 44.4 months, range 87-182 months; M/F: 6/2) and 5 affected by functional constipation with fecal retentive incontinence (FRI) (median age: 128.4 + 45.4 months, range 78-170 months; M/F: 4/1). At rest, the maximum and mean pressure were 100,28 mmHg (SD±33.7) and 70 mmHg (SD±18) in FC children and 92.6 mmHg (SD ± 27.6) and 69 mmHg (SD ± 7.9) in FRI children (p 0.6; p 0.8, respectively). The mean anal relaxation rate was 23.2% (SD ± 17) in FC children versus 15.6% (SD ± 9) in FRI children (p 0.3). The maximum squeeze mean pressure was 169 mmHg (SD ± 56) in FC children and 141 mmHg (SD ± 38.49) in FRI children (p 0.7). The mean RAIR was 37 mL (SD ± 14.9) in FC children and 36 mL (SD ± 8.9) in FRI (p 0.6). No statistical significant differences were found with regards to anal canal length values between the 2 groups (2.5 cm ± 0.2 vs. 2 cm ± 0.5; p 0.2). When comparing HRARM values of our children with Banasiuk *et al.*, we observed no differences in maximum resting pressure (97 mmHg vs. 100 mmHg) and anal canal length (2.2 cm vs. 2.6 cm). The maximum squeeze pressure and the mean resting pressure of our population study were lower (157 mmHg vs. 191 mmHg; 69 mmHg vs. 83 mmHg, respectively); the mean RAIR values resulted higher (37 mL vs. 15.7 mL, respectively).

Conclusion: Our preliminary data demonstrate that HRARM pressure values in children with FC with or without FI are comparable. When comparing with children without lower gastrointestinal symptoms, children with FC with or without FI show lower values of squeeze and resting pressure and higher values of RAIR. Further studies are needed to confirm the results of this preliminary work.

307 THE UTILITY OF CYP2C19 GENETIC TESTING IN PATIENTS WITH PERSISTENT GASTROESOPHAGEAL REFLUX DISEASE

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Background: The diagnosis of gastroesophageal reflux (GERD) and the use of proton pump inhibitors (PPIs) in children has significantly increased over the last decade. Cytochrome P450 enzymes are essential for the metabolism of PPI's, most specifically CYP2C19. Genetic variability in these enzymes may influence patient's response to PPIs. The use of genetic testing is becoming more prominent in an effort to provide more comprehensive individualized medicine.

We aim to assess the clinical utility of CYP2C19 genetic testing in the clinical management of children with refractory GERD.

Methods: We conducted a retrospective chart review of the electronic medical records (EMR) at Mayo Clinic from August 2014 to April 2016. Children age 0-18 years who had their genetic CYP2C19 status checked because of refractory GERD were included. Relevant data including clinical notes, laboratory studies, endoscopic evaluations and esophageal impedance studies was recorded. This study was approved by Mayo Clinic IRB.

Results: Ten patients (6 female, 4 male) with a mean age of 9.4 years were found to be ultrarapid metabolizers. All 10 of these patients were on a PPI metabolized by CYP2C19. All patients carried a diagnosis of GERD and their presenting symptoms were abdominal pain and vomiting. The mean length of symptoms prior to further investigation with genetic testing was 11 months. All 10 patients underwent an upper endoscopy. Five were found to be normal both visually and histologically and 5 were abnormal (4 had esophagitis and 1 had linear furrows). Out of 10 patients, 8 had esophageal pH impedance testing and 6 of those were found to have a gastric pH <4 indicating inadequate acid suppression. All 10 patients with ultrarapid metabolizer status underwent a change in their antacid therapy, 7 were switched to H₂ blocker (ranitidine or famotidine), 1 was switched to CYP2C19 independent PPI and 2 patients had their current PPI dose increased. Seven patients reported either improvement or resolution of their symptoms after an average of 2 months and all of these patients had been switched to H₂ blocker. One patient was lost to follow-up. The remaining 2 patients who did not improve were found to have functional abdominal pain or delayed gastric emptying; both of them had normal initial endoscopic assessment.

Conclusion: In children with refractory GERD symptoms despite adequate PPI therapy, genetic testing of CYP2C19 can be of clinical utility. Larger prospective trials are needed to further investigate the utility of CYP2C19 genetic testing in children.

308 GASTROESOPHAGEAL REFLUX IN NEUROLOGICALLY IMPAIRED CHILDREN: WHAT ARE THE RISK FACTORS?

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Background/Aims: Neurologically-impaired patients (NIP) frequently suffer from gastrointestinal tract problems such as gastroesophageal reflux disease (GERD). In this study, we aimed to define the risk factors for GERD in neurologically impaired children.

Methods: From May 2006 to March 2014, 101 neurologically impaired children who received 24 hr esophageal pH monitoring in Severance children's hospital were enrolled. The results of esophageal pH monitoring and the clinical characteristics of the patients were analyzed.

Results: Reflux index was higher in the abnormal EEG group than in the normal EEG group (p = 0.027). Mitochondrial disease was associated with a higher reflux index than epileptic disorders or cerebral palsy (p = 0.009). Patient gender, feeding method, scoliosis, tracheostomy, and baclofen use did not lead to statistical differences in reflux index. Age of onset of neurological impairment was inversely correlated with

DeMeester score and reflux index. Age at the time of examination, duration of the disease, and number of antiepileptic drugs did not correlate with GER severity.

Conclusions: Early-onset (less than 12 months) neurologic impairment, abnormal EEG, and mitochondrial disease are identified as risk factors for severe GERD.

309 VALUE OF 24-HOUR DELAYED FILM OF BARIUM ENEMA FOR EVALUATION OF COLON TRANSIT FUNCTION IN YOUNG CHILDREN WITH CONSTIPATION

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Purpose: To evaluate the utility of a 24-h delayed barium enema (BE) film for assessing colon transit function in young children with constipation.

Methods: In total, 93 children who met the Rome III criteria for constipation performed both single-contrast BE and radio-opaque marker colon transit time (RMCTT) test. Of these, the data from 70 children were analyzed (M:33, F: 37; mean age (range): 5.63 ± 2.94 (2 - 14) years). The basic principle of the study is velocity = distance/time. Time values were identified in both studies, and the colon length and distance of barium movement were measured on the 24-h delayed BE film. Thus, colon transit velocity values could be calculated using both methods. The correlation between colon transit velocity using a 24-h delayed BE film versus RMCTT test was analyzed statistically.

Results: Median value (IQR) of colon transit velocity using RMCTT test was 1.57 cm/h (1.07-2.89), and that using BE of that was 1.58 cm/h (0.94-2.07). The Spearman correlation coefficient was 0.438 ($p < 0.001$) for the overall group. The correlation was the strongest in children younger than 4 years ($r = 0.537$; $p = 0.032$).

Conclusions: Although the correlation between BE and RMCTT test was not very strong, the 24-h delayed BE film could provide broad information about colon transit function in young children, especially those under 4 years who usually cannot undergo RMCTT test.

310 ESOPHAGEAL HIGH RESOLUTION MANOMETRY FOR LOCATING LOWER ESOPHAGEAL SPHINCTER IN CHILDREN WHO UNDERGO 24-HOUR IMPEDANCE-PH MONITORING

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Background: Twenty-four-hour multichannel intraluminal impedance-pH monitoring (MII-pH) is a reliable investigation for the diagnosis of gastroesophageal reflux disease (GERD). Proper position of the catheter is crucial for the accuracy of reflux detection. In adults, the MII-pH catheter is generally placed under esophageal manometry (EM) which is considered as a gold standard method to locate lower esophageal sphincter (LES) but it is difficult to perform in children. Esophageal high resolution manometry (EHRM) is technically easier and more tolerable than conventional EM. However, EHRM is not widely available particularly in developing countries.

Objectives: Primary objective: To compare the esophageal length (EL, the distance from nostril to LES) identified by EHRM with the other techniques (Strobel formula and pH step-up technique); Secondary objective: To examine the position of pH sensor by using chest radiography. Study design: Cross sectional study.

Methods: Infants/children, age more than 6 months with suspected GERD, were enrolled. EHRM was performed to locate the LES and EL. Then, EL was estimated using Strobel formula and pH step-up technique. Finally, the MII-pH catheter was placed at 87% of EL in according to the EHRM measurement and chest radiography was performed to identify the pH sensor position.

Statistical analysis: Paired t-test and Bland & Altman limits of agreement.

Results: We enrolled 28 patients; 16 were female (57.1%), aged 6-126 months. The mean age was 42 (SD 39) months. The mean difference of EL using Strobel formula and pH step-up technique compared to EHRM was 1.3 and 0.69 cm, respectively. The mean difference of EL using Strobel formula compared to EHRM according to age groups were the following: -0.01, 1.26 and 3.77 cm in children aged 6-24 months (n=13); 25-60 months (n=8) and 61-126 months (n=7), respectively. The mean difference of EL using pH step-up technique compared to EHRM according to age groups were 0.38, 0.81, and 1.11 cm, respectively. The new model to predict EL was created; $EL \text{ (cm)} = 4.641 - [0.046 \times \text{age (months)}] + [0.263 \times \text{height (cm.)}]$ ($R^2 = 0.91$). The positions of pH sensor shown in chest radiography were at the 8th vertebral body (42.9%), the 9th vertebral body (28.6%) and the 7th vertebral body (21.4%).

Conclusion: In children aged 6-126 months, LES can be identified with sufficient accuracy by pH step-up technique while Strobel formula is appropriate in children aged 6-24 months. The position of pH sensor shown by chest radiography varies between the 7th and the 9th vertebral body.

*311 MOLECULAR AND GENETIC CHARACTERIZATION OF TASHT, A MOUSE MODEL THAT PHENOCOPIES THE MALE BIAS OF HIRSCHSPRUNG DISEASE

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Hirschsprung disease (HSCR), or aganglionic megacolon, is a congenital disease affecting 1/5000 birth, with a ratio of 4 boys for 1 girl. It is characterized by the absence of enteric nervous system (ENS) along variable length of the distal gut, leading to tonic contraction and lethal accumulation of feces. The ENS is a network of ganglia made up of multiple neuron subtypes and glial cells. The ENS is mainly subdivided into the myenteric plexus, which is responsible for controlling gut motility, and the submucosal plexus, which is notably important for regulating the intestinal barrier function. The ENS is derived from neural crest cells (NCCs) that colonize the prenatal bowel, a process in which Gdnf/Ret and Edn3/Ednrb signaling pathways play a key role. Accordingly, mutations affecting one of these two pathways are the main known genetic causes of HSCR. However, this represents only a minority of HSCR cases and none of these pathways can directly explain the intriguing male bias.

TashT is a mouse model—generated by random transgene insertion—that phenocopies HSCR, including its male bias. Indeed, these mice display aganglionic megacolon with weak penetrance and a 15:1 male to female ratio. Our previous studies showed that TashT NCCs fail to properly colonize the fetal intestines essentially because they migrate too slowly. The transgenic insertion in the TashT genome was revealed to disturb a gene desert that contains highly conserved non-coding sequences possessing silencer activity. Using chromatin conformation capture (3C) assays, we further found that these silencer elements normally interact with Fam162b, an uncharacterized gene located 3.6Mb away. In TashT, this repressive interaction is lost, resulting in the upregulation of Fam162b. However, targeted overexpression of Fam162b in NCCs

failed to fully recapitulate the TashT ENS defect. The TashT model is thus much more complex than we first thought. Accordingly, new preliminary studies using circular chromatin conformation capture (4C) assays point to the existence of multiple intra- and inter-chromosomal interactions between the silencer elements and other distant genes. Moreover, a sex-stratified transcriptomic analysis of TashT NCCs allowed us to identify Ddx3y upregulation as a likely cause of the male bias. In conclusion, with the TashT mouse line in hands, we are uniquely positioned for understanding the male sex bias of HSCR.

312 COMPARISON OF IDIOPATHIC AND PATHOLOGICAL LEAD-POINT IN PEDIATRIC INTUSSUSCEPTION

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Introduction: Intussusception in children is mostly idiopathic and is rarely caused by the pathological lead-point. We examined the possibility of finding the pathological lead-point of intussusception at an early stage.

Objects and Methods: The patients were 41 children with intussusception diagnosed for the first time at Aso Iizuka Hospital between April 2013 and September 2015. We retrospectively compared them with Idiopathic group (I group, 35 cases) and the pathological lead-point group (P group, 6 cases: 4 cases had Meckel's diverticulum, one had intestinal duplication and one had Henoch - Schönlein purpura).

Results: There was no statistically significant difference in age among I group and P group, 2.1 ± 1.4 years and 4.2 ± 3.7 years respectively. In the pressure of pneumatic reduction, P group (112.5 ± 8.3 mmHg) was significantly higher than I group (79.3 ± 26.1 mmHg) ($p = 0.01$).

Conclusion: Pediatric intussusception with the pathological lead-point required over 100 mmHg pneumatic pressure of reduction. It is preferable that the cases requiring high pneumatic pressure at the first reduction were positively evaluated with the organic lesion.

313 GENETIC VARIANTS IN REELIN GENE CONTRIBUTE TO THE RISK OF HIRSCHSPRUNG DISEASE IN THE HAN CHINESE POPULATION

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Background & Aims: Hirschsprung disease (HSCR, OMIM 142623), a congenital defect of the enteric nervous system, is one of the most common genetic causes of neonatal intestinal obstruction. However, only a small fraction of the total genetic risk for HSCR can be attributed to the identified mutations, suggesting the involvement of more genes in HSCR etiology. We performed genetic analyses to determine whether genetic variants in Reelin (RELN) gene is involved in HSCR susceptibility.

Methods: A combination of case-control strategy and MassArray system was applied in 104 HSCR cases (84 male and 20 female) and 151 normal controls (86 male and 65 female) in the Han Chinese population. We employed the iPLEX Gold technology and 8 single nucleotide polymorphisms (SNPs) (rs802788, rs17155888, rs2299374, rs727709, rs6977616, rs12536415, rs56345626 and rs2229864) within RELN to interrogate the effects of RELN gene on HSCR risk.

Results: With respect to the studied genetic markers, the observed genotype distributions showed no significant deviations from Hardy-Weinberg equilibrium in either HSCR or control group ($p > 0.05$). For the 104 HSCR subjects and 151 normal controls, we observed that rs802788, rs6977616 and rs56345626 were significantly associated with HSCR (rs802788, allele, $p = 0.006$, genotype, $p = 0.021$; rs6977616, allele, $p = 0.004$, genotype, $p = 0.008$; rs56345626, allele, $p = 0.008$, genotype, $p = 0.031$). Of note, the A allele and AA genotype of rs802788 were more common in HSCR group compared to control group (A allele, 67.3% versus 55.0%, OR 1.68, 95% CI, 1.16-2.44; AA genotype, 44.6% versus 29.5%), and likewise the T allele and TT genotype of rs6977616 and the G allele and GG genotype of rs56345626 presented strongly higher frequencies in the HSCR subjects than in the controls (rs6977616: T allele, 70.3% versus 57.5%, OR 0.57, 95% CI, 0.39-0.84; TT genotype, 46.5% versus 33.6%; rs56345626: G allele, 35.2% versus 24.2%, OR 0.59, 95% CI, 0.40-0.87; GG genotype, 15.8% versus 6.7%). Haplotype analysis also showed some significant findings, and one eight-SNP-based haplotype was the most significant, giving a global $p < 1.0 \times 10^{-4}$.

Conclusions: Our results for the first time indicate that genetic variants within RELN might contribute to the altered risk of HSCR in Han Chinese, suggesting a possible role of RELN in the pathogenesis of Hirschsprung disease and providing potential molecular markers for early diagnosis of clinical manifestations.

314 FECAL CALPROTECTIN IN CHILDHOOD IRRITABLE BOWEL SYNDROME

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Background: Fecal calprotectin (FC) is a marker of intraluminal intestinal inflammation and especially known to increase in inflammatory bowel disease (IBD). Irritable bowel syndrome (IBS) is the functional gastrointestinal disorder, but it has some similarities of the pathophysiology and clinical manifestation with IBD. The aim of the study was to evaluate the level of fecal calprotectin (FC) in IBS children and the difference between IBS children with each subtype and healthy control (HC).

Methods: 126 children with IBS and 28 healthy controls aged 4-16 years (85 boys, 69 girls, mean age 9.12 years) were included this study. IBS children were diagnosis by the ROME III criteria and classified to three types by clinical manifestation: IBS with constipation (IBS-C, n=39), IBS with diarrhea (IBS-D, n=41) and IBS with mixing constipation and diarrhea (IBS-M, n=46). Stool samples were analyzed for the FC level, using enzyme-linked immunosorbent assay. All of participants filled out a questionnaire regarding several demographic and clinical characteristics.

Results: IBS children had higher level of FC than HC, and the difference was significant (mean 54.95 vs. 17.77 mcg/g, $p = 0.004$). No one had the FC level above a cut-off level (50 mcg/g) in HC, but 32.5% of IBS children (n=41). Among three subtypes of IBS, the level of FC was highest in children with IBS-D (mean 87.59 mcg/g), followed by IBS-M (mean 43.37 mcg/g) and IBS-C (mean 34.30 mcg/g). This difference had a statistical significance compared with each groups ($p < 0.001$). There were no significant difference of gender and age between IBS groups and HC.

Conclusions: FC in IBS children was measured to higher level than HC and had a difference depending on subtype. Our results could support the hypothesis that IBS is a kind of low grade of bowel inflammatory disease and suggested a necessity of follow-up the IBS children who had the high FC level.

315 CORRELATION BETWEEN THE BRISTOL STOOL SCALE AND ROME III PEDIATRIC GASTROINTESTINAL SYMPTOMS SURVEY IN SPANISH IN SCHOOL CHILDREN AND ADOLESCENTS WITH FUNCTIONAL CONSTIPATION IN CALI, COLOMBIA

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Introduction: The Bristol Stool Scale (BSS) is used to identify the stool consistency in adults and older children. The pediatric gastrointestinal symptoms survey Rome III in Spanish involves questions related to stool consistency.

Objective: To determine the correlation as reported for schoolchildren and adolescents with functional constipation (FC) and the pediatric gastrointestinal symptoms survey Rome III in Spanish and the BSS, regarding to the stool consistency.

Methods: Schoolchildren (n=52) and adolescents (n=61) with FC from a public school in Cali, Colombia were asked to complete the pediatric gastrointestinal symptoms survey Rome III in Spanish, and to indicate their stool consistency according to the BSS (type 1 and 2: hard, type 3, 4, and 5: normal and type 6 and 7: liquid). To identify the correlation the R Pearson test was used.

Results: 113 children were analyzed (age 12.9 ± 2.9 years, 50.4% male). The correlation between the pediatric gastrointestinal symptoms survey Rome III in Spanish and the BSS, regarding to their stool consistency was positive and not significant ($R^2 = 0.0178$, $p = 0.2784$).

Conclusion: In this group of schoolchildren and adolescents, the reported stool consistency, besides having a weak correlation was not statistically significant, so in order to identify the stool consistency other types of instruments should be used

316 FUNCTIONAL GASTROINTESTINAL DISORDERS IN ECUADORIAN INFANTS AND TODDLERS AND POSSIBLE FACTOR RISKS

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Introduction: The prevalence of functional gastrointestinal disorders (FGDs) in infants and toddlers in Latin America is unknown. Social, biological, and psychological factors could be potential risk factors (RF).

Objective: To determine the prevalence and possible RF of FGDs in healthy Ecuadorian infants and toddlers from Quito, Ecuador through the FINDERS Questionnaire (Functional Digestive International Epidemiological Research Survey) in Spanish based on the Rome III criteria.

Methods: Prevalence study in 218 infants and toddlers. Family, sociodemographic and clinical variables were obtained. Statistical analysis included estimation of the proportion of children with FGDs and corresponding 95% CI; estimating percentages, percentiles, averages, medians and other descriptive measures with their corresponding standard deviations and ranges; univariate analysis; possible occurrence of association between the variables (ORs and 95% CI); Fisher's exact test with a value of $p < 0.05$, two-tailed, significant and multiple logistic regression analysis.

Results: We acquired data from 218 subjects, with age 17.3 ± 12.8 months, 53.7% male. FGDs' prevalence was 24.3%. 8.7% had functional constipation (FC), 5.5% had rumination, 4.1% had regurgitation, 3.7% infant colic, 1.8% had dyschezia and 0.5% had functional diarrhea. There was a higher chance of FGDs among males. Any possible RF was presented.

Conclusion: One-quarter of healthy Ecuadorian infants and toddlers between 1 and 48 months, present with one of the FGDs, with FC the most common, a predominance of male gender and without any possible risk factor.

NUTRITION & INTESTINAL REHABILITATION

***323 THE ROLE OF MATERNAL VITAMIN D AND IRON STATUS ON DEVELOPMENTAL OUTCOMES AND HEAD CIRCUMFERENCE IN HIV-EXPOSED UNINFECTED INFANTS**

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Some studies suggest that perinatally HIV-exposed uninfected (HEU) infants are at risk for neurodevelopmental delays. Fetal exposure to vitamin D and iron may have positive effects on neurocognition. Few have evaluated the association between the nutrition of HIV+ women in pregnancy and the developmental outcomes of their infants.

We evaluated the association between 3rd trimester maternal intake and serum levels of vitamin D and iron on infant neurodevelopmental outcomes and head circumference z-score (HC-Z) at 1 y of age.

HIV+ pregnant women enrolled in the Pediatric HIV/AIDS Cohort Study were recruited in the 2nd/3rd trimester for this sub-study. Third trimester diet and supplement intake were obtained using 3, 24-hour diet recalls over 2 weeks. Micro- and macronutrient intake were calculated. Maternal serum 25(OH)D and iron were measured near the time of diet recall. Maternal demographic and clinical variables were abstracted from the medical record. At the 1-year visit (range 9-15 months), HC-Z was calculated. Neurodevelopmental outcomes were assessed with the Bayley Scales of Infant Development-III. Dietary factors were categorized into quartiles, with the lowest quartile as reference. Linear regression models were fit to evaluate the association of dietary factors with HC-Z and 5 Bayley outcome scores (cognitive, motor, language, social-emotional, adaptive (composite score means 100; sd 15), unadjusted and adjusted for potential confounders: SES, maternal substance use, clinical site, maternal IQ, season, CRP, and HIV viral load.

193 mother-infant dyads were analyzed. Mean maternal age was 29 yrs (SD 6.07); 76% were black and 87% had viral load <400 copies/mL. Vitamin D and iron intake was below RDA in 56% and 12% of women, respectively. Median 25(OH)D and iron serum values were 34 ng/mL [IQR 24, 42] and 59 ug/dL [IQR 49, 84], respectively. Mean birth weight Z-score was -0.23 (SD 0.99) (adjusted for prematurity) and 18% were preterm. At 1 y, the median for each outcome was: HC-Z 0.40; Cognitive 105; Motor 97; Language 94; Social-Emotional 100; Adaptive 93. The average adjusted difference in HC-Z between the highest versus the lowest quartile of nutrient was 0.55 (95% CI, 0.02, 1.08, $p = 0.04$) for serum iron, 0.57 (95% CI, -0.06, 1.19, $p = 0.077$) for iron intake, and 0.61 (95% CI, 0.08, 1.13, $p = 0.024$) for vitamin D intake, but no association of serum 25(OH)D with HC-Z. The average adjusted difference in social-emotional score between the highest and 3rd versus lowest quartile of vitamin D intake were 5.51 (-2.65, 13.67, $p = 0.18$) and 8.44 (95% CI, 0.41, 16.48, $p = 0.040$), respectively.

Higher dietary intake of vitamin D and iron and serum levels of iron were associated with larger HC in HEU infants. These nutrients were generally not associated with developmental outcomes (Bayley scores). Since 1-year Bayley scores are not very stable except at lowest ranges, future studies should continue to examine these relationships in later childhood.

324 ENTERAL BILE ACID TREATMENT PRESERVES GUT MICROBIAL DIVERSITY AND REGULATES HEPATOBILIARY TRANSPORTERS IN ANIMALS ON PARENTERAL NUTRITION

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Background: Parenteral nutrition (PN) is a life-saving therapy; however, its benefits come at the cost of significant gut atrophy and cholestasis. While bile acids (BA) can modulate intestinal growth via gut receptors, the gut microbiome also likely influences gut proliferation and inflammation. BAs also regulate the key hepatobiliary transporter, Bile Salt Export Pump (BSEP) involved in cholestasis. We hypothesized that the BA receptor agonist oleanolic acid (OA) regulates the gut TGR5 receptor, and modulates the gut microbiota contributing to improved PN associated injury.

Methods: Neonatal piglets were randomized to approximately two weeks of isocaloric enteral nutrition (EN), PN, or PN + enteral OA treatment. Stool, serum, gut and liver samples were obtained. 16S rRNA sequencing was utilized for culture independent bacterial identification.

Results: PN resulted in marked gut atrophy which was prevented by OA treatment. The mean v/c ratio (\pm SD) was EN 3.28 ± 0.50 ; PN 1.88 ± 0.38 and OA 2.77 ± 0.59 ($p < 0.05$: EN vs. PN, OA vs. PN). OA upregulated gut TGR5 and hepatic BSEP however there was no statistically significant improvement in serum bilirubin with OA ($p = 0.08$). The mean microbial alpha diversity was significantly different between the groups at 0.6403, 0.1351 and 1.077 for EN, PN and OA respectively ($p < 0.05$) as assessed using the Shannon Diversity index. In addition to a decreased microbial diversity, a shift towards the proinflammatory phylum *Bacteroidetes* was seen with PN with no EN or OA differences.

Conclusions: OA improves PN associated gut injury. There is significant expansion of *Bacterioides* and decreased microbial diversity with PN, both prevented by OA treatment. This study provides a novel relationship between PN associated dysfunction, BA treatment and gut microbial changes.

325 EVOLUTION OF OVERWEIGHT AND OBESITY BY BMI ACCORDING TO WHO CLASSIFICATION IN CHILDREN AND ADOLESCENTS OF QUITO, ECUADOR DURING THE CONSECUTIVE YEARS 2012-2014

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Introduction: The prevalence of overweight (OW) and obesity (OB) in children has been increasing worldwide.

Objective: To determine the annual behaviour of OW and OB by BMI according to WHO classification in Ecuadorian children during the years 2012-2014.

Methods: Comparative prevalence study in children who regularly attend at the Care Unit and healthy schoolchildren and adolescent in Quito, Ecuador. We obtained sociodemographic and clinical variables. According to WHO classification, the anthropometric nutritional status by BMI was classified OB ($> +2$ standard deviations), OW (+1 and +2 SD), undernutrition (-2 and -3 SD), severe undernutrition (> -3 SD) and eutrophic (-2 and +1 SD). Statistical analyses included univariate and chi square tests, with a significance at $p < 0.05$.

Results: 626 children and adolescents were included in 2012, 260 in 2013, 362 in 2014 and 128 in 2015; the mean (SD) age was 14.7 (1.7) years, 55.0% was male, the mean weight was 49.8 ± 10.4 kg and mean height was 154.9 ± 9.5 cm. Malnutrition was presented in 29.4% (2012), 20.8% (2013), 24.3% (2014) and 26.6% (2015) ($p > 0.05$); corresponding to 22.5% the OW and OB (2012), 19.6% (2013), 23.8% (2014) and 25.0% (2015) ($p > 0.05$); statistical significance was found during the years 2013 to 2014 for the OW ($p = 0.048$). There was a predominance for malnutrition in females (OR 2.32; 95% CI, 1.57-3.44; $p = 0.0000$) and schoolchildren (OR 2.21; 95% CI, 1.24-3.88; $p = 0.0028$).

Conclusion: In this group of children and adolescents of Quito, Ecuador a high prevalence of OW and OB between 19.6% and 25.0% occurred during follow-up years, with a higher prevalence in females and in schoolchildren

326 BILE ACID COMPOSITION IN A NEONATAL PIGLET MODEL OF PARENTERAL NUTRITION ASSOCIATED LIVER DISEASE

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Background: Parenteral Nutrition Associated Liver Disease (PNALD) remains a leading cause of morbidity and mortality for neonates with intestinal failure. Use of fish oil containing parenteral lipid appears to prevent and treat PNALD. However, both the mechanisms for PNALD and how fish oil improves PNALD are poorly understood. The aim of this study was to investigate bile acid composition in neonatal piglets given PN - with and without fish oil - and to determine how this relates to PNALD.

Methods: Neonatal piglets (3 to 6 days old) underwent jugular venous catheter insertion, followed by 14 days of iso-caloric, iso-nitrogenous PN, with either Intralipid® (Fresenius Kabi) (IL, n=8), or fish oil containing SMOFLipid® (Fresenius Kabi) (SMOF, n=10). After 14 days, a terminal laparotomy was performed, the common bile duct cannulated, bile flow measured and bile collected. The composition of bile acids in the bile was then determined using liquid chromatography coupled to tandem mass spectrometry (LC/MS/MS). Comparison between PN groups used Student's t-tests. Normal ranges for all data was provided from sow-fed piglets studied at 16-22 days old (Ref, n=16). Linear regression modelling was undertaken to determine predictors of bile flow.

Results: There was a significant difference in bile flow between IL and SMOF (6.4 vs. 13.6; $p = 0.011$; Ref 6.5-14.4 μ g g⁻¹ liver-1 10 min⁻¹). Total bile acids (806 vs. 1408; $p = 0.04$; Ref: 1826-6892 μ g mL⁻¹) and secondary bile acids (628 vs. 1199; $p = 0.03$; Ref 589-5655 μ g mL⁻¹) were significantly different between the PN groups, greater with fish oil. Primary bile acids (8 vs. 14; $p = 0.36$; Ref: 11-53 μ g mL⁻¹) were similar between PN groups. Compared to Ref, PN led to a marked reduction in total, primary and secondary bile acids. Primary bile acids and treatment group (IL vs. SMOF) independently predicted 60% of the variance in bile flow ($p = 0.001$).

Conclusions: These findings reaffirm the physiological principal that primary bile acids are the major determinants of bile flow. The main difference in bile composition with PN is a decrease in total bile acids, both primary and secondary. The main difference with fish oil containing

lipid is a decrease in secondary bile acids. Therefore, the mechanism for improving bile flow with fish oil may not directly relate to altering bile composition. As secondary bile acids are formed under the action of luminal bacteria the role of dysbiosis should be further explored.

***327 MULTILEVEL DETERMINANTS OF POSITIVE OUTLIER STATUS IN A CHILDHOOD OBESITY INTERVENTION**

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Background: Many clinically-based RCTs to reduce a child's BMI have had limited success. One approach to optimizing interventions could be to examine characteristics and behavioral changes of children considered to be positive outliers in RCTs, e.g., those who succeed in reducing their BMI to below the 95th percentile or decreasing their BMI z-score by ≥ 0.5 units during an intervention.

Objectives: To examine multilevel characteristics and behavior change strategies associated with children being positive outliers in a childhood obesity RCT over a 1-year intervention period.

Design/Methods: We examined changes at 1 year for 340 children, ages 6-12 years, who were randomized to the intervention arm of the STAR cluster-RCT. At baseline, eligible children had a BMI \geq 95th percentile. Using logistic regression, we examined the independent effects of child (age, sex, race/ethnicity, and baseline severe obesity) and parent/household characteristics (age, education, annual household income, BMI, US born status, and language spoken at home) on child's positive outlier status during the 1-year intervention. We also examined parental and child behavior changes (i.e., SSB, fruit and vegetable intake, screen time, sleep, physical activity) that predicted positive outlier status.

Results: At baseline mean (SD) child age was 9.8 years (1.9 SD) and mean (SD) BMI Z-score at baseline was 2.0 (0.29). At 1-year, 65 children (27%) in the intervention met the definition for a positive outlier; 61 (94%) of the 65 had reduced their BMI to $<$ 95th percentile and 19 (29%) had reduced their BMI Z-score by ≥ 0.5 units. In multivariable analyses, children with severe obesity had lower odds of being a positive outlier (OR: 0.25 [95% CI, 0.09, 0.66]). Children who increased their sleep duration during the intervention had a higher odds of being a positive outlier (OR: 1.84 per 1-hour increase in sleep; 95% CI, 1.13, 3.01). We observed a trend towards Black or Hispanic children (OR: 0.52, 95% CI, [0.23, 1.18]) having lower odds of being a positive outlier vs. white children. Children of parents who were born outside of the US and those who increased their fresh fruit and vegetable intake had higher odds of being positive outliers but confidence limits spanned 1 and we lacked power to detect statistical significance.

Conclusions: The odds of being a positive outlier in a childhood obesity RCT was lower among those with severe obesity at baseline and higher among those who improved their sleep behaviors over time. Solutions learned from such positive outliers could be generalized and promoted to optimize interventions for other children with obesity.

***328 THE EFFECTS OF VITAMIN D ON CORTICAL APOPTOSIS AND SYNAPTIC DENSITY**

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Introduction: Vitamin D insufficiency is a global problem with severe deficiency most common in the Middle East and South Asia. Recently, vitamin D deficiency has been correlated with an increased risk and or progression of neurodevelopmental disorders including attention deficit hyperactivity disorder, autism spectrum disorders and schizophrenia. Previous research suggests vitamin D acts as a neuroprotectant. In the ketamine-induced injury model, vitamin D administration 24 hours prior to ketamine exposure in neonatal rats successfully reduced ketamine-dependent apoptosis in somatosensory cortical cells. Additional data indicates somatosensory neurons exposed to vitamin D display increased presence of Activity-Dependent Neuroprotective Protein (ADNP). Together, these studies suggest vitamin D plays a neuroprotective role through increased expression of ADNP. The aims of the current study were to determine if varying vitamin D concentrations have an effect on apoptosis in cortical neurons and also to determine if vitamin D influences cortical synaptic protein density.

Methods: Cortical neurons extracted from pre-natal rats were exposed to 500 nM, 5 μ M or 10 μ M concentrations of vitamin D for 2 hours on 3, 7, and 14 days post cortical neuron extraction and compared to control group cortical neurons (standard growth media without vitamin D exposure). Immunofluorescent staining (DAPI, PSD 95, Synapsin-1, and SNAP 25) was performed used to visualize nuclei and synaptic proteins within cell cultures. Non-biased stereologic cell count was performed using a Microbright Field Microscope with cell counts verified by an independent reviewer.

Results: No significant difference in nuclei counts between controls and each vitamin D treatment group was noted on 3, 7, and 14 days *in vitro*. Cortical cell culture numbers were not significantly different between study groups. Vitamin D treated cortical neurons (10 μ M) had significantly fewer apoptotic nuclei at each of the treatment days compared to controls (p 0.04). This same vitamin D concentration resulted in significantly increased PSD 95 staining, indicating increased post synaptic receptor density following exposure (p 0.01). Control cell cultures had progressive decreases in SNAP 25, a pre-synaptic protein, staining over time while vitamin D exposed neuron cultures progressively increased this cortical synaptic protein expression, although statistical significance was not reached.

Conclusions: The current study shows that all concentrations of vitamin D used protected against cortical apoptosis *in vitro*. Vitamin D was also shown to have possible protective presynaptic (SNAP 25) and postsynaptic (PSD 95) effects on cortical neuron protein density. This may provide greater insight into the pathophysiologic role of vitamin D in protection against neurodevelopmental disorders.

329 EXOCRINE PANCREATIC STATUS EFFECTS OUTCOMES FOLLOWING 3-MONTH IVACAFTOR THERAPY IN SUBJECTS WITH CYSTIC FIBROSIS GATING MUTATIONS

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Background: Ivacaftor is approved for use in patients with cystic fibrosis (CF) who have gating mutations. Prior studies have demonstrated improved weight gain, pulmonary function, and decreased sweat chloride concentration in subjects with CF following drug use. The effect of Ivacaftor in patients with pancreatic sufficiency (PS) compared to pancreatic insufficiency (PI) has not been explored.

Objectives: To determine if pancreatic status effects the response to 3 months of Ivacaftor treatment in subjects with CF and gating mutations.

Methods: Subjects with one or more CFTR gating mutations who were 5 years of age or greater were recruited from Italy, Canada, and the United States. Pancreatic status was determined by medical history. Outcomes were measured at baseline and after three months of Ivacaftor treatment. Height, weight, and BMI were measured. Spirometry was used to assess forced expiratory volume at one second percent predicted (FEV1 %). Fat mass (FM), fat free mass (FFM), and percent body fat (% fat) were determined by whole body dual x-ray absorptiometry (DXA). Resting energy expenditure (REE) was determined by indirect calorimetry and expressed as a percent predicted (Schofield equation, REE%). Fecal elastase ($\mu\text{g/g}$ stool) was used to measure pancreatic exocrine function and fecal calprotectin ($\mu\text{g/g}$ stool) was used to evaluate gut inflammation.

Results: 23 subjects completed the study ($17 \pm 13\text{y}$, 61% female). 17 subjects had PI ($15 \pm 9.9\text{y}$, 53% female) and 6 subjects had PS ($23.8 \pm 18.8\text{y}$, 83% female). Subjects had 19 different genotypes and 8 different gating mutations. At baseline, subjects with PS had a greater weight, BMI, FM, and FFM and a lower REE% than subjects with PI (Table 1). Subjects with PI had a significant decrease in calprotectin and significant improvement in FEV1, weight, height, BMI, FM, and FFM. Changes in outcome measures in subjects with PS were of a smaller magnitude. Fecal elastase was higher at baseline in PS and 4 out of 6 subjects had an increase following Ivacaftor that ranged from 52 to 390 $\mu\text{g/g}$ stool.

Conclusions: 3 months of Ivacaftor treatment in subjects with CF and gating mutations resulted in improved pulmonary function, measures of growth and fat stores, and reduced REE and gut inflammation. Subjects with PI demonstrated significant improvements in pulmonary function, growth and fat stores, and gut inflammation compared to minimal changes noted in the group with PS. Further studies are needed, but this suggests that Ivacaftor may be more effective in subjects with gating mutations who are pancreatic insufficient.

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	FEV1, % predicted	Weight, kg	Height, cm	BMI, kg/m ²	FM, kg	FFM, kg	REE %	Fecal Elastase, $\mu\text{g/g}$ stool	Calprotectin, $\mu\text{g/g}$ stool
PI Baseline	82.6	39.9	145.6	18	12.1	28	99.4	39	94
PI Change	11.4 **	3.0***	1.7***	0.9***	1.9***	1.2*	-6.0†	3	-37.4**
PS Baseline	93.7	56.1	160.7	21.4	19.1	37.3	82.9	248	34
PS Change	4	0.9	0.7	0.2	0.8	-0.2	-3.7	136	-11.7

*330 MICROBIOTA AND CORRELATIONS WITH HMO CONTENT IN BREAST MILK FROM CHINESE LACTATING MOTHERS

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The microbiota of breast milk from Chinese lactating mothers at different stages of lactation was examined in the framework of a Maternal Infant Nutrition Growth (MING) study investigating the dietary habits and breast milk composition in Chinese urban mothers. We used microbiota profiling based on the sequencing of fragments of 16S rRNA gene and specific qPCR for *bifidobacteria*, *lactobacilli* and total bacteria to study microbiota of the entire breast milk collected using standard protocol without aseptic cleansing (n 60), and the microbiota of the milk collected aseptically (n=30). We have also investigated the impact of the delivery mode and the stage of lactation on the microbiota composition. Ten human milk oligosaccharides (HMO) were quantified in the samples using a validated protocol in which the HMO were derivatized with a fluorescent tag then analyzed by liquid chromatography with fluorescence detection. In 80% of samples 2'-fucosyllactose (2'FL) was the most abundant HMO (present at levels between 1040 – 4430 mg/kg), the remaining 20% had 2'FL levels below 53 mg/kg. When 2'FL levels were below 53mg/kg the predominant HMO was either 3-fucosyllactose (3FL) or lacto-N-tetraose (LNT). 6'-Sialyllactose (6'SL) was present in higher quantities than 3'-sialyllactose in 88% of the samples, and in all samples but one, LNT predominated over lacto-N-neotetraose (LNnT). The microbiota of breast milk was dominated by *streptococci* and *staphylococci* for both collection protocols and, in the case of standard collection protocol, *Acinetobacter sp.* While the predominance of *streptococci* and *staphylococci* was consistently reported previously for other populations, the abundance of *Acinetobacter sp.* was reported only once before in a study where milk collection was done without aseptic cleansing of the breast and rejection of foremilk. Higher bacterial counts were found in the milk collected using standard protocol. *Bifidobacteria* and *lactobacilli* were present in few samples with low abundance. We observed no effect of the stage of lactation or the delivery mode on microbiota composition. We have observed negative correlations of LNnT, 6'-SL, Lacto-N-fucosylpentaose-I and sum of 10 HMOs with one of *Acinetobacter sp.* OTUs, but no association of the abundance of *Staphylococcus sp.* with any of the HMOs.

In conclusion, our study further substantiates the presence of bacteria in human milk, with a significantly higher number of bacteria identified in the "breastfeeding-associated microbiota" compared to milk obtained under aseptic conditions. We also confirmed the presence of the dominant species such as *streptococci*, *staphylococci*, as well as the low abundance of *bifidobacteria* and *lactobacilli*. The association of microbiota with other human milk components, notably HMOs, deserve further research.

331 HOME PARENTERAL NUTRITION IN FRANCE: A NATIONAL SURVEY

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Whatever the cause of chronic intestinal failure (CIF), long-term parenteral nutrition (PN) and home-PN (HPN) are the mainstay therapies. In France, according to the national health system, only 7 centers are certified as Pediatric Home-PN Expert Center (PHPN-EC). All patients requiring HPN must be referred to one of them to be supported by e French Social Security. The aim of this study was to review the HPN activity of the 7 French PHPN-EC from a national data base.

Population and Methods: The survey was conducted from January 1 to December 31, 2014. Data included: patients characteristics, indications for HPN, duration of HPN, patients turn-over, incidence and cause of PN weaning, complications: catheter-related blood stream infections (CRBSIs), cholestatic liver disease (CLD) defined as bilirubin >20 mol/l.

Results: a total of 268 patients < 18 years of age (56.9 % boys) were followed-up in a HPN program (17.5 patients per million < 18 years) with 54 new patients enrolled in 2014 (20.1 % of the cohort). Mean number of patients per center was 38 ± 33 (range 16-108). Age was 80.6 ± 25.8 months (4 months-18 years). Primary digestive disease (PDD) involved 257 children (98%). According to the different PHPN-EC, major indications for HPN were short bowel syndrome (SBS): 40.8 ± 7.3 % (31-50) - congenital enteropathies: 21.9 ± 8.5 % (5.5-31) - chronic intestinal pseudo-obstruction: 15.7 ± 8.9 % (4-31) – Total aganglionosis: 8.3 ± 6.8 % (0-24) and inflammatory bowel disease: 4.3 ± 4.2 % (0-12.5). Vascular access was a Broviac type central venous catheter in 98% of patients. All of them received tailored PN bags made by the hospital pharmacy (27%) or by Fasonut-Baxter® (73%). Intravenous lipid emulsions used were SMOFlipid® in 62.3 ± 42.8 % (0-100) or MCT/LCT. On December 31, 2014, 31 patients had left the HPN program after a duration of 3 months to 18 years (med 6.5 years) because of weaning (84.5 %)-, [SBS representing 90% of weaned patients], adult transfert: 10.5% or death: 5% (96% with non PDD; eg: cancer or immune deficiency).The major complication of HPN was catheter-related blood stream infections (CRBSIs), 0.94 ± 0.22 per 1000 days of PN (range: 0.7-1.37). Staphylococcus coagulase negative represented 75 ± 18 % of CRBSIs (range (50-100) and Staphylococcus aureus 12.0 ± 11.5 % (range 15-25) (no fungal infection). Only 38.4 ± 19.7 % (range 25-73) patients of the cohort received taurilidone locks. Twenty patients (7.5%) had total bilirubin >20 & molmol/l and 5 (2%) >50 mol/l, including 2 cirrhosis, listed for liver-intestine transplantation.

Conclusions: In this setting, HPN is a safe and efficient therapy. SBS is the main HPN indication, with the highest rate of PN weaning. CRBSIs and CLD are potentially life-threatening. Nevertheless, their rates were low and deaths (5%) were mostly due to the underlying disease. Patients must be referred early to expert centers (PHPN-EC) for optimal management and follow-up.

332 EVALUATION OF MALNUTRITION DEVELOPMENT RISK IN HOSPITALIZED CHILDREN IN TURKEY

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Introduction: Various screening methods are developed to prevent malnutrition and its overlook for pediatric patients, such as the Screening Tool for Risk On Nutritional status and Growth (STRONGkids) and the Pediatric Yorkhill Malnutrition Score (PYMS). We aimed to explore the prevalence of risk of malnutrition in hospitalized children, identify symptoms and contributing factors and also to examine the efficacy of malnutrition screening tools for hospitalized children in Turkey.

Methods: Between March and July 2015, STRONGkids and PYMS were applied to 1513 inpatients in 26 centers by 51 researchers. Newborns, emergency room or intensive care patients, patients who received appetite stimulant drugs or enteral nutrition treatment during last 3 months were excluded from the study. Physical measurements were performed during admission, day 3, day 7 and at discharge and Z-scores for length/height-for-age, weight-for-age, weight-for-length/height, body mass index-for-age were calculated using Anthro software developed by the World Health Organization. Sensitivity and specificity was calculated using results from screening tools divided into low and moderate-high risk of malnutrition.

Results: Mean age of the patients was 52.7 months and female/male ratio was 1:1.4. Most of the patients (91.4%) were hospitalized for ≥ 3 days and 47.5% of the patients had an underlying chronic disease. Height-for-weight Z-score was < -3 in 5.2% and < -2 in 11.2% of the patients in whom acute malnutrition was developed. STRONGkids and PYMS scores of these patients at baseline were significantly higher than other cases ($p=0.015$ and 0.024 , respectively). Development of acute malnutrition was correlated with longer hospitalization (> 3 days; $p=0.021$) and having a chronic underlying disease ($p<0.001$). Weight-for-age Z-scores reduced significantly in the group of patients who had high STRONGkids and PYMS scores at admission ($p=0.001$ and <0.001 , respectively). An underlying chronic disease was detected in 72.4% of the patients who had decreasing weight-for-age Z-scores. A negative correlation was observed between duration of hospitalization and weight-for-age Z-score ($p=0.001$). Most of the patients were short in height and height-for-age Z-score was < -3 in 8.7% and < -2 in 16.6% of the patients. These results were found significantly higher when compared to general characteristics of Turkish population (9.5%) in terms of height and stunting. Stunted patients with chronic malnutrition had higher STRONGkids and PYMS scores at admission and at discharge ($p=0.03$). Specificity of STRONGkids and PYMS tests were calculated as 93.0% and 96.9%, respectively and sensitivity was detected as 72.2% and 89.4%, respectively (Table 1).

Conclusion: STRONGkids and PYMS tests are widely used to detect risk of malnutrition and they are found highly specific and sensitive in our study. Application of these tests to each hospitalized child may reveal the risk of malnutrition and help in reducing morbidity and mortality.

Table 1. Weight-for-height Z-scores at baseline and STRONGkids/PYMS specificity and sensitivity results

Weight-for-height		STRONGkids		PYMS	
		Low risk	Moderate-high risk	Low risk	Moderate-high risk
<-2	n	25	65	5	42
	Percentage (row)	27,8%	72.2%*	10,6%	89.4%*
	Percentage (column)	7,0%	14,5%	3,1%	13,8%
>=-2	n	332	383	157	263
	Percentage (row)	46,4%	53,6%	37,4%	62,6%
	Percentage (column)	93.0%*	85,5%	96.9%*	86,2%
Total	n	357	448	162	305
	Percentage (row)	44,3%	55,7%	34,7%	65,3%
	Percentage (column)	100,0%	100,0%	100,0%	100,0%

* Mc Nemar test $p<0.001$

333 THE IMPACT OF GASTRO-ESOPHAGEAL REFLUX ON AROUSALS AND BRADYCARDIA IN INFANTS.

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Background: "Physiological" gastroesophageal reflux (GER) is a very common phenomenon in children and the dysfunction of this system is often suspected to be the cause of apparent life threatening events. These events occur more often during sleep. Arousals permit the protection of the infant by raising transiently the vigilance after a potentially threatening event such as gastroesophageal reflux. The link between arousals, the characteristics of the reflux (pH, time, height) and bradycardia in the infant has never been considered.

Methods: Seventeen neonates ranging from 30.3 ± 25 day-old, with suspected GER disease were studied. Two tests were performed simultaneously: a polysomnography and a Multichannel Intraluminal Impedance-pH monitoring (MII-pH) between January 2012 and January 2013.

Results: 30.2% of arousals were followed by GER. No significant association was found between the arousals and the characteristics of reflux or the sleep stage.

Bradycardia occurred more often in patients having a reflux detected by impedance (28.6%, $p < 0.05$) than reflux only detected by pH monitoring (8.6%). The occurrence of the bradycardia was different by the level of the height of the reflux (Z6 in 0%, 38% in Z5, 22.6% in Z4; $p < 0.05$).

Conclusions: Our results highlight the importance of considering the interaction between GER and sleep in the neonates. The fact that GER occurs more often in Rapid Eye Movement Sleep (REMS), raises the question of the potential harmfulness of gastric reflux during sleep, which remains a fragile period especially for GER weakly acid with important bolus. These results pave the way for multicenter prospective studies to identify the subpopulation of infant at risk of the apparent life threatening events and may benefit from MII-pH to detect pathogenic GER.

*334 LONGITUDINAL BONE MINERALIZATION ASSESSMENT BY DUAL ENERGY X-RAY ABSORPTIOMETRY IN CHILDREN WITH LONG TERM PARENTERAL NUTRITION FOR SEVERE INTESTINALE FAILURE

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Introduction: Intestinal failure (IF) is defined by dependence on long-term home parenteral nutrition (HPN). Metabolic bone disease is common in children receiving parenteral nutrition. Few pediatric studies have looked at the long-term evolution of bone mass in children with severe IF. The aims of our study were 1) to determine the prevalence of low bone mass (LBM) in a cohort of children receiving HPN for severe IF, 2) to evaluate the evolution of total bone mineral content (TBMC) during HPN with dual-energy x-ray absorptiometry (DXA); and 3) to identify related factors in TBMC changes.

Methods: All children referred in our HPN expert center from November 1, 2004 to January 1, 2014 were eligible. Inclusion criteria were HPN dependence due to non-inflammatory severe IF, at least 2 DXA assessments of TBMC, and a HPN duration of at least 2 years at last assessment. Longitudinal TBMC follow-up was expressed in Z-score for ideal weight for height (WFH). Longitudinal mixed effects models were used to analyze change in TBMC over time.

Results: 31 were included in the study. A total of 175 TBMC measurements were performed with 2 to 11 measurements per child (5.6 ± 2.9). At the first DXA assessment, 14 children (45%) had a TBMC WFH Z-score ≤ -2 SD. Children with chronic intestinal pseudo-obstruction (CIPO) and congenital enteropathy had LBM ($p = 0.023$) more frequently. The median time between first and last DXA recorded was 6.2 years (0.7;16.6). According to longitudinal follow-up TBMC WFH increased $+0.1 \pm 0.04$ Z-score per year of HPN ($p = 0.012$). Moreover the risk of a TBMC Z-score ≤ -2 SD decreased significantly with the duration of HPN (OR 0.9 per year of HPN; CI, 95%: 0.92 to 0.99, $p = 0.018$). The change of TBMC Z-score values for ideal WFH was positively correlated with the LM Z-score for ideal WFH ($p = 0.034$) and calcium HPN content ($p = 0.002$) whereas it was negatively correlated with the number of days of HPN per week ($p = 0.003$).

Conclusion: LBM is common in children with severe IF; however, we have shown that bone status could be improved with long-term HPN in those same children.

335 COW'S MILK ELIMINATION FOR TREATMENT OF EOSINOPHILIC ESOPHAGITIS: A PROSPECTIVE PEDIATRIC STUDY

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Background and Objectives: Eosinophilic esophagitis (EoE) is a chronic immune-mediated disorder of the esophagus mediated by food antigen(s). Empiric six food elimination diet (SFED) is effective and recommended as first-line therapy for treatment in children and adults. However, multiple food exclusion simultaneously is difficult and not practical for families. Eliminating a single food is an attractive option if it can lead to disease remission. Cow's milk was the most common food trigger identified in children treated with elimination diet. The objective for this prospective study is to assess the efficacy of exclusive single food milk elimination (ME) diet in inducing remission in children with EoE.

Methods: Children meeting the consensus guidelines for diagnosis of EoE were enrolled in this study and prospectively eliminated cow's milk from their diet temporarily. After 6-8 weeks of ME they underwent upper endoscopy with biopsies to establish histologic remission. Histologic remission was defined as esophageal peak eosinophil count < 15 eosinophils per high power field (eos/hpf).

Results: Thirty children (73% male, 8 years, 83% white, 73% atopic) were recruited for treatment with ME. Slow eating (37%), dysphagia (37%), vomiting (33%), and food impaction (33%) were the most common presenting symptoms. Histologic remission was demonstrated in 13 (43%) children with decrease in esophageal eosinophil count from 51 ± 31 eos/hpf to 5 ± 4 eos/hpf ($p < 0.0002$) post treatment. Exudates improved in 75% ($p < 0.002$), furrows in 45% ($p < 0.009$), and edema in 44%, ($p < 0.03$). One or more symptoms resolved in 58% of responders.

Conclusions: Empiric single food elimination of cow's milk is effective in children with EoE and induces clinical and histological remission.

The overall efficacy is lower than with SFED. ME diet is a viable option for children interested in diet elimination but find exclusion of multiple foods too restrictive and impractical.

336 THE STUDY OF NUTRIENT INTAKE FROM ENTERAL AND PARENTERAL NUTRITION AMONG PRETERM INFANTS IN SHANGHAI
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Objective: To understand the nutrient intake from enteral and parenteral nutrition support in preterm infants of every birth weight in Shanghai. We also compared intake with recommendation in order to provide the theoretical basis for improving nutritional support in premature infants.

Method: We retrospectively reviewed the clinical records of premature infants whose gestational age was < 37 weeks and who stayed in the hospital for more than 3 days from October 2012 to September 2015 in the neonatal intensive care unit in Xinhua hospital affiliated with Shanghai Jiao Tong University. For each case, we recorded the data in the perinatal period; the intake from both enteral and parenteral nutrition including energy, fat, protein, vitamin A, vitamin D, calcium and iron in week 1, week 2, week 3 and week 4 after birth. We also recorded the weight when discharged from hospital.

Outcome: According to exclusion criteria, such as non-Han nationality, incomplete medical records, death, operation on digestive tract, macrosomia, endocrine genetic metabolic diseases, selected for other clinical trials etc., 773 infants were selected from 960 preterm infants. Most of the energy, primary nutrients, some vitamins and trace elements from enteral and parenteral nutrition support were below the recommended daily amount. This can be seen in detail in Table 1. According to a 2013 Fenton curve, the incidence rate of EUGR at discharge is 47.5%.

Conclusion: Most of nutrients didn't reach the recommendation among preterm infants. In early life of preterm infants, neonatologists need to pay attention to not only intake of enough energy and primary nutrients, but also increasing the provision of vitamins and trace elements.

Key Words: preterm infant; enteral nutrition; parenteral nutrition; recommendation; intake

Table 1 Ratio of intake and Recommendation

	Age	NBW			LBW			VLBW			ELBW		
		EN%	PN%	PN%+EN%	EN%	PN%	PN%+EN%	EN%	PN%	PN%+EN%	EN%	PN%	PN%+EN%
N		130			541			91			11		
E	1w	42	45	87	32	8	40	6.5	76	82.5	0.3	74	74.3
	2w	82	0	82	58	39	97	30	61	91	13	87	100
	3w	88	0	88	69	0	69	46	43	89	29	69	98
	4w	100	0	100	82	0	82	60	31	91	56	59	115
Fat	1w	45	60	105	10	85	95	6.7	95	101.7	0	100	100
	2w	87	0	87	60	55	115	30	85	115	10	100	110
	3w	95	0	95	75	30	105	50	60	110	30	100	130
	4w	107	0	107	87	0	87	63	0	63	57	65	122
Pro	1w	37	45	82	29	59	88	5.7	75	80.7	0	72	72
	2w	72	0	72	53	37	90	27	59	86	8	75	83
	3w	80	0	80	67	19	86	45	40	85	27	61	88
	4w	93	0	93	77	0	77	56	32	88	53	51	104
VA	1w	7	39	46	5	39	44	0.9	40	40.9	0	45	45
	2w	12	0	12	8	36	44	4	34	38	1	43	44
	3w	24	0	24	12	0.2	12.2	7	24	31	4	39	43
	4w	22	0	22	12	0	12	11	28	39	7	27	34
VD	1w	27	71	98	13	71	84	2	71	73	0	71	71
	2w	44	0	44	27	57	84	4	57	61	1	71	72
	3w	50	0	50	35	14	49	12	57	69	3	71	74
	4w	137	0	137	41	0	41	28	43	71	16	57	73
Ca	1w	43	0	43	34	28	62	4.6	45	49.6	0	42	42
	2w	87	0	87	74	0	74	22	24	46	8	45	53
	3w	122	0	122	101	0	101	42	0	42	21	34	55
	4w	144	0	144	123	0	123	97	0	97	81	0	81
Fe	1w	40	-	40	30	-	30	5	-	5	0	-	0
	2w	90	-	90	70	-	70	20	-	20	5	-	5
	3w	110	-	110	90	-	90	35	-	35	20	-	20
	4w	130	-	130	105	-	105	85	-	85	75	-	75

"NBW: normal birth weight; LBW: low birth weight; VLBW: very low birth weight; ELBW: extremely low birth weight; EN%: ratio of intake and recommendation from enteral nutrition; PN%: ratio of intake and recommendation from parenteral nutrition; N: number of people; E: energy; Fat: Fat; Pro: protein; VA: vitamin A; VD: vitamin D; Ca: calcium; Fe: iron.

The numbers in red are higher than the recommendation.

337 HYPERTENSION IN OBESE AND OVERWEIGHT CHILDREN AND ADOLESCENTS IN TWO SCHOOLS IN BOGOTÁ

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Introduction: The global epidemic of obesity has been linked to an increased prevalence of hypertension in children.

Objective: To determine the frequency of hypertension in obese children and adolescents in Bogotá and to establish the association between hypertension and excess weight.

Methods: We invited 1190 students, 8 to 18 years old, in two schools in Bogotá to participate in a cross-sectional study. A total of 270 children had signed parental consent and were enrolled. Information on age, weight, height and blood pressure (average of 3 sequential measurements) was obtained; participants were classified according to body mass index (BMI). Data were analyzed in relation to the presence of hypertension as defined by percentile curves (NHLBI). The Research Committee of the Department of Pediatrics approved the protocol.

Results: The frequency of obesity was 5.9%, found predominantly in females. The prevalence of hypertension and prehypertension was 25.2 and 11.9 %, respectively. High blood pressure values were found in 68.8, 45.3 and 33.1% of obese, overweight and normal BMI students, respectively.

Conclusion: This study supports a relation between hypertension and excess weight in children and adolescents. The prevalence of hypertension seems to be increasing parallel to overweight and obesity in the pediatric population.

338 ORAL MOTOR SKILLS AND ORAL SENSORY SENSITIVITY IMPACT FOOD CHOICES

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Background: Childhood feeding difficulties can result in reduced dietary intake and variety, and contribute to nutritional deficiencies. Oral motor skills and oral sensory processing abilities contribute to feeding difficulties and may impact food choices.

Aims: The primary aim of this study was to determine the associations between oral motor impairment and oral sensory sensitivity with types of foods consumed in children with feeding difficulties.

Methods: Children aged 2-6 years with feeding difficulties (n=68, 33 autism spectrum disorder; 35 non-medically complex history) underwent multi-disciplinary assessment. All children were on a full oral diet and displayed no aspiration risk. Sensory processing was scored from the Sensory Profile and confirmed on clinical examination. Oral motor skills (eating from a spoon, chewing, biting, drinking from a cup) were assessed using the Pre-Feeding Checklist. Two experienced feeding therapists rated each child independently from video recording. A 3-day diet record assessed dietary intake, and a food list was used to determine dietary variety and group foods eaten according to broad categories (fruits/vegetables, protein-rich foods, and carbohydrate-rich foods).

Results: Children with oral motor delay consumed significantly more daily energy ($p<0.01$) than those with normal oral motor skills, however, this difference was not significantly different once drinks were removed from calculations. Children with oral motor delay and/or heightened oral sensory sensitivity consumed significantly less fruits and vegetables ($p=0.02$).

Discussion: Liquid energy, particularly from milk based drinks (including fortified) contributes to increased energy consumption in children with oral motor delay. This, in conjunction with reduced unprocessed fruits/vegetables is concerning, given that usual diet in childhood tracks into adulthood. Long-term preferences for easy-to-consume foods has implications for risk of overweight and obesity throughout life, as these foods are often energy dense at the expense of nutrients. In this context, oral motor abilities and oral sensitivity issues warrant attention in children with feeding difficulties.

339 ASSOCIATIONS BETWEEN CHANGES IN FEEDING BEHAVIORS AND PSYCHOSOCIAL FUNCTIONING IN PEDIATRIC PATIENTS WITH FEEDING DISORDERS AND THEIR FAMILIES FOLLOWING AN 8-WEEK INTENSIVE FEEDING PROGRAM

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Background: Research suggests that children with medical and developmental issues treated for feeding disorders in multidisciplinary intensive outpatient programs show success following treatment. Few studies report quantitative group results related to changes in health, feeding behaviors, and psychosocial functioning following treatment. The single related study conducted by Greer and colleagues in 2008 found that an intensive feeding program for the treatment of severe feeding problems was associated with improvements in caregiver stress, mealtime behaviors, weight, and caloric intake. This study reported on a combined inpatient and outpatient program and may not generalize to patients treated in an intensive outpatient program. The relative dearth of information regarding medical and psychosocial outcomes following intensive outpatient treatment, our pilot study examined associations between changes in body mass index, feeding behaviors, and psychosocial functioning in pediatric patients with feeding disorders and their families following an 8-week intensive feeding program.

Methods: Caregivers of 14 patients aged 1 to 15 years (mean age 5.79 years; 71% male) completed pre- and post-treatment measures of feeding behaviors and psychosocial function including the Behavioral Pediatrics Feeding Assessment Scale (BPFAS), Pediatric Assessment Scale for Severe Feeding Problems (PASSFP), Pediatric Quality of Life (PedsQL) General and Family Impact Modules, and the Parenting Stress Index (PSI). Anthropometric outcomes were abstracted from the medical record. Paired samples t-tests were used to evaluate differences between pre- and post-treatment psychosocial measures. Pearson correlations were used to assess associations between change scores computed for each relevant variable.

Results: Maladaptive mealtime behaviors improved significantly on both the BPFAS [$t(13) 9.45, p<0.001$] and PASSFP [$t(12) -8.82, p<0.001$]. Family Impact [$t(13) 2.36, p=0.035$] also showed significant improvements following treatment. No other variables met significance although change scores all indicated improvements post-treatment with the exception of parenting stress which showed no change. Correlations among change scores indicate that reductions in maladaptive feeding behaviors are associated with increases in both patient ($r =.895$) and family quality of life ($r =.608$) suggesting treatment may mediate the relations between enrollment in the Intensive Feeding Program and improvements in patient and family quality of life.

Conclusions: Results support the benefits of an intensive feeding program for children with severe feeding disorders on both feeding behaviors and family QL. Reductions in maladaptive behaviors are also associated with increases in caregiver-reported child and family QL.

340 A META-ANALYSIS ON THE EFFECT OF BOVINE COLOSTRUM IN CHILDREN WITH ACUTE DIARRHEA

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Objectives: To evaluate the effect of bovine colostrum in reducing stool frequency, stool output and duration of diarrhea. To evaluate the effect of bovine colostrum in improvement of oral rehydration salt intake.

Search methods: Systematic searches were conducted using PubMed, MeSH, Herdin, EMBASE, OVID and www.clinicaltrials.gov for randomized controlled trials (RCTs). A PICOM table was made to screen for studies to be appraised and those selected were assessed for methodological quality.

Data collection and analysis: Twenty-two possibly relevant articles were identified and 7 RCTs were assessed for methodological quality. Studies were divided into assessment of 4 outcomes specifically stool output, stool frequency, ORS intake and duration of diarrhea. The outcomes were analyzed using standardized mean difference as the principal measure of the effect size. Forest plots of comparison were obtained for effect of bovine colostrum in stool output, stool frequency, ORS intake and duration of diarrhea.

Results: Analysis of two of the 7 RCTs did not show a significant effect on the stool output. Evaluation of three of the 7 RCTs showed significant reduction in the stool frequency; however, there is insufficient evidence with regards to efficacy of bovine colostrum in improvement of ORS intake. Analysis of six of the 7 RCTs showed that bovine colostrum significantly reduced duration of diarrhea.

Conclusions: In this systematic review, analysis revealed evidence that bovine colostrum can decrease stool frequency and duration of acute diarrhea in children. Since there are still no guidelines in the use of bovine colostrum in children, consideration of the impact in the cost of medication among patients should be investigated in further studies.

341 HIGH-PROTEIN, MEDIUM-CHAIN TRIGLYCERIDE CONTAINING FORMULA AS AN ALTERNATIVE TO POST-DISCHARGE FORMULA

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Background: Post-discharge formula (PDF) has been proved to be superior to conventional infant formula in premature infants after hospital discharge, but its availability in Thailand is limited due to logistic and economic reasons. Alternatives to PDF are often needed.

Objective: To evaluate whether a locally-made high-energy, high-protein, medium-chain triglyceride containing formula (HPMCT) can be used as an alternative to PDF for feeding preterm infants after hospital discharge, by comparing growth, adverse symptoms, and costs.

Material and method: After written consents from their parents were obtained, preterm infants who had postconceptional age (PCA) 35+1 to 36+0 weeks and weight between 1800 and 3000 g at hospital discharge were randomly enrolled to receive either PDF or HPMCT starting from the discharge day. Intervention period lasted at least 28 days and until the infant's weight was at least 3000 g or PCA was at least 40+0 weeks. Body weight, length, and head circumference were measured on days 0, 14, 28, 56, and 84 after hospital discharge. Formula intakes and adverse symptoms (abdominal distension, diarrhea, and constipation) were recorded. Costs were calculated from estimated actual formula intakes.

Results: Six and five infants were enrolled into the PDF group and the HPMCT group respectively. Demographic data were not different between the two groups. Infants in both groups gained more than 200 g of body weight per week during the follow-up period. There were no significant differences in growth rates between the groups at days 28, 56, and 84 after hospital discharge. Adverse symptoms and costs were not different either.

Conclusion: HPMCT might be an appropriate alternative to PDF for feeding preterm infants after hospital discharge, as noted from growth, adverse symptoms, and costs. Due to the small sample size of this study, more studies with longer follow-ups in larger numbers of subjects, and with assessment of biochemical and neurodevelopmental parameters, are needed to more clearly evaluate the use of HPMCT in this population.

Keywords: preterm infants, infant nutrition, preterm nutrition, preterm feeding, post-discharge formula

342 FACTORS INFLUENCING THE QUALITY AND QUANTITY OF HUMAN BREAST MILK: IS THERE A NEED TO STANDARDIZE SAMPLING OF MILK FOR CHARACTERIZATION OF LIPIDS AND LIPOPHILES?

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Human breast milk (BM) composition is dynamic and is reported to vary, presumably to reflect the nutritional needs of growing infants.

Literature suggests that methodological aspects such as BM sampling, storage and analyses for research may influence the quantification of certain nutrients, and therefore must be carefully considered at the study design and execution stages. In order to gain insight into the nutritional needs and intake of the breastfed infants, it is imperative to eliminate the variability encumbered by these methodological aspects. Therefore, we holistically reviewed the impact of maternal factors (anthropometry, socio-demographics, obstetric history, health, medications, diet and lifestyle), infant factors (gestational age, anthropometry, gender, breastfeeding frequency and duration, and health), and methodological aspects of study that may impact BM quality and/or quantity, and eventually the validity of study conclusions. We emphasized the need for standardization of BM sampling to characterize nutrients that are known to be affected by the study methodology, and nutrients for which the effect has not been researched or clearly demonstrated. Keen attention was finally given on the choice of the analytical method to characterize and quantify nutrients in BM, with respect to their selectivity, accuracy, precision and robustness.

We searched SCOPUS database with predefined keywords for all scientific literature related to factors that are known to or could potentially influence BM quality and quantity across lactation.

Based on our assessment of degree of impact of each of these factors on BM quality and quantity, we summarized them in the following categories.

1. Low to minimal impact– infant suckling duration, maternal moderate physical activity, social factors, and stress.
2. Have an impact, and must be recorded for appropriate data interpretation– maternal diet, anthropometry, lifestyle (smoking, alcohol/caffeine consumption, severe physical activity), feeding frequency, obstetric history (e.g., parity, mode of delivery), infant birth weight, gender, lactation stage, maternal demographics.
3. Could affect the quality of results, and therefore must be standardized – time and type of BM sampling, treatment of samples post collection, temperature and length of BM storage until analyses, handling and transport of samples, freeze-thaw cycle and analytical procedures. Lipids or liposoluble nutrients appeared to be the most affected nutrients.

Evidence suggests that numerous maternal, infant and study methodological aspects have an impact on BM quality and quantity. To minimize the bias caused by these factors, facilitate the accurate interpretation of study results and ensure comparability across studies, it is critical to

standardize the methodology at the study onset, with special attention to sampling procedures for lipids and liposoluble nutrients, and appropriately consider all relevant factors at the data analyses stage.

***343 A MULTIFACETED PERSPECTIVE OF PROTEIN IN HUMAN MILK: THE DYNAMIC PROTEOME CONTRASTED WITH A REMARKABLY CONSISTENT AMINO ACID COMPOSITION**

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Background and Study: Quantity of protein in human milk is unquestionably important for healthy infant growth and development. These proteins provide not only amino acid building blocks but also play a wide spectrum of bioactive roles. The Global Exploration of Human Milk (GEHM) program includes a unique view of breastmilk over lactation and among mothers from 3 distinct global geographies, offering a unique opportunity to gain a multiplanar view of protein in human milk. Samples collected from GEHM and the Cincinnati Breastfeeding Cohort (CBC) have provided insights into the intersecting changes in the human milk proteome, total protein concentration and amino acid content over the course of lactation and across global populations.

Methods: Milk samples analyzed for protein and amino acids were full breast collections from 10 mothers in each of three GEHM cohorts in Mexico City, Shanghai, and Cincinnati at 4, 13, 26, and 52 weeks lactation. Protein (%w/w) was characterized via Dumas combustion based on conversion from total nitrogen. Total amino acid (TAA) concentrations (mg/dL) in milk were determined by specialized ion exchange chromatography with post column derivatization. The human milk whey proteome was characterized from full breast samples collected from 10 GEHM mothers in each cohort at 4 and 26 weeks as well as 10 Cincinnati mothers in the CBC (Cincinnati Children's Hospital) at 1, 4, 13, 26, 39, and 52 weeks lactation. The whey portion of human milk was analyzed through tandem mass tag, which differentially labels milk proteins and allows quantitation of relative protein abundances using mass spectrometry.

Results: Analysis of the individual proteins or proteome of human milk demonstrates a remarkable diversity of ~2000 proteins expressed in human milk over the course of lactation. Furthermore, the type and relative abundance of these proteins in milk evolves constantly from 1 to 52 weeks of lactation, demonstrating dynamic patterns of up- and downregulation of protein expression. Overlaying the changing human milk proteome are total protein levels that decrease over lactation ($1.40 \pm 0.14\%$ at 4 weeks to $1.17 \pm 0.13\%$ at 52 weeks), a trend that is consistent among samples from the 3 GEHM geographies encompassing mothers with distinct genetic, dietary, and environmental backgrounds. This decrease in protein content over lactation is also mirrored by TAA concentration in human milk, which indicates a similar decrease through 12 months of lactation. However, reframing amino acids in a purely compositional view by normalizing each amino acid as a percentage of total amino acid content shows a remarkable consistency in the TAA profile of human milk collected from all samples across 1 year of lactation and from each cohort.

Conclusion: Study findings offer evidence for a strikingly constant fingerprint for the amino acid profile in human milk provided to the infant regardless of overall protein level and the constantly evolving proteome.

344 TEMPORAL CHANGE OF THE CONTENT OF 10 OLIGOSACCHARIDES IN THE MILK OF CHINESE URBAN MOTHERS

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Human milk oligosaccharides (HMO) are the third most abundant solid component of human milk after lactose and fat. HMO have been postulated to protect the infant from infection by deflecting the binding of pathogenic bacteria, to help establish the microbial ecosystem of the gastrointestinal tract, to modulate the developing immune system, and to be a potential source of sialic acid for the developing infant. In this cross-sectional observational study, the HMO composition of milk from Chinese mothers was studied to determine the impact of stage of lactation, mode of delivery and geographical location. The content of 10 oligosaccharides was measured in the milk from 446 mothers living in 3 different cities in China. The samples were split in to 5 groups representing 5 different stages of lactation. Around 21% of the samples contained very low levels (below 53 mg/kg) of 2'-fucosyllactose (2'-FL), similar to the frequency of fucosyltransferase-2 non-secretors in other populations, but 2'-FL was detected (levels above 4.4 mg/kg) in all samples. Levels of most of the HMO studied decreased during the course of lactation, but the level of 3-fucosyllactose (3-FL) increased. Levels of 2'-FL and 3-FL seem to be strongly correlated suggesting some sort of mechanism for co-regulation. Levels of 6'-sialyllactose were higher than those of 3'-sialyllactose at early stages of lactation, but beyond 2-4 months 3'-sialyllactose was predominant. Neither mode of delivery nor geographical location had any impact on HMO composition. We conclude that the composition of oligosaccharides in the milk of Chinese mothers is quite comparable with mothers from other countries. Stage of lactation (and genetics) seem to be the major drivers for HMO composition, but environmental factors, such as diet, have yet to be explored.

345 GASTROINTESTINAL PROCEDURAL BURDEN DURING ADMISSIONS OF PATIENTS WITH CONGENITAL HEART DISEASE TO CHILDRENS' HOSPITALS

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Background: Gastrointestinal (GI) issues are relatively common in pediatric patients with congenital heart disease (CHD). Invasive GI procedures are often performed in these patients; however, accurate estimates of the magnitude of GI procedural burden are limited. Our objective was to characterize GI procedural burden in inpatient care for various CHD lesions across institutions of differing volumes.

Methods: Hospitalizations of patients (≤ 5 years old at admission and return visits not limited by age) from 39 children's hospitals were collected for 19 gastrointestinal procedure codes from 2004 to 2015 records of the Pediatric Health Information System (PHIS). Four CHD types: secundum atrial septal defect (ASD), ventricular septal defect, (VSD) tetralogy of Fallot (TOF) and Hypoplastic left heart syndrome (HLHS) were analyzed. Diagnosis, institutional volume, and billed charges were recorded. Differences in GI procedure burden by diagnosis and institutional volume, and differences in billed charges with and without GI procedure were calculated. Pairwise comparisons were made among CHD lesions, and among institutions based on volume (low, medium, high) with correction for multiple comparisons.

Results: There were 79390 total admissions (13140 ASD, 24319 VSD, 21965 TOF, 19966 HLHS). Of these, 18088 admissions (22.8%) had a GI procedure: 2690 (20.5%) ASD, 4348 (18%) VSD, 4350 (20.6%) TOF, and 6520 (32.7%) HLHS ($p < 0.001$). Proportion of patients receiving GI procedure varied significantly by CHD lesion ($p < 0.001$). Procedural burden was greater in low volume institutions than in medium and high volume institutions ($p < 0.001$), but medium and high volume institutions were not different. There was \$11,677,727,375 in billed charges, \$3,575,184,479 for admissions with GI procedure (30.6%) and \$8,102,541,878 for admissions without GI procedure (69.4%). Estimated mean increase (95% CL of difference) in charges (\$) per admission with GI procedure for each of the CHD was: 51,215 (39,220-63,210) for ASD, 40,164 (31,302-49,026) for VSD, 62,816 (47,996-77,636) for TOF, and 57,305 (44,816-69,794) for HLHS (all $p < 0.001$).

Conclusions: GI procedures are common during admissions (22%) of CHD patients to children's hospitals. The occurrence of GI procedures during these admissions varies based on the cardiac lesion, with HLHS emerging as the most commonly associated, and VSD the least. Procedural burden is highest at low-volume institutions. Regardless of the underlying CHD, admissions were more costly if they included a GI procedure. The role of GI disease in inpatient care of CHD patients may be under recognized, but it carries important implications for resource allocation and utilization.

CHD lesion	With GI Procedure		No GI Procedure		Estimated Difference (\$)	95% CL of Difference (\$)	p
	Mean \$	SD	Mean \$	SD			
ASD	130,507	311,300	79,292	120,747	51,215	39,220-63,210	<0.001
VSD	143,852	289,800	103,688	149,433	40,164	31,302-49,026	<0.001
TOF	211,269	483,826	148,453	240,918	62,816	47,996-77,636	<0.001
HLHS	251,780	454,843	194,475	345,252	57,305	44,816-69,794	<0.001
All	197,655	412,634	132,174	232,533	65,481	59,192-71,770	<0.001

SD=standard deviation, \$=charges, CL=confidence limits

346 SECONDARY CARNITINE AND BIOTIN DEFICIENCIES USING ACYLCARNITINE ANALYSIS BY TANDEM MASS SPECTROMETRY FROM DRIED BLOOD SPOTS

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Objective: This study aimed to evaluate whether tandem mass spectrometry (MS/MS) in dried blood spots (DBS) is useful in detecting carnitine and biotin deficiencies in pediatric patients.

Methods: Forty-two children (24 males and 18 females) were enrolled between December 2013 and December 2015. Blood tests, including measurement of serum free carnitine via the enzyme cycling method, and acylcarnitine analysis by MS/MS in DBS were performed for the evaluation of nutritional status.

Results: The age at the time of blood collection was 4.6 ± 4.8 years (range, 2 months to 14 years). The mean serum level of free carnitine was 41.8 ± 19.2 fÉmol/L. In six of the 42 patients, the serum levels of free carnitine were < 20 fÉmol/L. C0 and 3-hydroxyisovalerylcarnitine (C5-OH) levels that were measured by MS/MS in DBS were 33.8 ± 20.2 nmol/mL and 0.48 ± 0.22 nmol/mL, respectively. There was a strong positive correlation ($r_s = 0.89, p < 0.001$) in the serum free carnitine and C0 that were measured on the same day. In one patient who was fed hydrolyzed formula, the C5-OH level was > 1.00 nmol/L. Therapy-resistant eczema was improved by a generic formula and additional biotin administration.

Conclusions: C0 and C5-OH, which were measured by MS/MS in DBS, were useful for diagnosing carnitine and biotin deficiencies. MS/MS in DBS may be a useful tool for evaluating pediatric nutritional status, particularly for the detection of carnitine and biotin deficiencies, because only a small amount of blood is required.

347 THE USE OF ANTIBIOTIC LINE LOCKS TO REDUCE RATES OF CATHETER RELATED BLOODSTREAM INFECTIONS IN CHILDREN WITH INTESTINAL FAILURE

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Background: Children with type 3 intestinal failure (IF) require long-term parenteral nutrition (PN). There are several risks associated with long-term PN, including; electrolyte imbalance, liver disease and catheter related bloodstream infection (CRBSI). CRBSI is associated with significant morbidity and mortality as highlighted by recent National CQUIN (Commissioning for Quality and Innovation) guidance, identifying diagnosis and treatment of sepsis as a National CQUIN Goal. Current prophylactic techniques include tunnelling of long-term catheters and use of aseptic non-touch technique. However, few studies have investigated the use of prophylactic antibiotic line locks on the incidence of CRBSI in the pediatric population.

Aim: Based on previous audit data, as of August 2010, antibiotic line locks have been routinely used in children under the age of 5 and in older children with recurrent CRBSI. We aim to quantify the rate of reduction in CRBSI using a larger sample of comparable patients.

Methodology: A descriptive cohort study was carried out involving extraction of data from electronic health records (from the Cerner Millennium application) and pharmacy database. Data collected was for the time period of January 8, 2010 to January 8, 2015, and included episodes of confirmed CRBSI (positive blood culture and/or positive bacterial DNA) and dates on and off antibiotic line locks. Statistical

analysis was used to compare rates of CRBSI per 1000 catheter days while on and off antibiotic locks, using each child as their own historical control. Rates of CRBSI were also compared with previous audit data.

Results: A total of 27 patients with type 3 IF were included in this study, with 17 spending a proportion of time within the five year study period on antibiotic line locks. In the majority of cases IF was due to short bowel syndrome, often following surgery for necrotizing enterocolitis. Table 1 shows patient demographics.

The total number of CRBSI per 1000 catheter days was lower in children on antibiotic line locks, reducing from 104.46 to 55.08. Although not reaching statistical significance, use of antibiotic line locks reduced average rates of CRBSI per 1000 catheter days by 47.42%, from 3.88 to 2.04. Results of this study show that rates of CRBSI continue to fall, as evidenced by a 41.71% reduction in rates compared with the preceding five years.

Conclusion: Antibiotic line locks are safe and well tolerated among pediatric patients with type 3 IF. This research has shown that they are effective in reducing rates of CRBSI and associated hospital admission, as well as improving morbidity. Average rates of CRBSI recorded during this study are well below current published rates. Further larger scale studies are required to accurately assess the effectiveness of this strategy.

Table 1 - Patient demographics. Data is expressed as range (median).

Total number of patients	n=27 (17 male)
Age (years)	0.62 - 17.86 (6.45)
Time on PN (days)	92 - 1826 (1254)
Patients on antibiotic line locks	62.96%
Time on antibiotic line locks (days)	51 - 1634 (723)
Age of patients on antibiotic line locks (years)	2.14 - 17.86 (6.45)
Diagnosis	Short bowel syndrome 48.15% Pseudo-obstruction 29.63% Mucosal disorders 22.22% (Tufting enteropathy 83.33%)
Infective organisms affecting patients on antibiotic line locks	n=17 Gram negative 29.41% Gram positive 47.06% Fungal 23.53%

***348 OUTCOMES AND SAFETY OF TEDUGLUTIDE IN THE TREATMENT OF SHORT BOWEL SYNDROME IN CHILDREN**

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Introduction: In a 12-week, open-label, multicenter safety and pharmacodynamics study (NCT:01952080; EudraCT: 201300458830) teduglutide (TED) 0.05 mg/kg/day reduced the volume of and the days per week on parenteral support (PS; parenteral nutrition and/or intravenous fluids) and advanced enteral nutrition (EN; oral and/or tube feeding) in children with short bowel syndrome (SBS). Here we report additional outcome and the safety results from this study.

Methods: Patients were aged 1-17 years with SBS ≥12-month duration who required PS for ≥30% of caloric and/or fluid/electrolyte needs and who showed minimal/no advance in EN feeds for ≥3 months before baseline. Patients enrolled sequentially into 3 TED cohorts (0.0125 mg/kg/day [n=8], 0.025 mg/kg/day [n=14], 0.05 mg/kg/day [n=15]) or received standard of care (SOC; n=5). Data presented are median (min, max). Safety data were collected at all scheduled study visits.

Results: At baseline, 42 patients (age, 3.0 [1.0, 14.0] years; weight Z-scores, -0.2 [-1.9, 1.7]) received PS 7.3 (4.0, 16.0) L/week (5345.5 [1785.0, 11956.0] kcal/week) and had been PS dependent for 3.7 (0.5, 12.2) years. At Week 12, PS calories (kcal/kg/day) were reduced by 52%, 45%, and 6% in the 0.05-, 0.025-, and 0.0125-mg/kg/day cohorts, respectively, and by 1% in the SOC cohort. EN calories (kcal/kg/day) increased by 63%, 26%, and 7% in the 0.05-, 0.025-, and 0.0125-mg/kg/day cohorts, respectively, and by 41% in the SOC cohort. 4 patients achieved PS independence with TED (0.05 mg/kg/d, n=3/15; 0.025 mg/kg/d, n=1/14), 2 of whom resumed PS 4 weeks after TED ended. There were no reported deaths or discontinuations due to treatment-emergent adverse events (TEAEs). All patients experienced ≥1 TEAE; most were mild (95% TED, 100% SOC) or moderate (57% TED, 60% SOC). TEAEs reported in ≥10% of the combined TED vs. SOC groups are shown in the Table. There were no reports of AEs related to fluid overload, intestinal obstruction, hepatobiliary complications, or colon polyps. Serious TEAEs reported in ≥5% of the combined TED vs. SOC groups were central line infection (4 [11%] vs. 0), pyrexia (4 [11%] vs. 2 [40%]), catheter-related complication (3 [8%] vs. 1 [20%]), and parainfluenza virus (2 [5%] vs. 0). None were considered related to study drug. No patient developed neutralizing antibodies to TED. One patient was positive for non-neutralizing anti-teduglutide antibodies at the study follow-up visit (Week 16) but was negative at 3-month follow-up.

Conclusions: Data trends from this study indicate that TED treatment reduced PS dependence and increased EN intake in children with SBS whose intestinal rehabilitation had plateaued. TED has a generally good safety profile and is well tolerated. Most TEAEs were related to gastrointestinal complaints and/or central line-related issues.

Disclosure: The clinical trial was funded by NPS Pharmaceuticals, Inc., Lexington, MA, USA. NPS Pharmaceuticals, Inc., is a wholly owned indirect subsidiary of Shire PLC.

Table. TEAEs Occurring in ≥10% of the Combined Teduglutide Versus SOC Cohorts

TEAE, n (%)	Teduglutide (n=37)	SOC (n=5)
Vomiting	12 (32)	0
Upper respiratory tract infection	10 (27)	2 (40)
Catheter-related complication	9 (24)	1 (20)
Pyrexia	9 (24)	2 (40)
Cough	7 (19)	1 (20)
Abdominal pain	6 (16)	1 (20)
Reduced blood bicarbonate	5 (14)	2 (40)
Fatigue	5 (14)	0
Headache	5 (14)	0
Nausea	5 (14)	0
Central line infection	4 (11)	0
Diarrhea	4 (11)	1 (20)
Increased fecal volume	4 (11)	0

349 EATING ATTITUDES IN ADOLESCENTS WITH RESPECT TO THEIR BODY IMAGE

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Background: Adolescence is a transitional stage in one's life and roughly consists of three distinct periods – early, middle and late. Many pivotal influences exist during these years including changes (e.g. puberty) that affect one's body shape, weight and appearance. Teenagers are not only being exposed to various health risks of obesity and poor nutrition but have developed very unhealthy concerns regarding body image and shape.

Objective: To assess the eating attitudes in adolescents in correlation to their body image from a selected cohort of school children in Karachi, Pakistan.

Methods: A descriptive cross-sectional study was conducted on a total number of 334 school children in middle-adolescent of middle socio-economic strata, selected via non-probability convenient sampling, with age ranging from age 14 - 17 years. Data was collected from February to April 2016 by visiting the children during their school hours using the standard Eating Attitudes Test (EAT-26). Permission from parents and principal of the respective institution was obtained. IRB was taken from Karachi Medical and Dental College. The data was analyzed using SPSS 16 to calculate the frequency of different eating attitudes observed in the concerned population.

Result: The mean age of children was 14.92 ± 1.04 years, with 170 boys and 164 girls. The mean BMI was 18.06 kg/m². Using the standard EAT-26 scoring chart, it was calculated that a total of 109 (32.6%) children got a score greater than 20. This included 59 (17.7%) boys and 50 (15.0%) girls. Moreover, out of 334 participants, 139 (42.5%) children were terrified about being overweight, 21 (6.3%) vomit after eating, 183 (54.7%) said they are preoccupied with a desire to be thinner, and 71 (21.2%) children said that they felt extremely guilty after eating.

Conclusion: It could be concluded from our study that body image has an effect on the eating attitudes of both male and female adolescent children. Parents of children scoring more than 20 (threshold according to EAT-26 scoring chart) are recommended to visit psychologists to discuss their eating behaviors.

Keywords: Adolescent, eating attitude.

*350 GROWTH FALTERING, SMALL INTESTINAL CRYPT DYNAMICS, AND INTESTINAL STEM CELL ADAPTATION IN METHYL DONOR DEFICIENT MICE

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Introduction: Environmental enteropathy (EE) is a subclinical intestinal condition highly prevalent in low- and middle-income countries characterized, in part, by malabsorption, villous atrophy, and crypt hypertrophy. The pathogenesis of EE remains unclear, however supplementation with folate (a key micronutrient for proper DNA methylation) is an effective adjunct therapy for tropical sprue, i.e., persistent diarrhea on a background of EE. Building on previous work exploring the role of macronutrient deficiency in EE, we aimed to determine the extent to which methyl donor deficiency (MDD) provokes features of EE in mice and uncover mechanistic links between dietary MDD and small intestinal (SI) crypt hypertrophy in mice and murine SI crypt cultures (enteroids).

Methods: At gestational age 11-14 days, we randomized pregnant dams to one of four diets: 1) a standard control diet (CD), 2) an isocaloric MDD diet lacking folate and choline, and formulations of 3) CD and 4) MDD containing sulfamethoxazole to suppress production of folate by the intestinal flora. We weaned pups to their dams' diet on day of life 23. Mice were sacrificed at 7 weeks and another group at 16 weeks for generating jejunal enteroids by the Sato method. *In vivo* measured outcomes were growth, folate status, evidence of megaloblastosis, and histological features. Using light and confocal microscopy, we measured *in vitro* outcomes of enteroid formation, morphology, number of buds/crypt, crypt domain length, and Edu+ proliferative cells in enteroids grown under both standard and MDD conditions.

Results: Prenatal and continued postnatal exposure to MDD led to reduced birthweight, poor ponderal growth with inadequate catch up growth, and impaired linear growth. At 7 weeks of age, MDD mice showed significant folate deficiency with megaloblastic anemia. Histologically, we detected patchy areas of increased crypt depth in the SI of MDD mice. Interestingly, sulfamethoxazole-containing diets produced statistically significant increases in crypt depth in the duodenum and ileum. *In vitro*, we found enteroids from MDD mice are more viable in MDD media vs. CD enteroids. In addition, enteroids from MDD mice displayed highly dysmorphic features in MDD, as evidenced by elongated crypt domains and decreased circularity compared to CD enteroids. In contrast to CD enteroids, we observed a robust but aberrant pattern of proliferation in MDD enteroids maintained in MDD media.

Conclusions: Combined folate and choline deficiency impairs ponderal and linear growth in mice in association with dysmorphic SI crypts. The partial recapitulation of this dysmorphism in *ex vivo* enteroids may reflect epigenetic changes and metabolic adaptation of intestinal stem cells. Our results add to mounting evidence that diet modulates intestinal stem cell function and provide clues as to why folate supplementation is an effective adjunct therapy for tropical sprue and why EE is difficult to reverse.

351 PARENTAL FEEDING STYLE AND ITS INFLUENCE ON PARENTAL PERCEPTION OF FEEDING CONCERNS IN CHILDREN

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Background: Feeding concerns in children are increasingly recognized. Contributory factors include parental feeding styles. There are tools to help us assess mealtime behaviors and parental feeding styles.

Objective: Describe if there are any associations between parental feeding style and perception of feeding concerns in their child.

Methods: Children aged 12-35 months attending their routine general pediatric outpatient clinics were invited to participate. An anonymous survey of demographics, feeding information, the Behavior Pediatrics Feeding Assessment (BPFA) and Caregiver's Feeding Styles Questionnaire (CFSQ) were completed by parents. The BPFA consists of 4 separate sections: 2 objective (child feeding behaviors, parent mealtime responses) and 2 subjective (whether these were considered a problem for parents). Scores higher than specific cut-offs on the BPFA are suggestive of feeding difficulties.

Results: One hundred children (49 male) were recruited. The majority were term infants (76%), with normal (2.5-4 kg) birth weight (66%). 85% did not have medical conditions. Age at survey was: 12-17 months (33%), 18-23 months (26%), 24-29 months (26%) and 30-35 months (15%).

Almost a third (30%) of parents expressed concern about their child's feeding, with weight and solid intake being the top two. Despite this, the majority were at least satisfied with the quantity of food their child ate (77%) and with their child's eating habits (74%). Chinese parents (46%) were more likely to be concerned about their child's feeding compared to Malay (0%) and Indian (27%) ($p = 0.08$) parents.

Based on the BPFA, more children ($n = 80$) met "positive" cut-offs for feeding difficulties. Parents with concerns for their child's feeding were more likely to give positive responses to feeding behavior issues on the child behavior frequency component of the BPFA compared to those without (87% vs. 58%, $p = 0.00$). Parental feeding styles based on CFSQ: 16% authoritative, 32% authoritarian, 31% indulgent and 17% uninvolved. 59% (17/30) of those with feeding concerns were authoritarian, while 37% (25/70) of those without were indulgent ($p = 0.01$). Parents with authoritarian feeding style were more likely to view their child's feeding behavior as a problem (27%) than authoritative (15%), indulgent (11%) or uninvolved (8.3%) parents ($p = 0.07$). They were also more likely to display problematic parental feeding behaviors (97%) compared with authoritative (73%), indulgent (55%) or uninvolved (63%) parents ($p = .00$). Overall, authoritarian parents were most likely to have met positive criteria for the BPFA ($p = .034$) (97%) than authoritative (87%), indulgent (68%), or uninvolved (81%).

Conclusions: Not all parents who gave positive responses for child feeding behavior difficulties on the BPFA report being concerned about their child's feeding. Chinese parents and parents with authoritarian feeding styles were more likely to report both objective as well as subjective feeding concerns.

*352 UPREGULATION OF CHOLESTEROL AND BILE ACID GENE SYNTHESIS IN WILD-TYPE RATS WITH 4 WEEKS OF EXERCISE

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Background: We have recently found an upregulation of genes controlling bile acid and cholesterol synthesis in the livers of rats selectively bred over several generations for high aerobic capacity; findings that tracked with protection against hepatic steatosis following a high-fat diet.

Objectives: Because exercise training can robustly increase aerobic capacity, we sought to determine if various exercise modalities would induce an upregulation of bile acid and cholesterol in previously sedentary Sprague-Dawley rats.

Methods: 46 Male Sprague-Dawley rats were randomly assigned into sedentary (SED), voluntary wheel running (VWR), VWR that were overnight fasted (VWR-OF), treadmill endurance exercise (TM-END; 30 m.min⁻¹, 12% gradient, 60 minutes per day, 5 days per week), or treadmill interval sprint training (TM-IST; 50m.min⁻¹, 12% gradient, 6 x 2.5 minute bouts, 5 days per week) groups for a four week intervention. Rat livers were processed and gene expression of cytochrome P450 family 7 (CYP7A1), HMG-CoA reductase (HMGCR), Squalene epoxidase (SE), Farnesoid X receptor (FXR), Citrate Lyase (ACLY) and HSD17B2) were analyzed using real-time PCR.

Results: There was a significant upregulation of cholesterol and bile acid gene synthesis with various modalities of exercise, with the most pronounced and consistent changes found in the VWR-OF group. An upregulation of CYP7A1, HMGCR, and SE were noted in VWR-OF, TM-END, and TM-IST groups compared to SED. The VWR-OF group uniquely displayed an upregulation in ACYL and HSD17B2 genes compared to SED. FXR expression was down-regulated in the VWR-OF group but was not altered in the remaining groups.

Conclusions: We previously found that rats bred for high aerobic capacity display increases in genes controlling bile acid and cholesterol synthesis in association with increased fecal bile acid excretion and protection against hepatic steatosis. These results show that chronic exercise training can also up-regulate genes controlling bile acid and cholesterol synthesis. This effect was most significant in animals that performed wheel running without access to food.

Four weeks of exercise significantly increases genes controlling cholesterol and bile acid synthesis. Further work is needed to determine if exercise increases fecal bile acid secretion and if this is a mechanism that aids in protection against hepatic steatosis.

353 NUTRITION ASSESSMENT IN 126 HOSPITALIZED CHILDREN WITH HEPATIC DISEASE

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Objectives and study: To investigate the nutritional status and to explore the malnutrition prevalence of hospitalized children with hepatic disease.

Methods: We prospectively surveyed a total of 126 hospitalized children with hepatic disease in Children's hospital of Shanghai, Height for Z-score (HAZ), weight for age Z-score (WAZ), and weight for height Z-score (WHZ) were calculated.

Results: The prevalence of stunting (HAZ < -2), underweight (WAZ < -2), and wasting (WHZ < -2) was 9.6%, 13.5%, and 13.5%, while the nutritional risk (-2 ≤ Z < -1) was 12.7%, 7.9%, and 19.8%, respectively. The children were divided into cholestatic group and noncholestatic

group, the prevalence of stunting, underweight, and wasting was 13.3%/6.1%, 20.0%/7.6%, and 15.5%/13.1%, respectively. The differences in HAZ, WAZ, and WHZ were statistically significant ($p < 0.05$).

Conclusion: The malnutrition prevalence in hospitalized children with hepatic disease is higher than the common population, especially with cholestasis. Nutrition assessment is recommended for hospitalized children with hepatic disease.

Disclosure of interest: The authors have declared that no conflict of interest exists.

354 IMPROVED OUTCOME OF PEDIATRIC INTESTINAL FAILURE WITH EARLY REFERRAL TO A MULTIDISCIPLINARY TEAM

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Introduction: Intestinal failure (IF) requires a multidisciplinary approach to ensure better results, mainly, intestinal rehabilitation (IR). We hypothesize that patients referred early have better outcomes than those who come late.

Aim: To compare the outcome of pediatric patients with IF referred early versus late to a multidisciplinary IR and Transplantation Program (IRTP).

Material and Methods: Retrospective, descriptive analysis of medical records of pediatric patients with parenteral nutrition (PN) dependency greater than 3 months, who were referred to a multidisciplinary IRTP. Evaluated variables were: percentage of IR, PN complications, need for Intestinal transplantation (IT) and mortality. IF associated liver disease (IFALD) was defined as persistent elevation of liver function tests, 1.5 times above normal reference range. Main venous thrombosis were stratified according to Miami classification (1: no thrombosis, 2: one thrombosis, 3: 2 or more, 4: all thrombosed). Patients with history of more than 2 catheter related bloodstream infections (CRBI) per year were considered. Statistical analysis was performed with chi-square test.

Results: Between 2008 and 2016, 106 patients with IF were evaluated. 12 patients with less than 6 months of follow-up were excluded, the rest (94) were divided according to time of disease at the moment of first consultation. Group 1 (G1) included patients referred within 6 months of IF diagnosis (53/94) with a median age 0.25 y (0-14y) and group 2 (G2) patients who were first evaluated after 6 months from IF diagnosis (41/94) with a median age 2.5 y (0.6-14y). IR was accomplished in 31/53 (58%) from G1 versus 15/41 (36.5%) from G2 ($p = 0.035$). IFALD didn't show statistical significance during follow-up according to referral time: G1 24/53 (45%) versus 20/41 (49%) in G2 ($p = 0.73$). Advanced liver disease was present in 1/24 from G1 and 3/20 in G2. Miami 1-2 was described in 38/53 (72%) in G1 versus 20/41 (49%) in G2 and Miami 3-4 was described in G1: 15/53 (28%) versus 21/41 (51%) in G2 ($p = 0.023$). Two or more episodes of CRBI were present in 22/53 (41.5%) from G1 and in 27/41 (66%) from G2 ($p = 0.019$). Transplantation was performed in 6/94 (6%), 3 in G1 and 3 in G2 and 7/94 are still on the waiting list, 3 in G1 and 4 in G2. Mortality in G1 was 6/53 (11%) and 12/41 (29%) in G2 ($p = 0.028$).

Conclusion: To improve IR chances, survival and decrease PN complications in pediatric patients with IF, early referral to a multidisciplinary IRTP is mandatory. Working on prevention of PN complications is also essential to have better results and to avoid the need for transplantation.

355 INFLUENCE OF SCHOOL STRESS ON EATING BEHAVIOR IN ROMANIAN CHILDREN AGED 9 -11 YEARS

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Background: Several studies suggest that self-reported distress is related to increased caloric intake. Feeling pressured or stressed by schoolwork may influence eating behavior. Affected students characteristically engage in more health-compromising behaviors (such as smoking), have more frequent health complaints (such as headache, abdominal pain and backache) and experience psychological problems (such as feeling sad, tense and nervous).

Methods: We performed a cross-sectional study on a sample of 82 pediatric patients, hospitalized in the Pediatric Gastroenterology Service, St. Mary Children's Emergency Hospital, Iasi city, from January 2014 to January 2015. The criteria for selecting patients were age between 9 and 11 years and BMI (Body Mass Index) values. Participants completed Health Behavior in School-Aged Children (HBSC) questionnaires on eating habits, health-related behaviors, and emotional distress.

Results: The overweight was associated with increase prevalence of risk and health complaints as compared to normal weight students (headache and backache, 5 % vs. 0 %, weakness 6% vs. 0%, agitation, 11% vs. 8%, lower self-reported health 4% vs. 2%). Eating patterns in overweight school-aged children as compared to normal weight children were characterized by increased consumption of sweets (35% vs. 25%), Coca-Cola (25% vs. 0%) and French fries (22% vs. 5%).

Conclusions. School stress is associated with a range of health and well-being outcomes, which may influence eating behavior and leads to overweight.

356 REVIEW OF OUR 2-YEAR CLINICAL EXPERIENCE WITH INDIRECT CALORIMETRY: TECHNIQUE MATTERS

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Background: According to the American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines for nutrition of the critically ill child, patients with suspected metabolic alterations or malnutrition should have their energy expenditure measured. Ste-Justine University Hospital has acquired expertise to perform indirect calorimetry (IC) as part of the clinical care of children at risk of malnutrition. We present here our 2-year experience to underline the importance of applying a rigorous technique while measuring and editing the resting energy expenditure (REE) data to obtain reliable results in order to optimise patients' nutritional management.

Methods: REE is measured at the patient's bedside by open circuit IC using a computerized metabolic cart (Encore). A 60-minute REE assessment is performed. Raw data is subsequently edited to omit the data from the first ten minutes and from periods of documented physical movement or coughing. The remaining data is averaged and REE is calculated from the modified Weir equation in Kcal/day. A nutritional evaluation is also performed with each REE assessment by a clinical dietician. A retrospective chart review was completed for all the patients who underwent IC.

Results: Twenty-seven IC studies were performed on 16 patients. Twenty-one studies were performed with canopy while 6 IC were completed on mechanically ventilated patients. The edited results differed from the raw data by a mean of $4.25 \pm 7.33\%$. In some studies with cooperating adolescents, the edited REE result was almost identical to the unedited measurement, while differences as high as 32% were documented

between the raw data and edited results in younger patients. The edited result was lower than the raw data in 14 out of 27 REE measurements. Five patients underwent more than 1 REE measurement over 1 to 6 months with the same technique (3 with canopy and 2 with ventilator) and significant changes were observed varying from 9 to 34% with a mean change of $21.60 \pm 10.53\%$ over time.

Conclusions: IC is a useful tool to optimize and individualize nutritional management of critically or chronically ill patients, but a precise technique and thorough analysis are required to obtain reliable REE results. Significant changes in REE can occur over a few weeks therefore frequent IC monitoring is recommended to avoid under- or over-nutrition.

357 VITAMIN D NON-SUFFICIENCY IS COMMON IN CHILDREN WITH CHRONIC INFLAMMATORY BOWEL DISEASE AND CHRONIC LIVER DISEASE IN A TROPICAL COUNTRY

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Introduction: Vitamin D deficiency is common in children and adolescents with inflammatory bowel disease (IBD) and chronic liver disease (CLD) despite vitamin D supplement.

Objectives: To determine (1) the vitamin D status in patients with IBD and CLD on stable dose of vitamin D supplement; (2) the relationship between vitamin D status and dosage of vitamin D supplement, as well as disease activity.

Patients and Methods: A cross-sectional study on 26 patients with IBD (Crohn's disease, n=16; ulcerative colitis, n=10; mean age \pm S.D. 10.4 ± 3.9 years) and 71 patients with CLD (cholestatic liver disease, n=61, non-cholestatic liver disease, n=10; mean age \pm 5.4 years) had serum vitamin D and other related blood investigations measured at University Malaya Medical Center (UMMC), Kuala Lumpur. Vitamin D status (sufficiency: serum vitamin D ≥ 50 nmol/L, non-sufficiency: serum vitamin D < 50 nmol/L), vitamin D supplement (total vitamin D < 1000 units/day, ≥ 1000 units/day), disease severity (inactive/stable disease, inactive/progressive disease) and disease duration were analysed.

Results: The overall prevalence of vitamin D non-sufficiency was 46% (n=12 of 26) in IBD and 28% (n=20 of 71) in patients with CLD, respectively. In patients with IBD, vitamin D status was not affected by disease status (active vs. inactive, $p=0.25$) or daily vitamin D intake (< 1000 units/day vs. ≥ 1000 units/day; $p=0.39$). In patients with CLD, vitamin D status was not affected by disease status (active vs. inactive, $p=0.06$) or daily vitamin D intake (< 1000 units/day vs. ≥ 1000 units/day; $p=0.67$). On further analysis, however, patients with cholestatic liver disease having an inactive disease status was more likely to be associated with non-sufficiency in vitamin D (0%, n=0/7) as compared with those with an active disease (100%, n=7/7; $p=0.026$).

Conclusions: The current oral vitamin D supplement regime in a tropical country with plenty of sunlight is insufficient to maintain an adequate level of serum vitamin D in a significant number of children with IBD and CLD. Surprisingly, a vitamin D non-sufficiency was commonly observed in children with cholestatic liver disease with an inactive disease than in those with active disease. Close monitoring of vitamin D status in all children with IBD and CLD is mandatory, irrespective of their disease status.

358 A RETROSPECTIVE DUAL-CENTER STUDY OF PARENTERAL NUTRITION-ASSOCIATED CHOLESTASIS IN PREMATURE NEONATES: 15 YEARS' EXPERIENCE

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Background: Parenteral nutrition (PN) has become an essential measure for premature infants. PN-associated cholestasis (PNAC) is a major complication. The aim of this study was to describe PN practices in premature neonates and to explore potential risk factors for PNAC in order to suggest possible methods for decreasing PNAC incidence.

Methods: In this retrospective dual-center study, premature neonates were admitted to the neonatal intensive care unit (NICU) and received PN at least 14 days at Xin Hua Hospital and Shanghai Children's Medical Center Affiliated to Shanghai Jiao Tong University School of Medicine from January 2000 to December 2014. Infants with metabolic liver disease, cyanotic congenital heart disease, congenital syphilis, hepatitis B infection, and those who underwent surgery were excluded. Cholestasis was diagnosed as conjugated bilirubin (D.Bil) > 34 μ mol/L. Confirmed sepsis was defined as positive blood culture. Infants were divided into 3 groups: group A (2000-2004, n=50), group B (2005-2009, n=283), group C (2010-2014, n=741). A case-controlled study was conducted by comparing infants with PNAC to those without PNAC. Potential risk factors associated with PNAC in univariate analyses at a P-value < 0.10 were further analyzed using multivariate binary logistic regression.

Results: Of 1074 premature newborns, PNAC was confirmed in 53 infants (4.93%). The incidence of PNAC decreased slightly over past decades (8.0%, 4.2% in groups A and C respectively). In the meanwhile, sepsis declined from 52.0% to 5.1% ($p<0.001$). Compared with those without PNAC (n=1021), infants with PNAC (n=53) had significantly lower GA (30.1 vs. 31.7 weeks; $p<0.001$) and BW (1260 vs. 1550g; $P<0.001$). They also had longer PN duration (29 vs. 19 days; $p<0.001$), and higher rate of sepsis (22.6% vs. 5.8%; OR 4.772, 95% CI, 2.382-9.561; $p<0.001$). A slightly higher ratio of male gender was observed in neonates with PNAC (male, 71.7% vs. 59.3%; OR 1.742, 95% CI, 0.946-3.208; $p=0.072$). We further found that infants who received PN with dose of lipid > 2.0 g/kg/d ($p=0.004$), amino acid > 3.5 g/kg/d ($p=0.034$) or calorie > 80 kcal/kg/d ($p=0.046$) were more likely to develop PNAC. A logistic model showed that male gender ($p=0.019$; OR 2.342, 95% CI, 1.149-4.773), PN duration ≥ 43 d ($p<0.001$; OR 7.757, 95% CI, 2.867-20.986), and sepsis ($p=0.002$; OR 3.657, 95% CI 1.585-8.436) were statistically correlated to PNAC.

Conclusions: PNAC was more common in premature male newborns with sepsis, and prolonged PN duration. Several measures to limit PNAC can be suggested, such as avoiding overfeeding, decreasing sepsis, withdrawing PN as soon as possible, and individualized nutrition therapy administered by NST. Prospective randomized controlled trials are necessary to determine the optimal daily dose of nutrient, which are sufficient for adequate growth but not promote PNAC in premature neonates.

359 CURRENT NUTRITIONAL STATUS AND RISK FACTORS OF MALNUTRITION IN INFANT WITH CONGENITAL HEART DISEASE

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Background: Congenital heart disease (CHD) is now no longer incurable disease. However, it seems to be insufficiently studied to identify how CHD affect malnutrition. Malnutrition is observed more frequently from CHD infant than healthy infant. Since infantile malnutrition negatively affects lifelong physical and neurodevelopmental growth, recognition and prevention of malnutrition in this period is more important. This study aims to define how CHD affects malnutrition and what is the consequential risk factors from the malnutrition.

Subjects and Methods: This study was conducted with a group of newly hospitalized patients, aged 3 months to 1 year and diagnosed with congenital heart disease, between January 2010 and December 2013. Preterm infants less than 35 gestational age were excluded. We defined malnutrition as weight-for-age Z-score less than 5%. The investigation was performed for prevalence of malnutrition, age, sex, gestational age, weight at birth, type of congenital heart disease, genetic abnormality, accompanied anomaly, and number of previous surgeries, retrospectively. Nutritional status was assessed using weight-for-age and weight-for-height. The weight-for-age and the weight-for-height was calculated by using L-M-S data of 2007 Korean growth charts. The prevalence of malnutrition was assessed. The anthropometric data was analyzed by t-test, χ^2 -test and Fisher's exact test. And the risk of malnutrition was analyzed by logistic regression analysis.

Results: A total of 371 infants (199 boys and 172 girls) was analyzed. The average age at admission was 6.5 ± 2.6 (3.0-11.9) months. The mean Z-score of weight-for-age was -1.17 ± 1.56 . Eighty-eight infants (23.8%) were born between 35-37 gestational weeks. Of 371 infants, 133 infants (29.9%) were estimated as having malnutrition. Infant with pulmonary hypertension ($p < 0.001$), gestational age ($p = 0.019$), prematurity ($p = 0.008$), low birth weight ($p < 0.001$), genetic abnormality ($p < 0.001$), gastrointestinal anomaly ($p = 0.038$), history of heart surgery ($p = 0.001$), history of surgery ($p = 0.001$) and accompanied congenital anomaly ($p = 0.001$) were significantly related to malnutrition. Presence of cyanotic heart disease and type of congenital heart disease were not significantly associated with malnutrition. In multivariate analysis, pulmonary hypertension ($p < 0.001$, odds ratio 2.544, 95% CI, 1.420-4.560), genetic abnormality ($p < 0.001$, odd ratio 7.648, 95% CI, 2.739-21.356), history of heart surgery ($p = 0.003$, odds ratio 2.324, 95% CI, 1.333-4.052) and accompanied anomaly ($p = 0.026$, odds ratio 6.125, 95% CI, 1.240-30.246) were identified as the risk factors for malnutrition.

Conclusions: In our study, 29.9% infants with CHD showed malnutrition. Pulmonary hypertension, genetic abnormality, history of heart surgery and accompanied anomaly are risk factors of malnutrition in infant with CHD.

360 BREASTFEEDING AMELIORATES DYSBIOSIS OF GUT MICROBIOTA IN INFANTS BORN BY C-SECTION

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Early-life intestinal microbiota is influenced by various elements such as delivery and feeding modes, and can impact various aspects of health and disease in later years. While studies have focused mainly on *Bacteroides*, *bifidobacteria*, *lactobacilli* and to a lesser extent on *Clostridium difficile*, the colonization patterns of several specific anaerobes such as toxigenic *Clostridium perfringens* remain underexplored. Herein we examined the microbiota development of 89 healthy, full-term Japanese infants prospectively from the first week of life to 3 years of age, with a particular focus on the fecal carriage of α -toxigenic and enterotoxigenic *C. perfringens* and its association with delivery and feeding modes and also with other gut bacteria. *C. perfringens* was quantified by using qPCR assays; other intestinal bacteria were quantified by RT-qPCR. Alpha-toxigenic *C. perfringens* was detected in 3.4, 39.3, 33.7, 38.2 and 39.3% infants at day 7, 1 month, 3 months, 6 months, and 3 years, respectively, with counts ranging from 10^3 to 10^7 cells/g feces; however, its count at 3 years was significantly lower than those at previous time points. Enterotoxigenic *C. perfringens* remained undetected at day 7 but was detected in 1.1, 4.5, 10.1 and 4.5% infants at age 1 month, 3 months, 6 months and 3 years, respectively. Infants who had higher carriage of *Bacteroides fragilis*, *bifidobacteria*, *Lactobacillus* had lower levels of α -toxigenic *C. perfringens*. Compared to vaginal delivery, Caesarean-born infants had lower levels of *B. fragilis*, *Bifidobacterium*, *Lactobacillus* and fecal organic acids, and had higher carriage of α -toxigenic and enterotoxigenic *C. perfringens*. Furthermore, cesarean-born infants also had slightly higher bodyweight at age 3 years. Infants who started formula-feeding in the first week of life tended to be slightly more often colonized with *C. perfringens* compared to those who were exclusively breastfed during first 3 months. Whereas within the cesarean-born group, breast-fed infants had slightly lower levels of *C. perfringens* and higher levels of *B. fragilis* and several species of bifidobacteria and lactobacilli. These results might hint that while vaginally-delivered infants acquire a healthy microbiota, cesarean section could lead to a somewhat perturbed gut microbiota configuration; and breastfeeding during first few months could be particularly helpful in ameliorating the gut dysbiosis in these cesarean-born infants. The finding that healthy infants may also carry toxigenic *C. perfringens* at significant levels is intriguing and warrants further investigation of its sources and clinical significance in infants, particularly the Caesarean-born who appear to have a higher carriage of *C. perfringens* and hence may be more prone to associated illnesses. Studies are also needed to elucidate what impacts these early-life microbiota differences might have on the health of the newborn in later years.

361 CLINICAL OUTCOMES OF MILK ALLERGY IN INFANCY AND ATOPIC DISEASES IN CHILDHOOD: 15- YEAR EXPERIENCE IN A SINGLE CENTER

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Background: Milk allergy affects 2-7.5% of children under 1 year of age and is one of the most common childhood food allergies in the developed world. Despite 80% of children developing tolerance at five years of age, the risk of progressing to other atopic diseases is unclear. The goals of this study are to illustrate the clinical outcomes of milk allergy and the association with other allergic diseases.

Methods: A cohort of 10945 young infants between 1 day old to 4 months old admitted to the neonatal service at Taipei Veterans General Hospital during 1998 to 2010 was eligible for analyzed. The diagnosis of milk allergy was based on a definite disappearance of symptoms after elimination of cow's milk protein. From the same cohort, cases with milk allergy and a randomly nested control group were retrospectively follow-up by questionnaires in order to investigate the development of atopic disease during childhood. Standardized questionnaires on asthma, allergic rhinitis (AR), eczema and food allergy were answered.

Results: Overall, 90 infants (0.82%) were diagnosed with milk allergy in our study. Initial clinical symptoms occurred at an average of 34.4 days (2-154days) post-natal age. Bloody stool (64.4%) was the most common symptom, followed by diarrhea (15.6%), vomiting (7.8%), bloody vomitus(5.6%) and skin rash(2.2%). A serious case with skin rash as the initial presenting symptom resulted in mortality. Otherwise, all symptoms improved after cow milk protein elimination and medical treatment. Colonoscopy was performed in 33 (36.7%) infants and 17 cases were found to have typical hemorrhagic proctocolitis. Pathologic examination of biopsy specimens revealed chronic inflammation with predominant eosinophil infiltration in all cases.

Completed questionnaires were returned by 24 (26.7%) of the cases with milk allergy and 67 (18.6%) of the control group. In children with a known history of milk allergy, 8.3% and 41.7% was diagnosed as asthma and AR while 11.9% and 55.2% children of control group was diagnosed as asthma and AR, respectively. With a mean follow-up of 13.5 years, children with milk allergy were found to develop eczema more frequently than control subjects (66.7% vs. 15.0%, $p < 0.01$).

Conclusion: Milk allergy is the most common food allergy in early childhood and may manifest with gastrointestinal symptoms or skin rash. Eosinophilic proctocolitis is the major pathologic mechanism contributing to this disorder. There is no increased risk of developing asthma and AR in children with milk allergy after food elimination. However, the incidence of atopic eczema is significantly increased in late childhood in those patients with a history of milk allergy.

*362 ACQUISITION OF ORAL FEEDING SKILLS IN PRETERM INFANTS BORN <32 WEEKS

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Background: In pre-term infants, achievement of safe oral feeding skills is an important milestone. According to American Academy of Paediatrics guidelines, "prior to discharge, it is recommended that preterm infants establish competent oral feeding by breast or bottle, without cardiorespiratory compromise." Therefore these infants should learn gradually to make successful transition from gavage feeding to oral/suck feeds. The suitable time to introduce oral feeds has not been defined yet. It is important to recognise feeding performance and provide support towards development of sucking skills in order to achieve successful oral feeding.

Methods: A prospective cohort study was conducted including preterm infants born <32 weeks entering the NICU during 1-year-time period. Feeding performance and anthropometric parameters were recorded during hospital stay. Infants were divided in two groups on the basis of Gestational Age (GA): <28 weeks (Extremely preterm infants (EPI)); >28 weeks (very preterm infants (VPI)). To assess individual feeding performance, important time points were defined regarding tube feeding phase and oral feeding phase. Tube feeding phase included days to reach full enteral nutrition (FEN) and oral feeding phase included transition from gavage feeding to oral/suck feeds i.e., 1) 10% of total feed was fed orally, 2) 50% of total feed was fed orally, 3) 100% orally fed, 4) *ad libitum* feeds. The aim was to identify the time point regardless of the GA (at birth) when attainment of full oral feeding is possible.

Results: 83 infants were included in analysis. All preterm infants successfully acquired oral feeding skills before discharge, all infants were discharged on *ad libitum* feeds. EPI (n=27) compared to VPI (n=56) showed significantly different feeding performance during both tube feeding and oral feeding phase. EPI needed more time to reach FEN than VPI (21 vs. 8.6 days). Moreover, after having reached FEN, EPI needed longer to receive 10% of total feeds orally; (41.5 vs. 10.07 days). There was a significant difference between EPI and VPI in regard to the time needed from 10% to 100% oral feeds (18.6 vs. 14.9 days). Attainment of full oral feeding skills was reached at gestational age of 39.1 weeks in EPI and at gestational age of 35.9 weeks in VPI, discharge was about 1 week later in both groups. We found significantly lower weight increment in EPI group as compared to VPI group during 10-100% oral feeds period (13.5 vs. 15.02 g/kg/d).

Conclusion: All pre-term infants successfully acquired oral feeding skills before discharge. The time point of attainment of full oral feeding was significantly later in EPI compared to VPI. During 10-100% oral feeds mean weight gain per day was significantly lower in the EPI group compared to VPI group.

363 COW'S MILK AVOIDANCE AND COW'S MILK PROTEIN CHALLENGE IN 0-6 MONTHS INFANTS OF COW'S MILK PROTEIN ALLERGY -A MULTI CENTER STUDY

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Cow's milk avoidance and open CMP challenge is a relatively safe method for diagnosing these suspected CMA infants. During the period of cow's milk avoidance, we can choose amino acid formula as food replacement for more effective diagnosing CMA.

364 THE NUTRITIONAL SUPPORT STATUS OF HOSPITALIZED LATE PRETERM INFANTS: A MULTI-CENTER SURVEY IN BEIJING AREA

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Objectives: To evaluate the nutritional support status of hospitalized late preterm infants (34 to 36+6 weeks of gestational age) in hospitals of different levels in Beijing area, with the further aim of developing the nutritional management guideline to improve the short- term and long-term prognosis of late preterm infants.

Methods: Data on nutritional strategy and nutritional-related complications of late preterm infants were collected through a cross-sectional survey

Results: From October 2015 to March 2016, twenty-six hospitals and neonatal intensive care units in the Beijing area participated in this clinical study, of which five were level II hospitals and twenty one were level III hospitals. A total of 723 late preterm infants were enrolled, with mean gestational age of 35.6 ± 0.8 weeks. Infants with gestational age of 36+0~36+6 weeks accounted for 40.2%. The percentage of small for gestational age was 8.2%. The average birth weight, birth length and head circumference was 2509.4 ± 401.4 g, 46.6 ± 2.4 cm and 32.4 ± 1.7 cm respectively. Length of hospital stay was 9.3 ± 5.4 days, and the weight, length and head circumference at discharge was 2521.4 ± 507.4 g, 47.0 ± 3.0 cm and 32.9 ± 2.0 cm respectively. For enteral nutrition during hospitalization, the percentage of exclusive breastfeeding was as low as 4.6%; preterm formula constituted the majority (46.5%), post-discharge formula accounted for 18.5%, full-term formula accounted for 12.2%, and 18.3% of late preterm infants was fed a mix of human milk and formula. Nevertheless, most of the late preterm infants could not reach full enteral feeding at discharge; only 18.7% could reach 120kcal/kg.d of energy and 26.2% 150mL/kg.d of intake volume at discharge. It took an estimated 8.9 ± 2.9 days to reach 120kcal/kg.d of enteral feeding and 8.6 ± 2.9 days to reach 150mL/kg.d of enteral intake volume. The total calory of enteral nutrition at discharge was 91.7 ± 31.3 kcal/kg.d and enteral intake was 121.5 ± 40.6 mL/kg.d. About 37.6% infants received parenteral nutrition during hospitalization. The time at the lowest weight was 3.6 ± 1.8 days, and it took 6.2 ± 3.2 days to regain birth weight. 39.4% of late preterm infants were discharged without regaining birth weight. With the present nutritional support strategy, the incidence of hypoglycemia and hyperglycemia was 11.3% and 2.1% respectively, the incidence of hyperbilirubinemia was as high as 56%, the incidence of neonatal infections was 25.6% and 15.1% of infants were diagnosed with anemia.

Conclusions: The nutritional support survey of late preterm infants showed a low rate of exclusive breastfeeding and dominated preterm formula. A majority of the late preterm infants could not reach full enteral feeding and failed to regain birth weight when discharged. It is reasonable and urgent to standardize the nutritional management protocol of late preterm infants both during hospitalization and after discharge.

365 GROWTH FALTERING IN PEDIATRIC PATIENTS WITH CONGENITAL HEART DISEASE AND IMPACT ON POST-OPERATIVE OUTCOME: A SINGLE CENTER EXPERIENCE

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Objective: Malnutrition is a common cause of morbidity and mortality in children with CHD (congenital heart disease). The study aimed to assess the prevalence of growth restriction in children with CHD before operation and investigate the relationship between pre-operative malnutrition, cardiac classification and post-operative mortality.

Methods: This retrospective study was performed in a tertiary pediatric cardiac intensive care unit for the entire year of 2014. A total of 3279 patients who underwent corrective or palliative cardiac surgeries was enrolled. Anthropometric measurements included weight for age Z-score (WAZ), weight for height Z-score (WHZ) and height for age Z-score (HAZ) according to standard WHO procedures. The studied groups were classified into normal nutritional status and malnutrition with a cut-off Z-score -2 to classify low WAZ, low HAZ, and low WHZ.

Results: In total, 3252 patients were included. The prevalence of WAZ<-2, HAZ <-2 and WHZ<-2 was 23.3%, 23.4% and 24.3%, respectively. In the age subgroups, the <1 year subgroup had the highest prevalence of WAZ<-2 (29.7%, $p<0.0001$), HAZ<-2 (23.1%, $p<0.0001$) and WHZ<-2 (19.7%, $p<0.0001$) than that of 1-3 year, 3-6 year and > 6 year subgroups. Subgroups with weight no more than 10 kg had a higher prevalence of WAZ<-2 (29.7%, $p<0.0001$), HAZ<-2 (23.1%, $p<0.0001$) and WHZ<-2 (19.7%, $p<0.0001$) than the subgroup of more than 10 kg. Among the different types of cardiac diseases, the highest incidence of WAZ<-2, HAZ<-2 and WHZ<-2 was CAVC (complete atrioventricular canal) (47.7%), IAA (interrupted aortic arch) (48.6%) and PTA (persistent truncus arteriosus) (42.1%) separately. The single ventricle subgroup had the higher prevalence of HAZ<-2 (29.5%, $p<0.0001$) than the double ventricle subgroup, but there was no significant difference in the prevalence of WAZ <-2 or WHZ<-2 between the two subgroups. The cyanotic subgroup had the higher prevalence of HAZ<-2 (25.5%, $p<0.0001$), but the acyanotic subgroup had the higher prevalence of WHZ<-2 (18.0%, $p<0.0001$). The pulmonary hypertension subgroup had the higher prevalence of WAZ<-2 (24.2%, $p=0.0007$), and WHZ<-2 (18.2%, $p<0.0001$), but the group without pulmonary hypertension had higher prevalence of HAZ<-2 (24.8%, $p=0.0054$). By logistic regression analysis, risk factors of post-operative mortality were children no more than 10 kg (OR 0.49[0.27, 0.87]), WAZ<-2 (OR 2.26 [1.32, 3.86], $p=0.003$), and HAZ<-2 (OR 2.29 [1.63, 5.13], $p=0.0003$).

Conclusions: Malnutrition is more serious in the children with CHD younger than 1 year of age or weighing no more than 10 kg. Some types of cardiac defects were associated with a higher risk of malnutrition; therefore, we would pay more attention to the nutritional support in the peri-operative treatment of these susceptible groups. Malnutrition pre-operatively would affect post-operative mortality in CHD children weighing no more than 10 kg, WAZ<-2 or WHZ<-2.

*366 WITHDRAWN

TRANSPLANTATION

372 SEVERE SARCOPENIA AND INCREASED FAT STORES IN PEDIATRIC PATIENTS WITH LIVER, KIDNEY AND INTESTINE FAILURE

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Background: Recent research suggests that measures of frailty, such as nutrition status, may be important predictors of surgical and transplant outcomes. The objectively calculated degree of malnutrition, including muscle and fat stores, experienced by pediatric patients with end-stage organ failure has not been well studied. This study compares children with end-organ disease to healthy, age-matched controls to determine the disparity in muscle and fat stores.

Methods: Children younger than age 19 with end-stage liver, kidney and intestine disease were extracted from the transplant database. Those children with computed tomography (CT) imaging within 6 months of transplant were then age and gender-matched to healthy controls from the trauma database. Measures of nutrition status included core muscle mass, perinephric (visceral) and subcutaneous fat. Measurements of total psoas muscle area, total perinephric fat, and subcutaneous fat were measured at the L2/L3 disc space, and scaled to patient height. Results: Liver (n 35), kidney (n 20) and intestine (n 26) transplant patients were included in the final analysis, with each individual child matched to a healthy control. Liver failure patients' primary diagnosis was biliary atresia (54%). Kidney failure patients' primary diagnosis was focal glomerular sclerosis (20%) and obstructive uropathy (15%). Intestine failure patients' primary diagnosis was gastroschisis (31%) and necrotizing enterocolitis (23%). Body mass index for cases and controls was similar (range 17 to 21). Protein and albumin levels were higher in the healthy controls. Patients with end-stage liver disease had a 28% reduction in muscle, a 31% increase in visceral fat and an 8% increase in subcutaneous fat volume. Patients with end-stage renal disease had a 30% reduction in muscle and a 50% increase in subcutaneous fat volume. Visceral fat volume was not compared in this group because the atrophic kidneys resulted in unreliable measures of perinephric fat. Patients with intestine failure had a 44% reduction in muscle, a 12% increase in visceral fat and a 28% increase in subcutaneous fat. Conclusions: These results demonstrate significant sarcopenia in patients with end-stage liver, kidney and intestine failure. These children, however, have increased fat stores suggesting an active physiologic mechanism to store fat while losing muscle mass. Sarcopenia may be related to total body protein loss either from decreased synthesis (liver), wasting (kidney) or malabsorption (intestine). Standard measures of nutrition, including body mass index and serum albumin and protein failed to provide an adequate representation of the redistribution of muscle and fat in these children.

374 LIVER TRANSPLANTATION COMING OF METABOLIC AGE

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Liver transplantation has been a life-saving surgery for children with liver disease. Transplantation outcomes are excellent as it offers a consistent survival advantage in both short- and long-terms. This success allowed our transplant community to adopt a new paradigm of treatment for metabolic disorders: liver transplantation for brain protection. We report the changing demographics and outcomes in a single liver transplant program. We reviewed our pediatric liver transplantation demographics before and after the establishment of our metabolic transplant program. In period 1 (2003-2012): 101 patients received an isolated liver transplant, 11 of them for metabolic conditions (1 oxalosis, 6 UCD, 1 A1AT, 1 PA, 1 MMA, 1 galactosemia). Contrasting with period 2 (2013-2015): 54 patients received an isolated liver transplant, 23 of them for metabolic conditions (10 UCD, 2 PA, 7 MSUD, 1 A1AT, 1 NP C, 1 GSD1, 1 GSD4). Outcomes have been excellent and favorably compare to those of transplantation for primary liver disease. Current patient survival at 1, 3 and 5 years is 100%. One patient died 10 years ago from PA metabolic storm in the peri-operative period, resulting in a 97% survival for our cohort. 91% (30/33) of our patients are on single immunosuppressive drug, with normal LFTs and no portal HTN. Transplant-related complications have included: 4 graft losses, 5 HAT (all in infants < 12 months of age), 1PV thrombosis, 2 BD stenosis, 7 episodes of rejection. Metabolic control, quality of life and cognitive function are improved in all patients.

Conclusion: Liver transplantation is an excellent treatment option for metabolic disorders that can be cured or stabilized with a healthy liver. Specific metabolic support and expertise is crucial to guide those patients through peri-transplant times. Long-term outcomes of graft function are excellent. Rejection, in particular steroids-resistant one, appears to be more frequent in this patient population and needs to be confirmed in larger studies. As the concept of liver transplant for primary brain protection is gaining momentum, we noticed a solidly established trend towards transplantation at an earlier age (before the onset of any significant brain damage), and for transplantation of patients with other disorders than OTC and A1AT.

375 PEDIATRIC LIVER TRANSPLANTATION IN INDIA: LEARNING OUR LESSONS, COMING OF AGE

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Background: Liver transplant (LT) is now an established treatment modality for management of children with end-stage liver disease (ESLD). In the early-mid 90s, the scenario for patients with liver failure in India was grim. There was no center in the country that offered liver transplantation. All patients awaiting a LT needed to be transplanted at centers outside the country. The transplants done outside were not only costly but also entailed a long waiting period in view of the preference for patients enrolled in the country's own registries. Hence, there was a perceived need to develop a comprehensive liver transplant program in India.

Methods: A retrospective analysis of all liver transplants done at our center since 1998 was performed.

Results: The first successful pediatric LT in the country was performed in November 1998 in a boy with extra-hepatic biliary atresia who had previously undergone a portoenterostomy at our center in Delhi. Like any new program, our transplant program went through an initial teething period. The acceptability of the program among the medical fraternity and public was limited and in the absence of a national registry the task was herculean. Referrals for pediatric LT were few and only a miniscule proportion of those requiring LT could be transplanted. The first decade of LT (1997-2006) saw only 14 children and 88 adults being transplanted. Late referrals by primary care physicians, donor non-availability, economic and social constraints were the reasons for such few transplants. The year 2007 served as a watershed. Living-related LT offset the shortage of donors. The patients who were leading a normal life post-LT helped create awareness about its benefit. Refinement of surgical techniques, improvements in peri and post-operative care resulted in better outcomes. The patient survival post 2007 at our center is now 90%. Survival as high as 90% is also being reported in babies less than 7.5 kg. The average length of stay for both donors and recipients has decreased. Eighty-five children and 900 adults have been transplanted in the past 3 years.

The availability of generic immunosuppressants has greatly aided in bringing down costs. The average cost of LT in India is around 30000 USD. This is only a fraction of the cost in the West. Another positive aspect is the involvement of the community in arranging funds for the underprivileged who can't afford LT. Current concerns have shifted from the initial aim of early post-transplant survival to long-term quality of life. Another challenge is to increase the number of cadaveric donations.

Conclusions: The success of LT in India has shown that the program is reliable, replicable and affordable. Challenges in the form of establishing a national LT registry and providing better post-transplant care remain.

376 CONTRIBUTION OF GI ENDOSCOPIC BIOPSY FOR DIAGNOSIS OF ACUTE GRAFT-VERSUS-HOST DISEASE (GVHD) IN CHILDREN

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Introduction and Aims: GVHD remains a major complication of allogeneic Hematopoietic stem cell transplant (HSCT) with skin followed by GI tract commonly involved at the onset of acute GVHD (aGVHD). GI aGVHD is diagnosed by histological examination of endoscopic mucosal biopsies. This study was undertaken to better guide the investigation of children with suspected GI aGVHD (<100 days post-transplant). Our aim was to determine whether recto-sigmoid biopsies alone would be sufficient in establishing the diagnosis of GI aGVHD.

Methods: A retrospective case chart analysis was performed on all consecutive children (< 18 years) who had undergone endoscopy for suspected GI aGVHD within 100 days of an allogeneic stem cell transplant from July 2008 to August 2015 at a tertiary pediatric hemato-oncology centre. Electronic histology reporting services, the HSCT database and operating theatre records were utilised to identify patients. GI GVHD was defined histologically as the presence of gland apoptosis, not explained by other inflammatory or infectious etiologies. The patient was diagnosed with GI aGVHD if at least one biopsy site was positive.

Results: 22 patients with 24 endoscopic procedures, M14:F8 with a median age of 5.7 years (range 0.5 – 16.6) were included. Those children without histological evidence of GvHD or *Clostridium difficile* infection were excluded (n=7). All our patients underwent simultaneous upper GI and lower endoscopies. The common endoscopic finding was normal mucosa (27%) and the most common symptom was diarrhea (100%). Nearly 60% of children presented with predominantly lower GI symptoms and 9% with upper GI symptoms only. The diagnostic yield at oesophagus, stomach, and duodenum biopsies were 13%, 42% and 67% respectively. The overall yield from upper GI endoscopic biopsies was 79%. The diagnostic yield for recto-sigmoid biopsy was 96% including in patients presenting with upper GI symptoms. In a sub-group of 10 patients who had ileo-colonoscopy diagnostic yield at terminal ileum, cecum, colonic and recto-sigmoid was 83%, 88%, 100%, and 100% respectively. In only one patient diagnosis was achieved on upper GI endoscopy biopsy they then had a further endoscopy 3 weeks later showing GVHD on both upper and lower GI biopsies. No complications were identified secondary to endoscopy but one patient developed hypotension requiring fluid resuscitation, and another bled secondary to liver biopsy.

Conclusion: As suggested in other adult studies, biopsy of recto-sigmoid was best in diagnosing GI aGVHD regardless of symptom presentation in our cohort. In patients with a high index of suspicion with negative feature on sigmoidoscopy, a combined ileo-colonoscopy and upper GI endoscopy biopsy may be considered.

377 PILOT STUDY TO DESCRIBE THE PREVALNCE OF NEUROCOGNITIVE DISORDERS, THEIR MEDICAL PRECURSORS, AND ACCESS TO EDUCATIONAL SERVICES IN PEDIATRIC RECIPIENTS OF LIVER TRANSPLANT

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Advances in medical treatment have resulted in increased survival rates for children undergoing liver transplantation. With increased survival rates, our awareness of the significant neurocognitive deficits impacting these patients has been heightened. Recent studies have documented neurocognitive and academic deficits related to liver disease and subsequent liver transplantation though very little is known regarding the provision of early intervention (EI) and school-based educational services for those in need. As such, the present retrospective study aimed to describe the relations between documented neurocognitive or academic deficits and EI or school-based educational services in a sample of pediatric patients followed in the liver transplant clinic at a pediatric academic medical center located in the southeastern United States. We hypothesized that a significant proportion of patients with neurocognitive or academic deficits would not be receiving formal services to address these concerns, whether through EI or an individualized education plan delivered through their school. Our sample consisted of 74 patients who had been diagnosed with liver disease and had received or were listed to receive a liver transplant between the ages of 2 to 19 years (55% female, 47% Caucasian). In this sample, 37 (50%) had neurocognitive or academic deficits as determined by independent neuropsychological assessment or via school evaluation. The two most common diagnoses reported for patients were Global Developmental Delay (in patients 5 years or under) or Intellectual Disability (in patients age 6 and above). Of these patients, 21 (57%) were not receiving any kind of educational or academic services. The most common medical diagnosis for those with documented neurocognitive or academic concern was biliary atresia though more research is needed to understand the exact mechanisms underlying neurocognitive impairment in patients who have undergone liver transplantation. While preliminary, these results support the need for the development of a more standardized protocol for identifying patients at risk for neurocognitive deficits and helping families to obtain appropriate educational interventions in their local communities.

378 PELD EXCEPTION FOR METABOLIC DISORDERS AND THE IMPACT ON LIVER TRANSPLANTATION IN CHILDREN

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Background: The pediatric end-stage liver disease (PELD) score is used to prioritize pediatric liver transplants from deceased donors in the United States. For metabolic disorders characterized by episodes of life threatening decompensation a timely transplant may avert death or major neurologic injury. These patients are eligible for PELD exception under current United Network of Organ Sharing (UNOS) practices and therefore may impact children transplanted for other disorders.

Method: Data were reviewed from the report of the Organ Procurement and Transplantation (OPTN) on pediatric transplants in the modern era 2002-2015. Wait-list and outcome data for patients for designated metabolic disorders (MD) and the total (T) pediatric transplants and patients with biliary atresia (BA) (group with primary liver disease) were compared.

Results: The total (T) number of pediatric liver transplants during this time was 10637, of which 3268 (30.7%) were for BA and 447 (4.2%) for MD. For region 2 these were respectively, T, 1716, BA 387 (11.8%) and MD 132 (29.5%). There was a gradual increase in the number of wait-listed for transplant for MD during the time period while the numbers of BA have remained steady and total transplants peaked in 2005. The number of transplants followed a similar pattern. The most common PELD score at listing was <15 for 54%, 58.4% and 96.6% respectively, p<0.05. At transplant the most common PELD group was 15-35 for T (37.7%), 15-35 for BA (48.4%) and 1B (42.5%).

The median time (in days) to deceased donor transplant was the lower for MD vs. BA, 109 (91-123) and 176 (160-192) and particularly long for BA in region 2. The probability of death (%) on the wait-list was also lower for MD vs. BA, 3.81 vs. 2.02. However mortality on the wait-list for BA decreased over successive time periods 2002-2005, 5.05%, 2006-2010, 4.34% and 2011-2015, 2.31%.

The patient survival (%) was better for the MD versus BA at 1 year (96.2 vs. 93.04), 3 years (94.76 vs. 92.01) and 5 years (92.26 vs. 90.64); similarly the graft survival. These trends were maintained for successive time periods and in region 2, respectively (97.4 vs. 96.54), 3 years (94.84 vs. 92.86) and 5 years (92.96 vs. 92.86)

Conclusion: There is an impact on children with liver failure on the liver transplant wait-list, particularly the wait-list time in regions where a large proportion of children with MD receive exception scores in the PELD system.

379 DE NOVO AUTOIMMUNE HEPATITIS IN FIRST HIGH VOLUME PEDIATRIC LIVER TRANSPLANTATION PROGRAM IN SAUDI ARABIA

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Objectives and study: The development of de novo autoimmune hepatitis (AIH) after liver transplantation (LT) has been described in both pediatric and adult populations. Unlike classic AIH, this condition does not have defined diagnostic criteria and is diagnosed mainly by the exclusion of other conditions. We examined the clinical presentation, pathologic features, association and treatment of De novo autoimmune hepatitis occurring after liver transplantation (LT) that is unrelated to disease recurrence.

Material and Methods: Between January 2011 and December 2015, 198 pediatric liver transplants were performed at King Faisal Specialist Hospital and Research Centre, the first high-volume pediatric liver transplant program in Saudi Arabia, mostly from living donors (n=185, 93.4%). Seven percent of transplants were performed from deceased donors (n=13, 6.6%). The most common indications for liver transplants were Progressive familial intrahepatic cholestasis (PFIC), biliary atresia, Criglar najjar syndrome, urea cycle defect, Alagile Syndrome, hepatoblastoma, hepatocellular carcinoma, congenital hepatic fibrosis, tyrosinemia, hyperoxaluria type 1, bile acid synthesis defect, Wilson's disease, glycogen storage disease, sclerosing cholangitis and acute liver failure.

A retrospective review of all patients (n=198) who underwent liver transplantation at our institution from 2011 to 2015 was undertaken. Patients were selected based on a laboratory diagnosis of hepatitis. The patient's charts reviewed for possible causes or association, duration, and outcome.

Results: Six cases were identified (3%). They were transplanted for biliary atresia (n=4), urea cycle defect (n=1) and sclerosing cholangitis (n=1), and presented with the features of acute hepatitis in otherwise stable transplant recipients. All have positive autoimmune work-up and positive histopathological findings without significant correlation of their serum immunoglobulin level which is usually the case in *de novo* (AIH). It is of interest to mention that we are adopting a tacrolimus-based immunosuppression protocol. Mycophenolate will be added only in special cases as ABO-I and indications like nephrotoxicity and recurrent acute cellular rejections. Four of them were associated with biliary stricture either at time of diagnosis or shortly after.

All patients were successfully treated with steroids, azathioprine and low doses of tacrolimus to keep level (2-4 ng/mL).

Conclusions: We are reporting that even with differing indications for liver transplantation (LT) and being purely a living-related donor (LRD) program, the incidence of *de novo* AIH is low and does not impact long-term survival. Keeping in mind that familial and metabolic cases are the major indications for liver transplantations in our centre, and the high percentage of *de novo* (AIH) in biliary atresia cases (75%) strongly support that more studies to look for the pathophysiology of biliary atresia as an autoimmune disease are needed.

380 LONG-TERM OUTCOME OF 10-YEAR PEDIATRIC SURVIVORS AFTER LIVING-DONOR LIVER TRANSPLANTATION

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Background: Liver transplantation (LT) is a well-established treatment for children with end-stage liver disease. The overall life expectancy for adult LT is 22.2 years. However, the longevity of liver graft should be longer for children, most of whom have LT during the early period of life. The aim of the study was to determine health-related profiles of 10-year pediatric survivors after living-donor liver transplantation (LDLT) at a single center.

Methods: The study was a retrospective analysis characterizing patients alive 10 years among patients with LDLT from 1994 to 2014 at Seoul Asan Medical Center. From the study period, 101 children was identified. Patients who had died (n=19) and patients from whom data for 10-yr anniversary follow-up visit was not available were excluded from analysis.

Results: A total of 79 10-year survivors was identified, all of whom received daily immunosuppressant therapy. The indications of LDLT were biliary atresia (n=51, 64.6%), acute liver failure (n=11, 13.9%), and idiopathic cirrhosis (n=7, 8.9%), and others (n=10, 12.7%). Cumulative Rate of graft survival at 10 years among 10-yr survivors was 95.1%. Cumulative rates of acute and chronic rejection at 10 years post-transplantation were 51.6% and 3.7%, respectively. Impaired linear growth (Z-score <-2) was noted among 30 (38%) patient. The absence of health-related problems was associated with normal linear growth ($p=0.03$, Chi-square test). Six (7.6%) patients experienced seizure and two (2.5%) had neuropsychiatric symptoms. However, moderate-to-severe mental retardation was nil. Autoimmune hepatitis and *de novo* hepatitis B were noted in 2 (2.5%) and 9 (11.4%) patients, respectively. Co-morbidities associated with the post-LT course included post-transplantation lymphoproliferative disease (n=9, 11.3%), renal dysfunction (n=2, 2.5%), hypercholesterolemia (n=2, 2.5%), and diabetes mellitus (n=9, 11.3%).

Conclusion: Despite a long-term survival after LDLT, a variety of health-related problems may affect the life quality of 10-year pediatric survivors. To prevent impaired growth in long-term survivors, optimized health-care may be essential.

381 DIFFERENT ETIOLOGIES WITH VARIABLE PROGNOSIS IN CHILDREN WITH ACUTE LIVER FAILURE IN A SINGLE CENTER IN ARGENTINA: PELD PERFORMANCE AS A PROGNOSTIC MARKER

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Background and Aim: Acute liver failure is a critical medical condition and the prognosis in these patients is highly variable and depends on multiple factors. There is significant geographic variation in the etiologies and prognoses of acute liver failure (ALF). The aims of the present

study were to determine the causes and short-term outcomes of ALF and to evaluate the performance of prognostic criteria using PELD score over the course of fifteen years of experience.

Patients and Methods: Retrospective review of clinical charts of patients with ALF in 57 consecutive patients younger than 18 years who presented with ALF admitted to a liver transplantation program from January 2000 to December 2015.

Results: Mean (SD) age of patients was 6.02 ± 5.2 years (range 3 months–17 years); 77.7% females (n=39). Etiologies of ALF were autoimmune hepatitis (AIH) 31.6 % (18), hepatitis A 19.3% (11), metabolic 19.3% (11), indeterminate 15.8 % (9), toxic 10.5% (6) and other viral etiologies 3.5 % (2). Since 2007 no fulminant hepatic failure secondary to HAV was diagnosed due to the incorporation of the vaccine in our country No acetaminophen overdose was reported. Twenty-eight (35%) were included on the waiting list and LT was performed on 25 patients (43.85%). The one-year survival rate was 96%. Mean PELD score was 33.5 ± 10.3 (range 11-53). PELD scores obtained on admission were significantly higher among non survivors (39.1±10.5) and recipients of a LT (37.9 ± 7.5) compared with those who survived without LT (26.6 ± 9.1) ($p < 0.0001$, 95% CI, 6.9 -16.2). The poor outcome etiologies were viral, indeterminate and metabolic. They had a significantly higher PELD (37.3 ± 4.6) compared to those with a better outcome (AIH and toxic) with a PELD 30.69 ± 0.9 ($p = 0.0001$, 95% CI, 8.36-5.03). **Conclusions:** AIH, hepatitis A and metabolic were the most frequent causes of fulminant hepatic failure in our series. A PELD score ≥ 33 at admission was associated with poor outcome. These could help to establish the optimal timing for LT evaluation and listing depending on the etiology of ALF. Further validation in larger and more diverse populations is needed.

382 RISKS FACTORS FOR IMMUNE HEMOLYTIC ANEMIA AFTER PEDIATRIC LIVER TRANSPLANTATION.

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Objectives and Study: Immune hemolytic anemia (IHA) is a rare condition occurring after solid organ transplantation. The incidence of which is not known. The aim of this retrospective study was to analyze a single center cohort in order to identify potential risk factors.

Methods: Donor, recipient and surgical parameters were collected from the records of 96 children having received a liver transplant (LT) between the years 2000-2013. IHA was defined as acute anemia with positive direct Coombs. Using IHA as the outcome, univariate data's were compared by Fischer's exact test and by Mann-Whitney test. A p value of 0.05 was considered as significant. Early IHA was defined as IHA occurring during the first 3 months after LT and late IHA as IHA occurring more than 3 months after LT.

Results: Seven (7/96) patients with IHA were identified (Table 1). All patients received a primary immunosuppressive protocol consisting of tacrolimus, basiliximab and corticosteroids for three months. Patients with early IHA were treated by corticosteroids or immunoglobulins. All patients with late IHA (4/4) were refractory to this treatment but later responded to rituximab.

Development of IHA was significantly ($p = 0.04$) associated with biliary atresia (BA) and young age at LT ($p = 0.04$). The use of IGL1 preservation solution seemed also to favor the development of IHA ($p = 0.05$). Viral infections occurring more than 3 months after transplantation were also associated with development of late IHA ($p = 0.01$). Patients at high risk of CMV infection (defined as positive donor and negative recipient serology at LT) were also at higher risk of developing IHA ($p = 0.035$). Likewise, there was a significant association between the onset of IHA and CMV primary infection during first year post-LT ($p = 0.03$).

Table 1: Description of 7 cases of AIHA occurring before one year after transplantation. * At transplant BA Biliary Atresia. IHA: Auto-immune hemolytic anemia

Conclusion: The incidence of IHA following pediatric LT was 7% in this cohort. There were two distinct clinical phenotypes: early and late. They differed by differential response to treatment. These findings should encourage clinicians to look for IHA, especially among younger recipients, who may be more vulnerable to viral infections. The association between AIHA and the use of the IGL-1 preservation solution needs to be investigated further since this is a novel finding. It seems that CMV infection, known to be an important cause of morbidity early post-LT may also contribute to IHA, adding credence to the importance of primary prophylaxis. Therefore, it can be argued that others viruses should be sought and considered among potential culprits.

Primary diagnosis	Age* (months)	AIHA onset (time after transplant)	Direct Coombs test	Red blood cell antibody	Infectious trigger	Preservative Solution
EARLY AIHA						
BA	13	9 days	++	Anti A1 (Allo or Auto)	no	UW
BA	5	9 days	+	Not searched	Laryngitis	UW
Alpha 1 anti-trypsin deficiency	119	9 days	+++	Not searched	no	IGL 1
LATE AIHA						
BA	8	10 months	++++	Warm IgG Auto - AntiC	CMV Primary Infection	UW
BA	8	11 months	+++	Warm IgG and IgM Auto - Antibodies	Viral gastro-enteritis	IGL1
BA	7	7 months	+++	Warm IgG and IgM Cold agglutinins Auto - Antibodies	Viral gastro-enteritis	UW
BA	12	8 months	+++	Warm IgG Auto - Anti-e	Clostridium enteritis	IGL1

Table 1: Description of 7 cases of AIHA occurring before one year after transplantation. * At transplant

BA= Biliary Atresia. AIHA: Auto-immune hemolytic anemia

383 *EVALUATION OF INTESTINAL INFLAMMATION WITH FECAL CALPROTECTIN IN PEDIATRIC LIVER TRANSPLANT PATIENTS*
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Objectives and Study: Fecal calprotectin (FC) is a neutrophilic protein found in stool which is markedly elevated in inflammatory conditions affecting gastrointestinal system, even when symptoms are obscured and hematologic markers are negative. Risk factors that have been associated with development of intestinal inflammatory conditions after liver transplantation include acute CMV infection, gastrointestinal allergies and use immunosuppressant drugs. This study investigates frequency and etiologies of gastrointestinal inflammation in post-transplant children taking immunosuppressive medications.

Methods: All children younger than 18 years, who underwent liver transplantation between 2000 and 2013, transplanted at least 3 months ago during evaluation were included. The control group was healthy children not taking any medication and without gastrointestinal symptom or disease. Children with FC values >50 µg/g were asked to deliver an additional stool sample (one month apart from the first) in both groups. FC was measured with an improved enzyme linked immunosorbent assay method (Hycult® Biotech, Netherlands). All patients underwent a complete evaluation including: clinical status, erythrocyte sedimentation rate, C-reactive protein and total blood count determination.

Results: Stool samples from 80 children who underwent liver transplantation with average age of 97.4 months (± 53.6) were collected. The average age of the 25 children at control group was 111 months (± 52.8). The overall median FC concentration was 52 µg/g (min 4-max 440) in liver transplant patients and 45 µg/g (min 10-max 64) in healthy children. There was not statistical difference between two groups ($p=0.101$). All patients with high FC levels had negative CMV DNA study. Stool cultures for bacterial pathogens and *Clostridia difficile* toxin were negative. Children with average FC concentration 100-200 µg/g underwent upper endoscopy for excluding celiac disease and other diseases. In 2 children with FC levels above 200 µg/g colonoscopy was done. In first child colonic biopsy I was reported as lymphoid hyperplasia in all colonic segments (food allergy?), second patient: intra-epitelial lymphocytosis in all segments (20/100: lymphocytic colitis). First patient had intestinal amyloidosis detected 1 year after and second patient had diabetes mellitus, renal failure and heavy rejection detected 2 years after and both patient die because of this complications.

Conclusion: Post-transplant gastrointestinal inflammatory involvement may need to be considered in patients on immunomodulatory medications. High fecal calprotectin levels (especially if above 200µg/g) may show not only local intestinal inflammation, but may be associated with systemic involvement especially in transplant patients. Increased fecal calprotectin screening can be used as a non-invasive marker that might aid in the diagnosis both for local and systemic involvement.

384 *OUTCOME OF LIVER TRANSPLANTATION IN CHILDREN WITH HEPATOPULMONARY SYNDROME: A RETROSPECTIVE ANALYSIS OF THE UNOS DATABASE*

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Background: Hepatopulmonary syndrome (HPS) is diagnosed in the presence of hypoxemia due to intrapulmonary vascular shunting in patients with chronic liver disease and/or portal hypertension. Children with HPS associated with partial pressure of arterial oxygen < 60 mm Hg on room air are given exception points when listed for liver transplantation (LT) due to higher pre-transplant mortality. However, outcomes of LT in children with HPS have not been well-studied.

Aim: Evaluate the outcome of LT in children with HPS.

Methods: We performed a retrospective analysis of data from UNOS of all children aged <18 years who were listed for their first LT after the implementation of MELD (2/27/2002). Patients were then divided into 2 groups: those with at least 1 approved exception for HPS (the HPS group) and those with no approved exception for HPS (the non-HPS group). Propensity score matching was used to match each HPS patient to 3 non-HPS patients. Kaplan-Meier product limit estimates were used to assess 3-month patient and graft survival post-LT.

Results: A total of 364 children listed for LT were included in the analysis of which 273 belonged to non-HPS group and 91 belonged to HPS group. There was no significant difference in mean PELD/MELD between 2 groups at the time of listing. Median time on wait list was 3.3 months during which time 75% of subjects received LT and 6% of them died. There was no significant difference in cumulative pre-LT mortality rates between HPS and non-HPS group. 183 non-HPS and 72 HPS patients with a cadaveric donor were assessed for post-LT outcome. HPS group patients had a significantly longer length of stay in hospital post-LT (19 days vs. 15 days, $p=0.04$). There was no significant difference in post-LT patient survival, graft survival and re-transplantation between HPS and non-HPS groups.

Conclusion: Although patients with HPS required longer duration of hospitalization post-LT, there was no significant difference in pre-LT mortality, post-LT patient or graft survival, and re-transplantation.

385 *DEMOGRAPHIC AND EPIDEMIOLOGIC DESCRIPTION OF A PATIENTS WITH ALLERGIC DISEASES IN A PEDIATRIC LIVER TRANSPLANTATION PROGRAM IN CALI-COLOMBIA*

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Introduction: The incidence of allergic disease in pediatric patients post-liver transplantation is increasingly documented, a prevalence between 10% and 17% is estimated. Results of previous studies have suggested that immunosuppressive drugs such as tacrolimus may reduce tolerance and trigger allergic reactions. The objective of this study is to describe epidemiologically pediatric patients who underwent liver transplantation and then developed allergic disease.

Methodology: A systematic review of the medical records of patients who underwent liver transplantation during the period of January 2008 and December 2015.

Results: A total of 267 transplant patients were found, of whom ten have a diagnosis of allergic disease, confirmed by the performance of skin tests or specific IgE. Three of these patients were diagnosed with eosinophilic esophagitis and associated food allergy. Two patients had symptoms and signs of anaphylaxis triggered by food; one patient had respiratory allergy diagnosed with rhinitis. All patients were receiving immunomodulatory management with tacrolimus. Six of our patients had living donor liver transplantation and four with cadaveric donor.

Conclusions: The occurrence of allergic disease, particularly food allergy, is an established complication in post-liver transplantation children, which has an important impact in the quality of life of patients. Allergies reactions are mostly IgE-mediated and can be life-threatening. as

observed in two of our patients. The pathogenesis of allergic disease associated with liver transplantation remains unclear and is probably multifactorial; therefore, more studies should be conducted.

386 UTILITY OF ACOUSTIC RADIATION FORCE IMPULSE (ARFI) ELASTOGRAPHY IN PREDICTING GRAFT FIBROSIS AS COMPARED TO HISTOLOGY FROM LIVER BIOPSY IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

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Background: Liver fibrosis and graft rejection are among the main complications seen in pediatric liver transplant (LT) recipients. Post-transplant graft fibrosis may occur in more than 67% of patients and the degree of fibrosis can vary from mild to severe. Acoustic radiation force impulse (ARFI) is a noninvasive method that has been used to measure liver tissue stiffness using shear wave pulse in adult patients with chronic hepatitis C.

Objective: To predict the clinical utility of ARFI elastography in predicting liver graft fibrosis compared to liver histopathology in pediatric liver transplant recipients.

Material and Methods: This was a prospective study done between April 2015 and April 2016, comparing ARFI elastography with liver histopathology in pediatric liver transplant recipients. Thirty patients were enrolled after the study was approved by our Institutional Review Board and informed consent and assents were obtained. Patients underwent transplant protocol liver biopsies and had ARFI measurements taken at the liver biopsy site during ultrasound marking for the liver biopsy. The ARFI shear wave velocity (SWV) measurements were expressed as meters per second and were compared to the following patient groups: those who demonstrated no fibrosis versus any fibrosis (Metavir F0 vs. Metavir F1 to 4) on liver biopsy.

Results: There were equal numbers of male and female subjects in our study. Age of the graft at the time of liver biopsy ranged from 1 year to 19.4 years with a median age of 8.8 years. Most patients underwent liver transplantation for biliary atresia (57%). One-third of patients were transplanted with a graft from a living donor. Half of the patients (15/30) received a left lateral segment either from living donor or a cadaveric donor, while 43% received a cadaveric whole liver. Seventy percent (21/30) had no fibrosis on liver biopsy and none of the patients had cirrhosis. There was a significant difference (p values 0.041) in mean ARFI SWV measurements between the group with no fibrosis (Metavir F0) on liver biopsy versus the group in which any fibrosis was noted (Metavir F1 to 4). There appeared to be a trend showing an increase in ARFI SWV with increasing fibrosis grades on liver biopsy; however it did not reach significance, which could have been due to the small number of patients in our study.

Conclusions: Acoustic radiation force impulse (ARFI) elastography is a feasible, simple, quick, reliable and noninvasive method to measure liver stiffness in pediatric LT recipients and is able to detect the presence of fibrosis in post-liver transplant recipients. Future studies are needed to determine whether ARFI can distinguish between various grades of fibrosis in pediatric liver transplant patients.

387 PEDIATRIC LIVER TRANSPLANTATION FOR METABOLIC LIVER DISEASE IN KUWAIT

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Background: The liver is a highly metabolic organ where many pathways of intermediary metabolism are located. Dysfunction in any of those pathways may lead to deleterious hepatic or extrahepatic manifestations known as metabolic liver disease (MLD). MLD is currently being recognized as an important indication for pediatric liver transplantation (LT).

Objectives: To study pediatric MLD patients in Kuwait who were managed with LT.

Subjects and methods: The records of all LT patients followed up in the pediatric gastroenterology unit from January 2000 to May 2016 were retrospectively reviewed.

Results: Among the 62 pediatric LT cases followed, MLD was the indication in 52% of cases while biliary atresia in 24% and other disorders in 24% as well. Progressive familial intrahepatic cholestasis and Crigler Najjar syndrome were the main categories among MLD cases. Kuwaiti nationals were 81% and 56% were females. The median age at transplant was 5 years (Range: 0.4-13.5) and 22% were ≤ 1 year. Extrahepatic manifestations were the main problem in 50% of MLD cases before LT. The majority (72%) received a cadaveric transplant with a whole liver graft in 74%. Combined liver and kidney transplant was performed in 13% of cases. All patients were maintained on tacrolimus but a combination with mycophenolate mofetil and prednisolone were required in 41 and 28% respectively. Post-LT complications included hepatic artery thrombosis, biliary strictures and post-transplant lymphoproliferative disease were encountered in 6, 8 and 2 patients respectively. A re-transplantation was required in 3 patients due to acute graft dysfunction. The patient survival rates at 1 and 5 years were 97 and 94% respectively; however, the graft survival rates were 90 and 88% at 1 and 5 years respectively. On follow-up, 31% of the patients manifested with neurodevelopmental delay.

Conclusion: MLD constitutes the major indication of pediatric LT in Kuwait. Considering the high consanguinity rate, many MLD cases are pooled thus increasing the demand on LT, especially when most families prefer post-transplant quality of life.

388 SUBCLINICAL CARDIOVASCULAR CHANGES IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

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Background: Cardiovascular (CV) disease is a major cause of morbidity and mortality in adult liver transplant recipients. There is an increased prevalence of metabolic syndrome in children following liver transplantation. Despite a plethora of data on atherosclerosis and arterial stiffness in other pediatric solid organ transplant recipients, it is currently not known whether pediatric liver transplant patients have subclinical CV disease. The objective of this study was to investigate the presence of subclinical CV changes in pediatric liver transplant recipients.

Methods: This is a cross-sectional study performed in a single institution. Inclusion criteria were age 8-18 years and a minimum of 1 year since liver transplant. We performed detailed echocardiography, central pulse wave velocity (pWV) and carotid intima-media thickness (cIMT) measurements. We compared the results to age- and gender-matched healthy controls. Given the paucity of data in pediatric liver transplant recipients, sample size was calculated using pWV measurements from the pediatric renal transplant literature. Based on that, a sample size of 16 patients would be needed to detect a mean pWV difference of 0.75 m/sec (SD of 0.9) with a power of 0.9.

Results: Detailed measurements were obtained from 20 patients and 20 healthy controls (60% female). The most frequent pre-transplant diagnosis was biliary atresia (50%). Mean age was 5 years (SD± 5) with median time since transplant of 7.2 years (range 1.7-16.5 years). There was no significant difference in pWV between patients and healthy controls (6.9 ± 24.2 m/sec vs. 15.9 ± 208.2 m/s; *p*=0.84, respectively). There was also no difference in cIMT measurements between patients and healthy controls (0.043 ± .003 vs. 0.044 ± 2.1 mm; *p*=0.962, respectively). There was also no statistical significance in left ventricular mass between patients and healthy controls (1312 ± 3990 vs. 5558.4 ± 14747 gm, *p*=0.8711, respectively).

Conclusions: Despite reports suggesting an increased prevalence of metabolic syndrome in pediatric liver transplant recipients, this study does not reveal significant subclinical CV changes at a median time of 7 years post-transplant. Larger studies are needed to investigate this further.

389 OUTCOMES OF POSITIVE STERILITY CULTURES IN CHILDREN UNDERGOING TOTAL PANCREATECTOMY AND ISLET AUTOTRANSPLANT

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Purpose: Total Pancreatectomy and Islet Autotransplant (TPIAT) is increasingly being utilized as treatment for children with severe chronic pancreatitis refractory to medical and endoscopic-therapy. The pancreas is removed entirely and the pancreatic islets are isolated and infused back into the patient's liver, where they engraft and function. Cultures from the final islet preparation are frequently positive for bacterial organisms. It is unknown whether these positive cultures are associated with adverse short- or long-term effects for pediatric patients.

Methods: Children (n=86) who underwent TP-IAT between January 2006 and March 2015 were reviewed. Data reviewed included patient demographics, pancreatitis etiology, prior pancreatic interventions, operation duration, sterility culture results, islet yield, post-operative islet cell function, hospital length-of-stay (LOS), and 30-day post-operative infection. Outcomes were compared between patients with positive sterility cultures (n=57) and patients with negative sterility cultures (n=29).

Results: Patients who had undergone previous pancreas surgery are more likely to have positive cultures than those with intact pancreata (*p* value 0.0002). Positive cultures were also associated with increased number of pre-operative ERCPS: 3-3.5 ERCPS versus 1-1.4 (*p* value <0.0001). Patients with positive sterility cultures were less likely to be diagnosed with a post-operative infection (*P* = 0.05). Culture status did not impact hospital length of stay (*p* value 0.49). Patients with positive sterility cultures were less likely to achieve insulin independence at 3 months (*p* value 0.030) and more likely to develop graft failure at 2 years (*p* value 0.041).

Conclusions: Positive sterility cultures during TPIAT do not increase pediatric patients' risk of post-operative infection or prolong hospital length of stay. However, positive cultures are, however, associated with decreased rates of early insulin independence and increased rates of islet graft failure at 2 years, possibly due to increased inflammatory response interfering with engraftment. Patients are more likely to have positive sterility cultures if they have had previous pancreatic surgery or multiple ERCPS.

Originality: The data presented in this abstract is original and has not been previously published or presented.

Table 1. Patient Demographic Characteristics and Sterility Culture Results

	All patients (n = 86)	≥ 1 positive culture (n = 57)	2 negative cultures (n = 29)	P
Gender, n (%)				
Male	34 (39.5)	17 (29.8)	17 (58.6)	0.019
Female	52 (60.5)	40 (70.2)	12 (41.4)	
Age, mean ± SE, range	12.77 ± 0.42, 3-18	12.89 ± 0.54, 3-18	12.55 ± 0.70, 5-18	0.70
Year, mean ± SE, range	2011.24 ± 0.27, 2006-2015	2011.16 ± 0.34, 2006-2015	2011.41 ± 0.47, 2006-2015	0.66
Symptom duration in years, mean ± SE	7.57 ± 0.45	7.80 ± 0.57	7.08 ± 0.70	0.42
Hospital LOS, mean ± SE	20.95 ± 1.21	20.04 ± 1.29	22.76 ± 2.55	0.29
Previous ERCPS, mean ± SE	2.44 ± 0.34	3.19 ± 0.47	0.97 ± 0.28	<0.0001
Previous pancreas surgery, n (%)	12 (14.0)	12 (21.1)	0 (0)	0.007
IEQ/kg infused, mean ± SE	4697.08 ± 342.3	4697.91 ± 449.55	4695.45 ± 510.27	0.99
< 2,500, n (%)	25 (29.1)	19 (33.3)	6 (20.7)	0.32
2,500-5,000, n (%)	25 (29.1)	14 (24.6)	11 (37.9)	
>5,000, n (%)	36 (41.9)	24 (42.1)	12 (41.4)	
Posttransplant Infections, n (%)	41 (47.7)	27 (47.4)	14 (48.3)	1.00
Insulin independence, % at 1 year (n = 76), % at 2 years (n = 57)	32.9, 49.1	34.0, 48.7	30.8, 50.0	1.00, 1.00
Graft failure, % at 1 year (n = 76), % at 2 years (n = 57)	10.5, 17.5	12.00, 23.08	7.69, 5.56	0.71, 0.15

ERCP = endoscopic retrograde cholangiopancreatography; IEQ = islet equivalents; LOS = length of stay; SE = standard error

390 LAPAROSCOPIC-ASSISTED VERSUS OPEN TOTAL PANCREATECTOMY AND ISLET AUTOTRANSPLANTATION: A CASE-MATCHED STUDY OF PEDIATRIC PATIENTS

Srinath Chinnakotla, Megan Berger, Kaustav Majumder, Melena Bellin, Sarah J. Schwarzenberg, Ty Dunn, Timothy Pruett, Gregory Beilman, University of Minnesota, Minneapolis, MN, USA

Purpose: Chronic pancreatitis is a rare but debilitating disease affecting pediatric patients. Total Pancreatectomy and Islet Autotransplantation (TP-IAT) is a potential treatment for patients who are refractory to medical endoscopic or surgical drainage procedures. A partially laparoscopic approach allows for a smaller incision while simultaneously providing excellent visualization of the distal pancreas and spleen during resection. A minimally-invasive approach has proven advantageous for other pediatric procedures, but its value is not clear for this rare operation. This retrospective review compares short- and long-term outcomes between patients who receive laparoscopic-assisted versus open TP-IAT. **Methods:** Children (n=18) who underwent laparoscopic-assisted TP-IAT from 2013-2015 were compared with case-matched children (n=18) who underwent open TP-IAT from 2011 to 2015. Patients were matched based on age, gender, and duration of pancreatitis, previous surgery /endoscopic procedures, and pancreatic fibrosis scores. Data reviewed included operative time, hospital length-of-stay, estimated blood loss, intraoperative transfusions, post-operative complications, graft function, and narcotic use. Between-group differences were compared using Wilcoxon rank-sum, Fisher's exact, or T-tests.

Results: There was no perioperative mortality. Surgical complications were similar between the two groups ($p = 0.44$) and included wound complications (n=11), chyle leak (n=6), bowel obstruction (n 4), bile leak (n 3), and GI bleed (n 2). Operative times were not significantly different ($p = 0.11$) with a median of 562 minutes (IQR 483-615) for open and 577 minutes (IQR 520-678) for laparoscopic-assisted cases. Hospital length-of-stay did not differ between groups (21.89 vs. 22.78 days, $p=0.81$). There was no difference in long-term narcotic use ($p = .417$) or islet graft function ($p = .408$) between the groups.

Conclusions: Preliminary data indicates that outcomes for laparoscopic-assisted TP-IAT are equivalent to open TP-IAT. In young patients, a minimally-invasive approach does not compromise safety, effectiveness, or operative efficiency and may be used based on surgeon and patient preference.

Table 1. Patient Outcomes

	Open TPIAT (n = 21)	Laparoscopic- Assisted TPIAT (n = 21)	P
OR time in minutes, mean ± SE	567 ± 23	612 ± 23	0.2
EBL in mL, mean ± SE	313 ± 55	310 ± 55	1
pRBCs transfused/patient in units, mean ± SE	0.67 ± 0.17	0.43 ± 0.18	0.3
IEQ/kg transplanted, mean ± SE	4352.4 ± 650.5	5751.0 ± 679.2	0.2
Post-transplant Complications, n (%)			
None	12 (57.1)	8 (38.1)	0.5
Wound Complication	6 (28.6)	5 (23.8)	1
Bile Leak	1 (4.8)	2 (9.5)	1
Bowel Obstruction	1 (4.8)	4 (19.0)	0.3
Chyle Leak	1 (4.8)	6 (28.6)	0.1
Gastrointestinal Bleed	2 (9.5)	0 (0)	0.5
Pneumonia	1 (4.8)	0 (0)	1
Hospital LOS in days, mean ± SE	20.67 ± 2.40	22.1 ± 2.22	0.7
Insulin independence post-operatively, n (%)			
3 months	1/21 (4.8)	0/21 (0)	1
6 months	3/21 (14.3)	2/21 (9.5)	1
1 year	6/20 (30.0)	4/15 (26.7)	1
2 years	5/15 (33.3)	3/6 (50.0)	0.6
Baseline narcotic use in daily Oral Morphine Equivalents, mean ± SE	35.8 ± 9.6	58.7 ± 15.0	0.2
Narcotic use above baseline during first post-operative week in daily Oral Morphine Equivalents, mean ± SE	203.9 ± 141.3	264.2 ± 186.0	0.2
Narcotic use post-operatively, n (%)			
3 months	11/21 (52.4)	11/21 (52.4)	1
6 months	4/21 (19.0)	9/19 (47.4)	0.1
1 year	3/20 (15.0)	5/16 (31.3)	0.4
2 years	0/13 (0)	1/5 (20.0)	0.3
Patient Scar Assessment Questionnaire Score*, mean ± SE	59 ± 4	55 ± 4	0.4

SE = standard error; EBL = Estimated Blood Loss; IEQ = islet equivalents; LOS = length of stay. *minimum possible score = 28, maximum possible score = 112

Thursday, October 6, 2016

CONCURRENT SESSION II
2:00 PM

NUTRITION AND INTESTINAL REHABILITATION

391 FUT2 SECRETOR STATUS MODIFIES NEONATAL INTESTINAL ADAPTATION FOLLOWING PREMATURE BIRTH

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Preterm infants born <30 weeks gestational age (GA) are at high risk of extrauterine growth restriction (EUGR), which is associated with persistent neurodevelopmental and growth deficits. To achieve appropriate growth in preterm infants, early and aggressive nutritional therapy is key. As enteral function does not initially support nutritional needs, parenteral nutrition (PN) is used to supplement enteral feeding, but prolonged PN increases risk of sepsis and other complications. While clinical protocols for feeding advancement are effective, nevertheless, some preterm infants require prolonged parenteral nutrition, for reasons that are not fully defined. We hypothesize that fucosyltransferase 2 (FUT2) genotype influences intestinal adaptation, and thus, the time required to achieve full enteral feeding. FUT2+ individuals ("secretors") produce abundant carbohydrate on intestinal surfaces and in their milk. We and others have shown that "secretor" carbohydrate enables intestinal adaptation and supports gut homeostasis. In this study, we investigated the relationship between FUT2 secretor status and intestinal adaptation. We conducted a secondary analysis of a prospective cohort of 236 infants who delivered <30 weeks GA, survived to at least 30 days, and provided infant and maternal samples. Thirty infants (12.7%) required prolonged PN, defined as PN for 30 days or more; of these infants, 19 (63%) developed necrotizing enterocolitis (NEC) or late onset sepsis. Infants with prolonged PN were born significantly more premature (median, 25 weeks GA) compared to other infants (27 weeks GA, $p<0.001$). After adjustment for covariates (gestational age, location of birth, breastfeeding, and antibiotic treatment) by logistic regression, non-secretor infants were more likely than secretor infants to have prolonged PN (OR 4.4, CI, 1.5-13.0, $p=0.007$). The association with FUT2 status remained after NEC and sepsis cases were excluded ($p 0.008$). The association between secretor status and prolonged PN was even stronger when both mother and infant were non-secretors ($p 0.001$). We also found decreased growth at 36 weeks corrected GA among non-secretor infants with non-secretor mothers (WAZ -0.5, $p=0.05$; LAZ -0.7, $p=0.03$), after adjusting for significant confounding factors (antibiotic use, GA, breastfeeding, NEC and sepsis) by linear regression. Analysis of the fecal microbiome by whole genome sequencing identified differences between non-secretor and secretor infants, but the strongest difference was found by RNA-Seq analysis: non-secretors had significantly decreased expression of genes involving the citrate cycle and other metabolic pathways. We conclude that FUT2 secretor status impacts growth and intestinal adaptation in the preterm infant associated with alterations in gut microbial metabolism. Methods for augmenting the intestinal microenvironment of preterm infants may improve outcomes in this vulnerable population.

392 PROCESSED SUPERNATANTS FROM LACTOBACILLUS RHAMNOSUS GG CULTURE IMPROVE INTESTINAL BARRIER FUNCTION IN RATS AFTER MASSIVE SMALL BOWEL RESECTION

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Objectives: Intestinal barrier integrity plays an essential role for gastrointestinal health and disease. The aim of this study was to explore potential effects of specific preparations of soluble mediators derived from *Lactobacillus rhamnosus* GG (LGG) on intestinal barrier function in a rat model of short bowel syndrome (SBS).

Methods: 6-week old male SD rats underwent either 75% small bowel resection or bowel transection (sham-operated control), followed by re-anastomosis. Animals were supplemented with 5×10^8 CFU viable LGG, LGG soluble mediator preparation in an equivalent dose or PBS by intragastric gavage daily from day 2 throughout day 14 after small bowel resection. Body weight of the animals was measured regularly. On day 15, intestinal permeability (FD-40), serum levels of endotoxin and bacterial translocation to mesenteric lymph nodes, liver and spleen were assessed. sIgA, TNF- α and IL-6 levels in ileum content and serum were determined by ELISA. Intestinal adaptation was evaluated by assessing villus height and crypt depth. Expression of tight junction proteins including occludin, ZO-1 and claudin-1 and -4 in ileum was measured by western-blotting. Statistical analysis was performed using a one-way ANOVA or a non-parametric test.

Results: Compared with the sham operated group, bowel resection led to significantly lower body weight, increased villus height and crypt depth accompanied with increased intestinal permeability, endotoxin levels as well as bacterial translocation. Most parameters detrimentally affected in this SBS model were improved by the supplementation with viable LGG and LGG soluble mediator preparation, including increased weight gain, reduced bacterial translocation, decreased levels of FD-40 and endotoxin as well as increased levels of sIgA and tight junction protein expression at the end of the experiment. In addition, TNF- α and IL-6 levels in ileum and serum were reduced in the viable LGG and LGG soluble mediator preparation intervention groups.

Conclusions: Enteral supplementation of viable LGG or specific LGG soluble mediators improves intestinal permeability, reduces bacterial translocation, increases intestinal sIgA level and lowers both local and systemic inflammation in a rat model of SBS. The LGG soluble mediator preparation not only mimics some of the biological effects of viable LGG, but even shows stronger effects on reducing inflammation and supporting intestinal barrier integrity and function, likely through upregulation of specific tight junction protein expression.

393 DEVELOPMENT OF URINARY ADIPONECTIN AND FIBROBLAST GROWTH FACTOR-21 ASSAY RAPID KIT FOR THE POPULATION-BASED SCREENING OF PEDIATRIC METABOLIC SYNDROME

Jin Soo Moon, Ahlee Kim, Jae Sung Ko, Ju Young Chang, Youngwon Nam, Kyoungsoon Lee, Sang Hoon Song, Junghan Song, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Jongno-gu, Seoul, South Korea

Objectives and study: Obesity is one of the most important metabolic syndrome in current society, and the prevalence of obesity is increasing. Although there are well-known evaluating values of obesity such as body mass index (BMI) and waist circumference, we need more accurate and noninvasive biomarkers for early screening and evaluation of the pediatric obesity and metabolic syndrome. The purpose of this study is to

develop new biomarkers to clarify the risk stratification and treatment plan for the obese children by analyzing urinary adiponectin (AD) and fibroblast growth factor-21 (FGF-21).

Methods: We used the data from the cohort database of pediatric obesity biomarker project of Ministry of Science, Information & communication technology and Future Planning, South Korea. We selected 93 obese group whose BMI values were > 99 percentile of the population, and 92 controls whose BMI values were between 25 and 75 percentile. The physical information of all individuals were collected. A total of 184 serum and urine samples were obtained from the medical examination. Urinary AD and FGF-21 were measured by ELISA method. The diagnosis of metabolic syndrome was made using the International Diabetes Federation criteria for children and adolescents, using 2007 Korean National Growth Chart.

Results: Urinary AD and FGF-21 level were significantly higher in obese group than normal control ($p=0.021$, 0.006). Urinary AD and FGF-21 level were higher in children with metabolic syndrome, though they were not statistically significant ($p=0.068$, 0.065). When adjusted with creatinine or albumin, urinary AD and FGF-21 were significantly higher in metabolic syndrome ($p=0.013$, 0.037). When comparing metabolic syndrome group and non-metabolic syndrome, only creatinine-adjusted urinary AD was statistically significant ($p = 0.037$). The highest area under the curve (AUC) value was observed in albumin-adjusted urinary AD (0.703). In comparison between metabolic syndrome and normal group, AUC was slightly lower than former analysis. The highest AUC value was also observed in albumin-adjusted urinary AD (0.686). Among all cutoffs, creatinine- and albumin-adjusted cut-offs were determined as statistically significant ($p < 0.001$). In logistic regression analysis, albumin-adjusted urinary AD (Odds ratio 1.192, $p = 0.004$) and FGF-21 (Odds ratio 1.007, $p = 0.01$) showed positive effect on the diagnosis of metabolic syndrome.

Conclusion: Urinary AD and FGF-21 assays can be useful screening biomarkers for screening pediatric obesity and metabolic syndrome due to simple and noninvasive sampling method. Creatinine-adjusted urinary AD may be a reliable biomarker for screening pediatric metabolic syndrome.

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394 DIET QUALITY AND QUALITY OF LIFE IN CHILDREN AND ADOLESCENTS WITH CELIAC DISEASE

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Objective: The gluten-free diet (GFD) is the only treatment in individuals with Celiac disease (CD). However, the GFD has lower amounts of important micronutrients such as folate and is higher in saturated fat and simple sugars than gluten-containing diets. Hence, while many children with CD thrive on the GFD, reduced diet quality (DQ) and quality of life (QOL) is a concern. The study objectives were to compare DQ and QOL in youth with CD on the GFD with youth with minor gastrointestinal (GI) complaints (non-CD disease controls; CON).

Methods: A prospective multi-centre study (Stollery Children's Hospital, Hospital for Sick Children and McMaster Children's Hospital) was conducted. Demographic, anthropometric and laboratory data was collected. Macro-and-micronutrient intake, glycemic index, glycemic load (GL) and DQ were calculated from 24-hr recalls (one weekend/one weekday). DQ was measured using validated tools: Canadian Healthy Eating Diet Index (HEI-C), Dietary Guideline Index for Children and Adolescents (DGI-CA) and Diet Quality Index-International (DQI-I). Validated questionnaires to measure QOL included the PedsQLTM 4.0 (child/parent report) and CDDUX. GI symptoms were assessed using PedsQL GI symptom (parent report).

Results: A total of 130 youth with CD (10 ± 4 yrs; 42M/88F); treated with GFD for 2.0 ± 1.5 years and 70 CON (10 ± 4 yrs; 24M/46F) were recruited. Youth with CD had lower weight for age Z-score (-0.27 ± 1.19) than CON (0.52 ± 0.90) ($p=0.003$), but no differences in height Z-scores were observed between the groups ($p>0.05$). No significant differences were found in energy, macronutrient and glycemic index intake between groups ($p>0.05$). CD youth had lower intakes of folate (as dietary folate equivalents) (CD: 51 ± 24 $\mu\text{g/day}$ vs. CON: 218 ± 88 $\mu\text{g/day}$) and higher intake of GL (CD: 130 ± 43 vs. CON: 106 ± 32) than CON ($p<0.01$). HEI-C (CD: 72 ± 13 , CON: 67 ± 14) and DGI-CA (CD: 67 ± 13 , CON: 61 ± 16) scores were higher in CD than CON ($p<0.05$). Youth with CD and their parents reported better QOL (emotional, school, and psychosocial domains) than CON group ($p<0.05$). Reduced DQ (HEI-C and DGI-CA) was associated with reduced QOL from the parent and child perspectives (HEI-C: Physical, emotional, school and psychosocial; DGI-CA: School and psychosocial). Higher DQ (HEI-C and DGI-CA) scores were related to improved GI symptomology in CON group.

Conclusion: Low DQ was observed in youth with CD and CON; and was associated with worse GI symptomology and lower perceptions of QOL. Nutritional education is necessary to improve DQ in youth with CD and on GFD and youth with functional GI symptoms. Enhanced DQ in youth with CD and GI control may have a positive impact on some domains of QOL.

395 PROBIOTIC AND LACTOFERRIN SUPPLEMENTATION IN PREMATURE INFANTS: WHAT'S GOING ON IN THEIR INTESTINAL MICROBIOME?

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Background: Probiotics and lactoferrin are currently being used in the neonatal intensive care unit (NICU), and have been shown to reduce rates of sepsis and necrotizing enterocolitis. The present study describes the evolution and diversity of the intestinal microbiome of premature infants receiving probiotics with and without lactoferrin.

Methods: Seventy premature infants ranging from 23 0/7 to 30 6/7 weeks gestational age (GA) were recruited within 12 hours of their first enteral feed, from a tertiary care NICU. The subjects were randomized (35 infants per group), to receive a once daily dose of 500 mg of FloraBABY, a probiotic mixture of Bifidobacterium and Lactobacillus (Renew Life Canada, Oakville ON) alone (control group) or probiotic with the addition of a once daily dose of 100 mg of bovine lactoferrin (AOR, Calgary, AB) (intervention group). Infant meconium followed by weekly stool samples were collected for a month. DNA was extracted from the stools and the V6 hypervariable region of the 16S rRNA gene

was amplified by PCR and then sequenced using an Illumina HiSeq 2500 platform. We described the alpha diversity using the chao 1 and Shannon index as well as the beta diversity using UniFrac analysis of our samples. In addition we calculated the relative abundance of bacterial taxa.

Results: One hundred and twenty-seven unique stool samples (63 in probiotic alone group (P) and 64 in probiotic and lactoferrin group (PL)) obtained from 29 infants in the P group and 30 infants in the PL group were analyzed. The P and PL groups were phylogenetically similar and did not show a separation on principal coordinate (PCoA) analysis using UniFrac distance. Bacterial diversity and richness were no different between infants receiving P versus PL. When infants were stratified by gestational age, older infants (>28 and 26-28 weeks GA versus < 26 weeks GA) had increased diversity compared to more premature infants ($p=0.04$ and $p=0.008$). Furthermore, infants of 26-28 weeks GA increased their bacterial diversity at a faster rate compared to those younger than 26 weeks (comparison of fits test, $p=0.0385$). Diversity and richness scores were similar between infants who had never received antibiotics and those who were currently or had previously been receiving antibiotics. Probiotic strains were identified in the stool of infants with a relative abundance of 2.86% (P group) and 3.23% (PL group).

Firmicutes was the most abundant phylum in the P group (51.7% \pm 38%) and *Proteobacteria* was most abundant in the PL group (51.3% \pm 36.9%). Interestingly, twins and triplets from the same family clustered together on PCoA plots irrespective of their treatment group.

Discussion: Probiotic strains are identifiable in the stool of premature infants. Our results also suggest that probiotics and lactoferrin may have a protective role since diversity scores were unchanged in those that had been exposed to antibiotics compared to infants who had never received antibiotics.

396 EVALUATION OF INTESTINAL FAILURE IN CHILDREN BY USING CITRULLINE LEVELS AND PARENTERAL NUTRITION

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Rationale: Plasma citrulline (PC) concentration has been proposed as a biomarker of small bowel length (BL) in patients with short bowel syndrome (SBS). However, PC might be more related to bowel function than to BL. We assessed the relationship between PC, BL and an index of PN dependency in children with intestinal failure (IF).

Methods: We included 98 children on home-PN followed at our IF rehabilitation center: Mean age was 6 years and 8 months, diagnosis group were: SBS (n=53), congenital enteropathy (CE) (n=20), long-segment Hirschsprung disease (LSHD) (n=15) and intestinal pseudo-obstruction (CIPOS) (n=10). Protein and non-protein energy intake (NPEI) were adapted to achieve normal growth. PN dependency level was assessed by using the NPEI to resting energy expenditure (REE) ratio [NPEI/REE] expressed as a percentage. REE was calculated from Schofield formula according to sex, age, body weight and height. Regression analysis was performed to establish a correlation between PC levels, NPEI/REE in the different groups and bowel length in SBS and LSHD.

Results: For Citrulline levels ($\mu\text{mol/l}$), NPEI/REE (%) and small bowel length for SBS and LSHD (cm) are respectively. SBS: 14.9 ± 10.8 ; 98.1 ± 31.8 , 33.6 ± 24.0 ; LSHD: 11.4 ± 7.9 ; 105.8 ± 21.5 ; 63.4 ± 20 ; CIPOS: 28.8 ± 19.1 ; 99.9 ± 21.1 and CE: 9.8 ± 7.3 ; 116.2 ± 29.7 .

In the SBS group, plasma citrulline levels were correlated to bowel length ($p=0.0001$) and to NPEI/REE (0.0001); BL and NPEI/REE were correlated ($p=0.0003$). In the LSHD group, we found a correlation between PC and NPEI/REE ($p=0.03$). There were no significant correlation between PC and NPEI/REE in the CE group ($p=0.22$) and the CIPOS group ($p=0.09$).

Conclusions: Plasma citrulline levels are relevant in SBS and LSHD, but not in other groups of IF. PN dependency for achieving normal growth as assessed by NPEI/REE index is helpful for adapting PN intake and IF management.

Thursday, October 6, 2016

PLENARY SESSION II 4:00 PM

APFED OUTSTANDING EGID ABSTRACT AWARD

397 EPITHELIAL-FIBROBLAST INTERACTION DRIVES PRO-FIBROTIC MILIEU IN EOSINOPHILIC ESOPHAGITIS

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated disorder in which unchecked inflammation universally leads to fibrosis and stricture. Esophageal epithelial cells activate myofibroblasts, chief effector cells in fibrosis via EoE-relevant inflammatory cytokines (*Exp Cell Res.* 2013;319:850-9). However, little is known about the role of direct cell-to-cell contact between esophageal epithelial cells and neighboring fibroblasts in the EoE pathogenesis. Herein we describe novel experimental platforms to examine these intercellular interactions.

Methods: Primary human esophageal fibroblasts (FEF3) were co-cultured for 24-72 h with immortalized human esophageal epithelial cells (EPC2-hTERT). FEF3 were labeled with tdTomato fluorescent protein and EPC2-hTERT were labeled with green fluorescent protein (GFP) for cell-lineage tracing. Cells were purified with fluorescent activated cell sorting (FACS). Additionally, we have developed single cell-derived three-dimensional (3D) murine esophageal organoids co-cultured with murine esophageal fibroblasts.

Results: Co-cultured EPC2-hTERT cells appeared to have a significant ($p<0.05$) increase in the expression of lysyl oxidase (LOX), Periostin, type 1 collagen, and TGF β , all essential secretory factors implicated in myofibroblast activation. The co-cultured FEF3 showed upregulation of IL1- β and TNF α . Direct cell-to-cell contact between these cell types resulted in a robust (2-300-fold) enhancement of the expression of these fibrogenic genes compared to the mono-cultured EPC2-hTERT and FEF3 in the presence of conditioned media from FEF3 and EPC2-hTERT, respectively. Moreover, co-cultured EPC2-hTERT cells showed molecular changes compatible with epithelial-mesenchymal transition (EMT) with downregulation of E-cadherin and upregulation of mesenchymal markers including smooth muscle actin (SMA) and type 1 collagen (COL1A). While EPC2-hTERT gains fibroblast-like characteristics in EMT, GFP expression confirmed the cells of origin. Such molecular changes were further documented in murine esophageal 3D organoids where co-cultured fibroblasts were found to facilitate basal cell hyperplasia, common in active EoE.

Conclusions: Our highly innovative novel co-culture and 3D organoid systems recapitulate molecular and morphological changes in EoE pathobiology. Without requiring immune cell components or exogenous cytokine stimulation, these findings underscore the roles of the epithelial-fibroblast crosstalk in the pathogenesis of EoE-associated fibrosis. Pharmacological modifications of these cell-to-cell interactions may provide an alternative to targeting infiltrating inflammatory cells.

NUTRITION PRIZE

398 EARLY FECAL MICROBIOMES ARE DIFFERENT IN PREMATURE NEONATES WHO DEVELOP PARENTERAL NUTRITION ASSOCIATED CHOLESTASIS

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Introduction: Premature neonates often require parenteral nutrition (PN) until they reach enteral autonomy due to gut immaturity which puts them at risk of developing PN-associated cholestasis (PNAC). Since changes in the gut microbiota may potentially affect enterohepatic circulation of bile acids, we sought to compare longitudinal changes in fecal microbiomes of premature neonates who developed PNAC with those who did not despite being on similar PN doses.

Methods: Weekly fecal samples are collected from premature (gestational age <30 weeks) neonates admitted to our NICU. Neonates who developed direct bilirubin > 1.0 mg/dL while receiving PN with resolution of cholestasis after discontinuation of PN were included, after possible contributing factors were ruled out. Samples from cases were divided into pre-, cholestasis, and post-cholestasis based on bilirubin levels at the time of sample acquisition and control samples were accordingly time (groups 1, 2, 3) and demographically matched (Table 1). DNA was extracted using the Powersoil DNA isolation kit and PCR was used to amplify the V4 region of the 16S ribosomal RNA gene. 16S amplicons were pooled and sequenced using an Illumina MiSeq sequencer. The Ribosomal Database Project software was used to make taxonomic assignments and PC-ORD was used for microbiome analysis performed at the genus level.

Results: 80 fecal samples from 5 cases and 5 controls were analyzed. Both cases and controls show progressive longitudinal changes in fecal microbiomes. However, early fecal microbiomes (0-2 weeks; pre-cholestasis (n=6) vs. group 1 (n=10) of neonates who developed PNAC, in addition to being less diverse, were significantly more abundant in genii *Enterococcus* (order *Lactobacillales*), *Sneathia* (Order *Fusobacteriales*) and *Mycoplasma* (order *Mycoplasmatales*) ($p < 0.05$) whereas genus *Trabulsiiella* (order *Enterobacteriales*) was enriched in controls ($p = 0.01$). Nonmetric Multidimensional Scaling (NMS) ordination plot based on the taxonomic composition of early fecal samples revealed significant separation between cases and controls (T = -2.31, A = 0.08, $p = 0.03$). Based on indicator species analysis, *Enterobacteriaceae* were significantly more prevalent in group 1 ($p = 0.0006$). With feeding advances differences in microbiota decreased - genus *Acinetobacter* (order *Pseudomonadales*) was significantly more prevalent in the cholestatic samples (n=3) (vs. group 2, n=5; $p = 0.03$) but NMS ordination plots did not revealed significant separation. Finally, post-cholestasis fecal samples (n=16) did not significantly differ from group 3 (n=20) based on NMS plots, diversity, abundance and prevalence of microbiota.

Conclusions: Premature neonates who develop PNAC, compared to those who do not, show significantly different fecal microbiomes preceding the biochemical detection of cholestasis and these microbiota may be involved in its pathogenesis. The differences in microbiota resolve with weaning of PN and feeding advances.

Table 1. Demographic characteristics of the study participants (n=10)

	Cholestatic group (cases) (D.bili \geq 1.0)	Non-cholestatic group (controls) (D.Bili \leq 0.5)	p-value
Number of neonates (N)	5	5	-
Number of stool samples (n)	35	45	0.32
Gestational age (weeks)	25.2 (\pm 2.4)	27.2 (\pm 1.6)	0.17
Birth weight (grams)	813 (\pm 380.5)	797.43 (\pm 190.1)	0.77
Dextrose + Trophamine duration (days)	19.14 (\pm 5.1)	17.14 (\pm 2.6)	0.38
Intralipids duration (days)	17.29 (\pm 5.2)	16.43 (\pm 2.7)	0.71
Highest D. Bili (mg/dL)	1.98 (\pm 1.1)	0.48 (\pm 0.03)	0.005
<i>Comorbidities</i>			
Bronchopulmonary Dysplasia	100%	100%	-
<i>Medications</i>			
Diuretics	100%	100%	0.12
Proton Pump Inhibitors	0%	20%	0.73
H2 blockers	40%	20%	0.23
Urodiol	20%	0%	0.73
Antibiotics \geq 3 days	0%	0%	-
Feeds- Breast milk	100%	100%	-
Major surgeries	0%	0%	-

399 FECAL EXTRACTS FROM COLICKY INFANTS INDUCE VISCERAL HYPERSENSITIVITY IN MICE

Clara Garcia Rodenas¹, Hélène Eutamène², Sophie Yvon², Emilie d'Aldebert², Gabriela Bergonzelli¹, Francis Foata¹, Julien Sauser¹, Bernard Berger¹, Emmanuel Mas³, ¹Nestlé Research Center, Lausanne, Switzerland, ²Toxalim, University of Toulouse, Toulouse, France, ³Hôpital des Enfants, Toulouse, France

Objectives: The pathophysiology of infantile colic is poorly understood, though various studies report gut microbiota dysbiosis in colicky infants. Dysbiosis has been also shown in irritable bowel syndrome and have been associated with increased visceral sensitivity triggered by increased luminal protease activity. We aimed at testing the hypothesis that colic-related dysbiosis is associated with visceral hypersensitivity triggered by increased luminal protease activity.

Methods: Faecal samples from 7 breastfed colicky infants selected according to the Rome III criteria and from 7 breastfed non-colicky control infants were studied. Faecal supernatants (FS) were infused in the colon of male C57/Bl6 mice (n=10 per FS). Visceral sensitivity was subsequently assessed in the animals by recording their abdominal muscle electromyographic (EMG) response to colorectal distension (CRD). Serine and cysteine protease activities were assessed in the FS with specific substrates. Microbiota composition of the donor stools was analyzed by DNA extraction and 16S rRNA gene pyrosequencing.

Results: Compared to FS from controls, FS from colicky infants triggered higher EMG activity in response to the largest CRD volumes and overall, as assessed by the area under the curve (AUC) of the EMG activity across all CRD volumes (Table). Mean infant crying time strongly correlated with mouse EMG response to the largest distension volumes (R 0.7860, $p < 0.001$ at 0.06 mL; R 0.6821, $p 0.007$ at 0.08 mL and R 0.6126, $p 0.02$ at 0.1 mL) and with the EMG AUC (R 0.8416, $p < 0.001$). The microbiota was more diverse in stools from colicky than from control infants. *Bacteroides vulgatus* and *Bilophila wadsworthia* were significantly increased in the colicky specimens. The relative abundance of *B. vulgatus* significantly correlated with the visceral sensitivity data. No significant differences between the groups were found on FS protease activities.

Conclusion: We show for the first time that compounds in the intestinal milieu of colicky infants can trigger visceral hypersensitivity, which may explain the excessive crying behaviour in these infants. Additional studies are required to determine the nature of these compounds, their mechanism of action and the potential implication of the intestinal microbiota in their generation.

Table: EMG activity (mV/s) in response to CRD

Volume distension (ml)	Colic FS	Control FS	P value
0.02	4.41 ± 1.83	1.12 ± 0.89	0.527
0.04	18.45 ± 3.21	11.16 ± 9.23	0.162
0.06	75.58 ± 12.18	48.61 ± 9.27	<0.001
0.08	95.79 ± 7.57	75.29 ± 8.57	<0.001
0.1	111.07 ± 4.97	93.7 ± 11.03	0.001
AUC (ml x mV/s)	5.00 ± 0.36	3.66 ± 0.38	<0.001

400 CHARACTERIZING THE MECHANISM OF BILE RESISTANCE AND RELATED BIOFILM FORMATION IN SHIGELLA FLEXNERI

Christina S. Faherty¹, Kourtney P. Nickerson¹, Rachael B. Chanin¹, Jeticia R. Sistrunk², Peter Fink¹, Massachusetts General Hospital, Charlestown, MA, U.S.A., Deepak K.V. Kumar¹, David A. Rasko², ¹Massachusetts General Hospital, Charlestown, MA, USA, ²University of Maryland School of Medicine, Baltimore, MD, USA

Introduction: *Shigella flexneri* is a Gram-negative, facultative intracellular pathogen that causes millions of cases of diarrhea each year, predominantly in children under the age of 5 years in developing countries. While many aspects of colonic cell invasion are known, a crucial gap in knowledge remains regarding how the bacteria survive, transit, and regulate virulence gene expression prior to infection. *S. flexneri* is exposed to bile, a bactericidal host factor essential for digestion, as it enters the small intestine. Previous research has demonstrated that bile salts induce both *S. flexneri* adherence to and invasion of epithelial cells. In this study, we further characterized the effects of bile salts exposure on *S. flexneri* 2a strain 2457T.

Materials and Methods: The bile salts used in the study were a 1:1 mixture of cholate and deoxycholate. Growth curve analysis was performed in Luria Bertoni broth containing bile salts ranging from 0.2% weight/volume (w/v) to 10% w/v. RNA-sequencing analysis was performed as a comprehensive analysis of gene expression on RNA isolated from bacteria grown in the presence or absence of 0.4% w/v bile salts. To quantify bile salt-induced biofilm formation, electron microscopy, crystal violet staining and immunofluorescence analysis of concanavalin A for exopolysaccharide matrix production were performed. Finally, mutants were constructed using either a targeted mutagenesis approach with the λ red linear recombination method or the random insertion of transposon EZ-Tn5 into the 2457T genome. Mutants were assessed for bile salt sensitivity and the inability to form a biofilm.

Results and Conclusions: Growth curve analysis in the presence of bile salts revealed that 2457T grew normally within the physiological range of 0.2% to 2% w/v, but growth was slowed or inhibited at 5% and 10% w/v. Using RNA-sequencing, we identified 172 genes induced in 0.4% w/v bile salts that are involved with central metabolism, gene expression, membrane structure, drug resistance, and virulence. Interestingly, to mimic small intestine transit, extended periods of bile salts exposure led to biofilm formation, which was confirmed by crystal violet staining, analysis of exopolysaccharide matrix production, and electron microscopy. Analysis of additional *Shigella*, *Salmonella*, and *Escherichia coli* strains demonstrated a common theme of bile salt-induced biofilm formation among enteric pathogens. Finally, analysis of targeted and random transposon mutations identified several 2457T mutants unable to survive bile salt exposure or form a biofilm. Our data demonstrate that *S. flexneri* has several mechanisms to survive bile exposure, and we hypothesize that biofilm formation is crucial in that process. Moreover, bile serves as an *in vivo* signal to activate *S. flexneri* virulence prior to entry in the colon. This work has led to a greater understanding of how *Shigella* transits the host to establish infection in the colon.

Friday, October 7, 2016

PLENARY SESSION III
8:00AM

*** Poster of Distinction**

GERARD ODELL PRIZE

402 GESTATIONAL ALLOIMMUNE LIVER DISEASE: FATE OF UNTREATED PREGNANCY IN 152 WOMEN AND OUTCOME OF AFFECTED INFANTS

Sarah A Taylor, Susan Kelly, Peter F Whittington, Anne & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA

Gestational alloimmune liver disease (GALD) is the most common cause of fetal liver disease leading to fetal death, neonatal acute liver failure, congenital cirrhosis and the phenotype of neonatal hemochromatosis. GALD is preventable by intravenous administration of pooled human immunoglobulin G (IVIG) in pregnancies subsequent to one affected. Thus it is imperative to recognize GALD when it occurs.

Methods: We prospectively collected data on the gestational histories of women who were to receive gestational IVIG from 1997 through 2015. All had at least one affected pregnancy in order to qualify. We analyzed the data to better understand the natural history of GALD in this large cohort.

Results: Our cohort comprises 364 untreated gestations in 152 women, including 2 twin pregnancies. The outcomes were: 103 healthy live offspring; 157 live-born with liver failure; and 89 spontaneous fetal losses (approximately 1 in 4 untreated pregnancies), of which 37 were at < 20 weeks, 19 at 20 - 37 weeks, 7 at > 37 weeks, and 26 at an undetermined time. 130 women had 1 affected pregnancy, whereas 21 had multiple affected pregnancies (1 with no data): 15 had 2, 3 had 3, and 3 had 4. The apparent recurrence rate, i.e. repeat occurrence in sibships following the index case, was 100%; however there were 4 skipped pregnancies, yielding a per-pregnancy apparent recurrence rate of 92%. Interestingly, 72 index cases (47%) occurred in G1. The outcomes of the 157 live-born children with liver failure was poor: 28 (18%) survived with medical therapy and/or liver transplantation (Table) and 129 (82%) died. Of the 28 surviving infants 31% received IVIG ± double volume exchange transfusion (DVET) and 21% received a liver transplant. A greater proportion of survivors received IVIG ± DVET (31%) than non-survivors (8.5%).

Conclusions: These data capture the largest GALD cohort reported to date and provide important insight into this unique gestational alloimmune disease and treatment outcomes. The finding that 47% of cases occurred in G1 pregnancies supports the concept that a unique fetal antigen gains access to the maternal circulation and sensitizes her immune system early in gestation, making GALD substantially different from other gestational alloimmune diseases. The inordinate rate of fetal loss observed in these women suggests that GALD may be cause of fetal loss even before 14 weeks gestation. Once a woman has an offspring affected with GALD, it is highly likely that subsequent pregnancies will be affected. This and the fact that treatment during subsequent pregnancies can prevent recurrence make it imperative to diagnose GALD in the index case. The use of IVIG/DVET therapy may increase survival of live born infants with GALD.

Table: Treatment of GALD infants separated by outcome.

Treatment	Alive (% total)	Deceased (% total)
Cocktail	13 (46)	41 (32)
IVIG	6 (21)	4 (3.1)
IVIG and DVET	3 (10)	7 (5.4)
Liver transplant	6 (21)	9 (7.0)
Supportive	0	45 (35)
No treatment data	0	23 (18)
Total	28	129

GRAND WATKINS PRIZE

403 THE ROLE OF A NOVEL IL-10 PRODUCING REGULATORY T CELL (TR2) IN IMMUNE HOMEOSTASIS

Masaki Tajima, Ivan J. Fuss, Atsushi Kitani, Warren Strober, Mucosal Immunity Section, NIAID, National Institutes of Health, Bethesda, MD, USA

Suppressor T regulatory cells are comprised of two types of suppressor cells; FoxP3 T regulatory cells and Tr1 T cells. The former requires FoxP3 transcription factor and acts through TGF-β mediated suppression while the latter requires the transcription factor c-maf for expression and acts through secretion of IL-10. To better understand host defense homeostasis and the differentiation of these suppressor cells we stimulated naïve CD4+ T cells with bone marrow-derived dendritic cells in the presence of various stimulants, which included cytokines, TLR's, (toll-like receptor) zymogen isoforms, and yeast or hyphal forms of *C. albicans*.

We found a novel finding in that T cells specifically stimulated by zymogen-depleted stimulant or the hyphal form of *C. albicans* produced large amounts of IL-10; whereas the yeast form of *C. albicans* produced a pro-inflammatory response. This difference reflected that zymogen-depleted stimulant and the hyphal form of *C. albicans* stimulates specifically Dectin-1 receptor alone while the yeast form stimulated both Dectin-1 and the TLR 2 pathways (the latter TLR 2 eliciting the pro-inflammatory response). In further studies, to determine the molecular basis of the IL-10 response we found that it requires IL-4 secretion and is inhibited in IL-4, STAT-6 and GATA-3 deficient CD4+ T cells. In addition, as determined by microarray studies, IL-10 production was downstream of C/EBP-β (CCAAT/enhancer-binding protein) activation and C/EBP-β KO CD4+ T cells stimulated by hyphae exhibited deficient IL-10 production. Importantly, this C/EBP-β effect was dependent on the LIP isoform of C/EBP-β rather than LAP isoform as transduction experiments of C/EBP-? KO CD4+ T cells with LIP led to increased IL-10 production whereas transduction with LAP inhibited IL-10 production.

This positive effect of LIP was traced to enhancement of CREB mediated IL-10 transcription, as LIP but not LAP expressing T cells stimulated by Dectin-1 signaling pathway exhibited CREB binding to the IL-10 promoter. Parallel studies of Tr1 or conventional Th2 cells producing IL-

10 noted required c-maf transcription expression for the former and both expressed low levels of the LIP molecule and exhibited little CREB binding to the IL-10 promoter .

Furthermore, *in vivo* IV administration of *C. albicans* resulted in substantial increase in the numbers of TR2 T cells within the kidney at the sites of severe inflammation. Thus, stimulation via the Dectin-1 pathway induces a novel type of IL-10 producing T regulatory cell, which we have termed Tr2 regulatory T cells, which are well positioned to exert regulatory function at sites of inflammation. Present studies are evaluating the role these Tr2 T cells play in intestinal inflammation such as Crohn's disease and whether other fungal antigens (*Saccharomyces cerevisiae*) can act in a regulatory role.

404 AUTOIMMUNE PANCREATITIS IN CHILDREN: WORKING GUIDELINES FOR DIAGNOSIS AND TREATMENT

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Background and Aims: Autoimmune pancreatitis (AIP) is an increasingly recognized and potentially treatable cause of pancreatitis, but reports in children are limited. Until now, pediatric gastroenterologists relied on adult AIP guidelines for diagnostic criteria. However, the presentation of AIP might be different in the children. Thus we aim to develop a working definition and diagnostic approach for AIP in children.

Material and Methods: Data about clinical symptoms, imaging, histology, other organ involvement and treatment modalities were collected using 2 different approaches: (1) a systematic literature search identifying pediatric cases of AIP and (2) children with an established diagnosis of AIP from the largest multicenter study of chronic pancreatitis in children (INSPPIRE) and from Cliniques St-Luc (CUSL). (3) We sought expert opinion from pediatric pancreatologists about AIP definition, diagnostic criteria and treatment.

Results: We identified 44 AIP cases, 26 from literature review, 14 from the INSPPIRE cohort study and 4 from CUSL. The median age at diagnosis of AIP was 13.2 years (range 2-17y). Abdominal pain (39/44, 87%) and/or obstructive jaundice (20/44, 45%) were the most frequently reported symptoms at diagnosis. Serum IgG4 levels, a hallmark in adult AIP, was above the upper limit of normal in only 8/38 (21%). Imaging findings were abnormal in all children mainly showing hypointense global or focal gland enlargement (35/43, 81%), irregularity of the main pancreatic duct (29/43, 67%) and common bile duct stricture (25/43, 58%). Of those for whom pancreas biopsy was performed, a combination of lymphoplasmacytic inflammation, pancreas fibrosis and ductal granulocyte infiltration were the main findings (18/25, 72%). Children with AIP had a prompt clinical response to steroids. Twenty-two percent of AIP patients developed other autoimmune/inflammatory conditions, mainly ulcerative colitis. Complications of AIP included impaired exocrine function requiring pancreatic enzyme replacement therapy (4/25, 16%) and diabetes (3/27, 11%).

Conclusion: AIP in children is a distinct subtype of pancreatitis. Children with AIP have (1) a high frequency of abdominal pain at diagnosis, (2) a relatively low frequency of positive serum IgG4, (3) parenchymal and/or duct abnormalities on cross-sectional imaging and (4) parenchymal lymphoplasmacytic and granulocyte infiltration with fibrosis. The disease responded promptly to steroids. Based on these observations, we have established working guidelines to help identification and treatment of these children as well as to pave the way for future prospective studies.

405 CHARACTERISTICS OF PREFORMED AND DE NOVO DONOR SPECIFIC ANTIBODIES IN PEDIATRIC LIVER TRANSPLANTS

Dominique Schluckebier, Valérie McLin, Vladimir Cousin, Laetitia Marie Petit, Dominique Belli, Barbara Wildhaber, Anne-Laure Rougemont, Jean Villard, Sylvie Ferrari-Lacraz, Geneva University Hospitals, Swiss Center for Liver Disease in Children, Geneva, Switzerland

Introduction: Despite the growing interest about the impact of anti-HLA antibodies very little is known in liver transplantation especially in children. The negative impact of donor specific anti-HLA antibodies (DSA) in kidney, heart and lung transplantation is well established. There are 2 categories of DSA: preformed and de novo, the second one being more detrimental on the graft outcome. In adult liver transplant (LT) recipients, an association between DSA and acute cellular rejection (ACR) has been described with a negative effect on graft survival.

Objective: To analyze whether the presence of DSA was associated with the development of ACR in our cohort of pediatric LT recipients and to identify factors potentially associated with the development of de novo DSA post-LT.

Methods: Retrospective single-center study, involving all patients aged 0-16 years who had undergone deceased or living donor LT at the University Hospitals of Geneva between 01.01.2005-31.12.2013. Information on host- and donor-related factors (age, gender, weight, etiology of liver disease, presence of biliary complication after LT) was collected for all patients. Liver biopsy reports were analyzed retrospectively; the Banff criteria were used to evaluate for rejection. HLA-A,-B,-DR and DQ typing for both recipients and donors were performed by SSO-Luminex® method. with HLA identification performed by LABscreen® single antigen. Anti-HLA titers were considered positive with a normalized value of Mean fluorescence intensity (MFI) >1000 for class I and class II HLA antibodies. Patients were divided into 2 groups: those with and without ACR.

Results: 58/65 patients were included in our study. The overall prevalence of *de novo* DSA was 57%. We did not identify any differences concerning class I and II DSA between the two groups. Although the MFI of patients with *de novo* class II DSA was higher in children who did reject, this finding did not reach statistical significance ($p = 0.4$). 21 patients (36%) presented with at least 1 episode of ACR during the follow-up period, mostly (10/21) moderate rejection (Banff 6-7). Using a survival analysis, there was no significant difference in time to first ACR in patients with and without DSA, but recipients with a gender mismatch were at a significantly higher risk for the development of ACR. Biliary

atresia (OR 10.6 (2.1-54.1), $p=0.004$) and receiving a whole liver graft (OR 10.3 (1.8-58.1), $p=0.008$) were potential predisposing factors of the development of *de novo* DSA in our study cohort.

Discussion: The present study has shown a high prevalence of anti-HLA antibody in children after LT. In spite of this, patient and graft survival was excellent during follow-up and not influenced by the presence of *de novo* DSA nor by the event of one or several ACR during follow-up. There is a need for prospective studies to define time points for DSA identification, in order to advance our understanding about the possible link between circulating DSA and ACR or loss of graft function.

Friday, October 7, 2016

**Concurrent Session III
10:00AM**

HEPATOLOGY

417 MACROPHAGE DERIVED INTERLEUKIN-1-BETA SUPPRESSES LIVER X RECEPTOR AND HEPATIC PHYTOSTEROL TRANSPORTERS ABCG5/8 TO PROMOTE PARENTERAL NUTRITION ASSOCIATED CHOLESTASIS IN MICE

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Background: Parenteral nutrition-associated cholestasis (PNAC) complicates the care of infants with intestinal failure. In a mouse model, we have demonstrated that PNAC occurs following exposure to both soy lipid (phytosterol)-containing PN and intestinal injury, but neither alone. Mice with PNAC had pro-inflammatory macrophage activation, hepatic phytosterol retention and transcriptional suppression of hepatocyte sterol (Abcg5/8) and bile (Abcb11 and Abcc2) transporters. To determine the interplay between macrophage activation, phytosterol accumulation, and cholestasis in this model, we hypothesized that macrophage-derived pro-inflammatory IL-1 β played a critical role through suppression of hepatic sterol transporters and resultant phytosterol retention.

Methods and Results: Adult C57/BL6 mice were given dextran sulphate sodium (DSS) in drinking water to induce intestinal injury for 4 days followed by continuous infusion of phytosterol-containing PN through a central venous catheter for 3, 7, and 14 days (DSS-PN); controls included PN without DSS, DSS without PN, and chow only. Cholestasis (increased serum total bilirubin and bile acids) and hepatocyte injury (AST, ALT) first appeared at 7d DSS-PN, increased at 14d, and were absent in all controls. At all time points, Il1b mRNA was increased in intrahepatic mononuclear cells and hepatic mRNA for Abcb11, Abcc2, Abcg5/8, and Lxr was suppressed, indicating that Il1b induction and transporter suppression preceded PNAC. In DSS-PN mice, hepatic caspase1 was activated (promoting IL-1 β synthesis) and serum IL-1 β levels were increased relative to controls. PNAC was prevented in IL-1R $^{-/-}$ and Caspase1 $^{-/-}$ 14dDSS/PN mice and in 14dDSS/PN wt mice with pharmacological blockade of the IL1 receptor (Anakinra). These interruptions of IL-1 β signaling also restored Abcb11, Abcc2, and Abcg5/8 expression to levels observed in control mice. To determine the mechanisms of decreased hepatic expression of canalicular Abcg5/8 in PNAC mice, chromatin immunoprecipitation (ChIP) was performed on the Abcg5/8 promoter. Reduced binding of LXR to this promoter was observed in DSS-PN mice and was reversed in IL1R $^{-/-}$ DSS-PN mice. In primary mouse hepatocytes and in human hepatocyte cell lines (HuH7 and HepG2), recombinant IL-1 β activated NF κ B and suppressed mRNA for LXR and ABCG5/8. Overexpression of either p50 or p65 NF κ B subunits in HuH7 cells suppressed LXR driven expression of ABCG5/8. Conversely, pharmacological and genetic inhibition of NF κ B in IL-1 β -treated HuH7 cells restored LXR-dependent ABCG5/8 expression.

Conclusions: Hepatic IL-1 β is a critical early mediator in the pathogenesis of PNAC by promoting suppression of the hepatic phytosterol transporter Abcg5/8 through NF κ B-mediated suppression of LXR. We speculate that reduced Abcg5/8 then causes phytosterol retention in soy lipid emulsion PN-treated mice which can interfere with hepatocyte FXR signaling, thus promoting cholestasis.

418 EXOVESICLES ENRICHED IN miR-128-3p PLAY A CRUCIAL ROLE IN THE DEVELOPMENT OF LIVER FIBROSIS AND HSC ACTIVATION IN AN EXPERIMENTAL MODEL OF NASH-FIBROSIS AND HCC

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Liver fibrosis is a key histological feature associated with prognosis in patients with Non-alcoholic Steatohepatitis (NASH) progressing to liver cancer. Hepatic stellate cell (HSC) activation is crucial for this process. The triggers for HSC activation in NASH remain incompletely understood. Recently, we identified miR-128-3p encapsulated in extracellular vesicles released by hepatocytes (Hep-EVs) during lipotoxicity and efficiently internalize into HSCs. Here we tested the hypothesis that miR-128-3p contributes to liver fibrosis in NASH by modulating HSC phenotype.

Methods: An experimental model of NASH-fibrosis progressing towards hepatocellular carcinoma (HCC) was obtained by single injection of Streptozotocin followed by 60% HFD (STZ-HFD) for 10 and 20 weeks. Level of hepatic miR-128-3p and extent of liver fibrosis were determined by molecular and histological assays. EV-miR-128 were used on primary murine HSC to investigate cell activation *in vitro*. *In vitro* loss-of-function approaches were used in hepatocytes to generate miR-128-3p-depleted EV that were incubated with HSCs to determine their pro-fibrogenic profile by quantitative PCR, migration and proliferation assays. *In vivo* imaging analyses were conducted to trace Hep-EVs injected intravenously in C57/B6 mice.

Results: Flow cytometry analysis showed a progressive increase of circulating EVs in STZ-HFD mice. Morphometric and gene expression analyses showed that level of miR-128-3p was markedly associated with the extent of fibrosis (α -SMA 2-fold increase and Collagen1a1 6-fold increase compared to control). Significant amount of miR-128 was also identified in EV isolated from STZ-HFD compared to control mice (3-fold increase compared to control mice). Primary mouse HSCs isolated from wild-type mice and exposed to primary hepatocyte-EVs showed faster cell activation *in vitro* over time and expressed higher level of pro-fibrogenic genes compared to untreated HSCs. Transfection of fat-laden hepatocytes with antagoni-miR-128-3p resulted in 90% reduction of miR-128-3p in both cells and EVs. The exposure of miR-128-3p-depleted EVs to HSCs resulted in downregulation of pro-fibrogenic markers α -SMA, Collagen1a1 and TIMP-2 and upregulation of the HSC quiescent marker, PPAR- compared to miR-128-3p-expressing EVs. Furthermore, miR-128-3p depleted EVs showed reduced HSC proliferation

and migration compared to control EVs. *In vivo* tracing imaging analyses showed that FITC-labelled Hep-EVs accumulate in the liver as early as 1 hour post-injection, but mostly after 6 hours post-injection. Level of miR-128-3p were up-regulated in EV-injected mice compared to mice injected with EV-free supernatant or with saline solution.

Conclusions: In this study we identify a pivotal role of miR-128-3p in liver fibrosis and HSC activation during NASH-HCC development. These results uncover important aspects of molecular mechanisms of liver fibrosis and may identify novel therapeutic targets for fibrotic liver diseases.

419 MINIMAL HEPATIC ENCEPHALOPATHY IN CHILDREN WITH CHRONIC LIVER DISEASE: PREVALENCE, PATHOGENESIS AND ROLE OF MAGNETIC RESONANCE BASED INVESTIGATIONS IN DIAGNOSIS

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Introduction: Data on minimal hepatic encephalopathy (MHE) in children with chronic liver disease (CLD) is scanty. We evaluated the prevalence of MHE, its correlation with changes in brain metabolites by magnetic resonance spectroscopy (1HMRS), diffusion tensor imaging (DTI) derived metrics, blood ammonia (BA) and inflammatory cytokines and the accuracy of MR based investigations for diagnosis of MHE in CLD children.

Patients and methods: 67 (38 boys; age 12.7 ± 3.0 years) CLD children and 55 healthy controls (36 boys; age 13.8 ± 2.7 y) were evaluated with a battery of age appropriate neuropsychological tests (NPT). All CLD children and 37 controls were subjected to blood ammonia (BA), interleukin-6 [IL6] and tumor necrosis factor [TNF α] estimation, MR imaging, 1HMRS and DTI.

Results: 34 CLD children (50.7%, age 12.8 ± 3.0 y; 23 boys) had MHE based on NPT. There was with no difference in the age, gender and etiology of CLD between MHE and no-MHE. MHE subjects had higher BA (33.1 ± 19.4 vs. 18.8 ± 11.4 μ mol/L; $p=0.001$), IL-6 (11.7 ± 7.9 vs. 8.5 ± 4.4 pg/mL; $p=0.049$), TNF α [21.8 ± 14.9 vs. 14.9 ± 7.2 pg/mL; $p=0.019$], glutamine (2.6 ± 0.30 vs. 2.4 ± 0.28 ; $p=0.02$) and lower choline (0.20 ± 0.03 vs. 0.22 ± 0.03 ; $p=0.01$) and myoinositol (MI, 0.26 ± 0.07 vs. 0.32 ± 0.10 ; $p=0.005$) on 1HMRS. DTI showed significantly higher mean diffusivity (MD) in MHE patients in comparison to No-MHE in 6/11 brain areas i.e., frontal white matter (FWM, 0.85 ± 0.06 vs. 0.74 ± 0.04 ; $p<0.0005$), caudate nucleus (CN, 0.82 ± 0.05 vs. 0.76 ± 0.04 ; $p<0.0005$), anterior (ALIC, 0.80 ± 0.05 vs. 0.73 ± 0.02 ; $p<0.0005$) and posterior limb (PLIC, 0.78 ± 0.04 vs. 0.73 ± 0.02 ; $p<0.0005$) of internal capsule, globus pallidus (GP, 0.80 ± 0.04 vs. 0.75 ± 0.05 ; $p<0.0005$), and occipital white matter (OWM, 0.81 ± 0.06 vs. 0.74 ± 0.06 ; $p<0.0005$). There was no significant difference in the T1S1 signal intensity and fractional anisotropy values in cases with and without MHE. Brain glutamine had a positive significant correlation with BA ($r=0.36$, $p=0.01$), IL-6 [$r=0.40$, $p=0.01$], TNF α [$r=0.35$, $p=0.01$] and MD value of various brain regions. A significant negative correlation was seen between the performance on NPT and BA, IL6, TNF α , brain glutamine and MD values. MD on DTI performed better than 1HMRS metabolites for discrimination between MHE and No-MHE. FWM-MD value of 0.805 (AUC 0.89 (95% CI, 0.81-0.97, $p<0.0005$) had a sensitivity and specificity of 73.5% and 100 % followed by ALIC (AUC 0.87 (0.77-0.96; $p<0.0005$) and OWM (AUC 0.85 (0.74-0.95; $p<0.0005$) for diagnosis of MHE.

Conclusions 50% children with chronic liver disease have MHE on NPT. There is a significant positive correlation between markers of hyperammonemia (BA and brain glutamine), inflammation (TNF α and IL6) and brain edema (MD) and these are negatively correlated with the NPT scores. MD on DTI is a reliable tool for diagnosis of MHE in children.

420 LEDIPASVIR/SOFOSBUVIR FOR 12 WEEKS IS SAFE AND EFFECTIVE IN ADOLESCENTS WITH CHRONIC HEPATITIS C INFECTION

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Background: HCV-specific direct acting antivirals (DAAs) have been extensively studied in adults with chronic HCV, but few studies have evaluated these new treatments in children for whom standard of care is still pegylated interferon plus ribavirin for up to 48 weeks. Ledipasvir/sofosbuvir LDV/SOF is a fixed dose combination of two DAAs which has been shown to result in sustained viral response (SVR) rates $\geq 94\%$ in adult patients with genotype (GT) 1 HCV infection. The objective of this study is to evaluate the safety and efficacy of an all-oral, DAA regimen of LDV/SOF administered for 12 weeks in adolescents with chronic HCV infection.

Aims and Methods: Patients aged 12 to 17 years old with chronic HCV GT1 were enrolled into this open-label ongoing study to receive 12-weeks of treatment with LDV/SOF 90 mg/400 mg once daily. The primary and secondary efficacy endpoints are SVR12 and SVR24, respectively (HCV RNA <lower limit of quantitation 12 and 24 weeks after end of treatment). Safety was assessed by adverse events and clinical/laboratory data. Blood samples for pharmacokinetic analysis were collected over 12 hours in the first 10 patients to evaluate exposure in this age group relative to adults.

Results: 100 adolescents with GT1 HCV infection were enrolled and treated; 63 were female, mean age was 15 years, 20 had failed prior treatment, and 55 had baseline HCV RNA $\geq 800,000$ IU/mL. Plasma exposures of LDV, SOF and its predominant circulating metabolite were comparable to adult exposures. The overall SVR12 rate was 97%; the three patients who did not achieve SVR12 were lost to follow-up. No serious adverse events (AEs) have been reported. The most common AEs (reported by $\geq 10\%$ of patients) were headache (27%), diarrhea (14%), fatigue (13%), nausea (11%), vomiting (11%), cough (10%), and oropharyngeal pain (10%). Post-treatment follow-up is ongoing: SVR24 results will be presented.

Conclusions: In adolescents with chronic GT1 HCV infection, LDV/SOF once daily for 12 weeks resulted in a 97% SVR12 rate with no observed virologic failures by 12 weeks post-treatment. This interferon- and ribavirin-free regimen was well tolerated, supporting its potential as a treatment option for children. The study is continuing in children aged 3 to 11 years old.

421 NEURODEVELOPMENTAL OUTCOMES IN PATIENTS WITH BILIARY ATRESIA AND NATIVE LIVER AT AGES 1 AND 2 YEARS: RESULTS FROM CHILDREN: AN INTERNATIONAL MULTI-CENTER CONSORTIUM

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Background: One of the most serious consequences of liver disease and malnutrition early in life is neurodevelopmental (ND) delay for which prompt identification and intervention may improve long-term outcomes. We hypothesized i) biliary atresia (BA) patients with their native liver at ages 1 and 2 yrs will have significant ND delays and ii) that specific demographic and clinical variables will predict worse ND outcomes. Methods: Infants with BA, birth weight >2 kg, who received hepatoporoenterostomy (HPE) and were enrolled between 2004-2012 in the multi-center, prospective NIDDK-funded ChiLDReN study (PROBE-NCT00061828) underwent ND testing at ages 12 ± 2 mos (T1) and 24 ± 2mos (T2) using either Bayley Scales of Infant Development-2 (B2) or Bayley-3 (B3), based on era. A subset of these infants was also enrolled in a blinded randomized placebo-controlled study of corticosteroids as adjunctive therapy to HPE (START-CNCT00294684). Scores (normative mean 100 ± 15) were categorized as ≥100, 85-99, 70-84, <70 for chi square analysis. The expected distribution of Bayley standard scores in the normal population is 50% (>100), 34.1% (85-99), 13.6% (70-84) and 2.3% (<70). Risk for ND impairment (defined as at least one score ≤85 on B2 or B3) was analyzed using logistic regression. Demographic, pre-and post-HPE clinical and laboratory variables significant at $p \leq 0.10$ in univariate analysis were included in stepwise multivariate regression adjusted for B2 or B3.

Results: 148 children had 217 Bayley exams (T1 n=132; T2 n=85). Death and transplant (LT) reduced the numbers of infants eligible for testing at T1 (death n 15, LT n 82) and T2 (death n 4, LT n 52). ND score distributions were significantly shifted downward relative to the normal population at T1 and, less markedly, at T2 (% of scores < 85 at T1 and T2: B2-Mental 38%* and 40%*, B2-Motor 59%* and 35%*, B3-Cognitive 14% and 10%, B3-Language 33%* and 15%, B3-Motor 32%* and 17%, * $p < 0.05$ vs. expected based on 4 category comparison). Univariate analysis identified older age at HPE, ascites, and total bilirubin at T1 or T2, but not steroid use, as predictors of impaired ND. Risk factors for ND impairment in the final multivariate model were ascites (OR 3.50, 95% CI, 1.32, 9.30, $p = 0.012$) and height Z-score (OR 0.70, 95% CI, 0.50, 0.98, $p = 0.038$) at T1, and total bilirubin (OR 2.00, 95% CI, 1.18, 3.34, $p = 0.0094$) at T2.

Conclusions: Young children with BA and native liver are at increased risk for ND delays compared to the normal population. Risk was not increased by steroid exposure in the START trial. In this cohort, identification of ND may have been underestimated due to LT and death. Markers of advanced liver disease and stunted growth are associated with worse ND outcomes, suggesting that earlier LT and aggressive nutritional therapy may improve ND outcomes.

422 THE SAME GENETIC FACTORS IN HUMAN LEUKOCYTE ANTIGEN (HLA)-DP ARE IMPORTANT FOR BOTH HEPATITIS B, VACCINE RESPONSE AND THE CLINICAL OUTCOMES OF HEPATITIS B INFECTION

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Background: Hepatitis B (HB) vaccine, containing hepatitis B surface antigen (HBsAg), is the mainstay of HB prevention. However, 5 - 10% of recipients have no response and the mechanisms that determine this individual difference in vaccine response are not fully understood. The polymorphisms in class II human leukocyte antigen (HLA) including HLA-DP, -DQ, and -DR alleles and single nucleotide polymorphisms (SNPs) in these regions have been reported to be associated with both HB vaccine response and chronic hepatitis B (CHB) susceptibility. However the mechanism underlying these associations remains unclear. In addition, a well-known CHB biomarker, rs9277535, is located at the 3' UTR of HLA-DPB1, so that its functional mechanism has been interested.

Objective: To define the effects of 4-digit alleles and SNPs in HLA-DP on the response to primary HB vaccination, and to consider underlying mechanism for these associations.

Methods: We performed a case-control association study in 578 primary HB vaccine recipients among healthy Japanese university students. Cases (n=156) who produced anti-HBs < 100 mIU/mL were matched with controls (n 422) with anti-HBs ≥ 100 mIU/mL. The 4-digit alleles and SNPs of HLA-DPA1 and -DPB1 were genotyped by direct sequencing, PCR-SSOP method, TaqMan PCR, respectively. Next, we assessed the linkage disequilibrium between these alleles. Finally, we compared our results with the previously reported HLA-DP alleles associated with susceptibility to CHB infection.

Results: HLA-DPA1*02:02, HLA-DPB1*05:01, and G alleles of rs3077 and rs9277535 showed significant association with poor vaccine response (risk alleles). Conversely, HLA-DPA1*01:03, HLA-DPB1*04:02, and A alleles of rs3077 and rs9277535 showed significant association with sufficient vaccine response (protective alleles). The SNPs showed strong linkage disequilibrium with the 4-digit alleles. Furthermore, our identified factors and their risk/protective associations were exactly identical to those reported for CHB infection in unvaccinated Japanese cohort (Kamatani Y, *Nat Genet* 2009).

Conclusions: The present findings indicate that polymorphisms in HLA-DP regions are strongly associated with HB vaccine response. The SNPs in the 3' UTR may be detected by the strong linkage disequilibrium with the 4-digit alleles, which reflect the properties of antigen-binding site of HLA molecules. Taken together with a previous report of the association between HLA-DP alleles and CHB susceptibility, our results suggest that the interaction between HLA-DP molecules and HBsAg is a critical genetic factor modulating not only HB vaccine response but also CHB infection.

Friday, October 7, 2016

Concurrent Session III
10:00AM

CELIAC AND OTHER LUMINAL DISORDERS

APFED OUTSTANDING EGID ABSTRACT AWARD

423 EPITHELIAL BARRIER DYSFUNCTION IN A MOUSE MODEL OF EOSINOPHILIC ESOPHAGITIS

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Background: Growing evidence highlights an altered epithelial barrier in the pathogenesis of eosinophilic esophagitis (EoE). Transforming growth factor beta (TGF- β 1), a potent pleiotropic cytokine involved in fibrosis and remodeling, contributes to epithelial barrier dysfunction in other organ systems. Studies of EoE patient biopsies have shown increased phosphorylated-SMAD2/3 (p-SMAD2/3), a downstream molecule in the TGF- β 1 signaling pathway. Our preliminary data shows that esophageal epithelial cells treated with TGF- β 1 develop diminished barrier function *in vitro*, specifically decreased Claudin-7 expression. Our analysis of human EoE biopsies demonstrated that nuclear p-SMAD2 is increased and Claudin-7 mRNA is decreased, implicating TGF- β 1 in esophageal epithelial barrier dysfunction. With the potential for TGF- β 1 as a therapeutic target in EoE, we aimed to examine the role of TGF- β 1 on esophageal epithelial barrier in the L2-OXA mouse model of EoE (Masterson, JC et al. Gut 2014). We hypothesize that in this mouse model of EoE, elevated TGF- β 1 signaling will lead to altered epithelial barrier function, and indicate the potential utility of this mouse model to study the functional and molecular consequences of TGF- β 1 blockade. Methods: Transgenic mice with esophageal overexpression of IL-5 (L2-IL5) were sensitized and subsequently topically challenged with oxazolone (L2-OXA). These mice (L2-OXA) develop key histopathological features that are similar to human EoE when compared to control mice (WT-OXA). Mouse esophageal tissue was stained with H&E and assessed using a histological scoring tool (an indexed score measuring epithelial inflammation, epithelial remodeling, lamina propria fibrosis and intramuscular inflammation). Immunofluorescence was performed and quantified on paraffin embedded mouse esophageal tissues to evaluate p-SMAD2. Claudin-7 expression was analyzed by real-time RT-PCR (mRNA) and western blot (protein).

Results: In the L2-OXA mouse, histopathological changes such as dilated intercellular spaces and basal zone hyperplasia, suggest altered epithelial barrier. The epithelial histopathology score is significantly higher in L2-OXA mice than in WT-OXA control mice (9.1 vs. 1.3, $p < 0.001$, $n = 11$ or 6/group). L2-OXA mice exhibit significant increases in number and intensity of positively stained cells for nuclear p-SMAD2 protein compared to WT-OXA mice (149 vs. 73 cells/hpf, $p = 0.003$, $n = 4$ /group). Claudin-7 mRNA expression is significantly decreased in L2-OXA mice compared to WT-OXA (1.0 vs. 0.35, $p < 0.05$, $n = 5$ /group), which was confirmed with a 30% decrease in Claudin-7 protein expression in L2-OXA mice compared to controls.

Conclusion: Increased nuclear p-SMAD2 in esophageal tissues implicates a role for TGF- β 1 signaling in mouse esophagitis possibly through a Claudin-7 pathway. The L2-OXA mouse model of EoE may be utilized in future studies to determine the functional and molecular consequences of TGF- β 1 blockade.

424 FEASIBILITY OF A COMPETITIVELY SELECTED UNIVERSAL DONOR FECAL MICROBIOTA TRANSPLANTATION PROTOCOL AND CHARACTERIZATION OF POST-TRANSPLANT MICROBIOTA MODIFICATION

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Introduction: *Clostridium difficile* infection (CDI) is a serious cause of morbidity in pediatrics for the 17,000 pediatric patients diagnosed per year in the United States. With high treatment failure with oral antibiotics, Fecal Microbiota Transplant (FMT) has emerged as a promising treatment for recurrent CDI. Commonly, a related donor is used, without assessment of the quality of the microbiota being transplanted. Our team has established a competitive donor protocol process whereby a single universal donor is mindfully selected based on 3 parameters from the literature to provide microbiome for transplantation.

Methods: This longitudinal prospective cohort study aimed to demonstrate the feasibility of a FMT protocol with donor selection based on 3 parameters which have been associated with a healthy microbiota in the literature: increased stool butyrate concentration, high bacterial diversity, and *Bacteroidetes/Firmicutes* ratio > 1 . Screening of potential donors for infectious disease was completed in parallel with the stringent screening process of our collaborators, OpenBiome, thus exceeding minimum consensus screening.

The universal donor was then selected from among 9 potential donors based on the following parameters: a high butyrate concentration of 4.2 micromol/mL (range 2.5 – 5.1 micromol/mL), a Shannon Index of 6.07 (range 4.00 to 6.48), a Simpson Index of 0.93 (range 0.77 to 0.96), and high phylogenetic diversity on rarefaction curves.

Competitively selected donor stool was then utilized for FMT in recurrent CDI patients. Patients were followed prospectively for 10 weeks after transplantation during which time they were assessed for recurrence. Stool samples were obtained for microbiota sequencing pre- and at the following points post-transplant: 3 days, 1 week, 10 weeks, and if symptoms recurred.

Results: For the 10 patients treated via the competitive donor protocol, the rate of CDI clearance without recurrence with 1-2 FMTs was 100%. The cohort included 3 patients with high risk diagnoses including heart transplantation on dual immunosuppression therapy, liver transplant on monotherapy, and Complex Variable Immune Deficiency (CVID); no patient experienced any serious adverse events (SAEs). Eight patients

were age 5-23 years; 2 patients were >23 years. With a single FMT, 80% of patients cleared their CDI without recurrence, while 20% of patients required a single re-treatment. Microbiota sequencing is underway, and will better characterize the adaptation of the microbiota after transplantation.

Discussion: The competitive donor FMT approach is confirmed to be feasible and was accomplished without any SAEs including in immunosuppressed patients. Though not a comparative effectiveness study, the efficacy of CDI clearance without recurrence met or exceeded literature benchmarks. Microbiota analyses will provide insight into the post-transplant microbial evolution, which is largely undescribed in the pediatric literature.

425 LONG-TERM SAFETY AND EFFICACY OF RESLIZUMAB IN CHILDREN AND ADOLESCENTS WITH EOSINOPHILIC ESOPHAGITIS: A REVIEW OF 501 DOSES IN 12 CHILDREN OVER 8 YEARS

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Background: Eosinophilic esophagitis (EoE) is a chronic disease characterized by infiltration of eosinophils in the esophageal epithelium. There are limited treatment options for EoE.

Rationale: To evaluate the long term safety and efficacy of reslizumab (RSZ), a monoclonal antibody against interleukin-5, in pediatric patients who received RSZ in a randomized controlled trial (RCT) and expanded access program.

Methods: Records of patients who received RSZ in our center were reviewed. Patients received RSZ 2 mg/kg (or placebo) every 4 weeks as part of the RCT, open label extension (OLE), and compassionate use (CU). Data were analyzed as of their most recent evaluation in March 2016.

Labwork, history, and examinations were conducted every 12 weeks. Biopsy results were compared from baseline (prior to RCT) and at the most recent evaluation. Adverse events (AE) were recorded.

Results: 12 patients entered the RCT at our center. 6 patients completed the OLE. 4 received RSZ through CU. Between the RCT, OLE, and CU periods, patients received 501 doses of RSZ (median 37, range 2-97). No serious AE were attributed to RSZ. Symptoms improved on treatment: dysphagia (42% vs. 9%); abdominal pain (58% vs. 0%); heartburn (18% vs. 0%); vomiting (67% vs. 17%); reflux (58% vs. 0%). Median esophageal eosinophil count improved (35 eos/hpf vs. 0, p value < 0.001). Patients receiving reslizumab maintain a relatively unrestricted diet.

Conclusions: Reslizumab appears to be safe in children with eosinophilic esophagitis over 8 years of treatment experience. Symptoms and eosinophil count improved considerably during treatment with reslizumab despite a relatively unrestricted diet.

427 FECAL MICROBIOTA TRANSPLANTATION USING BANKED DONOR STOOL IS EFFECTIVE IN THE TREATMENT OF RECURRENT CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN

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Background: Fecal microbiota transplantation (FMT) is effective in eradication of *Clostridium difficile* infection (CDI) in children with success rates of 90-100%. FMT can be performed using either a related stool donor or stool from a donor bank. There is a paucity of efficacy and safety data of banked donor stool in children. In this study we present our experience of 8 patients treated with FMT for recurrent CDI with donor stool obtained from OpenBiome (Medford, MA), a nonprofit stool bank.

Methods: Children with recurrent CDI (> 3 recurrences) underwent FMT via colonoscopy using OpenBiome lower delivery microbiota preparation (total volume 250 mL). Patients underwent routine colon prep before the procedure with PEG 3350. If on vancomycin for symptom control this was held 48 hours prior to FMT. In children > 20 kg, 240 mL of the microbiota preparation was used. In children < 20 kg, 210 -240 mL was used (depending on the providers' discretion of volume the colon could accommodate). A small volume of the microbiota preparation (~10 mL) was reserved for future research purposes. In all cases, 90% of the microbiota preparation used was administered into the cecum with the remaining 10% being administered slowly as the scope was withdrawn from the patient. Loperamide was administered following the procedure. Children had either a clinic visit or telephone encounter at 2-10 weeks, 10-20 weeks and 6 months following FMT. *C. difficile* toxin B gene polymerase chain reaction was performed if there was concern for clinical recurrence. Clinical information regarding stool donors was provided by OpenBiome.

Results: Eight children underwent FMT with stool from 6 donors (Table 1). Recipient age range 2-21 years; 3 females; 5 males. Donor mean age +/- standard deviation (SD) of 30 ±5.5 years; BMI mean ± SD of 24.3 +/- 3.08; 4 males; 2 females. Of these 6 donors, donor efficacy aggregated from the OpenBiome database ranged from 75-92.3%. Follow-up period ranged from 2-12 months. One patient (Patient 8) had inflammatory bowel disease (IBD), 6 of the remaining 7 had other underlying diagnoses. At the time of FMT, Patient 8 was on immunosuppressive medication, 3 were on acid suppression therapy, none were receiving antibiotics other than vancomycin. Seven patients had resolution of CDI symptoms after FMT. Patient 8 had mild diarrhea which lasted for 1 day; otherwise there were no adverse events. Patient 8 also developed recurrence of diarrhea and documented positive *C. difficile* stool toxin assay 3 weeks after FMT. No changes were made to his IBD medications. The parents opted to repeat his FMT using a related stool donor.

Conclusions: FMT via colonoscopy using stool from OpenBiome donor bank eradicated CDI in our cohort with a success rate of 88%. There was one mild adverse event of transient, self-resolving diarrhea. Larger, long-term studies in pediatric patients are required to further evaluate efficacy and safety of banked donor stool.

Table 1: Recipient and Donor Clinical Information

Recipient	Recipient Age (years)	Recipient Gender	Underlying Diagnoses	Donor Stool Volume (mL)	Relapse of CDI after FMT	Adverse events	Follow-up time from FMT (months)	Donor ID #	Donor Gender	Donor Efficacy Clinical Cure/Treated (%)
1	3	Female	Fructose intolerance	210	No	No	12	37	Male	191/226 (84.5)
2	13	Male	Autism	240	No	No	10	52	Male	255/313 (81.5)
3	21	Male	Cardiofacio-cutaneous syndrome	240	No	No	6	52	Male	255/313 (81.5)
4	6	Male	Hypoxic ischemic encephalopathy	240	No	No	6	73	Female	17/19 (89.5)
5	16	Female	Irritable bowel syndrome, postural orthostatic tachycardia syndrome	240	No	No	5	84	Male	24/26 (92.3)
6	2	Male	Cystic fibrosis, alpha 1 anti-trypsin deficiency	210	No	No	4	82	Female	18/24 (75)
7	19	Female	None	240	No	No	3	82	Female	18/24 (75)
8	14	Male	Ulcerative colitis	240	Yes	*Yes	2	79	Male	49/56 (87.5)

*Had mild diarrhea for 1 day following FMT

428 MICROARRAY ANALYSIS ABOUT DEVELOPMENT OF NODULAR GASTRITIS WITH *HELICOBACTER PYLORI* INFECTION IN CHILDREN

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Background and aims: Chronic *Helicobacter pylori* (*H. pylori*) infection generally induces lymphoid hyperplasia called nodular gastritis on child's gastric mucosa. Nodular gastritis will gradually disappear with advancing age and atrophic gastritis is believed to replace on gastric mucosa. Although nodular gastritis is an ordinary finding of *H. pylori* infection among children with esophagogastroduodenoscopy, the key mucosal immune response leading to lymphoid hyperplasia is not clear. The aim of this study is to evaluate gastric immune responses of children with *H. pylori* infection by microarray using gastric samples and reveal key molecules that mainly cause lymphoid hyperplasia.

Methods: We obtained gastric mucosal samples from 14 child patients and 12 adult patients undergoing routine endoscopic evaluation of chronic abdominal complaints. 8 child patients (3 males and 5 females) aged 10.1-14.6 years were infected with *H. pylori*, and the remaining 6 child patients (3 males and 3 females) aged 4.8-15.5 years were not infected. 6 adult patients (4 males and 2 females) aged 37-58 years were infected with *H. pylori*, and the remaining 6 adult patients (3 males and 3 females) aged 40-46 years were not infected. The gold standard for the diagnosis of infection was both a culture and a urea breath test positive for *H. pylori*. If both a culture and a urea breath test were negative, the patient was considered to be uninfected. We found nodular gastritis on every antrum of *H. pylori*-infected children. 3 infected child patients had nodular gastritis both on antrum and corpus. To evaluate the immune response leading to lymphoid hyperplasia, we excluded them from the analysis of corpus samples. No adult patients had nodular gastritis. Microarray analyses were performed on those samples and analyzed up-regulated or down-regulated gene expression related immune response. Gene expression was compared between patients with or without infection.

Results: In microarray analysis, 20 genes in child antrum, 7 genes in child corpus, 19 genes in adult antrum and 17 genes in adult corpus showed significant changes of expression (fold change >5, $p < 0.01$) when comparing patients with or without infection. We found many of the same genes between different generations or positions of stomach. 9 genes showed significant changes of expression only on child antrum, where we found nodular gastritis. In 9 genes, the cluster of differentiation 20 and 21 (CD20 and 21) were activators of differentiation of B lymphocytes. We also found significant expressions of some oncogenes on child mucosa.

Conclusion: We analyzed the gene expression to investigate pediatric immune responses against *H. pylori* infection leading to lymphoid hyperplasia. Our study suggests that CD20 and CD21 play important roles induced to lymphoid hyperplasia in children with *H. pylori* infection.

Friday, October 7, 2016

**Concurrent Session III
10:00AM**

NEUROGASTROENTEROLOGY AND MOTILITY

NEUROGASTROENTEROLOGY AND MOTILITY PRIZE: CLINICAL (Supported by a grant from LABORIE)

429 SACRAL NERVE STIMULATION FOR TREATMENT OF CONSTIPATION IN CHILDREN: LONG-TERM OUTCOMES, PATIENT BENEFIT, AND PARENT SATISFACTION

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Background: Treatment options for children with constipation refractory to medical treatment are limited. Recent studies suggest that sacral nerve stimulation (SNS) is an effective treatment option for children with defecation disorders. However, the long-term outcomes of SNS in children with constipation have not been described. The aims of our study were to evaluate the long-term efficacy of SNS for children with constipation and to describe patient benefit and satisfaction.

Methods: Using a prospective patient registry, we identified patients up to 21 years old who initiated SNS >2 years ago for treatment of constipation. Encounters were selected at baseline prior to SNS and at the most recent follow-up visit. We compared medication usage, PedsQL GI Symptom Scale (GSS), Fecal Incontinence Quality of Life Scale (FIQL), and Fecal Incontinence Severity Index (FISI) at baseline and follow-up. In addition, we contacted parents by phone to administer the Glasgow Children's Benefit Inventory (GCBI) and a parent satisfaction questionnaire. Wilcoxon signed-rank test and McNemar's test were used for comparison.

Results: We included 25 children (52% male, mean age 14.0 years): 17 had functional constipation, 6 had an anorectal malformation, 1 had Hirschsprung's disease, and 1 had tethered cord. In addition to constipation, 18 (72%) had fecal incontinence and 16 (64%) had urinary symptoms. Thirteen (52%) were using antegrade continence enemas (ACEs) at baseline. As shown in Table 1, use of laxatives and ACEs had decreased at follow-up. Of the 13 subjects using ACEs, 8 (62%) had undergone closure of their appendicostomy or cecostomy at follow-up and the remaining 5 (38%) were able to decrease ACE frequency. GSS, most FIQL domains, and FISI were significantly improved at follow-up. Sixteen parents (64%) completed the GCBI and parent satisfaction questionnaire after a mean of 2.5 years. Median GCBI was +42.7 (IQR 23.4-77.1) and 15 (94%) reported GCBI scores >0, indicating positive health-related benefit. Fourteen (88%) said they would still proceed with SNS if given the opportunity to remake their decision. All parents would recommend SNS to patients with similar symptoms. Six subjects (24%) had complications requiring surgery, including 4 requiring SNS replacement.

Conclusion: SNS is a promising treatment for children with constipation. In our cohort, SNS led to continued symptomatic improvement in children with constipation 2 years after treatment initiation. Despite a 24% complication rate requiring additional surgery, nearly all parents reported health-related benefit and would recommend SNS to others. Further long-term studies are needed to identify predictors of outcome, particularly risk factors for complications from SNS placement.

Table 1: Outcomes of SNS for treatment of constipation in children.

Outcome (n=25)	Baseline	Follow-up	
<i>Constipation treatment</i>			
Laxative doses per week; median (IQR)	7.0 (0.0-7.0)	0.0 (0.0-7.0)	p=0.06
ACEs per week (n=13); median (IQR)	7.0 (7.0-7.0)	0.0 (0.0-3.3)	p=0.001
Subjects using laxatives; n (%)	16 (64%)	11 (44%)	p=0.16
Subjects using ACEs; n (%)	12 (48%)	5 (20%)	p=0.03
<i>Symptom scores; median (IQR)</i>			
GSS	59.7 (42.4-72.2)	80.6 (55.6-88.9)	p=0.01
Constipation	37.5 (25.0-50.0)	75.0 (50.0-100.0)	p=0.003
FIQL			
Lifestyle	3.0 (2.3-3.9)	3.9 (3.3-4.0)	p=0.005
Coping/Behavior	2.8 (2.2-3.9)	3.7 (3.3-4.0)	p=0.001
Depression/Self-Perception	2.8 (2.4-3.6)	3.3 (2.9-3.6)	p=0.08
Embarrassment	3.0 (1.7-3.3)	3.3 (2.3-4.0)	p=0.005
FISI	32.5 (26.0-39.0)	30.0 (12.0-40.0)	p=0.007

430 USE OF CALRETININ IMMUNOSTAINING IN THE EVALUATION OF CHILDREN WITH POSSIBLE HIRSCHSPRUNG'S DISEASE
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The diagnosis of Hirschsprung's disease (HD) is made by the absence of ganglion cells in rectal biopsies. Rectal suction biopsies are usually obtained, but they are often inconclusive, mostly because of technical issues. Patients therefore require repeated biopsies. The recent addition of calretinin immunostaining (CI) may provide a more accurate diagnosis, and obviate the performance of subsequent biopsies. The objective of the present study was to evaluate the sensitivity and specificity of CI to aid in the diagnosis of HD. We also set out to determine if the CI would help in the initial diagnosis of inconclusive biopsies to avoid a second biopsy, and what is the CI like in patients with internal anal sphincter achalasia (IASA).

Methods: A total of 169 rectal biopsies were obtained at Boston Children's Hospital since the CI was introduced in 2010. Biopsies were reviewed in a blind fashion without knowing the final diagnosis. All biopsies were stained with H&E and classified as: ganglion cells present, absent, or inadequate for evaluation (too superficial). All biopsies with CI were classified as normal (no HD), abnormal (HD) or inconclusive. In many patients acetylcholinesterase(AChE) was also performed and its results were compared with CI. Patients were well characterized after long-term follow-up into three groups: No HD, classic HD (absence of ganglion cells), and IASA (normal ganglion cells and non-relaxing internal anal sphincter).

Results: A total of 169 patients were included: Mean age 5.7 ± 5.4 years (range 0-25y). *Table 1* shows the results of the biopsies according to the final clinical diagnosis. H & E (n=169) sensitivity 68.4% and specificity 86.4% to diagnose HD. CI stain (n=169) sensitivity was 96.3% specificity was 95.5%, while AChE stain (n=103) sensitivity 85.9% and specificity 100% for final diagnosis.

Comparing CI and AChE showed the following: no HD group 87.5% had both normal stains, 1.4% had both abnormal stains, 8.3% had normal CI and abnormal AChE, and 2.8% had abnormal CI and normal AChE. In the HD group 0% had both normal stains, 100% had both abnormal stains, 0% had normal CI and abnormal AChE, 0% had abnormal CI and normal AChE. In the IASA group CI showed was always normal (n=6) Regarding superficial biopsies (n=63) a total of 58 patients had CI performed. There were no false positives or false negatives with CI in these patients and the CI was always accurate to predict final diagnosis.

Conclusion: The addition of CI is useful in the evaluation of rectal biopsies of children with suspected HD with a high specificity and sensitivity. It was particularly useful in superficial biopsies in which other stains resulted in inconclusive results, allowing an accurate diagnosis. We also demonstrate for the first time that calretinin is normal in patients with IASA.

431 RET RECEPTOR TYROSINE KINASE PLAYS A SEXUALLY DIMORPHIC ROLE IN THE REGULATION OF GASTROINTESTINAL MOTILITY AND IS EXPRESSED BY DISTINCT SUBSETS OF ENTERIC NEURONS IMPORTANT FOR PERISTALSIS.

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The receptor tyrosine kinase Ret is essential for normal development of the enteric nervous system (ENS) and absence of Ret causes aganglionic bowel distal to the cardiac stomach. Ret expression is maintained in post-natal enteric neurons but its functions in the mature ENS remain unclear. Identifying these functions is important because altered Ret signaling may contribute to the pathophysiology of digestive disorders and drugs that target receptor tyrosine kinases are increasingly being used to treat cancer. To investigate Ret function in the mature ENS, we used heterozygous Ret-CFP mice, in which cyan fluorescent protein (CFP) is knocked into the Ret locus. Ret-CFP mice are haploinsufficient for Ret but have normal enteric neuronal density and exhibit no obvious deficits. To determine the role of Ret in the mature ENS, we analyzed gastrointestinal (GI) motility in adult Ret-CFP mice and control littermates. Total GI transit time was accelerated in male, but not female, Ret-CFP mice (n=7, $p < 0.03$). Gastric emptying and small intestinal transit were unchanged, suggesting that Ret function is selectively required for normal colonic motility in males. To identify Ret-expressing enteric neurons that might be important for GI motility, we used whole mount immunostaining to quantify the proportions of enteric neurons that express Ret in Ret-CFP mice. While all enteric neurons are CFP+ at the time of birth, by 12 weeks of age CFP co-localizes with the neuronal marker ANNA-1 in $59 \pm 6\%$ of myenteric neurons in the ileum (mean \pm SEM; $p < 0.0002$; n=8 mice) and $55 \pm 6\%$ of myenteric neurons in the colon ($p < 0.0001$; n=8), suggesting that only a subset of mature enteric neurons maintain Ret expression. Analysis of Ret co-expression with markers of neuronal subsets important for motility revealed that $32 \pm 2\%$ of Ret+ myenteric neurons in the ileum and $51 \pm 3\%$ in the colon express neuronal nitric oxide synthase (nNOS), which primarily marks inhibitory motor neurons (iMNs). Virtually all nNOS+ myenteric neurons express Ret ($99 \pm 1\%$ ileum, $97 \pm 1\%$ colon; n=4) suggesting that mature iMNs maintain Ret expression. Vasoactive intestinal peptide (VIP), another marker of iMNs, also co-localizes with Ret. Intrinsic primary afferent neurons (IPANs), which are critical for initiation of peristaltic reflexes, are marked by expression of the protein, calbindin. We found that $30 \pm 3\%$ of Ret+ myenteric neurons in the ileum and $19 \pm 3\%$ in the colon express calbindin. In contrast to iMNs, Ret expression in calbindin+ myenteric neurons is restricted to a subset. These data show that Ret expression is maintained within specific subsets of enteric neurons and that diminished Ret function is associated with a sex-dependent defect in GI motility. Altering Ret expression or function may thus offer a sexually dimorphic therapeutic strategy for GI motility disorders.

432 GUT MICROBIOTA-MEDIATED GENE X ENVIRONMENT INTERACTIONS IN THE TASHT MOUSE MODEL OF HIRSCHSPRUNG DISEASE

Nicolas Pilon, Ouliana Souchkova, University of Quebec at Montreal, Montréal, QC, Canada

Background: The enteric nervous system (ENS) is subdivided into two major plexuses: the myenteric plexus and the submucosal plexus. While the former mainly controls gastrointestinal (GI) motility, the latter regulates several mucosal functions. Although the ENS is formed from neural crest cells during prenatal development, its maturation persists in the early post-natal period. Emerging evidences suggest that the molecular factors required for proper post-natal maturation might be modulated by the gut microbiota. Accordingly, germ-free and antibiotics-treated rodents display enteric neural defects and gut dysmotility similar to what is observed in genetic models of enteric neuropathies. However, efforts to assess the impact of altered microbiota on the expressivity of these genetically-induced enteric neuropathies are lacking. To begin to address this question, we took advantage of a recently described insertional mutant mouse line called TashT in which $\sim 13\%$ of homozygotes (TashTTg/Tg) succumb to aganglionic megacolon around weaning age, with a striking 15:1 male to female ratio. TashTTg/Tg mice that do not develop megacolon display male-specific reduced colonic motility which is associated with a strong male bias in the severity of colonic aganglionosis/hypoganglionosis as well as with an increase in nNos+ myenteric neurons restricted to the distal ganglionated colon.

Methods: Pregnant wild-type (FVB/N) and TashTTg/Tg mice at mid-gestation are divided into antibiotics-treated (A+) and control (A-) groups. For the antibiotics treatment, mice are given drinking water containing 1 mg/mL of ampicillin, 1 mg/mL of metronidazole, 0.5 mg/mL of vancomycin, 0.5 mg/mL of neomycin and 10 mg/mL of sucrose for 5 weeks (i.e. until weaning of their pups). The neural composition of the myenteric plexus and intestinal motility parameters is then assessed in P22-23 and P30-35 male pups from each group.

Preliminary results: A+ wild-type mice display an increased proportion of both Calretinin+ and nNos+ myenteric neurons in the duodenum and ileum and a decreased proportion of only Calretinin+ myenteric neurons in the distal colon. These changes of neurochemical coding are detected as early as at P22-23. Furthermore, while GI transit is delayed in the proximal gastrointestinal tract, it is enhanced in the distal colon.

Surprisingly, in P22-23 TashTTg/Tg males, antibiotics treatment was found to induce a net increase in myenteric neuron numbers that is accompanied by a decrease in the proportion of nNos+ neurons in the distal ganglionated colon.

Conclusion: This study demonstrates for the first time that the gut microbiota can influence the expressivity of a genetically-induced enteric neuropathy.

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NEUROGASTROENTEROLOGY AND MOTILITY PRIZE: BASIC (Supported by a grant from MMS)

433 THE ABILITY OF HIGH RESOLUTION ESOPHAGEAL MANOMETRY TO DISTINGUISH PRIMARY FROM SECONDARY RUMINATION EPISODES IN CHILDREN AND ADOLESCENTS

Franziska Righini-Grunder, Ann Aspirot, Christophe Faure, CHU Sainte Justine, Université de Montréal, Montréal, QC, Canada

Introduction: The diagnosis of rumination syndrome is mainly clinical and based on the Rome III criteria. Pathophysiology of rumination syndrome remains unknown, but involves a voluntary contraction of the abdominal wall muscles with a rise in intragastric pressure and painless retrograde movement of gastric contents into the esophagus up to the mouth with following rechewing or expulsion of food. We recently described the high resolution esophageal manometry (HREM) pattern in children and adolescents with rumination syndrome and showed that HREM can be a helpful and useful tool for confirmation of rumination syndrome. The aim of this study is to analyze the mechanisms leading to rumination namely primary (abdominal pressure increase occurs before the rumination episode) or secondary (increase in abdominal pressure following the onset of a reflux event) rumination using HREM in children and adolescents.

Patients and methods: Evaluation of HREM patterns of fifteen pediatric patients with rumination syndrome according to Rome III criteria between January 2011 and March 2016. Ten wet swallows followed by 100 mL of water or a test meal were administered during HREM. A primary rumination was defined as a clinical rumination episode (exteriorisation of the gastric content without retching, nausea or vomiting effort) associated to a rise of gastric pressure >30mmHg. A secondary rumination was defined as a clinical rumination episode (exteriorisation of the gastric content without retching, nausea or vomiting effort) associated to a rise of gastric pressure occurring during a transient inappropriate LES relaxation (TLESR).

Results: Ninety-two clinical episodes of rumination were demonstrated during HREM study in 12 out of the 15 patients (80%; range 1-29 episodes per patient; median pressure 49.6mmHg, range 30.2-126.7). Analysis of the mechanism of rumination was possible in 28 out of 92 (30%) episodes. Among the 28 episodes, 8 were classified as primary rumination and 20 as secondary rumination. The 64 remaining non-classified episodes occurred during repetitive swallows leading to LES relaxation precluding any mechanistic analysis in 2 patients. Primary rumination occurred in 3 patients and secondary rumination in 5 patients. 1 patient had both primary and secondary rumination episodes. In 3 patients no classification was possible.

Conclusion: Differentiation between primary rumination with gastric pressure overcoming LES pressure and secondary rumination occurring during a TLESR may help to accurately diagnose rumination in adolescents and in children, by providing an objective evaluation in addition to clinical symptoms. Further research is needed to study whether HREM results may influence treatment and outcome of children and adolescents suffering from rumination syndrome.

434 NEUROSTIMULATION WITH IBSTIM ATTENUATES AMYGDALA NEURONS AND PREVENTS POST-INFLAMMATORY VISCERAL AND SOMATIC HYPERALGESIA IN RATS

Adrian Miranda, Reji Babygirija, Medical College of Wisconsin, Milwaukee, WI, USA

Introduction: Hyperalgesia following TNBS colitis has been extensively used as an animal model for IBS. Recent clinical evidence from our group suggests that auricular electrical stimulation with the IBstim device (Innovative Health Solutions, Indiana) can have antinociceptive properties. We aimed to examine the role of neurostimulation with this device on visceral and somatic hyperalgesia following colitis in rats and to investigate its effect on amygdala neurons, a central structure known to be involved in nociception.

Methods: In two groups of male Sprague-Dawley rats, colitis was induced by application of TNBS (50% in EtOH). One group (n=8), received stimulation starting on the day of TNBS administration and continued daily for 4 hours x 5 days. The control group (n=8) had an inactive "sham" device. On day 7 following TNBS, a visceromotor response to colorectal distension was recorded using EMG. The paw withdrawal response with Von Frey filaments was used as a measure of somatic sensitivity. Experimenters were blinded to all groups. A separate group of TNBS treated rats (n 5) underwent extracellular, *in vivo*, single-unit recordings from neurons in the central nucleus of the amygdala (CeA) using glass-insulated carbon filament electrodes. Following baseline firing recording, a brief (30 s) compression of the paw was applied twice, 5 min apart to induce firing of CeA neurons. IBstim was then placed on the ipsilateral ear and after 15 minutes, the baseline firing of the neuron and response to compression of the paw was again recorded and compared.

Results: Control animals with the "sham" device showed a much higher VMR at CRD pressures >30mmHg compared to those with IBstim (0.67 ± 0.09 and 0.85 ± 0.08 vs. 0.33 ± 0.02 and 0.54 ± 0.07 , respectively). Thus, active stimulation significantly prevented the development of visceral hyperalgesia compared to control ($p < 0.05$). Similarly, rats with IBstim required much higher forces to induce a paw withdrawal (780 ± 120 mN) when compared to inactive devices (190 ± 10 mN) ($p < 0.05$), suggesting the prevention of somatic hyperalgesia. Extracellular recordings from amygdala neurons and were recorded only from excitatory neurons. Prior to stimulation, the mean spontaneous firing of the neurons was 1.15 ± 0.36 imp/sec with an excitatory response to 3.05 ± 0.46 after paw compression (190mN). There was a 52% decrease in the spontaneous firing of the neurons after just 15 minutes of auricular stimulation (0.56 ± 0.21 imp/sec). Similarly, the response to compression of the paw was decreased by approximately 66% after auricular stimulation (1.04 ± 0.29 imp/sec) ($p < 0.05$).

Conclusion: Auricular stimulation with IBstim prevented the development of post-inflammatory visceral and somatic hypersensitivity. Stimulation also significantly decreased the baseline firing of amygdala neurons and the response to somatic stimulation. This attenuation could theoretically account for the modulation of pain responses in both humans and animals.

Friday, October 7, 2016

Poster Session II
12:00 – 2:00 PM

*** Poster of Distinction**

APGNN

435 CASE OF COMBINATION OF FRUCTOSE-1,6-BISPHOSPHATASE DEFICIENCY WITH COW'S MILK AND EGG WHITE ALLERGY
Burcu Kumru¹, Burcu Öztürk Hıþmi², Miray Karakoyun², ¹Gaziantep Children's Hospital, Gaziantep, Turkey, ²Tepecik Education and Research Hospital, Ýzmir, Turkey

Background: Fructose-1,6-bisphosphatase (FBPase) deficiency is a very rare autosomal recessive disorder caused by a mutation of the fructose-1,6-bisphosphatase gene (FBP1). Disease is mainly revealed by hypoglycemia and lactic acidosis, both symptoms being characteristic for an enzymatic block in the last steps of the gluconeogenesis. Symptoms usually accompany prolonged fasting associated with illness but they have been reported following ingestion of a large single dose of fructose, especially after a period of fasting. The majority of children should keep well without dietary fructose restriction between episodes of intercurrent illness. Most serious food allergies start in infancy and early childhood. They are caused by a relatively small number of different foods. IgE-mediated food allergies cause children's immune system to react abnormally when exposed to one or more specific foods such as milk, egg, wheat or nuts. Milk and egg allergy are the most common food allergy. The symptoms caused by food allergy are varied. They usually cause gastrointestinal symptoms such as bloating, diarrhea, nausea and vomiting.

Case report and Results: A 25-month-old boy, born at term of first-cousin parents, had FBPase deficiency. His younger sibling was diagnosed with FBPase deficiency by DNA testing (homozygous mutation in the FBP1 gene c.961insG;p.Ser321Val(fs)13X)) at the age of 7 months. He requires regular meals containing a complex carbohydrate source to provide 'slow release' glucose. Uncooked cornstarch has been advocated daytime and late evening (2 g/kg/dose). After 1 year of age, although he didn't eat a large single dose of fructose, he experienced vomiting and diarrhea with frequent hypoglycemia episodes. This hypoglycemia occurred as a result of reduced food intake. During these episodes, he requires an Emergency Regime (ER) (15% unflavored glucose polymer drink) at home. If his blood glucose didn't increase through ER, hypoglycemia was treated with infusions of IV 10% glucose solution in hospital. It was thought that the allergic reactions to food might be caused by these symptoms. Laboratory tests showed serum total IgE level 332.25 IU/mL (0-100) and positive-specific IgE to cow's milk and egg white. t. After the elimination diet, symptoms disappeared. Consequently, food allergies should be considered in patient with inherited metabolic disease who is suffering from unimproved vomiting and diarrhea.

436 RISK FACTORS FOR DIARRHEA, FOUND IN THE GROWTH AND DEVELOPMENT OF A HEALTH FACILITY IN VITORIA-PE MUNICIPALITY

Raphael Henrique Gomes da Costa, Vitória Carla Conceição Almeida, José Teles de Oliveira Neto, Mariana Boulitreau Siqueira Campos Barros, Recife, Pernambuco, Brazil, Vanessa Karla Santos de Souza, UFPE, Recife, Pernambuco, Brazil

Most of the pathogens that cause diarrhea are transmitted by the fecal-oral route and the risk may be higher in infants in a developing period due to the ease of contact between caregivers through the contaminated hands of family members, lack of hygiene in the preparation of food and aseptic deficiency of infants. The preparation of food and poor hygiene conditions appear to be a potential source of contamination for the child who gets diarrhea. The aim was to identify the incidence of diarrhea in infants where hygiene and care of utensils are poor, confirm the risk factors associated with the disease and check for contamination in the care of the infants followed. Prospective cohort of 100 infants followed in the growth and development consultations and home visits to a healthcare facility's Vitória-PE municipality in the period from November to January 2015/2016. Infants exposed to poor hygiene and sanitation or not exposed to these conditions the possible risk factors described in the literature were followed throughout the study for the occurrence of diarrhea diagnosed according to the criteria of the National Nosocomial Infection Surveillance System / Centers for Disease Control and Prevention (NISS / CDC). Within 3 months of the study were diagnosed 38 episodes of diarrhea with cumulative incidence. Children who were exposed to risk factors had an incidence of diarrhea 95.2%, compared with those who were not 4.8%, a statistically significant risk for diarrhea. In the analysis where variables were included: poor hygiene and sanitation exposed to these conditions, the probability had over 90% of contracting diarrhea plus get the following result: to breastfeed during growth and development and administration of the vaccine rotavirus were protective factors and aid in the recovery of affected infants from diarrhea, while those who did not receive the vaccine and those who were not breastfed were at higher risk of getting diarrhea. The infants hygiene conditions are directly linked to diarrhea, although it was observed that the precarious hygiene is directly linked to risk factors for diarrhea in infants. The fact of being exposed to poor hygiene and sanitation was a risk factor for the occurrence of the disease, requiring rigorous evaluation in home consultation and visit the care of infants as the exposure of risk factors. The more care, breastfeeding and vaccination was considered a protective factor for the outcome of the disease.

437 GASTROSTOMY TUBE LENGTH: DOES IT GROW WITH THE CHILD

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Rationale: Advances in medicine enable increased life expectancy of children with disabilities, and the number of children fed through gastrostomy tubes has also increased. The tube preferred by most parents is the skin level-button which allows better function. The button is placed after measuring the length of the tract created through the skin, abdominal wall and stomach wall. Accurate estimation of the stoma tract length is important to prevent gastric ulcer formation and/or skin damage. The children are followed at the gastrostomy- ube clinic, to ensure that the length of the tube fits the child's growth. Tubes are changed periodically and a change in length over 0.2 cm requires a tube exchange. Our long-standing observation shows that the tube length is almost unchanged during the child's growth and development.

Our primary aim is to examine whether change in BMI predicts a change of gastrostomy tract length. Secondary aim is to examine the correlation between the patient's age, height, weight and the length of gastrostomy tract, and to evaluate how often gastrostomy stoma tract has to be measured in children, considering the natural growth.

Methods: A retrospective chart review of 65 patients under 18 years of age, followed by attendant nurses at the gastrostomy-tube clinic between January 1,2000 and July 31,2015. All of the children had a Mic Key gastrostomy. Clinical demographic and anthropometric data and measurements of the gastrostomy tract over time were retrieved from the patients' charts: age, gender, background diagnosis, ability to swallow, age at gastrostomy insertion, type of procedure, fundoplication performance, weight and height measurements, body mass index (BMI), and stoma-tract measurements.

Results: Of the 65 patients, aged 0.5-18 years, with at least 2 measurements of the gastrostomy tract length, 36 were males and 29 were female. Mean age was 4.7 and 7.1 years at first and second measurements respectively. A change of >2 mm in the tube length was found in 14 patients within 31 months of follow-up. The main predictor we found for increase in tract length was increase of the BMI percentile. Out of 22 children with a BMI % increase of more than 10%, an increase in the tract length was found in 27.3%. In children with a BMI% increase of $\leq 10\%$, a change in tract length was found in only 18.2%. The time interval between tract measurements was longer in those with change in length compare to those with no change (51.3 months and 28.4 months, respectively). A change in tract length occurred in only 15% of patients after <3 years interval, in 36% of patients after >3 years interval, and in 42% of those after >4 years interval.

Conclusions: A change in the gastrostomy tract length is uncommon within the first 3 years post-insertion, and therefore tract measurements are not necessary. An increase in BMI% is a predictor of increase in tract length.

438 COMPARISON OF THE WEIGHT Z-SCORE, PROTEIN AND CALORIE INTAKE BETWEEN SMALL AND APPROPRIATE FOR GESTATIONAL AGE PRETERM INFANTS DURING HOSPITAL STAYS

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Comparison of the weight Z-score, protein and calorie intake between small and appropriate for gestational age preterm infants during hospital stays.

Objective: To investigate the possible differences of the weight Z-score, practical protein and calorie intake between SGA (small for gestational age) and AGA (appropriate for gestational age) preterm infants during hospital stays.

Methods: A total of 493 preterm infants admitted to the NICU in Xinhua hospital from January 2012 to December 2014 were enrolled, parenteral nutrition was initiated within 24 hours of birth and participants were divided into gestational age <34 weeks group (gestational age <34 w, 314 cases) and ≥ 34 weeks group (gestational age 34-37 w 179 cases); then each group was classified into AGA and SGA subgroups by birth weight <34 w AGA 268 cases and <34 w SGA groups 46 cases; ≥ 34 w AGA 125 cases and ≥ 34 SGA 54 cases). General information, weighted Z-score, actual protein and calorie intake, history of pregnancy and delivery and preterm infants' complications were compared between AGA and SGA preterm infants in different gestational age brackets.

Results: (1) in preterm infants with gestational age <34 w, calorie intake in the SGA group was less than that in the AGA group on the fourth, eighth and tenth day ($p < 0.05$); total protein intake in the SGA group on the eighth day was less than that in the AGA group ($p < 0.05$); in preterm infants with gestational age ≥ 34 w, there is no statistical difference in protein intake between the AGA and SGA group in two weeks after birth ($p > 0.05$). Calorie intake in the SGA group was more than that of the AGA group on the sixth day ($p < 0.05$). (2) On the side of weight gain, preterm infants in the SGA group had a higher rate of weight growth after regained birth than the infants in the AGA group ($p < 0.05$); however, it is shown that the weight Z-score of each group in two weeks after birth were moving away from the average, and SGA groups were lower than AGA groups.

Conclusion: Compared to the AGA premature infants, SGA premature infants had a higher rate of weight growth after regained birth weight, lower weight Z-score in two weeks after birth, less protein and energy intake and more complications. More importance should be attached to actual protein and calorie intake of SGA preterm infants, especially for the SGA prematures with gestational age <34 weeks, and an individualized nutritional strategy should be established to improve their poor growth.

Key words: parenteral nutrition; protein intake; calorie intake; weight Z-score; SGA preterm infant.

439 THE ADVENTURES OF CAPTAIN IMMUNITY: A COMIC BOOK STORY THAT TEACHES ADOLESCENTS ABOUT THE STAGES OF HEPATITIS B

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Project Description (including objectives and approach): Boston Children's Hospital's Center for Childhood Liver Disease ("Center") specializes in helping infants, children, adolescents and young adults who have a wide variety of liver, gallbladder and bile duct disorders.

Doctors refer children with liver disease to this program at Boston Children's from all over the world.

A small patient population seen at the Center is children with chronic hepatitis B, a life-long infection of the liver that can lead to serious health issues such as liver cancer. Infants and young children who become infected with the hepatitis B virus are often more susceptible to developing chronic hepatitis b. Statistics from the Centers for Disease Control and Prevention show that 90 percent of infants infected with hepatitis B become chronically infected, compared with 2 to 6 percent of adults. Therefore, education about chronic hepatitis b and its management are crucial for young populations who must live with this lifelong disease.

At Boston Children's, the median age of the chronic hepatitis B patient is 15 years old; however, an audit of internally available education materials about the virus revealed that all materials were geared toward parents. The Center's clinical team, in partnership with the hospital's patient and family education department, set an objective to create an educational tool that taught pre-teen and teen populations about chronic hepatitis B and the stages of infection, in particular. After conducting an environmental scan of externally available chronic hepatitis B education for these populations, it was determined that a comic book could serve as a novel and engaging mode of education for Boston Children's pre-teen and teen chronic hepatitis B patients.

The project, which took approximately a year to complete, had many phases:

•Storyboarding: Determining the storyline of the comic book and characters while ensuring an accurate representation of both the effects of and treatment for chronic hepatitis B. •Writing the Narrative: Morphing medical jargon about chronic hepatitis B effects and treatments into language that is simple and easy to understand by young audiences.

•Design: Drawing the characters and scenes for the comic, keeping in mind cultural considerations (more than half of Boston Children’s chronic hepatitis B patient population is Asian).

•Family Engagement: Involving families in the design and review process of the comic book.

Target Population: Young children/adolescents (ages 8 and up) with chronic hepatitis B.

Outcomes/Impact:

•Reading Level: Given that information about chronic hepatitis B contains hard-to-understand medical language (such as “immune tolerance” and “latent”), the comic book reads at a seventh-grade reading level.

•Patient and Family Satisfaction: Since its launch in the Center beginning December 2015, *The Adventures of Captain Immunity* comic book has received positive feedback from patients and families. Here is feedback we have received so far:

o Said one parent, “This is AWESOME! I feel as though I learned TONS on Hep B. It was easy to follow and understand, not scary or overwhelming. Incredibly well done that both a parent and child can follow.”

o Patients and families feel that the comic book is gender neutral.

o Patients enjoy the characters and find them engaging.

o Patients enjoy the interactive activities in the comic book (i.e., a word puzzle of common chronic hepatitis B terms. Said one 12-year-old boy: “Oh cool a word puzzle, I love these.”

o A common theme of feedback is that the book is simple to understand. It takes something as complicated as hepatitis B and simplifies it for patients and parents to understand.

Implications for Policy, Delivery or Practice: Since the beginning of the twentieth century, comic books have been used to transform real-life sensitive information or events into a fictional format to help the target audience to more easily understand — and accept — this information.

For example, Captain America is a comic famous for helping the American public temporarily escape from their anxieties and insecurities caused by the Great Depression.

Comic books play a powerful role in health education. They, too, can help patients and families with their anxieties and insecurities around a new diagnosis and/or treatment plan. A 2014 journal article in *Medical Humanities* sums up the benefits: “Health information comics have the potential to do much more than simply convey facts about an illness; they can also support patients in dealing with the social and psychological aspects of a condition.”

For Boston Children’s, *The Adventures of Captain Immunity: A Comic Book on Hepatitis B for Adolescents* aids in facilitating sometimes challenging conversations between clinicians, parents, and young adults. It also helps the child to visualize an otherwise invisible disease and reconcile the effects chronic hepatitis B has on his or her own body. Finally, the comic book style creates a fun narrative for adolescents to follow through the use of action, thrill and adventure popular in media aimed at younger generations.

440 THE IMPACT OF PEDIATRIC HOME PARENTERAL NUTRITION (HPN) SERVICE ON THE CLINICAL OUTCOME AND HEALTHCARE COSTS IN QATAR

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Introduction: Home Parenteral Nutrition (HPN) is recognized to be the best option for improving the quality of life the children with intestinal failure, and their families, within the constraints of the disease (Koletzko *et al.*, 2005). Before starting HPN in Qatar, such children were kept as in-patients for many years, which was associated with high mortality and morbidity rates. In developed countries, private Homecare companies run the HPN service. However, since no such private companies were available in Qatar and the neighboring region, an innovative approach had to be developed to allow the provision of such service.

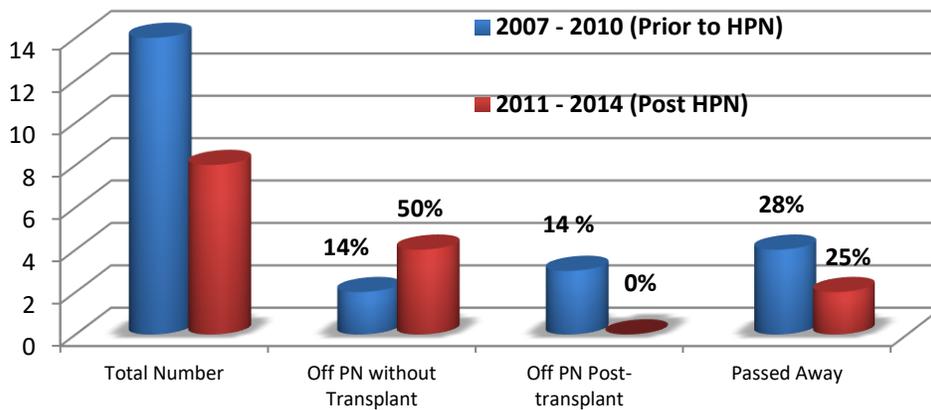
Objectives: 1) To describe the impact of HPN service on the patients and families in Qatar; 2) To describe the impact of HPN service on the savings to health service in Qatar.

Method: This is a retrospective study done at Hamad Medical Corporation (HMC) in Qatar. The medical files of all the pediatric patients who had TPN for more than 3 months between January 2007–December 2014 were reviewed to find out the impact before and after introduction of HPN service.

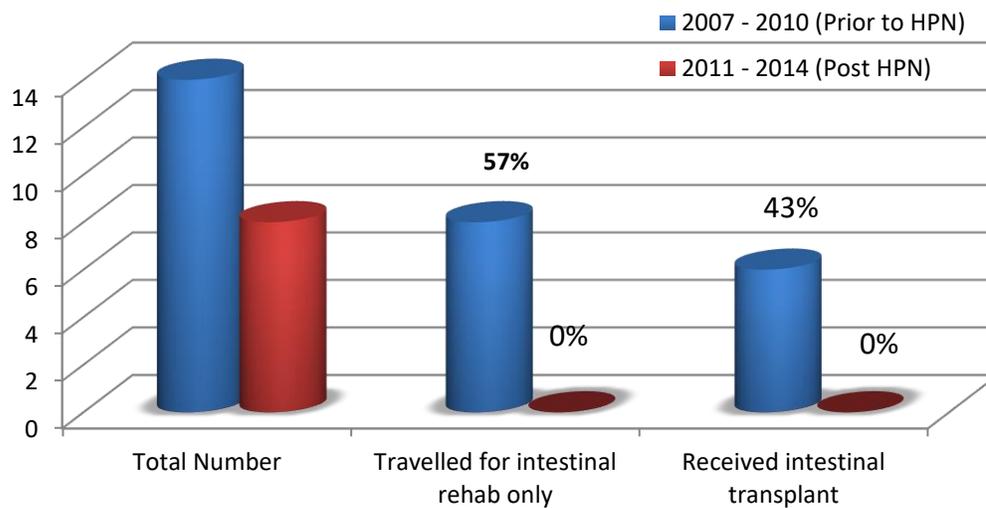
Results: Between 2011-2014, 10/11 (90 %) long-term TPN patients were successfully discharged on HPN. One eligible patient could not be discharged home for social reasons. Significant reduction in the rate of CVL sepsis was demonstrated in 8/10 (80 %). In the 4 years period prior to starting HPN, 14/14 (100%) patients traveled abroad, 6 of them more than once, for intestinal rehabilitation and/or intestinal transplantation. 5 of them (36%) underwent intestinal transplantation, 2 unsuccessful and both patients died. Post-HPN service, no patient (0%) traveled abroad or had intestinal transplantation done ($p<0.001$) with huge savings to the health service authority in Qatar.

Conclusion: Pediatric HPN program in Qatar is the only program in the whole of the Arab region that provides full pediatric HPN service. It has significantly reduced the mortality and morbidity rates of long-term TPN. It has proved that when families are trusted, engaged and trained; they can successfully deal with high tech TPN pumps and clinical care. It has demonstrated that, even in a small country, it is possible to establish and run a successful HPN service using the local resources available.

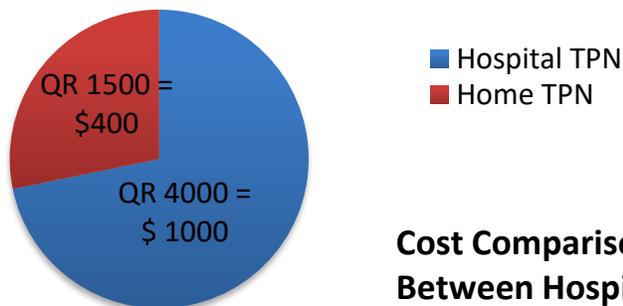
Reference: Koletzko *et al.* Guidelines on Paediatric Parenteral Nutrition of the ESPGHAN and the ESPEN. *JPGN.* 2005;Nov41 Suppl 2:S1-87.



Clinical Outcome Pre- & Post-HPN Service



Number of Patients Who Travelled Abroad Pre- & Post- HPN



Cost Comparison Between Hospital and Home TPN in Qatar

441 RISK FACTORS FOR DIARRHEA IN A PEDIATRIC ICU IN THE CITY OF VITORIA-PE

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Most pathogens that cause diarrhea is transmitted by the fecal-oral route and the risk may be higher in infants hospitalized due to ease of contact between patients through contaminated hands of family members and health professionals. Pacifiers similar to bottle nipples appear to be a potential source of contamination for the child acquiring nosocomial infectious diarrhea. To determine the incidence of nosocomial diarrhea (DN) in infants who use pacifiers or not, to identify risk factors associated with the disease and check for fecal contamination in the pacifier of hospitalized infants. Prospective cohort of 78 infants hospitalized in the pediatric ICU of Hospital João Murilo, Vitória-PE, in the period from April to October 2015. Patients exposed or not the use of pacifiers with possible risk factors described in the literature were followed over admission for the occurrence of nosocomial diarrhea diagnosed according to the criteria of the National nosocomial Infection Surveillance System / Centers for Disease Control and Prevention (NISS / CDC) or to exit. During the 7 months of the study were diagnosed 33 episodes of DN with cumulative incidence and incidence density of 8.7% and 11.25 / 1000 patient-days, respectively. Children who used a pacifier had an incidence of DN 8.2% when compared with those who did not use (9.2%), with no statistically significant risk in the bivariate analysis controlled for length of stay. In multivariate analysis where we included the variables in the bivariate were associated and the use of pacifiers and rotavirus vaccine for biological plausibility was obtained the following result: be nursed during hospitalization and each day of stay in the ICU were protective factors, while the risk factors were associated with the highest number of days of use of oxygen by nasal catheter and antimicrobial. They were isolated from fecal coliforms in 16% of samples placed in culture and about ¾ of the positive (77.8%) had more than 100,000 CFU / mL per pacifier. Pacifier use by infants was not associated with nosocomial diarrhea, although it has been observed fecal contamination in samples placed in culture. The highest number of days of antibiotic use was a risk factor for the occurrence of the disease, requiring rigorous evaluation as to the indication and the duration of use of antimicrobials. The highest number of days of use of supplemental oxygen by nasal catheter was considered a risk factor for the outcome and was probably associated with catheter manipulation by the mother and / or healthcare professional during the installation and maintenance of the same in medically ill children with instability hemodynamics.

442 PREVALENCE AND MICROBIOLOGY OF CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS AMONG CHILDREN WITH BILIARY ATRESIA LISTED FOR LIVER TRANSPLANTATION

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Introduction: The commonest indication for liver transplantation (LT) in children is biliary atresia (BA). Pre-transplant nutritional status is directly related to post-operative outcomes, however, malnutrition is prevalent in patients with BA, and can be refractory to even aggressive enteral therapy. Parenteral nutritional (PN), therefore, may be required for nutritional rehabilitation of the LT candidate with BA. While the use of PN in malnourished patients with BA has been shown to improve nutritional status, PN comes with tradeoffs, chief among them the risk for central line associated bloodstream infection (CLABSI). We sought to define the rate and microbiology of CLABSI among children transplanted for BA at our large, pediatric LT program, and to investigate potential risk factors associated with CLABSI.

Methods: We reviewed medical records of all children with BA who were transplanted at our institution from 2008-2015, and were waitlisted before the age of 2 years. We defined CLABSI based on the Centers for Disease Control and Prevention/National Healthcare Safety Network definition to include only primary bloodstream infections, not those secondary to infections at another body site. In contrast to these criteria, though, we captured all CLABSI, whether they originated in an outpatient, or an inpatient setting. Univariate analysis was used to compare characteristics of patients with CLABSI, to those without CLABSI; chi square for frequency data and Mann Whitney for continuous data.

Results: A total of 83 children with BA met inclusion criteria. Fifty-five of 83 children (66%) had a central venous catheter for PN. Twenty-one episodes of CLABSI were documented among 15 of 55 (27%) patients receiving PN; yielding a rate of 5.5 CLABSI per 1,000 line days. More CLABSI occurred among inpatients (13/21, 62%) than outpatients (8/21, 38%). Gram-negative bacteria were most frequently isolated (12/21, 57%), followed by Gram-positive bacteria (6/21, 29%), and yeast (3/21, 14%). Regarding risk factors for CLABSI (Table 1), only serum albumin was significantly different among patients with CLABSI and those without CLABSI (2.8 vs. 3 g/dL, $p=0.03$, respectively).

Conclusions: PN is frequently used for nutritional rehabilitation of patients with BA on the LT waitlist. CLABSI represents a significant morbidity, with rates that eclipse those previously observed in ambulatory or inpatient pediatric oncology patients (0.65 and 2.2 CLABSI per 1,000 line days, respectively, Rinke, *Pediatr Blood Cancer*, 2013). While most CLABSI were associated with Gram-negative bacteria, Gram-positive bacteria and yeast were also encountered, underscoring the importance of broad empiric antibiotic coverage initially. A preliminary univariate analysis of potential risk factors for CLABSI only identified albumin as a significant discriminator between the groups. This needs to be confirmed in a multivariable model, which is our future direction with this work.

	CLABSI (n=15)	No CLABSI (n=40)	p-value
Age (years) [median, range]			
At listing	0.56 (0.29-1.74)	0.5 (0.29-1.48)	0.4
At transplant	0.85 (0.53-1.81)	0.8 (0.42-3.1)	0.36
Sex			
Female	12 (80%)	28 (70%)	0.46
Race [n (%)]			
White	12 (80%)	33 (82%)	0.83
Non-white	3 (20%)	7 (18%)	
Language [n (%)]			
English	12 (80%)	32 (80%)	1
Spanish	3 (20%)	8 (20%)	
Insurance [n (%)]			
Public	11 (73%)	21 (52%)	0.21
Private	3 (20%)	18 (45%)	
Charity	1 (7%)	1 (3%)	
Length Z-score [median, range]	-1.26 (-4.1-0.96)	-1.23 (-5.73-1.05)	0.39
Weight Z-score [median, range]	-1.43 (-3.1-0.74)	-1 (-5.22-1.81)	0.5
Weight-for-length Z-score [median, range]	-0.48 (-2.27-0.55)	-0.18 (-3.24-2.32)	0.67
ALT (U/L) [median, range]	143 (35-789)	124.5 (33-1598)	0.67
GGT (U/L) [median, range]	353 (51-1028)	287.5 (51-2249)	0.56
Albumin (g/dL) [median, range]	2.8 (2.3-4)	3 (2.2-5.1)	0.03
Conjugated bilirubin (mg/dL) [median, range]	4.2 (0-11.2)	3.75 (0-19)	0.55
Total bilirubin (mg/dL) [median, range]	12 (0.3-22.5)	10.85 (0.6-36.8)	0.41
Leukocytes (x 10 ⁹ /L) [median, range]	13.6 (6.2-24.8)	10.18 (3.34-30.1)	0.51
Hemoglobin (g/dL) [median, range]	10.7 (7.2-11.8)	9.9 (7-13.7)	0.84
Platelets (x 10 ⁹ /L) [median, range]	164 (80-508)	123.5 (39-502)	0.92
INR [median, range]	1.4 (1-2)	1.35 (0.8-3.2)	0.3
Blood urea nitrogen (mg/dL) [median, range]	10 (3-22)	8 (3-29)	0.79
Prealbumin (mg/dL) [median, range]	9 (5-15.8)	9.1 (3.7-22.6)	0.27

443 NURSING CARE A CHILD WITH ACUTE GASTROENTERECOLITIS(GECA)

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Acute gastroenterocolitis also known as acute diarrheal disease (ADD) is a syndrome because of different etiologic agents (bacteria, viruses and parasites) whose predominant manifestation is the increased number of bowel movements with watery stools\liquid or little consistency. The disease is characterized by sudden onset of diarrhea, with or without other symptoms such as nausea, vomiting, abdominal pain and fever. The study aims to provide information on acute gastroenterocolitis as well as implement the Systematization of Nursing Assistance (SAE) Patient with GECA. The study was conducted in a state hospital in the city of Vitoria-PE; the data were collected from patient records, along with information obtained through the responsible reporting and literature. T.S.H patient, 1 year and 7 months, male, residing in a rural area of the same city. The patient, accompanied by his mother was admitted on April 29, 2016 complaining of diarrhea, with diagnosis of GECA hypothesized. Physical examination: weight 11,500kg, regular condition, eupneic, afebrile, tearful, normal skin color, Pelé and intact mucous related ecchymosis will peripheral venipuncture. regular heart rhythm. Abdomen plan, oral diet, low acceptance of diet food. Eliminations + and spontaneous bladder, bowel: diarrhea more than 6 days, melena. Decreased hemoglobin levels, erythrocyte and hematocrit indicating mild anemia from blood loss in the stool were observed from the day of admission. Prescription: lactose-free diet, oral serum, hydrolyzed ecology, SG a5% 250mL, 250mL SF 0.9%, chloramphenicol, pediatric Florax, metronidazole, paracetamol (if fever), account for number and appearance of bowel movements and thermal control. The care plan was prepared based on symptoms and patient's needs. The main nursing diagnoses were: diarrhea, reinfection risk, electrolyteimbalance , impaired skin integrity risk. The main nursing interventions: control, watch, write down

the amount and appearance of feces, administer medicines and rehydration therapy according to medical prescription, correctly perform aseptic techniques, monitor standard electrolytic hydro, perform oral rehydration therapy with serum as prescribed, supervise the skin, clean the perineal region after episodes of evacuation and keep the skin free of moisture. It was concluded that both science and the nursing care developed for the child led to improvements after the implementation of nursing interventions.

444 FOCUSING ON THE FUTURE DURING SIGNIFICANT CHANGE: TUBING CONNECTION STANDARDIZATION IN THE PEDIATRIC HEALTHCARE SETTING

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Background: A new global design standard for tubing connections, supported by The International Organization of Standardization (ISO), is being implemented to help reduce the incidence of misconnections. Tubing misconnections can be life threatening and the impacts are detrimental to both patients and caregivers who make the errors. The Joint Commission issued a Sentinel Event Alert in 2006 related to tubing misconnections and again in 2014 regarding risks during transition to the new ISO connectors. In response to these patient safety concerns, an international network of organizations is planning for five phases of tubing changes, with the first of those being enteral feeding products. The new enteral connector has been named "ENFit". As addressed in the 2014 Joint Commission Sentinel Alert, the ISO connectors being developed and manufactured to eliminate the risk of misconnections are not without concern. Gaps in aligned products are elucidating clinical conundrums such as low dose syringe accuracy or Foley/Cecostomy connection challenges.

Objective: The current enteral tubing standardization process has highlighted some significant challenges for safe pediatric medication delivery and for small doses of liquid medications administered to adults. Nursing leaders must advocate for safe and reliable conversion practices.

Intervention: A steering committee of key stakeholders at Children's Hospital Colorado (CHCO) was identified to represent all disciplines, including those that represent community partners. The committee addressed anticipated challenges with the ISO connectors which include: gaps, risks and changes. A Failure Mode Effects Analysis (FMEA) process was utilized to address challenges of product alignment. The group also investigated the impact of: clinical work flows, finance, education, physical space, patient safety, technology and partnerships.

Results: The FMEA process identified 27 potential risks of stocking both oral and ENFit syringes. Other patient safety concerns identified include off label use and products not intended for enteral use such as Foley or Cecostomy tubes which require enteral product adaption.

Evaluation: Enteral tubing connection standardization will impact hundreds of products, which require significant efforts put towards coordination of product delivery and timing. Multiple vendor partnerships will be impacted. Coordinated communication with robust education is required to meet the needs across departments, disciplines and community partners. Ongoing evaluation of changes will occur and this interdisciplinary model approach will be utilized for future phases of tubing connection changes.

Conclusion: An interdisciplinary problem solving model approach, led by a clinical nurse specialist, is a useful process improvement tool to identify gaps, risks and challenges and implement current and future tubing standardization changes in order to provide optimal safe patient care.

445 PRELIMINARY OUTCOMES OF A REGISTERED NURSE DRIVEN FECAL MICROBIOTA TRANSPLANTATION (FMT) PROCEDURE TO TREAT CLOSTRIDIUM DIFFICILE (C.DIFF) INFECTION IN PEDIATRICS

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Background: Fecal Microbiota transplantation (FMT) is considered standard of care for treatment of recurrent *Clostridium difficile* infection (CDI) unresponsive to standard antibiotic regimens. We initiated a nurse-driven FMT procedure delivering stool donor bank-derived fecal material into the stomach via nasogastric tube (NGT) or gastrostomy tube (g-tube), when available. Retention enema and oral capsule administration are also available if unable to administer via NGT.

Methods: Eligible patients to receive an FMT procedure included inpatient and outpatient pediatric patients, ages 1 to 21 years, with a diagnosis of recurrent CDI, defined as having failed 2 courses of antibiotics including one course of oral vancomycin therapy. After providers obtain consent, a nurse-driven FMT protocol which includes orders and guidelines for practice is initiated by the nurse. The FMT procedure is performed by the nurse in an ambulatory setting utilizing an order set. All donor stool product was obtained from the stool bank Openbiome (Cambridge, MA). Follow-up was performed at two week and three and six month intervals after the procedure to assess outcome of FMT.

Treatment success was defined as: symptom resolution at 3 months post-FMT. Treatment failure was defined as: return of symptoms (abdominal pain, diarrhea, hematochezia) and a positive stool PCR for *c.difficile* toxin.

Results: A total of 31 FMT procedures were performed in 27 patients over a 15 month period at Children's Hospital Colorado. Patient age ranged from 2 to 18 years old. 25 patients received FMT in the ambulatory setting, 2 patients were hospitalized. Of the 27 patients, 8 were healthy previous to acquiring CDI, 9 had inflammatory bowel disease, and 10 were medically complex. 56% of treated patients were female. 22 procedures were performed via NGT, 8 via G-tube, and 1 procedure was performed orally using frozen stool capsules. All 27 patients had follow-up at 3 months to assess treatment outcome. 19 of 27 patients (70%) experienced a treatment success. 3 of 8 treatment failures underwent a second round of FMT and only 1 of these patients ultimately experienced a treatment success. Treatment success varied based on underlying disease. FMT achieved treatment success in 7 of 8 previously healthy patients (87%), 5 of 9 patients with IBD (55%), and 8 of 10 medically complex patients (80%). 4 of 27 patients experienced a single vomiting episode within 24 hours of FMT; all quickly recovered.

Conclusion: A nurse-driven FMT procedure, utilizing donor stool bank product administered into the stomach, achieves treatment success in pediatric patients comparable to published norms. At a tertiary pediatric referral center, patients with IBD and medical complexity made up the majority of patients referred for FMT. The presence of IBD appears to decrease the efficacy of FMT for treatment of recurrent CDI.

446 STORMFALL: A DIFFERENT ANGLE TO MULTIDISCIPLINARY COLLABORATION IN MANAGEMENT OF COMPLEX IBD PATIENT

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Background: There are pediatric GI patients unable to receive care due to severe psychological/psychiatric impediments. We present such a case, a severely ill child, unable to receive adequate care due to severe psychological impediments and describe the unique multidisciplinary approach to her management.

Case: 15-year-old female, 2-year history of abdominal pain, weight loss, recurrent mouth sores and cheilitis, undiagnosed due to intense fear of invasive medical procedures or anything being introduced into her orifices. Examination revealed pale female, markedly swollen and cracked lips, with some abdominal tenderness. There was a high index of suspicion for IBD. The challenge was overcoming her anxiety of invasive medical procedures to allow for necessary testing. With the help of the psychologist and child life specialist, the patient created "stormfall", a futuristic machine coming in for a maintenance check. Each caregiver had assigned roles: anesthesiologist (mechanic)-to make stormfall idle, nurses (technicians) that check plumbing and wires and physicians (mechanic) to check out stormfall while idle. Stormfall was a machine at all times during the period of testing and participants agreed to play their roles for the benefit of the patient. Stormfall arrived with headphones listening to music, nurses (technicians) checked it in, and set up the videogame for stormfall to immerse itself in. Stormfall was idled and its plumbing/wires (EGD/Colonoscopy) checked out and also drained mechanical fluids (blood) to analyze (test). Results showed hemoglobin 8.8g/dL, plt-630 k/uL, crp-3.9 mg/dL, esr-33mm/hr, alb-3.6 g/dL. EGD and colonoscopy revealed severely erythematous, friable, inflamed and ulcerated mucosa in the entire colon. The IC valve was stenotic and we were unable to pass the scope into the terminal ileum. Biopsies confirmed a diagnosis of Crohn's disease and therapy initiated.

Discussion: We present a case of a 15-year-old female that had been undiagnosed with IBD for 2 years because of her severe anxiety for invasive medical testing and showcase a creative use of the multidisciplinary team: nurses, psychologist, child life specialist, physician and anesthesiologist in the management of this complex patient. The physician recognizing the need for psychological intervention, child life specialist/psychologist creating "stormfall" with guidance from the patient, and of course the nurses for quarterbacking the script for her procedure and for future intravenous infusions and blood.

447 CONSTIPATION IN A 5-YEAR- OLD: CAN IT BE HIRSCHSPRUNG DISEASE?

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Introduction: Constipation in children is often a long-lasting disorder affecting up to 30% of children. Functional constipation is responsible for more than 95% of cases in healthy children age one year and older. Approximately 3-5% of outpatient visits are to treat constipation every year and many of these children require referral to a specialist. Hirschsprung Disease, a birth defect characterized by complete absence of neuronal ganglion cells from a portion of the intestinal tract, occurs in approximately 1 per 5000 live births, and is four times more common in males than females. Nearly all children with Hirschsprung are diagnosed during the first 2 years of life.

The Case: A 5-year-old male was referred to Pediatric Gastroenterology for concerns with constipation and fecal soiling. He was born 40 weeks gestation vaginal delivery, no complications with a birth weight of 7 pounds 6 ounces. He passed meconium in the first 24 hours of life and was formula fed Enfamil. During the first 3 months of life, he could go 1 week without the passage of a bowel movement. This stool pattern continued throughout his toddlers years despite use of multiple laxative agents (Karo syrup, MiraLAX, fiber, milk of magnesia). Stool pattern evolved, and every 1-3 weeks he would present to ED for manual disimpaction with or without enemas. This intervention would produce a large volume and watery bowel movement.

Findings: Barium enema was completed January 19, 2016 and revealed a markedly dilated cecum measuring 12.7 cm in diameter and possible Hirschsprung Disease. Anorectal manometry was completed and failed to produce a recto-anal inhibitory reflex (RAIR). Following manometry, a full thickness rectal biopsy was performed to evaluate for presence of ganglion cells. No ganglion cells were identified and surgery was scheduled and performed.

Discussion: This case supports the consideration of Hirschsprung Disease to remain on the differential while evaluating causes of constipation even in children older than 2 years of age.

448 ASSESSMENT OF NURSE DRIVEN EDUCATION PROGRAM FOR NURSING STAFF IN THE DIGESTIVE HEALTH INSTITUTE AT CHILDREN'S HOSPITAL COLORADO

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Background: Newly hired registered nurses and medical assistants in the Digestive Health Institute (DHI) have limited knowledge of digestive health diseases. Ambulatory nursing care management involves telephone or electronic triage, consultation, evaluation, support and advocacy between visits; this necessitates a broad knowledge of digestive diseases and ongoing education to keep up to date. Further, Children's Hospital Colorado requires yearly continuing education credits for all nurses.

Objective: The purpose of this project was to develop a formal education program promoting knowledge of digestive health disease topics. The goals were to improve the comfort, knowledge and expertise of DHI staff; enhance patient/family education and satisfaction; improve compliance and outcomes for patients; facilitate staff collaboration; and improve job satisfaction.

Methods: Education topics were selected with consultation and mentorship from our advance practice clinical nurse specialist. Presentations were scheduled for late afternoon during the work day to minimize time constraints and maximize accessibility. Documentation was submitted to attain continuing education unit (CEU) credits. In 2015, selected CHCO experts delivered monthly presentations and anonymous evaluations were obtained to assess staff satisfaction of content and provider. At the conclusion of the series, an anonymous electronic survey was sent to staff soliciting feedback on effectiveness, impact on practice, and suggestions for future educational topics.

Results: 9 presentations were delivered, and 7 were able to provide continuing education units (CEUs). Challenges included attaining CEU accreditation, procuring expert presenters, organizing satellite and phone access, and advertising. 12 of 26 (46%) surveys were returned. Presentations received favorable evaluation scores (4 or 5) on a 5 point Likert scale regarding helpfulness and relevance. Participants noted a positive impact on job satisfaction (mean 3.75, 1 no impact and 5 extreme impact). Fecal Microbiota Transplant and liver disease were the highest rated topics, and Functional Abdominal Pain was the most requested topic for future presentations. The individual evaluations from each of the topics scored greater than 4 (out of a 5 point scale).

Conclusion: A nurse-driven education program can improve staff knowledge and promote staff satisfaction while fulfilling organization requirements of yearly continuing educational credits. Vigilant attention to documentation and formatting requirements can facilitate CEU accreditation.

449 A COMPARISON OF SCHOOL /EXTRACURRICULAR ATTENDANCE IN CHILDREN WITH FUNCTIONAL ABDOMINAL PAIN (FAP) AND INFLAMMATORY BOWEL DISEASE (IBD)

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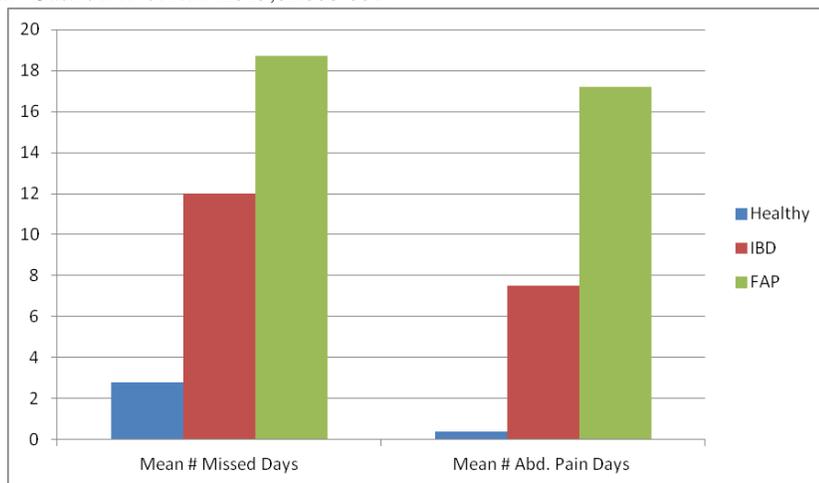
Inflammatory bowel disease, including Crohn's disease, and ulcerative colitis, is associated with gastrointestinal symptoms such as abdominal pain and diarrhea. Functional or chronic recurrent abdominal pain is manifested primarily with a complaint of periumbilical abdominal pain without other significant gastrointestinal symptoms. Both conditions alter a child's quality of life and result in missed days of school. A recent study by Assa et al. identified that children with inflammatory bowel disease and functional abdominal pain (FAP) missed significantly more school than healthy, age-matched controls (Assa, Ish-Tov, Rinawi, & Shamir, 2015). However, there was found to be no difference in school attendance and functioning between children with IBD and those with FAP. Unlike Assa et al it has been our observation that children with IBD do however attend school, even though they are feeling ill, and those with functional abdominal pain, miss significantly more school than those with pathologic disease.

Methods: The purpose of this project was to assess absences at school and related activities for reasons of gastrointestinal symptoms among healthy controls, those with recently diagnosed IBD (within the last 6 months) and those with confirmed chronic recurrent or functional abdominal pain. IRB review and approval as an exempt protocol was obtained from the Boys Town National Research Hospital IRB. We enrolled subjects between 7 and 18 years of age with 26 females and 27 males between February and May 2016. Parents were asked to complete a recall survey to assess absences from various activities since September of 2015 to the present. Differences were assessed via ANOVA.

Results: Among healthy controls mean total number of days of school missed was 2.8 days, 12 days for IBD and 18.7 days for FAP and of those days the mean number missed due solely to abdominal pain were 0.38, 7.53 and 17.2 respectively. Also assessed were absences from school trips, extracurricular activities, clinic, ER/hospital visits, and after school programs and these numbers did not differ significantly.

Conclusion: Children with FAP missed more school due to abdominal pain $p=0.038$ than those with IBD. Frequent school absence due to abdominal pain appears more reflective of functional rather than organic disease in our population.

Assa A., Ish-Tov A., Rinawi F. Shamir R. School Attendance in Children With Functional Abdominal Pain and Inflammatory Bowel Diseases. *J Pediatr Gastroenterol Nutr.*2015;61:553-557.



450 IBDECIDING: DEVELOPMENT, IMPLEMENTATION AND EVALUATION OF A NEW SHARED DECISION-MAKING APP FOR ADOLESCENTS

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Background: Adolescence is a stage of growth and development where individuals begin to show signs of independence through expression of ideas, thoughts, actions, and concerns. This marks transition of healthcare decision making from parents to the patients themselves.

Unfortunately, adolescents are not always active participants in their own medical decision-making. Reasons for this may include historical parental management of care, lack of knowledge regarding care and treatment, and healthcare providers not providing the time and resources to ensure adolescents' participation in self care. Since they are technology-oriented, an app might provide the best mode of sharing knowledge to empower the adolescent in a healthcare partnership. Based on this gap analysis, the IBD Center engaged a patient partner to build an IBD decision-making app.

Objective: To improve care and decision-making of IBD adolescent patients through the use of an app called IBDeciding, which provides information about traditional and non-traditional treatment for IBD.

Methods: The IBD team met with an adolescent patient to analyze strategies that would be useful in clinical decision-making. Throughout the course of several months, the patient attended team meetings to discuss development and revision of the app. The patient also met with community IT resources to assist with platform choice (BuildFire) and app build. Once completed, the IBDeciding app was placed in the Apple Store and Google Play for free access. An evaluation survey, developed by the IBD team, assessed ease of use, applicability and feedback. The app was presented and evaluated by patients in two settings, clinic and at a national conference. During clinic, patients 12 years and older were

asked to download the app and complete the survey. It also garnered favorable accolades at the ImproveCareNow (ICN) conference which consisted of healthcare providers, patients and parents.

Results: In the initial pilot involving a few adolescents with a long-standing history of IBD, the app was met with positive feedback including ease of use, relevant information and improved communication. Continued patient engagement will facilitate feedback to improve content and update current practice.

Conclusion: The IBDeciding app is an effective clinical decision-making tool for adolescents struggling with multiple treatment options. Empowering patients may improve clinical outcomes, patient satisfaction, and successful transfer to adult healthcare.

451 SUCCESSFUL THALIDOMIDE THERAPY FOR ATYPICAL CROHN'S DISEASE

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The oral manifestations (OM) of Crohn's disease (CD) are well documented and may precede the onset of intestinal disease by several years. OM are more common in children than adults with a male predominance (Plauth *et al*, 1991). OM include nonspecific findings such as aphthous ulcers and those clearly associated with CD such as granulomatous cheilitis, pyostomatitis and deep ulceration. Biopsies of oral lesions are positive for granulomas in about 70 percent of cases, but their absence does not preclude the diagnosis of CD (Hegarty *et al*, 2003).

Thalidomide is available for use in the United States under a restricted distribution program (Thalomid REMS®) due to the risk of embryologic defects. The mechanism of action of thalidomide is not fully understood, but it possesses immunomodulatory, anti-inflammatory and anti-angiogenic properties. It is indicated for multiple myeloma and leprosy, but has established efficacy for HIV-related oral ulceration (Porter & Jorge, 2002), and there are case reports of its use in oral CD (Hegarty *et al*, 2003).

Case Study: 12-year-old female diagnosed with non-granulomatous oral ulcerations at age 5. She suffered from recurrent painful flares of both oral and anal ulcerations necessitating frequent hospital admissions. Multiple endoscopic procedures were performed that showed esophagitis with ulceration as well as patchy colonic inflammation and erosions with granulation tissue in the terminal ileum consistent with CD. Repeated oral biopsies were obtained and revealed deep ulceration with associated necrosis, acute and chronic inflammation, gingivitis and abscess formation. No viral cytopathic changes or granulomas were identified. Immunology and rheumatology work-up was negative. Behcet's disease was ruled out. Her disease responded to corticosteroids, but would recur as doses were tapered. She failed to respond to multiple steroid-sparing medication regimens that included colchicine, immunomodulators, biologic agents including TNF α and IL-6 antagonists, and calcineurin inhibitors. She required gastrostomy tube placement for enteral feeding as she was unable to eat during flares.

At age 9 years, thalidomide was initiated and her condition gradually improved. Hospitalizations decreased and her oral symptoms were maintained in remission as corticosteroids were eventually discontinued. She has remained in steroid-free remission for one year and 5 months and endoscopy and colonoscopy at age 12 years demonstrated tissue healing of the gastrointestinal tract.

Summary: Oral manifestations of CD can be difficult to manage and adversely affect the patient's quality of life. Thalidomide may have efficacy in healing oral lesions that are not responsive to more conventional treatments. GI nurses should be aware of its use in Crohn's disease and the restrictive prescribing program.

452 BODY MASS INDEX QUALITY IMPROVEMENT PROJECT

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Background: Childhood and adolescent obesity has become epidemic both nationwide and globally. Nationally, rates of obesity among African American, Hispanic and other minority children continues to rise. Obesity increases the risk of multiple co-morbid health issues including Type II Diabetes Mellitus (T2DM), hypertension (HTN) and Non-alcoholic fatty liver disease (NAFLD).

Objective: To identify and record a diagnosis of overweight or obesity for all children ages 2-18 years with a BMI >85%. This diagnosis will be added to the electronic medical record (EMR) problem list. Secondary aims include improving their evaluation for NAFLD and referral for obesity care.

Methods: Baseline data was established through review of the EMR. Improvement approaches including divisional education on the prevalence and complications of NAFLD and obesity for both practitioners and families. Educational materials for families were developed in both English and Spanish. The EMR was utilized to create a best practice alert (BPA) to notify practitioners of all patients with elevated BMI. The BPA is linked to order sets for the evaluation of NAFLD that include targeted laboratory evaluation, and/or liver ultrasound and referral for obesity therapy. The BPA must be addressed prior to chart closure. This BPA serves several purposes, namely the identification of patients most at risk for fatty liver disease and its comorbid conditions and more efficient use of the electronic medical record. Provider level feedback was published weekly. The Quality Improvement (QI) team met monthly to evaluate data and make changes.

Results: 30% of patients attending Nationwide Children's Hospital (NCH) Gastroenterology clinic were found to be overweight or obese. After the implementation of the interventions described, the percent of patients with BMI >85% with this indicated on the problem list increased from a baseline of 30% to 70%. The identification of patients with BMI > 95% increased from a baseline of 50% to 85%. Identified barriers to project implementation included time constraints during office visits, parent resistance to discussing obesity, limited obesity providers outside of a tertiary care setting, and poor insurance coverage for obesity-related problems. Unanswered questions include patient selection targeting obesity interventions related to the limitations of providers focusing upon obesity treatment. Financial limitations for families also create barriers to treatment plan implementation.

Conclusion: This QI project has the potential to advance nursing knowledge and practice among a large population of patients at high risk for long-term co-morbidities. Advanced practice nurses are ideal practitioners to work with members of a multidisciplinary team to address the increasingly prevalent healthcare problem of obesity.

453 USEFULNESS OF A PEDIATRIC INFLAMMATORY BOWEL DISEASE DATABASE FOR NURSE FOLLOW-UP OF A BIG COHORT

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Background and Aims: A dedicated Nurse for inflammatory bowel disease (IBD) is part of the quality of care in IBD. Nurse interventions in IBD clinics have proven to increase patient education, access and continuity of care. In centers with huge numbers of patients and many

physicians, nurse activities might be complicated. Thus, a tool to facilitate their work could be of great benefit. In 2013 a clinical IBD database (PediData) was built in our unit to help improve the follow-up of these children. The aim of the present work was to discuss the usefulness and satisfaction of the nursing team after three years of usage.

Methods: The gastroenterology unit of Sainte Justine Hospital includes 10 senior physicians, 6 fellows, and 3 clinical nurses (one of them dedicated to IBD patients). Each year 90-100 new cases of IBD are diagnosed in our unit. The active cohort includes nearly 500 patients. Usual nurse activities are: phone call from or to parents/children related to children's symptoms/treatments/lab results, in-hospital visit for educational teaching, etc. PediData is a prospective database that was built in-house. It includes different sections organized in tabs: administrative, imaging, treatments, follow-up, lab results. This database is hosted internally in a server in our hospital; access is granted by a private password for each user (physician, nurse and dietitians). Since January 2013, every new case of IBD has a new form created in PediData. Nurse follow-up is recorded in the database; this report is printed and sent to the medical file.

Results: From January 2013 to December 2015, there were a total of 2149 nurse notes (encounters) in the database related to follow-up of 407 patients (median entry per patients, 5). Among these notes, 1166 were related to patients newly diagnosed during the study period (n=288). The majority of notes were phone call follow-ups for disease symptoms, changes in medication or lab results. Medication logs and lab results logs were two of the most useful tools that enhanced the usefulness of the database. For example, there were 361 notes in the medication tab for anti-TNF therapy for 220 patients. These notes include new initiation of therapy, modification of frequency/dose. The visual presentation of data including date of beginning/end, reason for change etc. enabled easy tracking of these changes. Lab results entries in the database helped tracking changes in specific values such as liver tests, lymphocyte count etc.

Conclusions: PediData enhanced the quality of nurse follow-up of children with IBD in a big cohort setting. This database enables a synoptic view of the patient. We have noticed a usability of the database as regards to symptoms recording, medication and lab results tracking. Other tools included in the database facilitate communication with physician/patients, such as integrated email. There was great satisfaction of the nursing team after more than two years of utilization of this database.

454 *QUALITY IMPROVEMENT INITIATIVE: THE ADMINISTRATION OF EARLY NUTRITION FOLLOWING PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE PLACEMENT IN CHILDREN*

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Gastrostomy tubes are placed in children who require long-term dietary support. The purpose of placing a gastrostomy tube is to reverse or prevent malnutrition and in return improve the child's well being. Providers routinely delay the introduction of enteral nutrition following the placement of a percutaneous endoscopic gastrostomy tube in pediatric patients. This postponement of enteral feedings can lead to unnecessary hospital stay, increased healthcare costs, deprivation of nutrition, and disruption of family life. Currently there is no established approach for initiating early enteral nutrition following the placement of a percutaneous endoscopic gastrostomy tube. At our institution, the type of formula, strength of formula, as well as the time and amount in which to advance the feeding was variable based on the ordering provider. The quality improvement initiative's objective was to create guidelines outlining electronic ordering, standard calculations, and administration instructions for the initial feedings with a goal of beginning enteral nutrition four hours post-procedure. The interprofessional healthcare teams involved in the project were asked to evaluate the new process using anonymous questionnaires. Of the gastroenterology providers that responded, one hundred percent either agreed or strongly agreed to the following: (a) the standard calculations assisted providers in ordering the correct amount of initial bolus feedings; and (b) the diet order added to the post-procedure order set assisted providers in ordering the correct diet administration process. For project sustainability purposes we also addressed barriers that had previously affected a timely discharge for patients following their percutaneous endoscopic gastrostomy tube placement. Changes were made to the quality improvement initiative based on the feedback gained. With guidelines for the administration of early enteral nutrition following gastrostomy tube placement we intend to improve patient outcomes and enhance the quality of care our families receive following the child's procedure.

455 *TOTAL BODY SODIUM DEPLETION AS AN ETIOLOGY OF GROWTH FAILURE IN AN INFANT WITH INTESTINAL FAILURE WITHOUT A DIVERTING ENTEROSTOMY*

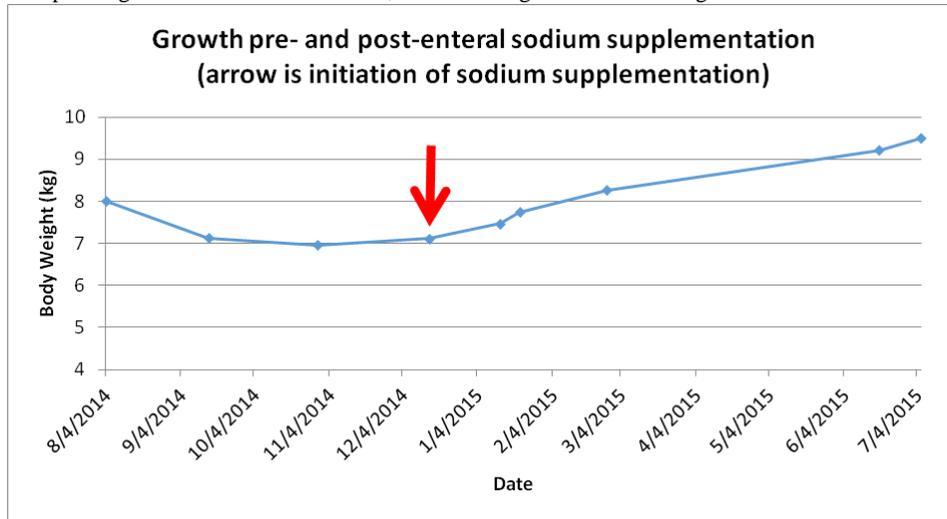
Danielle Stamm, Christopher Duggan, Boston Children's Hospital, Boston, MA, USA

Background: Children with intestinal failure have various possible causes for growth failure, including malabsorption, inadequate dietary intake, higher energy needs, and micronutrient deficiencies. Previous case series have identified total body sodium depletion, indicated by a urine sodium concentration <10 mmol/L, as a risk factor for poor growth in intestinal failure patients with a high output enterostomy. It is likely that total body sodium depletion can also occur in intestinal failure patients with rapid transit and frequent diarrhea despite restoration of intestinal continuity, but this has not yet been described.

Methods: A retrospective chart review was performed on an infant with intestinal failure who presented for a series of visits over 5 months during which she exhibited no weight gain despite multiple medical and nutritional interventions.

Results: Our patient was a 10-month-old girl with intestinal failure due to complications of an abdominal teratoma resection leading to thrombus of the celiac axis and subsequent hepatosplenic infarct requiring duodenoduodenostomy and Roux-en-Y hepaticojejunostomy. She retained nearly all of her small bowel and her full colon. She had chronic diarrhea and known exocrine pancreatic insufficiency which was being treated with pancreatic enzyme replacement therapy (PERT). Due to lack of weight gain over a 5 months, numerous interventions were made including changing her formula, increasing PERT, treating empirically for small bowel bacterial overgrowth, and increasing the caloric density and volume of her feeds. During this time, her weight-for-age decreased from the 58th percentile to the 8th percentile, at which time she was admitted to our hospital for further workup. Admission labs were notable for a low urine sodium level (<10 mmol/L). All serum electrolytes including sodium (139 mmol/L) were normal. She was started on an enteral sodium supplement at a dose of 4 mEq/kg/day, and her urine sodium level normalized to 81 mmol/L. She exhibited rapid and substantial weight gain, and her weight-for-age had improved to the 12th percentile at the time of discharge. She continued to receive enteral sodium supplements following discharge, and her weight-for-age was at the 20th percentile 6 months later (see Figure 1).

Conclusions: Total body sodium depletion and growth failure in intestinal failure patients with a small bowel enterostomy has been reported. We describe marked growth failure in an infant with limited intestinal resection and intestinal continuity, who was found to be total body sodium deplete based on assessment of her urinary sodium concentration. Enteral sodium supplements led to improvement in her growth trajectory. Pediatric intestinal failure patients in intestinal continuity may still be at risk for total body sodium depletion due to chronic diarrhea and corresponding loss of sodium in the stool, and screening for this cause of growth failure should be liberally employed.



456 PARENTERAL NUTRITION IN NEONATES: INDICATION AND EVOLUTION IN MARKERS OF LIVER FUNCTION DURING 2014 AT THE NATIONAL INSTITUTE OF PEDIATRICS

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Background: Parenteral Nutrition (PN) is one of the most important therapeutic modalities invented in recent decades. This has saved thousands of lives of premature infants with intestinal immaturity and pediatric patients with intestinal failure as a result of mainly gastrointestinal tract malformations.

Material and Methods: We included prospective hospitalized patients in the Neonatology Service of the National Institute of Pediatrics, during the period from January 1 to December 31, 2014, indicating receiving PN. We excluded patients who had received PN in less than the last 48 hours. The information was obtained from the physical and electronic records and sheet data collection by Nutrition Service, and included general patient data, clinical diagnosis at the onset of PN, the indication for it, daily prescription data, route of venous access and grounds for suspension of parenteral support. The PN was maintained until a suitable transition to oral or enteral was achieved. During the period of PN administration: serum electrolytes (magnesium, phosphorus, sodium, chloride, calcium and potassium), liver function tests (direct and indirect bilirubin, alkaline phosphatase, alanin amino transferase, aspartate amino transferase and gamma glutamyl transpeptidase, albumine, glucose, triglycerides and cholesterol were monitored.

Results: 49 infants required PN for more than 3 days. Of these, 47 were nourished with a parenteral central line and 2 peripherally. The TPN duration in days was 17 (range 66-3 days). The median weight gain was 367.2g. 55% had enteral stimulation at 72 hours. As a preventive measure for cholestasis secondary to parenteral nutrition, PN cycled 23 infants. The GGT values were similar at the initial time of PN to the end.

Conclusion: Our report of this study confirmed that congenital malformations of the digestive tract treated surgically were the most frequent indication for PN (96%). On the third day of the beginning of PN, about 86.8% of the energy requirement was covered, and by the seventh day, 100%. Cholestasis associated with parenteral nutrition in neonatology has been associated with various risk factors such as prematurity, low birth weight, initiation of enteral stimulation, sepsis and gastrointestinal surgeries.

CELIAC AND OTHER LUMINAL DISORDERS

485 EOSINOPHILIC OESOPHAGITIS: A PROSPECTIVE STUDY ON DEMOGRAPHICS AND DISEASE CHARACTERISTICS IN CHILDREN

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Aims: Eosinophilic oesophagitis (EoE) is a rare, chronic, and relapsing immune/antigen-mediated disease characterised by symptoms of oesophageal dysfunction with an eosinophil predominant inflammation of the oesophageal mucosa. There is a paucity of data among the NZ pediatric population. Our 3-year prospective study aimed to characterize this disease better in NZ children, and to verify initial treatment strategies adopted by physicians throughout the country. Here we present preliminary data from the first 19 months of the study.

Methods: Information on new diagnoses of pediatric EoE was obtained via the NZPSU through monthly questionnaires sent out to all pediatricians & other specialists working with children throughout NZ.

Results: 31 new cases (28 male) were reported to the NZPSU from February 2014 to August 2015. 74% were of European descent with a median age of 8 years (0.6-15). Dysphagia was the most common symptom (35%) followed by vomiting (29%), food refusal (26%), epigastric pain (19%) and weight loss (19%). Other symptoms reported were food impaction, nausea, failure to thrive, non-specific abdominal pain, and

diarrhea. 2 patients were asymptomatic. 71% had a history of atop or food allergy, with 55% having a family history of the same. 61% had abnormal endoscopic findings, of which linear furrows and white plaques were the most common. 39% had normal oesophageal mucosa on endoscopy. Only 35% received a proton pump inhibitor (omeprazole) prior to endoscopy; 4 patients continued this post-endoscopy. 9 patients (29%) were initially managed with dietary manipulation alone (7 with an elimination diet, 2 with an elemental formula); 1 patient required a nasogastric tube for their feeds. 19 (61%) and 3 (10%) patients were treated with swallowed fluticasone propionate and oral prednisone respectively. Leukotriene receptor antagonists and immunosuppressive therapy were not used. 25 patients (81%) have a repeat endoscopy planned to monitor response to treatment.

Conclusions: The demographics and disease characteristics of our patients with pediatric onset EoE in NZ are similar to that reported in the current medical literature. Long-term prospective observational data obtained from this cohort of patients, should significantly improve our knowledge of this rare condition.

486 DETECTION OF GLUTEN CONTENT IN THE NATURALLY GLUTEN FREE AND GLUTEN FREE LABELLED COMMERCIALY AVAILABLE FOOD PRODUCTS IN ITALY

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Background: Gluten-free diet is the only accepted treatment for celiac disease and other glute- related disorders. Lack of gluten contamination is usually ensured by a certified food chain but is not routinely checked in gluten-free food that are available in the Italian market. The aim of this study was to test the level of gluten contamination in Italian gluten-free products, an issue that is frequently enquired by gluten intolerant patients on treatment.

Method: We planned to test at least 100 different products. In the initial phase 32 commercially food products (naturally gluten-free and/or labeled as gluten-free) available in Italian super markets were collected. Gluten content was determined by commercially available sandwich ELISA coated with specifically designed R5 monoclonal antibody that reacts with the gliadin fraction from wheat and the prolamins from rye and barley.

Results: So far, 26 (81%) food samples (including naturally gluten-free and/or labeled as gluten-free) were detected with a gluten content lower than the accepted threshold (20 mg/kg or ppm). However, 6 (19%) samples including one product labeled as gluten-free were found to have a gluten level higher than 20 mg/kg. Contamination was observed in buckwheat, oat and lentil-based products, ranging from 30 mg/kg to 53 mg/kg.

Conclusion: Preliminary results of this study raise doubts of the reliability of the gluten-free foods that are commercially available in the Italian supermarket. Complete absence of gluten is not achieved by some manufacturers. These gluten traces could be responsible for the persistence of mucosal damage in treated celiac patients. Ongoing analysis will be performed on a larger sample of additional products. However, many naturally gluten-free products remain safe from gluten contamination.

487 ADIPONECTIN SERUM LEVELS IN NCGS VERSUS CRC PATIENTS AND HEALTHY CONTROLS: A POTENTIAL BIOMARKER OF INFLAMMATION

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Background: The adipose tissue is no longer considered inert and mainly devoted to storing energy; it is emerging as an active tissue in the regulation of physiological and pathological processes, including immunity and inflammation. Adipose tissue produces and releases a variety of adipokines (leptin, adiponectin, resistin, and visfatin), as well as pro- and anti-inflammatory cytokines (tumor necrosis factor- α , interleukin [IL]-4, IL-6, and others). Adiponectin regulates glucose and lipid metabolism, insulin sensitivity, and food intake. It also seems to protect against chronic inflammation. Low adiponectin levels and insulin resistance have been linked to several obesity-related disease entities, such as type 2 diabetes mellitus, hypertension, and atherosclerosis. Adiponectin has also been proposed as a biological link between obesity and several malignancies, including Colon Rectal Cancer (CRC). Specifically, low adiponectin levels are considered as a prognostic biomarker that may improve the ability to identify cancer patients at high risk of disease progression and mortality.

The aim of our study was to investigate the correlation of the circulating concentration of adiponectin among neo-diagnosed CRC patients, Healthy controls and Non Celiac Gluten Sensitive (NCGS) patients and compare them to their Body Mass Index (BMI), anthropometric, biochemical parameters and lifestyle variables (diet), as well as diabetes mellitus status.

Material and Methods: Determination of serum adiponectin, obesity and other variables were performed in samples from 10 newly diagnosed CRC, 8 NCGS patients, and 16 age- and sex- matched healthy controls. Adiponectin levels were measured by ELISA. Circulating concentration of IL-6, IL-8, TNF α were also detected in NCGS patients by MSD Assay System.

Results: BMI was moderately higher in CRC patients compared to Healthy controls and NCGS, whereas Adiponectin levels were decreased in CRC patients (63.2 ± 3.0 mean \pm SE) versus controls (69.8 ± 5.4). Diabetes Mellitus status and other variables did not influence those levels. Interestingly, adiponectin was significantly increased in NCGS (80.2 ± 7.7) in respect to CRC patients ($p= 0.0270$), and was correlated with higher IL-6, IL-8 and TNF α serum levels independently from the diet.

Conclusion: Our data confirm the observation reported in other studies of low adiponectin levels in CRC patients, suggesting its possible involvement in cancer progression. Conversely, the significantly increased adiponectin levels in NCGS patients could play a role in modulating inflammatory process in Non Celiac Gluten Sensitivity. The exact nature of the association and the underlying patho-physiological mechanisms need, however, to be further examined in large prospective studies assessing adiponectin and its receptors as novel targets for exploring both diseases.

488 RELATIONSHIPS BETWEEN DIETARY INTAKES AND PERSISTENT GASTROINTESTINAL SYMPTOMS IN PATIENTS ON ENZYME TREATMENT FOR GENETIC SUCRASE-ISOMALTASE DEFICIENCY

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Introduction: Genetic sucrase-isomaltase deficiency (GSID) was first described in 1960, yet remains under-diagnosed in clinical practice. Absent or reduced enzyme activity allows undigested and malabsorbed disaccharides to culminate in symptoms of abdominal cramping, distension, excessive gas, and diarrhea. Enzyme treatment with Sucraid® (sacrosidase) Oral Solution is effective in replacing sucrase. However, persistence of symptoms and symptom severity may be related to the amount or frequency of sugars consumed. Moreover, consumption of high starch foods may be contributing to maldigestion/malabsorption and clinical symptoms. This study was designed to characterize dietary intakes of patients treated for GSID and determine relationships between carbohydrates consumed and gastrointestinal (GI) symptoms.

Methods: 49 subjects (26 children, 14 adolescents, 9 adults) treated with Sucraid® for ≥3 months were enrolled in a 30-day observational study to assess dietary intakes (24-hour recall interviews), GI symptoms, and Sucraid® intake. Dietary data were analyzed using Nutrition Data System for Research (v. 2014) and compared to the Recommended Daily Allowances and National Health and Nutrition Examination Survey data by sex and life stage. Relationships between nutrients and GI symptoms were assessed by Spearman Rho coefficients.

Results: Sucraid® dose averaged 5.2 ± 3.1 mL/day. Subjects reported 1.3 ± 0.9 bowel movements daily and ~1 episode of excess gas, burping, stomach pain and/or distension per day. Having less frequent GI symptoms was associated with higher Sucraid® intake. Energy intakes averaged 1562.5 ± 411.5 kcal/d in children, 1964.7 ± 823.6 kcal/d in adolescents, and 1952.6 ± 546.5 kcal/d in adults. Macronutrient composition was 44% carbohydrate, 39% fat, and 17% protein. Total carbohydrate was 35% starch, 8% fiber, and 57% sugars. Of total sugars, added sugars were 41% of the national average for children (37.8 ± 28.7 vs. 92.2 ± 58.3 g/d) and adolescents (42.2 ± 29.8 vs. 104.1 ± 64.8 g/d), and 61% of the national average for adults (47.8 ± 25.6 vs. 78.5 ± 52.1 g/d). Sucrose and fructose intakes were not associated with GI symptoms. Maltose intake was associated with nausea, distension, and reflux. Lactose intake was associated with diarrhea. With regard to nutrient inadequacies, fiber and potassium were 50% of recommended intake. Adolescents and adults also had inadequate calcium, magnesium, and folate intakes.

Conclusions: Overall, intakes were higher in fat and lower in carbohydrate than the typical American diet. Importantly, daily gastrointestinal functions were normal. While sucrose and fructose intakes were not associated with GI symptoms, higher maltose and lactose intakes were associated with more frequent symptoms. Intake of fiber, folate, and key minerals were insufficient. These novel findings provide specific evidence to guide diet and nutrition counseling with patients treated for GSID.

489 PANCOLITIS AND H. PYLORI GASTRITIS AS THE CLINICAL PRESENTATIONS OF HUMORAL IMMUNE DEFICIENCY IN A TEENAGER

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Introduction: Primary antibody deficiency syndromes such as x-linked agammaglobulinemia and common variable immunodeficiency disorder lead to abnormal development of B-lymphocytes and/or hypogammaglobulinemia. These disorders usually present with recurrent bacterial infections during infancy. Here we describe a 14-year-old boy with no significant past medical history, who presented with pancolitis and *H. pylori* gastritis, which led to the diagnosis of primary humoral immunodeficiency.

Case report: 14-year-old Vietnamese boy presented to our clinic with a 2-year history of mild watery, non-bloody diarrhea with mild weight loss. Symptoms had worsened in the last 2 months following a course of Clarithromycin for a respiratory infection. Denied nausea, vomiting or abdominal pain. Past medical history was remarkable for recurrent mild ear infections during infancy, one of which had required surgical drainage. Weight and height were noted below the 3rd percentile with an otherwise normal physical examination. Labs were remarkable for microcytic anemia (Hb 9.1, MCV 61), normal inflammatory markers and agammaglobulinemia (immunoglobulin 1.2, IgM<8, IgA<7, IgG<28, completely absent B cell count). Stool studies were negative. Upper endoscopy was remarkable for severe chronic *H. pylori* gastritis and chronic active duodenitis with villous blunting and increase intra-epithelial lymphocytes. Colonoscopy was significant for mild active pancolitis with lamina propria edema. Subsequently, he was treated with antibiotics for *H. pylori* infection and monthly infusions of intravenous immunoglobulin. Three weeks after treatment he had clinically improved, showing good weight gain and with diarrhea resolved.

Discussion: As the gastrointestinal tract is the largest lymphoid organ in the body, immunodeficiency disorders can result in extensive gastrointestinal pathology. These clinical manifestations often present during infancy. While they may mimic classic forms of gastrointestinal diseases such as celiac sprue and IBD, they differ in both pathogenesis and treatment. This case report, therefore, illustrates the importance that physicians consider an underlying immune deficiency in patients with diffuse gastrointestinal pathology, regardless of their age.

490 IS THERE AN ASSOCIATION BETWEEN FAT-SOLUBLE VITAMIN AND PLASMA LIPOPROTEIN LEVELS IN CELIAC DISEASE?

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Introduction: Celiac disease (CD) is an immune-mediated enteropathy caused by a permanent sensitivity to gluten in genetically susceptible individuals. It affects approximately 1% of the population. Fat-soluble vitamin deficiencies are noted in about 10% of children with CD. Low levels of LDL and HDL have been reported among 10 to 30% of patients with CD. Because fat-soluble vitamins are carried in plasma associated with lipoproteins, the low lipoprotein levels in CD could explain the low serum levels of fat-soluble vitamins. This association has not been examined in children with CD to date.

Objectives: 1) To determine the prevalence of fat-soluble vitamin deficiencies and hypolipoproteinemia in children with CD; 2) To determine if there is an association between fat-soluble vitamin and lipoprotein levels among children with CD; and 3) To determine if plasma lipoprotein levels correlate with the Marsh classification of the biopsied intestinal tissue.

Methods: We conducted a retrospective chart review of 23 small-bowel biopsy confirmed new cases of CD seen at our institution between July 1, 2013 and September 1, 2015. The demographic and laboratory data at diagnosis were collected. Data were analyzed using Pearson's correlation, the Chi-square test and analysis of variance.

Results: Fat-soluble vitamin deficiencies were observed in 21% (5/23) of children. Low lipoprotein (LDL, VLDL) levels were present in 39% (9/23) children. A significant positive correlation was observed between Vitamin E and LDL levels ($r = 0.51, p = 0.016$). The levels of other fat-soluble vitamins did not correlate with any lipoprotein. Plasma lipoprotein levels did not correlate with the Marsh classification. Conclusion: Fat-soluble vitamin deficiencies and hypolipoproteinemia are common in children with CD. The observed correlation between Vitamin E and LDL levels is supported by the fact that Vitamin E depends exclusively on lipoproteins, especially LDL, for its transport. Plasma lipoprotein levels do not correlate with the degree of intestinal mucosal inflammation.

491 ESOPHAGEAL DISTENSIBILITY INCREASES WITH AGE AND PROVIDES MEASURE OF REMODELING IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS

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Introduction: Sequelae of eosinophilic esophagitis (EoE) include repeated food impactions and esophageal strictures. Duration of inflammation is currently seen as the dominant risk factor; however development of these complications remains unpredictable. Functional endoluminal Imaging Probe (EndoFLIP) has been used in adults to measure esophageal distensibility; adult EoE subjects demonstrated altered distensibility which associated with risk of food impaction. Given uncertainty around the natural history of EoE, assessing distensibility as a surrogate for remodeling across ages is important. This has yet to be done in children. We hypothesize distensibility increases with age in normal patients and is reduced during active EoE inflammation. Herein we compared esophageal lumen distensibility in pediatric EoE to controls.

Methods: Under IRB approval, patients age 8-18 years old (y/o) undergoing upper endoscopy at 2 tertiary care sites were prospectively studied. Subjects: 1. Active EoE—symptomatic and >15 eosinophils per hpf; 2. Inactive EoE—treated, asymptomatic with <5 eos/hpf; 3. Controls—no esophageal inflammation and normal biopsies. EoE subjects were on twice-daily proton pump inhibitor for at least 6 weeks prior to diagnosis. EndoFLIP: Following endoscopic inspection, the EndoFLIP (Crospon) was positioned within the esophageal lumen and the balloon inflated to a max luminal pressure of 50 mmHg. Analysis: Data was filtered to minimize distortion from peristalsis and respirations. Pressure-geometry measurements of the esophageal body were analyzed. Luminal distensibility was determined based on minimum cross sectional area (CSA) at a luminal pressure of 40 mmHg. Adjusting for age, distensibility was compared between EoE and normal using t-tests.

Results: 113 subjects (mean age 11.7 y/o, 70% male, 80% Caucasian) were enrolled; including 44 controls, 43 active and 26 inactive, with no significant difference in mean age between groups. Distensibility increased with age in controls ($R^2 = 0.84, p < 0.001$). Controlling for age, EoE subjects had decreased distensibility compared to controls (152 ± 53 mm² vs. 216 ± 87 mm²; $p = 0.001$). EoE subjects ≥ 12 y/o with inactive inflammation had improved distensibility compared to active EoE subjects (184 ± 50 mm² vs. 137 ± 11 mm²; $p = 0.01$). History of food impaction was associated with decreased distensibility when compared to age balanced uncomplicated EoE ($p = 0.01$).

Conclusion: Our results demonstrate that esophageal lumen distensibility increases with age in normal children and suggests active inflammation in EoE reduces distensibility in children greater than 11 years old. Treatment of inflammation may improve distensibility. We propose EndoFLIP will provide insights in to the pathophysiology of EoE and may identify patients at risk for clinically significant fibrostenosis.

492 PERSISTING ENTEROPATHY AND DISTURBED ADAPTIVE MUCOSAL IMMUNITY DUE TO MHC CLASS II DEFICIENCY

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Regulatory dysfunction of the mucosal immune system leads to mucosal inflammation, tissue damage, and enteropathy. Major histocompatibility complex class II (MHCII) molecules are essential for adaptive immune response. Therefore, it is not surprising that MHCII deficiency, a primary immunodeficiency disease characterized by a lack of MHCII molecules on immune cells, often presents with gastrointestinal disorders. We report on history, course and gastrointestinal features of seven children out of six families with confirmed MHC class II deficiency.

Intestinal biopsy samples were analysed regarding HLA-DR, CD74 and immunoglobulin expression. In addition, aeces were analysed in six patients.

Immunohistochemistry revealed a loss of HLA-DR and invariant chain CD74 expression in enterocytes, which persisted after successful stem cell transplantation. Paucity of IgA expressing enterocytes was accompanied by the lack of faecal sIgA, which was not compensated by mucosal IgM expression.

A multifaceted disturbance of the adaptive mucosal immunity is found in patients with MHCII deficiency. Moreover, as it could not be restored by stem cell transplantation our results indicate a major role of enterocytes in adaptive immune response and may account for serious infectious complications and worse outcome.

493 THE SPECTRUM OF BLEEDING MECKEL DIVERTICULUM IN A TERTIARY PEDIATRIC CARE CENTER

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Introduction: Meckel diverticulum (MD), a vestigial remnant of the omphalomesenteric duct, is found in approximately 2% of the population and reportedly presents with hematochezia in 55% of pediatric cases. The purpose of this study was to identify features of bleeding MD which would preclude unnecessary testing.

Methods: We retrospectively reviewed the charts of children <18 years diagnosed with MD on pathology from 2005-2015. Patients with other known causes for gastrointestinal (GI) bleeding were excluded. We collected patient data including: demographics, bleeding history, medical history, exam findings, laboratory, imaging and endoscopic procedures. A diagnosis of MD was defined as evidence MD in pathology reports.

Results: We identified 206 patients with MD; 44 (21%) presented with hematochezia and 162 (79%) without. Non-bleeding intestinal presentations occurred in 60 (37%) including: intussusception in 19 (32%), bowel obstruction in 22 (37%), meckel diverticulitis in 10 (17%) and meckel perforation in 9 (15%). The others were found incidentally during other interventions.

Of the 44 with hematochezia, 25 (57%) were healthy and 4 (9%) had history of rectal bleeding. Pallor was the most common exam finding – present in 23 patients (52%). Hemoglobin was <7g/dL in 15 (34%) patients and 23 (52%) received transfusions. A meckel scan (MS) was performed in 36 (82%) – 26 (72%) were positive, 8 (22%) were negative and 2 (6%) were equivocal. Fluid resuscitation was required in 21 (48%) of patients and only 7 (16%) and 6 (14%) underwent esophagogastroduodenoscopy (EGD) and colonoscopy respectively. Conclusion: MD is a common small intestinal anomaly which can present in numerous fashions. Our cohort highlights important clinical features of MD: anemia is common, MS was frequently positive, and children frequently require blood transfusions, but not endoscopy. In healthy children with anemia, transfusion requirement, and appropriate history, patients should be triaged to laparoscopy, which is diagnostic and therapeutic. Identifying clinical and/or biochemical predictors of MD can optimize the use of healthcare resources.

494 ETIOLOGY, ENDOSCOPIC AND HISTOLOGIC FINDINGS OF IMMUNOCOMPROMISED CHILDREN PRESENTING WITH GASTROINTESTINAL BLEEDING

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Background: Gastrointestinal bleeding (GIB) is one of the potential causes of increased morbidity and mortality in immunocompromised patients. These patients may also suffer from opportunistic infectious complications such as bacterial infections, candidiasis or cytomegalovirus infection involving gastrointestinal tract, or specific conditions such as graft-versus host disease in children undergo bone marrow transplantation. However, data on characteristics of GIB in immunocompromised children are limited.

Objective: To identify etiology, endoscopic and histologic findings of GIB in immunocompromised children.

Methods: We conducted a structured medical record review of patients aged < 20 years old between January 2007 and April 2015 at a large tertiary care and teaching hospital to include patients with GIB who underwent gastrointestinal endoscopic procedures with one of the following immunosuppressed conditions: 1) history of bone marrow or solid organ transplantation; 2) malignancy that was treated with immunosuppressive agents such as corticosteroids, chemotherapy or radiation; 3) human immunodeficiency virus infection or immunodeficiency syndrome.

Results: We identified 33 patients, 45 GIB episodes (23 with upper GIB, 22 with lower GIB) and 71 endoscopic procedures. The three most common immunocompromised conditions were liver transplantation (21%), treatment with chemotherapy (21%), and bone marrow transplantation (12%). Most had either esophagogastroduodenoscopy or colonoscopy (65/71, 92%). Mean age at endoscopy of 10.7 years (SD 4.6). Most common manifestations for endoscopy were melena in upper GIB and hematochezia in lower GIB. The median duration between GIB presentation to arrival to the hospital was 24 hours but a median delay from the GIB presentation to timing at endoscopy was 4 days (IQR: 2, 11). All but one child had at least one endoscopic abnormality. However, endoscopic biopsy was omitted in some patients with defined abnormal endoscopic abnormalities (e.g., varices, hemorrhoids). The most common identifiable cause of upper GIB was cytomegalovirus-related gastrointestinal disease (35%) followed by esophageal varices (26%). The most common cause of lower GIB was cytomegalovirus-related gastrointestinal disease (55%), as shown in the Table.

Conclusion: Among immunocompromised individuals aged < 20 years presenting with GIB, cytomegalovirus-related gastrointestinal disease is the commonest in our study population. However, the etiology of immunocompromised state needs to be taken into consideration when evaluating these children presenting with GIB.

Table Primary final diagnoses of immunocompromised children presented with gastrointestinal bleeding.

Diagnosis	Upper GIB N= 23	Lower GIB N=22	Total N= 45* (%)
Cytomegalovirus-related gastrointestinal disease	8	12	20 (44)
Esophageal varices	6	0	6 (13)
Graft-versus host disease	2	2	4 (9)
Others**	7	7	14 (31)

Abbreviation: GIB, gastrointestinal bleeding.

*One patient had both negative endoscopic and histologic findings.

**including radiation esophagitis (1), gastritis (1), granulocytic sarcoma of stomach (1), duodenitis (1), duodenal ulcer (2), cow’s milk protein allergy (1), cryptosporidiosis (1), colonic polyps (1), inflammatory bowel disease (2), hemorrhoids (3).

495 APPLICATION OF CONJOINT ANALYSIS AND QUALITY IMPROVEMENT PRINCIPLES TO IMPROVE RELIABILITY OF DIETICIAN CONSULTATION IN NEWLY DIAGNOSED CELIAC DISEASE

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Background: Celiac disease management involves lifelong adherence to a gluten-free diet, making the dietician a key member of the multidisciplinary team. Although dietary consultation is recommended by multiple professional societies, adherence to these guidelines is unknown. In general, it is reported that children receive less than 50% of recommended ambulatory care. Quality improvement methodology may be utilized to achieve higher reliability in care processes. Conjoint analysis is a useful tool to understand provider or patient/family preferences when making changes to a healthcare system.

Aims: To improve reliability of dietician consultation in newly diagnosed celiac disease and to utilize conjoint analysis to identify important factors when redesigning the care process.

Methods: We used a 24-1 fractional factorial study design to generate 8 scenarios for our conjoint analysis. The four factors studied [2 levels each] were a) initial follow-up provider [celiac specific or primary gastroenterology (GI) provider], b) interval from diagnosis to follow-up [1 week or 4 weeks], c) timing of dietary consult [concurrent with GI visit or separate], and d) on-going follow-up provider [celiac specific or primary GI provider]. 15 pediatric GI providers at a tertiary care academic center completed the forced ranking survey of the 8 scenarios. Care was standardized in 7/2014 and reliability of dietary consultation was monitored by plotting the days between diagnosis and dietician consult on an I-control chart and frequency of patients not seen by a dietician on a G-control chart.

Results: Conjoint analysis identified that a shorter time to initial follow-up visit [effect size 2.57] and having a concurrent GI/dietician visit [effect size 2.59] as important attributes in newly diagnosed celiac follow-up. The type of follow-up provider during the first [effect size 0.5] or subsequent visits [effect size 0.31] were identified as less important attributes. No significant interactions between factors were identified. In July 2014, care was standardized so that newly diagnosed patients were seen in one pediatric GI clinic session per week, concurrently with a dietician. Prior to standardization, the baseline time from celiac diagnosis to dietician consultation was 30 days. A special cause (8 points below the mean) was identified on the I-control chart beginning in December 2014, with a reduction in the mean days from diagnosis to consultation to 20 days (32% reduction). A special cause (point above the upper control limit) on the g-control chart was noted in February 2015, with 12 patients being diagnosed with celiac before a patient was not seen by a dietician compared to a baseline of 1.9 patients.

Conclusion: We used conjoint analysis to identify factors which GI providers identified as important in the care of patients with newly diagnosed celiac disease. By redesigning the care process, we improved timeliness and reliability of dietary consultation.

496 BASELINE LEVELS OF ANTITRANGLUTAMINASE ANTIBODIES (tTG-a) AT DIAGNOSIS IN CHILDREN WITH CELIAC DISEASE ARE ASSOCIATED TO TIME OF NEGATIVIZATION?

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Introduction: Celiac disease (CD) is an autoimmune enteropathy triggered by the ingestion of wheat, barley and rye. Negativization of antibodies occurs in most patients between 3 to 6 months after diagnosis with gluten-free diet (GFD). However varying levels of tTG-a in children show they can do it much later.

Objective: To evaluate with longitudinal data tendency to negativization in two cohorts by level of baseline tTG-a in celiac patients and evaluate the percentages of negativization at 6 and 12 months in both cohorts.

Methods: Retrospective cohort study. Sample of children was included with confirmed CD according to ESPGHAN criteria and GFD for a period of 1 year without transgressions attended to Pediatric Gastroenterology and Nutrition Section at Pirovano Hospital during 2010-2014.

The cohort analysis were: celiac children with baseline tTG-a value lower (Group I) and greater than or equal to 100 IU/mL (Group II). The mean values of tTG-a at 6 (time I) and 12 months (Time II) diagnosis with ANOVA repeated measures were evaluated (previously validating their assumptions of normality, homogeneity of variance matrix and sphericity) and the percentages of negativization in each of the groups at both times. Other variables considered were: sex, age, weight, height and presenting symptoms.

Results: n=78 patients. Age x: 7.87 ±SD 4.72 years (GI) and 7.50 ± SD 3.79 years (GII). Sex: women 57.7%. There were no differences by groups regarding age (GI 7y 10m vs. GII 7y 6m [Welch Test $p=0.70$]) and sex (GI 57.5% [n=23] vs. GII 57.9% [n=22] [Z proportion Test $p=0.95$]). The behavior of longitudinal data showed a downward trend in parallel between the two groups with more lower mean values for the basal group of less than 100 IU/mL tTG-a ($p=0.038$) and for the 12-month assessment ($p<0.0001$) repeated measures ANOVA. The mean values were: GI 17.84 IU / mL (95% CI, 9.26-26.41), GII 27.68 IU/mL (95% CI, 18.89-36-48), TI 36.28 IU/mL (95% CI, 25.73-46-83), TII 9.23 IU/mL (95% CI, 6.44-12-03). At one year of treatment, GII (ATTG ≥ 100 IU/mL) had a 23.7% positive antibodies that had not yet proved to be negative (n=9) in relation to GI (ATTG <100 IU/mL) that showed a 10% with antibodies positive (n=4) with Fisher test $p=0.13$ not significant but clinically considerable.

Conclusions: The tendency of mean decreasing by groups and times was confirmed being the negativization percentages favorable to GI but without sufficient evidence.

*497 COMPARING DUODENAL BRUSHING AND ASPIRATE SAMPLING METHODS TO DIAGNOSE SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO) USING METAGENOMIC PROFILING

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Background: Duodenal brushing offers a more convenient method of obtaining duodenal microbiome than duodenal aspiration using sterile catheters. We have previously reported a strong correlation between brushing and aspirates in paired samples for cultivable microbiome. The purpose of the current study is to look at non-cultivable bacteria in aspirates and brushings to assess differences between luminal and mucosal microbiome. Understanding profiles in microenvironments may help define role in disease, and also optimal sampling method. We report preliminary findings of 25/50 paired samples in children undergoing diagnostic endoscopy for IBS symptoms. We used duodenal brushing and aspirate samples for bacterial profiling by 16S metagenomic sequencing

Methodology: Total genomic DNA was extracted from duodenal brushing, transport media (Amies TM brushing samples, and aspirates). Bacterial 16S rRNA gene target was amplified from all the samples following the guidelines of Illumina, Inc to sequence with MiSeq instrument. The sequenced data were analyzed using QIIME software. Total cultivable bacterial load and identified species were compared with the bacterial profile detected by 16s metagenomic sequence analysis. Correlations among the samples were measured using beta diversity metrics. Preliminary data is presented.

Results: Of 25 brushing samples in Amies transport media and 10 paired brushing and aspirate samples (10x 2 20) were selected for microbiome profiling. Cultivable bacterial growth was obtained in 11 samples. Bacterial species were detected in both of these samples with relative abundances of different taxa. Identified bacterial profile included both cultivable and non-cultivable genera and species. Firmicutes, proteobacteria, actinobacteria, bacteroidetes, and fusobacteria were the main phyla present in the brushing samples. Minor presence was reported for TM7 and Thermi. The data showed the high abundance of phylum proteobacteria over the firmicutes, bacteroidetes, and

actinobacteria (80%, 13%, 6%, and 5%, respectively) in both brushings as well as aspirates. There were significant differences between patients at the genus levels.

Conclusion: Duodenal brushings are closely related to luminal fluid aspirate at genus and species level, both with cultivable bacteria when present, as well as the much larger non cultivable microbiome. This supports brushing as an alternate and technically easier method, given lack of fluid for aspiration in most cases at the time of endoscopy.

The bacterial taxonomy revealed a perfect correlation with the quantitative culturing methods. Some bacterial species, such as Streptococcus and Haemophilus, were identified in culturing method and microbiome analysis as well. However, further analysis is pending to look for differences between mucosal brushing and luminal microbiome at the species level.

498 CHARACTERIZING PEDIATRIC CELIAC DISEASE IN THE HISPANIC POPULATION: THE US-MEXICO BORDER EXPERIENCE Sherief Mansi¹, Eduardo Rosas Blum¹, Marcelo Lacayo-Baez¹, Claire Zeorlin^{1,2}, Chelsie Hollas^{1,2}, Geri Villanueva^{1,2}, ¹Texas Tech University Health Sciences Center El Paso, El Paso, TX, USA, ²Paul L. Foster School of Medicine, El Paso, TX, USA

Background: Celiac Disease (CD) is an immune-mediated disease triggered by ingestion of the prolamins found in gluten with subsequent intestinal and extraintestinal manifestations. CD is the most common pediatric autoimmune disease and almost all patients with CD carry the HLA DQ2 or DQ8 haplotypes. The Hispanic population is the fastest growing population in the US and the literature on pediatric CD in the Hispanic population is scant.

Objective: Characterize the presentation, diagnosis, and management of pediatric celiac disease in Hispanic children.

Methods: We performed an IRB-approved chart review of all patients with CD at the Pediatric Gastroenterology outpatient clinic from February 2012 to October 2015. Demographic data, celiac serology levels, duodenal biopsy results, gastrointestinal symptoms, extra-intestinal symptoms, gluten-free (GF) diet compliance, and symptomatic improvements with GF diet were recorded. We excluded all patients without a Hispanic ethnicity, negative celiac serology (with the exception of selective IgA deficiency), absence of duodenal biopsy result, or with a duodenal biopsy score of Marsh 2 or less.

Results: A total of 96 charts were reviewed and 30 patients were included in our study. The mean age of diagnosis was 8.47 years. BMI Z-scores at time of diagnosis averaged -0.49 SD. There were 19 females (63%) compared to 11 males (36%) diagnosed with CD. About 90% of our cohort had no family history of CD. A total of 76% of our patients had a positive celiac serology at the time of diagnosis. The most common serological test used was TTG IgA followed by TTG IgG, EMA IgA, and DGP IgA. Of our cohort, there were 16 patients with selective IgA deficiency and CD. Regarding patient symptomatology at the time of diagnosis, 56% of our patients had abdominal pain, 30% had constipation and 3% had diarrhea. Weight loss was seen in 10% of the cohort compared to 30% in patients diagnosed with failure to thrive. Short stature was associated with celiac disease in 13% of the patients. About 5 patients had CD associated with Diabetes Mellitus and 2 patients had Down's syndrome at the time of CD diagnosis. Regarding GF diet, only 46% of the patients were compliant but 83% of patient reported significant symptomatic improvement with dietary modification.

Conclusion: To the best of our knowledge this study represents the largest description of Hispanic children with CD. Although considered a rare disease in Hispanics, the diagnosis of CD is rising in our population. Our study accurately represented commonly known parameters such as higher prevalence of disease in female gender, abdominal symptoms and diagnostic testing. There was a high GF diet non-compliance rate in our cohort that could be related to the lack of specific ethnicity-based education for this disease. Future studies should address the needs of Hispanic CD patients in regards to education and accessibility of gluten-free products.

499 GASTROINTESTINAL OUTCOMES OF RECESSIVE DYSTROPHIC EPIDERMOLYSIS BULLOSA AFTER HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Recessive dystrophic epidermolysis bullosa (RDEB) is one of the most severe of an inherited group of blistering disorders where loss of integral skin scaffolding proteins occurs due to defects in type VII collagen production. The presence of type VII collagen in mucous-type squamous epithelium of the oropharynx, esophagus, and rectum also leads to significant and severe gastrointestinal (GI) complications such as esophageal strictures, esophageal reflux, and malnutrition. Whereas previous therapies addressed supportive care, hematopoietic cell transplantation (HCT) offers partial type VII collagen deficiency correction and improves wound healing of squamous epithelium. A paucity of literature exists surrounding the effects of HCT on GI symptoms in RDEB.

Objectives: To assess improvement of GI symptoms in patients with RDEB after HCT based on the severity of esophageal stricturing disease and presence of comorbid GI complaints pre- and post-HCT.

Methods: A total of 30 patients with EB underwent HCT at the University of Minnesota between 2/2010 and 10/2015. RDEB patients were included in this retrospective chart review study if they received non-myeloablative conditioning, and had at least 6 months follow-up. Patients with other subtypes of EB, and those who received myeloablative conditioning, were excluded.

Results: 16 patients met criteria for this study, as described in Table 1. The average weight-for-age Z-score pre-HCT at -1.43 improved to -1.05 at 6-month follow-up (p 0.05). The rate of esophageal dilatations at 0.98 per pt-yr surrounding HCT (day -180 to +180), improved to 0.75 per pt-yr following HCT (day +180 to +545) (p 0.67).

Conclusions: GI symptoms were common pre- and post-HCT. The impact of HCT on these symptoms is unclear, likely related to the small cohort size and often objective, transient nature of symptoms. Post-HCT GI side effects confound assessment of improvement in EB-related GI symptoms, thus patients need evaluation further out.

Esophageal strictures needing dilatation were present in almost half the cohort pre- and post-HCT. Trends toward improvement were seen in the rate of dilatations pre- and post-HCT, suggesting esophageal healing that may mirror skin healing, but this was not statistically significant.

Future research could attempt to quantify esophageal healing.

Weight-for-age significantly improved post-HCT. Mechanisms could include fewer nutrient losses through skin, fewer infections, and decreased hypermetabolic state.

This study was limited by its retrospective nature and small cohort size. In addition, as our center treats patients from all over the world, they may have received different standards of care, or no significant care, prior to evaluation and transplant. This would impact symptom management, nutritional rehabilitation, as well as the absolute number of dilatations prior to HCT if a center does not have the expertise or technology to offer dilatations.

Table 1: Patient characteristics, outcomes, and select GI symptoms after hematopoietic cell transplantation for recessive dystrophic epidermolysis bullosa

Pt	Gender	Age at HCT (years)	Follow-up after HCT (years)	Origin	Dermatologic outcome ¹	Mucocutaneous chimerism %	Esophageal dilatations		Esophageal reflux		Constipation		Weight z-score	
							pre	post	pre	post	pre	post	at transplant	at 6mos follow-up
1	M	20.4	4.1	American	Improvement	9-23	0	0	y	y	n	y	n/a (>20yo)	n/a (>20yo)
2	F	2.8	2.1	American	Improvement	0-2	0	0	n	n	n	y	-2.28	-1.98
3	F	6.4	3.1	African	Improvement	3-7	1	3	y	n	y	n	-2.74	-1.07
4	F	7.7	0.3	Indian	No engraftment	0	12	1	y	n	y	n	-1.49	n/a
5	M	0.9	2.6	American	Improvement	0-15	0	0	y	n	y	n	0.65	-0.35
6	M	3.2	0.2	European	Death	8-11	3	0	n	n	y	n	-1.53	n/a
7	F	0.9	0.6	South American	Improvement	0-3	0	0	y	n	n	y	0.61	0.12
8	M	3.3	2.3	Middle Eastern	1st: Waning chimerism	0-16	1	0	n	y	y	y	-3.35	-3.4
					2nd: Improvement		0	2	n	y	y	y	-4.12	-3.23
9	F	1.3	1.5	European	Improvement	0-22	2	7	n	y	y	y	-0.16	-0.11
10	M	0.9	1.4	Middle Eastern	Improvement	0-47	0	2	y	y	y	y	-1.93	-1.25
11	F	4.9	1.2	Middle Eastern	Improvement	0	1	4	n	y	y	y	-2.47	-1.98
12	F	0.4	1.0	European	Improvement	3-8	0	0	n	n	y	n	-0.17	-0.26
13	M	0.5	0.6	American	Improvement	13	0	0	y	y	y	y	1.44	2.3
14	M	5.2	0.7	European	Death	51	0	1	y	y	n	y	-3.74	-3.35
15	F	0.7	0.5	American	Improvement	10	0	0	y	y	n	n	-0.45	0.49
16	M	6.0	0.5	European	Improvement	n/a	6	0	y	y	n	n	-1.36	-0.65

Abbreviations: M=male, F=female, y=yes, n=no

1: C7 expression, % body surface area affected, resistance to blistering

***500 BREATH VOLATILE ORGANIC COMPOUND TESTING CAN BE USED TO DIFFERENTIATE CHILDREN WITH CELIAC DISEASE FROM HEALTHY CONTROLS**

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Background: Celiac disease (CD) affects an estimated 0.3-2.4% of the population. It is commonly screened for in patients with diarrhea, abdominal pain, and weight loss. Diagnosis is confirmed with upper endoscopy, and adherence to the gluten-free diet (GFD) is monitored with serial laboratory draws and possible endoscopy. This suggests the need for noninvasive tests for diagnosing and monitoring compliance with the GFD. Volatile organic compounds (VOCs) in the exhaled breath, have been shown to correlate in unique patterns with certain disease states. The aim of this study was to determine if there is a unique VOC pattern, or “breath print”, found in CD.

Methods: We collected single exhaled breath specimens from patients aged 6-21 with new diagnosis/untreated (n=24) or an existing/ treated CD (n=46) as well as from healthy controls (HC) (n 55) during well child examinations. Breath specimens were analyzed per protocol with selective ion flow tube mass spectrometry for VOC concentrations.

Results: Patient characteristics were similar between groups. Of the 22 known compounds, 16 were noted to be significantly different in patients with CD (both untreated CD and patients following the GFD) compared to HC. There were no differences in VOC compounds between untreated celiac and celiac patients following the GFD. Stepwise discriminant analysis was performed and showed that a combination of breath VOCs could be used to classify subjects into CD or HC, with a very low misclassification rate of 6.4%. A model was calculated using ROC analysis with various marker combinations and showed excellent accuracy of prediction for differentiating CD vs. HC, with AUROC of 0.95 (95% CI, 0.91, 0.99). The final proposed multivariable logistic regression prediction model for CD utilizes ethanol, isoprene, and trimethylamine. Internal validation of the model showed AUROC or 0.948, and a score of 35.5 or higher would provide sensitivity of 98.6% and specificity of 99%.

Conclusions: Breath VOC testing can be used to classify patients with CD from HC with excellent accuracy, suggesting a breathprint exists for CD. Breath VOC testing did not differentiate untreated patients from those following the GFD in our current study.

501 CLOSTRIDIUM DIFFICILE INFECTION ASSOCIATED BOWEL HABIT CHANGE IN INFANT

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Background: Incidence of the functional diarrhea in infancy is relatively uncommon, but the causes are little known. Clinical symptoms associated with *Clostridium difficile* infection (CDI) vary widely, and the carrier state without apparent symptoms is relatively common in infancy. Therefore, we identified the association between CDI and bowel habit change, and the effect of CDI treatment on the restoration of bowel habit.

Methods: Between 2008 and 2014, infants less than 12 month of age with more than 2 weeks of diarrhea who did not improved with conservative care were collected in Gachon University Gachon Children's Hospital. And the infants who followed by at least over 2 weeks were included after excluding the patients who were or were suspected lactose intolerance, milk allergy and prior gastrointestinal surgery. Whether CDI or not, effect of metronidazole, other medical records, such as birth history and vaccination were reviewed. For identifying the association between CDI and bowel habit change in infancy, logistic regression analysis was used.

Results: Of 126 infants, 27 patients (21.4 %) were CDI; 74 (58.7%) were male .CDI-associated risk factors are artificial milk feeding, prior rotavirus vaccination and antibiotic use (OR 4.310; 95% CI, 1.564-11.878, OR 4.217; 95% CI, 1.242-14.314, OR 2.873; 95% CI, 1.066-7.746, $p<0.05$). Regardless of CDI, there were improvement in bowel habit after the metronidazole therapy (OR 0.34; 95% CI, 0.15-0.79, $p<0.05$).

Conclusions: There was no correlation between bowel habit change and CDI in infancy, but metronidazole can be one of the optional methods for the management of functional gastrointestinal disorders.

502 *HELICOBACTER PYLORI* INFECTION ALTERS GUT MICROBIOTA IN CHILDREN

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Background: *H. pylori* infection causes peptic ulcer diseases, iron deficiency anemia, and growth retardation in children. Compositional difference of gut microbiota is tightly associated with susceptibility of many diseases, including inflammatory bowel diseases, obesity, diabetes mellitus, cancer, and atherosclerosis. The relationship between dysbiosis and *H. pylori* infection have not been studied extensively.

Purpose: The aim of the study was to elucidate if there was alteration in the composition and diversity of gut microbiota in children infected with *H. pylori*.

Methods: Sera of healthy schoolchildren aged 10-12 years were tested for anti-*H. pylori* antibody using ELISA test, and confirmed by C-13 urea breath test (13C-UBT). The diversity of gut microbiota between *H. pylori*-infected and non-infected children were analyzed by the next generation sequencing (NGS).

Results: The seroprevalence of *H. pylori* infection was 12.8% In 179 healthy children. The 13C-UBT confirmed that 22 of 23 seropositive people have sustained *H. pylori* infection. A total of 19 stool samples (10 from *H. pylori*-infected and 9 from controls) were processed for NGS analysis. In phylum level, a significant difference of fecal microbiota diversity (weighted UniFrac algorithm $p < 0.001$) between *H. pylori*-infected and non-infected children. In genus level, we found a significantly higher *Clostridium* XIVa and *Rikinellaceae* and lower *Ruminococcaceae* in infected children than non-infected ones by Linear discriminant analysis (LDA).

Conclusions: This is the first time to evaluate the gut microbiota by the NGS tool and to find *H. pylori* infection altering gut microbiota in children. The functional significance of these genus or species desired further investigation.

503 WHETHER THE APPROPRIATE ANTIMICROBIAL THERAPY AFFECTS FECAL EXCRETION TIME IN PEDIATRIC PATIENTS WITH NONTYPHOID SALMONELLOSIS: A PRELIMINARY REPORT

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Objective: Antimicrobials are not generally recommended for the treatment of isolated uncomplicated nontyphoid *Salmonella* gastroenteritis because they may prolong both the excretion of nontyphoid *Salmonella* and the remote risk for creating the chronic carrier state. However, most studies didn't classify the salmonellosis with different severity. The present study is to investigate whether the appropriate antimicrobial therapy affects fecal excretion time in pediatric patients with nontyphoid salmonellosis.

Methods: Children with nontyphoid salmonellosis admitted to Kaohsiung Veterans General Hospital, Taiwan who consented to receive consecutive stool cultures every 4-7 days till two consecutive negative results between 2005 and 2015 were enrolled. Fecal excretion time was defined as the timeframe of the first positive stool culture and the first of two consecutive negative results. The Severity Score previously published (CLIN PEDIATR, 967-74, 2014) was used to stratify the patients as the severe (score: 4), moderate (score:2-3) and mild group (score:0-1) according to their fever days before admission, band cells in peripheral blood and C-reactive protein. Patients were classified into no antibiotics, appropriate (A group) (bacteremia or severe patients receiving antibiotics active *in vitro*) and inappropriate antimicrobial therapy group (I group) (mild and moderate patients receiving antibiotics or severe patients receiving antibiotics resistant *in vitro*).

Results: One hundred and ten patients were enrolled; 61 were in no antibiotic group, 21 were in A group and 28 were in I group. Compared with no antibiotic group, although A group had significantly longer fever days before admission (3.90 vs. 2.16 days) and higher C-reactive protein (9.55 vs. 5.05 mg/dl), A group had comparable fecal excretion time (11.76 vs. 9.92 days) and fever days after admission (3.19 vs. 2.15 days). However, A group had significantly longer hospital stay (8.19 vs. 6.30 days) than no antibiotic group. The I group had not only significantly longer fecal excretion time (20.43 vs. 9.92 days), but also longer fever days after admission (3.21 vs. 2.15 days) and longer hospital stay (8.11 vs. 6.30 days) than no antibiotics group. With further multiple regression analysis, fecal excretion time was only affected by inappropriate antibiotic therapy significantly.

Conclusions: Appropriate antimicrobial therapy in patients with bacteremia and severe salmonellosis do not prolong fecal excretion time, but inappropriate antimicrobial therapy not only prolong fever days after admission and hospital stay, but also prolong fecal excretion time. The Severity Score and surveillance of antimicrobial resistance could be served as guides for antibiotic use in children with salmonellosis and antimicrobials should be reserved for severe cases to improve clinical outcomes in terms of fever days after admission and avoid the longer fecal excretion time.

504 ASSOCIATION BETWEEN PROTON PUMP INHIBITOR MEDICATION CYP2C19 EXTENSIVE METABOLIZER PHENOTYPE AND ANTI-REFLUX SURGERY IN CHILDREN

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Funduplication (FP) surgeries are among the most common operations performed by pediatric surgeons frequently for the indication of failed medical management of gastroesophageal reflux disease (GERD). Proton pump inhibitor (PPI) medications are metabolized by the CYP2C19 enzyme which is encoded by the CYP2C19 gene and which harbors SNPs that give rise to extensive, normal and poor metabolizer (EM, NM, PM) phenotypes. We hypothesized that the distribution of the EM phenotype among children undergoing FP surgery after failing PPI therapy would differ compared to controls (children with no history of FP surgery). Across the Nemours Health System between 2000-2014, we identified 367 FP children > 2 years of age of which 34 children had stored endoscopic tissue samples available and had previously undergone esophageal pH testing while on PPI therapy. Children were 73.5% Caucasian, 64.7% male, 9 (± 5.3) years old and were taking 1.37 mg/kg (± 0.51) mean PPI dose. Loss-of-function CYP2C19 SNPs (rs4244285, *2; rs4986893, *3; rs41291556, *8; rs17884712, *9) and a gain-of-function SNP (rs12248560, *17) were genotyped by TaqMan, and children were classified as PM, NM and EM phenotypes. CYP2C19 phenotypes from FP patients were compared to 136 race matched controls: EM 41.2% FP vs. 25.0% control; NM 55.9% FP vs. 47.8% control; PM 2.9% FP vs. 27.2% control; $p < 0.005$. At the SNP level, *2 that corresponds to PM phenotype was underrepresented in FP children with a minor allele frequency (MAF) of 4.4% relative to 16.5% in controls (OR 0.23; CI, 0.07-0.77; $p < 0.05$) while *17 that corresponds to EM phenotype was overrepresented in FP children with a MAF of 29.4% FP relative to 16.5% in controls (OR 2.10; CI, 1.14-3.88; $p < 0.05$). To further explore the EM phenotype, logistic regression analysis was performed for FP vs. entire control cohort with race as a confounding

variable (OR 10.5; CI, 1.3-83.7; $p=0.03$). PPI CYP2C19 EM phenotype was significantly more frequent among FP children who had failed PPI therapy compared to controls.

In conclusion, genotype-guided dosing of PPI medication therapy may help to guide indications for fundoplication surgery.

505 STEROID THERAPY DOES NOT PRECLUDE THE NEED FOR DIETARY RESTRICTION IN EOSINOPHILIC ESOPHAGITIS

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Background: Food restriction and topical steroid therapy are two of the most common treatments for eosinophilic esophagitis (EoE). Typically, these treatments are used separately. Neither treatment is effective in all patients.

Methods: We identified patients with EoE who failed dietary restriction and were subsequently placed on topical steroids. Those who achieved a response to steroid therapy (<15 eosinophils per microscopic high powered field (hpf) on biopsy) were prospectively followed as foods were reintroduced into their diet.

Results: 10 patients were identified who remained on some form of dietary restriction while starting steroid therapy. Of those 10 patients, 6 underwent food challenges with some of the previously restricted foods while remaining on steroid treatment. All 6 patients had a response to steroids, and all 6 had histologic relapse after reintroducing some of the previously restricted foods. The median eosinophil count per microscopic high powered field prior to starting steroids was 43 eos/hpf (range, 20-98 eos/hpf). The median eosinophil count on steroid therapy, before food challenge, was 2 eos/hpf. Median eosinophil count increased to 43 eos/hpf after food challenge, p value 0.021.

Conclusion: Patients who are responders to topical steroid therapy can develop active EoE during food challenge, even when steroid therapy is continued. This finding calls into question the common approach of using either topical steroids or dietary therapy and suggests that combination therapy may be necessary in a subset of patients with EoE. This also may account for the less than complete response rates seen in trials of topical steroids in the literature.

*506 PROSPECTIVE STUDY EVALUATING DIAGNOSTIC AND POST-TREATMENT ENDOSCOPIC FINDINGS IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: Diagnostic guidelines for eosinophilic esophagitis (EoE) are based on clinical and histologic features. The role of endoscopic findings in diagnosis, or as a biomarker of active disease has not been established in children. We aimed to determine the diagnostic utility of the EoE Endoscopic Reference Score (EREFS) and assess the relationship between endoscopic changes and treatment response.

Methods: EoE was diagnosed by the 2011 consensus guidelines. Children undergoing diagnostic upper endoscopy and those diagnosed with EoE undergoing follow-up endoscopy were prospectively scored using an EREFS atlas from 2012-2016. This assesses severity of five endoscopic findings: edema, rings, exudates, furrows and strictures. Inactive disease was considered as peak eosinophil count <15 eosinophils/hpf (eos/hpf). Endoscopic findings were correlated with eosinophil counts, and prevalence, sensitivity, specificity, positive (PPV) and negative (NPV) predictive values for each finding was determined for diagnostic and follow-up endoscopy. Longitudinal treatment changes in EREFS were assessed with regards to treatment response.

Results: Data from 166 diagnostic and 543 follow-up endoscopies was evaluated in 372 children (mean age 10 years, 57% male, 90% white at diagnosis and mean age 10 years, 77% male, 88% white at follow-up). At diagnostic endoscopy, 69 children met criteria for diagnosis of EoE. Endoscopic abnormalities were present in 87% of patients with EoE including furrows (83%), edema (72%), exudates (46%) and rings (29%); 92% had multiple findings. At follow-up, active disease (≥ 15 eos/hpf) was present in 248 endoscopies and 84% had endoscopic abnormalities including furrows (74%), edema (70%), exudates (44%) and rings (27%); 85% had multiple findings. No strictures were found. Inflammatory endoscopic findings (edema, furrows and exudates) correlated significantly with increased eosinophil counts at diagnostic and follow-up endoscopy ($p<0.001$). Eosinophil counts increased by 17 (diagnostic) and 18 (follow-up) eos/hpf for each additional endoscopic finding ($p<0.0001$, r 0.64). Multiple inflammatory endoscopic findings present at diagnostic endoscopy had a sensitivity of 83%, specificity 93%, PPV 88%, and NPV 89%. At follow-up, this had a sensitivity of 77%, specificity 82%, PPV 80%, and NPV 79%. Pre- and post-treatment longitudinal data from 80 patients demonstrated a significant reduction in a EREFS-inflammatory severity score (2.3 vs. 0.6, $p<0.001$) for treatment responders vs. non-responders with 98% of responders demonstrating score reduction.

Conclusions: Inflammatory EREFS findings are prevalent in most children with EoE at diagnosis (87%) and with active disease at follow-up (84%). These findings correlate well with eosinophilia and the presence of multiple inflammatory EREFS findings appears to be a reliable biomarker for active disease. Patients that respond to therapy have a significant reduction in EREFS inflammatory severity.

507 CHANGING DISTRIBUTION OF AGE, CLINICAL SEVERITY, AND GENOTYPES OF ROTAVIRUS GASTROENTERITIS IN HOSPITALIZED CHILDREN AFTER THE INTRODUCTION OF VACCINATION: A SINGLE CENTER STUDY IN SEOUL BETWEEN 2011 AND 2014

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Background: This study aimed to explore changes in clinical epidemiology and genotype distribution and their association among hospitalized children with rotavirus gastroenteritis after the introduction of vaccines.

Methods: Between November 2010 and October 2014, hospitalized children with acute gastroenteritis were enrolled. Rotavirus genotypes were confirmed through reverse transcription-polymerase chain reaction (RT-PCR), semi-nested PCR, and sequencing. Clinical information including vaccination status and the modified Vesikari scores were collected.

Results: Among 179 children with rotavirus infection, nineteen (10.6%) were completely vaccinated. During the study period, the number of children between three and 23 months of age decreased significantly compared to the number of children older than 24 months of age ($p = 0.010$), who showed lower diarrhea severity (duration, $p = 0.042$; frequency, $p = 0.021$) but higher vomiting severity ($p = 0.007$, 0.036) compared to the former. Vaccination status was also significantly associated with lower vomiting severity after adjustment for age (frequency only, $p = 0.018$). The predominant genotypes were G2P[4] (18.4%), G1P[8] (14.5%), and G1P[4]P[8] (12.8%), and the prevalence of genotypes with

uncommon and mixed combinations was more than 50%. Children infected with G2P[4] strains tended to be older ($p = 0.005$) and had more severe vomiting ($p = 0.018, 0.006$) than those with G1P[8].

Conclusions: Increase in age of infected, hospitalized children was accompanied by change in clinical severity during 2011-2014 after the introduction of vaccines in Seoul. Clinical severity was also associated with vaccination status and genotype. Long-term large scale studies are needed to document the significance of the increase in genotypes of uncommon and mixed combinations.

508 VARIABILITY AND ATTITUDES TOWARDS COW'S MILK PROTEIN ALLERGY MANAGEMENT BY PEDIATRIC GASTROENTEROLOGISTS IN SPAIN

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Objective: To analyze the variability in cow's milk protein allergy (CMPA) management by pediatric gastroenterologists in Spain.

Methods: A fifty-item questionnaire was sent by a distribution mail list where the vast majority of pediatric gastroenterologists in Spain are included. The questionnaire comprised open and closed items in a Likert's scale from 0 to 5. Data were anonymously included in a database and then analyzed with SPSS 20.0. Those items scored 0-1 were considered "disagree", 2-3 "undefined" and 4-5 "agree".

Results: Seventy-three questionnaires were received, 41 corresponding to full members of the Spanish Society of Pediatric Gastroenterology, Hepatology and Nutrition (30.5% of the total members). In 11 items, the median score fell into the undefined category. Only 3 items showed a concordance greater than 90%. Regarding diagnosis, 25% considered that symptom relief after CMP removal was enough for the diagnosis of CMPA. Oral Challenge should be performed in a hospital setting by 43% of the participants, although 83.5% considered reintroduction of milk at home in non IgE mediated CMPA cases. Oral challenge protocols were almost different in every unit. Regarding treatment, 11% considered a soy formula appropriate for children younger than 6 months of age and 5.7% considered milk from other mammals as a treatment option. In children older than 3 years 66.2% did not consider a milk free diet in their protocols. Casein hydrolysates were the preferred treatment choice, soy formulas and elemental formulas being less used. Regarding prognosis and safety, 8.5% do not consider CM exposition as a possible death hazard at any age, and 39.4% are not sure if non IgE-mediated CMPA infants develop tolerance before or after IgE-mediated CMPA.

Almost all the participants are aware of the existence of clinical practice guidelines on CMPA, with the ESPGHAN guidelines the most used (64%). Twenty-three percent of the participants considered their knowledge on CMPA outdated and low.

Conclusions: Although CMPA is a very prevalent condition which pediatric gastroenterologists have been treating for decades, there is still a huge variability on its management. Efforts should be made to try to unify patterns. There is room for future improvement in this field among pediatric gastroenterologists.

*509 17-BETA ESTRADIOL PROTECTS THE ESOPHAGEAL EPITHELIUM FROM IL-13-INDUCED BARRIER DYSFUNCTION

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Background: Eosinophilic esophagitis (EoE) is an emerging chronic esophageal disease that is associated with esophageal eosinophil-predominant inflammation and barrier dysfunction. Similar to other esophageal disorders including GERD and Barrett's esophagus, the incidence of EoE in males is 3-4.5 times higher than that observed in females. While the molecular basis for the heightened incidence of esophageal disorders in males remains unclear, estrogen has been linked with a protective effect in other esophageal diseases, including GERD. Aim: To define the effect of 17-beta estradiol (E2) on esophageal epithelial barrier function.

Methods: Primary human esophageal keratinocyte cells (EPC2 cells) were grown in air-liquid interface and exposed to IL-13 (100 ng/mL), with or without exposure to E2 (100 nM) and esophageal epithelial barrier properties (transepithelial resistance (TER)), esophageal epithelial remodeling and gene expression (RNA-seq) was examined.

Results: IL-13 stimulation of EPC2 cells decreased TER (TER Ohms.cm²; 2021 +/- 516 vs. 1258 +/- 334; Vehicle vs. IL-13 respectively; mean +/- SD; n=10 per group; $p < 0.001$). Pretreatment of EPC2 cells with 100 nM E2 24 hours prior to IL13 exposure attenuated the IL-13-mediated decrease in TER (TER Ohms.cm²; 1291 +/- 190 vs. 1597 +/- 363; Vehicle + IL13 vs. E2 + IL13 respectively; mean +/- SD; n = 10 per group; $p < 0.05$). Simultaneous exposure of EPC2 ALI cells with IL-13 and E2 resulted in mean TER of 1205 +/- 268.6 Ohms.cm². Western blot analyses revealed that E2 abrogation of IL-13-induced esophageal barrier dysfunction was associated with decreased expression and activation of pSTAT-6. In accordance with this, RNA-seq analyses revealed that IL-13-induced SOCS1 expression (+6.91 FC, $p < 0.05$), which was abrogated following E2 pretreatment (-1.96 FC, $p < 0.05$).

Conclusions: E2 has a protective effect against IL13 mediated esophageal barrier dysfunction if treated prior to IL13 exposure. The E2-mediated suppression of IL13 was associated with reduced STAT6 activation and expression. These studies suggest that E2 may protect against IL13 induced changes similar to those observed in EoE. Further studies are needed to explore the role E2 may play in EoE.

*510 MID-PREGNANCY AND CORD BLOOD IMMUNOLOGICAL BIOMARKERS, HLA GENOTYPE AND CELIAC DISEASE

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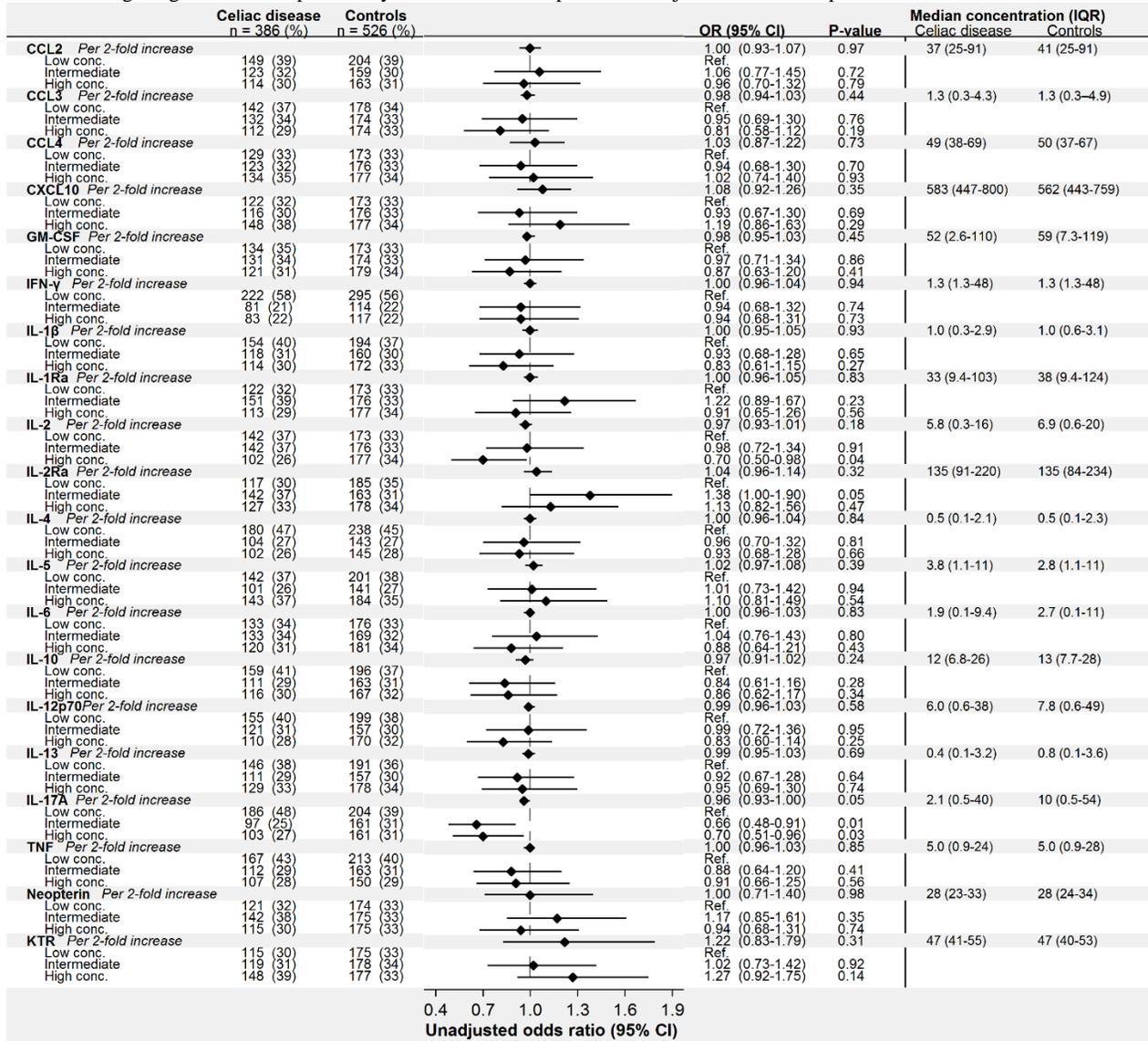
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Background: Motivated by observations suggesting that the perinatal environment may influence pediatric celiac disease (CD) development we aimed to test whether multiple prenatal immunological biomarkers, next to HLA haplotype, predicted increased risk of CD.

Methods: This case-control study, nested within the prospective Norwegian Mother and Child Cohort study, included 413 children with CD and 568 randomly selected controls (median age 9.5 and 8.5 years, respectively). Twenty biomarkers of cellular and humoral immune activation were measured in mid-pregnancy plasma (CCL2, CCL3, CCL4, CXCL10, granulocyte-macrophage colony stimulating factor, interferon- γ , interleukin [IL]-1 β , -2, -4, -5, -6, -10, -12p70, -13, -17A, IL-1 receptor antagonist, IL-2 receptor- α , tumor necrosis factor- α) and umbilical-cord plasma (neopterin, kynurenine/tryptophan ratio). Logistic regression yielded odds ratios adjusted for covariates retrieved from national registries, parental questionnaires and CD-associated HLA haplotypes.

Results: Odds ratios for CD per two-fold increase in cytokine concentration in pregnancy ranged from 0.96 (95% confidence interval [CI], 0.93-1.00) for IL-17A to 1.08 (95% CI, 0.92-1.26) for CXCL10 (Figure 1); neither inflammatory markers at birth differed significantly between cases and controls (p values ≥ 0.10 for trend per two-fold increase in concentrations). OR for childhood CD according to summary cytokine scores reflecting Th1- and Th2-immunity in mid-pregnancy approximated one and restriction to children with CD-prone HLA-DQ2.5 haplotype as well as adjustments for multiple potential confounders yielded essentially unchanged results. Conclusions: This comprehensive study observed no significant association of immune markers in mid-pregnancy or at birth with childhood CD. The results argue against that the prenatal systemic immune response is a major risk factor for pediatric CD.



511 PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS PRESENTING WITH FOOD IMPACTION: A POSSIBLE DISEASE SUBPOPULATION?

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune- or antigen-mediated esophageal disease, characterized by eosinophilic inflammation in the esophagus. Children who suffer from EoE can present with esophageal food impaction (EFI). The underlying pathophysiology of EFI in children without an anatomical disorder and suffering from EoE is not well understood. Studies have suggested the presence of motility abnormalities in patients with untreated EoE, but no specific studies have focused on characterizing EoE patients that experience EFI. Mast cells have been associated with dysphagia in EoE and have been suggested to modulate esophageal contractility by the expression of TGF- β 1. TGF- β 1 can also cause fibrosis in the esophagus. Nitric oxide (NO) is an important inhibitory neurotransmitter of the esophageal myenteric plexus. A decrease in NO causes simultaneous esophageal body contraction and failure of swallow-induced lower esophageal sphincter relaxation. It is possible, therefore, that smooth muscle dysfunction may also play a role.

Objective: To investigate the esophageal mRNA expression in pediatric patients with EoE who have had an EFI.

Methods: The patient population consisted of 5 pediatric EoE patients that presented with EFI. 12 age-matched EoE patients who did not experience EFI were selected as controls. Patients with a diagnosis of Crohn's, achalasia, esophageal atresia or trachea-esophageal fistula, were excluded. In those with EFI, biopsies were obtained at time of follow-up endoscopy after PPI treatment. Gene expression data was collected for all individual using Digital mRNA profiling with nCounter® NanoString technology.

Results: 4 EFI patients and 4 controls were male. Average age at diagnosis was 14.8 years for EFI patients and 14.3 years for controls. All children underwent allergy workup: 3 of 5 EFI patients and all 12 controls had a history of proven allergies ($p=0.02$). This might implicate that EoE patients presenting with EFI have a different disease phenotype. None of the patients required dilation of their esophagus. *Table 1* shows the gene expression of a sample of the investigated genes. No significant differences were seen in esophageal expression of genes associated with fibrosis, inflammation or mast cell involvement. However, the overall pattern of inflammatory gene expression and nitric oxide related genes were lower in children experiencing EFI.

Conclusions:

- Patients with EoE experiencing EFI did not show evidence of elevated esophageal gene expression associated with fibrosis.
- The significant difference in genes associated with the regulation of NO production, suggests that there may be an underlying motility disorder causing EFI in children with EoE.
- Children presenting with EFI might be a disease subpopulation, characterized by a unique inflammatory esophageal mRNA pattern.

512 *HELICOBACTER PYLORI* INFECTION IN MOTHERS MODIFIES FECAL MICROBIOTA IN THEIR NEWBORNS ACCORDING TO THE DELIVERY ROUTE

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Background: Interactions of resident intestinal microbes with the luminal contents and the mucosal surface play important roles in normal intestinal development, nutrition and immunity. Long-standing infections such as gastric *H. pylori* modify the gastric microbiota and might modify fecal microbiota composition.

Objective: To evaluate the fecal microbiota of mother-child pairs and its relation to *H. pylori* status.

Methods: Consecutive mothers and their newborns were recruited in the maternity unit, immediately after delivery. After signing informed consent, we took one stool sample of the mother before hospital discharge and one stool sample of the newborns at home (15 days old).

Maternal *H. pylori* status was evaluated by *H. pylori* antigen detection (Platinum HpSA, Meridian Diagnostics, Ohio, USA). Collected samples were stored at -80°C until processing. The V4 region of the 16S rRNA gene was sequenced using Illumina MiSeq platform. Sequences were analyzed using the QIIME pipeline.

Results: 22 mother-child pairs were recruited and 11 of them have positive maternal *H. pylori* status (50%). Thirteen babies were vaginally delivered and 9 were born by Caesarean section. All babies were fully breastfed. *H. pylori* was not detected in the feces of newborns. The analyses showed that there were differences in the structure of the microbiota by maternal *H. pylori* status only in infant feces born vaginally (PERMANOVA, $p=0.01$). Although with similar bacterial alpha diversity level, infants born vaginally to *H. pylori*-infected mothers had higher abundance of Enterobacteriaceae and Veilonella (LEfSe analysis, LDA > 3.0-fold).

Conclusions: Maternal *H. pylori* status affects the fecal microbiota composition in babies born by vaginal delivery, but not in babies born by Caesarean section. The results suggest that the effect of the maternal *H. pylori* on the infant fecal microbiota is mediated by the acquired vaginal microbiota at birth.

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513 COST COMPARISON OF STEROIDS VS. DIFFERENT ELIMINATION DIET FOR THE TREATMENT OF EOSINOPHILIC ESOPHAGITIS IN CHILDREN

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Background: Standard of care treatment for eosinophilic esophagitis (EoE) includes either swallowed steroids or dietary elimination of empiric or all food proteins. While the efficacy of these treatments has been well studied, there are no published studies comparing the cost of these treatments in children.

Methods: Medical records were reviewed to determine hospital charges and physician fees associated with the management of pediatric patients with EoE treated with swallowed steroids (budesonide and Flovent), elemental diet, six-food elimination (SFED), four food elimination (FFED), and milk elimination. For patients on diet elimination therapy, pre- and post-treatment food diaries were reviewed to determine the cost of each treatment regimen. For each specific diet treatment, cost was assessed for five patients. Parents were contacted to assess their perception of the estimated cost of their child's treatment. Assumptions were made regarding costs associated with clinic follow-up, number of endoscopies, formula needs, as well as medication costs.

Results: The initial cost of diagnosis for each patient was \$18,808. The first-year costs from steroid therapy were \$20,691, elemental diet was \$60,643, SFED was \$80,485, FFED was \$55,864, and milk elimination diet was \$17,772. During the second year of treatment, patients treated with steroids incurred charges of \$20,691, empiric elimination diet \$17,524 and on elemental diet \$60,643. The detailed cost analysis is shown in *Table 1*.

The challenges perceived by parents related to steroid therapy included difficulties in obtaining insurance approval for the prescription, resulting in delays in starting the treatment, and concerns of side effects of long-term steroid therapy. Parents' perceived benefit of steroid therapy was the lack of dietary restrictions and thus improved quality of life.

The perceived challenges identified relating to elimination diet included difficulty finding the right foods at the start of the treatment and the need to visit multiple grocery stores to find the right foods. The increased cost of the groceries was also an impediment. The parents' perceived benefit of completing diet elimination therapy was identification of the specific food(s) triggering their child's EoE.

Conclusion: The cost of steroid treatment and single food elimination diet incurred the lowest cost in the first year of treatment. From the second year onwards the costs of the different elimination diets were lower than those incurred by steroids.

***514 CHARACTERIZATION OF CULTURED ESOPHAGEAL EPITHELIAL CELLS FROM PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS**

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Background: Eosinophilic Esophagitis (EoE) is an allergic, immune-mediated, clinicopathologic disease, characterized by eosinophilic infiltration of the esophageal epithelium. The disease is believed to be Th2 driven, however, the role of the epithelium in this process is not well understood. Integrins (found on epithelial cells) are transmembrane proteins that mediate cell adhesion and have important immune-mediated roles including cell migration. In this study, our aim was to isolate, culture and expand esophageal epithelial cells obtained from patients with or without EoE and characterize any differences observed over time in culture.

Methods: Biopsies were obtained at the time of esophagogastroduodenoscopy (EGD) from pediatric patients with EoE or suspected to have EoE. The biopsies were digested with dispase and 0.05% Trypsin-EDTA to isolate the epithelial cells. Cells were then, plated on irradiated 3T3 feeder cells and expanded utilizing conditional reprogramming methods. Cells from Passage 1 and Passage 3 were stained, and analyzed via flow cytometry for integrin characterization. We also isolated RNA and performed qRT-PCR to characterize gene expression between the biopsy and cells obtained at passage 3.

Results: Integrin profiling demonstrated that the $\alpha 2$ integrin was not as highly expressed in EoE patients compared to normal patients. In addition, the $\alpha 1$ and $\beta 1$ integrins were significantly lower at passage 3 in EoE patients compared to normal controls. qRT-PCR revealed significant overexpression of TSLP and IL-33 in EoE vs. normal controls, which is expected based on the disease process. The integrin profiles and gene expressions did not seem to change significantly within the groups from passage 1 to passage 3.

Conclusion: In this study, we were able to isolate, culture and expand esophageal epithelial cells from pediatric patients. Furthermore, we characterized their phenotype and integrin profile to determine key differences and similarities between pediatric patients. The data suggests that the cells maintained their phenotype from biopsy/passage 1 to passage 3. This method will help us in developing an *ex-vivo* individualized, patient-specific model for diagnostic or drug testing.

515 COMPARISON OF BONE MINERAL DENSITY, TISSUE TRANSGLUTAMINASE AND MARSH STAGING IN ADOLESCENTS AND CHILDREN WITH NEWLY DIAGNOSED CELIAC DISEASE

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The importance of celiac disease has been increased recently owing to wide use of serological screening tests. We aimed to determine relationship between BMD, histopathologic findings and plasma tTG levels in children and adolescent with newly diagnosed celiac disease. A total of 118 biopsy proven celiac patients (61 females and 57 males) were included in the study. Cut-off point for tTG was accepted equal and above 20 U/mL. Mean diagnostic age of cases was 105.1 ± 50.1 month (22 – 207 month). While the mean height Z-score was -2.20 ± 1.55 SD the weight Z-score was -1.54 ± 0.85 SD. Failure to thrive was the most prominent complaint in our cases as seen in 65 (55%) of 118. First BMD Z-score values of cases were -5.2 to 0.7 (mean: -1.54 ± 1.15). Histological evaluation of biopsy specimen revealed that 10 patients (9%) were Marsh 2, 27 patients were (23%) Marsh 3a, 50 patients were (42%) Marsh 3b and 31 patients were (26%) Marsh 3c. There was no statistically significant difference between Marsh groups BMD Z-score and tTG value (respectively, $p=0.190$, $p=0.379$). There was significant negative correlation between cases' first BMD Z-score and their tTG values ($r = -0.281$, $p=0.002$) statistically. In conclusion, comparison of Marsh score with first BMD Z-score and tTG value was not correlated; however, BMD Z-score and tTG levels were correlated in children and adolescent with celiac disease.

ENDOSCOPY

534 COMPARISON OF ILEAL INTUBATION RATES AND DIAGNOSTIC YIELDS IN ILEOCOLONOSCOPY BETWEEN FOUR TERTIARY PAEDIATRIC GASTROENTEROLOGY CENTRES IN THE UNITED KINGDOM: A MULTICENTRE, RETROSPECTIVE COHORT STUDY.

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Introduction: Pediatric gastrointestinal endoscopy is integral to the diagnosis and management of many gastrointestinal conditions in children, especially pediatric inflammatory bowel disease (PIBD). With the increasing numbers of pediatric endoscopies performed worldwide, terminal ileum intubation (TII) rate at ileocolonoscopy has been gaining increasing importance, and indeed now constitutes a pivotal mandate in the revised Porto Criteria to improve IBD diagnosis, establishing itself as an integral part of PIBD management.

Several service evaluation studies have looked at TII rates and diagnostic yields in individual centres, and the factors influencing the same. In our study, we have compared this data among four major pediatric gastroenterology centres in the UK, in order to identify practice variations and local factors that may influence these outcomes, with a view to using this knowledge to further improve practice nationwide.

Methods: A service evaluation study to evaluate the diagnostic yield of ileocolonoscopy was originally conducted in Sheffield Children's Hospital, United Kingdom. Subsequently, further data was collected as per an agreed proforma across 3 other pediatric gastroenterology training units in the UK – Bristol, Chelsea & Westminster (London) and Kings College Hospital (London). 50 consecutive cases were selected from each of these 3 centres and data collected retrospectively for demographic details, indication for ileocolonoscopy, macroscopic and histopathological findings, ileal intubation rates and scope details. The number of procedures per list, both scheduled and actually performed, was also reviewed for its impact on TII rates. While the arithmetic mean was used as the measure of central tendency, the diagnostic yield was calculated from the Sheffield data and the sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) from all the other centres were calculated for comparison.

Results: Data from a total of 297 children who underwent endoscopy across 4 UK centres were analysed. The diagnostic yield from Sheffield was 18.9% and 32.6% for esophagogastroduodenoscopy and ileocolonoscopy respectively in this cohort. Overall, the endoscopic procedures had comparable sensitivities, specificities, PPV and NPV across all centres, as per Table 1 below.

Conclusions: Our data compares the TII rates and positive diagnostic yields across the four UK centres in the cohorts that were studied. This evaluation suggests that full pediatric ileocolonoscopy in UK tertiary centres seem to be adhering well to established guidelines, with an overall high ileal intubation rate (>95%) across all centres, without any significant impact of the number of procedures done per list, use of scope guide or use of scope stiffener. Further studies looking at international trends and practices will throw light on how robustly PIBD is being managed on a global scale.

	Bristol	Kings	Sheffield	Chelsea	Cumulative
Number	50	50	147	50	297
Mean age (years)	10.5	11.8	9.58	11.85	10.49
M:F ratio	1.6:1	1.5:1	1:1.42	2.8:1	1.15:1
Average no. of procedures/list (scheduled)	5.36	4.68	Data not collected	6.1	5.38
Average no. of procedures/list (performed)	5.3	4.32	Data not collected	5.68	5.10
Upper GI abnormalities (macroscopy)	14/43 (32.5%)	12/50 (24%)	35/147 (23.8%)	13/41 (31.7%)	74/281 (26.33%)
Upper GI abnormalities (histology)	26/43 (60.4%)	16/48 (33.33%) (2 not done)	36/147 (24.4%)	17/41 (41.4%)	95/279 (34.05%)
Lower GI abnormalities (macroscopy)	23/50 (46%)	34/50 (68.7%)	33/103 (32%)	31/50 (62%)	121/253 (47.8%)
Lower GI abnormalities (histology)	29/50 (58%)	28/48 (58.33%) (2 not done)	23/103 (22.33%)	31/50 (62%)	111/251 (44.2%)
Scope Type	Fujinon	Olympus	Olympus	Olympus	
Scope guide used	No	No	Yes	No	
Scope stiffener used	No	No	Yes	No	
TII rate	42/44 (96%) (6 not indicated)	48/50 (96%)	144/147 (98%)	40/47 (85%) (3 not indicated)	274/288 (>95%)
Normal ileocolonoscopy	21/50 (42%)	20/50 (40%)	70/103 (67.9%)	19/50 (38%)	130/253 (51.38%)
Sensitivity	75%	73.3%	71.4%	94.5%	77.8%
Specificity	90%	77.7%	71.4%	92.3%	77.3%
PPV	91.30	84.61	65.21	97.22	79.87
NPV	74.07	63.63	76.90	85.71	75.17

535 NOT YOUR TYPICAL FOREIGN BODY INGESTION

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Introduction: It is well-known that foreign body ingestions are commonly encountered in pediatric patients. However, the identification of ingested objects is not always straightforward.

Case: A 10-year-old male presented to the office with generalized abdominal pain of two weeks duration. He had initially been seen by his PCP for this issue and was referred after an abdominal x-ray revealed multiple radiopaque objects scattered throughout his colon. The patient had no history of foreign body ingestion. He had not started any new prescriptions or OTC medications. Because his initial x-ray had also showed a prominent stool burden, a bowel cleanout was attempted in order to alleviate symptoms. Repeat x-rays demonstrated migration of the radiopaque objects and an overall decrease in number from 25 to 8-10. Given their continued presence, the decision was made to proceed with colonoscopy for further evaluation. Two tablets were identified in the ascending colon during the colonoscopy and after successful removal were determined to be naproxen. This medication was immediately discontinued. In review of excipients found in naproxen formulations, it was

discovered that iron oxides are frequently used for coloring. We hypothesize that iron oxides contributed to the radiopaque nature of the retained naproxen tablets.

Discussion: This case poses a unique understanding that while we may initially discount the “usual suspects” in a child with evidence of foreign body ingestion, careful review of medications may provide diagnostic clues and help guide medical management.

536 FEASIBILITY OF PATENCY CAPSULE EXAMINATION PRIOR TO CAPSULE ENDOSCOPY IN CHILDREN

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Background: Capsule ingestion is key to successful noninvasive capsule endoscopy (CE) in children; an ingestion trial with a patency capsule (PC) can predict capsule retention in CE. We retrospectively evaluated the feasibility of PC use, focusing on capsule ingestion.

Methods: Data from pediatric patients (6 - 18 years old) examined for intestinal patency by PC were analyzed for determinants of PC ingestion difficulty and relationships in outcomes of PC and CE examinations. Patients taking 30 minutes or more, or failing to ingest the PC were considered to have ingestion difficulty.

Results: Among 61 patients (median age, 12.9 years; 40 boys) who underwent PC examination, 39 (64%) successfully ingested the PC without ingestion difficulty. The other 22 had ingestion difficulty; compared with those who succeeded, they were significantly younger (11.7 ± 2.2 vs. 13.0 ± 1.8 years; $p = 0.04$) and shorter (143.3 ± 14.0 vs. 154.6 ± 12.5 cm; $p = 0.003$). Multivariate analysis shows that the most significant factor for predicting PC ingestion difficulty was body height (cut-off value, 152 cm). Five of seven patients who initially failed to ingest the PC succeeded on retreat. The time to ingest the CE was significantly shorter than that for PC ingestion (8 ± 32 vs. 20 ± 58 minutes; $p = 0.01$).

Conclusion: PC is a useful noninvasive tool for evaluating intestinal patency and facilitating the performance of CE, but attention needs to be paid to the possibility of PC ingestion difficulty in children shorter than 152 cm who lack experience with capsule ingestion. We recommend that the physician estimate and explain the risk of PC ingestion difficulty to the patient or legal guardian by considering the child's body height prior to performing a PC ingestion trial.

537 LAPAROSCOPIC CHOLECYSTECTOMY AND ERCP IN A SINGLE SESSION REDUCES THE NEED FOR MULTIPLE GENERAL ANESTHETICS IN PEDIATRIC PATIENTS WITH CHOLEDOCHOLITHIASIS

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Introduction: Symptomatic pediatric gallstone disease is increasing in prevalence, with up to a third of patients presenting due to biliary obstruction. Many of these children will require both ERCP and laparoscopic cholecystectomy (LC), traditionally resulting in two separate general anesthetics. Laparoscopic cholecystectomy and ERCP in a single anesthesia session (LESS) offers an alternative to staged procedures that necessitate multiple anesthesia sessions.

Methods: A multicenter prospective ERCP database (the PEDI database) was queried for all ERCP performed from May 2014 to November 2015. Inclusion criteria: ERCPs performed for suspected choledocholithiasis, age <19, complete data entry and had both LC and ERCP performed within the index admission. Exclusion criteria: patients presenting with pancreatitis or cholangitis, those with prior intervention for choledocholithiasis. Patient and procedural characteristics were compared for patients managed with LESS to those managed with the traditional staged ERCP/LC approach. Variables were compared using two-sided Fisher's exact test for categorical variables and the Student's t-test for continuous variables.

Results: Twenty-two procedures met inclusion criteria and included for analysis. The mean age was 14.7 (range 11.2-18.3), mean ASA score was 2.5 (range 2-3), and 6 (27%) of the patients had hemolytic disease. Twelve patients (55%) were managed with LESS, while 10 (45%) were managed by the traditional staged ERCP/LC approach. Table 1 compares patient and procedural characteristics the two groups. One planned LESS was aborted due to prolonged ERCP time and post-ERCP abdominal distension. Two patients with hemolytic disease in the LESS required repeat ERCP for retained stones. There were no episodes of post-operative or post-procedural complications experienced in this series in either group.

Conclusion: This is the first described series of LESS in pediatric patients for choledocholithiasis. Patients undergoing LESS had fewer general anesthetics. This data suggest the LESS method may confer an advantage over staged ERCP and LC. Further data needed to delineate patient selection and factors contributing to outcomes including procedure and hospitalization times.

Patient and procedure characteristics in LESS vs. traditional choledocholithiasis management

	LESS (n=12)	Traditional management (n=10)	pvalue
Age, years (range)	15.4 (11.2-18.3)	13.8 (11.2-16.8)	0.06
ASA >2 (%)	7 (58%)	3 (30%)	0.23
History of hemolytic disease	5 (42%)	1 (10%)	0.16
Anesthetic sessions >1 (%)	2 (16%)	10 (100%)	<.0001*
Time from presentation to first procedure, days (range)	1.7 (0-5)	0.9 (0-4)	0.17
Time from first procedure to discharge, days (range)	2.6 (1-6)	3.3 (2-9)	0.40
Time from presentation to discharge, days (range)	4.3 (2-8)	4.2 (3-10)	0.89
% of patients > 1 day from first procedure to discharge	8 (67%)	10 (100%)	0.10
% of patients > 2 days from first procedure to discharge	4 (33%)	6 (60%)	0.39
ERCP procedure time, min (range)	18 (10-50)	22 (10-55)	0.51
LC procedure time, min (range)	105 (62-252)**	88 (50-130)	0.40
Total procedure time, min (range)	123 (75-262)	109 (62-164)	0.51
Total anesthesia time, min (range)	194 (118-333)	196 (134-269)	0.91

* $p < .05$ ** One LC required prolonged operative time due to severe inflammation and dense intra-abdominal adhesions

538 OUTCOME FROM ENHANCED ENDOSCOPE PROCESSING AND MICROBIOLOGIC SURVEILLANCE, SINGLE INSTITUTION EXPERIENCE

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There has been increased concern over risks associated with endoscopy and patient contamination with dangerous, antibiotic resistant infectious agents. *Pseudomonas*, *Enterobacteriaceae* (*Klebsiella*, *Salmonella*, *Serratia*, etc.) and more recently carbapenem-resistant *Enterobacteriaceae* (CRE) have been linked to inadequately processed endoscopes. Failure in scope processing was thought to be at fault in many of these cases but more recently contamination of elevator-wire channel in ERCP and Linear EUS scopes has been noted to be an issue. Outbreaks have occurred in spite of facilities abiding by manufacturer scope processing recommendations. Scope processing techniques were modified at our institution in response to this in 2015.

Methods: Currently, all ERCP and EUS scopes are cleaned per manufacture's recommendations: Cleaning starts in the procedure room post-procedure. Meticulous manual cleaning in the instrument processing room using specially designed brushes that are focused on the scope's elevator, scopes are checked for leaks and enzymatic detergent (Intercept, Medivator Inc.) is purged through all channels with the use of manual power, duodenal scopes are put through the disinfection process using Medivator DSD-201 and 2.5% glutaraldehyde solution (Rapidex, Medivator Inc.). Scopes are processed twice after each use to reduce bioburden and once if not used in 7 days. All microbiology samples are collected by 2 trained RN's. Samples are collected quarterly from elevator wire channel, suction channel and biopsy port. For the elevator channel 3 mL of sterile water is irrigated x3, total 9 mL, and collected for culture. Quarterly scope cultures are performed.

Results: From 6 quarters of scope microbiologic surveillance we have had only 2 positive cultures for clinically "significant" agents. 1 strain of Coagulase-negative *Staphylococcus* and *Streptococcus sanguis* isolated in 2 ERCP scopes. These cultures were felt to be not unexpected considering prior reports and after reprocessing, scopes were put back in circulation.

Results: pending changes in elevator system design by manufacturers, changes in reprocessing techniques for scopes containing elevator-wire channels is warranted and has been successful in preventing any microbiologic mishaps at our institution. It must be noted that we possess Olympus 130 (duodenoscope), 140 (EUS), 160(EUS) and 180 (duodenoscope) series scopes so age of device was not a factor here. Olympus is changing the elevator-wire channel design to close the wire channel in the 180 series only so reprocessing issues will persist as a problem with 130 and 160 series ERCP scopes still in use. Other manufacturers are modifying processing techniques recommendations only. Devising adequate endoscopy processing techniques for the Endoscopy Unit has become a critical Quality Metric and we hope our experience will help figure out the ideal "best practice" for most major academic centers.

539 USING NEXT GENERATION SEQUENCING TO STUDY INHERITABLE PEUTZ-JEGHERS SYNDROME

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Introduction: High Mendelian susceptibility to colorectal cancer is a critical issue in patients with hereditary polyposis syndrome. Peutz-Jeghers syndrome (PJS) is one of these polyposis disorders and characterized by intestinal hamartomatous polyps with skin and mucosal melanin depositions. GermLine mutation in the serine/threonine kinase 11 gene (STK11) is known as one of the major causes, and predisposes patients

to early-onset colon, breast, and pancreatic cancers. However, clinicians make the presumptive diagnosis of PJS largely based on clinicopathological information. We aim to use genetic testing to make the diagnosis more accurate and convincing, and optimize subsequent treatment, counseling, and surveillance.

Materials and methods: We recruited 11 unrelated patients who were clinically diagnosed with PJS in National Taiwan University Hospital. GermLine genomic DNA was extracted and used for multigene study by next-generation sequencing (NGS). In order to comprehensively check the genetic variants in related genes of intestinal polyposis syndromes, NGS method sequencing to screen variants through the entire genomic areas, upstream promoter regions, 3'-UTRs and miRs of not only STK11 gene, but also APC, SMAD4, BMPR1A, PTEN, MUTYH, POLD1, and POLE genes were performed. Indel, nonsense mutation and splicing mutation were considered as pathogenic mutations and missense mutations were predicted by bioinformatics. The pathogenic and deleterious mutations were confirmed by Sanger's sequencing.

Results: Among these patients, the median age at the onset of symptoms was 14.4 years. Six (54.5%) and one (9.1%) patients suffered from intussusception and gastrointestinal (GI) bleeding as complications, respectively. Hamartomatous polyps occur most commonly in small intestine (72.7%). In addition to GI tract involvement, mucocutaneous pigmentations of lip or buccal mucosa were also frequently found in our group (90.9%). A total of 7 patients (63.6%) were found germline pathogenic mutations among STK11 gene; however, no gene mutation related to other hereditary polyposis syndromes encompassed in our gene panel was identified. Two cases carrying STK11 mutations had malignant disease; one patient had pancreatic cancer at age 5 and the other had breast cancer at age 51.

Conclusion: Peutz-Jeghers syndrome poses a threat to patients with various symptoms, and higher potential to develop cancers at an early age. NGS methods serve as an efficient tool in the molecular diagnosis, helping to establish relevant surveillance strategy. Some patients were not found to have causative genetic mutation, and further studies for novel gene identification is required.

Case	Age/sex	Age at diagnosis	Pigmentation	Familial History	Mutation found by NGS	Clinical history and polyp locations
1	29/F	15	Yes	No	STK11:NM_000455:exon1:c.117dupC;p.R39fs	GI bleeding with Anemia. Enterotomy and polyps resection at 17 y/o (duodenal polyp)
2	52/M	28	Yes	Yes	STK11:NM_000455:exon1:c.C180G;p.Y60X	Small bowel resection at 28 y/o.(intussusception; jejunum polyps)
3	24/F	12	Yes	No	STK11:NM_000455:exon5:c.T715G;p.W239G	Laparotomy, manual reduction and polyp resection at 12 y/o. (intussusception, 3 ileal polyps)
4	28/F	11	Yes	No	STK11:NM_000455:exon8:c.G923A;p.W308X	Jejunum resection at 14 y/o.(intussusception;1 jejunum polyp)
5	32/F	13	Yes	Yes	STK11:NM_000455:exon4:c.T569G;p.L190R	1. Manual reduction and polypectomy at 13 y/o; segmental resection of terminal ileum at 16 y/o (2 jejunum-jejunum intussusception and ileum-T-colon intussusception; several jejunum and ileum polyps) 2. Open reduction + segmental ileum resection at 21 y/o (ileal-ileal intussusception; multiple ileum polyps)
6	20/F	2	Yes	Yes	Uncertain	Open reduction and polypectomy at 7 y/o (intussusception; D-colon polyp)
7	15/M	12	Yes	Yes	Uncertain	Endoscopic polypectomy at 12 y/o (Multiple small gastric polyps)
8	18/F	14	Yes	No	STK11:NM_000455.4:c.153_154delGG	Exploratory laparotomy and intestinal polypectomy at 14 y/o (multiple gastric, jejunum, ileum, and colon polyps)
9	20/M	3	Yes	No	Uncertain	Endoscopic polypectomy at 3 y/o (Multiple gastric and colon polyps)
10	15/M	12	Yes	Yes	Uncertain	Endoscopic polypectomy at 12 y/o (Multiple gastric, ileal, and ascending colon polyps)
11	54/F	36	No	Yes	STK11:NM_000455:exon7:c.C910T;p.R304W	1. Operations with small bowel resection for 2 times at 36y/o and 43 y/o, respectively (intussusception; Multiple gastric and duodenal polyps) 2. Lt side breast cancer, invasive carcinoma, s/p modified radical mastectomy at 51 y/o.

540 EGD FOR UPPER GASTROINTESTINAL BLEEDING IN CHILDREN: A SYSTEMATIC REVIEW

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Background: EGD is an important diagnostic and therapeutic intervention in children presenting with upper gastrointestinal bleeding of unknown etiology. We performed a systematic review of studies examining children undergoing EGD for symptoms consistent with upper gastrointestinal bleeding. We examined the diagnostic yield, endoscopic interventions, underlying conditions, and histological findings reported in the existing literature.

Methods: All full-length articles published in English during 1966-2015 were included if: 1) participants had EGD for evaluation of hematemesis, coffee-ground emesis or melena, 2) etiology of bleeding was unknown prior to EGD, 3) EGD outcomes (e.g., gross findings, histopathology, interventions) were reported; and 4) age of participants was under 18 years.

Results: Twenty-nine studies including 4,763 EGDs in 4,631 children fulfilled the inclusion criteria. Eight studies were performed in North America, 8 in Asia, 4 in Europe, 6 in the Middle-East, 2 in Africa, and 1 in South America. The largest study examined 1000 procedures and 9 studies examined less than 50 procedures. Specific endoscopic findings included: 321 (6.7%) cases of erosive gastritis, 280 (5.9%) varices, 256 (5.4%) duodenal ulcers, and 125 (2.6 %) gastric ulcers. Out of eleven studies reporting histopathology findings, 9 reported the presence of *H. pylori*. The presence of *H. pylori* was reported in 299 cases, and the prevalence of *H. pylori* ranged from 4.0% to 55%. The most common endoscopic interventions included 260 cases of sclerotherapy, 33 band ligations, local drug injection in 39 cases, and hemoclip application in 24 cases. The primary non-endoscopic intervention was PPI use (346 cases). No articles attempted to describe the impact of EGD on quality of life or cost-effectiveness.

Conclusions: We reviewed 29 studies including 2136 EGDs in children with upper gastrointestinal bleeding of unknown etiology and discovered that peptic ulcers was the most common finding followed by erosive gastritis.

541 PREVALENCE OF EOSINOPHILIC GASTROINTESTINAL DISORDERS WITH ESOPHAGEAL EOSINOPHILIA IN JAPANESE CHILDREN: A RETROSPECTIVE STUDY AND SYSTEMATIC REVIEW

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Background and Aims: Eosinophilic gastrointestinal disorders (EGIDs) are rare diseases that are characterized by food-induced, eosinophil-dominant inflammation in various segments of the gastrointestinal tract. Diagnosis of EGIDs, particularly eosinophilic esophagitis (EoE), is increasing in adults and children. However, the prevalence of EoE in Japanese children is unknown. This study aimed to determine the prevalence and clinical manifestations of EGIDs with esophageal eosinophilia (EE) in Japanese children.

Methods: We conducted a retrospective review of EGIDs, including EoE, eosinophilic gastritis, eosinophilic gastroenteritis, and eosinophilic colitis, in Japanese children. The review was based on literature published from 1977 to 2016. We collected data on the profile of patients with EoE and EGIDs with EE, histological findings, treatment, and clinical improvement.

Results: A systematic review of 36 studies, including eight studies on patients with EoE and EGIDs, was performed. The clinical features of 21 patients, including our patients, are shown in *Table 1*. The median age of the patients was 8 years (range: 0 - 17 years), and 15 were boys and six were girls. Six patients had congenital esophageal atresia and stenosis, and they underwent esophageal biopsy or surgical resection. The main clinical presentation was vomiting in 11 (52%) patients. Fifteen (71%) children also had a history of atopic dermatitis, allergic rhinitis, food allergies, or bronchial asthma. Endoscopic findings in patients with EoE showed linear or longitudinal furrows in four cases, white plaques in four cases, and four children had an endoscopically normal-appearing esophagus. Fourteen (67%) children responded to a proton-pump inhibitor.

Conclusions: Many Japanese children might have EGIDs with EE. Pediatric gastroenterologists should perform an esophageal biopsy, including in all patients who undergo upper endoscopic evaluation, regardless of the endoscopic appearance or findings.

Table 1 The clinical features of patients with eosinophilic esophagitis and eosinophilic gastrointestinal disorders with esophageal eosinophilia

Case no.	Age (years)	Sex	Symptoms	Histological eosinophilic infiltration (HPF)		
				esophagus	stomach	duodenum
1	10	M	hematemesis, cough, dysphagia	>50	-	-
2	9	M	abdominal pain and vomiting after egg intake	>30	>30	>30
3	5	M	abdominal pain	>20	>20	>20
4	6	M	recurrent vomiting, abdominal pain	22	5	50
5	8	M	abdominal pain, tarry stool	>100	>100	20
6	10	F	recurrent vomiting, abdominal pain	60	0	10
7	13	M	epigastralgia, heartburn, dysphagia	>20	-	-
8	10	M	recurrent vomiting, fecal occult blood	+	+	+
9	6	F	vomiting, dysphagia	+	+	-
10	4	M	vomiting, diarrhea	17	6.5	80
11	6	F	abdominal pain, tarry stool	60	60	250
12	6	M	abdominal pain, diarrhea	46	9	30
13	17	M	back pain, epigastralgia	40	-	40
14	9	M	recurrent vomiting, hematemesis	290	NA	NA
15	11	F	nausea	13	NA	NA
16	6	M	hematemesis	193	NA	NA
17	1	M	vomiting	48	NA	NA
18	1	M	post-operative follow-up (CEA)	36	NA	NA
19	0	F	post-operative follow-up (CEA)	250	NA	NA
20	14	M	fever	23	NA	NA
21	2	F	vomiting, poor weight gain, feeding difficulty	106	-	72

CEA :congenital esophageal atresia

NA: not available

542 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN CHILDREN: 8-YEAR EXPERIENCE IN A SINGLE CENTER

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Background: Experience regarding the diagnostic and therapeutic utility of endoscopic retrograde cholangiopancreatography (ERCP) in children is limited. The low incidence of pancreatobiliary disease in children, and the lack of formal training programs in therapeutic endoscopy for pediatric gastroenterologists may play a role.

Objective: To evaluate the indications, findings, therapies, safety, and technical success of ERCP in infants and children, performed by an adult gastroenterologist at a university hospital.

Methods: Retrospective analysis by medical records. The charts of patients under 18 years who underwent ERCP from 2007 to 2015 in Hospital Universitario Santa Fe de Bogotá were reviewed. The following data were analyzed: indications, findings, therapies, success rate and complications.

Results: Thirty children (mean age 8.2 years, SD 3.2; 63% female) underwent a total of 65 diagnostic or therapeutic ERCPS. Of those patients, 15 (50%) had a pancreatic indication, whereas 15 (50%) had a biliary indication for the procedure. Main findings were biliary duct stones or sludge (n=12), pancreatic duct stricture (n=7), bile duct stricture (n=8), failed cholangiogram (n=1), and choledochal cyst (n=2). Successful cannulation was achieved in 80% (52/65) of cases. Endoscopic therapies were performed in 78.5% of the procedures, with a success rate of 96% (49/51). The complication rate was 12.3% (8/65), and included pancreatitis (n=4), bleeding (n=2), bacteriemia (n=1), and creation of a submucosal tunnel in the duodenum (n=1). No mortality related to ERCP occurred.

Conclusions: Diagnostic and therapeutic ERCP, when performed by a trained endoscopist, is a safe and valuable procedure for children of all ages with suspicion of pancreaticobiliary diseases (Table 1).

***543 PRIMARY CLINICAL EXPERIENCE WITH THE USE OF DUODENAL: JEJUNAL BYPASS LINER IN MORBIDLY OBESE ADOLESCENTS**

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Objectives and study: The duodenal-jejunal bypass liner (DJBL) (Endobarrier) is an endoscopic implant that mimics the duodenal-jejunal bypass component of the Roux-en-Y gastric bypass. Studies in adults have shown relevant weight loss and improvement in type 2 diabetes. The aim of this prospective study was to investigate for the first time safety and efficacy of DJBL in severely obese adolescents with obesity complications up to 12 months after implantation.

Methods: The device was successfully implanted in 14 morbidly obese adolescents out of 17 who underwent the procedure (10 females, mean age 17.7 years (range 15.0 - 19.2); average BW 124.3 kg (range 93.2 - 158.8)). Inclusion criteria were; \geq BMI 35 kg/m² with obesity complications such as hypertension, prediabetes or type 2 diabetes. Their metformin was discontinued prior to DJBL placement. The exclusion criteria are described in detail at www.ClinicalTrials.gov (NCT02183935). The procedure was performed endoscopically under general anesthesia. Subjects were under observation in the hospital for 2 days following the procedure for possible complications. According to the protocol they were receiving esomeprazole 40 mg BID throughout follow-up.

Results: In the safety analyses there were no severe procedure or post-procedure related complications. The most frequent adverse events were of gastrointestinal origin: nausea (6/14), abdominal pains (8/14), and diarrhea (2/14) in the first two weeks after implantation. One subject developed cholecystitis 3 months after endoscopy and one patient had transiently elevated pancreatic enzymes. The BMI (kg/m²) was measured at 0, 3, 6, 9 and 12 months and decreased at all time frames (42.3 (range 36.7 to 48.8), 38.0 (range 34.1 to 44.5), 37.7 (range 33.3 to 44.8), 37.5 (range 33.1 to 45.5), 36.7 (range 32.4 to 45.9), respectively). In addition, glucose metabolism significantly improved: mean HOMA-IR level at the beginning of the study was 5.6 (\pm 2.2) and decreased at 6 and 12 months after implantation (3.8 (\pm 1.6), 2.7 (\pm 0.9), respectively).

Conclusion: This is the first report on the use of endoscopically placed DJBL in adolescents being followed-up to 12 months. Relevant weight loss was determined in most adolescents and glucose metabolism improved in all. No serious device-related adverse effects were detected.

Disclosure of interest: None declared.

***544 DEVELOPMENT AND VALIDATION OF A SATISFACTION QUESTIONNAIRE FOR PEDIATRIC DIGESTIVE ENDOSCOPY**

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Background: Assessment of patients' perspective is a crucial determinant for a good quality improvement process. There is currently few data in the literature about the quality and security of pediatric digestive endoscopy. Only one questionnaire has been identified after a thorough literature search but this has not properly been validated in children.

Objectives: To develop and validate a patient satisfaction questionnaire for children aged 10-18 years, undergoing a digestive endoscopy.

Methods: This prospective study took place in the digestive endoscopy unit of Sainte Justine University hospital, a tertiary center in Montreal, Canada. The study was established in many steps (1) Literature search and items selection, (2) Writing of questions, (3) Questions validation with nurses, gastroenterologists, an expert in questionnaire conception and among a group of healthy children, (4) Internal validation during two periods. The final questionnaire included 41 questions in two parts: preprocedure and post-procedure.

Results: A total of 219 children aged 10 to 18 years old were included in the study in two different time periods. The items included in the final version of the questionnaire were distributed into six domains: 1) knowledge about the disease and the procedure, 2) waiting times, 3) knowledge about colonoscopy procedures and satisfaction regarding bowel cleaning, 4) satisfaction regarding personal manners, 5) anxiety, pain and comfort before, during and after the procedure and 6) overall satisfaction about the whole process of endoscopy. Globally, 67.8% of children felt enough informed about the indication of the procedure, 58.3% about the different steps of the endoscopy and 51.8% about the sedation. The delay was more than 3 months for 18.1%, 1 to 3 months for 43.2%, 1 to 4 weeks for 23.1% and less than 1 week for 13%. The majority (84.9%) judged the delay appropriate. Bowel cleaning was found to be very uncomfortable for 68.9% of children. Overall, the satisfaction of the team was good: 71.4% very happy with their meeting with the nurse and the majority found the medical team very kind. Pain and anxiety were a great concern for many children; 45.7% of them were afraid before the endoscopy, 33.7% felt pain during the exam and 7.5% judged the level of discomfort completely unacceptable. The global satisfaction on the whole process was good: 76.9% would do the procedure in the same conditions if they had to.

Reliability of the questionnaire was evaluated using Cronbach's alpha coefficient: 0.47.

Conclusions: The pediatric endoscopy satisfaction questionnaire (PESQ) is a valuable tool to assess the patients' experience and is part of the implementation of a quality improvement process in pediatric digestive endoscopy. It has a good internal validity. An external validation will have to be done in other pediatric endoscopy centers.

545 PREDICTORS OF PROLONGED FLUOROSCOPY EXPOSURE TIME IN PEDIATRIC ERCP: A REPORT FROM THE PEDI DATABASE

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Introduction: Ionizing radiation exposure during ERCP is emerging as an important quality issue. The deleterious health effects of ionizing radiation may be amplified in pediatric populations. Identifying factors associated with prolonged fluoroscopy time (FT) is the first step to developing best practices aimed to minimize radiation exposure in children during ERCP.

Aim: To identify factors associated with extended FT in children undergoing ERCP.

Methods: Consecutive ERCP on children ≤ 18 years from 13 IRB approved centers were entered prospectively into an electronic database to evaluate several outcome and quality measure. Inclusion criteria for this analysis included: Cases entered between 5/1/2014 to 4/27/2016, both the pre-procedure and post-procedure forms were completed and FT was recorded. Cases were excluded if additional procedures requiring fluoroscopy exposure were performed during the same session. Fischer's exact test was utilized to identify pre-procedural factors associated with procedures with top quartile FTs.

Results: 433 ERCPs performed in 343 unique patients met inclusion criteria and were included for analysis. The mean age at the time of ERCP was 12.2 years (IQR 9.6-15.6). 301 (70%) patients had native papillae. 404 (93%) ERCPs were performed for therapeutic indications and 334 (77%) were done for a biliary indication. The average FT was 208 seconds (IQR 67-263). Factors associated with top quartile FTs included ERCPs with ASGE difficulty grade ≥ 3 ($p=0.0007$) and ERCPs performed for pancreatic indications ($p=0.0006$), especially when the indication was improving drainage in the setting of chronic pancreatitis ($p=0.0021$). ERCPs associated with FTs less than the top quartile included procedures performed for biliary indications ($p=0.002$), particularly when the indication was treatment of suspected choledocholithiasis ($p=0.0004$). FT variability was also seen between participating centers as one center was associated with FTs outside the top quartile ($p<0.0001$) and two centers were associated with FTs within the top quartile ($p=0.006$ and 0.003 respectively). No statistical difference was seen in children ≤ 3 years ($p=0.39$), weight ≤ 10 kg ($p=1.00$), prior failed ERCP ($p=1.00$), native papilla ($p=0.19$), having pancreatitis at the time of the procedure ($p=0.77$), or type of facility where the procedure was performed ($p=0.29$).

Conclusion: Several pre-procedural factors are associated with top quartile FTs in pediatric ERCP. Significant differences between participating centers were also identified. This data can help us better identify children with higher risk for radiation exposure during ERCP and potentially allow us to identify best practices to decrease fluoroscopy time and improve quality in pediatric ERCP in the future.

546 ABOVE AND BEYOND TRAINING: COLONOSCOPY LEARNING CURVES AND EXPECTED ANNUAL PROCEDURAL VOLUME OF CREDENTIALLED PEDIATRIC GASTROENTEROLOGISTS

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Studies of pediatric and adult endoscopy learning curves have consistently demonstrated that the completion of ≥ 250 colonoscopies are required to reliably, independently and efficiently achieve cecal and ileal intubation rates of $>90\%$. Current pediatric GI training guidelines require the performance of 120 colonoscopies prior to fellowship completion. The volume of colonoscopies generally performed annually by fully credentialed pediatric endoscopists has not been reported.

Aim: To quantify procedural volumes of a wide practice spectrum of North American pediatric gastroenterologists, ranging from research-focused to fully clinical, with the goal of estimating how many years it may require after fellowship to reliably demonstrate optimal procedural performance.

Methods: Deindividuated colonoscopy procedural volume data from 10/1/14-9/30/15 (FY15) was collected from electronic reporting systems at university - and community - based sites, representing various practice settings. Procedures were excluded if they were coded as flexible sigmoidoscopy or pouchoscopy. Descriptive analyses and non-parametric comparisons of data were performed.

Results: Data were collected from 12 sites (10 university-, 2 community-based) across 9 states (CA, CO, MA, MD, NJ, NY, PA, TX, WI) and Canada, representing 154 endoscopists (MDs) and 5,765 (5254 university-based) colonoscopies. Eleven MDs (7.1%) were in community-based practices. Five sites had <8 MDs, while 2 had >20 . Across all sites, MDs performed a range of 0-118 colonoscopies in FY15, with a median (IQR) of 31.5 (17 (25th%ile), 53 (75th%ile)). 24 (15.6%) MDs performed ≤ 10 ; 84 (54.5%) performed 11-49; and 46 (29.8%) ≥ 50 colonoscopies in the single year. There was no difference in the median (IQR) number of colonoscopies performed by university- vs. community-based MDs (31 (15, 51) vs. 33 (28, 62), $p=0.13$). Across both practice settings, smaller centers with fewer MDs had moderately less range in procedural volume across MDs ($r=.62$, $p<.035$). Assuming that fellows achieve 120 colonoscopies during training, and subsequently perform a median of 31 colonoscopies per year as attendings, we estimated that ~ 4.2 years may be required for a new graduate to accumulate the minimum 250.

Conclusions: A greater understanding of learning curves and colonoscopy skills, as well as transparency in expected annual procedural volume, may be critical to supporting both new pediatric GI graduates and the programs who hire them. Limitations to our study include that it does not account for individual job descriptions, presence of trainees, or cecal/ileal intubation rates. Additional research is required before we can discern any relationships between annual procedural volumes and colonoscopy outcomes for pediatric endoscopists with widely different clinical practices, at all stages of their careers.

547 COMPARISON OF ALTERED RESPIRATORY EVENTS DETECTION BY TRANSCUTANEOUS RESPIRATORY RATE, CAPNOGRAPHY, PLETHYSMOGRAPHY, AND PULSE OXIMETRY IN PATIENTS UNDERGOING ESOPHAGOGASTRODUODENOSCOPY AND COLONOSCOPY UNDER PROCEDURE-RELATED SEDATION

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Background: Microstream capnography (mCAP) has been shown to be more sensitive than traditional monitoring modalities (pulse oximetry, plethysmography, clinical observation) in detecting altered respiratory events (ARE) in children undergoing endoscopy. Acoustic transcutaneous respiratory rate monitoring is a newer monitoring modality that has not been widely studied in children undergoing procedures.

Study Aim: To compare the number of altered respiratory events detected mCAP versus Rainbow Acoustic Respiratory Rate transcutaneous monitoring (aRR) in pediatric patients undergoing endoscopy.

Methods: This IRB-approved prospective observational study was conducted at a single center. After informed consent was obtained from parents or guardians, consecutive patients 6 months to 18 years old undergoing upper or low endoscopy were monitored using aRR, mCAP, pulse oximetry, and plethysmography. All patients underwent deep sedation per institution standard of care guidelines. ARE were defined as one or more of the following clinical events: (1) alteration of mCAP or aRR waveform lasting >15 seconds, (2) change in mCAP CO₂ value of >20% from baseline, (3) pulse oximetry of <93%, decrease of respiratory rate >10 from baseline for >20 seconds, (4) clinical changes consistent with respiratory distress, reduction in respiratory rate to less than 50% of baseline based on aRR. The rate of ARE detected by mCAP and aRR were compared using appropriate statistical tests.

Results: 42 subjects (21 females, 21 males; 12.3 years mean age) underwent 58 endoscopic procedures. A total of 132 ARE were detected among the participants with 93.4% (124/132) of the events associated clinically identifiable activity such as intraprocedural agitation or gagging. Rate of ARE detection were as follows: mCAP 0.179 ARE/minute, aRR 0.065 ARE/minute, pulse oximetry 0.019 ARE/minute, and plethysmography 0.003 ARE/minute. Of the 132 detected ARE, 50% required no intervention by the endoscopy team, 24% required additional sedative, 17% required suctioning, and 3% required increased oxygen delivery. The following factors were associated with an increased rate of ARE detected by mCAP: procedure type (EGD>Colonoscopy), lengthier procedure duration, higher ketamine dose, and lower weight. Age, gender, and procedure indication were not associated with a higher rate of ARE detection by mCAP.

548 THE CURRENT ROLE OF COLONOSCOPY IN JAPANESE YOUNG CHILDREN

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Backgrounds: The incidence of immune related disorders, including autoimmune and allergic diseases, has increased among children, and it is presumed that diseases that cause gastrointestinal symptoms in children have also changed. Although pediatric colonoscopy is increasingly performed in young children due to better anesthetic techniques and better designed pediatric endoscopes, reports showing distribution of diseases required colonoscopy and usefulness of colonoscopy in young children have been limited.

Methods: We retrospectively reviewed 903 colonoscopies (...18 years old) which had been undergone from April 2011 to Mar 2016 in tertiary pediatric gastroenterology units of two representative children's hospitals in Japan. We defined young children as children ...6 years old.

Results: Of all colonoscopies, 315 procedures (35%) for 201 children were performed in young children, aged from 5 day-6.9 years (mean 3.3}1.9 years, median 2.8years). Colonoscopies were performed for the purpose of diagnosis (194/315; 62%) and follow-up (120/315; 38%). Clinical indications of colonoscopy for diagnosis were hematochezia (61%), diarrhea (30%), failure to thrive (13%), and abdominal pain (8.8%). Moreover, 144 of 194 diagnostic cases (74%) had macroscopic and/or histological positive findings. Colonoscopy is more useful for diagnosis of hematochezia than for the other clinical indications [positive finding; 101/119 (85%) vs. 43/75 (57%); $p<0.001$]. The diagnoses of children who underwent colonoscopy for diagnosis were eosinophilic gastrointestinal disease (EGID; 38/144; 26%), colonic polyps (28/144; 19%), inflammatory bowel disease (IBD; 27/144; 19%), primary immunodeficiency (PID; 13/144; 9.0%) and others (38/144). PID in this case series included 6 chronic granulomatous disease, 2 severe combined immunodeficiency, 2 familial Mediterranean fever, and others. Comparison between children <2 years of age and those >2 years of age revealed that EGID, including gastrointestinal allergy, is a more common cause of hematochezia in children <2 years of age (52% vs. 3%, $p<0.001$), and colonic polyps is a more common cause in children >2 years of age (6% vs. 36%, $p<0.001$). The diseases that required follow-up colonoscopy were IBD (72/120, 60%), PID (20/120, 17%), and EGID (13/120, 11%), and others (15/120).

Discussion: Seventy-four percent of young children who underwent colonoscopy had positive findings. Thus, colonoscopy appeared useful for the diagnosis in young children. Most of those diseases that required colonoscopy for diagnosis were related to immune abnormalities (EGID, IBD, and PID), irrespective of their low morbidity rates. As the number of patients with such diseases are increasing in pediatric population, the demand of colonoscopy would be expected to increase further.

549 NONINVASIVE MARKERS OF ESOPHAGEAL VARICES IN CHILDREN WITH CHRONIC LIVER DISEASE

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Background: According to recent guidelines, all cirrhotic patients should undergo screening endoscopy at diagnosis to identify patients with varices at high risk of bleeding who will benefit from primary prophylaxis. This approach implies a heavy burden upon endoscopy department and the repeated testing over time may have a detrimental effect on patient compliance. Noninvasive identification of patients at highest risk for oesophageal varices would limit investigation to those most likely to benefit.

Objectives: To identify noninvasive markers of esophageal varices in children with chronic liver disease.

Methods: It was a cross sectional analytic study conducted at the department of Pediatric Gastroenterology & Nutrition of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh between January 2014 through June 2015. A total of 50 consecutive patients with chronic liver disease aged 2-14 years of both sexes, who had not experienced any active/recent bleeding, didn't have any prophylactic management or not gone through surgery for esophageal varices were included in study. All patients underwent a thorough history, physical examination and necessary investigations including upper gastrointestinal endoscopy (gold standard test). Based on endoscopic findings patients were divided into two groups. Group-I, chronic liver disease with esophageal varices (33 patients) and Group-II, chronic liver disease without esophageal varices (17 patients). Univariate analysis was used to determine the association of patient's clinical (jaundice, stigmata of CLD,

hepatomegaly, splenomegaly, and ascites) and laboratory parameters (S. bilirubin, ALT, S. albumin, platelet count and INR) with presence or absence of varices. Then performance of each significant variables were evaluated individually and with combination.

Results: Among 50 cases, 52% were male and the male:female ratio was 1.1:1. Mean age at admission was 9.03 ± 3.6 years in Group I and 8.38 ± 3.6 years in Group II (range 2-14 years in both). Wilson's disease appeared to be the most common cause of cirrhosis (40%) followed by celiac disease in 2nd highest position (8%). Along with 40% unknown etiology, 6% were Budd-Chiari syndrome, 4% hepatitis B and 2% biliary cirrhosis. Significant identified parameters were splenomegaly and thrombocytopenia (Platelet count $<150000/\text{mm}^3$) (p value 0.000 and 0.012 respectively). Splenomegaly has the highest sensitivity (90.9%) and accuracy (80%) followed by thrombocytopenia (66.7% sensitivity and 68.0% accuracy) and y splenomegaly with thrombocytopenia (63.6% sensitivity and 68.0% accuracy). Specificity was greatest in splenomegaly with thrombocytopenia (88.2%).

Conclusion: Splenomegaly may identify the presence of esophageal varices whereas at the same time absence of splenomegaly with thrombocytopenia can assure the negativity.

550 PREPARATION, SEDATION AND SELECTION OF EQUIPMENT IN PEDIATRIC GASTROINTESTINAL ENDOSCOPY: A QUESTIONNAIRE SURVEY OF PHYSICIANS

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Background and Aim: Specifications for patient preparation, sedation, and equipment used in pediatric gastrointestinal endoscopy in Japan is not well documented. Thus, the aim of this study was to investigate how Japanese pediatric endoscopy specialists perform gastrointestinal endoscopy in children.

Methods: A questionnaire, requesting information regarding patient preparation, sedation, and decisions regarding scope size used in esophagogastroduodenoscopy, colonoscopy, balloon enteroscopy, or endoscopic retrograde cholangiopancreatography, was sent to all 17 members of Japanese Pediatric Gastrointestinal Endoscopy Guideline Committee.

Result: We received a response from all 17 members. General anesthesia was most frequently used as sedation in infants undergoing esophagogastroduodenoscopy; midazolam and general anesthesia were equally used for those undergoing colonoscopy. Peroral balloon enteroscopy was generally performed under general anesthesia even in adolescents; however, peranal balloon enteroscopy was performed under general anesthesia and midazolam sedation equivalently. For preparation prior to esophagogastroduodenoscopy, topical lidocaine was used in adolescents, who did not receive general anesthesia. As preparation for colonoscopy, magnesium citrate and polyethylene glycol were widely used, often in combination with picosulfate sodium. These specialists decided the size of the scope used according to the patients of age, purpose of endoscopy, and body weight.

Conclusions: In Japan, general anesthesia and intravenous sedation with midazolam is used extensively for sedation in pediatric gastrointestinal endoscopy. Indications for these vary according to institutions, number of staff, and hospital facilities. We recommend the development of universal guidelines for patient preparation and equipment use in pediatric endoscopy to standardize this procedure.

551 USE OF NON-ENDOSCOPIC TREATMENT FOR OESOPHAGEAL FOREIGN BODY IMPACTION IN CHILDREN IN THE ERA OF EOSINOPHILIC OESOPHAGITIS

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Background: Foreign body ingestions are common to Pediatric Emergency department. Interventions (non-endoscopic or endoscopic) are often required for oesophageal foreign body impactions due to the severity of symptoms and risk of complication. Non endoscopic measures such as glucagon injections and fizzy drinks have been described in adults for symptom resolution and aid the passage of food bolus impaction; however, there are only a few studies in the pediatric literature. Eosinophilic esophagitis (EoE) is a relatively 'new' clinicopathological disease entity with rising prevalence that may present with food bolus impaction and is often the first presenting symptom. We studied the outcome of non-endoscopic treatments (Glucagon injection and fizzy drinks) for oesophageal foreign body impaction in children, especially in the setting of EoE.

Methods: A retrospective chart review was performed using the ICD codes and the emergency department database of patients presenting with oesophageal foreign body from January 2010 to December 2014. Response to non-endoscopic treatment (glucagon and/or fizzy drinks) was defined as symptomatic relief of obstruction prior to endoscopic intervention. The age of the patient, object ingested, non-endoscopic treatment, subsequent diagnosis of EoE, complications and outcome were recorded.

Results: Two hundred seventy seven oesophageal foreign body impactions in 262 children were identified during the study period. Non-organic foreign bodies accounted for 157 (56.7%) and organic for 120 (43.3%) impactions. Non-endoscopic treatment was used for 7 episodes with non-organic foreign body impactions with 4 (57.1%) achieving symptom resolution; for organic foreign body it was trialled for 42 (21 with EoE, 21 without EoE) with resolution of symptoms in 16 patients (38%). One child with EoE responded to non-endoscopic treatment compared to 15 of those without EoE (4.8% vs. 71.4%). Out of 78 episodes with organic foreign bodies with no non-endoscopic treatment, 33 (42.3%) underwent endoscopy whereas 45 (57.6%) had spontaneous resolution of symptoms.

Conclusions: Non-endoscopic treatment measures to relieve oesophageal foreign body impactions are commonly used in children and mostly for those with organic foreign body ingestion or food bolus obstruction. These measures are ineffective in children with EoE but may be effective in about 70 percent of patients without EoE. There were no complications identified in its use in children.

552 ENDOSCOPIC BALLOON DILATATION FOR POST-OPERATIVE ESOPHAGEAL STRICTURE IN PATIENTS WITH CONGENITAL ESOPHAGEAL ATRESIA

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Introduction: Evidence suggests that post-operative esophageal stricture (ES) frequently develops after correction of congenital esophageal atresia (EA). However, clinical experience of endoscopic balloon dilatation (EBD) in children with post-operative ES in patients with EA is limited.

Patients and Methods: Sixty-one neonate diagnosed EA were included. The demographic data of EA patients were collected and stricture rate was determined. Significant esophageal stricture was investigated, and technical and clinical success rate of EBD was identified. All data were analyzed in a single-institution retrospective study.

Results: Among 65 patients, 64 patients underwent esophageal anastomosis with or without resection of TEF. Thirty-eight (58.5%) of 65 was male and seventeen (26.2%) were prematurity. Mean birth weight was 2.55 ± 0.60 kg. Most of the patients (95.4%, 62/65 patients) presented esophageal atresia with distal tracheoesophageal fistula type. Forty-nine patients (75.4%) had combined anomaly other than EA. Except two patients, 62 patients underwent barium esophagography on post-operative day 7 and esophageal leakage was observed in 7 patients, while 5 of them recovered without surgery. Among 64 patients underwent surgery, thirty-six patients (56.3%) experienced clinically significant post-operative esophageal stricture during mean follow-up period of 21.5 ± 19.2 months. Patients with ES had significantly longer gap compared to patients without ES (1.6 ± 0.8 cm and 1.0 ± 0.6 cm, respectively, $p=0.008$). Of 36 patients clinically significant esophageal stricture who underwent EBD, 28 patients (77.8%) were clinically successful, while eight patients (22.2%) eventually underwent further surgeries or procedures. Three of 65 patients were dead of multiple comorbidities. Thirty-six patients underwent EBDs 87 times. Mean body weight at EBD was 5.41 ± 2.78 kg. Mean procedure time was 13.5 ± 5.2 minutes, and the mean balloon diameter was 8.9 mm (6.0-12.0mm). Of 87 EBD procedures, 82 procedures (94.3%) were technically successful without complications, two procedures (2.4%) failed due to complete obstruction, two patients experienced respiratory holding, and one procedure experienced pneumothorax related to intubation before EBD. Seven patients underwent EBDs more than four times up to seven times; five of them were clinically successful without further surgery.

Conclusions: Clinically significant ES developed in 56.3% patients who underwent EA surgery. Clinical and technical success rate of EBD was 77.8% and 94.3%, respectively. EBD up to 12mm in very young children is an effective and safe procedure to decrease the rate of further surgery.

553 NATIONWIDE MULTI-CENTER STUDY OF PEDIATRIC SMALL BOWEL CAPSULE ENDOSCOPY IN JAPAN

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Aim: The aim of our study was to determine the safety and feasibility of small bowel capsule endoscopy (SBCE) in children.

Methods: We performed a retrospective survey on SBCE in 252 pediatrics (10 months to 18 years of age) by the Japan Pediatric Small-bowel Endoscopy Study Group (Japanese Society for Pediatric Gastroenterology, Hepatology and Nutrition) at 17 nationwide institutions from October 2007 to August 2013. Data were collected including demographics, swallowing ability, indication of SBCE, outcome and clinical impact on treatment, use of patency capsule and complications.

Results: The youngest patient was 10 months old and minimum BW was 7.4kg. Forty-six patients (18%) had past history of abdominal surgery. In 188 patients (75% of 252 subjects), aged >6 years, capsule endoscope could be successfully swallowed. Most common application was small-bowel investigation for known Crohn's disease following obscure gastrointestinal bleeding and surveillance of small bowel polyposis. In 95% patients, whole small bowel investigation was achieved. Abnormal findings were observed in 68% and the result had clinical impact on changing therapy in 35% of the patients. Patency capsule was safely performed in 82 patients. In this cohort, none had capsule retention. Overall retention rate was 1.6% (N 4) including 3 cases of post-abdominal operations, no other serious complication was reported. All 4 patients had organic disease such as arteriovenous malformation or ulceration in small intestine, but none of them had Crohn's disease. Among 9 patients aged <2 years, capsule retention didn't occur.

Conclusion: Safety and feasibility of SBCE were not different from those shown in adult patients. According to our result and the post-marketing data, use of capsule endoscopy was approved in patients aged <18 years on February 2015 by the Ministry of Health, Labour and Welfare in Japan with general and special precautions in children.

GLOBAL HEALTH

555 CLINICAL FEATURES OF ULTRASOUND DIAGNOSED ACUTE SEGMENTAL NECROTIZING ENTERITIS IN TAIWANESE CHILDREN

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Objective: This was a retrospective study designed to review the clinical features of acute segmental necrotizing enteritis (ASNE) managed in a medical center located at Northern Taiwan. All patients fulfill the ultrasound criteria of segmental bowel edema with wall thickness of > 3 mm. **Patients and Methods:** From year 1996 to 2016, a total of 48 children (<18 years) diagnosed as ASNE were collected. Patients' demographics, clinical features, laboratory data and treatment were collected and analyzed.

Results: In this study, 35 (73%) children were diagnosed between 2 to 6 years old. Two third of them had abdominal pain with duration 3 to 7 days before diagnosis. The majority (93.3%) of pain located at epigastric and periumbilical area. 15 had vomiting and only 3 presented with bilious vomitus. For children with laboratory data, 23 of 47 (48.9%) had leukocytosis (defined as WBC > 10000/ul) and 11 of 33 (33.3%) had elevated CRP (defined as CRP > 0.5 mg/dL). Those with serum blood urea nitrogen and creatinine checked showed normal. 4 out of 35 children had hyponatremia. Under ultrasound examination, the swollen intestines were detected at left upper quadrant (17 cases), left lower quadrant (13 cases), right lower quadrant (11 cases) and other locations (4 cases). The longitudinal length was 1.5 to 4 cm in 40 cases and wall thickness 0.3 to 0.6 cm in 41 cases. 44 children received steroid treatment and all of the symptoms resolved within 5 days. Four of them had recurrent symptoms happened 3 days, 21 days, 5 months and 1 year after the steroid treatment, respectively.

Conclusion: The diagnosis of ASNE by ultrasound in children with suspicious clinical features is possible. Of those who received steroid treatment, the symptoms resolved within 5 days.

556 CURRENT STATUS OF FOOD ALLERGY IN TAIWAN: A QUESTIONNAIRE-BASED SURVEY

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Background: To investigate the prevalence and pattern of food allergy in Taiwan over the past few years.

Methods: This is a nationwide, cross-sectional, randomized questionnaire survey performed in 2012. Elementary school children aged six to thirteen years old and their family members above nineteen were randomly enrolled from seventy-two schools located in six strata of Taiwan. Respondents' demographics, dietary habits, food allergy history and associated allergic diseases were collected and analyzed.

Results: Over the study period, 20801 questionnaires were completed and returned. The average response rates over the six strata were over 90%. After exclusion of ineligible cases, there were 10196 (52%) children and 9413 adults. The prevalence of food allergy in children and their family members was 11.45% and 8.76%, respectively. Overall, among the twenty most common food allergens, shellfish, fruit, nuts, egg and milk accounted for around 80%. For respondents with dietary pattern recorded (19443 cases), 94.96% consumed regular diet and others were vegetarian. Comparing with age-matched healthy children consuming regular diet, vegetarian children had a lower incidence of both egg and milk allergy.

Conclusions: The current prevalence of food allergy in Taiwan was 11.45% in children and 8.76% in adults. Shellfish, fruit, nuts, egg and milk were common allergens encountered. Allergic reactions to egg and milk seemed to be lower in vegetarian children.

557 DIAGNOSTIC UTILITY OF CLINICAL, RADIOLOGICAL, MANOMETRIC, ENDOSCOPIC, HISTOLOGICAL AND IMPEDANCE DATA COMPARED TO pH MONITORING ALONE IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE

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Introduction: Due to the high prevalence of Gastroesophageal Reflux Disease (GERD) and its clinical, social and economic implications; the aim of the study was to determine the association and diagnostic utility of risk factors, clinical data as well as various diagnostic tests compared to pH monitoring alone to determine if one of them is as sensible and specific as the latter in order to simplify the diagnosis.

Methods: We conducted an evaluation of diagnostic tests in a third-level hospital in Mexico City from January 2008 to June 2015. Patients had to be younger than 18 years old and have had a pH monitoring or a combined impedance and pH monitoring test performed to be included. Demographic data included family history of GERD and/or esophageal cancer as well as personal risk factors such as prematurity and obesity. All the signs and symptoms considered related to GERD were evaluated and divided in two main age groups: infants/toddlers and school-aged /adolescents. Upper GI series was considered abnormal only in case of anatomical anomaly. Gastric emptying scan was considered prolonged after 110 minutes for solid food and after 65 minutes for liquids. Esophageal manometry was considered abnormal in case of dysmotility and/or hypotonic lower esophageal sphincter. Endoscopic esophagitis was evaluated using Los Angeles scale. pH monitoring was considered positive with a RI > 7% and impedance with SAP ≥ 95%.

Results: 100 patients were included, most of them younger than 8 years old and male. There was significant association between obesity and abnormal pH monitoring but none with the rest of risk factors evaluated. There was no significant association between any clinical sign or symptom with abnormal pH monitoring; regurgitation was the most common symptom for all age groups. Endoscopic esophagitis and symptom correlation from impedance monitoring were both highly specific compared to pH monitoring alone, but low in sensitivity. Gastric emptying scan and esophageal manometry were much less sensitive and specific than pH monitoring. The diagnostic utility of upper GI series and histological esophagitis was not evaluated properly due to the small number of patients with abnormal results for the first test and normal results for the second one.

Conclusion: In this study, the first of its kind made in our country, it was found that no clinical data or test used in the study of GERD can be compared to pH monitoring regarding diagnostic utility, only coming close the presence of endoscopic esophagitis and symptom association from impedance in specificity. However, even though no test can replace pH monitoring, they can improve the diagnostic approach of this entity. For diagnostic confirmation of this disease it is required a detailed clinical evaluation to determine which tests are needed in each particular case with the ultimate goal of achieving a prompt and adequate treatment at the lowest possible cost.

558 INCREASED EMERGENCE OF RECOMBINANT HUMAN NOROVIRUS IN SOUTH KOREA DURING 2007-2012

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Backgrounds: Norovirus-associated gastroenteritis is a persistent threat to global health. Among different geno-groups and -types of the noroviruses, genotype II.4 often predominated in seasonal outbreaks. Previous molecular epidemiologic studies have revealed fairly frequent recombination between different norovirus genotype es, and recently indicated the global emergence of intra-genotypic recombinants such as GII.4/2008 variants. However, systematic large scale analyses of noroviruses genetic sequences are rare in Korea. This study aimed to analyze systemically noroviruses sequences which were isolated at a tertiary hospital in Korea.

Methods: In this study, we performed systematic, large-scale genetic analyses of the noroviruses (n=281) circulating in South Korea from 2007 to 2012, which were collected in hospitalized patients with AGE in the pediatric ward of Inje University Sanggye Paik Hospital.

Results: Our phylogenetic analyses capture the progressive emergences and evolution of GII.4/2008i and 2008ii since 2009. After the first detection in 2008 winter, these two intra-genotypic recombinants become co-circulating (taking up 10-20% of proportion of GII.4 infections) with the pre-existing GII.4/2006b variants in South Korea. Strikingly, such co-circulation of three variants has engendered an unprecedentedly massive number of independent recombinants (n=12) in last three years, which unexpectedly appeared earlier than their parent first surfaced in the population. Although the recent discovery of a number of intra-genotypic recombinant variants and their worldwide emergence has posed significant concerns on the future increase of gastroenteritis outbreaks and severity, their real impact has yet to be determined. Our data conjecture that the intra-genotypic recombinants might have advanced compatibility to recombine with other contemporary variants, and thus generate many recombinants as observed in our survey.

Conclusions: It is conceivably a critical moment where a number of norovirus pure and recombinant variants are co-circulating in South Korea and other countries, and that novel potent strains might eventually emerge from the chaos of recombinant progenies.

559 USING FECAL CALPROTECTIN TO DIFFERENTIATE THE PATHOGENIC CAUSE OF INFECTIOUS DIARRHEA AND EVALUATING THE DISEASE SEVERITY.

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Objective: Calprotectin is an intestinal inflammatory marker which has been widely used in the evaluation of inflammatory bowel disease.

However, its diagnostic value in infectious diarrhea is still unknown. By using quantitative test of stool calprotectin, we wish to determine its value in differentiate the pathogen of infectious diarrhea as well as the disease severity.

Methods: This is a prospective research conducted in a tertiary teaching hospital from June 2014 until July 2015. Pediatric patients aged from 5 months old to 16 years old who were admitted with the diagnosis of acute gastroenteritis were collected. A total of 99 patients were enrolled and tested for stool calprotectin. Among them, only 52 patients were isolated with definite cause of pathogens. The values of fecal calprotectin were analyzed along with the disease severity as well as other clinical and laboratory parameters.

Results: *Salmonella* was isolated from 26 patients, rotavirus antigen was positive for 16 patients and norovirus was identified in 10 patients. The mean value of fecal calprotectin for the *Salmonella* group was 1117.57£gg/gm, for rotavirus group was 604.53£gg/gm and for norovirus group was 680.95£gg/gm. Statistical analysis showed significant higher calprotectin levels of bacterial gastroenteritis (*Salmonella*) than that of viral induced (rotavirus and norovirus) ($p=0.02$). However, further evaluation of the clinical severity failed to show any statistical correlation between fecal calprotectin with the Vesikari score, the total days of diarrhea, vomiting, fever, the value of C-reactive protein, white count, hemoglobin, platelet, sodium, potassium, blood glucose level and stool pus cell.

Conclusions: Fecal calprotectin levels increased higher during bacteria infection in compare to viral gastroenteritis. However, it showed inconsistent results with the clinical disease severity, probably due to the small sample size. Larger study populations are needed to further confirm the diagnostic value of this test.

560 FAECAL CALPROTECTIN AND EOSINOPHIL-DERIVED NEUROTOXIN VALUES. A PILOT STUDY TO ESTABLISH REFERENCE VALUES IN HEALTHY CHILDREN

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Objectives: To establish reference values for fecal calprotectin (fCP) and faecal eosinophil-derived neurotoxin (fEDN) levels in young healthy children to further investigate their potential role as biological markers.

Methods: Prospective, multi-centre study including 128 healthy children, 0 to 16 years, from the general population. 128 faecal samples were collected in plastic containers, sent to the laboratory no later than 7 days after collection and stored at -20°C until analysis. The extraction procedure was performed with the fecal sample preparation kit (Roche Diagnostics). fCP and fEDN levels in the stool samples were measured by EliA Calprotectin 2 and an EDN research assay developed on the ImmunoCAP platform, respectively (Thermo Fisher Scientific).

Results: We found a statistically significant association for median fCP concentration values and age ($p<0.001$) and median fEDN concentration values and age ($p<0.001$). This association was stronger at younger ages and sharply decreased around 36 months of age. Moreover, for children up to 36 months, a large variability was found both for fCP and fEDN values, especially in the first month of life. No statistically significant association was found for gender, neither for fCP ($p=0.09$) nor for fEDN ($p=0.15$).

Breastfed babies aged up to 6 months showed overall higher fCP and fEDN values as compared to non-breastfed infants, but this difference was not statistically significant ($p=0.93$ and $p=0.66$).

Comments: The variability of fCP and fEDN for children up to 3 years of age justifies the need for different cut-off levels in this age range. It also suggests that the main utility of both markers could be intra-individual variation monitoring, allowing assessment of disease progression or response to therapeutic intervention. Beyond the age of 3 a unique cut-off level can be used through childhood, and the lower variability allows for a better discrimination between true positive and true negative results.

In the first month of life, due to the extremely high variability of both fCP and fEDN, efficiency of any of these two markers in clinical practice as a diagnostic tool is controversial.

***561 SODIUM, POTASSIUM, CALCIUM, AND PHOSPHORUS CONTENT OF HUMAN MILK OVER THE FIRST YEAR OF LACTATION: A GEHM STUDY OF THREE GLOBAL COHORTS**

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Objectives: Minerals in human milk are critical to infant growth and development; however, multiple factors, e.g., maternal genetics, body mass index, and diet, may introduce variability into the elemental composition of human milk. This study expands the longitudinal and geographic resolution for sodium, potassium, calcium, and phosphorus content in human milk through the first 12 months of breastfeeding by characterization of samples collected from three distinct geographies.

Methods: Human milk was collected from mother-infant pairs participating in the Global Exploration of Human Milk (GEHM) in Shanghai, China, Mexico City, Mexico, and Cincinnati, United States. A total of 435 milk samples from 90 mothers at 2, 4, 13, 26 and 52 wks were analyzed by inductively coupled plasma-mass spectrometry.

Results: Human milk exhibited similar mineral concentrations and temporal patterns by geographic site over the first year of lactation. Mean calcium concentration remained stable between 2 and 13 wks at 0.29 g/L before decreasing to 0.22 g/L through 52 wks ($p<0.001$). From 2 to 52 wks post-partum, mean potassium and phosphorus content of human milk decreased ~30% across lactation, ranging from 0.59 to 0.41 g/L for potassium ($p<0.001$) and 0.17 to 0.12 g/L for phosphorus ($p<0.001$). Sodium displayed a high level of interindividual variability throughout lactation with a resulting mean concentration of 0.26 g/L at 2 wks, dipping to 0.10 g/L at 26 wks, and then increasing through 52 wks to 0.17 g/L ($p<0.001$). Characterization of mineral ratios demonstrated the Na:K ratio of human milk to have a modestly U-shaped, significant trend ($p<0.001$) over the first year of lactation with ratios of 0.47 at 2 wks, 0.23 at 26 wks, and 0.38 at 52 wks post-partum. Human milk Ca:P ratio also showed longitudinal trending increasing from 1.7 at 2 wks to 2.1 at 13 wks, then decreasing to 1.9 at 52 wks; however, the Ca:P ratio did not demonstrate statistical significance across lactation.

Conclusion: This study offers a global perspective of sodium, potassium, calcium, and phosphorus content in human milk including similarity in concentrations over lactation between mothers with diverse genetic, dietary, and geographic influences. The demonstration of distinct concentration patterns across lactation for these abundant minerals may also offer insight into mineral intake provided via human milk during infant growth and development.

562 VAGINAL pH IS ASSOCIATED WITH BIRTH WEIGHT AND BIRTH LENGTH IN BANGLADESHI INFANTS

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Preterm birth and low birth weight (LBW) are associated with a number of short- and long-term consequences for future health. South Asia suffers from particularly high rates of both prematurity and LBW. The impact of vaginal health on birth outcomes is a subject of debate, and the data from South Asia are particularly scarce. We set out to examine the impact of maternal vaginal health on infant outcomes in 300 pregnant Bangladeshi women recruited at the 3rd trimester of pregnancy to a birth cohort study with the follow-up of infants until their second birthday. Medical examination with special focus on urogenital health was carried out at 32 weeks of pregnancy. Vaginal microbiota was evaluated by 16S rRNA gene sequencing. The gestational age was estimated based on 3rd trimester ultrasonography and infant weight and length were measured at birth. Candidiasis was detected in 13% of women, and bacterial vaginosis in 21% according to Nugent criteria and 42% when using Amsel criteria, while other urovaginal infections were rare. The dominant taxa of vaginal microbiota were *L. crispatus*, *L. iners* and *G. vaginalis*. Twenty percent (54/268) of infants were born LBW and 19% (54/284) were premature, defined as born before completed 37 weeks of gestation. The only parameter of vaginal health which had clear impact on infant outcomes was vaginal pH, with a significant association with birth weight and length (Spearman for both $r = -0.16$; $p=0.01$), and marginally significant for gestational age (Spearman $r = -0.13$; $p=0.036$). From the lowest, healthiest, pH category of <4.5 to the highest values of $\text{pH}>6$, infants showed 100g decrease in weight at birth, 1 cm in length, and 3 days decrease in gestational age. No other measured parameter, including Amsel and Nugent scores, had impact on birth outcomes (ANOVA and t-test, NS). Overall microbiota composition was associated with infant birth length in multivariate analysis (RDA, $p<0.05$) but not infant weight or prematurity (NS). However, this was not measurable on the level of individual bacterial taxa. Microbiota composition was, as expected, dominated by *L. crispatus* in healthy women, while those with bacterial vaginosis had high abundance of *G. vaginalis* and high bacterial diversity. The clear association of vaginal pH with infant birth weight and length was surprisingly not reflected in specific bacterial taxa. It is usually assumed that vaginal bacteria are the key factor controlling the vaginal pH. While ultimately the best approach to vaginal health might be promoting optimal vaginal microbiota, improving vaginal pH during pregnancy should not be neglected. To better understand the long-term impact of vaginal health on later in life outcomes, the health of infants in this cohort will be monitored for at least 2 years of life.

563 RANDOMIZED, DOUBLE BLIND, PLACEBO CONTROLLED, CLINICAL TRIAL ON THE SAFETY, EFFICACY AND PHARMACOECONOMIC ANALYSIS OF RACECADOTRIL IN CHILDREN WITH ACUTE DIARRHEA

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Rationale: Acute diarrhea (AD) continues as a public health problem worldwide. The efficacy and safety of adjuvant racecadotril has demonstrated 10 years ago. There is no published economic analysis of drug.

Objectives: To evaluate the safety, efficacy, tolerability and costs associated with racecadotril vs. placebo as an adjunct in the treatment of AD in Mexican children.

Material and Methods: Controlled clinical trial, double-blind, randomized (RCTs) with economic drug analysis, clinicaltrials.gov NCT01153854, conducted in 454 children 1 to 24 months with AD (270 hospitalized for dehydration, and 184 ambulatory). Children were randomly assigned to Racecadotril (1.5 mg/kg/dose/t.i.d., for up to five days), plus oral rehydration solution (ORS) vs.. placebo plus ORS. Stool output, duration of diarrhea, need for intravenous hydration (IVNs) and frequency of adverse events were analyzed in hospitalized patients. Stool frequency, stool characteristics, duration of diarrhea and frequency of adverse events were analyzed in ambulatory. In both groups, a cost-minimization analysis (CMA) was performed. Statistical analysis was made through STATA 11.0 and Tree AD Pro Healthcare 1.2.0 2009. **Results:** In hospitalized children, stool output at 48 hours (102 ± 18 g / kg. vs.. 189 ± 34 g / kg., $p<0.01$), the average rate of stool output during the study (176 ± 24 g / kg vs.. 398 ± 27 g / kg, $p<0.001$), duration of AD (33 ± 8 h vs. 97 ± 11 h, $p<0.02$) and percentage of IVNS (6% vs.. 17%, $p<0.02$) was better in the racecadotril group. In ambulatory, the frequency of bowel movements at second day (9.8 ± 2.8 vs.. 14.6 ± 3.1 , $p<0.01$), the frequency of diarrheal stools on the second day (5.6 ± 1.7 vs. 11.3 ± 2.7 , $p<0.001$), and duration of diarrhea (75.5 ± 11.6 h vs. 142.5 ± 15.4 h, $p<0.001$) was better in the racecadotril group. No patient receiving racecadotril had a new event of dehydration, while in the placebo group, 20 patients were readmitted for dehydration (22%, $p=0.02$). In the cost analysis, the average incremental cost per patient was significantly higher in the placebo group (18.94 USD, $p<0.05$). **Conclusions:** This RCT provides additional evidence that supports the positive effects of Racecadotril in the treatment of AD in children. Considering the results of drug studio is economically possible to recommend as a cost-effective adjuvant

***564 DETECTION OF BOVINE PROTEINS IN HUMAN MILK AND AMNIOTIC FLUID USING PROTEOMICS**

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Background and Objectives: Human milk (HM) and human amniotic fluid (HAF) have previously been thought to be "bovine-free". However, mass-spectrometry (MS)-based proteomics have uncovered cow milk proteins (CMP) in human milk. It has been speculated that the presence of CMP may drive either tolerance or cow milk protein intolerance in early childhood. Further understanding of bovine proteins in both HM and HAF through proteomics may offer insights into the occurrence of allergies or development of tolerance in breastfed infants. Using MS-based proteomics, this study explores a possible mechanism of exposure of fetuses and infants to bovine proteins in human milk whey (HMW) and HAF through the mother-fetus/infant dyad.

Methods: This prospective analysis included preterm HM from 1 - 3 wks of lactation (n=6) and HAF from 34 - 37 wks of gestation (n=6), both collected by Cincinnati Children's Hospital. Proteins were extracted and tryptically digested, followed by MS analysis and search against Uniprot database under human and bovine taxonomy. Peptides with association to both human and bovine organisms were excluded from comparison. An exponentially modified protein abundance index (emPAI) estimated relative intensities of proteins.

Results: A total of 36,882 human-specific and 3044 bovine-specific peptides were characterized in HAF and assigned to 1,739 human and 267 bovine proteins, respectively. Analogously, 33,937 human-specific and 3,673 bovine-specific peptides were identified in HMW and assigned to 1705 human and 330 bovine proteins, respectively. In this study, 124 bovine proteins including B-lactoglobulin were present in both HAF and HMW whereas alpha-s1-casein was specifically found in HAF and lactotransferrin only in HMW. Relative abundances of these three bovine proteins are at least four orders of magnitude lower than the most abundant human proteins in HAF and HM.

Conclusion: Using proteomic technology, bovine proteins beyond B-lactoglobulin and caseins were identified in human milk whey and/or human amniotic fluid. Future work is needed to validate the presence and composition of non-human proteins in HM/HAF through proteomic and complementary approaches and to examine correlation of these proteins with clinical outcomes such as cow milk protein intolerance.

565 THE DIAGNOSTIC ACCURACY OF TWO CLINICAL SCORING SYSTEMS FOR SUSPECTED APPENDICITIS AMONG CHILDREN THREE TO EIGHTEEN YEARS OLD IN A TERTIARY HOSPITAL

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Background: Acute appendicitis is the most common surgical emergency performed each year. However, its diagnosis often poses a challenge to the clinician owing to the difficulty in interpreting the clinical presentation in children. Scoring systems have been utilized to aid in its early diagnosis.

Objective: To determine the diagnostic accuracy of Alvarado Score (AS) and Samuel's Pediatric Appendicitis Score (SPAS) in the diagnosis of appendicitis (AP).

Design: Retro-prospective, cross-sectional study.

Setting: Emergency Department of tertiary, private hospital.

Participants: Three hundred fifty (350) patients aged 3-18 years old with complaints of abdominal pain in the emergency department were included in the study. Excluded were patients with chronic medical condition, pregnant, radiologic imaging done two weeks prior to the study, and previous abdominal surgery.

Main Outcome measure: Overall diagnostic accuracy, specificity, sensitivity of both scoring systems.

Results: AS revealed an 84% sensitivity, 92.6% specificity, and overall accuracy 88.3% with the cut-off point at ≥ 7 . SPAS revealed a 48% sensitivity, 98.6% specificity, and overall accuracy of 73.4% at a cut-off point of ≥ 8 .

Conclusions: Both scoring systems can be used as practical aids in risk-stratifying patients suspected of AP; however, neither can be solely used. Clinical judgment remains the mainstay for the diagnosis especially in patients with equivocal scores.

Appendicitis, Accuracy, Alvarado, Samuel Scoring, Pediatrics.

566 PRIMARY ANTIBIOTIC RESISTANT OF HELICOBACTER PYLORY ISOLATED IN VIETNAMESE CHILDREN PATIENT WITH GASTRITIS AND PEPTIC ULCER

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Background: *Helicobacter pylori* (*H. pylori*) has been considered as a major cause of gastritis and peptic ulcer disease (GPUD). Treatment of *H. pylori* induced GPUD is challenging. Effectiveness of treatment regimens depend on antibiotic resistance status where currently treatment effectiveness is about 80%, under the desired level due to high drug resistance.

Aim: We conducted this study to identify the prevalence of antibiotic resistance in *H. pylori* strain isolated from Vietnamese children in the national Pediatric hospital, Vietnam between 2011 and 2013.

Materials and Methods: We performed gastro-endoscopy, biopsy, dyeing *H. pylori* shed for histopathology, and culture for *H. pylori* bacteria among 624 patients who had symptoms of gastro-duodenal disease, with no previous history of eradication of *H. pylori*. Anti-microbial susceptibility tests were also performed to determine antibiotic resistance by diffusion test.

Results: We found 588 strains with primary antibiotic-resistant *H. pylori* (94.2%). Resistance rate to clarithromycin was the most serious with the highest proportion of 56.6%. Resistance rates to azithromycin, metronidazole, amoxicillin, cefixime and ciprofloxacin were 55.8%, 29.2%, 18.3%, 11.5% and 1.8%, respectively, while the resistance rates to tetracycline and levofloxacin resistance were as low as 0.5 and 0.3%, respectively. Resistance to two antibiotics was mostly observed for azithromycin and clarithromycin (30.6%), and the rate was lower for clarithromycin and metronidazole (9.8%). Resistance rate to three antibiotics was as low as 6.6% for azithromycin, clarithromycin, and metronidazole. The resistance rate to four antibiotics was only 0.6% for azithromycin + clarithromycin + metronidazole + cefixime. Previous history of antibiotic use increased the risk of clarithromycin resistance by 2.45 times (95% CI, 1.69-3.55), boy increased the risk by 1.42 times (95% CI, 1.02-1.98) and peptic ulcer disease increased the risk by 3.06 times (95% CI, 1.27-7.36).

Conclusions: Primary antibiotic resistance of *H. pylori* children on gastritis and peptic ulcers are commonly observed among children with gastro-duodenal disease. Therefore, it is necessary to effectively manage the use of antibiotics in the treatment of other diseases to reduce status of antibiotic resistance of *H. pylori*.

567 FECAL CALPROTECTIN IN PEDIATRIC GASTROINTESTINAL PATHOLOGIES IN A PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION REFERENCE CENTER OF COLOMBIA

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Introduction: Fecal calprotectin (FCP) is a stable and highly sensitive biomarker that provides information about the inflammatory condition of the bowel. Therefore, it is useful for tracking and predicting relapse in some diseases of inflammatory origin, including for addressing gastrointestinal pathologies (GIPs) noninvasively.

Objective: To describe the levels of FCP in different GIP in a pediatric population of a gastroenterology and nutrition reference unit (Gastronutriped).

Materials and Methods: In a case series, patients ≤ 18 years of age who attended a consultation at Gastronutriped between May 2013 and May 2014 and for whom FCP was requested were included. Data were extracted from the medical histories. The description of continuous variables was performed with the mean or the median, with their respective measure of dispersion (standard deviation and interquartile range). Discrete variables were expressed as proportions. FCP levels were determined according to subgroups for different variables. The difference between groups was established by calculating the p-value with the Wilcoxon rank test or the Kruskal-Wallis test. A p value < 0.05 was considered significant.

Results: 29 patients were found, whose median age was 46.8 months, 55.2% male, and 58.6% (n=17) exhibited some degree of malnutrition. FCP values ranged between 15 and 429 ug/g with a median of 59 μ g/g. The most frequent suspected diagnoses that caused a request for FCP were intestinal malabsorption syndrome and food allergy (FA). FA was the most frequent confirmed diagnosis. In 65.5% of patients, organic type GIP was documented, with higher values of FCP. No statistically significant difference in levels of FCP was found between subgroups of the study, which in part can be explained by the sample size. In patients with definitive diagnoses of peptic esophagitis (280 ug/g) and enteropathy (429 ug/g), very high values of FCP were found.

Conclusions: FCP is useful for monitoring inflammatory bowel disease in children and adults. However, the results of its application in other GIPs have been contradictory. In our study, no statistically significant relationship between levels of FCPs and GIP was observed, which could be related to the sample size, although high values were documented in patients with peptic esophagitis, malnutrition, and allergic enteropathy. Since they are elevated in patients with FA, they could be a useful marker for inflammatory bowel diagnosis and monitoring. Further studies with a larger sample size are required in order to assess normal FCP behavior and that in functional and organic gastrointestinal diseases by age group in the pediatric population.

568 LOW PREVALENCE OF HELICOBACTER PYLORI INFECTION AMONG SYMPTOMATIC CHILDREN IN HANGZHOU, CHINA

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Background and Aim: The prevalence of *Helicobacter pylori* (*H. pylori*) is high in developing countries. *H. pylori* infection is acquired in childhood. The aim of our study was to evaluate the characteristics of *H. pylori* infection among children with gastrointestinal symptoms in Hangzhou, China.

Methods: A systematic surveillance of *H. pylori* infection according to the delta over baseline value of 13C-urea breath test was conducted in outpatient department and inpatient wards from January 2007 to December 2014 in the children's hospital, Zhejiang University School of Medicine. The demographic information and main symptoms of every subject were recorded.

Results: A total of 12,796 subjects were enrolled in this study and 18.6% (2382/12796) children evaluated as having a *H. pylori* infection. The positive rates were 14.8% in 3-6 years age group, 20.2% in 7-11 years age group, and 25.8% in 12-17 years age group, which increased with age and were statistically significant (116.002, $p < 0.01$). The prevalence in boys was significantly higher than girls (15.090, $p < 0.01$). We did not find any difference in the positive rate of *H. pylori* infection in children with or without gastrointestinal symptoms (18.9% vs. 17.5%), and any significant relationship between the status of *H. pylori* infection and each kind of gastrointestinal symptom. The *H. pylori* infection rate was higher in children with a history of an *H. pylori* infected family member than those without an *H. pylori* infected familial history. n

Conclusions: The prevalence of *H. pylori* infection in our study was lower than most of what is reported in mainland China. Comprehensively understanding the characteristics of *H. pylori* infection will be helpful to *H. pylori* management strategies in children in China.

HEPATOLOGY

584 FOLLOW-UP OF BONE STATUS IN CHILDREN WITH CHRONIC LIVER DISEASES

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Background: Twenty to 50% of children with chronic liver disease develop osteoporosis and/or osteomalacia. Even if it improves after liver transplantation, these anomalies increase morbidity and persist few months following the intervention.

Design: A retrospective longitudinal cohort study was carried out. Patients were children diagnosed with chronic cholestatic disorders recruited from the gastroenterology clinics of CHU-Sainte-Justine Hospital, Montreal. All children who had 2 or more bone mineral density (BMD) measures post-diagnosis were identified. Information on time-invariant covariates such as date of diagnosis, age at diagnosis, gender, type of disease at diagnosis, date at liver transplantation etc. was abstracted. Data on time-varying covariates such as doses of vitamins (A, E, D) administered blood levels of calcium (and other minerals) and bilirubin etc. during follow-up was also ascertained.

Statistical analysis: Evolution of BMD and potential modification by covariates was assessed using generalized estimation equations (GEE). A linear model plus quadratic model was fit to the data with the non-transformed BMD score as the outcome assuming an exchangeable correlation structure. BMD modification by potential covariates was examined by incorporating appropriate interaction terms in the models and adjusting for potential confounders such as age at diagnosis, duration of follow-up, gender etc. A *p*-value cut-off of 0.05 was considered for ascertaining statistical significance.

Results: A total of 36 patients were identified. The mean (\pm SD) age at diagnosis of the cohort was 0.3 (\pm 0.3) yrs. Fifty-eight percent (21/36) of the patients were male. The cohort was followed up for a mean (range) duration of 2468 (515 to 6510) days. After accounting for potential covariates, regression analysis using GEE indicated that for the cohort overall there was a statistically significant annual linear increase of BMD of 0.05 units (95% CI, 0.03-0.06; *p*<0.001). With increasing time, however, the rate of evolution of BMD was slower (*p* 0.02). Children who were administered higher calcium doses during follow-up were likely to have greater evolution in their BMD (0.02 units greater, *p* 0.03) than those administered lower doses. Although initially there was no association with vitamin D or vitamin A dosage, with increasing time, those on higher doses showed better evolution in their BMD scores (*p* values of 0.05 and 0.047 respectively). Evolution of BMD was much slower for those with higher blood levels of total bilirubin (*p*<0.001). After liver transplantation, 10 out of 15 patients showed normal BMD.

Conclusions: Children with chronic cholestasis should have a close follow-up of their bone density, and be treated with high doses of vitamin D (sometimes administered intra-muscularly) and calcium to prevent bone complications.

585 INCIDENCE AND CLINICAL FEATURES OF PEDIATRIC PATIENTS WITH AUTOIMMUNE HEPATITIS IN THE PROVINCE OF SANTA FE (ARGENTINA)

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Background and Objectives: Autoimmune hepatitis (AIH) is a chronic necroinflammatory disease of liver parenchyma. Epidemiologic data among pediatric populations are scarce, especially from developing countries. We aimed to investigate the incidence and clinical features of AIH in children from the province of Santa Fe (Argentina) over a period of ten years.

Methods: Retrospective analysis of clinical records of patients <18 years, followed by all pediatric gastro-hepatologists from the province of Santa Fe, diagnosed with AIH according to the IAHG score (>13 points) from January 2003 to December 2013. Population data were extracted from the 2010 national census. Values were expressed as percentages and median \pm interquartile range. Mann-Whitney test was used for comparison between groups.

Results: 67 patients fulfilled the inclusion criteria, from which 11 (16.4%) were later reclassified as sclerosing cholangitis (SC) according to biochemical, histological and radiological findings. Therefore, a final sample of 56 patients (39 F) with AIH was analyzed, giving an annual incidence of 0.56/100000. Median age at presentation was 8 years (5-11 years), and the median follow-up was 4 years (2-7 years). Type 1 AIH was diagnosed in 89%, 13/56 (23%) suffered from other immune-mediated disease, being ulcerative colitis (n=3), type-1 diabetes (n=2), celiac disease (n=2), and psoriasis (n=2) the most common. An acute (icteric) form of presentation was observed in 53%, 3 (5%) patients developing severe acute liver failure, while 13 (23%) showed cirrhosis on initial biopsy. Meprednisone (87%), and azathioprine (60%) were the most common drugs prescribed, but mycophenolate (7%), cyclosporine (5%), tacrolimus (3.5%) and rituximab (3.5%) were occasionally used. Complete remission was achieved in 68% at the end of first year of treatment, and 53/56 (95%) were alive at the end of follow-up. There were 3 deaths (2 sepsis, 1 bleeding), and 4 patients (7%) received a liver transplantation (2 acute, 2 chronic) being alive and well. When comparing AIH vs. SC children, only GGT levels at presentation showed statistical differences: AIH 71 IU/L, (37-140 IU/L); SC 481 IU/L (107-864 IU/L), (*p*=0.007).

Conclusion: AIH has an estimated incidence of 0.56/100000/year in children from the province of Santa Fe (Argentina). Combined current therapies achieved an overall survival of 95%. A subgroup of patients diagnosed as AIH develops biliary changes akin to SC, and should probably be better classified as "autoimmune cholangitis".

586 DIAGNOSTIC APPROACH AND MEDICAL MANAGEMENT OF BILIARY ATRESIA IN CANADA: RESULTS OF A SURVEY BY THE CANADIAN BILIARY ATRESIA REGISTRY

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Purpose: The Canadian Biliary Atresia Registry (CBAR) has been established to prospectively follow all biliary atresia (BA) patients nationally with the goal of improving care practices and outcomes. There are no standardized clinical care pathways for the management of BA. We report the current practices among Canadian pediatric gastroenterologists (PG) involved in the care of children with BA.

Methods: With REB approval, PG and surgeons in Canadian pediatric tertiary care centers were invited to complete an online survey of their current practices for the assessment and management of children with BA.

Results: Surveys were completed by 24 PGs from 8 centres. Of the 24, 21 provide long term care of BA children post-Kasai procedure (KP). Diagnostic procedures varied with 92% (22/24) performing liver biopsies, 58% (14/24) performing HIDA scans and 46% (11/24) percutaneous cholangiograms. Liver biochemistries and tests to exclude other causes of cholestasis were routinely done in all centers. The post-operative management was coordinated by both medical and surgical teams. For the majority of PGs, the post-operative nutritional approach included breast milk (90%; 19/21), formula (52%; 11/21) and TPN (10%; 2/21). In the immediate post-operative period, use of corticosteroids and IV antibiotics were reported by 24% (5/21) and 85% (17/20) of PGs respectively. At discharge, 80% (16/20) prescribed oral antibiotics, 95% (20/21) ursodeoxycholic acid, and 100% one or more fat-soluble vitamins. Vitamins A, D, E, and K were prescribed by 81% (17/21), 100% (21/21), 81% (17/21), and 67% (14/21), respectively. There was considerable variation in the timing of follow-up appointments, monitoring of laboratory parameters, and imaging studies. Follow-up ultrasounds were routinely requested by 57% (12/21). Endoscopic surveillance for varices was reported by 33% (7/21). No centre had a standard protocol for the evaluation for suspected ascending cholangitis. Most reported that the diagnosis was based on clinical presentation such as fever and/or jaundice along with liver biochemistries (100%), blood cultures (96%), and liver biopsy (26%). There was a lack of consensus on what defined a failed KP and the criteria for referral for transplant evaluation.

Conclusion: In Canada, the diagnostic approach of BA is variable; however, the majority of PGs include a liver biopsy as part of the assessment. The immediate and long term post-operative management, including the schedule for routine follow-up visits and laboratory testing, medication use, as well as the evaluation for BA related complications, were highly variable between the centres. Furthermore, there was considerable variation in the definition of what constitutes a failed Kasai procedure and the criteria for referral to a liver transplant center. Collaboration through the CBAR will allow for the development, implementation and evaluation of standardized protocols for this rare and serious pediatric liver disease.

587 BILIATRESONE, A TOXIN CAUSING BILIARY ATRESIA, LEADS TO INCREASED EXPRESSION OF CX3CL1, A LEUKOCYTE ADHESION LIGAND, IN MOUSE CHOLANGIOCYTES

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Background and Aims: Biliary atresia (BA) is a neonatal inflammatory fibrosing cholangiopathy of unknown etiology. Our group previously isolated a novel toxin, biliatresone, from plants responsible for outbreaks of BA in Australian livestock. We showed that biliatresone causes luminal obstruction in cholangiocytes in 3D and explant culture. In our current study, we aimed to identify changes in pro-inflammatory cytokines/receptors triggered by biliatresone that could potentially explain the progressive inflammatory bile duct injury seen in BA.

Methods: Cultured cholangiocytes were exposed to either biliatresone or DMSO (control) for 24 hours, mRNA was isolated, and gene expression evaluated using a Qiagen PCR array for 84 pro-inflammatory cytokines and receptors. RT-PCR testing was done to evaluate and confirm changes in expression of different cytokines. Enzyme-linked immunosorbent assay (ELISA) was performed on conditioned media to assess for changes in specific soluble cytokines.

Results: The initial PCR array reported an increase in 7 cytokines/receptors in cholangiocytes treated with biliatresone compared to control: CX3CL1 (known as fractalkine or neurotactin), CSF1, CSF3, IL17a, IL1r1, IL6ra, and Tnfsf13. The increased expression in CX3CL1 was confirmed by RT-PCR which showed an 11.8 ± 0.644 (mean \pm SEM)-fold increase in biliatresone treated cholangiocytes. CX3CL1 exists as a soluble and membrane-bound form. Membrane-bound CX3CL1 is known to be expressed on epithelial cells and functions to promote the adhesion of leukocytes. An ELISA for CX3CL1 showed no increase in soluble CX3CL1 in biliatresone treated media compared to DMSO treated media. RT-PCR testing did not show increased expression of CSF1 in biliatresone treated cholangiocytes. We have not yet confirmed an increase in expression of the other cytokines reported to be increased on the initial PCR array.

Conclusions: Biliatresone causes increased CX3CL1 mRNA expression in cultured cholangiocytes. A detectable increase in soluble CX3CL1 was not demonstrated via ELISA experiments. This suggests that the increased expression may lead to increased membrane-bound, rather than soluble, CX3CL1. Increased expression of CX3CL1 by cholangiocytes after exposure to biliatresone could explain the ongoing inflammatory response in the extra-hepatic biliary tree and liver parenchyma in BA after exposure to an initial insult. Further studies are required to demonstrate a direct increase of membrane-bound CX3CL1 after exposure to biliatresone and to validate other cytokine changes.

588 BACTERIAL INFECTION IN CHILDREN WITH LIVER DISEASE: FREQUENCY, SITE, TYPE, RISK FACTORS, MICROBIAL RESISTANCE PATTERN AND EFFECT ON OUTCOME

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Background and aims: Risk of infections is increased in patients with acute liver failure (ALF) and decompensated chronic liver disease (DCLD). We evaluated the frequency, site, type and risk-factors for bacterial infections in children with ALF and DCLD and its effect on outcome.

Methods: ALF or DCLD children were enrolled prospectively from March, 2013 to May, 2014. Clinical and laboratory details were recorded. Cultures (blood, urine and ascites) and chest x-ray were done at admission followed by weekly surveillance cultures.

Results: 173 patients, 68 ALF [48 boys, age 72 [0.5 - 192] months] and 105 DCLD [70 boys, age 84 [3-204] months] were enrolled. Viral hepatitis (48, 70.5%), was the most common cause of ALF, followed by idiopathic (10, 14.7%), autoimmune (6, 8.8%), drug induced (3, 4.4%) and hemophagocytic lymphohistiocytosis (1, 1.4%). The most common cause of CLD was autoimmune liver disease (21, 20%) followed by Wilson's disease (18, 17.1%), Budd-Chiari syndrome (17, 16.1%), biliary atresia (16, 15.2%), cryptogenic (16, 15.2%), chronic hepatitis B (4, 3.8%), secondary biliary cirrhosis (4, 3.8%), galactosemia (4, 3.8%), and others (5, 4.7%).

Infections were more common in DCLD than ALF cases (60/105 [57.1%] vs. 27/68 [39.7%]; $p= 0.02$). Ascitic fluid infection, pneumonia, urinary tract infection and bacteremia were seen in 19%, 17.9%, 13.2% and 12.1% patients respectively. Healthcare-associated (HCA) infections were most frequent (39/87, 44.8%), followed by nosocomial (32%) and community-acquired (23%). Nearly three-quarters of bacterial isolates were resistant to cephalosporins and quinolones, 23% being multiresistant bacteria (MRB). DCLD patients with infection had higher Child- Pugh Score (10(6-14) vs. 7(6-14); $p= 0.008$), need for ICU care (26/60 vs. 3/45; $p= 0.01$), in-hospital mortality (24/60 vs. 8/45; $p= 0.04$) and mortality at 3 months (32/60 vs. 9/45; $p=0.00$). Infection did not affect the outcome in ALF.

Conclusions: Infections develop in 40% ALF and 57% DCLD children. HCA and NC infections account for 77% of infections. Most culture isolates are resistant to cephalosporins and fluoroquinolones and 23% have MRB. Risk of infections is higher in DCLD patients with advanced liver disease.

Parameter	ALF	DCLD
Number of patients	68	105
Total culture specimens	249	424
Number of patients with infection	27/68 (39.7%)	60/105 (57.1%)
Single site: multiple site infection cases	24:03:00	46:14:00
CA: HCA:NC (number of cases)	4:12:11	16:27:17
Yield of culture	19/249 (7.6%)	42/424 (9.9%)
Nature of isolates	GPC -10, GNB -9, MRB -5	GPC-17, GNB-25, MRB-9

589 A JAPANESE CHILD WITH IDIOPATHIC COPPER TOXICOSIS

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We experienced a Japanese child with idiopathic copper toxicosis (ICT), who was diagnosed with special features of liver histology.

Case: A seven-year-old boy was referred to our hospital because of a deep jaundice. He was suffering from itching and growth retardation since 3 years of age. His physical findings were jaundice, angioma spider on his cheeks, hepatosplenomegaly (liver palpable 6 cm in right costal margin, spleen palpable 5 cm in left costal margin), and scratches with bleeding in skin. His laboratory findings were WBC 6,420/ micro L, hemoglobin 10.3 g/dL, platelet 174,000/ micro L, total bilirubin 13.5 mg/dL, direct bilirubin 10.6 mg/dL, AST 1,477 U/L, ALT 457 U/L, LDH 393 U/L, GGT 162 U/L, Alb 2.9 g/dL, UA 2.4 mg/dL, PT 37.7%, APTT 49.4 sec, and haptoglobin 9mg/dL. His copper associated profiles were serum Cu 215 micro g/dL, ceruloplasmin 48.6 mg/dL, and 24-hour urine Cu 472.8 micro g/d.

Clinical Course: He was diagnosed with Wilson's disease (WD) with normal serum ceruloplasmin level and no abnormality of ATP7B gene. He was treated with trientine hydrochloride in addition to zinc acetate for 30 days. His 24-hour urine Cu levels were increased to >2,500 micro g/d, while his condition was deteriorating. His new Wilson Index reached up to 17. He was transferred to the Transplantation Center and underwent cadaveric liver transplantation. Histology of explanted liver: Liver surface and divided face showed multiple nodular formations. Lobular architecture was disturbed with severe fibrosis. Inflammation was minimal. Mallory body like materials was markedly found in hepatocytes. A copper content in the explanted liver was 1482.3 micro g /g dry weight. Both Orcein and Rhodanine stainings were strongly stained in hepatocytes.

Discussion and Conclusion: ICT is one of the copper metabolic disorders, less recognized than Wilson's disease. The pathogenesis of ICT is still unknown, but the clinical features of ICT are similar to hepatic type of Wilson's disease. Cases of Wilson's disease with normal or high level of serum ceruloplasmin should consider ICT. The liver histology is helpful to diagnose ICT.

590 INFANTILE CHOLESTASIS ADVANCES IN ITS UNDERSTANDING: NEW CONCEPTS

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Neonatal Cholestasis is an important cause of chronic liver disease in young children. Late referral and lack of precise etiological diagnosis are reasons for poor outcome.

Hyperbilirubinemia, if lasts more than 14 days defined as prolonged jaundice. This requires differential diagnosis between benign unconjugated hyperbilirubinemia and pathological conjugated hyperbilirubinemia.

The role of liver biopsies is changing with the development of new diagnostic methods, advances in imaging techniques, non-invasive biomarkers, proteomic and genomic studies. There are multiple causes and morphological patterns related to genetic defect in hepatic metabolism including synthesis of bile acids, formation and function of membrane transporters, alterations in the development of the bile ducts. Inherited syndromes produce intrahepatic cholestasis and biliary atresia are the most common causes of chronic liver disease leading liver transplantation in children.

Recent progress in basic research has enhanced our understanding of the molecular mechanisms of normal bile secretion and their alterations in cholestasis. Genetic transporter variants contribute to entire spectrum of cholestatic liver diseases and cause hereditary cholestatic syndromes or determine susceptibility and disease progression in acquired cholestatic disorders. Cholestasis is associated with complex transcriptional and post-transcriptional alterations of hepatobiliary transporters and enzymes participating in bile formation. Ligand-activated nuclear receptors for bile acids and other biliary compounds play a key role in the regulation of genes required for bile formation. Nuclear receptors (NRs) play a key

role in the transcriptional control of critical steps of hepatobiliary transport and phase I/II metabolism of endo and xenobiotics such as bile acids and drugs, NRs also play a key role in the control of hepatic inflammation. Hereditary and acquired alterations of NRs contribute to the pathogenesis of cholestasis and gallstone disease.

Mutations in NR1H4, which encodes the farnesoid X receptor (FXR), a bile acid-activated nuclear hormone receptor regulates bile acid metabolism.

Cholestasis is an impairment of bile formation/flow at the level of the hepatocyte and/or cholangiocyte. The first, and for the moment, most established medical treatment is bile acid, ursodeoxycholic acid. Limited efficacy of UDCA in cholestatic conditions urges development of novel therapeutic approaches. These include nuclear and membrane receptor agonists and BA derivatives. The nuclear receptors farnesoid X receptor, retinoid X receptor, peroxisome proliferator-activated receptor α , and pregnane X receptor are transcriptional modifiers of bile formation. Membrane receptors fibroblast growth factor receptor 4 and apical sodium BA transporter deserve attention as additional therapeutic targets.

591 MODALITY OF TREATMENT AND POTENTIAL OUTCOME OF WILSON'S DISEASE IN TAIWAN: A POPULATION-BASED LONGITUDINAL STUDY

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Purpose: This study aimed to investigate the epidemiology, the preference of medication, and the long-term outcome of Wilson's disease in Taiwan.

Methods: Data was obtained from the National Health Insurance Research Database (NHIRD), which stores detailed clinical records of all insurers in Taiwan. The database used in this study is a randomized sample of two million out of 23 million beneficiaries in Taiwan's NHIRD in 2005. And the integrated medical records of these two-million cases were collected from 2000 to 2011. Subjects of Wilson's disease were identified as those with International Classification of Diseases, Ninth Revision (ICD-9) code 275.1 and the specific prescription drugs (including D-penicillamine, zinc, and trientine) in either outpatient clinic or inpatient records.

Results: During the study period, 66 cases of Wilson's disease were identified. The male to female ratio was 1.75. The average prevalence rate was 1.81 per 100,000 and the average annual incidence rate was 0.22 per 100,000. The age-specific incidence rate peaked at 10 - 14 years of age, followed by 20 - 24 years, and 25 - 29 years. 54 of all subjects (81.8%) started the treatment with D-penicillamine, compared with zinc (12.1%) and trientine (6.1%). Among these 66 cases with Wilson's disease, 27 (40.9%) had liver cirrhosis and 3 (4.5%) underwent liver transplantation due to liver failure.

Conclusions: D-penicillamine is still the drug most prescribed for patients with Wilson's disease, followed by zinc monotherapy. Although chronic liver injury cannot be avoided, a favorable long-term outcome is well demonstrated in this population-based study. Liver failure or mortality was rarely found.

592 CHANGES OF HEPATITIS B VIRUS ANTIBODY TITER BY CHILDREN'S AGE AND EFFECTIVENESS OF BOOSTER VACCINATION IN ENDEMIC AREA

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Introduction: In intermediate HBV endemic area as South Korea, the most common cause of liver disease is Hepatitis B virus (HBV) infection. Because of the high prevalence of hepatitis B, the main route of HBV infection is vertical transmission from the mother to the newborn during childbirth. So through management of carriers and vaccination, spread of the disease has become inhibited. After vaccination, hepatitis B surface antibody (HBsAb) titer decrease over time but immunologic memory is maintained for more than 10 years. Even if HBsAb titer decreased, a booster is generally not recommended. This concerns HBsAb titer by children's age and effectiveness of booster in Korea's children.

Method: From May 2012 to April 2015 we retrospectively went through 6159 medical records aimed at patients from 7 months to 17 years who underwent a hepatitis B antigen/antibody tests at Chung-Ang University Hospital. People with a previous history who underwent a booster, were inoculated with HB immunoglobulin, had no titer test result and repeatedly conducted the test were excluded. Titer criteria was classified as positive with a titer of 100IU/mL or more, as weakly positive with 10IU/mL or more, yet less than 100IU/mL, as negative when less than 10IU/mL. In addition, we compared the titer investigated one month after booster 1 time.

Results: Full research subjects were 5658 (male 3016, female 2642) people. 8 patients were hepatitis B surface antigen (HbsAg)-positive (0.14%). HBsAb average titer was lowest in patients aged 14 years old, then 8 years old, and the age group that switched HBsAb titer to negative in 50% of patients was 7 years old. Until three years of age, antibodies were significantly continually decreased; thereafter, patients 7 years of age were found to be consistently negative in at least 50% of patients. When the booster vaccination was given once, the titer tests conducted after one month (n=72) 4.2% (n=) were negative, 31.9% (n=23) were weakly positive, and 63.9% (n=46) were positive.

Conclusion: In our study, we have recently checked the trend of hepatitis B antibodies in children of South Korea. In conclusion, immunological memory of hepatitis B vaccine was decreasing over time, especially in the more than half of school-age children after age 7 years converted to negative. In addition, the majority of children (95.8%) showed a one-time vaccination antibody seroconversion which is considered to be good to determine whether a booster through regular hepatitis B antibody test after this period.

593 CHARACTERISTICS OF HBV-ASSOCIATED HEPATOCELLULAR CARCINOMA IN CHILDREN: A MULTI-CENTER STUDY

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Background: Pediatricians and liver specialists in the United States and Canada continue to encounter hepatitis B virus (HBV) infection in high-risk populations, including unvaccinated children, adopted children, and immigrants. Although hepatocellular carcinoma (HCC) is a known complication of HBV, there exists a paucity of data regarding clinical presentation of HBV-associated HCC in children in these countries.

Methods: Investigators at four medical centers with large numbers of HBV-positive children queried their pathology and/or oncology databases to identify all cases of HBV-infected children <18 years presenting with HCC between 1990 and 2015. Clinical data were extracted from chart review.

Results: The group identified 8 patients, 8 to 17 years old, including 6 (75%) males. All individuals were assumed to be infected through vertical transmission. Three (38%) presented initially to the emergency room, 2 (25%) to a general pediatrician, 1 (13%) to a hepatologist, and the initial location was not documented in 2 (25%) cases. Three patients were asymptomatic, but the most common symptoms were jaundice, abdominal pain, and fatigue in 3 patients. Hepatomegaly was present in 5 (63%) patients. Viral load was not documented in any patient. Only three patients had their HBV envelope status documented and in all instances, the envelope antigen was negative and the envelope antibody was positive. Aspartate aminotransferase (AST) ranged from 13 to 575 IU/L, and alanine aminotransferase (ALT) ranged from 14 to 212 IU/L; four patients had AST and ALT < 1.5 times the upper limit of normal. Bilirubin and gamma glutamyl transpeptidase (GGT) were both elevated in 3 patients, both normal in 3 patients, and not documented in 2 patients. Alpha fetoprotein (AFP) was elevated in 3 patients (range 2,556 to 7,600 ng/mL), normal in 2 patients, and not documented in 3 patients. Ultrasound was initially used to identify the tumor in 5 patients whereas computerized axial tomography (CT) scan was used in 3 patients. Six patients had multiple nodules on initial imaging.

Conclusion: Although rare, HBV-associated HCC occurs in young children, often with normal liver enzymes, bilirubin, GGT, and AFP. Only routine imaging with ultrasound or CT scan consistently identified the tumor. These data may help inform screening for HCC including age of initiation and the role for imaging over laboratory testing.

594 FAT STORES, MUSCLE MASS AND BONE MINERAL DENSITY CORRELATE WITH LINEAR AND CENTRAL NERVOUS SYSTEM GROWTH IN INFANTS AND TODDLERS WITH CHRONIC LIVER DISEASE

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Objective: The aim of our study were to demonstrate the correlation of linear and central nervous system growth with fat stores, muscle mass and bone mineral density in infants and toddlers with chronic liver disease.

Methods Design: Cross-sectional. Setting: A pediatric referral hospital. Sample: 15 patients with CLD, age 3-36 months. Variables: a) Anthropometrical: weight, height and head circumference (HC) b) DXA: Fat stores (FS), muscle mass (MM) and bone mineral density (BMD). Protocol: Anthropometric data were handled with CDC reference pattern; criteria of normality $\pm 2SD$. DXA was performed with a whole-body scanner (Hologic Discovery W-series QDR) with pediatric software, Fomon's and Butte's reference patterns. Statistics: Frequencies, %, means, SD and Pearson correlation.

Results: Patients: 10 females, median age 14 months. Anthropometrics: Height for age was <-2SD in 67% (n=10), head circumference for ages was <-2SD in 60% (n=9). Body composition analyzed with Fomon's reference pattern, 80% had low MM and 67% FS (% of median <80). 47% of patients had FS depletion with Z-score <-2DE (Butte reference). All patient had affected BMD Z-score <-2 DE. FS and MM correlated strongly with height (r 0.90, $p < 0.001$; r 0.89, $p < 0.001$). FS correlated significantly with head circumference (r 0.90, $p < 0.001$). BMD correlated with FS (r 0.64, $p 0.01$), height (r 0.58, $p 0.03$) and head circumference (r 0.56, $p 0.03$).

Conclusions: Significant correlations of FS and MM with height and head circumference may underline the association of energy stores and linear and central nervous system growth.

595 AUTOIMMUNE HEPATITIS IN BRAZIL. RETROSPECTIVE MULTICENTER STUDY OF 797 CASES

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Background: There are scarce data on demographic and clinical presentation features of AIH in children and adolescents of South America.

Aim: To analyze epidemiology, immunology, histology and clinical aspects of children adolescents with AIH in Brazil and to evaluate the prognostic factors predictive for disease remission and survival with and without liver transplantation (LTx).

Methods: We conducted a retrospective analysis of medical records of patients diagnosed with AIH in 15 Brazilian centers that integrate the Brazilian Study Group on Pediatric Hepatology (GEHPed) in Brazil. Case validation was done according to the IAIHG diagnostic criteria (1999). Most patients were treated with combination therapy comprising prednisone and azathioprine.

Results: Among the 797 children/adolescents with AIH under study, 577 a (72.4%) were female, 716 (89.8%) with AIH-1 and 81 (10.2%) with AIH-2. Age at diagnosis was [mean(dp)] 115.9 \pm 44.3 months, being lower in AIH-2 ($p < 0.001$). Personal or family history of autoimmune disease were detected in 21.8% and 25% respectively. HBV and HCV serology were negative in all patients. Onset of symptoms: acute 421 (55.7%), insidious 335 (44.3%), liver failure 249 (32.9%) and fulminant hepatitis 32 (4.2%), the latter being more common in AIH-2 ($p = 0.001$). Liver enzymes' serum levels were similar in both groups. The AIH-2 group showed lower gamma globulin ($p < 0.001$) and C3 ($p = 0.05$) levels, and IgA deficiency ($p < 0.001$). Serum IgG/globulin was increased in 91.3% of patients. The IAIHG diagnostic criteria (1999) were not met in 42.9% of patients, who were, even so, treated as AIH. Histopathology: Interface hepatitis was found in 520 (84.1%) biopsies, mainly plasma-cell infiltrate in 331 (51.6%), rosettes in 315 (49.2%), biliary changes in 57(8.8%), cirrhosis in 503 (78.8%). Rosettes and plasma cells were more frequent in AIH-1 ($p = 0.004$ and $p < 0.001$, respectively). Autoimmune sclerosing cholangitis was diagnosed in 92 (12.7%), more frequently in AIH-1 ($p = 0.009$). Biochemical and clinical remission were observed in 563 (75.4%) patients, more commonly in AIH-2 ($p = 0.006$).

Remission reduced the need of LTx in 97% of the cases. The need of LTx occurred in 32 (4.3%) patients, being tripled in the presence of

fulminant presentation. Fifty-one patients with AIH (6.9%) died without LTx. Death risk was 7.7 times higher in the presence of autoimmune sclerosing cholangitis. Death risk increased by 18.8% for each mg/dl of serum direct-reacting bilirubin. Predictive factors of disease remission were higher levels of both ALT and hemoglobin at presentation. Higher levels of platelets at presentation were correlated with disease remission, and its decline, with the death and need of LTx.

Conclusions: In this large multicenter retrospective study, irrespective of the high cirrhosis index a successful treatment prevented the occurrence of LTx and death.

596 LIVER AND SPLEEN STIFFNESS MEASUREMENTS BY TRANSIENT ELASTOGRAPHY AS A POTENTIAL NON-INVASIVE MONITOR OF CYSTIC FIBROSIS ASSOCIATED LIVER DISEASE

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Background: Cystic fibrosis-associated liver disease (CFALD) is the third leading cause of death in CF after lung disease and transplant complications. Severity of CFALD is typically diagnosed based on liver histological, ultrasonographical findings or endoscopically with evidence of portal hypertension. The emergence of Transient Elastography (TE; Fibroscan) as a means of measuring both liver and spleen stiffness (LSM and SSM) in chronic liver disease patients may allow for better assessment and monitoring of liver disease in children CF. The aim of this study is to assess the feasibility and efficacy of LSM and SSM as a marker of CFALD and the development of GI varices. Methods: Fibroscan measurements were performed on children attending our centre for their cystic fibrosis annual review. LSM was recorded in all patients, while 16 also had SSM. Biochemical data were collected at the same time. The Clinical Prediction Rule (CPR) derived from spleen size, platelet count and albumin. Aspartate transaminase to platelet ratio index (APRI) was derived from aspartate transaminase and platelet count.

Results: 32 patients (11M), median age 10 years underwent transient elastography. LSM was obtained in all 32 patients; SSM was attempted in 20 patients, and successfully recorded in 16. SSM was successfully recorded in all patients who had splenomegaly. LSM was significantly higher in patients with CPR below the cut-off point of 116 (n 6, median 23.9kPa v 6kPa, p 0.04) a cut-off point of 10.3kPa gave an AUC of 0.96 (p 0.003). SSM was also significantly higher in patients with a CPR <116 (37.8 kPa vs. 10.5 kPa, p 0.04) a cut-off point of 18.7 kPa gave an AUC of 1 (p 0.003). APRI was not significantly different between those above and below the CPR cut-off of 116. Patients with abnormal liver enzymes had a higher LSM (15.1kPa v 5.5 kPa, p 0.005) with a cut-off point of 10.3kPa giving an AUC of 0.78 (p 0.01) and SSM (26.6 kPa v 12.2 kPa, p 0.03) with a cut-off point of 18.7 giving an AUC of 0.74 (p 0.04), compared to the ones with normal liver function tests, while only SSM was significantly increased in clinical CFLD (25.3 kPa vs. 9.3 kPa, p 0.04) with a cut-off point of 16.5 kPa giving an AUC of 0.87 (p 0.01). Two of the 4 patients who underwent a surveillance endoscopy were found to have varices (median LSM 18.7 kPa, SSM 43.1 kPa).

Conclusions: Fibroscan measurement of both LSM and SSM are feasible in CF patients with 100% success of SSM in patients with splenomegaly. Both can distinguish between low and high-risk groups for varices. SSM could distinguish patients with heterogeneous livers on ultrasound from those with a normal appearance. Thus, transient elastography and particularly SSM may be a promising tool for non-invasive measurement of CFLD.

597 SURVEY OF SERUM HEPATITIS B VIRUS DNA, GENOTYPES, SURFACE ANTIGEN MUTANTS AND REVERSE TRANSCRIPTASE MUTANTS IN IMMUNIZED SUBJECTS 25 YEARS AFTER UNIVERSAL INFANT IMMUNIZATION IN TAIWAN

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Background & Aims: To investigate breakthrough hepatitis B virus (HBV) infections and genetic characteristics of HBV isolates in immunized children and young adults, 25 years after universal infant immunization (UII) program in Taiwan.

Methods: Serum HBV DNA was detected using PCR and sequence analysis in 2853 <25-year-old subjects enrolled during 2009 serosurvey. HBV genotypes, surface antigen mutants and nucleoside analogue-resistant (NAr) mutants were determined. We then compared these data in these subjects with our five previous serosurveys conducted every five years in the same area.

Results: In the 2009 survey, the anti-HBc prevalence was low in those <23 years (1.90%-5.51%) and the prevalence of HBV DNA was even lower (0.51%-1.13%), implying that breakthrough infection was uncommon and rarely became persistent. Nonetheless, a significant in seroprevalence of anti-HBc and HBV DNA was found in 23-25-year-old individuals. Between those 17-23 and 23-25 year olds, the prevalence of anti-HBc was 5.51% and 12.38% ($p=0.001$), respectively. That of HBV DNA was 1.13% versus 3.96% ($p=0.007$), respectively. The increase in seroprevalence of anti-HBc and HBV DNA between 17-23 and 23-25 year-old was probably due to incomplete infant immunization during the early period of the immunization program rather than acquisition of HBV infection during young adulthood. Well-characterized NAr mutants, potential NAr mutants and surface "a₁" determinant mutants were detected in none, 15 (45%) and 9 (27%) of 33 HBV DNA-positive subjects <25 year-old, respectively. Among those subjects (<18 years) seropositive for both HBsAg and HBV DNA, the prevalence of genotype C in six serosurveys seems to increase slowly with time. Nonetheless, there was no significant difference in genotype C frequency between vaccinated and unvaccinated cohorts (14/79 [17.7%] versus 25/98 [25.5%], $p=0.188$).

Conclusions: The 25-year UII in Taiwan was associated with a slow, gradual increase in genotype C prevalence in children with immunization failure. There was a stable low prevalence of vaccine escape mutants and rare emergence of classical NAr mutants in immunized population, and no real increase of breakthrough infections beyond adolescence. These results suggest that routine booster vaccination is currently not recommended in young adult subjects who had been immunized in infancy.

598 BASELINE QUANTITATIVE LEVELS OF HEPATITIS B CORE ANTIBODY IN CHILDREN PREDICTS SPONTANEOUS HBeAg SEROCONVERSION DURING FOLLOW-UP

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Background: Whether baseline quantitative hepatitis B core antibody (anti-HBc) in children predicts HBeAg seroconversion in the long-term natural history of chronic hepatitis B virus (HBV) infection remains unclear. This study was aimed to investigate the correlations between anti-

HBc and clinical parameters in the childhood, especially the effect of baseline anti-HBc level to predict spontaneous HBeAg seroconversion during follow-up.

Methods: Children with untreated HBeAg positive chronic HBV infection were followed longitudinally. Anti-HBc level was determined by a double-sandwich immunoassay. The impacts of anti-HBc levels on the nature course of chronic HBV infection, including elevation of ALT levels and HBeAg seroconversion were assessed. Other factors influence HBeAg seroconversion such as gender, HBV vaccination history, and maternal HBV status were also studied.

Results: A total of 225 children (134 male) were followed for 17.8 ± 5.9 years with initial ages of 11.6 ± 3.6 years. Among them, 115 cases achieved spontaneous HBeAg seroconversion (51.1%) during follow-up. Anti-HBc levels were positively correlated with ALT levels ($r = 0.523$, $p < 0.001$). Baseline anti-HBc level > 500 IU/mL during childhood predicted spontaneous HBeAg seroconversion during follow-up (hazard ratio, HR 2.78, $p < 0.001$, based on multivariate survival analysis)

Conclusions: Baseline anti-HBc level > 500 IU/mL in children with chronic HBV infection predicted spontaneous HBeAg seroconversion during follow-up.

Note: Correction requested / not provided.

*599 SIMULTANEOUS DETECTION OF MUTATIONS IN CHOLESTASIS GENES AND NOVEL PATHWAY RELATED GENES USING TARGET-ENRICHMENT NEXT GENERATION SEQUENCING

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Background: Diagnosis of genetic cholestasis diseases or syndromes is a great clinical challenge because of common symptoms, signs and pathology presentation. Conventional sequencing based on phenotype-predicted candidate genes has been time and cost consuming. We aimed to develop an efficient method to identify known and novel cholestasis genes using next-generation sequencing.

Methods: A target-enrichment next generation sequencing cholestasis panel (TE-NGS cholestasis panel) including analysis of 34 known cholestasis/jaundice related genes, and 18 cholestasis pathway-related genes were developed. The whole genomic regions of target genes were captured and libraries were paired-end sequenced.

Results: The 23 previously identified genetic mutations identified by Sanger sequencing in 19 patients were confirmed using this panel. We further tested 54 patients with pediatric cholestatic liver disease. A total of 45 disease-causing mutation/variants in 14 different genes were found in 25/54 tested patients. A higher yield of genetic diagnosis was obtained in 19 or 24 patients (79.2%) with distinct phenotypic or biochemistry diagnosis, including progressive familial intrahepatic cholestasis (PFIC), inborn errors of bile acid synthesis, Wilson's disease, and polycystic disease. A lower yield of genetic diagnosis was obtained from 7/31 (22.6%) of patients with cholestasis that may be caused by heterogeneous causes, such as autoimmune hepatitis/cholangitis, neonatal hepatitis, neonatal liver failure, cholestasis in extreme prematurity. A newly recognized genetic cholestatic disease: NR1H4 (FXR) in the pathway-related gene list was identified in one patient with neonatal cholestasis with early liver failure and mortality. A novel phenotype was found in one patient with benign recurrent intrahepatic cholestasis with compound heterozygous CFTR mutations. Of those patients without identifiable disease-causing variants/mutations, 14/29 (48.3%) were found to have at least one heterozygous genetic mutation with predicted functional significance, which may contribute partly in the disease pathogenesis.

Conclusions: This TE-NGS cholestasis panel provided high throughput detection of mutations in multiple cholestasis genes, as well as may identify novel disease-causing genes or phenotypes. The panel shows great potential to facilitate diagnosis and research of cholestatic diseases.

*600 EFFICACY AND SAFETY OF SOFOSBUVIR IN HEPATITIS C INFECTION IN CHILDREN

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Hepatitis C is endemic in world population with a prevalence of 170 million. Chronic HCV infection leads to cirrhosis and hepatocellular carcinoma over decades. Standard therapy with pegylated interferon and Ribavirin has variable efficacy, with poor response against HCV genotypes 1 and 4; and serious side effects like cytopenias, thyroid dysfunction and anorexia. This study was planned to evaluate the efficacy and safety of oral Sofosbuvir and Ribavirin combination in children with hepatitis C infection.

Methods: The study was planned as a randomized controlled trial. Patients PCR positive for HCV were randomized to study group (sofosbuvir and ribavirin) and control group (pegylated interferon α -2a and ribavirin). Of the first 8 patients in control group, 1 with genotype 1 failed to respond at 12 weeks while one with genotype 3 showed EVR but end of treatment PCR was positive while 1 patient developed cytopenias requiring cessation of therapy. However, no such side effects were observed in study group and all patients showed RVR. Afterwards, study design was changed to uncontrolled open labeled trial and all patients subsequently included in the study were given sofosbuvir 400 mg once daily and ribavirin 10-15mg/kg/day. Monthly follow-up was done and PCR was done at 4 weeks and end of treatment. If PCR was positive at 4 weeks, it was repeated at 12 weeks also.

Results: At the moment, 19 patients, 10 (52.63%) male and 9 (47.37%) female with mean age 10.76 ± 2.76 years have completed the treatment. Thalassemia major was present in 4 (21.05%) patients, 1 (5.26%) had von-Willibrand disease, 1 (5.26%) each treated for Hodgkin's disease, non-Hodgkin's lymphoma, rhabdomyosarcoma and 1 (5.26%) had Down Syndrome. Vertical transmission was documented in 3 (15.79%) patients while 7 (36.84%) had history of blood component transfusion, 2 (10.53%) had history of surgery and 1 (5.26%) patient had tattooing. The rest of the patients had no identifiable risk factors. 16 (84.21) patients had genotype 3 while 3 (15.79%) had genotype 1. All patients had normal pre-treatment blood counts except 1 who had hemoglobin 8g/dl; while 10 (33.33%) had elevated pre-treatment ALT (mean 86.63 ± 68.15 iu/mL). All patients had normal end of treatment blood counts and ALT (mean 17.89 ± 5.7 liu/mL). All patients with genotype 3 achieved RVR while 2 patients with genotype 1 achieved RVR but 1 achieved EVR. All patients had negative PCR at the end of treatment. One patient with developmental delay achieved RVR but dropped out at 8 weeks because of intractable headache. She remained HCV PCR negative till 06 months after stopping treatment. No major adverse effects were observed in rest of the patients. 4 patients had headache that improved without any treatment gradually and 1 developed constipation requiring an oral laxative.

Conclusion: Sofosbuvir and ribavirin in combination has 100% response in HCV genotypes 1 and 3. No major undesirable side effects are observed in the short-term.

601 ANTIVIRAL EFFICACY OF TENOFOVIR MONOTHERAPY COMPARED WITH LAMIVUDINE MONOTHERAPY IN CHILDREN WITH NUCLEOS(T)IDE-NAÏVE CHRONIC HEPATITIS B

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Purpose: Tenofovir disoproxil fumarate (TDF) has a higher genetic barrier to antiviral resistance and a more potent antiviral efficacy than lamivudine (LMV). The aim of the study was to compare the therapeutic efficacy of TDF with that of LMV in children and adolescents with nucleos(t)ide-naïve chronic hepatitis B (CHB).

Methods: Eight patients (age range of 10.1-20.9 years with a mean age of 13.9 ± 3.4) with HBeAg-positive chronic hepatitis B were first treated with TDF (TDF group), when confirmed to be in the immune-clearance phase. Pre-treatment HBV-DNA level was over 10^5 IU/mL. The TDF group was compared with the control group comprising 23 patients (age range of 9.4-16.5 years with a mean age of 12.8 ± 2.0) initially treated with LMV. HBV-DNA titer decrement ($>3 \log_{10}$ IU/mL) was monitored after the initiation of each treatment, and compared with pre-treatment HBV-DNA levels. HBV-DNA clearance (<357 IU/mL) was also analyzed. The follow-up period was 48 weeks.

Result: The mean duration for HBV-DNA titer decrement ($>3 \log_{10}$ IU/mL) was 6.0 weeks in all 8 patients (100%) of the TDF group, but was 17.9 weeks in 17/23 patients (73.0%) of the LMV group. The HBV-DNA clearance (<357 IU/mL) in the TDF and LMV groups was respectively, as follows: 75.0% (6/8) and 30.4% (7/23) at 12 weeks ($p=0.043$), 87.5% (7/8) and 43.5% (10/23) at 24 weeks ($p=0.045$), and 100% (8/8) and 52.2% (12/23) at 48 weeks ($p=0.028$). After initiation of the treatment, 12 of 23 patients (54.5%) in the LMV group were found to have an inadequate virologic suppression (>2000 IU/mL) at 24 weeks ($p=0.023$). This was not the case in the TDF group

Conclusion: TDF monotherapy shows a significantly more effective virologic response than LMV monotherapy in children with nucleos(t)ide-naïve CHB.

Keywords: Therapeutic effects, Antiviral agents, Tenofovir, Lamivudine, Chronic hepatitis B

602 CLINICAL VARIABILITY FOLLOWING PARTIAL EXTERNAL BILIARY DIVERSION IN FAMILIAL INTRAHEPATIC CHOLESTASIS 1 DEFICIENCY

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Objectives: Familial intrahepatic cholestasis 1 (FIC1) deficiency is caused by a mutation in the ATP8B1 gene. Partial external biliary diversion (PEBD) is pursued to improve pruritus and arrest disease progression. Our aim is to describe clinical variability following PEBD in FIC1 disease.

Methods: We performed a single-center, retrospective review of genetically confirmed FIC1 deficient patients who received PEBD. Clinical outcomes following PEBD were cholestasis, pruritus, fat-soluble vitamin supplementation, growth, and markers of disease progression that included splenomegaly and aspartate aminotransferase-to-platelet ratio index (APRI).

Results: Eight patients with FIC1 disease and PEBD were included. Mean follow-up was 32 months (range 15-65 months). Following PEBD, total bilirubin was <2 mg/dL in all patients at 8 months after surgery, but 7/8 subsequently experienced a total of 15 recurrent cholestatic events. Mean pruritus score decreased (4.3 vs. 1.5; $p<0.0001$), but itching exacerbation occurred during cholestatic episodes. High dose fat-soluble vitamin supplementation persisted, with increases needed during cholestatic episodes. Weight Z-scores improved (-3.4 to -1.65 , $p<0.01$). Splenomegaly did not worsen or develop and 1 patient developed an APRI score of >0.7 suggesting development of fibrosis 24 months following PEBD.

Conclusions: Clinical variability is evident among genetically defined FIC1 deficient patients following PEBD, even among those with identical mutations. Recurrent, self-limited episodes of cholestasis and pruritus is reminiscent of the benign recurrent intrahepatic cholestasis phenotype. Despite diversion of bile from the intestinal lumen, weight gain improved while fat soluble vitamin requirements persisted. Significant progression of liver disease was not evident during follow-up.

603 FREQUENCY AND RISK FACTORS FOR VARICEAL HEMORRHAGE IN CF FOUNDATION REGISTRY PATIENTS WITH CYSTIC FIBROSIS CIRRHOSIS

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Cirrhosis and portal hypertension occur in 5-10% of patients with CF; variceal bleeding (VB) is a common presentation. We analyzed VB and associated risk factors in subjects with cirrhosis from the CFF registry database. Kaplan-Meier was used to estimate 10 year incidence rate for VB, adverse liver outcomes (hemorrhage, transplant, or liver death) and all-cause mortality rate. Cox proportional hazard model with time-dependent covariates was used to study risk factors for these events. From 2003-2012, 943 participants (41% female, mean age 18.3 years) were newly reported to have cirrhosis and had follow-up. 24.5% were on insulin and 85% had pseudomonas (PA). 73 subjects had reported VB. 38 had the first VB recorded on the same date as cirrhosis. In 35, VB was reported after diagnosis of cirrhosis, with 10-year cumulative VB rate of 8.8%. Worse lung function (HR 1.16, 95% CI, 1.05, 1.28 for 10% decrease in FVC) and CFRD (HR 2.09, 95% CI, 1.28, 3.44) were associated with higher risk of adverse liver outcomes, while history of PA was associated with a 51% reduction in risk. The estimated 10-year cumulative rate of liver-related events was 21.2% and overall death rate was 39.2%. Mortality was not increased in cirrhotic patients with VB compared to those without (HR 1.072, CI, 0.568, 2.022). Risk factors for mortality included older age at cirrhosis diagnosis, worse lung function, underweight and insulin-dependent diabetes; PA was associated with lower risk. Subjects with VB history were more likely to undergo liver transplantation; death rate in transplanted subjects was 24% vs. 20% in those who were not transplanted. VB is a common complication of CF cirrhosis and can announce the diagnosis; it does not affect all-cause mortality. Better data regarding natural history and management of VB in CF cirrhosis are needed.

604 HBEAG(+) IMMUNE TOLERANT PHENOTYPE IS RARE AMONG CHILDREN IN THE LARGEST NORTH AMERICAN COHORT WITH CHRONIC HEPATITIS B VIRAL INFECTION

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Background: Chronic hepatitis B (HBV) infection progresses through virologic phases, or phenotypes, characterized by differences in viral load, HBeAg status, and alanine aminotransferase levels (ALT). Phenotypes of HBV infection may influence prognosis and response to therapy, although many aspects of these phenotypes remain poorly understood. A large proportion of children with HBV are thought to be "immune tolerant" (IT) phenotype, which is defined as HBeAg(+) with high viral load and normal ALT levels. IT children are thought to have slow progression of liver injury, and are unlikely to respond to treatment with viral clearance.

Objective: Determine the characteristics and significance of phenotypes in the largest, well characterized cohort of US and Canadian children with HBV.

Methods: We examined baseline enrollment data of pediatric subjects in the Hepatitis B Research Network. Phenotype definitions were: Inactive carrier (IC): (HBeAg(-), low DNA, normal ALT), immune tolerant (IT): (HBeAg(+), high DNA, normal ALT), or chronic hepatitis B (CHB): HBeAg(-) or (+), high ALT. HBV DNA levels for CHB definitions were >10⁴ IU/mL for HBeAg(-) and >10⁵ for HBeAg(+). Past definitions of IT were based on upper limit of normal (ULN) ALT levels from local laboratories. New, more accurate, population based, data sets for ULN ALT levels are lower than previously believed (Table 1).

Results: 323 subjects were analyzed with 242 HBeAg(+) and 81 HBeAg(-). 97% of HBeAg(+) had HBV DNA above 105IU/mL. If local lab ULN ALT levels were used, then 36% met the IT phenotype, but if more accurate absolute ALT levels were used, then only 37 (11%) were IT (Table 2). Of these 37 IT, 81% were female, 97% Asian, 87% adopted and 57% genotype B. 198 of 242 (82%) of HBeAg(+) subjects had elevated ALT and HBV DNA levels, the definition of HBeAg(+) CHB, and were 84% Asian, 49% adopted, but no majority genotype. 84% of HBeAg(-) subjects had HBV DNA below 104 IU/mL and therefore not CHB. Of these, 51 of 68 (75%) had elevated ALT levels using updated ULN, and therefore, an indeterminant phenotype. No genotype dominated this indeterminant group, and 37% were adopted.

Conclusions: Most HBV infected children in North America are HBeAg(+) with high viral load. The IT phenotype with normal ALT levels is rare, and most are Asian adoptees with genotype B. Other phenotypes are more mixed genotypes and race. Past data might need re-interpretation with regard to prognosis and treatment response of children with ALT levels now recognized to be elevated, but previously interpreted as normal. Most HBeAg(-) children have an indeterminant phenotype of low viral load, but elevated ALT levels. These children need further study to define the course of their disease. Longitudinal follow-up of this cohort will explore the outcomes of various phenotypes and the transitions between phenotypes.

Table 1

ALT ULN IU/L	Age	*Updated		Previous Protocol		Typical Local Lab	
		Male	Female	Male	Female	Male	Female
	<1y	33	33	60	55	30	30
	1-12y	25	25	40	35	32	24
	13-17y	25	22	40	35	46	31

Characteristic	Phenotype					
	Total (N=323)	IT (N=37)	CHB HBeAg(+) (N=198)	CHB HBeAg(-) (N=12)	IC (N=17)	Indet (N=59)
Age (yrs), mean	10.5	9.2	9.9	11.5	12.3	12.8
Sex, %						
Male	42.1	18.9	41.9	50.0	41.2	55.9
Female	57.9	81.1	58.1	50.0	58.8	44.1
Race, %						
White	7.8	0.0	3.6	16.7	23.5	20.7
Black	10.9	2.7	9.1	16.7	29.4	15.5
Asian	78.2	97.3	83.8	58.3	47.1	60.3
Other	3.1	0.0	3.6	8.3	0.0	3.4
Adopted, %	52.0	86.5	48.5	33.3	70.6	40.7
BMI-for-age percentile, mean	53.7	42.6	55.3	49.8	56.9	55.5
HBV Genotype, %						
A	3.4	0.0	4.0	0.0	5.9	3.4
B	31.6	56.8	36.9	8.3	5.9	10.2
C	22.6	24.3	24.7	33.3	17.6	13.6
D	13.0	0.0	8.1	16.7	29.4	32.2
Other	4.6	2.7	2.5	25.0	0.0	10.2
Not Determined	24.8	16.2	23.7	16.7	41.2	30.5

605 THE IMPACT OF microRNA DYSREGULATION IN LIVER CARCINOGENESIS IV FROM LIVER STEM/PROGENITOR CELLS TO CANCER STEM CELLS IN HUMAN

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Objectives: This study aimed to elucidate the roles of microRNA (miRNA) on the carcinogenic process from liver stem/progenitor cells (LSPCs) to cancer stem cells (CSCs) of hepatoblastoma (HB) and hepatocellular carcinoma (HCC).

Methods: We assessed the LSPCs markers in human HB, HCC tumor samples and hepatoma cell lines by immunohistochemistry staining, and validated their roles on CSCs characteristics. The difference of miRNAs between LSPCs marker-carrying human HB, HCC, and fetal hepatocyte were assessed by miRNA microarray, and confirmed by quantitative real-time polymerase chain reaction. The roles of identified miRNAs on CSCs characters and clinical data were then studied.

Results: EpCAM was identified to be the most prevalent LSPCs' marker in both human HB and HCC tumors and hepatoma cell lines. EpCAM-positive HB and HCC cells had greater self-renewal and tumorigenicity ability than EpCAM-negative counterparts and EpCAM-positive fetal hepatocytes. In comparison to EpCAM-positive fetal hepatocyte, down-regulation of miR-126, miR-144, and miR-451 in EpCAM-positive HCC cells, and miR-126 in EpCAM-positive HB cells were confirmed. In EpCAM-positive fetal hepatocytes, the miR-126 expression level increased with increasing gestational age. Sphere and colony formation ability decreased in HepG2 HB cells transfected by miR-126-mimic, and Huh7 HCC cells by miR-126-mimic, miR-144-mimic, and miR-451-mimic. The miR-126, miR-144, and miR-451 increased the apoptosis in hepatoma cells. High HCC pathologic grade, multifocal HCC, and presence of distant metastasis of human HCC are also associated with lower miR-126, miR-144, and miR-451 expression levels, respectively, ($p < 0.05$). Lower miR-451 levels in HB patients is associated with younger age at diagnosis ($p = 0.001$).

Conclusions: The miRNAs dys-regulation of EpCAM-positive LSPCs during development and differentiation is associated with the anti-apoptotic, proliferation, and carcinogenesis of HB and HCC CSCs in human.

Keywords: hepatoblast, hepatoblastoma, hepatocellular carcinoma, fetal liver stem/progenitor cell, cancer stem cell

606 ABERRANT TH1 IMMUNE RESPONSES ACCELERATE LIVER FIBROSIS OF BILIARY ATRESIA THROUGH THE IFN- γ /STAT1 PATHWAY

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Regulatory T cells (Tregs) and CD4+ T helper (Th) cells play important roles in bile duct injury of biliary atresia (BA). However, the dynamics of these cells and their impacts on liver fibrosis in BA remain undefined. Between 2013 and 2015, 106 patients at different stages of BA were enrolled in this study. Flow cytometry, magnetic cell sorting and live cell imaging were used to characterize lymphocytes from BA patients.

Successive sections from liver biopsies of BA patients were applied for immuno-staining. Persistent deficiency in Tregs and rTregs was observed along with aberrant Th1, Th2 and Th17 frequencies in BA. The levels of peripheral blood and intrahepatic Th1 cells positively correlated with the stage of liver fibrosis. Furthermore, Th1 cells were enriched in the livers and localized in close proximity to activated hepatic stellate cells (HSCs) and areas of fibrosis. In culture, Th1 cells activated HSCs through the IFN- γ /STAT1 pathway. In addition, phagocytosis of Th1 cells by HSCs also contributed to HSCs activation. Despite the intrinsic pro-fibrogenic effects of Tregs, the Th1-mediated activation of HSCs was attenuated by Tregs. For Treg subsets, BA patients manifested a decrease in rTreg subset with concomitant increase in aTreg subset expressing high level of CTLA-4. Of note, the CTLA-4 expression by Tregs correlated with their ability to inhibit cytokines secretion by Th cells.

Conclusions: Aberrant Th1 cells-associated responses in BA accelerate liver fibrosis through the IFN- γ /STAT1 pathway, and phagocytosis of Th1 cells represents a potentially important mechanism regulating the development of hepatic fibrosis. The decreased inhibition by Tregs in BA contributes to the persistence of activated Th1 cells, which may promote the progression of liver fibrosis.

607 CHARACTERISTIC AND OUTCOME OF DENGUE FEVER ASSOCIATED LIVER FAILURE IN CHILDREN: A CASE SERIES

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Background: Dengue fever is common in Southeast Asia although liver failure is a rare complication with up to 50% mortality rate reported in children [1].

Objective: To evaluate the characteristics and treatment outcome of dengue fever associated liver failure (DFALF) in a case series of 4 pediatric patients. DFALF was defined as severe liver dysfunction with peak INR>2, with concurrent dengue infection.

Material and methods: Patients with DFALF, admitted to a tertiary pediatric centre in Singapore over a 6-year period (January 2009 to December 2015) were identified from the Gastroenterology and Infectious Disease database. Case records were retrospectively reviewed.

Results: Four patients, all boys, age 5 months to 6 years, presented at the acute febrile phase of illness with Dengue Shock Syndrome. Table 1 shows the characteristics, management and outcome of all 4 patients. Aspartate Transaminase (AST) and Alanine Transaminase (ALT) peak at day 4 to 7: median ALT 1871.5 \pm 917 u/L, median AST 7802.5 \pm 5453.8 u/L. Median peak International Normalised Ratio (INR) was 2.9 \pm 1.6, median peak ammonia 106 \pm 144.6 mmol/L, median peak lactate 7.4 \pm 8.4 mmol/L. All patients had hepatomegaly and mild conjugated hyperbilirubinaemia: median peak total bilirubin 73.5 \pm 36.9 μ mol/L. Two patients received N-Acetylcysteine. One patient received intravenous dexamethasone for dengue associated Hemophagocytic Lymphohistiocytosis (HLH). All achieved full recovery with early supportive treatment. Liver function normalized at mean 6.25 \pm 2 days from onset of liver failure. INR normalized at mean 13 \pm 2 days of illness.

Conclusion: Patients with DFALF can achieve normalization of liver function and full recovery with early supportive treatment.

References: 1. Chongsrisawat V, Hutagalung Y, Poovorawan Y. Liver function test results and outcomes in children with acute liver failure due to dengue infection. *Southeast Asian J Trop Med Public Health* 2009;40:47-53.

Case No.	Age	Clinical presentation	Max ALT (u/L)	Max AST (u/L)	Max GGT (u/L)	Max INR	Max bil / direct bil (umol/L)	Min Alb (g/L)	Max Lactate (mmol/L)	Max ammonia (mmol/L)	Max LDH (u/L)	Final diagnosis	Treatment
1	9m	Fever, vomiting, lethargy, status epilepticus	1441	2970	129	2.2	24/18	18	2.08	-	-	Dengue shock syndrome (severe dengue)	• Supportive
2	6y	Fever, headache, coffee ground vomiting, abdominal pain, diarrhoea, shock	2161	11725	128	5.5	102/57	22	10.6	106	2364	Dengue shock syndrome (severe dengue) with hepatic encephalopathy	• Supportive • IV NAC
3	5y	Fever, abdominal pain and rash	1582	3880	867	2.1	95/79	21	4.2	103	7812	Dengue shock syndrome with dengue associated HLH	• Supportive • IV dexamethasone for HLH, subsequently completed 4 week of weaning doses of corticosteroids
4	5m	Fever, vomiting, status epilepticus	3453	13754	290	3.6	52/44	17	20.8	355	7082	Dengue shock syndrome (severe dengue) complicated by dengue associated encephalitis and acute leukaemoid reaction	• Supportive • IV NAC • IV Sodium Benzoate for hyperammonaemia

ALT= Alanine aminotransferase AST= Aspartate aminotransferase GGT=Gamma-glutamyl transferase PT= Prothrombin time Bil= bilirubin Alb=albumin
LDH= Lactate dehydrogenase HLH= Hemophagocytic Lymphohistiocytosis NAC=N-acetylcysteine Max= Maximum Min= Minimum IV= intravenous

Table 1: Characteristics, management and outcome of children with dengue fever-associated liver failure

608 EFFECT OF SEBELIPASE ALFA ON SURVIVAL AND LIVER FUNCTION IN INFANTS WITH RAPIDLY PROGRESSIVE LYSOSOMAL ACID LIPASE DEFICIENCY: 2-YEAR FOLLOW-UP DATA

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Sebelipase alfa (SA) prolongs survival in infants with Lysosomal Acid Lipase Deficiency (LAL-D), compared with historical controls. Two-year survival data are presented here from an ongoing phase 2/3 study of SA in infants with LAL-D, providing insight into extent of survival, and details of weight, functional development and hematological effects over extended duration. All 9 patients enrolled had significant liver dysfunction at baseline; 8 had early growth failure. Median (range) age at SA treatment initiation was 3.0 (1.1-5.8) months. As of 26-July-2015, 5 subjects remain on study and have survived beyond age 2 years (range, 2 years 5 months-4 years 7 months) with a mean time in the trial of 33.8 months, and all 5 continue to receive SA. The oldest subject has been receiving SA for 4 years 3 mos. Surviving patients demonstrate improvements in median percent change (range) for serum alanine aminotransferase -45.59% (-68.46% to 80.00%), aspartate aminotransferase -

39.36% (-65.33% to -4.26%), hemoglobin 29.79% (4.21 to 61.11%), albumin 11.84% (3.81% to 73.68%), median weight percentile from 3.59% baseline to 35.09%, and improvement in gastrointestinal symptoms and reduction in hepatosplenomegaly. Median percent change (range) in platelets was 0.39% (-10.59 to 97.69%). At the most recent assessments (Week 74-218) of the Denver II developmental screening test, 4/5 ongoing subjects scored normal, with one subject suspect. One patient experienced treatment-related serious AEs (tachycardia, pallor, chills, and pyrexia) that resolved; no patient discontinued treatment because of tolerability or infusion reactions. Of 7 patients tested, 4 had detectable anti-drug antibody titers; 2 of whom developed neutralizing antibodies; all 4 continue treatment. In conclusion, SA is associated with a substantial survival benefit, a favorable safety profile, and now improvement in disease activity parameters sustained over prolonged treatment in infants with LAL-D can be demonstrated. The majority of patients demonstrated normal development.

609 ANTIVIRAL EFFICACY OF TENOFOVIR MONOTHERAPY COMPARED WITH TENOFOVIR PLUS LAMIVUDINE COMBINATION THERAPY IN CHILDREN WITH NUCLEOS(T)IDE-RESISTANT CHRONIC HEPATITIS B

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Purpose: Tenofovir (TDF) has a high genetic barrier to antiviral resistance such that it could be used alone or in a combination protocol as a rescue therapy for patients with nucleos(t)ide resistance. The aim of this study was to compare the therapeutic efficacy of TDF monotherapy with that of TDF plus lamivudine (LAM) combination therapy in children and adolescents with chronic hepatitis B (CHB) who had developed nucleos(t)ide resistance.

Methods: A total of 12 children and adolescents (eight male subjects; age range of 9.1-20.5 years, with a mean age of 15.3±4.1) with CHB were enrolled between April 2013 and July 2015. Either HBV-DNA or HBeAg was not cleared in all patients with clinical or sero-proven nucleos(t)ide resistance. The treatment protocol was switched to a rescue therapy including TDF, and the patients were divided into TDF monotherapy and TDF and LMV combination therapy groups. Six patients (two male subjects; age range of 10.7-20.5 and a mean age of 17.2±3.6) were treated with TDF monotherapy while the other six patients (six male subjects; age range of 9.1~18.1 and a mean age of 13.5±4.0) were treated with TDF and LMV. Prior to the rescue therapy, the distribution of HBV-DNA titer in the groups was as follows: over 104 IU/mL (two patients in the TDF group, three in the TDF and LAM group); 20-357 IU/mL (three patients in the TDF group, one in the TDF and LMV group); and non-detectable HBV-DNA titer (one in the TDF group - reconverted HBeAg, two in the TDF and LAM group - sustained low HBeAg level). The duration for HBV DNA clearance (<20 IU/mL) was compared in both groups (patients with initially undetectable titer levels were not counted).

Result: The duration of the HBV-DNA clearance (<20 IU/mL) was 25.0 weeks in four out of five HBV-DNA-positive patients in the TDF group. Conversely, 13.0 weeks elapsed for four out of four HBV-DNA-positive patients in the TDF and LMV group. At 12 weeks after the initiation of treatment, HBV-DNA titer decreased by over 3 log₁₀ IU/mL in 40% (2/5) and 100% (4/4) patients of the TDF and the TDF and LMV groups, respectively. At 24 weeks after the initiation of treatment, HBV-DNA clearance (<20 IU/mL) occurred in 60% (3/5) and 100% (4/4) patients in the TDF and the TDF and LMV groups, respectively. HBV clearance occurred in all patients at 48 weeks after the initiation of the rescue therapy.

Conclusion: TDF monotherapy or TDF and LMV combination therapy could be useful in children and adolescents with CHB who have developed nucleos(t)ide resistance or have not achieved complete remission.

Keyword: Therapeutic effects, Antiviral agents, Tenofovir, Lamivudine, chronic hepatitis B, Nucleosides resistance

*610 BIRTH WEIGHT IS AN IMPORTANT LIFE STAGE FACTOR FOR CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Objective: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children in the United States.

Studies have suggested a possible connection between birth weight and conditions that are risk factors for NAFLD such as obesity or insulin resistance. We hypothesized that birth weights at both tails of the normal curve, either low or high, influence the risk for NAFLD. The study aims were to evaluate: 1) the distribution of birth weight in children with NAFLD compared to the general U.S. population and 2) the relationship between birth weight and severity of NAFLD.

Methods: We included children with biopsy-proven NAFLD enrolled in the NASH CRN. Liver biopsies were reviewed centrally by the Pathology Committee. Birth weights were recorded and categorized as: low birth weight (LBW), 1,500 to 2,499 grams, normal (NBW), 2,500 to 3,999 grams, or high (HBW), ≥4,000 grams. The distribution of birth weight categories was compared to national data from the CDC. The odds ratios (OR) for steatosis severity, NASH, and advanced fibrosis were calculated for children with LBW or HBW compared to children with NBW as the reference group, and were controlled for age, sex, race/ethnicity, as well as height, and weight at the time of diagnosis of NAFLD. Results: We included 538 children with NAFLD with a mean age of 13 years of whom 143 (27%) had definite NASH histologically. Advanced fibrosis was present in 77 (14%). Children with NAFLD had a significantly different distribution of birth weights compared to the general population of the United States with overrepresentation of both low and high birth weight (LBW 9.3%, NBW 75.8%, HBW 14.9% vs. LBW 6.1%, NBW 83.5%, HBW 10.5%; $p < 0.0001$). Among children with NAFLD, there was no difference in age, ethnicity or gender by birth weight category. At the time of the diagnosis of NAFLD, there was, however, a significant ($p < 0.001$) difference in height and weight by birth weight category. Children in the HBW group were significantly heavier and taller than children in the NBW group, while children in the LBW were significantly shorter and lighter than children in the NBW group. Children with HBW had significantly greater odds of having more severe steatosis (OR 1.83, 95% CI, 1.15-2.91) and to have frank NASH (OR 2.03, 95% CI, 1.21-3.41) than children with NBW. In contrast, children with LBW had significantly greater odds (OR 2.65; 95% CI, 1.26-5.58) of having advanced fibrosis than children with NBW.

Conclusion: Birth weight involves both maternal and *in utero* factors that may have long-lasting consequences. Children with both LBW and HBW may be at increased risk for developing NAFLD. Among children with NAFLD, those with LBW or HBW appear to be at increased risk for more severe disease. These data illustrate areas for further exploration of the underlying pathogenesis of pediatric NAFLD.

611 IMPACT OF THE ASSOCIATION OF COELIAC DISEASE IN CHILDREN WITH AUTOIMMUNE HEPATITIS

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Celiac patients are at risk to develop an autoimmune liver disease. The association of Autoimmune Hepatitis (AIH) and Coeliac Disease (CD) has been described in a limited number of patients. The prevalence is estimated between 4 to 11.5% according to different population.

Aim: To evaluate prevalence of celiac disease in patients with Autoimmune Hepatitis and analyze clinical features, histological characteristic and the course of this association.

Materials and Methods: A retrospective and transverse study was realized in pediatric patients with AIH associated with CD, between 1 year to 18 years, from 1989 to 2014. AIH diagnosis was realized according to the diagnostic criteria of the International Group of Autoimmune Hepatitis and liver histology. CD was studied by transglutaminase ticular (TG) antibodies and Marsh's classification for the diagnostic confirmation.

Results: 152 patients with AIH were evaluated. 13/152 (8.55%) presented with association AIH (11/13 Type 1, 1/13 Type 2 and 1/13 Gigantocellular hepatitis) with CD. In 7/13 (54 %) presented other associated diseases (hypothyroidism, diabetes, and IgA deficit). The median age of the AIH associated to celiac disease was 10.3 years ($r=-2.3 - 18$ years). The histology showed necroinflammatory activity (piecemeal necrosis) in 100% of the patients, necrosis of the lobule in 87.5%, injury ductal in 62.5% and fibrosis in 50%. Histological characteristics were compared with other 13 AIH patients. It showed a statistically significant difference ($p=0.0399$) in the variable Necrosis intralobulillar, demonstrating a severe activity in this association. All received a gluten-free diet and immunosuppressant treatment with prednisone and azathioprine in 9/13 and cyclosporine in 3/13; one patient (Gigantocellular hepatitis) received Anti CD 20. Two patients demonstrated bad adherence to diet and immunosuppressant treatment leading to cirrhosis and later to transplant.

Conclusion: Autoimmune liver disease is associated with celiac disease, but they might remain undiagnosed. The prevalence of AIH and CD association in our population is 8.5%; however, liver severe inflammatory activity was shown, but with good evolution. Patients with autoimmune liver disease might have a hidden celiac disease, suggesting a rigorous check of this. The diet and immunosuppressant treatment adherence are the essential requirements for a good prognosis.

612 THE CHRONIC REGULATION OF LEPTIN METHYLATION BY MELATONIN IN PROGRAMMING LIVER STEATOSIS

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Melatonin can rescue a prenatal dexamethasone exposed liver with steatosis in young rats. In this study, we aimed to explore the mechanisms of adult chronic liver steatosis in prenatal dexamethasone exposure and examine whether melatonin can rescue the adult offspring with liver steatosis. Pregnant at gestational day 14-21, one group of Sprague-Dawley rats was administered intraperitoneal dexamethasone (DEX). Another group of rats received prenatal dexamethasone and melatonin treatment between gestational day 14 and post-natal day ~120 (DEX+MEL). Chronic programming effects in the liver were assessed at post-natal day ~120. Liver steatosis was increased in DEX than vehicle group and decreased in (DEX+MEL) group. The expression of leptin and the leptin receptor were decreased in DEX and increased in DEX+MEL group by liver RT-PCR and leptin by liver Western blot study. Increased TNF- α and IL-6 protein expressions were seen in DEX group compared with vehicle group and decreased in DEX+MEL group. Liver DNA methyltransferase activity and leptin methylation were increased in DEX and decreased in DEX+MEL group. The present study showed that prenatal dexamethasone induces liver steatosis at ~120 days via altered leptin expression and liver inflammation, not cell apoptosis. Melatonin may reverse leptin methylation and leptin expression, decrease inflammation, and chronic liver steatosis.

613 TRANSIENT ELASTOGRAPHY AND DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN COMPARISON TO LIVER BIOPSY FOR ASSESSMENT OF LIVER FIBROSIS FOR CHILDREN WITH CHRONIC LIVER DISEASE

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Introduction: Evaluation of liver fibrosis is an important step in managing children with chronic liver diseases. Liver biopsy for assessing liver fibrosis in children with chronic liver diseases pertains several risks specially if there is bleeding tendency. Transient elastography (TE) and diffusion-weighted magnetic resonance imaging (DW-MRI) as noninvasive tools can be used in staging liver fibrosis and evaluating the disease activity.

Aim of Study: To evaluate transient elastography and diffusion-weighted magnetic resonance imaging as noninvasive tools in staging liver fibrosis and evaluating the activity in comparison with liver biopsy for children with chronic liver diseases.

Patients and Methods: A total of 81 children with chronic hepatitis C virus (HCV) with a mean age of 12.01 ± 3.95 years (55 males and 26 females), underwent liver stiffness measurement (LSM) using TE and measurement of apparent diffusion coefficient (ADC) of liver and spleen using DW-MRI. Liver biopsies were evaluated for fibrosis by Ishak score. LSM, liver and spleen ADC were compared in different fibrosis stages and were correlated with fibrosis and other studied variables using spearman correlation.

Results: The majority of patients had moderate fibrosis (73.5%) and the remaining (26.5%) had mild fibrosis, and none had severe fibrosis or cirrhosis. The majority of patients (68.8%) had mild activity, while only 7.8% had moderate activity. Ishak scores had a significant direct correlation with LSM ($p=0.008$), but negatively with both liver and spleen ADC with no statistical significance ($p=0.086$ and 0.145 respectively). Similarly, histopathological activity correlated significantly with LSM ($p=0.002$) but not with liver or spleen ADC ($p=0.84$ and 0.98 respectively).

Conclusion: LSM using TE appears more reliable than ADC using DW-MRI in predicting liver fibrosis. According to these results it is worthwhile to undertake further studies on larger population of children with different chronic liver diseases.

Key words: Pediatric Chronic Liver diseases, Chronic hepatitis C, Children, Liver Fibrosis, Liver Stiffness, Transient Elastography, Diffusion-Weighted Magnetic Resonance Imaging.

614 *INSULIN RESISTANCE IN CHILDREN WITH CHRONIC HEPATITIS C AND ITS ASSOCIATION WITH RESPONSE TO TREATMENT*

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Background: Aim of the study was to evaluate the association between insulin resistance and response to the treatment given in pediatric patients with chronic hepatitis C.

Methods: Twenty-six patients with chronic hepatitis C (mean age: 12.5 ± 1.96 years, M/F:3.33) were involved in the study. Fasting glucose, insulin, and c-peptide levels, HOMA-IR, QUICKI were assessed. The association between these parameters and response to the treatment given was determined.

Results: Five (19.2%) of the total patients, 2 (21.4%) of the patients with response to treatment and 3 (16.6%) of the patients without response to treatment had IR ($p=1.00$). No significant differences were obtained between the patients with response to the treatment and without response to treatment in terms of fasting glucose, insulin, and c-peptide levels, IR, HOMA-IR, and QUICKI values ($p>0.05$).

Conclusion: No significant association was established between insulin resistance and response to treatment in children with chronic hepatitis C who were treated with interferon-alpha and ribavirin.

Key words: Children; hepatitis B; hepatitis C; HOMA-IR; insulin resistance.

*615 *ASSESSMENT OF THE UTILITY OF DIFFERENT SCREENING STRATEGIES FOR NAFLD IN OBESE CHILDREN AND ADOLESCENTS: REAL LIFE DATA FROM A WEIGHT MANAGEMENT PROGRAM*

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children. Yet, there is currently no agreement on whether to screen for NAFLD in children at risk, and the appropriate tests to do so. While the American academy of pediatrics (AAP) recommends screening for NAFLD using alanine aminotransferase (ALT) in obese and overweight children with risk factors, more recent European guidelines (ESPGHAN) proposed using both ALT and abdominal ultrasound (US). Furthermore, the cutoff values for ALT as a screening tool for NAFLD are not well defined. The aim of this study was to assess the prevalence of NAFLD in obese children based on screening strategies that are recommended by different practice guidelines.

Methods: Consecutive overweight and obese children seen at a multidisciplinary weight management program were included. Each child underwent a liver US and had ALT level measured at the time of their first visit. Three screening strategies were compared: AAP strategy using ALT above the local laboratory specific upper limit of normal (our laboratory cut-off is 45 U/L), ESPGHAN strategy using elevated ALT > 45 U/L and/or fatty liver on US, new strategy using sex-specific cut-off of ALT > 26 for boys/ ALT > 22 for girls and/or fatty liver on US. Other etiologies of chronic liver disease were ruled out. A univariable and multivariable analyses were performed to assess predictors of normal ALT in subjects with evidence of NAFLD on US.

Results: 344 overweight/obese children were included. The median age was 13 years, 55% were male and 58% were severely obese (BMI > 99th percentile). The majority were Caucasian (65%), 12% were Hispanic, 17% were Black and 6% were other races. The prevalence of NAFLD was as follows according to each screening strategy: AAP strategy 28.3%, ESPGHAN strategy 58.4%, and the new strategy 66.9%. NAFLD was present on US in 184/344 (53%). ALT was > 45 U/L in only 43.5% of children with evidence of fatty liver on US indicating that by relying on the AAP strategy, NAFLD would have been missed in 56.5% of obese children. Lowering the ALT cut-off to 26 for boys and 22 for girls would have identified 75% of children with NAFLD on US but 25% would have been missed. Univariable analysis indicated that children with NAFLD on US and low ALT (< 26/22) were less likely to have metabolic syndrome and insulin resistance as indicated by lower fasting insulin levels and HOMA-IR. Multivariable analysis confirmed that the absence of metabolic syndrome was associated with increased likelihood of having normal ALT in obese children with NAFLD on US (OR 2.6 (1.08, 6.4), $p=0.033$).

Conclusion: Screening for NAFLD in real life clinical settings should rely on both liver US and sex-specific ALT values to increase the identification rate of this rapidly rising chronic liver disease. Children with NAFLD on US and completely normal ALT were less likely to have metabolic syndrome.

616 *SERUM ZINC DISCRIMINATE INDETERMINATE : ACUTE LIVER FAILURE FROM WILSON'S DISEASE : ACUTE LIVER FAILURE*

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Objectives and Study: Wilson's disease (WD) is a rare autosomal recessive disorder of copper metabolism. Combined clinical and laboratory findings are needed for early diagnosis. There is the hypothesis suggested that low serum Zinc (Zn) is related to phenotypic severity of WD. Indeed, alkaline phosphatase (ALP), a Zn-containing metallo-enzymes that reflects the real Zn deficiency is relatively low in WD patients might support this presumption. However, few studies underscore the role of these biomarkers in WD pathogenesis and severity.

Our study aimed to observe the values of serum Zn, ALP and other baseline laboratory results in acute liver failure (ALF) of indeterminate cause and WD.

Patients and Methods: The medical records from children with WD (n=43) and ALF of indeterminate cause (n=9) at King's College Hospital between 2005 and 2015 were retrospectively reviewed. All WD children had disease causing mutations identified. WD is classified into WD-non-ALF (n=28) and WD-ALF (n=15). The values of serum Zn, copper, ceruloplasmin (CP) and liver function tests were collected. Free serum copper and corrected Zn formula were calculated as following;

Free copper (μ mol/L) = total copper (μ mol/L) – bound copper (μ mol/L)

(Bound copper = $0.0472 \times$ ceruloplasmin (mg/L)) and

Corrected Zn patient = $0.25 \times$ Zn normal + ((albumin normal ÷ albumin patient) \times (Zn patient – (0.25 \times Zn normal)))

Results: Our study demonstrates, a significantly lower level of serum Zn, corrected Zn and ALP in WD-ALF compare to WD non-ALF and ALF of indeterminate cause (Table 1).

Conclusion: The present study showed that the dramatic aberrance of serum Zn in WD-ALF can discriminate WD-ALF from indeterminate ALF.

***617 ALPHA 1-ANTITRYPSIN LEVELS CAN DIFFERENTIATE ALLELIC PHENOTYPES IN CHILDREN**

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Purpose of Study: Alpha 1 anti-trypsin (A1AT) is a liver protein whose alleles have multiple phenotypes. Deficiency of A1AT is the most common genetic cause of liver disease in children and is caused by homozygosity or compound heterozygosity for the A1AT mutant Z or S alleles estimated to occur in 1 in 2000-5000 live births. These allelic combinations are also known to result in a low A1AT plasma level. A1AT heterozygosity has been shown to have a role as a modifier of other forms of chronic liver disease in both adults and children however there is a lack of data on the pattern of A1AT plasma levels in such heterozygous phenotypes.

Methods: We performed an IRB approved retrospective review of the electronic medical records at Cincinnati Children's Hospital Medical Center (CCHMC) for the time period 2007 through 2015. We queried for patients that had A1AT levels and phenotype performed simultaneously. Subjects were divided into three categories by A1AT allelic phenotype; i) normal (MM, M1M1, M1M2, M1M3, M2M2, M2M3, M3M3, BM, CM, DM, EM, FM, GM, IM, LM.), ii) diseased (SS, SZ, ZZ), and iii) Heterozygous (M1S, M1Z, M2S, M3Z, MS, MT, MX, MZ, MZ PRATT, PM). Differences in A1AT levels across categories were analyzed by one way analysis of variance (ANOVA), *posthoc* Tukey's multiple comparison test and Area under Receiver Operator Curve (AUROC) analyses, using Graphpad Statistical software.

Results: We found a total of 1688 patients with paired A1AT levels and phenotype in the study period: 41 patients in the disease category (mean age 9.3 years, 44.9% female); 1401 in the normal category (mean age 11.7 years, 43.9% female); 246 in the heterozygous category (mean age 12.3 years, 42.1% female). There was no difference in age or sex between groups. The A1AT level (mean ± SD) was significantly different across the three categories of normal (144.2 ± 37ng/mL), diseased (42.8 ± 18ng/mL), and heterozygous phenotype (104.6 ± 32ng/mL) [One way ANOVA *p*<0.0001; and *post hoc* Tuckey's *p*<0.05 for all comparisons, normal vs. disease, normal vs. heterozygous, and disease vs. heterozygous]. All normal phenotype subjects had A1AT levels greater than 95 ng/mL, except for one outlier. AUROC for disease causing phenotype identification was 0.995 with an optimal cut-off of A1AT<83.5 ng/mL giving a sensitivity of 95.87% and a specificity of 95.12%. Similar analyses for other group comparisons are detailed in the table below.

Conclusion: Our study confirms that A1AT levels can accurately predict a normal or diseased A1AT phenotype in children. However, we found that the power of A1AT levels to distinguish heterozygous phenotypes from diseased or normal phenotypes is less robust. We recommend A1AT levels be used as a primary analysis for determining A1AT disease state and A1AT phenotyping be obtained as a secondary confirmatory test when the A1AT level is ± 83.5ng/mL and there is a need to determine heterozygote phenotype as a potential disease modifier.

COMPARISON GROUPS	AUROC	A1AT CUT OFF LEVEL (ng/ml)	SENSITIVITY (%)	SPECIFICITY (%)
Disease causing phenotype vs. all other phenotypes	0.995	<83.5	95.87	95.12
Disease causing phenotypes vs. Normal Phenotypes	0.997	<87.5	100	99.93
Disease vs. Heterozygous	0.971	<69.5	94.31	87.8
Normal vs Heterozygous	0.831	<118.5	74.39	78.94

618 GENETIC DELETION OF CXCL10 IS PROTECTIVE AGAINST DIET-INDUCED NON-ALCOHOLIC STEATOHEPATITIS IN MICE.

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Background and Aims: NASH is an inflammatory lipotoxic disorder, but how inflammatory cells are recruited and activated within the liver is still unclear. We previously reported that activated mixed lineage kinase 3 mediates the release of C-X-C motif chemokine 10 (CXCL10) enriched extracellular vesicles (EVs) from lipotoxic primary mouse hepatocytes. These CXCL10 loaded EVs are potently chemotactic for macrophages *in vitro*. However, the role of CXCL10 inhibition in reducing NASH-associated inflammation *in vivo* is unclear. In this study, we tested the hypothesis that CXCL10^{-/-} mice are protected against diet-induced NASH.

Methods: We employed C57BL/6J CXCL10^{-/-}; and wild-type (WT) mice. Mice were fed a high saturated fat, fructose, and cholesterol (FFC) or chow diet for 20 weeks. Metabolic cages were used to examine their metabolic phenotype. Liver injury, inflammation, and fibrosis were assessed histologically and biochemically. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated.

Results: FFC-fed CXCL10^{-/-} and WT mice displayed insulin resistance (HOMA-IR >10), similar weight gain, and metabolic profile. Histological examination of hepatocyte steatosis and biochemical determination of hepatic triglyceride content were also similar in FFC-fed WT vs. CXCL10^{-/-} mice. In contrast, there was prominent inflammatory infiltrates in FFC-fed WT vs. CXCL10^{-/-} mice. The serum ALT levels were also significantly reduced in FFC-fed CXCL10^{-/-} vs. WT mice (mean; 393 vs. 564 U/L, *p*<0.01), as were the number of TUNEL positive cells (0.5 vs. 6.3 cells, *p*< 0.001). Immunohistochemistry for Mac-2 a marker of phagocytically active macrophages, showed reduced stained surface area in FFC-fed CXCL10^{-/-} vs. WT mice. Likewise, the mRNA expression of markers of macrophage activation, including TNF alpha, IL1 beta and MCP-1 were all significantly decreased. The mRNA expression for markers of other innate immune cells (dendritic cells, NK cells and neutrophils) were all increased to a greater extent in WT FFC-fed mice compared to chow-fed mice, although their expression was not statistically different in the FFC-fed CXCL10^{-/-} vs. WT mice. Fibrosis was assessed by the Sirius red stain and by mRNA levels of osteopontin, collagen 1a1 and alpha smooth muscle actin, which were all significantly decreased in FFC-fed CXCL10^{-/-} vs. WT mice.

Conclusion: Our results suggest that CXCL10^{-/-} mice are protected against macrophage associated inflammation during diet-induced hepatic steatosis. Macrophage-associated inflammation appears to be the lynch pin for the CXCL10-mediated sterile inflammatory response observed in NASH in our model, as liver injury correlated with this inflammatory cell type, but not other cell types of the innate immune system. We speculate that CXCL10 inhibition is a potential therapeutic strategy for human NASH.

619 LIVER SPACE: LEVERAGING FACEBOOK TO ENHANCE COMMUNITY, ENGAGEMENT AND PATIENT-CENTERED RESEARCH
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Introduction: Increasing numbers of individuals are using social media to obtain health information and share health data. Facebook currently contains thousands of groups that regularly exchange information. Liver Space is a "Facebook app" designed to strengthen the functionalities of the Facebook platform in order to build stronger digital communities.

Methods: The following search terms were queried within Facebook in order to identify the largest groups: "biliary," "Alagille," "alpha-1," "Wilson," "autoimmune hepatitis," "hepatitis," "primary sclerosing," "fatty liver," "liver transplant" and "NAFLD." Adult (18+ years) members of Facebook liver disease groups were asked to complete an anonymous survey to evaluate and rank features of Liver Space.

Results: We identified 26 liver-related groups on Facebook with over 1000 members and 9 groups with over 2000 members. The largest groups were centered around pediatric liver transplant (7828), fatty liver (5146), viral hepatitis (4822; 4271; 3025, 2638), biliary atresia (4063) and alpha-1-antitrypsin deficiency (2192). The survey had 289 respondents and 277 (96%) met eligibility requirements. The mean age of respondents was 40 years (SD 11; range 18 to 67) and 88% were female. The study sample included 173 (66%) parents of children with liver disease, 26 (10%) adults with a liver disease acquired in childhood, 46 (17%) adults with a liver disease acquired in adulthood, as well as 2 (1%) spouses, 9 (3%) friends, and 8 (3%) other. Study participants reported spending an average of 13 hours per week on Facebook and 3 hours per week on other social media. On a 100-point scale (0 definitely not, 25 probably not, 50 neutral, 75 probably yes, and 100 definitely yes), mean interest in an enhanced app was 88 (SD 18). Mean (SD) interest in Liver Space functionalities included: hot topics 91 (17), ask an expert 90 (20), survey participation 85 (23), forums 85 (23), education 85 (23), lab/weight tracking 84 (27), and medication reminders 72 (34).

Conclusion: Thousands of Facebook users engage other members with liver-related issues. These individuals are interested in using Liver Space functions. In particular, members are interested in the enhanced platform in order to receive the latest news about their disease, ask questions to an expert, and participate in research.

***620 FONTAN-ASSOCIATED PEDIATRIC LIVER DISEASE: NON-INVASIVE EVALUATION WITH ACOUSTIC RADIATION FORCE IMPULSE (ARFI) ELASTOGRAPHY**

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Background: Described in 1971, the Fontan operation is the standard of care for congenital heart disease (CHD), single ventricle (SV) physiology. Hepatic fibrosis is a significant complication in adult Fontan patients. Noninvasive modalities used to assess hepatic fibrosis include serum hepatic biomarkers, FibroSure (patented biomarker panel) and acoustic radiation force impulse (ARFI) ultrasound elastography. Pediatric Fontan patients are not routinely assessed for liver disease due to absence of a proven, low-risk screening method. We aimed to characterize the prevalence of liver disease in pediatric Fontan patients ≥ 1 year status post-Fontan operation by using noninvasive modalities and to determine if ARFI may be useful to detect hepatic fibrosis.

Methods: Subjects were prospectively enrolled and had ARFI values (shear wave speed (SWS), m/s) and serum testing including FibroSure. Echocardiogram and cardiac catheterization data within 1 year of the study were obtained. Statistical analysis was performed using Pearson's correlation coefficient, Wilcoxon rank-sum test and Kruskal-Wallis test.

Results: Forty subjects were studied, 75% male and median age at enrollment was 11 years (range 2-34). Median time since Fontan was 6.50 years (range 1-28). Platelet count had negative correlation with age at study ($p=0.0009$) and decreased with increasing years of Fontan $p < 0.0001$. Alanine transaminase (ALT) and aspartate aminotransferase (AST) were elevated in subjects with extracardiac conduit Fontan compared to extracardiac pericardial and lateral tunnel Fontans, $p=0.0338$ for ALT and $p=0.0088$ for AST. FibroSure was recorded in subjects ≥ 14 years of age ($n=13$) and predicted fibrosis in 77% of these subjects (31% with bridging fibrosis). Subject age and longer duration of Fontan circulation correlated with heterogeneous liver echotexture, $p=0.0026$ and $p=0.0224$ respectively. The association between years of Fontan and ARFI mean SWS were not significant, $p=0.9963$. Extracardiac conduit Fontan subjects had mean SWS of 2.282 m/s, 2.039 m/s for extracardiac pericardial Fontan and 2.073 m/s for lateral tunnel Fontan; $p=0.0662$. Ventricular function was abnormal in 4 subjects with right ventricle anatomy and extracardiac conduit Fontan.

Conclusion: All subjects had elevated SWS, suggestive of increased hepatic stiffness. The lack of correlation between SWS and time since Fontan suggests that hepatic congestion may affect SWS and limit its usefulness in this population. Platelet count correlated with increased duration of Fontan circulation but no correlation was noted with other serological biomarkers. Individual serum biomarkers are not sufficient in ruling out disease. The use of multiple indices may be warranted to increase diagnostic accuracy. ARFI elastography may be a useful tool for pediatric Fontan patients but additional testing is warranted to correlate gold standards and non-invasive screening modalities in this patient population.

621 BETWEEN CHOLANGITIS AND LIVER TRANSPLANTATION IN PATIENTS WITH BILIARY ATRESIA AFTER KASAI PORTOENTEROSTOMY: A 14-YEAR NATIONWIDE COHORT STUDY

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Objectives: The aim of this study was to examine the association between occurrence of cholangitis and liver transplantation (LT) in children with biliary atresia (BA) after Kasai portoenterostomy (KP).

Methods: Data were obtained from the National Health Insurance Research Database of Taiwan from 1998 to 2011. All BA patients born after 1998 and receiving KP were followed until the end of 2011. They were then divided into LT and non-LT groups. Cholangitis occurrence and total episodes of cholangitis for all patients were recorded, and compared between the two groups.

Results: A total of 366 BA patients were enrolled. Ninety-six (26.8 %) patients received LT during the study period. More patients with KP < 60 days of age survived with their native liver ($p < 0.05$). The mean age of first cholangitis was 0.9 years, 95 % confidence interval (CI), 0.6-1.2 years in the LT group and 0.8 years, 95 % CI, 0.6-1.1 in the non-LT group, respectively ($p = 0.868$). The accumulated incidence of cholangitis within 2 years after KP was not different between the two groups (hazard ratio 1.2; 95% CI, 0.9-1.6). However, the total number of episodes of cholangitis was higher in the LT group within 2 years after KP ($p < 0.05$).

Conclusions: Repeated occurrence of cholangitis within 2 years after KP in BA patients was associated with a greater risk of future LT.

622 ZINC MONOTHERAPY IN YOUNG CHILDREN WITH ASYMPTOMATIC WILSON'S DISEASE: MULTICENTER STUDY IN JAPAN

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Background and Aims: AASLD and EASL guidelines recommend zinc monotherapy as a treatment for asymptomatic patients with Wilson disease (WD). We previously reported that a reasonable goal in treating young children with asymptomatic WD using zinc to be maintaining 24-hour urinary copper excretion between 1 and 3 $\mu\text{g}/\text{kg}/\text{day}$ for the first 1-2 years (Mizuochi, et al. *JPGN* 2011;53:365). Here, we aimed at evaluating long-term efficacy and safety of zinc monotherapy for young children, under 10 years old, with asymptomatic WD in Japanese pediatric centers and establishing appropriate benchmarks of maintenance therapy.

Methods: We performed a retro- and prospective study to examine 21 children (median age 6 years, range 1-9) who satisfied diagnostic criteria for WD and were treated solely with zinc acetate prior to symptom onset at 10 participating pediatric centers in Japan. No additional WD sequelae, such as jaundice, hepatomegaly, or neurologic abnormalities were noted. We monitored serum AST and ALT, nonceruloplasmin serum copper, and 24-hour urinary copper for 1-7 years after initiation of zinc monotherapy. Additional monitorings included white blood cell count, hemoglobin, platelet count, γ -glutamyltransferase, total bilirubin, albumin, iron, amylase, lipase, and prothrombin time, as well as 24-hour urinary zinc excretion. We performed abdominal ultrasonography and evaluated clinical WD manifestations, drug compliance, and adverse effects of zinc. The prescribed dosage of zinc acetate for patient ≤ 5 years was 25 mg twice daily; for those children 6 years or older, the dose was 25mg 3 times daily. We increased the dosage of zinc if the patients had AST/ALT > 50-70 U/L, and decreased it if they had adverse effects of zinc such as iron-deficiency anemia or pancytopenia.

Results: At time of diagnosis, AST/ALT and 24-hour urinary copper were $148 \pm 118/234 \pm 151$ U/L and 124 ± 54 $\mu\text{g}/\text{day}$ (5.8 ± 2.9 $\mu\text{g}/\text{kg}/\text{day}$), respectively. All patients continued to take zinc without any evidence of zinc toxicity. None of our 21 patients became clinically symptomatic. AST/ALT significantly decreased to $54 \pm 30/77 \pm 49$ U/L ($P < 0.001$) at 1 month after initiation of treatment and was mostly maintained under 50 U/L for 1-7 years (AST/ALT: $33 \pm 7/38 \pm 17$ and $29 \pm 5/34 \pm 6$ U/L at 1 and 7 years after initiation of treatment, respectively). Twenty four-hour urinary copper significantly decreased to 49 ± 21 $\mu\text{g}/\text{day}$ (2.2 ± 1.1 $\mu\text{g}/\text{kg}/\text{day}$; $P < 0.001$) at 6 months after initiation of treatment and was mostly maintained under 75 $\mu\text{g}/\text{day}$ and between 1 and 3 $\mu\text{g}/\text{kg}/\text{day}$ for the remainder of the study (2.2 ± 0.6 and 1.5 ± 0.2 $\mu\text{g}/\text{kg}/\text{day}$ at 1 and 7 years after initiation of treatment, respectively).

Conclusions: Long-term zinc monotherapy for young children with asymptomatic WD proved highly effective and safe. A reasonable goal in treating young children with asymptomatic WD using zinc appears to be maintaining both AST/ALT under 50 U/L and 24-hour urinary copper excretion between 1 and 3 $\mu\text{g}/\text{kg}/\text{day}$ (and under 75 $\mu\text{g}/\text{day}$).

623 IMPLEMENTATION OF A NEW PROTOCOL TO PREVENT MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS INFECTION IN JAPAN

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Introduction: A major route of hepatitis B virus (HBV) transmission and subsequent chronicity is from mother to child. In Japan selective immunization of HBV was started in 1985. Carrier rate of mother to child infection decreased 0.26% in 1985 to 0.024% in 1995. While hepatitis B immunoglobulin (HBIG) and HB vaccine joint immunoprophylaxis has reduced mother-to-child transmission of HBV, vaccination for HBV that does not follow protocol became a concern in Japan and the protocol was changed in 2013. Old protocol was as follows: HBIG at birth and 2 months (if mother's HBe antigen positive) and HB vaccines at 2, 3, and 5 months. New protocol was as follows: HBIG at birth and HB vaccines at birth, 1, and 6 months.

Methods: We aimed to determine whether or not the new protocol is currently being implemented by sending surveys to obstetrics departments in Aichi Prefecture during 2015. This study was approved by the ethical committee of Nagoya City University.

Results: Among 92 (64%) institutions that responded, 91 (99%) had implemented the new protocol. The prevalence of HBs antigen and of HBe were 0.29% (135/45,067) and 0.08% (36/45,067), respectively, among pregnant women during 2014. Ninety-nine infants received immunoprophylaxis against HBV and none became HBV carriers. Among the respondents, 96% checked for HBe antigen, if the mother was positive for HBs antigen. Infants were followed up in internal pediatrics departments, by specialists and in internal obstetrics departments at 46%, 46% and 8% of institutions, respectively. Infants who were positive for HBs antigen were followed up in internal pediatrics departments, by specialists, and in internal obstetrics departments in 39%, 60% and 1% of institutions, respectively. Mothers carrying HBV were recommended to internal medicine departments in 75% of institutions.

Discussion: This study contains several limitations because it involved retrospective questionnaires. Outcome of the infants who received HBV immunoprophylaxis could not be revealed. Moreover, the response rate was low (64%). Non-responded institutions might have low interest for HBV mother to child transmission and might not have started the new protocol. In the present study, 45,067 pregnant women were enrolled. The subjects represented 70% of the birth at Aichi prefecture in 2014. Antiviral therapy for HBV such as entecavir and tenofovir has progressed and mothers infected with HBV should be referred to hepatologists.

Conclusion: This study indicates that the new protocol for preventing mother-to-child HBV transmission is currently being implemented in Aichi Prefecture. Thorough and further collaboration of obstetricians, neonatologists, and pediatricians is needed to decrease HBV mother-to-child transmission.

624 OCCULT HEPATITIS B VIRUS INFECTION IN HEALTHY VACCINATED CHILDREN, CHILDREN WITH NON-A TO E HEPATITIS, THALASSEMIC CHILDREN WITH POLY-TRANSFUSION AND CHILDREN WITH CHRONIC HEPATITIS C VIRUS INFECTION
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Background: Occult hepatitis B virus infection (OBI) has been defined as the presence of HBV DNA in livers or sera in subjects who are serologically negative for HBsAg. OBI was detected in 10.9% vaccinated Taiwanese children who visited hospital with other medical illnesses. OBI was detected in 28% Iranian HBsAg-negative, immunized children born to carrier mothers. OBI has been found in coinfection with HCV, in hemodialyzed patients, and in the context of transfusion and non-A to E hepatitis.

Aim: To assess the prevalence of OBI and genetic characteristics of HBV isolates in apparently healthy children and children with different clinical settings. Subjects: enrolled in 2009 HBV serosurvey who were HBsAg-negative and <18 years were considered for entry into this study. All subjects seropositive for anti-HBc who had sufficient serum samples for HBV DNA testing were included (Anti-HBc-positive only: N 23; Both anti-HBc and anti-HBs-positive; N 58). For subjects seronegative for anti-HBc, only 5-10 subjects in each age group were randomly selected (both anti-HBc and anti-HBs-negative: N 141; anti-HBc-negative but anti-HBs-positive; N 151). Serum samples from 17 infants and children, aged 4 months to 13.8 years, with non-A to E hepatitis. None of them were seropositive for HBsAg, anti-HCV, IgM anti-HAV, anti-HDV or anti-HEV. HBsAg was checked by RIA or EIA; anti-HCV was checked by second-generation EIA; HCV RNA was detected by RT-PCR; serum HEV was detected by EIA. 24 non-thalassemic children with chronic hepatitis C who were seropositive for anti-HCV and HCV RNA were included. Serum samples at the last visit were studied. 50 thalassemic children who had multiple blood transfusions during long-term follow-up but were without HCV infection were also enrolled. Serum samples at the last visits were studied.

Methods: HBV DNA was extracted from serum Pre-S, S and pre-core/core genes were amplified by using nested PCR under strict precautions, followed by direct sequencing. Children who were HBV DNA-positive at least two of three regions (Pre-S, S and pre-core/core) by nested PCR were classified as occult HBV infection. Serum HBV DNA was quantified by a real-time PCR amplification assay using a LightCycler. HBV genotype was determined as described in our previous studies.

Result: Among apparently healthy children, the frequency of OBI was 8.6% (7/81) in anti-HBc-positive subjects, compared to 0% (0/292) in anti-HBc-negative subjects ($p < 0.001$). 4 of 7 occult HBV isolates had mutations within "a" determinant of HBsAg (I110L, T115A, T126A and G145R). One occult HBV isolate from chronic HCV infection children had T126A mutation

Discussion: Although infrequent, OBI can be observed in vaccinated, apparently healthy individuals. In a post-vaccination era, anti-HBc can be a good marker for screening OBI in HBsAg-negative subjects. Selective pressure from immunization may result in the generation of OBI with mutations capable of causing immune evasion. Multiple blood transfusions carried a low risk in transmission of OBI.

625 CEREBROTENDINOUS XANTHOMATOSIS: A RARE DISEASE WHICH IS EASILY MISDIAGNOSED AS BILIARY ATRESIA IN INFANCY: CASE REPORT AND REVIEW OF LITERATURE

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Objective: To summarize and review the clinical data of an infant diagnosed with cerebrotendinous xanthomatosis (CTX) so as to identify the disease early and improve our understanding of cholestasis.

Methods: Report clinical features of a 2-month-old girl with an onset of cholestatic jaundice. Bile duct exploration and laboratory examinations were done and she was finally diagnosed with CTX by urinary acid mass spectrometry analysis and CYP27A1 gene detection. Clinical features of similar cases from published literatures were summarized. All literature was retrieved systematically.

Results: A 2-month-old girl was admitted to our hospital due to jaundice from one week after birth to the present. Laboratory findings showed cholestasis jaundice, normal or mildly elevated TBA (total bile acid), mildly elevated GGT (γ -glutamyltransferase) and TCH (total cholesterol). Biliary atresia was excluded by bile duct exploration. Absence of Cholesterol 27-hydroxylase activity measured by Urinary bile acid mass spectrometry analysis and Pathogenic compound heterozygous mutations of CYP27A1 gene: p.R127W(c.379C>C/T) and p.Q116X c.346C>C/T was confirmed for CTX. She then received therapy with cholic acid tablets. Followed-up for 9 months after discharge from the hospital, her jaundice faded and she had no discomfort. Three related literatures concerning CTX with cholestatic jaundice onset were searched from the PubMed database. Combined with this case, common manifestation is cholestasis jaundice in the second-third month, normal or mildly elevated GGT, mildly elevated TBA and TCH.

Conclusion: CTX reports on the onset of cholestasis in infancy were extremely rare. It is necessary to consider the possibility of this disease when there is normal or mildly elevated TBA, slightly elevated GGT and TCH. Diagnosis was confirmed by urinary bile acid mass spectrometry and CYP27A1 gene detection.

626 THE PHOSPHODIESTERASE-5 INHIBITOR SILDENAFIL POTENTIATES THE CYTOSTATIC EFFECT OF DOXORUBICIN IN PEDIATRIC EPITHELIAL LIVER TUMOR CELLS

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Introduction: Epithelial liver tumors (hepatoblastoma (HB) and pediatric hepatocellular carcinoma (pHCC)) are the most common liver tumors in infancy and childhood. Treatment results of these malignancies have been constantly improved during recent years, mainly because of integrated treatment protocols combining the multimodal therapeutic approaches (neo-)adjuvant chemotherapy and surgery.

However, the 5-year survival rate for High-Risk HB is below 50% stating that the survival of an advanced stadium of this disease is still poor. Therapeutic results for children with pHCC are generally unsatisfactory although a general increase in survival rates for most solid tumors among this age group had been observed. In the present study, we aim to investigate whether the established phosphodiesterase 5 (PDE5) inhibitor sildenafil interacts with doxorubicin to strengthen the antitumor effectiveness in pediatric malignant liver tumor cells.

Methods: The growth inhibition in the HB cell line HepT1 and the pHCC cell line HC-AFW1 under treatment with sildenafil in combination with doxorubicin was measured by MTT-assays. Apoptosis, ROS production as well as csc (cancer stem cells)-rate were measured by flow cytometry and the intracellular signaling was detected by using RT-PCR and Western Blot. All experiments were performed to determine any differences between the effects of solitary chemotherapy by its own and in combination with sildenafil.

Results: The concomitant treatment of HepT1 and HC-AFW1 cells with sildenafil and doxorubicin resulted in a suppressed tumor cell growth and enhanced apoptosis rates. The latter was mediated by an augmented generation of reactive oxygen species and a downregulation of β -catenin and correspondingly cyclin-D1. In addition a decline in expression of intracellular ALDH suggests a reduction of the csc-population and might therefore indicate a delay in the formation of a multi-drug-resistance. The majority of results where sildenafil was added vary significantly from these with a singular treatment of doxorubicin.

Conclusions: In summary, the obtained findings provide evidence that sildenafil might help to improve treatment results in advanced pediatric epithelial liver tumors.

627 FUNCTIONAL CHANGE OF NATURAL KILLER CELLS COCULTURED WITH HEPATITIS C VIRUS INFECTED HUH7.5 CELLS IN VITRO

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Background and Aim: Hepatitis C virus (HCV) infection has been a big problem threatening public health and an important pathogen resulting chronic liver diseases. More than 170 million of the world's population is infected, and 55-85% of those persons develop chronic HCV infection in absence of effective treatment. Natural killer (NK) cells play an important role in innate defense against some transformed cells and many pathogens including viruses without sensitization in advance. Amount, subset and function of NK cells altered in chronic HCV infected patients, indicating its association with chronic HCV infection, but the actual mechanism has been still unclear.

Methods: Human hepatoma Huh7.5 cells were transfected with genomic RNA from cell culture adapted JC1 genotype 2a HCV strain tagged with biotin Flag2 (Huh7.5-HCV), establishing HCV *in vitro* infected system and generating infectious HCV virus stock. NK cells were freshly isolated from whole peripheral blood of concentrating healthy donors by Ficoll Paque plus density gradient centrifugation and L-Phenylalanine methylamine ester treatment and then cocultured with Huh7.5-HCV. Assess the functional effect of HCV infection on NK cells by testing cytokine-secreting and cytotoxicity before and after coculture.

Results: The NK cells purity would be more than 90 percent and concentration would be about 1.7×10^6 /mL. We assess NK cytotoxicity with an MTT assay by E: T ratio of 5:1, 10:1, 20:1 and 40:1, and we found that NK cytotoxicity increased with the E/T ratio. After 72 hours *in vitro* cultured with recombinant human interleukin-2 (rhIL-2), the levels of IFN- γ , TNF- α and IL-10 secreted by NK cells were 220.0+25.6pg/mL, 530.2+55.4pg/mL and 1707.6+323.1pg/mL, respectively. When cocultured with Huh7.5-HCV of MOI 4.8, the levels of IFN- γ , TNF- α and IL-10 secreted by NK cells were inhibited. The inhibition of secreting IFN- γ was specially significant at 6 ($p < 0.0001$), 9 ($p < 0.0001$) and 12 ($p = 0.00127$) hours cocultured with Huh7.5-HCV. The inhibition of secreting TNF- α was specially significant at 6 ($p < 0.0001$), 9 ($p < 0.0001$) and 12 ($p = 0.00121$) hours cocultured with Huh7.5-HCV. And the significant inhibition of secreting IL-10 appeared at 6 ($p = 0.00196$) hours cocultured with Huh7.5-HCV. The strongest cytokine-secreting inhibition appeared at 6 hours cocultured with Huh7.5-HCV, by rate of 24.1%, 20.7% and 24.3%, respectively. The cytotoxicity decreased significantly at 6 hours cocultured with Huh7.5-HCV, p value 0.0023.

Conclusions: When *in vitro* is cocultured with Huh7.5-HCV of MOI 4.8, the function of IFN- γ , TNF- α and IL-10 cytokine-secreting was inhibited. The significant cytokine-secreting inhibition of IFN- γ and TNF- α appeared at 6, 9 and 12 hours cocultured with Huh7.5-HCV, and IL-10 at 6 hours. The NK cells cytotoxicity was also inhibited significantly and the strongest cytotoxicity inhibition arose at 6 hours cocultured with Huh7.5-HCV.

628 ALTERED LEVELS OF FIBROBLAST GROWTH FACTOR 19 ARE ASSOCIATED WITH LIVER DISEASE IN PEDIATRIC CHRONIC INTESTINAL PSEUDO-OBSTRUCTION PATIENTS

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Background: Chronic intestinal pseudo-obstruction (CIPO) is a severe digestive syndrome which resembles mechanical obstruction in absence of any lesion occluding the intestinal tract. Although the mortality associated with liver disease has been observed in pediatric patients with CIPO, the pathogenesis of CIPO-associated liver disease is uncertain.

Objective: To investigate the association of FGF19 with liver disease in pediatric patients with CIPO.

Design: Serum levels of FGF19, IL-6 and, TNF- γ were measured in pediatric CIPO patients and were matched to healthy controls using ELISA assay. Liver injury and fibrosis were determined by histology, TUNEL analysis and Masson's trichrome stain. Ultrapformance liquid chromatography-tandem mass spectrometry (UPLC-MS) was used to measure the bile acid composition in serum and liver.

Results: Histological evidence of pediatric CIPO patients exhibits liver injury characterized by liver bile duct proliferation, inflammatory infiltrate, hepatocyte apoptosis and different stages of fibrosis. The serum FGF19 levels were lower in CIPO patients, and those of IL-6 and TNF- γ were higher compared to healthy matched controls (all $p < 0.01$). FGF19 levels were inversely associated with IL-6 concentration ($r = -0.32$, $p < 0.05$) and were negatively correlated with ileal inflammation grades ($r = -0.50$, $p < 0.05$). Bile acid composition in pediatric CIPO patients was altered and reflected a primary bile acid-dominant composition. Intestinal and hepatic regulation of bile acid synthesis was characterized by altered FXR/FGF19 signaling activation and increased expression of CYP7A1.

Conclusion: In pediatric CIPO patients, the FGF19 levels corresponding to liver injury were associated with concurrent bile acid dysmetabolism.

Table. Liver biochemistry, serum lipids, glucose and inflammatory cytokines in the patients

Variable	Control	CIPO	p-value	Correlation with FGF19	
	n=21	n=23		r	p-value
Liver enzymes					
Plasma alkaline phosphatase, ALP (U/L)	51.76 ± 69.24	90.34 ± 66.99	0.08	-0.34	0.03
Plasma alanine aminotransferase, ALT (U/L)	23.23 ± 16.01	55.77 ± 19.91	<0.01	-0.19	0.24
Plasma aspartate aminotransferase, AST (U/L)	36.35 ± 16.66	61.67 ± 27.51	<0.01	-0.3	0.06
Markers of cholestasis					
Plasma total bilirubin (µmol/L)	5.33 ± 2.55	6.24 ± 1.35	0.15	-0.15	0.37
Plasma conjugated bilirubin (µmol/L)	3.16 ± 1.43	3.19 ± 2.26	0.97	-0.07	0.67
Serum lipids					
Serum HDL cholesterol (mmol/L)	0.76 ± 0.26	0.63 ± 0.19	0.09	0.07	0.64
Serum LDL cholesterol (mmol/L)	1.50 ± 0.56	1.83 ± 0.45	0.04	0.02	0.92
Serum total cholesterol, TC (mmol/L)	2.00 ± 0.47	2.4 ± 0.61	0.02	-0.16	0.32
Serum triglycerides, TG (mmol/L)	0.79 ± 0.31	1.13 ± 0.60	0.03	0.08	0.6
Plasma glucose (mmol/L)	3.80 ± 1.16	3.21 ± 0.88	0.21	0.18	0.26
Markers of inflammation					
Serum IL-6 (pg/mL)	13.28 ± 21.78	50.63 ± 45.99	<0.01	-0.32	0.04
Serum TNF-α (pg/mL)	0.41 ± 0.2	0.89 ± 0.43	<0.01	-0.33	0.32

629 SERUM BIOMARKER LEVELS IN WEST VIRGINIAN OBESE CHILDREN

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Background: Obesity, an epidemic among West Virginia children, is a well established high risk factor for the development of fatty liver, non-alcoholic fatty liver disease (NAFLD), and steatohepatitis (NASH). The reported prevalence of NAFLD and NASH among obese children is estimated at 30% and 9%, respectively. Liver biopsy is the most accurate method to identify NASH and steatohepatitis, but it is invasive, costly, and may be associated with complications. A panel of serum biomarkers were previously used in adults and showed close correlation with histology.

Objective: Several serum biomarkers related to obesity-associated complications were examined including: fat metabolism and out flow (EGF-21/Apo B), apoptosis marker (CK-18), inflammatory marker (IL-6), oxidative stress marker (8-isoprostane), and antioxidant marker (bilirubin). The levels of those biomarkers were compared between obese and normal weight children.

Design/Methods: Children who attended the gastroenterology clinic were prospectively recruited into the study. Fasting serum samples were drawn and biomarker levels were measured via ELISA and RT-PCR. The children were divided into 3 groups: normal weight without insulin resistance (IR) (Control, Group 1), obese without IR (Group 2), and obese with IR (Group 3).

Results: Seventy children participated, of whom 28 were in Group 1 (control), 15 in Group 2, and 27 in Group 3. Serum biomarker results are shown in Table 1.

Conclusions: The serum biomarkers associated with obesity complications significantly correlated with obese children, especially with those who developed IR. The data may suggest that those markers could be utilized to screen and monitor obese children for liver-related complications.

Groups (#pts)	BMI	8-Isop	CK-18	FGF-21	Apo-B	Bilirubin	IL-6
G1 (28)	21±0.5	7.34±0.37	57.9±10.8	0.72±0.1	1.4±0.1	0.74±0.04	2.4±0.6
G2, neg. IR (15)	29.7±1.3*	10.54±0.39*	68.7±21.9	0.99±0.09*	1.69±0.2*	0.46±0.03*	1.85±0.2
G3, pos. IR (27)	32 ±1.1*	11.02±0.44*	98.9±17.4*#	0.68±0.1	1.99±0.1*#	0.43±0.02*	2.78±0.3*
p-value vs. control*	< 0.02	< 0.02	< 0.02	< 0.02	< 0.02	< 0.02	< 0.02

Values represent means ± SEM. *p<0.02 vs. control; # p<0.02 vs. obese-IR negative.

***630 COMMON VARIANTS IN THE AUTOPHAGY-RELATED GENE IRGM CONFER SUSCEPTIBILITY TO NON-ALCOHOLIC FATTY LIVER DISEASE IN OBESE CHILDREN AND ADOLESCENTS**

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Background and aims: A growing body of evidence has shown a crucial role of autophagy in the regulation of the intracellular lipid stores in hepatocytes. We aimed to identify whether sequence variants in immunity-related GTPase family M (IRGM) genes (an autophagy-related gene) confer non-alcoholic fatty liver disease (NAFLD) susceptibility in obese children and adolescents.

Methods: A total of 832 obese children and adolescents aged 6 - 18 years were recruited. NAFLD was determined by liver ultrasonography. We genotyped 5 IRGM single nucleotide polymorphisms (rs13361189, rs9637876, rs10065172, rs1000113, and rs11747270), which were reported to be associated with human diseases. We assessed the independent effects of IRGM variants on NAFLD after controlling for PNPLA3 rs738409 and GCKR rs780094 polymorphisms.

Results: 22.8% of recruited obese children and adolescents had NAFLD. We found significant associations with NAFLD at genetic variants in IRGM, PNPLA3 and GCKR. Multiple logistic regression analysis showed that, after controlling for the effects of age- and gender-adjusted body mass index, gender, PNPLA3 rs738409 and GCKR rs780094 polymorphisms, variant IRGM rs10065172 TT genotype independently increased the odds ratio of NAFLD by 2.059 (95% confidence interval 1.238-3.423; $p=0.005$), as compared to the CC genotype. Subjects with a variant IRGM rs10065172 TT genotype had a higher mean serum ALT concentration than that of subjects with the CC genotype (31.7 - 39.8 IU/L vs. 24.8 - 24.4 IU/L, $p=0.019$).

Conclusion: The genetic variants in IRGM are significantly associated with an increased risk of NAFLD in our population of obese children and adolescents.

631 INCREASED LIVER STIFFNESS MEASURED BY TRANSIENT ELASTOGRAPHY CORRELATES WITH CENTRAL VENOUS PRESSURE AND TIME SINCE SURGERY IN PATIENTS AFTER FONTAN OPERATION

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Background: Liver cirrhosis is becoming a serious long-term complication in patients after the Fontan operation for congenital heart malformations, but the progression of post-surgical liver fibrosis is not fully understood.

Objective: We aimed to clarify the correlation between liver stiffness and clinical and laboratory characteristics in patients after the Fontan operation.

Method: Forty-three patients (median age 11.5 years, range 4.2 to 26.7 years) who had undergone Fontan operation (median time since surgery 9.7 years, range 2.6 to 18.7 years) were examined for liver fibrosis (as liver stiffness measurement, LSM) by using @liver transient elastography (FibroScan[®]). Their LSM was compared with a control group comprised of 173 patients (median age 12.1 years, range 1.31 to 17.7 years) without liver dysfunction, liver disease, or obesity. The correlation between LSM and clinical and laboratory characteristics was analyzed with Spearman's rank-correlation coefficient.

Results: LSM was significantly higher in the Fontan group than in the control group (mean \pm SD; 15.3 ± 8.5 kPa vs. 4.0 ± 1.0 , $p<0.001$). In the Fontan group, time since surgery was highly correlated with LSM ($r=0.621$), and central venous pressure was moderately correlated with LSM ($r=0.479$). Other laboratory parameters (AST, ALT, hyaluronic acid, type 4 collagen, and AST to platelet ratio index) showed no correlation with LSM in the Fontan group.

Conclusion: Increased liver stiffness correlates with central venous pressure and time since surgery in patients after Fontan operation. Our results indicate that chronic elevated central venous pressure may lead to liver fibrosis.

632 THE CLINICAL VALUE OF ALBUMIN IN DIAGNOSING THE NEONATAL INTRAHEPATIC CHOLESTASIS CAUSED BY CITRIN DEFICIENCY

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Objective: Neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD) is an autosomal recessive disorder caused by a mutation in the SLC25A13 gene, which is an important cause of infantile intrahepatic cholestasis in China. The incidence of NICCD is high in East Asia. NICCD is characterized by intrahepatic cholestasis, including jaundice and hepatomegaly and laboratory tests have indicated that the patients might also experience abnormal liver function, coagulopathy, hypoglycemia, hyperammonaemia and elevated alpha fetoprotein (AFP). This paper analyzed clinical data from ninety patients at Fudan University Children's Hospital diagnosed with NICCD in order to investigate the clinical value of albumin (Alb) in diagnosing NICCD.

Methods: From January 2007 to December 2014, clinical data from ninety patients at Fudan University Children's Hospital diagnosed with NICCD were retrospectively analyzed. Patients were divided into an Alb <30 g/L (LA) group and an Alb ≥ 30 g/L (NA) group. Clinical characteristics, biochemical tests, blood tandem mass spectrometry, urine GC-MS results and genetic sequencing results were analyzed. Normal distribution data were expressed as mean \pm SD and skewed distribution data using median (P25, P75). T-test and X2 tests were used for statistical analysis, and $p<0.05$ was considered to be statistically significant.

Results: Ninety patients were evaluable (50 males and 40 females), their average age of onset was 20 days (range 1-225), and birth weight was 2.98 ± 0.43 kg. The clinical manifestations included jaundice, hepatomegaly, etcetera. There were no statistically significant differences between the LA and NA groups with respect to gender, birth weight and the age of onset. However, there was a statistically significant difference seen for the degree of splenomegaly (3.28 ± 1.95 cm vs. 92 ± 1.06 cm, $p=0.030$). The laboratory tests indicated that all the patients had elevated serum total bile acid (TBA), total bile (TB), direct bile (DB), gamma glutamyl endopeptidase (GGT) and AFP levels and many of the children had elevated alanine transaminase (AST) and alanine aminotransferase (ALT) levels. The following measurements were observed for the LA group compared to the NA group: AST/ALT [3.15 (0.38 - 5.93) vs. 2.14 (0.26 - 6.67), $p=0.010$], activated partial thromboplastin time (APTT) (53.27 ± 11.68 s vs. 45.06 ± 9.79 s, $p=0.003$), international normalized ratio (INR) (1.92 ± 1.35 vs. 1.29 ± 0.33 , $p=0.001$). However, the differences of TBA, TB, DB, GGT and AFP were not statistically significant ($p>0.05$). The results of blood tandem mass spectrometry showed

that there was a statistically significant difference for valine (uM) (80.93 ± 25.70 uM vs. $VS101.53 \pm 33.80$ uM, $p=0.026$). SLC25A13 mutations were tested in 34 patients, and the mutation (851_854del4) of SLC25A13 had correlation with Alb ($X2$ 4.76, $p=0.025$), and the difference was statistically significant.

Conclusion: The children with Alb <30 g/L who are highly suspected of NICCD need genetic, blood and urine testing. An early intervention is necessary in order to prevent complications and improve prognosis.

INFLAMMATORY BOWEL DISEASE

657 IMPROVING NUTRITIONAL SURVEILLANCE AND SUPPLEMENTATION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE Julia Fritz, Jose Cabrera, Cassandra Walia, Children's Hospital of Wisconsin, Milwaukee, WI, USA

Background: Children with inflammatory bowel disease (IBD) are at risk for nutritional deficiencies even when in clinical remission. Studies suggest that iron, vitamin D, and vitamin B12 deficiencies may go unrecognized in these patients and favor routine screening blood work.

Although international societies have put forth recommendations, there is no consensus for nutritional surveillance in children with IBD. In March 2015, the IBD group at Children's Hospital of Wisconsin (CHW) developed evidence-based guidelines for annual laboratory screening and supplementation of micronutrient deficiencies for children with IBD.

Purpose of the Project: The goal of this project was to improve the recognition and supplementation of nutritional deficiencies in the IBD population of CHW. The specific aim was to increase the rate of nutritional surveillance according to our institution-specific guidelines from 25% to 75%.

Methods: We performed Plan-Do-Study-Act cycles to implement our guidelines. Interventions were based on provider-identified barriers and included: creation of an order set within the electronic medical record (EMR), provider education, reminder emails, and targeted feedback. We reviewed the medical records of IBD patients seen at CHW between December 1, 2014 through March 1, 2016 to obtain laboratory measurements (CBC, iron, vitamin D, and B12) and supplementation regimens for iron, vitamin D, and multivitamins. Our outcome measures were: 1) proportion of IBD patient visits with appropriate nutritional laboratory surveillance and, 2) proportion of patients receiving micronutrient supplementation. EMR order set use was obtained as a process measure.

Results: We reviewed 722 visits for 396 patients (66% of total CHW IBD population). Of these visits, 94.8% had bloodwork in the preceding year. After implementation of our CHW IBD nutritional surveillance guidelines, the rate of obtaining serum iron levels increased from 44% to 87%. Monitoring of vitamin D levels also increased from 56% to 73%. Similar increases were seen in the monitoring of iron saturation, ferritin level, and vitamin B12, although only 1 patient was identified with B12 deficiency. Paralleling the increase in surveillance, rates of iron supplementation increased from 31% to 60% and vitamin D supplementation increased from 43.7% to 53.5%. There was no significant increase in multivitamin supplementation. By March 2016, 10/19 (52.6%) of IBD providers were using the EMR order set.

Conclusions and Implications: The standardized implementation of evidence-based guidelines for IBD nutritional surveillance improved the rate of screening for nutritional deficiencies and supplementation of essential micronutrients in patients at CHW. Without a quality improvement cycle focused on multivitamin use, there was no change in multivitamin supplementation. Similar strategies could be effective in improving supplementation of multivitamins and addressing cost-effectiveness of current guidelines.

658 DIAGNOSTIC VALUE OF FECAL CALPROTECTIN IN PEDIATRIC PATIENTS WITH SUSPECTED INFLAMMATORY BOWEL DISEASE

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Background: Children constitute approximately 20% of all patients with inflammatory bowel disease (IBD). It is very important to identify markers that could be used to navigate the management of IBD in the pediatric population. Fecal calprotectin (FC) is one of the markers that was proposed to identify mucosal inflammation in patients with IBD. Although several studies have investigated the value of FC with respect to IBD, the accuracy and precision of this test is still under discussion. The aims of this study were to evaluate the diagnostic value of FC in pediatric patients with clinically suspected IBD and to determine if FC can be used as a reliable screening test to identify those children who need further evaluation.

Methods: Medical records of children who were followed at the Pediatric Gastroenterology Clinic at the JSUMC between June 2013 and January 2016 were analyzed. A standardized data extraction tool was applied to collect demographic and clinico-laboratory data. Patients were included if FC, upper endoscopy and colonoscopy results were available for verification. Data was statistically analyzed using ANOVA and Chi-square tests. In addition, Kappa statistics and accuracy test assessments, including estimation of FC sensitivity, specificity, positive and negative predictive value (PPV and NPV), and Likelihood ratio (LR) for positive (+) and negative (-) results were provided. Data are presented as means with 95% confidence interval (95% CI) and proportion (%).

Results: Among the 93 patients included in this study, 32 (34.4%) had IBD, including Crohn's disease (n=20), ulcerative colitis (n=11) and indeterminate colitis (n=1). The rest had a variety of functional and organic GI disorders including, but not limited to, irritable bowel syndrome (n=15), eosinophilic diseases of the GI tract (n=8), non-specific colitis (n=4), polyp lesions (n=3) and solitary rectal ulcer syndrome (n=1). IBD patients were older and comparable to non-IBD patients by gender. Duration of symptoms prior to presentation was significantly longer in the non-IBD group with 50 days (95% CI, 36 - 65) compared to 20 days (95% CI, 7 - 34) in the IBD group. The FC test had a sensitivity for IBD histopathology of 84%, a specificity of 75%, PPV of 64% and NPV of 90%. The LR+ of FC was 3.4 (95% CI, 2.15 - 5.45) and LR- was 0.2 (95% CI, 0.09 - 0.46). The observed agreement based on Kappa statistics between FC and IBD histopathology was 56% (95% CI, 38-73%).

Conclusion: Fecal calprotectin was found to have moderate agreement and high negative predictive value with IBD histopathology. This study demonstrated that FC assays could be useful in the investigation of children with GI symptoms suggestive of IBD. A negative test may indicate a low probability of active IBD and could help avoid unnecessary endoscopy, while positive result could facilitate the decision.

659 RELATIVE BIOAVAILABILITY, EFFECT OF FOOD, AND SWALLOWABILITY OF A NEW, AGE-APPROPRIATE, DELAYED-RELEASE MESALAMINE FORMULATION IN HEALTHY VOLUNTEERS

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Introduction: An updated formulation of mesalamine 400 mg delayed-release capsules containing four 100 mg tablets (Delzicol®) has been developed as an age-appropriate treatment for young patients with ulcerative colitis who may have difficulty swallowing the existing capsule formulation. Two studies were conducted, one to examine the comparative bioavailability of Delzicol to Asacol® (mesalamine) delayed-release tablets and to determine the effect of food on Delzicol bioavailability in healthy adults, and one to evaluate the swallowability of Delzicol tablets in healthy children.

Methods: In the open-label, replicate-treatment, randomized, single-dose, crossover, comparative bioavailability study, healthy adult volunteers were randomized to receive one of four treatment sequences: Asacol 400 mg (fasted) twice, Delzicol (fasted) twice, and Delzicol (with food) once, with ≥7 days between treatments. Blood samples for plasma mesalamine concentration were collected up to 72 h post-dose and pharmacokinetic (PK) parameters were calculated using non-compartmental analysis and were statistically analyzed using the reference-scaled average bioequivalence (RSABE) procedure. Adverse events were recorded. In the open-label, single-dose swallowability study, healthy children aged 5-11 years were asked to swallow eight placebo tablets identical to those contained in two Delzicol capsules.

Results: In the bioavailability study (n=160), Delzicol and Asacol in fasted volunteers exhibited similarly delayed mesalamine absorption (mean T_{max} was 14.4 h and 17.1 h; mean T_{lag} was 6.5 h and 8.0 h, respectively). Point estimates of the Delzicol/Asacol geometric mean ratio for C_{max}, AUC₍₈₋₄₈₎, and AUC_(0-tldc) (within 80.00 - 125.00%) [Table], 95% upper confidence bounds of the linearized criterion (<0), and within-volunteer standard deviation values (data not shown) met the criteria for determination of bioequivalence using the RSABE approach. Administration with food did not substantially affect the delayed-release performance of Delzicol (mean T_{max} and T_{lag} increased vs. the fasted state by 3.2 h and 3.3 h, respectively). Slightly increased mesalamine bioavailability was observed when Delzicol was administered with food as a result of decreased gastrointestinal transit rate (Table). The overall safety profiles of Delzicol and Asacol were similar. In the swallowability study (n=60), 70% of children were able to swallow all eight placebo tablets, including 85% of those aged 7 - 11 years, and 40% of those aged 5 - 6 years.

Conclusion: Evaluation of PK parameters using the bioequivalence criteria for highly variable drug products confirmed that the updated formulation of Delzicol is bioequivalent to Asacol. Delzicol capsules were well tolerated and can be administered with or without food. Delzicol capsules are an age-appropriate product for children aged 5 - 11 years.

Table. Plasma mesalamine PK parameter values following oral administration of Asacol and Delzicol (fasted), and Delzicol (with food) (n=146)

PK parameter	Arithmetic mean (SD)	Geometric mean (LSM)	Ratio (%)	95% upper bound of the linearized criterion		
<i>Delzicol (test) and Asacol (fasted state) [reference]</i>						
	Delzicol	Asacol	Delzicol	Asacol	Delzicol/Asacol	
C _{max} (ng/mL)	204 (375)	158 (312)	68.9	59.4	115.96	-1.11
AUC ₈₋₄₈ (ng·h/mL)	707 (752)	886 (738)	465	484	96.07	-1.54
AUC _{0-tldc} (ng·h/mL)	1021 (1109)	1114 (988)	618	586	105.52	-1.53
<i>Delzicol in fed (test) and fasted (reference) state</i>						
	Fed	Fasted	Fed	Fasted	Fed/Fasted	
C _{max} (ng/mL)	214 (321)	204 (375)	91.1	69.0	132.11	-0.825
AUC ₈₋₄₈ (ng·h/mL)	948 (853)	707 (752)	681	466	146.22	-0.152
AUC _{0-tldc} (ng·h/mL)	1128 (975)	1021 (1109)	802	620	129.39	-0.354

AUC, area under the curve; AUC_{0-tldc}, AUC from time 0 to time of last determinable concentration; AUC₈₋₄₈, AUC from time 8 h to time 48 h; C_{max}, maximum plasma concentration; LSM, least squares mean from analysis of variance model; PK, pharmacokinetic; ratio, ratio of geometric means; SD, standard deviation

660 EFFICACY AND SAFETY OF CO-THERAPY OF BIOLOGICS AND METHOTREXATE IN A PEDIATRIC INFLAMMATORY BOWEL DISEASE (pIBD) COHORT: A SINGLE CENTRE EXPERIENCE

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Background: Biological therapies (infliximab and adalimumab) are an established therapy for pIBD, as single treatment or combined with azathioprine. There is a paucity of data regarding the usage, efficacy and safety of biological therapy combined with methotrexate in pIBD.

Aim: The aim of this study was to evaluate the efficacy and safety of biological medications combined with methotrexate as therapy for pIBD.

Methods: A retrospective, observational study was performed in our centre over a 4 year period in pediatric patients with a diagnosis of IBD who were prescribed infliximab or adalimumab combined with methotrexate for at least 3 months. Demographic, efficacy and safety data were collected and analyzed via the ImproveCareNow (ICN) database.

Results: Data from 22 patients were included in the study and analyzed. Eleven patients were boys (50%) and the median age of the cohort was 13 years (IQR: 11.5 - 14). Crohn's disease was diagnosed in 12 patients, ulcerative colitis in 5 and indeterminate colitis in 5. The combined therapy was adalimumab and methotrexate in 15 (68.2%) patients and infliximab and methotrexate in 7 (31.8%). In 20 patients the co-therapy was prescribed because of failure with prior therapies and in 2 patients due to juvenile idiopathic arthritis. For all patients, methotrexate was prescribed once per week (oral or subcutaneous) followed by folic acid rescue treatment. In only 3 (13.6%) patients, methotrexate was discontinued because negative side effects were observed (2 patients had abnormal liver function and 1 was had nausea and vomiting). 19 patients were using co-therapy, with the median time on therapy being 2 years (IQR: 1 - 2). 18 patients had a good response to co-therapy with disease improvement, whereas 10 were asymptomatic/quiescent and 8 had partial improvement with mild symptoms. Only 1 patient showed no improvement at all.

Conclusion: Co-therapy (biologics and methotrexate) was effective and safe in the majority of cases in our cohort and should be considered as a good alternative for patients with poor response to azathioprine or biologics. Larger studies should be considered to verify our observation.

661 VARIATION IN INFLAMMATORY BOWEL DISEASE CARE AMONG SAUDI PEDIATRIC GASTROENTEROLOGISTS

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Objective: Although international guidelines in inflammatory bowel disease (IBD) management are currently available, variations in IBD care still exist. The aim of this study was to determine the extent of the variation in IBD care among Saudi pediatric gastroenterologists.

Methods: A cross-sectional survey was sent to all pediatric gastroenterologists who were members of the Saudi Society of Pediatric Gastroenterology, Hepatology, and Nutrition (SASPGHAN) from August 2015 to December 2015. The questionnaire included items on demographic characteristics and utilization of different diagnostic and therapeutic interventions in IBD care.

Results: Of the 45 registered pediatric gastroenterologists surveyed, 37 (82%) returned the survey from 20 centers across the country. Overall, 75.7% of the respondents were practicing in tertiary care centers. The majority of the respondents were male (89%). We found a significant variation in the use of calprotectin assays, MRI enterography, and DEXA scans, which were utilized more frequently by the physicians practicing at the tertiary care centers compared to those practicing at the secondary care centers ($p=0.005$, $p=0.006$, $p=0.001$, respectively). Physicians practicing at the secondary care centers tended to utilize computed tomography (CT) enterography more often to evaluate small bowel disease ($p=0.041$). There were no statistically significant differences in the utilization of the other diagnostic tests. The physicians' years of experience did not influence the utilization pattern between the two groups. Twenty-four (64.9%) of the respondents used biological therapy at least once in their practice, with anti-tumor necrosis factor (anti-TNF), particularly infliximab, being their first choice. Among the biological therapy prescribers, 62.5% reported using combination therapy (anti-TNF with IMM), while 37.5% reported using anti-TNF as a monotherapy. Eighteen (48.6%) of the respondents reported stopping at least one of the immune-suppressant medications (immunomodulators and/or biological therapy) for patients with sustained remission. Of these, 44.4% reported stopping the medications within 2 - 3 years of achieving a full clinical and biochemical remission, 27.8% reported stopping therapy after 3 years, 11.1% reported stopping after 6 - 12 months of achieving full clinical and biochemical remission, while the remaining (16.7%) of respondents did not answer this question. There were statically significant differences in the prescription of biological therapy medications and the presence of a local policy for the transition of care of adolescents between the two groups.

Conclusions: We found considerable variation in the use of different diagnostic and therapeutic interventions in the management of pediatric IBD patients. Implementation of the available evidence-based guidelines may limit such variations and could ultimately improve the quality of IBD care.

662 FECAL CALPROTECTIN IN MONITORING INTESTINAL INFLAMMATION IN ASYMPTOMATIC PEDIATRIC CROHN'S DISEASE PATIENTS

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Introduction: Fecal calprotectin (FC) is a calcium-binding protein found in the cytoplasm of neutrophils, monocytes and macrophages. FC is measured in stool samples and can be used as a marker of active intestinal inflammation in Crohn's disease (CD) patients. Indeed, FC is becoming more widely used in clinical care, as studies suggest that it is more sensitive for intestinal inflammation than current serum biomarkers and subjective disease activity scoring tools.¹

Aims: In asymptomatic pediatric CD patients, this study aimed to 1) explore the role of FC in detecting active intestinal inflammation, 2) identify if FC can predict disease relapse and 3) compare FC to current clinical and biochemical assessments.

Methods: A prospective, non-interventional study of asymptomatic pediatric CD patients on maintenance Remicade® infusion therapy at BC Children's Hospital was performed. At enrollment, all subjects must have been classified as being in disease remission, defined by a Pediatric Crohn's Disease Activity Score (PCDAI) of less than or equal to 10. Stool for FC levels, standard routine blood work (including C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]) were collected and a PCDAI score was determined for three consecutive infusion visits. Throughout sample collection, and for an additional period of 12 months, any episodes of disease relapse were recorded.

Results: To date, 55 patients have been enrolled, and 25 have completed the study. At enrollment, despite a PCDAI <10, 16 patients (64%) had FC levels >150 µg/g (mean 940 µg/g, range 186 - 2231 µg/g) indicating active inflammation and 9 (36%) had significant elevations of FC >500 µg/g. Of those with FC >150 µg/g, 10 (63%) had either a normal ESR or CRP. Nine patients (36%) had a flare of disease during the study period, defined by a PCDAI score >10 with at least a 10-point difference from the prior visit. At the time of the flare, 6/9 (67%) had either a normal ESR or CRP. FC levels were elevated >150 µg/g for a mean of 204 days prior to a disease flare (range 48 - 378 days). The study is ongoing and additional results will be presented.

Conclusion: FC is a valuable, non-invasive test for monitoring inflammation in children with CD on therapy. FC detected inflammation in a significant number of asymptomatic pediatric patients with CD on biologic therapy despite normal screening inflammatory markers (ESR and

CRP). The FC level was also elevated prior to a clinical flare of disease. These data suggest that the role of FC in early detection of inflammation is valuable in helping predict patients who are likely to have disease relapse and to optimize treatment.

Reference: 1. Chang S, Malter L, Hudesman D. Disease monitoring in inflammatory bowel disease. *World J Gastroenterol.* 2015;21(40):11246-59.

***663 SAFETY AND EFFICACY OF FECAL MICROBIOTA TRANSPLANT IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE**

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Background: Inflammatory bowel disease (IBD) is a chronic inflammatory condition due to immune dysregulation and associated with decreased bacterial diversity. Fecal microbiota transplantation (FMT) could have a potential role in the treatment of IBD by altering the composition of gut microflora. We report the safety and efficacy of FMT for *Clostridium difficile* infection (CDI)-negative and medically refractory Crohn's disease (CD) or ulcerative disease (UC)-related colitis (clinicaltrials.gov NCT02108821).

Aims: To evaluate the safety and efficacy of FMT in children with active IBD.

Methods: Patients aged 2-22 years with mild-to-moderate active colitis failing standard medical therapy and who were CDI-negative were eligible. Patients with small bowel only disease, stricture, abscess, small bowel obstruction, active fistulizing disease or on treatment with biologicals with high-dose steroids (>1 mg/kg/day) were excluded. Healthy family members who tested negative for infections were selected as donors. FMT was performed using a fresh sample by both duodenoscopy/jejunoscopy and colonoscopy routes. Disease activity was assessed at baseline and then at 7, 30 and 180 days post-FMT using the Pediatric Crohn's Disease Activity Index (PCDAI) or the Pediatric Ulcerative Colitis Activity Index (PUCAI) and/or fecal calprotectin/lactoferrin. Response was defined as a decrease of 12.5 in PCDAI or 15 points in PUCAI. Remission was defined as a PUCAI or PCDAI <10 or normalization of calprotectin/lactoferrin.

Results: The median age at diagnosis was 8.4 y (4.5 - 17) and the median age at FMT was 12 y (8 - 21). Median disease duration was 3 y (0.6 - 10). The initial diagnosis was UC in 14 patients and CD in 9 patients. Of the 23 subjects enrolled, 12 with UC and 4 with CD have completed 6 months' follow-up. Response at day 180 was noted in 16.6% and 75% of UC and CD patients, respectively, as shown in the table below. All patients tolerated FMT well (n=23). Adverse events related to FMT were mild and most were observed within one week after FMT. These included abdominal pain (n=13), gassiness (n=10), bloating (n=5), vomiting (n=4), diarrhea (n=3), fever (n=2), and nausea (n=1).

Table. Response at day 180

Diagnosis	Total	Response to FMT			Remission at D180					
		None	Day 7	Day 30	D180					
UC 14	Completed D180				12	4	2	4	2	0
	Not completed		D180	2	1		1	NA	NA	
CD 9	Completed D180				4	0	1	0	3	2
	Not completed		D180	5	1		4	NA	NA	

Conclusions: FMT was found to be a safe procedure in IBD patients with mild-to-moderate colitis. Most patients had short-term responses that lasted less than 6 months. There was a trend towards more sustained responses in patients with CD compared to those with UC. Large-scale randomized studies are needed to study various routes and efficacy of single vs. multiple FMT.

664 DIAGNOSTIC DELAY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Background: Early recognition of IBD may avoid complications and improve treatment outcomes. Lower socioeconomic status (SES), younger age and Crohn's disease (CD) have been linked with longer times to diagnosis, but much remains unknown about the contributors to diagnostic delay in pediatric IBD. This study was undertaken as a quality improvement initiative within the Canadian Children Inflammatory Bowel Disease Network (CIDsCaNN). We aimed to identify sources of diagnostic delay in incident pediatric IBD cases enrolled in CIDsCaNN at Sick Kids, Toronto.

Methods: This single-centre, prospective cohort study included children diagnosed with IBD between January 1, 2013 and December 31, 2015. Patient and disease characteristics were retrieved from the CIDsCaNN dataset. Hospital data sources were queried for referring physician specialty/practice location, GI ward census and endoscopy suite activity. We examined the interval from symptom onset to diagnosis (time to diagnosis) and its component intervals: symptom onset to referral, referral to GI consult, and consult to diagnosis. Cox proportional hazard modelling was used to identify items associated with diagnostic delay.

Results: 112 children were included (median age 12.4 years, 59% male, 59% CD). 62% had ≥1 hospital contact while awaiting GI consultation. The median time to diagnosis was 138 (IQR 63 - 271) days. Time from symptom onset to referral was the main contributor to this delay (median 89 [IQR 45 - 248] days), compared to time from referral to GI consult (median 6 [IQR 0 - 15] days) and GI consult to diagnosis (median 8 [IQR 5 - 28] days). Lower albumin, blood per rectum and colitic symptoms (bloody diarrhea) were associated with a shorter time to diagnosis in univariable analyses, while colitic symptoms and oral involvement displayed significant associations in a multivariable model. Lower height-for-age Z-score (HAZ) and community referral were independently associated with longer delays from symptom onset to referral, and from referral to GI consult, respectively. Community referral was also independently associated with a longer time from consult to diagnosis, while lower albumin, colitic symptoms and abdominal pain were associated with a shorter time from consult to diagnosis. Ulcerative colitis was associated with a shorter time to diagnosis, even after adjusting for disease activity and extent (HR 3.07 [95% CI, 1.60, 5.91]). No association was observed between diagnostic delay and age or income quintile.

Conclusions: This study provides insight into factors that influence diagnostic delay in pediatric IBD. Several symptoms indicative of more severe disease were associated with faster diagnosis. The longer time to referral associated with reduced HAZ may reflect the time required for growth delay to manifest. Community referrals had a longer time to consult and diagnosis, even after adjusting for disease severity, suggesting that tertiary centre referrals may be inappropriately prioritized.

Table 1. Unadjusted and adjusted survival analysis examining the association between various factors and time from symptom onset to diagnosis

Predictor	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Disease Activity¹				
None	Ref			
Mild	0.91 (0.45, 1.86)	0.8		
Mod	1.66 (0.85, 3.25)	0.14		
Severe	1.64 (0.87, 3.12)	0.13		
Albumin	0.97 (0.94, 0.996)	0.025*	0.97 (0.95, 1.00)	0.067
CRP	1.00 (1.00, 1.00)	0.8		
ESR	1.00 (1.00, 1.01)	0.44		
Hemoglobin	0.99 (0.98, 1.00)	0.19		
Income				
Quintile 1	Ref			
Quintile 2	0.74 (0.39, 1.38)	0.34		
Quintile 3	1.45 (0.79, 2.64)	0.23		
Quintile 4	1.13 (0.61, 2.07)	0.7		
Quintile 5	1.08 (0.60, 1.98)	0.79		
Referring MD				
Tertiary centre	Ref	0.81		
Community	0.77 (0.53, 1.14)	0.19		
Comorbidity				
None	Ref			
IBD-associated ²	0.62 (0.28, 1.35)	0.23		
Other	0.84 (0.52, 1.35)	0.48		
GI referrals ³	1.00 (0.96, 1.05)	0.94		
GI inpatients ⁴	1.04 (0.97, 1.12)	0.23		
Endoscopies ⁵	0.99 (0.96, 1.02)	0.49		
Holidays ⁶	1.27 (0.84, 1.92)	0.26		
Female	0.92 (0.63, 1.36)	0.69		
Diarrhea	1.50 (0.98, 2.31)	0.064*	0.75 (0.39, 1.43)	0.38
Blood PR	1.54 (1.01, 2.36)	0.044‡		
Colitic symptoms ⁷	1.89 (1.26, 2.83)	0.0019*	2.20 (1.22, 3.98)	0.0086
Abdominal pain	0.98 (0.62, 1.57)	0.95		
Anemia ⁸	0.93 (0.57, 1.51)	0.77		
Fever	1.25 (0.79, 1.99)	0.34		
Extraintestinal symptoms ⁹	0.88 (0.55, 1.43)	0.62		
BMI z-score	1.00 (0.88, 1.14)	0.96		
HAZ ¹⁰	1.10 (0.94, 1.29)	0.22		
Age at diagnosis (years)	0.99 (0.94, 1.05)	0.76		
Family history of IBD ¹¹	0.96 (0.52, 1.75)	0.87		
Oral IBD ¹²	2.23 (0.90, 5.54)	0.084*	7.67 (2.24, 26.29)	0.0012
Perianal disease	0.97 (0.62, 1.52)	0.9		

* Included in multivariable analysis; ‡ Excluded from multivariable analysis due to collinearity

1 Based on established Pediatric Ulcerative Colitis Activity Index (PUCAI) and weighted Pediatric Crohn's Disease Activity Index (wPCDAI) cut-offs

2 Conditions with a known association with IBD (i.e., arthritis)

3 Number of referrals for suspected IBD to the GI department in the 4 weeks preceding a patient's diagnosis (total)

4 Number of inpatients on the GI service during the week of a patient's diagnosis (daily average)

5 Number of endoscopies performed in the hospital during the week of a patient's diagnosis (total)

- 6 Hospital holiday(s) in the 2 weeks preceding a patient's diagnosis
- 7 Bloody diarrhea
- 8 Anemia and/or iron deficiency
- 9 Oral ulcers, skin manifestations, arthralgia and/or arthritis
- 10 Height-for-age Z-score
- 11 In a first-degree relative
- 12 IBD involvement of the oral region (excluding simple oral ulcers)

665 RELIABILITY OF ULTRASOUND AS AN IMAGING MODALITY IN PATIENTS WITH CROHN'S DISEASE

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Crohn's disease (CD) is a chronic, relapsing, transmural, inflammatory disease of the gastrointestinal tract. The diagnosis of these relapses requires, more often than not, the use of various imaging modalities such as ultrasound, CT scans or MRIs. The latter two are more expensive and time consuming, with CT causing increased risk of exposure to radiation over a lifetime.

Ultrasound is a safe, non-invasive, inexpensive, readily-available imaging technique with good patient tolerability. The purpose of this study was to determine the reliability of ultrasound in the evaluation of transmural involvement and assessment of Crohn's disease activity versus MRE or CT scan. We performed a retrospective chart review of 9 patients (7 females, 2 males; age range 11 to 19 years) seen at Medstar Georgetown University Hospital with Crohn's disease diagnosed between September 2014 and April 2016. Ultrasound examination was performed on eight out of nine patients who all showed increased bowel wall thickness and increased vascularity was noted on color doppler flow. In one patient, fatty changes near the terminal ileum were noted and, in another, absence of peristalsis was noted. Seven out of nine patients underwent MRE which showed abnormal bowel wall thickness and abnormal vascularity pattern and fat proliferation. These ultrasound and MRE findings correlated with each other and patients' clinical presentation, laboratory values and pathology findings at the time of evaluation.

Conclusion: Ultrasound examination can be utilized as a reliable, non-invasive technique in diagnosing and following up in patients with Crohn's disease. Bowel wall thickness, mesenteric inflammation, abnormal peristalsis, presence/absence of strictures, and vascularity based on color doppler flow were some of the ultrasound findings that can be used to localize the affected bowel segments.

666 OUTCOME AT 8 WEEKS IN CHILDREN WITH EXCLUSIVE ENTERAL NUTRITION (MODULEN®) AT DIAGNOSIS OF CROHN'S DISEASE IN A CANADIAN TERTIARY HOSPITAL

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Efficacy of exclusive enteral nutrition (EEN) as first-line treatment in newly diagnosed pediatric Crohn's Disease (CD) has been shown to be comparable to corticosteroids for induction of clinical remission. Nevertheless, usage of EEN in induction of remission in CD patients in North America has been reported as low in comparison to Europe. Since May 2011, EEN has regained interest among physicians in our hospital.

Aims: The main goal of this study was to assess the remission and response rate at week 8 in children receiving EEN (Modulen, Nestlé) at diagnosis. Secondary aims were to assess: 1) clinical and biological factors associated with remission, 2) the proportion of newly diagnosed CD receiving EEN as first-line therapy between 2011 and 2015, and 3) if clinical or biological factors have an impact on the choice of induction treatment at diagnosis.

Methods: This was a retrospective study of patients (0 - 18 years) followed at Ste-Justine University Hospital for CD and treated by EEN during a minimum of 4 weeks from January 1, 2011 to November 1, 2015. Data collected were related to phenotype, localization, sex, age, weight, height, BMI, biological markers of inflammation and adverse effects. We calculated wPCDAI at diagnosis and at 8 weeks. Remission was defined as wPCDAI <12.5 and response as a decrease of 17.5 points. Statistical analyses were performed using SAS version 9.3.

Results: During the study period, 266 patients were diagnosed with CD. Seventy patients were treated with EN as first-line therapy. Twelve patients were excluded for not meeting inclusion criteria. Among the remaining 58 patients, 8 had less than 4 weeks of EEN due to noncompliance (n=4), vomiting (n=3) or early inefficacy (n=1). In total, more than 80% (n=50, 32 males) completed more than 4 weeks of EEN (median: 8.1 weeks, range: 3.7 to 12.4 weeks). The median age at diagnosis was 13.5 (IQR: 4.7) and the median delay between diagnosis and beginning of EEN was 3 days (IQR: 5). More than 2/3 of patients began EEN during hospitalization with the support of medical and dietician teams. The percentage of induction treatment by EEN as compared to steroids increased slightly between year 1 and year 4. In a per-protocol analysis for children who completed at least 4 weeks of EEN, remission at 8 weeks was 73.5% and response was 89.8%. In an intent-to-treat analysis, the remission rate was lower (62.1%). None of the clinical or biological factors at diagnosis were associated with a risk of failure at 8 weeks. Physicians tend to use Modulen more often when the BMI and weight are low, when patients describe a weight loss and when the disease affects the small bowel. When the localization of the disease is colonic, and when the patient has rectal bleeding, physicians chose an other type of induction treatment.

Conclusion: We found good efficacy of EEN in children with CD. Nearly 1/3 of newly diagnosed patients received EEN as first-line therapy.

667 SEASONAL PATTERNS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASES

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Objective: Inflammatory bowel disease (IBD) might be associated with environmental factors, such as seasonal patterns and low vitamin D levels. We aimed to assess the association between IBD onset and flares with seasonality and vitamin D levels in a large cohort of children.

Design: The medical records of 623 pediatric-onset IBD patients were retrospectively reviewed. Baseline characteristics included age at onset, gender, severity indices, month of first symptom, and vitamin D levels at diagnosis. In a subgroup of patients, data were extracted, including date of first flare onset and vitamin D levels during flare onset and remission.

Results: Median age at diagnosis was 14 years (IQR 11.66 - 15.58). Distribution of disease onset did not vary significantly between either months ($p=0.367$) or seasons ($p=0.460$) of the year. Vitamin D deficiency at the time of diagnosis was prevalent among 19.7% of patients with

no significant association with either month/season of the year or type of disease. Analysis of 169 first flares showed that IBD flares were more common in February, May and June and less common in April, August and December ($p=0.016$). Mean vitamin D level was significantly lower during flares compared with periods of clinical remission (55.25 ± 19.28 vs. 64.16 ± 26.6 , respectively, $p=0.012$).

Conclusion: IBD onset in school-aged children is not associated with seasonal patterns, whereas flares are more common in February, May and June and are associated with low vitamin D levels. These findings have implications on the possible role of school-related stress and thus warrant further research.

668 TRANSITION READINESS IN YOUTH WITH INFLAMMATORY BOWEL DISEASE

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Transition readiness is the acquisition of behaviors that support self-care, effective healthcare decision-making, and self-advocacy. Successful preparation for transition helps ensure continuity of care as an adolescent or young adult (AYA) moves from pediatric to adult healthcare, whereas poorly planned transition can result in poorer health-related outcomes. We sought to describe parent and youth perceptions of AYA involvement in key domains of healthcare behaviors known to be important for successful transition to adult care and to evaluate predictors of transition readiness in patients with inflammatory bowel diseases (IBD).

Methods: AYA (ages 16-20) with IBD and their parents were recruited during GI clinic appointments at three Midwestern children's hospitals. Participants completed study-developed measures of patient-provider transition-related communication and a validated measure of transition readiness, the Readiness to Transition Questionnaire (RTQ). The RTQ provided an overall transition readiness score (RTQ-Overall) and an AYA responsibility score (RTQ-AYA Responsibility). AYA also reported on demographics and self-efficacy via the IBD Self-Efficacy Scale. Results: Seventy-six AYA participated [M(SD) age 17.37 (1.20); 54% female]. Most AYA had Crohn's disease (75%), and time since diagnosis was M(SD) 5.64(3.83) years. Most AYA (>75%) perceived high involvement ("often" or "almost always" responsible) in the following healthcare behaviors: taking medications as prescribed, attending medical appointments, explaining medical condition to others and communicating with medical staff. Behaviors in which AYA perceived low levels of involvement ("not at all" or "sometimes" responsible) included: knowing insurance coverage details, scheduling medical appointments and ordering medication refills. Parents identified similar domains of high and low AYA involvement. Older age and more frequent transition-related communication were the most consistent predictors of transition readiness in regression analyses. Age accounted for 8 - 12% of variance in RTQ-Overall scores and 17 - 29% in RTQ-AYA Responsibility scores. Transition-related communication explained 9 - 15% of variance in RTQ-Overall scores and 4% in RTQ-AYA Responsibility scores. AYA self-efficacy also accounted for 7% of variance in parent report of RTQ-Overall scores.

Conclusions: AYA are highly involved in illness-management tasks (e.g., taking daily medications, attending medical appointments), but less involved in knowledge of healthcare resources (e.g., insurance details, scheduling, ordering refills). Transition readiness increases with age, suggesting that transition to adult care may be most appropriate as youth enter young adulthood. Furthermore, discussion of healthcare resources and transition-focused education during clinic appointments are critical strategies for enhancing transition readiness and improving transfer to adult IBD care.

669 DIAGNOSTIC AND PROGNOSTIC FACTORS OF PEDIATRIC CROHN'S DISEASE

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Background: Approximately a quarter of cases of Crohn's disease begin in childhood or adolescence. Despite extensive research, it is not yet possible to identify prognostic factors at presentation that may predict progress in clinical practice. There have been attempts to build complex algorithms that include clinical, genetic, serological and morphological characteristics to predict the individual risk of children with Crohn's disease who develop complications. However these resources are difficult to apply in clinical practice.

Objectives: To evaluate the role of certain histological and clinical parameters as predictors of Crohn's disease severity, supporting the early use of biological therapy and to characterize the relevance of granulomas as a prognostic factor and the role of upper endoscopy in establishing the diagnosis.

Methods: Clinical records of 128 patients with Crohn's disease from the São João Hospital (Porto, Portugal) with at least 12 months of follow-up were reviewed. Clinical information, laboratory, pathology and imaging results were recorded.

Results: Thirty-three percent and 49.6% of patients had endoscopic and histological criteria, respectively, consistent with the involvement of the upper digestive tract in Crohn's disease. Granulomas were found in 39.4% of the patients. From these, 34.0% were found in the upper digestive tract. There was a trend for granulomas being more frequent in male subjects ($p=0.065$). Granulomas were associated with higher values in the weighted score of the Pediatric Crohn's disease Activity Index (wPCDAI) at diagnosis and a greater need for biological therapy ($p=0.048$ and $p=0.042$, respectively), despite the use of an elemental diet as first-line therapy in all patients. The wPCDAI and the presence of granulomas in the upper digestive tract were associated with a greater need for biological therapy ($p=0.006$ for both) with an associated risk of 1.025 (95% CI, 1.002 - 1.046) and 3.988 (95% CI, 1.191-13.352), respectively, within 1 year after diagnosis.

Conclusions: These results reinforce the importance of performing upper endoscopy in the diagnostic protocol. The presence of granulomas, particularly in the upper digestive tract, and higher wPCDAI values at presentation, may be potential predictors of the need for early biological therapy.

Keywords: pediatric Crohn's disease; esophagogastroduodenoscopy; granulomas; prognosis

670 THE EXPERIENCE OF ANTI-TNF THERAPY FOR PEDIATRIC INFLAMMATORY BOWEL DISEASE. MANCHESTER EXPERIENCE

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Background and Aims: The introduction of anti-TNF therapy for the treatment of pediatric inflammatory bowel disease (IBD) more than a decade ago has significantly changed the management of this condition. However, there is limited evidence on its safety in long-term use. Here, we aimed to get an overview of the use of biologics, focusing primarily on their safety profile.

Methods: Patients with IBD who were receiving biologics were selected from the IBD register from October 2007 to October 2014. An electronic search of created letters for clinics, hospital admissions, IBD specialist nurse helplines, letters to GPs and other healthcare professionals at periphery hospitals, as well as medical notes, were examined.

Results: 57 children with IBD on biologics were identified: 54 with Crohn's disease, 3 with ulcerative colitis and none with indeterminate colitis. 33 children received infliximab (IFX) and 24 received adalimumab (ADA). Of the patients on IFX, 1 developed psoriatic rash, 1 had a hypersensitivity reaction and 4 had symptoms of IBD that were not fully controlled. 2 on IFX were previously on ADA but stopped due to injection site pain and needle phobia. 9 required a course of steroids and 3 had two courses of steroids while on biologics. For patients on ADA, 1 had injection site inflammation and 4 had symptoms of IBD that were not fully controlled. 16 patients on ADA were previously on IFX but stopped, as 3 developed hypersensitivity reactions, 1 developed numbness in the arms and legs and 12 experienced inefficacy in controlling symptoms. 6 had one course of steroids, 2 had two courses of steroids, 1 had four courses of steroids and 1 had seven courses of steroids while on biologics. There were no serious adverse events or deaths reported. 24 patients had repeat endoscopy within 12 - 18 months of biologic treatment, 21 did not have repeat endoscopy and 12 were not due for a repeat.

Conclusion: This study shows that treatment with an anti-TNF is safe and well tolerated by patients. It is moderately effective in patients with moderate-to-severe IBD. Less than half of patients were getting endoscopic reassessment within 18 months of commencing biologics, which could have implications on cost-effectiveness in the long run.

671 PREDICTORS OF PERIANAL FISTULA HEALING IN CHILDREN WITH NEWLY DIAGNOSED CROHN'S DISEASE

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Background: Perianal fistulas are among the most severe complications of Crohn's disease (CD). Patients with perianal fistulas have increased morbidity and worse clinical outcomes compared to those without them. There are limited data about perianal fistulas in children. Our objective was to determine the predictors of perianal fistula healing among newly diagnosed pediatric CD patients.

Methods: We conducted a single-center, retrospective cohort study of all pediatric patients with newly diagnosed CD from January 2005 to November 2015. Perianal fistula identification was based on documented exam and/or cross-sectional imaging. Patients with prior history of inflammatory bowel disease, perianal fistula occurrence later in disease course, or ambiguity of fistula diagnosis were excluded. Patients were followed until fistula healing, defined by documented resolution on imaging or exam if no further imaging was done. Bivariate associations between those with and without fistulas were compared with χ^2 or Fisher's exact test. Time to healing was analyzed using bivariate and backward stepwise Cox proportional hazard regression models considering relevant covariates, including treatment within three months of diagnosis, surgical procedures, and patient demographics.

Results: Of 362 patients identified, 57 (15.7%) had a perianal fistula at CD diagnosis. These patients were more likely than those without a perianal fistula to have perianal lesion (skin tag, hemorrhoid) removal (11% vs. 0%; $p<0.001$), fistulotomy (12% vs. 0%; $p<0.001$), or incision and drainage of a perianal abscess (12% vs. 3%; $p<0.001$) prior to CD diagnosis. After diagnosis, patients with a fistula were more likely to be treated with antibiotics (77% vs. 16%; $p<0.001$) and less likely to receive steroids (21% vs. 59%; $p<0.001$). Body mass index (BMI) of patients with a fistula was ≤ 10 th percentile for age for 33% (14/43) of patients treated with anti-tumor necrosis factor α (TNF- α) and none (0/8) for those on other treatments ($p<0.001$). Bivariate analyses revealed no predictors of time to healing (Table 1). On multivariate analysis (Table 1), seton placement was associated with shorter time to healing (hazard ratio (HR) 5.11, $p=0.031$) and delayed fistula healing was associated with fistulotomy (HR 0.18, $p=0.022$), higher BMI at diagnosis (HR 0.98; $p=0.021$), and anti-TNF- α use (HR 0.037, $p=0.022$). Healing time was not different with concomitant anti-TNF- α and immunomodulator therapy compared to monotherapy.

Conclusions: Perianal lesion removal prior to CD diagnosis was only seen in patients with a perianal fistula. Seton placement was the only predictor of shorter time to fistula healing. Patients with fistulotomy and elevated BMI had longer healing times. Anti-TNF- α usage was associated with longer healing times, which was likely confounded by indication as a marker of disease severity. Further research is needed to better understand predictors of fistula healing in order to develop improved treatment strategies.

	Bivariate HR (95% CI)	Multivariate HR (95% CI)
Patient Demographics		
Sex	1.19 (0.64 - 2.22)	—
Race	0.75 (0.40 - 1.41)	0.83 (0.43 - 1.60)
Age at Diagnosis	0.97 (0.88 - 1.06)	—
Body Mass Index at Diagnosis	0.99 (0.98 - 1.004)	0.98 (0.97 - 0.99) *
Paris Classification	0.99 (0.57 - 1.72)	—
Procedures		
Perianal lesion removed before diagnosis	0.79 (0.33 - 1.89)	—
I&D at or before diagnosis	0.8 (0.37 - 1.72)	0.41 (0.10 - 1.67)
Fistulectomy at or before diagnosis	0.53 (0.21 - 1.36)	0.18 (0.04 - 0.78) *
Seton placement at or before diagnosis	0.92 (0.44 - 1.91)	5.11 (1.17 - 22.4) *
Treatment		
Anti-TNF α use	0.72 (0.44 - 1.20)	0.37 (0.16 - 0.87) *
Dual therapy (Anti-TNF α + immunomodulator)	0.91 (0.55-1.52)	—
Antibiotic use	0.62 (0.31 - 1.23)	0.6 (0.24 - 1.49)
Corticosteroid use	1.16 (0.57 - 2.34)	0.72 (0.31 - 1.65)

* $p<0.05$; HR Hazard Ratio; CI, Confidence interval

672 UNDER-CARBOXYLATED AND CARBOXYLATED OSTEOCALCIN STATUS AS AN INDICATOR OF VITAMIN K2 DEFICIENCY IN INFLAMMATORY BOWEL DISEASE CHILDREN AND HEALTHY CONTROLS

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Objective: Vitamin K, its K2 form in particular, acts as a co-factor for the post-translational carboxylation of glutamate residues in such proteins as osteocalcin, a protein synthesized by osteoblasts. Several studies in adults suggest a beneficial role for vitamin K in bone mineral metabolism and bone fracture prevention, although precise mechanisms have not been elucidated. In pediatric populations, especially in groups with chronic diseases such as inflammatory bowel disease (IBD), deficiencies of vitamin K may have significant consequences, such as loss of bone mineral density or growth impairment.

Aim: To assess the circulating levels of under-carboxylated (inactive) osteocalcin (ucOC), carboxylated fraction of osteocalcin (cOC) and ucOC:cOC ratio (UCR) (indicator for vitamin K2 status), in healthy children and children with IBD.

Methods: A pilot, prospective, cohort study in a total of 24 children, including 15 healthy children and 9 with IBD in clinical remission. The mean age for both groups was 12 years. There were 11 boys and 13 girls. From every study participant, a blood sample was taken by venepuncture. After serum preparation, the samples were frozen and kept at minus 40°C until use. Accurate concentrations of under-carboxylated and carboxylated fraction of osteocalcin in human serum was measured by a highly specific enzyme-linked immunoassay (Takara, Japan). Conjunction of the two tests allowed us to obtain more complete bone metabolic data. Serum vitamin D3 concentrations were also measured using standardized methods.

Results: The median ucOC serum concentration in the whole examined group equaled 34.30 ng/mL (7.37 - 37.51, SD 8.37). It was 32.29 ng/mL (20.38 - 37.51, SD -5.48) in healthy children and 35.03 ng/mL (7.37 - 36.40, SD -12.03) in the IBD group. The median UCR serum concentration was 1.85 ng/mL (0.94 - 4.30, SD 1.04) in the healthy group and 1.11 ng/mL (0.48 - 3.46, SD 1.15) in the IBD group. There were no significant differences between boys and girls in both groups. The median vitamin D serum concentration was surprisingly low in both groups, especially in healthy children 15.40 ng/mL (10.00 - 44.80) compared to the IBD group 27.20 ng/mL (20.40 - 43.30, $p=0.0027$). Only 7/24 (29%) children received vitamin supplementation daily, 6 from the IBD group and only 1 from the healthy group.

Conclusion: Based on our study, children in both groups had high levels of ucOC and low levels of UCR, which indicate vitamin K2 deficiency. In the IBD group, we found that ucOC concentrations were higher and the UCR level was lower than in the healthy group, suggesting a higher bone turnover and lower vitamin K2 levels in that group. Surprisingly, levels of vitamin D3 were extremely low in both groups, only 7 children received the recommended daily supplementation of that vitamin, thus contributing to further loss of bone mineral density. Further studies on larger groups are needed to verify our results.

673 PYODERMA GANGRENOSUM, AUTOIMMUNE THYROIDITIS AND CROHN'S DISEASE IN A THAI MALE ADOLESCENT

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Pyoderma gangrenosum (PG) is a rare, chronic, inflammatory disorder of the skin, associated with immune dysregulation and other systemic diseases. We report a case of PG with inflammatory bowel disease (IBD) in a 17-year-old Thai male patient who presented with large, multiple, painful ulcers on his hands, legs and feet. He had concomitant persistent diarrhea, weight loss and episcleritis. He also had had poorly controlled autoimmune thyroiditis for four years. Laboratory tests revealed hypochromic, microcytic anemia, high erythrocyte sedimentation rate and C-reactive protein, hypoalbuminemia, positive anti-*Saccharomyces cerevisiae* antibody and antinuclear antibody. Colonoscopic examination demonstrated multiple mucosal erosions predominately at the sigmoid colon and cecum with rectal sparing. Histological findings were compatible with Crohn's disease. He was treated with a systemic corticosteroid, oral mesalazine and azathioprine along with nutritional support and local skin care. His symptoms improved after two weeks of therapy. In conclusion, IBD may be found in young Asians with PG and other extraintestinal manifestations.

674 SURGICAL MANAGEMENT OF REFRACTORY CROHN'S COLITIS: A SINGLE-CENTER, RETROSPECTIVE REVIEW

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Background: Pediatric patients (pts) with medically-refractory Crohn's colitis (CC) require surgical management with either total colectomy with end ileostomy (TC) or diverting loop ileostomy (DLI). Data on outcomes of these treatments is lacking.

Methods: We retrospectively reviewed pts <18 yrs who underwent surgery for refractory CC (January 1998 - January 2016). Demographics, surgical complications and subsequent operations were recorded. Pre- and post-operative serology, anthropometric data and medications were also collected.

Results: We identified 22 TC pts and 5 DLI pts (16 males, 59%) with a median age at surgery of 15 yrs (3 - 18). Mean follow-up was 45 months (3 - 120). Indications for surgery included medically refractory disease (81%), failure to thrive (85%) and toxic megacolon (7%). Comorbidities secondary to CC were common: 73% had anemia, 29% required TPN and 82% had features of growth impairment. Pre-operatively, all pts received corticosteroids, 25 were on anti-TNF agents and 25 were on immunomodulators. At 1yr post-operatively, 10 pts required no medications, 6 received at least 1 course of corticosteroids, and 6 were on immunomodulators. Ten pts continued on anti-TNF agents and 4 received other biologic agents. A laparoscopic approach was used in 23 pts versus open techniques in 4, with a mean length of stay of 5.2 days (2 - 13). Two pts (6%) underwent stoma revision within 30 days of operation. Long-term complications occurred in 23 pts and included: ileostomy issues (stenosis, prolapse, or hernia, n=7), proctitis (n=7), ileitis (n=8), fistulae (n=6), small bowel strictures (n=2), and recurrent obstruction (n=1). Four DLI pts had persistent colitis. The majority of TC pts (59%) attempted restoration of continuity; 9 with ileorectal anastomosis, 4 with proctectomy and ileoanal anastomosis, at an average of 21 months (range 0 - 73). IPAA was only offered if the diagnosis of Crohn's was not definitively established at that time. One DLI pt (20%) underwent ileostomy takedown but subsequently needed re-diversion. At last follow-up, 10 (45%) TC pts and 0 DLI pts were in intestinal continuity. Of the 12 TC pts who had ileostomies at last follow-up, future restoration of continuity is planned for at least 6 pts (50%). Average anthropometric measures of growth all improved for TC pts by 1yr post-operatively (Table 1). These did not improve for the DLI pts. TPN dependence continued in 2 TC pts and 1 DLI pt.

Conclusions: This retrospective study demonstrates that colectomy significantly improves nutritional and growth parameters in children with medically refractory Crohn's colitis. Intestinal continuity was able to be restored in 45% of these pts. In contrast, those who underwent isolated diverting loop ileostomy had poor outcomes. For pediatric patients with medically-refractory Crohn's colitis, colectomy may offer an opportunity to improve growth and wean medications, with a good long-term likelihood of achieving intestinal continuity.

675 TOLL-LIKE RECEPTOR 1 POLYMORPHISMS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE (IBD) IN PEDIATRIC POPULATION

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Background: Toll-like receptors play an important role in innate and mucosal immunity. Defective toll-like receptor 1 signaling has been shown to be associated with defective immune responses and disrupted mucosal immunity in animal studies. We studied 2 common TLR1 polymorphisms associated with defective TLR1 signaling and its association in IBD susceptibility. TLR1 I602S polymorphism causes defective cell surface trafficking. TLR1 N248S polymorphism causes defective ligand recognition by protein change. Both these polymorphisms cause decreased TLR1 function. We hypothesized that TLR 1 polymorphisms would be associated with IBD susceptibility in a pediatric population. Methods: We conducted a multicenter study (Children's Hospital Los Angeles [CHLA] and University of Chicago) with a control population from a healthy pediatric clinic at CHLA. DNA was extracted from buccal swabs and genotyping for I602S and N248S was performed using quantitative PCR technique.

Results: A total of 230 IBD patients were analyzed (African American 29, Hispanic 43, Caucasian 135, other 23). A total of 100 controls were analyzed (African American 6, Caucasian 9, Hispanic 82, other 3). Refer to table 1 for details. There was increased expression of the variant homozygous genotype and heterozygous genotypes in IBD compared to control group in which homozygous expression of non-variant allele was more frequent (*P*-value significant). There was also a difference in the expression of the homozygous variant genotype seen between different racial groups (*P*-value significant).

Conclusion: Although there was a difference in racial composition of the IBD and control populations (more Caucasians in the IBD group and more Hispanics in the control group), our data suggest that there is a significant difference in expression of homozygous variant genotype in TLR1 polymorphism I602S and N248S between the control and IBD populations. Further studies with genotype-phenotype correlation are required with larger sample sizes.

	IBD (n=230)	Control (n=100)	Difference <i>P</i> -value
<i>Gender</i>			
Male	134 (58.3%)	45 (45.0%)	0.045
Female	94 (40.9%)	55 (55.0%)	
<i>Race</i>			
White	135 (58.7%)	9 (9.0%)	<0.0001
Black	29 (12.6%)	6 (6.0%)	
Hispanic	43 (18.7%)	82 (82.0%)	
Other	23 (10.0%)	3 (3.0%)	
<i>Age onset</i>			
A1a	67 (29.1%)	-	NA
A1b	151 (65.6%)	-	
A2	9 (3.9%)	-	
<i>Age onset (years)*</i>	13 (9-16)	-	
<i>Age (years)</i>	-	4.72 (1.40 - 11.63)	NA
<i>IBD type</i>			
CD	125 (54.3%)	-	NA
UC	95 (41.3%)	-	
Indeterminate	8 (3.5%)	-	
<i>TLR1 I602S</i>			
II	73 (31.7%)	58 (58.0%)	<0.0001
SI	102 (44.3%)	37 (37.0%)	
SS	55 (23.9%)	5 (5.0%)	
<i>TLR1 N248S</i>			
NS	93 (40.4%)	46 (46.0%)	0.001
SS	65 (28.3%)	24 (24.0%)	
NN	44 (19.1%)	30 (30.0%)	

	White (n=135)	Black (n=29)	Hispanic (n=43)	Other (n=23)	Difference P-value
<i>TLRI 1602S</i>					
II	22 (16.3%)	18 (62.1%)	23 (53.5%)	10 (43.5%)	<0.0001
SI	66 (48.9%)	9 (31.0%)	18 (41.9%)	9 (39.1%)	
SS	47 (34.8%)	2 (6.9%)	2 (4.6%)	4 (17.4%)	
<i>TLRI N248S</i>					
NS	48 (35.6%)	9 (31.0%)	25 (58.1%)	11 (47.8%)	<0.0001
SS	51 (37.8%)	1 (3.4%)	8 (18.6%)	5 (21.7%)	
NN	14 (10.4%)	16 (55.2%)	9 (20.9%)	5 (21.7%)	

676 PROACTIVE INFLIXIMAB CONCENTRATION MONITORING IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: A PILOT OBSERVATIONAL STUDY

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Infliximab (IFX) is used to treat pediatric inflammatory bowel disease (IBD). Proactive concentration monitoring of IFX is gaining more ground in clinical practice, as it can improve drug efficacy. The role of pre-medication with corticosteroids in preventing antibody formation to infliximab (ATI) is controversial. A change in clinical practice has occurred at our institution: IFX and ATI levels are proactively checked at 14 and 54 weeks. The primary objective of this study was to evaluate clinical outcomes after this practice change. Additionally, we aimed to assess ATI prevalence and potential correlating factors.

Methods: This was a retrospective, observational cohort of pediatric IBD patients that initiated IFX between 11/1/2013 and 4/30/2015, had IFX and ATI levels measured at 14 (IFX14/ATI14) and 54 weeks (IFX54/ATI54) and received pre-medication with methylprednisolone. IFX therapy was escalated by dose increase or decreased in frequency as per each treating physician's discretion. Data included demographics, concomitant medications, laboratory markers [albumin, C-reactive protein (CRP), calprotectin], Pediatric Crohn's Disease or Ulcerative Colitis Activity Index (PCDAI/PUCAI), as well as IFX dose and frequency at 14 and 54 weeks. IFX/ATI level testing was done by the same electrochemiluminescence immunoassay. Data were analyzed with descriptive statistics; T-test for continuous variables and Fisher's exact for categorical variables. $P < 0.05$ indicated statistical significance. This study was IRB approved.

Results: Of a total of 51 patients started on IFX, 11 (22%) did not have IFX/ATI levels checked because of insurance issues, 3 (6%) had secondary loss of response, 1 switched to another anti-TNF because of patient preference and 3 (6%) transitioned to another facility. We studied the remaining 33 patients. Cohort demographics are seen in Table 1. PCDAI/PUCAI at 54 weeks was available in 31 patients. Of those, 29/31 (94%) were in clinical remission (score < 10) and the remaining 2 had a score of 10. Escalation of IFX therapy was seen in 1/3 of the cohort by week 14 and in 21/33 (64%) by the end of 1 year. 13/33 (39%) received an immunomodulator during the 1 year course. 9/33 (27%) patients had detectable (> 22 ng/mL) ATI14 and 14/33 (45%) ATI54. Detectable ATI14 correlated with abnormal CRP and lower IFX14 levels (< 10 ug/mL) without reaching statistical significance (p 0.16 and 0.27, respectively). Undetectable ATI54 correlated with lower activity index scores (PCDAI/PUCAI of < 5 , p 0.004) and higher IFX54 levels of > 10 ug/mL ($p = 0.04$). Immunomodulator use was associated with undetectable ATI54 ($p = 0.07$).

Conclusion: Proactive IFX concentration monitoring leads to desired clinical outcomes. In this cohort with pro-active drug monitoring, clinical remission at week 54 was seen in 94% of patients. ATI prevalence at 54 weeks was 45% despite pre-medication. A planned, future study will aim to compare clinical outcomes before and after pro-active monitoring was implemented.

Table 1: Patient demographics and disease characteristics

Baseline Demographics	n=33
Age at diagnosis, mean \pm SD (year)	14.0 \pm 3.3
Sex [(male (%):female (%)]	12 (36%):64 (64%)
BMI, mean \pm SD (%)	47.4 \pm 36.8
Disease type	Crohn's disease: 25 (76%) Ulcerative colitis: 7 (23%) Indeterminate colitis: 1 (3%)
Disease duration before IFX treatment, median (months)	2.9 months
PCDAI/PUCAI score, median	22.5
CRP level, median, mg/dL	2.3

677 THE IMPACT OF OBESITY ON THE NATURAL HISTORY OF PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Background: Links have been made between obesity and a pro-inflammatory state leading to the development of various inflammatory diseases. Data on the clinical course, response to treatment, as well as epidemiologic factors of obese patients with inflammatory bowel disease (IBD) are quite limited. We used this retrospective study to investigate the impact of obesity on IBD severity, complications, and treatment.

Methods: This is a retrospective analysis of prospectively collected data of patients at the Children's Medical Center, Dallas with a diagnosis of IBD over the past 5 years. Patients with IBD were categorized by body mass index (BMI). Biochemical markers of inflammation, response to medical therapy, develop of anti-drug antibodies, as well as factors such as age, race, gender, and socioeconomic background were characterized. Obesity was defined as a BMI ≥ 30 (type I: 30 - 34.9, type II: 35 - 39.9, and type III: ≥ 40).

Results/Hypothesis: Among the patients with a diagnosis of IBD over the past 5 years at the Children's Medical Center, we expect roughly 30% to be classified as having a BMI ≥ 30 . We predict that obesity in IBD will be associated with a more pro-inflammatory state, with higher values

of serological makers of inflammation, such as CRP, ESR, and platelets compared to IBD patients with normal BMI. In addition, we anticipate that the obese population will have worse disease, requiring more aggressive medical therapies and more hospitalizations and will be more likely to develop anti-drug antibodies. We also postulate that there will be an association between obese patients with IBD and female gender, white race, and lower socioeconomic status. We predict that these differences in IBD patients with obesity compared with IBD patients with normal BMI will be more significant in patients with ulcerative colitis compared to those with a diagnosis of Crohn's disease.

Conclusions: We have identified 89 patients who fulfill the inclusion criteria with a BMI greater than 30. An initial sample of those patients revealed a higher utilization of biologics, lower socioeconomic class and early progression to complicated disease. A full chart review will lend power to these observations. We are conducting this investigation to determine whether or not obesity in IBD is associated with worsening disease needing more aggressive therapy, and to determine whether there is an association with female gender, white race, and lower socioeconomic status.

678 TASTE AND SMELL IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Introduction: The inflammatory bowel diseases (IBD) have a multifactorial pathogenesis. In adult IBD patients, diet modifications were reported, bringing interest to the gustative and olfactive capacities of these patients, which were shown to be distorted in several studies. Up until now, no evaluation had been done in children with IBD. The main objective of this work was to assess the olfactive and gustative capacities of children with IBD.

Methods: We conducted a prospective study to test the sensibility, identification and characterization of the sense of smell and taste in 41 IBD patients aged 7 to 18 years old. The results were compared with those of a healthy control population of the same age. We also analyzed correlations between the results of the tests and the clinical and biological characteristics of the patients.

Results: The olfactive capacities were altered with a significant decrease in sensibility (-0.9 ± 1.1 DS/age, $p < 0.0001$), identification (-1.6 ± 1.4 DS/age, $p < 0.0001$), and global change of the subjective criteria ($p < 0.05$). The capacities of identification (-0.4 ± 1.3 DS/age, $p = 0.03$), recognition (-0.4 ± 1.2 DS/age, $p = 0.046$) and perception of the intensity of the flavors (-0.5 ± 1.2 DS/age, $p = 0.009$) were decreased. The hedonic score was significantly increased for the sweet and acid flavors and decreased for the salty flavor ($p < 0.05$). The olfactive sensibility correlated to the age of the patient and disease duration.

Conclusion: This study highlighted a global disorder of olfaction and changes in the perception of taste in children with IBD. These changes were not significantly associated with the nutritional status or activity of the disease.

679 SURGERY IN PEDIATRIC CROHN'S DISEASE, 2002-2014

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Background: Patients with Crohn's disease (CD) often require surgical intervention. Observations of pediatric patients prior to 2008 showed that the risk for bowel surgery at 5 years from diagnosis was 14% (Schaefer *et al. Clin Gastro Hepatol.* 2010).

Aim: To evaluate the cumulative probability of bowel surgery in an inception cohort of pediatric patients with CD prior to, and after, 2008 and to identify risk factors associated with bowel surgery.

Methods: Patients ≤ 16 years of age with newly diagnosed CD were enrolled in the Pediatric IBD Collaborative Research Group Registry, a prospective, North American 31-center, observational study from 2002 to 2014. Diagnosis of CD was by conventional criteria. Patients were managed according to the practice of their individual physician. Uniform data were collected at diagnosis, 30 days, and then quarterly. Bowel surgery was defined as stricturoplasty, ostomy, and resection of small bowel, colon, or both.

Results: From 2002 to 2014, 1442 CD patients were enrolled in this observational study; mean age at diagnosis was 11.8 years, 41% were female. 171 of the 1442 enrolled patients underwent an initial bowel surgery. Kaplan-Meier analysis indicated that the overall risk of bowel surgery was 4% within the first year of diagnosis, 9% at 3 years, 13% at 5 years and 26% at 10 years (Figure 1). Of the 171 patients who underwent a first bowel surgery, 15% (25/171) had their surgery within 3 months of their initial diagnosis, including 7% (12/171) within the first 30 days from diagnosis. One-third (56/171) of the surgeries recorded occurred during the first year after diagnosis and 65% (111/171) within 3 years of diagnosis. Kaplan-Meier analysis further demonstrated that disease behavior at diagnosis (penetrating vs. stricturing vs. inflammatory) significantly affected the risk of surgery (Figure 2). Neither the year of diagnosis, nor the age of the patient at diagnosis, affected the risk of surgery. The five-year risk of bowel surgery was similar in patients diagnosed before 2008 compared to those diagnosed after 2008. With regard to gender, after 5 years of disease, 12.5% of males and 14% of females had undergone bowel surgery. After 10 years, the risk of bowel surgery was 20.1% for males and 32.3% for females ($p = 0.058$).

Conclusion: The cumulative risk of first bowel surgery in this cohort of children with CD was 26% at 10 years. The significant, very early risk of surgery, within the first three months of diagnosis, attests to the significant therapeutic challenges in dealing with patients who present with

aggressive, penetrating disease. Disease behavior at diagnosis strongly predicted risk for surgery. Even with the limitations of this observational study, the importance of strategies that prevent progression to penetrating disease is emphasized.

Fig 1

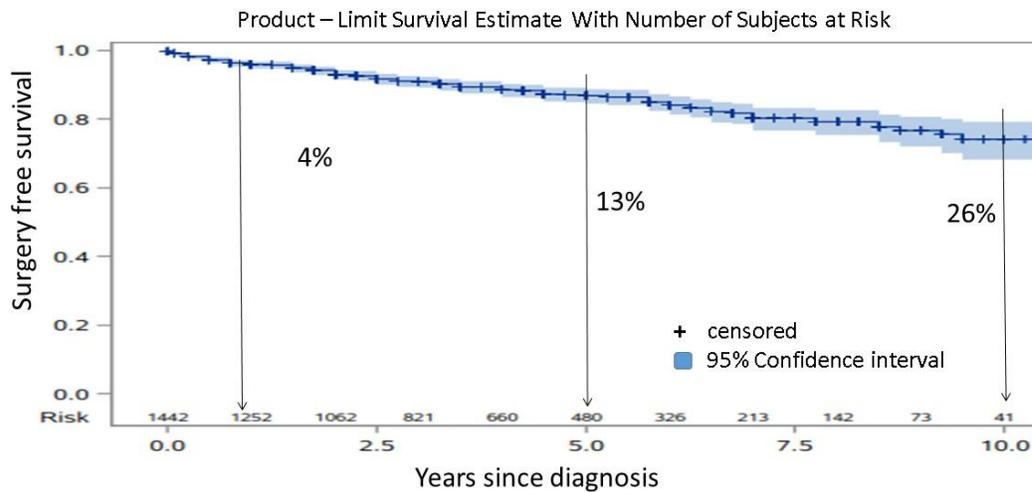
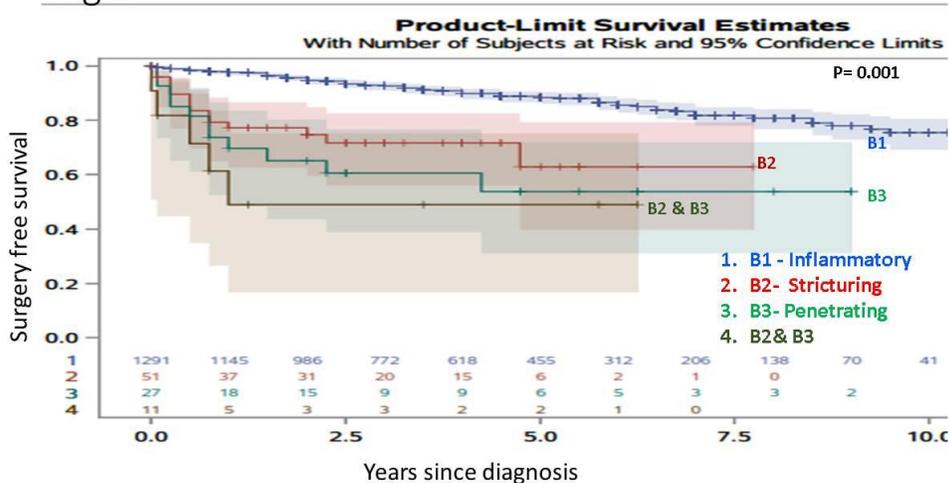


Fig 2



680 SERUM INFLIXIMAB TROUGH LEVELS ARE ASSOCIATED WITH MUCOSAL HEALING IN PEDIATRIC CROHN'S DISEASE PATIENTS

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Background and Aims: There is limited data regarding the association between serum infliximab trough levels and mucosal healing in the pediatric population of Crohn's disease. We aimed to investigate whether serum infliximab trough levels were associated with mucosal healing and to identify the cut-off level required for mucosal healing in pediatric Crohn's disease patients under maintenance treatment.

Methods: We performed a single-center, retrospective, cross-sectional study of 98 patients with pediatric Crohn's disease who had been receiving infliximab for at least 1 year. Mucosal healing was defined as a Simple Endoscopic Score for Crohn's disease (SES-CD) of <3. Logistic regression analyses were performed to examine the association between demographic, clinical and biological variables including serum infliximab trough levels and mucosal healing. Receiver operator characteristic curves were used to derive the cut-off level of serum infliximab trough concentration required to achieve mucosal healing.

Results: Median serum infliximab trough levels were significantly higher in patients with mucosal healing compared to those without mucosal healing (4.8 ± 2.3 vs. 3.4 ± 2.0 $\mu\text{g/mL}$, $p=0.002$). According to multivariate analysis, only infliximab trough levels were associated with mucosal healing (odds ratio 1.26, 95% CI, 1.05 - 1.57, $p=0.022$). The cut-off level of infliximab trough concentration in identifying mucosal healing was 5.1 $\mu\text{g/mL}$ (area under the curve 0.685, 95% CI, 0.578 - 0.791, $p<0.001$).

Conclusions: There was a significant association between serum infliximab trough levels and mucosal healing in pediatric Crohn's disease patients under maintenance infliximab. Patients with a serum infliximab trough level higher than 5.1 µg/mL may better achieve and maintain mucosal healing.

681 LINEAR GROWTH FAILURE IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS

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Introduction: Growth failure is common in children with inflammatory bowel disease (IBD), mainly in those with Crohn's disease (CD). Its etiology is multifactorial, such as increased energy expenditure, malabsorption and low dietary intake secondary to abdominal complaints. However, it is mainly induced by the damaging effects of chronic inflammatory process on the growth hormone axis. The aim of this study was to analyze height and linear growth rate of the patients with IBD.

Material and Methods: Linear growth data of 36 (60%) UC and 24 (40%) CD patients were obtained from our database and retrospectively analyzed in this study. The severity of disease for UC and CD was determined at admission and at the end of the first year by using PUCAI and PCDAI, respectively. The height for age z (HAZ) scores were calculated for each patient at diagnosis (baseline) and at the end of the first year. In order to evaluate the linear growth of the children with IBD, height velocity z (HVZ) scores were calculated for each patient at the end of the first year. HAZ and HVZ scores below -1.0 were considered as linear growth failure.

Results: The mean age of the children with IBD was 141 months ± 46.8 at diagnosis and 60% were female. PUCAI was moderate in 41% and severe in 29% of UC patients, while 67% of cases with CD had moderate-severe disease activity. Overall, 75% of the patients were in clinical remission at the end of the first year. At diagnosis, the mean HAZ scores were -0.15 ± 1.26 and -0.64 ± 1.05 in UC and CD patients, respectively ($p=0.12$). However, HAZ scores of the patients with UC (-0.17 ± 1.19) and CD (-0.72 ± 0.93) were not better at the end of the first year compared to the z scores at diagnosis. There was a statistical significance between HAZ scores of patients with UC and CD at the end of the first year ($p=0.048$). When the linear growth was evaluated at the end of the first year of follow-up, the percentage of children who had a HVZ score below -1 was 41.7% and 45.8% in children with UC and CD, respectively ($p=0.75$).

Conclusions: Growth failure usually existed at the diagnosis of IBD and often persisted during follow-up period. Although the mean HAZ scores of the IBD patients were not less than -1 at diagnosis and after one year of treatment, the rate of patients whose HVZ scores below -1 were very high despite clinical remission in 75% of patients. Hence, growth velocity might be a more sensitive indicator for those who acquire IBD during childhood and the pre-adolescent period.

682 CHARACTERIZATION OF HISTOLOGIC CHANGES IN CHILDREN NEWLY DIAGNOSED WITH ULCERATIVE COLITIS: THE PROTECT STUDY

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Background: Studies describing histologic changes in children with ulcerative colitis (UC) at diagnosis are sparse. It has been suggested that baseline histology may differ between adults and between younger and older children.^{1,2}

Aim: To describe the histologic changes in a well-characterized inception cohort of children newly diagnosed with UC with respect to age and severity of clinical disease.

Methods: The PROTECT (Predicting Response to Standardized Pediatric Colitis Therapy) Study enrolled children ≤17 years of age, newly diagnosed with UC by standardized criteria. A central pathologist evaluated baseline rectal biopsies for histologic grade of inflammation (I-V), eosinophilic inflammation (none to severe using 32/HPF as a threshold value for EI) and architectural changes (presence/absence). Findings at age <12 yr and ≥12 yr were compared. Disease activity was determined by PUCAI (0-85), Mayo score (0-12), and Mayo endoscopy subscore (MSS) (0-3).

Results: 368 biopsies were scored. Mean patient age was 12.9 ± 3.1 yrs (30% <12 yrs, 50% female). Extensive/pancolitis at diagnosis was observed in 76% of patients. Grades of histologic changes were mild acute cryptitis without abscesses (64%), moderate/marked including crypt abscesses (25%) and chronic only (11%). 56% of biopsies contained >32 eos pHPF. Architectural changes included crypt distortion/atrophy (98%), surface villiform changes (38%), basal plasmacytosis (53%), and basal lymphoid aggregates (64%). Eosinophilic inflammation and grades of histologic inflammation did not differ by age or gender. Eosinophilic inflammation and more severe grades of histologic inflammation were associated with the presence of basal plasmacytosis ($p=0.01$, $p<0.0001$) and basal lymphoid aggregates ($p=0.00003$, $p<0.0001$). Compared to histology grades I/II, grades IV/V were associated with more severe clinical indices including PUCAI ($p=0.003$), total Mayo score ($p=0.002$) and MSS ($p=0.04$). 70% of patients with an MSS of 3 had only chronic or mild inflammation.

Conclusion: This is the first demonstration of the relationships among various aspects of inflammation in UC rectal biopsies at diagnosis and prior to therapy in children. Histologic changes were similar across gender, age, or disease distribution. Eosinophilic inflammation is common in rectal biopsies at baseline, is associated with chronic changes and may contribute to architectural changes, even in biopsies that lack marked acute inflammation. More severe grades of histologic inflammation are associated with increased PUCAI, total Mayo and MSS.

Supported by 1U01DK095745-01. References: 1. Washington K *et al. Am J Surg Pathol.* 2002;26:1441. 2. Robert ME *et al. Am J Surg Pathol.* 2004; 28:183.

683 CANNABIS USE IN ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Complementary and alternative therapies are frequently used by patients to treat their inflammatory bowel disease (IBD).

Cannabis, now legal and increasingly accepted in Colorado, is commonly used by adolescents, both recreationally and for medical treatment. *In*

vitro and *in vivo* models suggest cannabis may be beneficial for treatment of IBD due to its anti-inflammatory, anti-diarrheal and analgesic properties. We sought to examine patterns of cannabis use and measure blood levels in adolescents with IBD.

Methods: We designed an observational study with a validated questionnaire (CIDI supplement) to investigate cannabis use among adolescent IBD patients followed at the Children’s Hospital Colorado IBD center. At the time of consent, all subjects received substance use counseling information. Serum cannabinoid levels (THC and cannabidiol and metabolites) were measured by gas chromatography mass spectrometry in a CLIA compliant and GLP standard laboratory.

Results: Of the first 26 subjects, 8 (31%) reported cannabis use. Of the 8 subjects who reported using cannabis, 5 did so for medicinal reasons, including for pain relief and to stay healthy. Five subjects reported cannabis use weekly or more frequently and all had detectable serum levels. Three subjects had very high THC concentrations, above the Colorado legal limit to drive. None of the non-users had detectable levels. Subjects using cannabis reported administering it in multiple ways including ingestion of edibles and oils, and inhalation by smoking, vaping, and dabbing. The one patient reporting use of CBD oil alone had no detectable levels of the psychoactive metabolite 11-hydroxy-THC.

Conclusions: Our data suggest that adolescents with IBD commonly use cannabis, often for medical reasons, and that, when asked, they are honest about reporting use. Adolescents with IBD who use cannabis are at risk for substance use problems, including addiction and impaired driving and judgment. Care providers should ask about cannabis use and be aware of its impact. Further study is needed to delineate both the benefits and the risks of cannabis use by adolescents with IBD.

IBD patients n=26	
% reporting cannabis use	31
% reporting use weekly or more frequent	19
Cannabis users n=8	
Age in year, SD	17.6, 1.5
% Male	62.5
% Caucasian race	75
% non-Hispanic or non-Latino ethnicity	87.5
% with Disease type	
Crohn’s	75
Ulcerative colitis	25
THC value range	3.2 - 18.3 ng/mL
% with THC levels above legal limit (5ng/mL)	37.5
CBD value range	1.7 -26.8 ng/mL

684 AN INTEGRATED MICROBIOME AND GENETIC ANALYSIS OF PEDIATRIC CROHN’S DISEASE

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Background: Inflammatory bowel disease (IBD) is an increasingly common disorder that causes inflammation in the gastrointestinal tract, affecting over 5 million people worldwide. IBD encompasses both ulcerative colitis (UC) and Crohn’s disease (CD). Although causes are elusive, recent findings have uncovered over 200 risk loci for IBD in the human genome. Moreover, the gut microbiome has also been shown to play a prominent role in IBD pathology. The relationship between the gut microbiome and host genetics has yet to be integrated into an analysis of pediatric patients presenting with *de novo* IBD.

Purpose: A primary objective in this study was to determine if sufficient host DNA from shotgun metagenomic data could be used to identify human single nucleotide polymorphisms (SNPs). We then investigated which is a stronger diagnostic predictor of IBD risk: human genetics or microbiome variation.

Methods: Metagenomic shotgun sequencing and 16S rRNA gene sequencing was carried out on intestinal biopsy samples from 20 pediatric patients with Crohn’s disease (CD) and 20 controls from a previously studied cohort. After filtering human reads from metagenomic samples, SNPs were called using an established bioinformatics pipeline. Bacterial taxonomy was analyzed using 16S rRNA sequencing data. Host genome and bacterial taxonomy data sets were integrated in a predictive modelling program to determine predictive accuracy of each in predicting CD risk.

Results: We successfully gathered information on host genetic variation from metagenomic reads, with a mean sequencing depth of 7.5x at 16,333,869 SNPs in the human genome across 40 samples. Genetic risk scores based on IBD loci were found to not significantly differ ($p=0.74$) between CD patients (0.79) and controls (0.70). Despite a lack of genetic variation between CD and controls, microbial community composition significantly differed, as measured by beta-diversity ($R=0.06$, $p=0.0259$) and bacterial species richness, as measured by OTU counts (CD 174, control 216, $p=0.0015$). Upon integration of both data sets into a predictive modeling program using machine learning, microbiome data had a significantly greater predictive accuracy compared to human genetics alone (microbiome: 69%, genetics: 61%, $p=0.0013$), but not to both data sets combined (combined: 61%, $p=0.41$).

Conclusions: Our study is the first attempt at integrating human genetics and microbiome data from a single sample source in a cohort of CD patients. Our microbiota diversity findings are consistent with previous analyses of CD; however, further analysis is needed to validate the role of host genetics in CD. Furthermore, we have demonstrated the novel ability to profile both human genetics and microbiota from a single sample source, presenting a streamlined bioinformatics pipeline for analyzing and integrating data for IBD clinical research. Future studies can leverage our findings for clinical diagnostics that involve both human and microbiome.

685 CANNABINOID RECEPTOR 2 FUNCTIONAL VARIANT CONTRIBUTES TO THE RISK OF PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Background: Endocannabinoids may limit intestinal inflammation via cannabinoid receptor 1 and/or 2 (CB1, CB2). We conducted a case-control association analysis to establish the role of a common CB2 functional variant, Q63R, in the susceptibility to inflammatory bowel disease (IBD).

Methods: We genotyped 217 pediatric IBD patients (112 Crohn's disease, [CD], 105 ulcerative colitis [UC]), and 600 controls for the CB2-Q63R variant by Taqman assay. The disease activity was measured with Pediatric Crohn's Disease Activity Index or Pediatric Ulcerative Colitis Activity Index. Additional data were collected from clinical records on age at diagnosis, disease duration and location, extraintestinal manifestations, therapy, clinical relapses and need for surgery.

Results: We found a significant association of the CB2-R63 variant with IBD (allele frequencies $p=0.04$; genotype distributions $p=0.0006$), in particular with CD (allele frequencies $p=0.002$; genotype distributions $p=0.00005$) and with UC only for genotype distributions ($p=0.03$). RR-carriers showed an increased risk to develop a kind of IBD (OR 1.82, $p=0.0002$ for IBD; OR 2.02, $p=10^{-3}$ for CD; OR 1.63, $p=0.02$ for UC). Upon genotype-phenotype evaluation, RR patients showed an increased frequency of moderate-severe disease activity at diagnosis in both CD and UC ($p=0.01$ and $p=0.02$, respectively) and also an earlier clinical relapse in UC ($p=0.04$). In UC, all the clinical features related to the CB2 risk allele were still significantly associated to the variant when analyzed using a multivariate logistic regression model ($p=0.001$).

Conclusions: The CB2-Q63R variant contributes to the risk of pediatric IBD, in particular CD. The R63 variant is associated with a more severe phenotype in both UC and CD. Taken together, our data suggest the involvement of CB2 receptor in the pathogenesis and clinical features of pediatric IBD.

686 UTILITY OF REGULAR INFLIXIMAB LEVELS IN PEDIATRIC CROHN'S DISEASE

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Introduction: Infliximab (IFX) has an established role in treating Crohn's disease. Serum trough IFX levels and anti-drug antibodies are increasingly used to optimize drug dosing in those losing response (LOR) and, in some adult studies, to predict and manage potential LOR. We report performance of routine IFX levels in children and the value of regular levels for guiding management.

Methods: Retrospective chart review of children with Crohn's disease receiving IFX in a tertiary pediatric centre. Patient age, clinical phenotype, duration of therapy, IFX level, biomarkers and changes in management were recorded. Standard induction and maintenance therapy regimes were employed. Remission was defined as clinically well with normal CRP (<5) and FC (<200).

Results: 117 IFX levels were recorded in 46 patients from January 2014 to March 2016. 43/46 (93%) children were on combination therapy with immunosuppression (IS) and only 2 developed IFX antibodies. 43 episodes of relapse (clinical, CRP >5 , FC >200) were documented and IFX levels at this time were significantly lower (mean 4.6 $\mu\text{g/mL}$) than those in remission (mean 6.6, $p=0.02$). 17/43 (40%) in relapse had IFX levels <3.0 vs. 16/74 (22%) in remission with IFX levels <3.0 . 27/117 (23%) of IFX levels led directly to a change in management: 15 episodes of treatment escalation, 7 of de-escalation and 5 changes to adalimumab. Of 15 escalations in treatment, 5 resulted in complete clinical and biochemical improvement to normal. 6/7 treatment de-escalations remained in remission with therapeutic IFX levels. 19 children had IFX levels at completion of induction (mean 8.5) significantly higher than those during maintenance (mean 5.5, $p<0.01$). All 9 children with post-induction IFX level >7 remained in clinical and biochemical remission over the following 6-12 months. 3 children had post-induction IFX levels <3 , 2 failed to go into remission and 1 relapsed at 12 months.

Conclusions: IFX trough levels help guide optimal management of IFX in children, including escalation and de-escalation of dosing, or change to adalimumab. They have some utility as a biomarker, with higher levels associated with ongoing clinical and biochemical remission. High post-induction IFX levels >7 predict a favourable 6-12 month response and low post-induction levels <3 predict a poor response or early relapse. Study numbers are small, but results are consistent with the emerging literature.

687 INFLUENCE OF GENETIC VARIATION IN THE RESPONSE OF MESALAMINE IN ULCERATIVE COLITIS

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Background: Mesalamine is a commonly-prescribed medication that is used to treat ulcerative colitis (UC), although response rates are only 50-72%. The reason for the variable response to mesalamine is poorly understood. Common variation in genes involved in absorption, distribution, metabolism and excretion (ADME) has been shown to play a strong role in predicting response to certain medications, such as warfarin. Mesalamine is inactivated by acetylation and this has been proposed as a possible mechanism for diminished mesalamine response. Our hypothesis was that genetic variability in ADME genes would explain the variable clinical response in UC to mesalamine.

Methods: Subjects with UC who were enrolled in a 6-week clinical trial assessing the efficacy of mesalamine (ASCEND III) were genotyped using the Psych chip that combines genome-wide SNP coverage and common exome variants. Analysis was primarily focused on coding variants in ADME genes that had minor allele frequency (MAF) in controls of $>10\%$ ($n=180$). Mesalamine response was defined as an improvement in both the rectal bleeding score at Week 3 and the physician's global assessment (PGA) at Week 6. Mesalamine non-response was defined as a lack of improvement in PGA at Week 6. Quality control (QC) included individual genotyping rate of $>90\%$ and single nucleotide polymorphism (SNP) genotyping rate of $>98\%$. All included variants must have met Hardy-Weinberg equilibrium ($p<0.001$). Chi-square analysis was performed by genotype for the analyzed genes. A p -value threshold of 2.7×10^{-4} was set for significance. Quality control and analysis was performed using the PLINK toolset.

Results: There were 461 adults with UC included in the study. 55.8% of subjects were male and 97.8% were Caucasian. The cohort included 282 mesalamine responders and 179 mesalamine non-responders. There were no common coding variants in ADME genes that were associated with response to mesalamine. SNPs (outside of ADME gene loci) that demonstrated marginal association with mesalamine response included rs11629409 ($p=6.8 \times 10^{-7}$), rs804956 ($p=5.2 \times 10^{-6}$), rs11159581 ($p=7.4 \times 10^{-6}$), and rs2882618 ($p=7.5 \times 10^{-6}$).

Conclusions: Common genetic variants in ADME genes were not associated with clinical response to mesalamine in adult UC. Further investigation is needed to determine the role of the identified variants in non-ADME gene loci. These data suggest that factors other than host genetics might explain the variable response of mesalamine.

688 INVESTIGATION OF THE ROLE OF DEATH-ASSOCIATED PROTEIN KINASE IN VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE (VEOIBD)

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Background and Aims: VEOIBD is a severe form of IBD that is often intractable due to complexity and heterogeneity in pathogenesis. Over the past years, our NEOPICS group has demonstrated a strong genetic component in this patient population. Recently, a homogenous mutation in DAPK was identified in a male infant with non-specific chronic pan-colitis that presented at 5 months of age with microcephaly, dysmorphic features and motor delay. This study aimed to elucidate the critical role of DAPK in intestinal inflammatory immune responses and IBD.

Methods: NF-KB, IFN α promoter-directed luciferase reporter activity, downstream genes expression, signaling pathway, as well as protein interaction were compared between wild and mutation DAPK in over-expression cell lines.

Results: Pathology samples demonstrated a striking increase in apoptosis in the patient's intestinal biopsy samples. Mutant DAPK abrogated DAPK-induced signaling, as shown by increasing TNF- α -induced NF-KB and increasing secretion of TNF- α and other pro-inflammatory cytokines compared to wild type DAPK, suggesting DAPK-dependent, anti-inflammatory regulation is disrupted in cells overexpression of mutant DAPK. Mutant DAPK also decreased interaction with IFN regulatory factor 3 (IRF3) and Sendai virus-induced ISRE promoter-directed luciferase reporter activity, showing DAPK-dependent, anti-viral immune response is also damaged.

Conclusions: A mutation in the DAPK gene was identified in patients with VEOIBD, resulting in disruption of DAPK-dependent, "negative feedback" regulation and hyper-inflammatory immune response in the intestine, suggesting that DAPK could be a new disease marker and a therapeutic target for patients with very early onset IBD.

No conflicts of interest.

689 ADALIMUMAB TREATMENT FOR LUMINAL INFLAMMATORY PEDIATRIC CROHN'S DISEASE: LONG-TERM, SINGLE-CENTER EXPERIENCE

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Objectives: Real-world experience with infliximab in children treated for luminal inflammatory Crohn's disease (CD) demonstrates that durability of responsiveness is enhanced by concomitant immunomodulation (IM) (Church, 2014; Grossi, 2015), but pediatric studies comparing adalimumab (ADA) with and without IM have not been performed. We reviewed the effectiveness of ADA treatment in achieving short- and long-term clinical remission and the effect of concomitant IM on durability of response in a single-center cohort.

Methods: From 2007 to 2015 at SickKids, Toronto, 106 children (63% male; median age 14.3 yrs, IQR 12.8 - 15.8) with luminal inflammatory CD (25% L1, 16% L2, 59% L3) received standard, 2-dose ADA induction, either to treat active CD (n=96) or as maintenance therapy (n=10) following other active treatments (steroids 1, enteral nutrition 4, infliximab 5). Median duration of diagnosed CD at initiation was 22 months. 64 (60%) were anti-TNF naïve; the remainder had prior secondary loss of response (LoR) and/or intolerance to infliximab. Responders, as judged by physician global assessment (PGA) and Pediatric Crohn's Disease Activity Index (PCDAI), continued regularly scheduled maintenance injections \pm IM. Records were retrospectively reviewed to extract PGA of continued response/remission vs. loss of response (LoR), PCDAI, levels of ADA and antibodies. Linear growth and follow-up colonoscopic and imaging data were recorded. Durability of response was explored using survival analysis.

Results: Rates of clinical response (≥ 20 drop in PCDAI) and remission (PGA quiescent and PCDAI < 10) following induction therapy in anti-TNF-naïve and infliximab-experienced patients treated for active disease are shown in *Table 1*. Clinical remission was achieved more often in those patients that were anti-TNF naïve, 83% vs. 62% ($p=0.02$). Responders, and those in remission at ADA initiation (n=92, anti-TNF naïve: 60), continued ADA as every other week maintenance. Concomitant IM was given more often to those with prior infliximab (50%) vs. anti-TNF naïve (25%). During the first year of follow-up, 19% of patients escalated to weekly dosing to maintain clinical remission. During a median follow-up of 20.7 months (IQR 11.7 - 35.2), 17 patients (7 [12%] of anti-TNF naïve; 10 [31%] of prior infliximab) discontinued ADA, 1 due to unsatisfactory primary response. 8 due to intolerance and 8 due to secondary LoR. Concomitant IM use was not significantly associated with a reduced hazard of experiencing secondary LoR (HR 1.46, 95% CI, 0.29 - 7.31; $p=0.64$), while controlling for prior anti-TNF use.

Conclusion: In this cohort of pediatric patients treated with ADA for luminal inflammatory CD, response was greater and more durable in anti-TNF-naïve patients than in those with prior secondary LoR to infliximab. First anti-TNF, ADA response appears durable, even given as monotherapy, but this important question should be further addressed in a prospective randomized controlled trial of ADA \pm IM.

690 FECAL CALPROTECTIN IS INFERIOR TO STANDARD LABORATORY TESTS IN PREDICTING SEVERITY OF DISEASE: THE PREDICTING RESPONSE TO STANDARDIZED PEDIATRIC COLITIS THERAPY (PROTECT) STUDY

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Background: Disease activity assessment at ulcerative colitis (UC) diagnosis is important in selecting initial therapy. Fecal calprotectin (FC) has become a popular method for this assessment, though little data are available comparing it to laboratory tests or clinical disease indices.

Aim: To compare the utility of FC to standard laboratory tests and disease activity indices in reflecting extent and severity of UC at diagnosis.

Methods: The PROTECT Study enrolled children ≤ 17 years, newly diagnosed with UC by standardized criteria. Pediatric Ulcerative Colitis Activity Index (PUCAD), Partial Mayo Scoring Index (PMSI), serum albumin (ALB), erythrocyte sedimentation rate (ESR), hemoglobin (HB),

platelet count (PLT) and FC were determined prior to therapy. Two scenarios were tested: ‘severe vs. non-severe’ and ‘mild vs. non-mild’. ‘Severe’ disease was defined as Montreal E3 (disease to hepatic flexure or beyond) and Mayo Endoscopy Sub-score (ESS) 3. ‘Mild’ disease was defined as Montreal E1/2 with Mayo ESS 1/2 or Montreal E3 with Mayo ESS 1. Descriptive statistics are shown as [medians (IQR)].

Performance of diagnostic modalities was by Area Under Receiver Operating Characteristic curve analysis (AUC). Results: Data were available for 399 participants (median age 13.9 years; IQR 11.3 - 15.7 yrs; 50% female) among whom 112 (28%) had ‘severe’ disease; and 103 (26%) had ‘mild’ disease. For the analyses, 100% had PUCAI and PMSI, 90-95% had standard labs, and 72% had FC. PUCAI, PMSI, ALB and ESR showed the greatest differences between severe disease and non-severe disease. Median PUCAI was clearly higher in severe disease than non-severe disease [65 (50-75) vs. 45 (30-55); $p < 0.001$], as was ESR [33 mm/Hr; (20 - 50) vs. 20 mm/Hr (10 - 35); $p < 0.001$]. ALB was clearly lower (3.5 g/L; IQR 2.9 - 3.9 g/L) (3.9 g/L; IQR 3.4 - 4.3 g/L; $p < 0.001$). Comparatively, median FC was minimally different in severe vs. non-severe [2910 $\mu\text{g/g}$ feces (1474 - 4436) vs. 1891 $\mu\text{g/g}$ feces (979 - 3808); $p = 0.048$). Likewise, when contrasting mild and non-mild patients, whilst median PUCAI, PMSI, ESR PLT and ALB clearly differed, there was no significant difference in FC [mild: 1741 $\mu\text{g/g}$ feces (1013 - 3758) vs. non-mild: 2376 $\mu\text{g/g}$ feces (1160 - 3956); $p = 0.16$]. The discriminative performance of the different tests for each scenario are shown in Table 1.

Conclusions: FC was generally inferior to PUCAI, Partial Mayo Scoring Index and standard laboratory testing in distinguishing extensive and severe mucosal disease from non-severe disease. FC was not helpful in identifying mild disease.

Table 1. Supported by 1U01DK095745-01

	‘Severe’ vs The Rest (112 vs 287)		‘Mild’ vs The Rest (103 vs 296)	
	AUC	95% CI	AUC	(95% CI)
F cal	0.59	0.52-0.66	0.55	0.48-0.63
Alb	0.69*	0.63-0.74	0.66*	0.60-0.73
ESR	0.66*	0.60-0.72	0.73*	0.67-0.79
Hb	0.61	0.55-0.68	0.65	0.59-0.71
Plt	0.61	0.55-0.67	0.68	0.61-0.74
Partial Mayo	0.78*	0.73-0.83	0.78*	0.73-0.83
PUCAI	0.78*	0.73-0.83	0.79*	0.74-0.84

* $p < 0.001$

691 DYSREGULATION OF TNFAIP3 (A20) IS ASSOCIATED WITH INFLAMMATION IN PEDIATRIC CROHN'S DISEASE

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Introduction: Inflammatory bowel diseases (IBD), including Crohn’s disease (CD) and ulcerative colitis (UC) are debilitating pediatric intestinal disorders. Failure in suppressing inflammation contributes to IBD pathogenesis; identification of factors that regulate inflammation can improve IBD management. A20, also known as tumor necrosis factor α -induced protein 3 (TNFAIP3), is a cytoplasmic protein that inhibits NF- κ β -induced inflammation. A20 interacts with A20-binding inhibitor of NF- κ β activation 1 (ABIN-1) and Tax1 binding protein 1 (TAX1BP-1) to attenuate inflammation. IKK β (inhibitor of nuclear factor κ -B kinase subunit β) phosphorylates A20 and stabilizes it. A20 expression is reduced in adult CD patients. We hypothesized that dysregulation of A20 contributes to uncontrolled inflammation in pediatric IBD.

Methods: A total of 39 patients were included in the study (14 non-IBD controls, 15 CD, and 10 UC patients). Gene expression of A20, IKK β , ABIN-1, and TAX1BP, as well as A20 protein and cytokine levels in the TI of IBD and non-IBD patients, were analyzed and compared to disease markers. A20 gene expression and protein levels in T-84 cells and *ex-vivo* biopsies of patients after treating with TNF- α or *Escherichia coli* strains LF-82 and HB101 were analyzed.

Results: TNF- α level and A20 gene expression were significantly elevated in the TI of pediatric CD patients compared to non-IBD and UC. In contrast, A20 protein levels and ABIN-1 expression were significantly low, IKK β was unchanged, and TAX1BP1 expression was high. A20 gene expression positively correlated with biopsy TNF- α levels, serum C-reactive protein and erythrocyte sedimentation rates in CD patients. Polar findings regarding A20 gene expression and protein levels in CD biopsies led us to assess the possibility of bacterial effects on A20 stability. Infection with *E. coli* strain LF82 triggered A20 expression in TI biopsies from CD patients and T84 cells, but did not cause an increase in A20 protein levels.

Conclusions: Our study reports a possible mechanism for failure of A20 to down-regulate inflammation in pediatric CD. We have shown, for the first time, a unique signature profile in pediatric CD patients in the form of high A20 and TAX1BP1, low ABIN-1, unchanged IKK β expression levels, and low A20 protein levels. The discrepancy between A20 expression and protein levels is possibly due to the concomitant lower expression of ABIN-1 and instability of A20 protein, due to lack of post-translational phosphorylation related to lower expression of IKK β . *E. coli* strain LF82 augments A20 expression, but not A20 protein, suggesting that microbes could hinder the capacity of A20 to limit inflammation. Thus, factors affecting A20, and microbes, negatively impact the protein’s anti-inflammatory action in pediatric CD, and contribute toward unremitting inflammation.

692 PHENOTYPIC CHARACTERIZATION, INDICATION AND OUTCOME OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE RECEIVING BLOOD TRANSFUSIONS

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Background: Anemia is a frequent complication of inflammatory bowel disease (IBD), and is present in 6-74% of patients at time of diagnosis. The incidence of acute major gastrointestinal hemorrhage is quite rare in IBD patients and has been reported in 0.1% of ulcerative colitis and 1.2% of Crohn’s patients hospitalized in one adult study. Transfusions in patients with IBD have been associated with a higher risk of alloimmunization and peri-operative infections or complications in adults, but no data have been published in children.

Aims: The primary objective of this study was to describe the prevalence, indications for red blood cell transfusion and the outcomes after RBC transfusions in a pediatric IBD cohort.

Methods: We undertook a retrospective review of all IBD children transfused with allogenic RBCs in the Sainte-Justine Hospital between January 2008 and December 2015. We used Pedidata, an ongoing prospective database established in our hospital, that includes all new cases of IBD. Transfusion records, including detection of alloantibodies, transfusion reactions and number and volume of transfusions, were obtained from the hospital's electronic blood bank database and cross-referenced with the IBD patient database.

Results: During the study period, 662 new cases of IBD were identified in the database. A total of 32 children received 1-6 units of RBC transfusion for treatment of their anemia. This represented 14 children with Crohn's disease, 14 children with ulcerative colitis and 4 children with indeterminate colitis. Ninety percent of transfusions were related to acute intestinal bleeding and the remaining had chronic anemia unresponsive to oral iron therapy. The median delay between diagnosis and the first transfusion was 10 days (IQR 45). Two-thirds of transfusions were given less than 1 month after diagnosis and 99% less than 1 year after diagnosis. More than one transfusion was needed in 19 children due to active bleeding. Severe anemia was the indication for transfusion in all children with a median level of hemoglobin (Hb) before transfusion of 65 g/dL (IQR 11). The response to transfusion was adequate with median post-transfusion levels of Hb reaching 87 g/dL (IQR 17). A total of seven patients had surgery (3 ileocaecal resections and 4 colectomies) within 3 months of transfusion. Benign adverse reactions to transfusion were noted in 2 patients.

Conclusions: In children with IBD, 5% needed a RBC transfusion, the majority of which occurred during the first three months after diagnosis. Acute intestinal bleeding is the most frequent cause of transfusion in these patients. The threshold Hb for transfusion in our cohort was 70 g/dL. Although transfusion in acute intestinal bleeding appears safe, it might be a prognostic marker or a risk factor for poor outcome (need for surgery). Seven children had a post-transfusion antibody analysis; none were positive. We are planning to investigate the presence of antibodies in the remaining 25 patients.

693 PERIPHERAL EOSINOPHILIA IN INFLAMMATORY BOWEL DISEASE PATIENTS ON INFLIXIMAB IS NOT ASSOCIATED WITH ADVERSE OUTCOMES

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Introduction: Inflammatory bowel disease (IBD) is a non-infectious inflammatory condition affecting the intestinal tract. The two most common types of IBD are Crohn's Disease (CD) and ulcerative colitis (UC). Infliximab (IFX) is a human chimeric anti-tumor necrosis factor antibody used in the treatment of moderate and severe IBD to alter the immune response and related inflammation. Eosinophils have been shown to be common in chronically inflamed tissue in IBD, and recently peripheral eosinophilia (PE) has been implicated as a possible marker of disease severity at diagnosis of IBD. A high degree of PE has been noted in our population of IBD patients receiving IFX. The two main aims of this study were to investigate whether an association exists in this population with the development of PE from the use of IFX and, if present, whether this results in a loss of treatment efficacy or in other adverse outcomes.

Methods: A comprehensive, retrospective chart review of all patients aged 4 to 22 years old with pediatric IBD who began induction therapy with IFX between January 2006 and July 2015 was performed. Data were collected at these time points: prior to starting IFX, after 1st infusion, after induction, after the 3rd induction dose and at 6, 12, and 24 months on treatment for PE, as well as for development of Human Anti-Chimeric Antibodies (HACA), infusion reactions, development of cancer or psoriasis, or loss of response to IFX. For this study, PE was defined as any episode of absolute eosinophil count (AEC) >500 at any time with return to normal in between.

Results: A total of 123 patients (mean age at diagnosis 12.4 ± 3.5 years, range 4 - 22 years, 61 males) with IBD starting IFX (108 with CD, 13 with UC, 1 indeterminate) were identified. Of these, 33 (27%) had >1 episode of PE. 43 patients (35.3%) had atopic conditions, but this was not associated with increased risk of PE ($p=0.96$). An independent risk factor for PE was UC (OR 3.2; 95% CI, 0.98-10.49; $p=0.066$) while female gender (OR 0.37; 95% CI, 0.17-0.81; $p=0.0138$) showed lower risk of PE. Incidence of PE decreased 16% per year (95% CI, 6%-26%) for age at diagnosis (OR 0.84; 95% CI, 0.75-0.94; $p=0.003$). However, the mean AEC in the study group did not significantly change over time (215 cells/uL \pm 337 prior to IFX, 228 cells/uL \pm 180 at 24 months). Furthermore, those patients with PE were not found to have any increased risk of HACA, infusion reactions, development of cancer or psoriasis, or loss of response to IFX, either alone or in combination therapy.

Conclusions: PE at diagnosis of IBD has been previously shown to correlate with higher disease activity indices. In IBD patients on IFX, time on IFX was not associated with increases in mean AEC. PE in this patient population was not correlated with increased risk of adverse outcomes or loss of treatment efficacy.

694 NATURAL HISTORY OF PEDIATRIC EOSINOPHILIC COLITIS AND ITS RELATIONSHIP TO INFLAMMATORY BOWEL DISEASE

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Background: Colonic eosinophilia represents a confounding histological feature of pediatric patients undergoing evaluation for common gastrointestinal complaints. While this finding is classically associated with food allergies and parasitic infections, it may also be seen in patients who ultimately have inflammatory bowel disease (IBD). Recent studies provide more details about another group of patients with what has been termed eosinophilic colitis (EoC). Currently, there are no definite diagnostic criteria for EoC and little is known about the prognosis or pathogenesis of this type of colitis.

Objective: The primary objective of this study was to define the clinical presentation and natural history of colonic eosinophilia. The secondary objective was to define findings that could guide the provider to a diagnosis in the setting of colonic eosinophilia.

Methods: To address these questions, we performed an 8-year, retrospective analysis of clinical, histopathological and laboratory data recorded from children between the ages of 1 and 21 years whose colonic pathology reports included the key words suggesting colonic eosinophilia (n=78) and compared them to control patients with normal biopsies (n=38). Members of the gastroenterology section reviewed clinical records independently and eosinophil enumeration was completed on these biopsies and reported as peak eosinophil counts/high power field (eos/hpf).

Results: Patients identified as having colonic eosinophilia were noted to have an increased number of eos/hpf at all locations in the colon compared to normals ($p<0.001$). Similar to normal controls, and to what has been seen previously, there was a decrease in number of eosinophils moving distally from the terminal ileum. Patients diagnosed with IBD did not have this decrease in eos/hpf moving distally. Of the 78 patients

identified to have colonic eosinophilia, 28 (36%) were ultimately diagnosed with IBD. The three most common presenting symptoms associated with colonic eosinophilia were abdominal pain, hematochezia and diarrhea. Findings of more chronic or severe disease (hemoglobin, $p<0.02$; elevated ESR, $p<0.0001$) and chronicity on biopsies ($p<0.001$) were more common in patients with IBD, while vomiting ($p<0.0065$) was more common in patients not diagnosed with IBD. Finally, a subset of the patients ($n=33$) had at least one repeat colonoscopy and 61% of those patients had a change in their diagnosis due to those colonoscopic findings. Overall, we find that colonic eosinophilia is a complex finding, but up to 36% of these patients are ultimately diagnosed with IBD. We note that there are associated findings that can guide the provider in making the final diagnosis and that repeat colonoscopy can help to ultimately define the diagnoses associated with colonic eosinophilia.

695 QUALITY OF LIFE IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: FACTORS THAT CORRELATE WITH WORSENING SOCIAL AND MENTAL HEALTH

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Introduction: Inflammatory bowel disease (IBD) is a chronic, immune-mediated disease, which results in a relapsing and remitting state of debilitating symptoms, requiring frequent clinic visits and stressful hospitalizations. Up to one-quarter of IBD patients present before the age of 20. Many therapies for IBD are given either intravenously (IV) or intramuscularly (IM), which can be an added source of stress for children and adolescents. While many studies have shown that IBD can lead to a decreased quality of life, few have identified which factors, such as type of treatment, severity of disease, or duration of illness are most predictive of worsening social and mental health.

Methods: All pediatric patients aged 7-17 years with a diagnosis of IBD who were seen in either our pediatric gastroenterology clinic or the hospital infusion center were recruited for the study. Patients and parents who agreed to enroll completed the NIH PROMIS paper survey on four quality of life measures: anger, anxiety, depression and peer relationships. Once the responses were obtained, a retrospective chart review was performed to document patient demographics, including age, gender, medications and any comorbidities. In addition, disease activity at the time of survey completion was determined using the standardized Pediatric Ulcerative Colitis Activity Index and the Pediatric Crohn's Disease Activity Index. Raw scores generated from PROMIS instruments were translated into standardized T-scores. Pearson correlation was used to assess the magnitude of association between various disease characteristics and patient scores.

Results: 100 patients were recruited with an average age of 13.8 years. 52 (52%) were male, 83 (83%) had a diagnosis of Crohn's disease (CD) and 15 (15%) had a diagnosis of ulcerative colitis (UC). Correlation between the 4 PROMIS domains and factors such as disease duration, disease activity and mode of medication (IV and IM versus oral) was performed. Disease activity scores in patients with CD correlated with all 4 domains tested: anxiety, depression, anger and peer relationships ($p<0.001$). Disease activity scores in patients with UC correlated with 3 of the 4 domains: anxiety, depression and anger. Neither disease duration, nor the type of medication used, correlated with decreased quality of life in any of the 4 tested domains.

Conclusion: This study suggests that increased disease activity scores in pediatric patients with both CD and UC are associated with decreased quality of life across social and mental health domains. Interestingly, decreased quality of life scores on the PROMIS survey did not correlate with type of medication used, nor did they correlate with disease duration. We suggest that physicians consider formally screening pediatric IBD patients with increased disease activity scores for potential mental and social health-related issues they may be facing, including anxiety, anger and depression.

696 SAFETY OF ADALIMUMAB IN PEDIATRIC PATIENTS WITH POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS, ENTHESITIS-RELATED ARTHRITIS, PSORIASIS, AND CROHN'S DISEASE

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Background: Adalimumab (ADA) is a tumor necrosis factor (TNF) inhibitor used for the treatment of chronic immune diseases. The safety of ADA treatment in pediatric patients (pts) is particularly important since prolonged treatment for these conditions is often required.

Objectives: To evaluate the safety of ADA, alone or in combination with concomitant therapy, in pediatric pts with polyarticular juvenile idiopathic arthritis (pJIA), enthesitis-related arthritis (ERA), psoriasis (Ps), and Crohn's disease (CD).

Methods: Safety data from 6 clinical trials and their open-label extension studies were analyzed. Pts treated for pJIA (NCT00048542, NCT00775437, and NCT00690573) and ERA (NCT01166282 [interim week-52 data]) received ADA 24 mg/m² body surface area every other week (eow) or 20 mg eow (<30 kg) to 40 mg eow (≥30 kg). Pediatric pts treated for Ps (NCT01251614) received ADA 0.4 mg/kg (up to 20 mg) or 0.8 mg/kg (up to 40 mg) at week 0, then eow from week 1. Pediatric pts treated for CD (NCT00409682) received open-label ADA induction therapy (160 mg and 80 mg at weeks 0 and 2, respectively, if ≥40 kg; 80 mg and 40 mg if <40 kg), followed by double-blind maintenance dosing (high dose: 40 mg eow if ≥40 kg or 20 mg eow if <40 kg at week 4; low dose: 20 mg eow if ≥40 kg or 10 mg eow if <40 kg at week 4); weekly dosing was allowed for disease flare at week 12 or later; pts received high-dose eow or weekly ADA during an open-label extension (NCT00686374). Events (E) per 100 pt-years (PY) were calculated using adverse events (AEs) reported after the first ADA study dose through 70 days after the last study dose.

Results: The analysis included 577 pediatric pts, representing 1423.3 PY of ADA exposure (Table). Over 90% of pts across indications reported treatment-emergent AEs. Common AEs were headache (13.8, 46.9, and 23.8 E/100 PY for pJIA and ERA, Ps and CD, respectively), nasopharyngitis (12.4, 57.6 and 14.1 E/100 PY, respectively), and upper respiratory tract infection (30.1, 24.7 and 14.9 E/100 PY, respectively). The rates of serious AEs (E/100 PY) were 13.4 for pts with pJIA and ERA, 7.4 for pts with Ps and 32.3 for pts with CD. One death was reported from an accidental fall (pt with Ps). There were no reports of malignancies, demyelinating disorders, cardiovascular events, pulmonary embolism, reactivation of hepatitis B, Stevens-Johnson syndrome, or erythema multiforme.

Conclusions: The safety profile of ADA in pediatric pts with pJIA, ERA, Ps, or CD was similar across indications, and no new safety signals specific to the pediatric population were identified.

Table. Treatment-Emergent Adverse Events Occurring in ≥1% of Patients in Pediatric Adalimumab Clinical Trials

Treatment-Emergent Event	pJIA and ERA*		Pediatric Ps		Pediatric CD	
	N=274		N=111		N=192	
	Exposure, PYs=797.4		Exposure, PYs=121.5		Exposure, PYs=504.4	
	N (%)	Events (Events/100 PY)	N (%)	Events (Events/100 PY)	N (%)	Events (Events/100 PY)
Any AE	265 (96.7)	4204 (527.2)	100 (90.1)	628 (516.9)	189 (98.4)	2838 (562.6)
Serious AE	67 (24.5)	107 (13.4)	8 (7.2)	9 (7.4)	92 (47.9)	163 (32.3)
AE leading to discontinuation of ADA	24 (8.8)	30 (3.8)	3 (2.7)	3 (2.5)	61 (31.8)	78 (15.5)
Severe AE	45 (16.4)	66 (8.3)	17 (15.3)	24 (19.8)	67 (34.9)	114 (22.6)
Drug-related [†] AE	200 (73.0)	1530 (191.9)	48 (43.2)	176 (144.9)	115 (59.9)	609 (120.7)
Infection	224 (81.8)	1195 (149.9)	82 (73.9)	203 (167.1)	144 (75.0)	657 (130.3)
Serious infection	20 (7.3)	21 (2.6)	1 (0.9)	1 (0.8)	25 (13.0)	34 (6.7)
Opportunistic infection (excluding tuberculosis and oral candidiasis)	0	0	0	0	4 (2.1)	4 (0.8)
Oral candidiasis	2 (0.7)	2 (0.3)	0	0	4 (2.1)	7 (1.4)
Tuberculosis	3 (1.1)	3 (0.4)	2 (1.8)	2 (1.6)	1 (0.5)	1 (0.2)
Active	1 (0.4)	1 (0.1)	0	0	0	0
Latent	2 (0.7)	2 (0.3)	2 (1.8)	2 (1.6)	1 (0.5)	1 (0.2)
Parasitic infection	3 (1.1)	5 (0.6)	0	0	1 (0.5)	1 (0.2)
Allergic reaction ^{‡,§}	41 (15.0)	62 (7.8)	7 (6.3)	9 (7.4)	18 (9.4)	24 (4.8)
Intestinal perforation	0	0	0	0	3 (1.6)	3 (0.6)
Intestinal stricture	—	—	—	—	6 (3.1)	6 (1.2)
Worsening/new onset of psoriasis [‡]	5 (1.8)	6 (0.8)	10 (9.0)	11 (9.1)	6 (3.1)	7 (1.4)
Hematologic disorders	10 (3.6)	16 (2.0)	2 (1.8)	3 (2.5)	27 (14.1)	36 (7.1)
Liver event [†]	5 (1.8)	5 (0.6)	0	0	1 (0.5)	1 (0.2)
Injection site reaction [‡]	101 (36.9)	844 (105.8)	11 (9.9)	17 (14.0)	42 (21.9)	104 (20.6)

—, analyzed only in the CD population; ADA, adalimumab; AE, adverse event; CD, Crohn's disease; ERA, enthesitis-related arthritis; pJIA, polyarticular juvenile idiopathic arthritis; Ps, psoriasis; PYs, patient-years.

*The ERA study includes interim week-52 data.

[†]Investigator assessed as possibly or probably related to study drug.

[‡]None were serious.

[§]Events included hypersensitivity (n=36), urticaria (n=27), asthma (n=16), eye pruritus (n=3), rash (n=3), bronchospasm

Events included anemia (n=24), leukopenia (n=17), neutropenia (n=10), lymphopenia (n=1), macrocytic anemia (n=1), microcytic anemia (n=1), and pancytopenia (n=1); 10 events were serious (leukopenia, n=2 and neutropenia, n=2 [JIA]; anemia, n=6 [CD]).

Events included liver disorder (n=3), hepatotoxicity (n=1), and hepatocellular injury (n=1) in the pJIA and ERA group, and 1 serious event of hepatitis in the CD group.

***697 BASELINE FACTORS ASSOCIATED WITH THERAPEUTIC RESPONSE TO ADALIMUMAB IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE: DATA FROM IMAGINE 1**

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Aim: The safety and efficacy of adalimumab (ADA) in pediatric patients (pts) with Crohn's disease (CD) has been demonstrated in the IMAGINE 1 trial.¹ Response and remission to ADA induction treatment (at week 4) and after 1 yr of therapy are assessed by subgroups. Methods: Pts 6 – 17 yrs old with PCDAI >30 at BL who failed or were intolerant to conventional therapy received ADA for 52 weeks (wks) in IMAGINE 1.¹ At wk 4, pts were randomized to double-blind high dose (HD) or low dose (LD) ADA according to body weight. Pts could escalate to blinded weekly ADA after week 12 for disease flare or non-response, followed by weekly open-label (OL) ADA for continued

flare/non-response. Remission (PCDAI ≤ 10) and response (PCDAI decrease ≥ 15 points from BL) at week 4 and week 52 were assessed in the All ADA group by sex, BL median PCDAI (< 40 , ≥ 40), prior infliximab (IFX) use (yes, no), BL corticosteroid use (yes, no), BL immunomodulator (IMM) use (yes, no), BL disease duration (< 2 yrs, ≥ 2 yrs; < 3 yrs, ≥ 3 yrs), BL albumin level (< 32 g/L, ≥ 32 g/L), BL CRP level (< 5 mg/L, ≥ 5 mg/L), and dose at week 4 (LD, HD). The proportion of pts in remission and response at weeks 4 and 52 by subgroup was compared using odds ratios (OR), with 95% confidence intervals. *P*-values were based on univariate analysis from a Chi-squared test. Modified non-responder imputation (mNRI) was used for missing data and that obtained after moving to OL weekly ADA. Pts who moved to blinded weekly dosing were considered as responders or non-responders according to their observed response.

Results: Among ADA-treated pts, ORs for the proportion of pts achieving response or remission by subgroup at wks 4 and 52 are shown in the Table. Statistically significantly more pts with BL CRP levels ≥ 5 mg/L achieved response and remission at wk 4 than pts with BL CRP < 5 mg/L (response=86.6% vs 72.9%, $p=0.03$; remission=35.4% vs 10.2%, $p<0.001$). In addition, a greater proportion of pts with shorter BL disease duration (< 3 yrs) achieved response at wk 4 compared to pts with longer BL disease duration (87.1% vs 75.0%, $p=0.04$). Wk 52 response rates were statistically greater in pts with BL IMM use (59.0%), pts receiving HD ADA (59.1%) and IFX naive pts (63.8%) compared to pts not using IMM at BL (36.6%), pts receiving LD ADA (42.1%), and IFX experienced pts (33.7%). Similar results were observed for wk 52 remission, except numerically greater, but not statistically different, proportion of pts receiving HD ADA than LD ADA achieved remission at wk 52 (41.9% vs 28.4%, $p=0.053$). Treatment-emergent adverse events for pts receiving ≥ 1 dose of ADA during the IMaGINE 1 study have been previously published(1).

Conclusion: Children with CD with higher BL CRP levels and < 3 yrs disease duration were more likely to achieve a clinical benefit with induction ADA therapy, whereas IFX-naive pts, pts with BL IMM use, and pts receiving HD ADA in IMaGINE 1 were more likely to achieve efficacy at 1 yr of treatment. Reference: 1. Hyams *et al. Gastroenterol.* 2012;143:365.

Table. Odds ratios for proportion of patients achieving clinical remission or response at week 4 and 52 by subgroup (mNRI)

Response	Week 4			Week 52		
	n/N (%)	OR (95% CI)	p value	n/N (%)	OR (95% CI)	p value
Sex						
Male vs	88/105 (83.8)	1.24	0.58	48/105 (45.7)	0.65	0.14
Female	67/83 (80.7)	(0.58, 2.62)		47/83 (56.6)	(0.36, 1.15)	
Dose at Week 4						
LD vs	80/95 (84.2)	1.28	0.52	40/95 (42.1)	0.50	0.02
HD	75/93 (80.6)	(0.60, 2.72)		55/93 (59.1)	(0.28, 0.90)	
BL Disease duration						
< 2 yrs vs	65/73 (89.0)	2.26	0.06	41/73 (56.2)	1.45	0.22
≥ 2 yrs	90/115 (78.3)	(0.96, 5.32)		54/115 (47.0)	(0.80, 2.61)	
BL Disease duration						
< 3 yrs vs	101/116 (87.1)	2.24	0.04	65/116 (56.0)	1.78	0.06
≥ 3 yrs	54/72 (75.0)	(1.05, 4.80)		30/72 (41.7)	(0.98, 3.23)	
BL median PCDAI						
< 40 vs	61/80 (76.3)	0.48	0.06	46/80 (57.5)	1.63	0.10
≥ 40	94/108 (87.0)	(0.22, 1.02)		49/108 (45.4)	(0.91, 2.92)	
BL Albumin						
< 32 g/L vs	13/15 (86.7)	1.42	0.66	5/15 (33.3)	0.46	0.17
≥ 32 g/L	142/173 (82.1)	(0.30, 6.61)		90/173 (52.0)	(0.15, 1.41)	
BL CRP						
< 5 mg/L vs	43/59 (72.9)	0.42	0.03	28/59 (47.5)	0.86	0.64
≥ 5 mg/L	110/127 (86.6)	(0.19, 0.90)		65/127 (51.2)	(0.46, 1.60)	
Prior infliximab use						
yes vs	64/83 (77.1)	0.52	0.09	28/83 (33.7)	0.29	<0.001
no	91/105 (86.7)	(0.24, 1.11)		67/105 (63.8)	(0.16, 0.53)	
BL Corticosteroid use						
yes vs	60/71 (84.5)	1.26	0.56	31/71 (43.7)	0.64	0.14
no	95/117 (81.2)	(0.57, 2.79)		64/117 (54.7)	(0.35, 1.16)	
BL IMM use						
yes vs	93/117 (79.5)	0.56	0.18	69/117 (59.0)	2.49	<0.01
no	62/71 (87.3)	(0.25, 1.29)		26/71 (36.6)	(1.36, 4.57)	

Remission						
Sex						
Male vs	24/105 (22.9)	0.58 (0.31, 1.11)	0.10	34/105 (32.4)	0.76 (0.42, 1.39)	0.38
Female	28/83 (33.7)			32/83 (38.6)		
Dose at Week 4						
LD vs	29/95 (30.5)	1.34 (0.70, 2.54)	0.38	27/95 (28.4)	0.55 (0.30, 1.01)	0.053
HD	23/93 (24.7)			39/93 (41.9)		
BL Disease duration						
< 2 yrs vs	21/73 (28.8)	1.09 (0.57, 2.10)	0.79	28/73 (38.4)	1.26 (0.68, 2.32)	0.46
≥ 2 yrs	31/115 (27.0)			38/115 (33.0)		
BL Disease duration						
< 3 yrs vs	33/116 (28.4)	1.11 (0.57, 2.15)	0.76	43/116 (37.1)	1.25 (0.67, 2.34)	0.48
≥ 3 yrs	19/72 (26.4)			23/72 (31.9)		
BL median PCDAI						
< 40 vs	22/80 (27.5)	0.99 (0.52, 1.88)	0.97	34/80 (42.5)	1.76 (0.96, 3.22)	0.07
≥ 40	30/108 (27.8)			32/108 (29.6)		
BL Albumin						
< 32 g/L vs	6/15 (40.0)	1.84 (0.62, 5.46)	0.27	4/15 (26.7)	0.65 (0.20, 2.13)	0.48
≥ 32 g/L	46/173 (26.6)			62/173 (35.8)		
BL CRP						
< 5 mg/L vs	6/59 (10.2)	0.21 (0.08, 0.52)	<0.001	19/59 (32.2)	0.87 (0.45, 1.67)	0.67
≥ 5 mg/L	45/127 (35.4)			45/127 (35.4)		
Prior infliximab use						
yes vs	18/83 (21.7)	0.58 (0.30, 1.12)	0.11	18/83 (21.7)	0.33 (0.17, 0.63)	<0.001
no	34/105 (32.4)			48/105 (45.7)		
BL Corticosteroid use						
yes vs	21/71 (29.6)	1.17 (0.61, 2.24)	0.65	21/71 (29.6)	0.67 (0.36, 1.26)	0.22
no	31/117 (26.5)			45/117 (38.5)		
BL IMM use						
yes vs	31/117 (26.5)	0.86 (0.45, 1.65)	0.65	48/117 (41.0)	2.05 (1.07, 3.92)	0.03
no	21/71 (29.6)			18/71 (25.4)		

698 FREQUENCY OF SEVERE INFUSION REACTIONS ASSOCIATED WITH OUTPATIENT INFUSION OF INFLIXIMAB WITHOUT PRE-MEDICATIONS

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Introduction: Infliximab is associated with the potential to cause severe infusion-related hypersensitivity reactions. Medications, such as antipyretics, antihistamines, and corticosteroids, are often administered prior to infusion to prevent such reactions. The efficacy of these medications and the incidence of medically-serious hypersensitivity reactions are unknown. Although evidence suggests pre-medications can reduce the severity of infusion reactions once an instigating event has occurred, it is unclear if pre-medicating in the absence of an infusion reaction serves any additional benefit. Additionally, there is high variability in current standard of care, even among practitioners within the same health system, regarding pre-medication use and the infusion rate of infliximab. In this study, we aimed to determine: 1) the variability in the standard of care that may be associated with increased risk of an adverse reaction during an infliximab infusion, and 2) the number of patients requiring rescue epinephrine and/or rapid response/code blue events as the result of a reaction to infliximab infusion.

Methodology: We performed a review of ambulatory infliximab infusions between January 2014 and December 2015. Hospital-wide longitudinal data were available from a total of 427 infusions in 2014 and 466 infusions in 2015. This information was cross-referenced with pharmacy records of epinephrine removal from the automated dispensing cabinets and with data collected by the hospital code committee regarding rapid response and code blue calls.

Results: During the two-year review period, two major practice changes occurred. In 2015, the gastroenterology service converted to a 1-hour infliximab infusion, while rheumatology maintained their infusions at 3 hours. Also in 2015, one provider omitted pre-medications from all infliximab infusions. Over a 1-year time span, these changes resulted in a 51% decrease in total infusion hours (from 1281 to 630 infusion hours), despite a 9% increase in total number of infusions. There were no epinephrine administrations associated with infliximab maintenance infusions in 2014 or 2015. Additionally, there were no code blue or rapid response calls associated with infliximab maintenance infusions.

Conclusion: In our experience, the frequency of severe infliximab infusion reactions requiring epinephrine is very low and corresponds with recently published literature. Infusing infliximab over 1 hour rather than 3, and omitting standard pre-medications, did not increase the risk of severe infusion reactions. Our findings highlight a quality-improvement opportunity and potential non-drug cost savings to standardize infliximab infusions to streamline care in an ambulatory setting.

699 CHARACTERISTICS OF CHILDREN WITH CROHN'S DISEASE FAILING SUSTAINED REMISSION DESPITE ANTI-TNF EXPOSURE

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Introduction: The identification of patients at risk for failure to reach sustained remission despite exposure to anti-TNF remains challenging in pediatric Crohn's disease (CD).

Methods: Data from BELCRO (Belgian observational prospective cohort of pediatric CD) were analyzed after 5 yrs follow-up. Disease severity was scored at diagnosis, and yearly thereafter, as inactive, mild, and moderate-to-severe on a 3-point scale based on PCDAI/PGA scores. Sustained remission was defined as inactive disease for ≥ 2 yrs follow-up. Univariate analyses were performed between anti-TNF exposed patients with(out) sustained remission and correlations assessed between variables and the outcomes average disease severity and sustained remission.

Results: Of 66 anti-TNF exposed patients (median (IQR) age 13.1 (11.5 – 15.2) yrs, 50% male), 17% failed to reach sustained remission. Disease location was similar in both groups and mild disease at diagnosis (45% vs. 16%; $p = .03$) more frequent in the group failing sustained remission. There were no differences between age, gender, WBC or CRP at diagnosis and treatment between both groups. Percentages of infliximab and adalimumab use were similar in both groups, including drug switching and dose or interval adjustments. When stratified by follow-up clinic, infliximab in pediatric follow-up was less frequently associated with failure to reach sustained remission (Table). Higher average disease severity (2.1 (2.0 - 2.3) vs. 1.6 (1.3 - 1.8); $p < .001$), adult follow-up (73% vs. 27%; $p < .01$), surgery for CD (1 (0 - 3) vs. 0 (0 - 3); $p < .01$) and active disease after 5 yrs (91% vs. 24%; $p < .05$) were associated with failure to reach sustained remission. Both colonic disease and adult follow-up (AUC = .66; both $p = .04$) correlated with average disease severity (no correction for multiple testing). No other correlations were found.

Conclusions: Patient phenotype at diagnosis does not predict failure to reach sustained remission despite anti-TNF exposure. Mild disease may not trigger appropriate treatment and lead to an active and complicated disease course. Sustained remission occurred most with infliximab in pediatric follow-up. Information on serum levels is lacking.

Variable, number (%)	No sustained remission (n= 11)	Sustained remission (n= 55)	P value
Paediatric follow-up and infliximab	3 (27)	37 (67)	.01
Paediatric follow-up and adalimumab	1 (9)	8 (15)	.63
Adult follow-up and infliximab	6 (55)	14 (25)	.05
Adult follow-up and adalimumab	2 (18)	4 (7)	.25
Paediatric follow-up and adjustments	1 (9)	8 (15)	.63
Adult follow-up and adjustments	1 (9)	3 (11)	.65

700 VEDOLIZUMAB FOR REFRACTORY PEDIATRIC ULCERATIVE COLITIS: REPORT OF THREE CASES

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Background: Ulcerative colitis (UC) is a chronic, remitting disease which has significant complications and morbidity. A subgroup of patients affected by this disease respond poorly to therapy and may become dependent on corticosteroid treatments. With the arrival of new molecules, novel therapeutic options are available for patients with moderate-to-severe UC. Vedolizumab, which has recently come onto the market, is an integrin receptor antagonist. It has been shown to be superior to placebo in inducing clinical response and maintaining remission in adult patients with moderate-to-severe UC and Crohn's disease, but has not yet been studied in children.

Aims: To describe safety and efficacy of intravenous vedolizumab in pediatric patients with refractory UC.

Methods: We report the cases of 3 patients who received open-label vedolizumab in our institution between June 2015 and April 2016 for UC refractory to anti-TNFs. Data was retrieved retrospectively from medical charts.

Results: There was 1 boy and 2 girls. Two patients were 17 years old at initiation of vedolizumab, and one was 15 years old. Median duration of illness was 12 months (12 - 53). All patients presented with severe pancolitis (Paris classification E4). Two patients presented with severe colitis and were initiated near diagnosis on anti-TNF and one failed thiopurines prior to beginning anti-TNF. The decision to start vedolizumab was made for all patients based on cortico-dependance. All patients received standard vedolizumab induction with an infusion of 300 mg at 0, 2 and 6 weeks, followed by a q8 weekly regimen. Patient 1 had a PUCAI of 40 at the initiation of therapy, which decreased to 25 by 1 month and to 5 by 3 months. His blood work demonstrated an improvement in his albumin level from 38 to 41 g/L. ESR also improved from 21 to 13 mm/h. However, the patient felt he remained tired and experienced abdominal pain the week prior to his infusion. He was transferred to an adult gastroenterologist 5 months into therapy. Patient 2 had a PUCAI of 15 at the initiation of therapy, which decreased to 5 by 1 month and to 0 by 5 months. Her fecal calprotectin also improved from 1307 to 36 $\mu\text{g/g}$. She was in clinical and biochemical remission by her 5-month follow-up and continues on this therapy. Patient 3 had a PUCAI of 25 at the initiation of therapy. However, she developed *C. difficile* colitis in the following months, which worsened her symptoms. She required metronidazole treatment followed by vancomycin PO treatment. However, by 6 months of treatment, she entered clinical remission and was weaned off prednisone. Her CRP improved from 25 to 7 and she continues on therapy.

Conclusions: Vedolizumab is well tolerated in pediatric patients and shows promising results. Further investigation is required in this patient population to assess efficacy.

701 TREATMENT OF IRON-DEFICIENCY ANEMIA FOLLOWING HOSPITAL DISCHARGE IN PEDIATRIC ULCERATIVE COLITIS

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Background: Iron deficiency anemia (IDA) occurs in up to 25% of patients diagnosed before the age of 20 and is the most common extra-intestinal manifestation of inflammatory bowel disease (IBD). As such, IDA represents a significant burden for growing and developing pediatric patients with IBD. In children admitted for management of worsening IBD, identification and management of IDA often takes a backseat to efforts directed at addressing the underlying inflammatory disorder. The primary aim of this study was to evaluate the response of oral iron treatment of IDA in pediatric patients with ulcerative colitis following admission to a tertiary care center for management of disease flare.

Methods: We conducted a retrospective chart review of all pediatric patients with ulcerative colitis disease admitted to a tertiary medical care center's GI service between January 2001 and December 2012. The diagnosis of IDA was based on low hemoglobin for age and gender (using NHANES database norms) and a lower 2.5% cut point. Patients who had received oral iron supplementation, IV iron supplementation, or parental nutrition in the 3 months prior to admission were excluded from analysis, as were patients with pre-admission diagnoses of leukemia, inherited RBC defects, or end-stage renal disease requiring dialysis.

Results: 232 patients with known anemia status were included in the study. 59.9% of patients demonstrated serologic evidence of IDA at admission. 189 patients had longitudinal hematologic data collected at admission, discharge and at the time their first ambulatory follow-up visit. Ad hoc analysis of data collected from these patients, controlling for age, disease phenotype, ASA use and hematologic parameters at discharge, demonstrated that patients discharged from the hospital on oral iron supplementation therapy experienced, per 1 g/dL decrease of hemoglobin during the admission and a 0.42 g/dL increase in hemoglobin at time of their first out-patient follow-up visit as compared to a 0.22 g/dL decrease in hemoglobin noted in those patients not discharged on iron supplementation.

Conclusions: IDA is prevalent in pediatric patients with ulcerative colitis, particularly in patients with active disease and ongoing intestinal blood loss. However, this deficiency is generally unrecognized and under-treated. This reluctance to treat may be related to physician bias about medication tolerance and efficacy. However, our data demonstrate that those patients discharged on oral supplementation responded favorably with improved hemoglobin levels at the time of their first outpatient follow-up visit.

702 PEDIATRIC INFLAMMATORY BOWEL DISEASE IN INDIA: A CHANGING TREND

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Objectives: To evaluate the clinical spectrum of IBD in Indian children and to evaluate any change in the disease trend in this decade.

Methods/Design: Retrospective study of prospectively collected data in 76 patients (less than 18 years of age) between January 2001 and May 2016.

Methods: The demographic profile, presenting symptoms, severity of colitis, blood parameters (CBC, ESR, albumin), endoscopic, radiologic and histologic profile of IBD patients were assessed. Diagnosis was made based on the above parameters. Severity of ulcerative colitis (UC) was assessed by PUCAI scoring. Data from the last five years (Group B) was compared to the previous ten years (Group A) in terms of frequency and distribution of the disease. Anemia was defined as Hb <10 mg/dL, high ESR >20 and hypoalbuminemia <3.5 mg/dL.

Results: Out of 76 IBD patients, 45 patients had UC and 31 patients had Crohn's disease (CD). Group A and Group B had 34 and 42 patients, respectively. In UC patients (n=45), the male:female ratio was 1:1 and the mean age was 10.2 years (range: 10 months to 18 years). Twelve patients had growth failure. Diarrhea and blood in stools were the most common symptoms seen in about 90% of patients, followed by abdominal pain (55.8%), growth failure (27%) and fever (23%). Pan-colitis was seen in 27 (60%) patients, left-sided colitis in 7 (15.5%), recto-sigmoid alone in 7 (15.5%) and left-sided colitis plus transverse colon in 4 (9%). Backwash ileitis was seen in 2 patients. Moderate-to-severe UC was seen in 82% of patients. Anemia was seen in 19 (42%) patients, hypoalbuminemia in 15 (33%) and raised ESR in 33 (73%). In CD patients (n=31), the male:female ratio was 1.4 and the mean age was 11.2 years (range: 18 months to 15 years). The most common presenting symptoms were abdominal pain (88%), growth failure (76%) and diarrhea (65%). Twenty patients (66%) had small plus large bowel involvement based on endoscopy, histology and radiological features, while seven patients had isolated small bowel involvement (on both imaging and capsule endoscopy) and 4 had isolated colonic involvement. Anemia was seen in 16 (51.6%) patients, hypoalbuminemia in 18 (58%) and high ESR in 25 (80.6%). The ratio of UC:CD in the first decade of this century was 1.8, in contrast to 1.1 in the present decade. The clinical presentation and the pattern of gut involvement were comparable in both groups.

Conclusion: There has been an increase in the incidence of IBD in Indian children. UC was almost twice as common as CD previously and presently the incidence of CD is almost equal to UC in North Indian children. The presentation and spectrum of gut involvement in both these diseases remains the same.

703 TAKE CHARGE! A TELEHEALTH SKILLS-BASED INTERVENTION TO PREPARE YOUTH WITH CHRONIC ILLNESS FOR THE TRANSITION FROM PEDIATRICS TO ADULT HEALTH CARE

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Background: The challenging developmental period of adolescence and emerging adulthood is a critical time for youth with chronic illness to set the stage for good health through the life course. Numerous strategies have been proposed to better prepare young adults for adulthood and the transition to adult health care. However, interventions are often limited by cost, access and uptake. We developed Take Charge!, a coaching program focused on building skill and confidence for the management of health among youth with chronic illness. To increase accessibility, uptake and value, the intervention is delivered via videoconference. Take Charge! is comprised of 6 one-to-one sessions: 1) linking health to values and goals, 2) problem solving to manage health, 3) communicating effectively with healthcare providers, 4) talking to friends and family about health, 5) managing stress, and 6) putting it all together. The aim of this study was to assess the feasibility and preliminary effectiveness of the Take Charge! intervention.

Methods: Youth aged 15-25 years were recruited from outpatient gastroenterology and diabetes clinics at a large children's hospital. Surveys upon enrollment and completion of the study assessed patient activation for chronic disease self-management (Patient Activation Measure; PAM), health-related quality of life (PedsQL), and transition readiness (Transition Readiness Assessment Questionnaire; TRAQ). Pre- and post-

intervention scores on instruments were compared using paired Student's t-tests and effect size determined with Cohen's d. This study was approved by the relevant Institutional Review Board.

Results: Fourteen youth completed the intervention and one consented, but withdrew after the first session. See the Table for a description of participants. At the conclusion of the program, patient activation improved (PAM score increased from mean of 62.8 to 76.4; $p=0.03$; Cohen's d 0.87). There was a trend toward increased transition readiness (TRAQ score 3.48 to 3.97; $p=0.06$; Cohen's d 0.80) and improved health-related quality of life (PedsQL score 73.8 to 82.6; $p=0.08$; Cohen's d 0.57). Overall satisfaction rating for the program was high (mean 4.6 on a 5-point Likert scale: 1, not very satisfied; 5, very satisfied). The use of role-plays in practicing new skills was reported as a beneficial learning format.

Conclusion: Telemediated delivery of health coaching to youth with chronic illness is feasible. Findings of this small study demonstrate that participation in this telehealth skills-based health coaching program improved activation for chronic disease self-management with a substantial effect size. Although not statistically significant, likely due to small sample size, results suggest improvement in other key domains for youth with chronic illness, including transition readiness and health-related quality of life. A larger study of effectiveness with assessment of health outcomes is planned.

Table. Demographics and Study Outcomes

	Value (% or SD)
Mean age	17 (2.0)
Gender	
Male	9 (64%)
Female	5 (36%)
Diagnosis [†]	
Diabetes (type 1 and 2)	9 (64%)
Systemic lupus erythematosus	1 (7%)
Recurrent cholangitis	1 (7%)
Crohn's disease	2 (14%)
Ulcerative colitis	1 (7%)
Eosinophilic esophagitis	1 (7%)
<i>Mean pre-post intervention change in study outcomes</i>	
	Δ Value
PAM	
PAM score (0-100)	13.57*
PAM level (1-4)	0.57
TRAQ Score (1-5)	
TRAQ Total	0.49
Managing meds subscale	0.43*
Appointment keeping subscale	0.47
Tracking health subscale	0.86**
Talking with providers subscale	0.07
PedsQL (0-100)	
PedsQL total	8.81
Psychosocial health subscale	6.6

[†] Cells do not sum to N due to multi-morbidity.

* p -value <0.05

** p -value =0.01

704 TETRATRICOPEPTIDE REPEAT DOMAIN 7A GENOTYPE-PHENOTYPE CORRELATIONS DEFINE OUTCOMES IN INTESTINAL DISEASE

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Background: The tetratricopeptide repeat domain 7A (TTC7A) protein modulates signal transduction in a range of biochemical pathways including phosphoinositide-3-kinase (PI3K) trafficking, maintenance of cell polarity and regulation of cell survival. Patients carrying deleterious mutations in TTC7A typically present very early with severe combined immunodeficiency (SCID), characterized by lymphopenia, hypogammaglobulinemia, VEOIBD and multiple intestinal atresia (MIA). However, disease course and severity can vary, as hypomorphic phenotypes have been observed. The underlying genetic basis for this variation has not been elucidated.

Hypothesis: The severity of TTC7A-mediated immunodeficiency and atresia is correlated with mutation location and degree of coding disruption.

Methods: Fifty-four patients with validated TTC7A mutations, including 3 recently identified probands, were included for analysis. New patients were identified through whole exome sequencing and validated by Sanger sequencing. Phenotypic information was collected and processed to map clinical observations to Human Phenotype Ontology (HPO) database terms. Phenotypic correlations were analyzed using a hierarchical visualization package called Phenostacks. Association testing was also performed on phenotypic and patient subsets.

Results/Discussion: Across the full cohort, strong correlation (as determined by high information content [IC] scores) was observed in a subset of patients for the hallmark manifestations of MIA, including intestinal atresia, intestinal obstruction and severe combined immunodeficiency (SCID). This subset clustered during hierarchical analysis. These patients represented the early onset subgroup characterized by mutations leading to stop codon gain/loss or frameshifts. Stop codon gain/loss and frameshift mutations were also associated with high morbidity and mortality by association testing. Less severe manifestations were defined by greater phenotypic complexity (multiple phenotypes, low IC scores). Genetically, this cluster of patients possessed predominantly point mutations, with a subset containing exonic splice variants.

Hierarchical analysis further subdivided this group, wherein patients with mutations located in tetratricopeptide repeat (TPR) protein domains clustered and were associated with higher disease morbidity.

Conclusions: TTC7A mutation location and severity correlates with disease course and outcome, with highly deleterious changes leading to a SCID-MIA phenotype. Conversely, point mutations or exonic splice variants lead to less severe, but more diverse, disease. Understanding the genetic basis underlying the variation in TTC7A disease severity will provide physicians with greater prognostic ability, an important tool, given the high morbidity associated with the standard clinical and surgical interventions. In addition, further characterizing the TTC7A signalling axis will assist in the development of future targeted therapeutics.

705 EXPLORING THE ACCEPTABILITY AND EFFICACY OF A MINDFULNESS-BASED PARENTING WORKSHOP FOR PARENTS OF ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Mindfulness-based interventions (MBI) have emerged as a promising treatment for individuals with chronic diseases, such as inflammatory bowel disease (IBD), given their versatility in targeting both physical and mental health outcomes. MBI studies in adolescents with various chronic diseases are just emerging, with most showing positive effects, including significant improvements in sleep and worry, well-being, self care and reductions in mental health diagnoses. MBIs for parents have targeted selected populations, such as parents of children with ADHD, autism, or risk-taking behavior. These interventions have shown reductions in child behaviour problems, enhanced parent-child relationships and improved parental well-being. As yet, no research studies have investigated MBIs for parents of children with chronic health issues. The aims of this project were to determine the acceptability, satisfaction and preliminary efficacy of a one-time MBI parenting workshop for parents of adolescents with IBD.

Workshop Content: Main themes reviewed during the workshop included: a) responding versus reacting to parents' own experience of distress related to their child's IBD, b) using mindfulness awareness to direct purposeful responses towards our children according to parenting values and c) an introduction to mindful meditation techniques.

Methods: Parents of adolescents enrolled in an ongoing MBI group for adolescents with IBD were invited to a one-time two-hour mindful parenting workshop. Parents completed questionnaires assessing mindful awareness (Mindful Attention Awareness Scale), psychological flexibility (Parent Psychological Flexibility Questionnaire) and satisfaction with the workshop prior to, and several days following, the workshop.

Results: A total of 17 parents (fall session n=8 and spring session n=9) participated in the workshop. All adolescents involved in the MBI group had at least one parent attend the workshop, with 3 adolescents having both parents attend the workshop. Overall, mean satisfaction rating out of 10 was 8.06 ± 1.03 (range 7 - 10). The majority of participants were mothers (n=13; 76%). There were no significant differences in mindful awareness, but parents demonstrated increased psychological flexibility immediately post-workshop ($Z = -2.18, p < 0.05$).

Conclusions: Parents of adolescents with IBD are accepting of, and satisfied with, a one-time in-person workshop targeting mindfulness-based approaches to parenting their child. Preliminary results demonstrate that MBI parenting workshops are a promising avenue to promote well-being in families of youth with IBD. Future research is needed to determine long-term outcomes for parents, as well as the potential need for more intensive MBI parent-training options. Full workshop content and qualitative comments from parents will be presented.

*706 LOSS OF TUMOR NECROSIS FACTOR RECEPTOR 1 INDUCES SEVERE EARLY-ONSET COLITIS IN INTERLEUKIN 10 KNOCKOUT MICE IN A MICROBIOME-DEPENDENT MANNER

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Tumor necrosis factor (TNF) is a therapeutic target in inflammatory bowel disease (IBD). TNF receptor 1 (TNFR1) polymorphisms have been described in IBD patients. Although TNF and TNFR1 have been implicated in IBD pathogenesis, TNFR1 also provides protective physiological roles in host defense and inflammatory resolution, suggesting that TNFR1 may regulate inflammatory responses to the commensal microbiome in IBD. *Il10*^{-/-} mice provide a spontaneous model of colitis driven by the lack of immune tolerance to normal gut microbiota. We hypothesized that TNFR1 protects against colitis in *Il10*^{-/-} mice by restraining dysbiosis and inflammation.

Il10^{-/-}*Tnfr1*^{+/-} mice were crossed to generate *Il10*^{-/-}*Tnfr1*^{-/-} mice and control *Il10*^{-/-}*Tnfr1*^{+/+} littermates. Co-housed littermates were euthanized at 2 and 8 weeks of age for comparison. 8 week-old mice also underwent colonoscopy and barrier function assay (FD4 absorption) prior to euthanasia. A separate group of 8 week-old *Il10*^{-/-}*Tnfr1*^{-/-} mice were treated with either antibiotics (neomycin and metronidazole) or water for 2 weeks. Mice underwent colonoscopy before and after antibiotics and endoscopic appearance was scored. Colon tissues were analyzed for histologic scoring and mucosal immune cell populations were characterized by flow cytometry. Microbiome analysis was performed by 16s rRNA sequencing of cecal content from 8-week old mice.

Il10^{-/-}*Tnfr1*^{-/-} mice developed severe colitis in a highly reproducible manner by 8 weeks of age, evidenced by both endoscopic and histologic scoring ($p < 0.01$). *Il10*^{-/-}*Tnfr1*^{-/-} mice presented with extreme mucosal thickening and granularity by colonoscopy and florid inflammation,

crypt abscesses, marked enterocyte loss and epithelial hyperplasia by histology, whereas Il10^{-/-} littermates appeared healthy. Features of colitis were not seen at 2 weeks of age prior to weaning. FD4 absorption was increased in Il10^{-/-}Tnfr1^{-/-} mice ($p < 0.0001$). There were increases in colonic macrophages (F4/80⁺) and dendritic cells (MHCII+CD11c⁺) in mice lacking TNFR1. Furthermore, survival was reduced in Il10^{-/-}Tnfr1^{-/-} mice vs. Il10^{-/-} littermates ($p < 0.001$), with 50% mortality by 12 weeks. Antibiotics significantly improved colitis in Il10^{-/-}Tnfr1^{-/-} mice, inducing remission with reduced endoscopic ($p < 0.01$) and histologic ($p < 0.01$) scores. 16s rRNA sequencing of cecal content showed Il10^{-/-}Tnfr1^{-/-} mice had distinct microbiome profile compared to age-matched Il10^{-/-} littermates at 8 weeks.

Il10^{-/-}Tnfr1^{-/-} mice develop severe early-onset colitis in a predictable manner and antibiotic depletion rapidly induces remission. TNFR1 may inhibit colitis by restraining dysbiosis and mucosal immune responses, potentially through macrophages and/or dendritic cells. Studies will determine how TNFR1 regulates disparate cell types in colitis and how these impact host-microbial interactions and which microbial factors determine disease severity in this model.

707 IL-27 IS ESSENTIAL FOR THE MAINTENANCE OF IMMUNE HOMEOSTASIS IN BLIMP-1 DEFICIENCY-MEDIATED EXPERIMENTAL COLITIS

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IL-27, composed of Epstein-Barr virus-induced gene 3 (EBI-3) and p28, works with TGF- β to promote IL-10-producing T-cell differentiation and is also reported to enhance the production of IL-10 in various T-cell subsets, resulting in the conversion of inflammatory effector T-cells into immunosuppressive Tr1-like cells. To understand the importance of IL-27-dependent regulation of IL-10 production in intestinal inflammation, we knocked down IL-27 *in vivo* by introducing a shRNA transgene to target the p28 subunit in a T-cell-specific Blimp-1 knockout (Blimp-1 CKO) mouse model and subsequently analyzed the clinical onset and severity of disease and colon histology in these BLIMP-1 CKO/IL-27p28 knockdown (KD) mice. Activation status, cytokine profiles and transcription factors in T-cells were further analyzed. The body weights of Blimp-1 CKO/IL-27p28 KD mice started to decrease at an earlier age than those of Blimp-1 CKO mice. Blimp-1 CKO/IL-27p28 KD mice developed soft stools at earlier age than Blimp-1 CKO mice did, suggesting a regulatory potential of IL-27 in T-cell deficiency-mediated colitis. Although T-cell pathogenicity was downregulated by suppressing the levels of IFN- γ , IL-17, GM-CSF and TNF- α in CD4⁺ T-cells from Blimp-1 CKO/IL-27p28 KD mice, the proportions and expression levels of IL-10 and IL-10R in Th1 and Th17 cells were significantly lower in the lymphoid organs of Blimp-1 CKO/IL-27p28 KD mice, suggesting that a regulatory role of IL-27-induced IL-10 production overrides the T-cell pathogenicity to aggravate colitogenic progression in these mice. The percentage of c-Maf expression in Th1 and Th17 cells from these Blimp-1 CKO/IL-27p28 KD mice was decreased, inferring an association of c-Maf with IL-10 production in Blimp-1 deficient T cells. IL-27-induced IL-10 expression by effector T-cells is essential for modulating the colitogenic pathogenesis of T-cells as a self-regulatory mechanism to protect BLIMP-1-deficiency mice from colitis.

708 INCIDENCE OF BOTH CROHN'S DISEASE AND ULCERATIVE COLITIS IS CONTINUING TO RISE AND IS HIGHER IN THE CITY POPULATION

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Background and Aims: The first prospective national survey¹ of pediatric inflammatory bowel disease (pIBD) in the UK documented an incidence of 5.2/100,000 children per year. A higher incidence was noted in the north (Scotland: 6.5) as compared to the south (England: 5.2) and Ireland (4.4). This prospective study aimed to: 1) document any change in incidence of pIBD in southwest England (SWE) from 2003 to 2014, 2) document any difference in incidence of pIBD in the city of Bristol population compared to the whole of SWE.

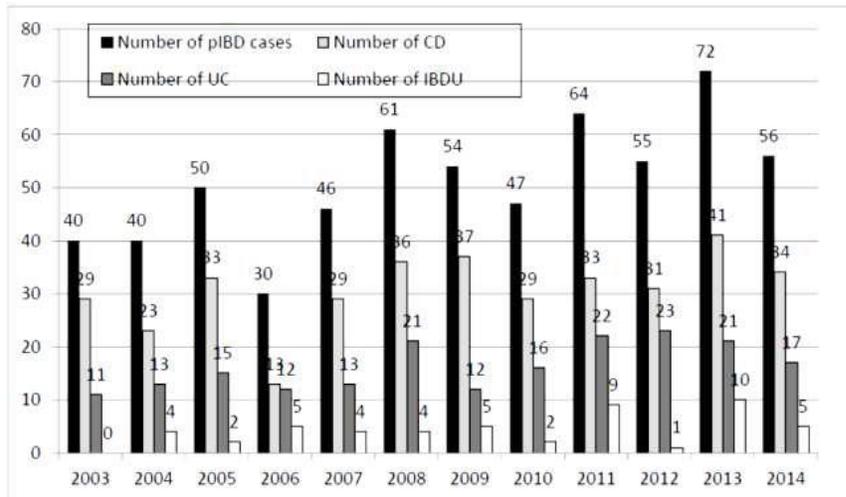
Methods: Bristol is the single specialist pediatric gastroenterology centre for SWE to which all children (aged 0 - 16 years) suspected of having IBD from the 12 pediatric centres are referred for endoscopy. Prospective data were collected on all new pIBD cases between 2003 and 2014, including types of IBD, gender and postcode address for the City of Bristol.

Results: 615 new cases of pIBD were diagnosed over a 12-year period (2003 - 2014). Male (n=361) to female (n=254) ratio was 1.4:1. The cumulative incidence rates over two consecutive 6-year periods for the city of Bristol were much higher than the whole SWE: 9.5 per 100,000 versus 5.0 per 100,000 (2003 - 2008) and this increased to 10.6 versus 6.2 (2009 - 2014). Cumulative incidence increased for all subtypes of IBD: Crohn's disease (CD) increased from 3.06 (2003 - 2008) to 3.63 (2009-2014), ulcerative colitis (UC) from 1.6 to 1.96 and IBD-unclassified (IBDU) from 0.36 to 0.57. Figure 1 shows the overall rising incidence for both UC and CD in SWE.

Conclusion: Cumulative incidence of IBD over two consecutive, 6-year periods increased from 5.0 (2003 - 2008) to 6.2 (2009 - 2014) in SWE. This was noted for both CD and UC with male preponderance. This study documents significantly higher incidence in the city population, suggesting environmental factors have a role.

Reference: 1. Sawczenko A *et al.* Prospective survey of childhood inflammatory bowel disease in the British Isles. *Lancet*. 2001;357(9262):1093-4.

Figure 1: Overall rising incidence for both UC and CD in SWE



709 PREVALENCE AND EFFECTS OF MARIJUANA USE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Recent studies in adults report symptom relief with marijuana use in patients with inflammatory bowel disease (IBD). To the best of our knowledge, there are no data on use of marijuana in pediatric patients with IBD. We assessed the prevalence, pattern, effects and adverse effects of marijuana use in pediatric patients with IBD. In particular, we evaluated the medicinal use of marijuana and assessed patients' views on legalization of marijuana use for IBD.

Methods: We conducted a prospective, questionnaire, survey study at a tertiary academic pediatric IBD clinic. All consecutive patients older than 18 years of age answered anonymous questionnaires about their demographics, IBD and medications. The survey included questions about current and past use of marijuana, reasons for use, costs, frequency, duration of use and views on legalization of marijuana use. If patients used it for medicinal reasons, detailed questions were asked whether marijuana was ineffective, slightly helpful, moderately helpful, very helpful, or led to complete relief in controlling their symptoms, such as abdominal pain, diarrhea, poor appetite and nausea. We also included the Short Inflammatory Bowel Disease Questionnaire (SIBDQ) to assess the health-related quality of life.

Results: Fifty patients (mean age 18.8 years, 30 males) were enrolled. 32 patients (64%) had Crohn's disease and 18 patients (36%) had ulcerative colitis. Thirty-four patients (68%) reported using marijuana currently or in the past. There was no statistically significant difference between the users and non-users of marijuana regarding demographics, disease activity, or medications. Despite prolonged use of marijuana, 71% of patients did not discuss it with their gastroenterologists. Twenty-two patients used marijuana medicinally for IBD symptoms, in addition to conventional therapy. While the majority found marijuana to be moderately/very helpful, complete relief of symptoms, such as abdominal pain, poor appetite, nausea and diarrhea, was seen in 32%, 32%, 21% and 6% of patients, respectively. Only half of patients reported knowledge of possible adverse effects of marijuana and 18% of patients reported mild neuropsychiatric adverse effects. Overall, 98% of patients supported legalization of marijuana and 84% were interested in using medical marijuana if it became legally available.

Conclusions: Marijuana use is very prevalent in young adults with IBD. The majority of users did not inform their physicians. Symptomatic improvement was common with marijuana and almost one-third of patients reported complete relief of abdominal pain and poor appetite. Many patients are interested in medicinal marijuana use. Pediatric gastroenterologists should be aware of this trend and future well-controlled studies are necessary to assess the role of marijuana in IBD therapy.

710 A REAL-WORLD STUDY FOCUSED ON THE EFFICACY AND SAFETY OF ADALIMUMAB AS FIRST-LINE TREATMENT OF PEDIATRIC CROHN'S DISEASE

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Background and Aims: Adalimumab (ADA), a monoclonal humanized anti-TNF antibody, is usually prescribed as a second-line therapy in pediatric Crohn's disease (CD) patients who have lost response or developed intolerance to infliximab (IFX). Data published thus far on the efficacy of treatment with ADA in children come from cases series, mainly retrospective studies and a clinical trial (IMaGINE 1). In the case-series reported, more than 70% of patients had initially been treated with IFX. Data on short- and long-term efficacy of ADA in anti-TNF-naïve patients are limited. The aim of the present study was to evaluate the efficacy and safety of ADA in achieving clinical remission and maintaining it over the time in an anti-TNF-naïve pediatric CD patients. The need for treatment intensification and growth velocity were also evaluated. **Methods:** Multicenter, retrospective study that included anti-TNF-naïve, pediatric CD patients treated with ADA as a first-line anti-TNF. All patients were naïve to anti-TNF, but could have been previously treated with corticosteroids and/or an immunomodulator (azathioprine, mercaptopurine, or methotrexate).

Results: Sixty-two patients (34 males) were included. The mean age at diagnosis was 11.6 years (SD, 3.1). The median disease duration before initiating ADA treatment was 7.3 months (IQR, 2.7 - 21.0). Clinical remission was achieved at week 12 in 50 of 62 (80.6%) patients. At week 52, 56 out of 60 patients (93.3%) were in clinical remission. Two patients discontinued treatment with adalimumab after week 12. Eight patients

(13%) reported some adverse events. There were no reports of allergic reactions, serious infections, or malignancies. C-reactive protein and erythrocyte sedimentation rate decreased at week 12 and remained low until the end of the follow-up. Mean height, growth velocity and BMI Z-scores improved significantly between baseline and week 52, mainly in patients with growth failure. The shortening of the interval between injections was necessary in 16/62 (25.8%) patients. During the study period (2008 - 2015), 103 patients with CD were treated with anti-TNF, 70 received ADA (68%) and 33 (32%) IFX. Of the patients receiving ADA, 63/70 did by patient or their parents' preference versus 7/33 of those who received IFX (90% vs. 15%, $p < 0.0001$).

Conclusion: ADA as first-line anti-TNF therapy induces and maintains clinical remission in pediatric patients with CD. Moreover, ADA has a beneficial effect on nutritional and growth parameters and is also well tolerated. Some patients maintain remission for prolonged time periods under monotherapy. Adalimumab is often the first choice of treatment for children and their families.

711 THERAPEUTIC DRUG MONITORING IMPACTS DECISION-MAKING FOR CHILDREN WITH INFLAMMATORY BOWEL DISEASE ON INFLIXIMAB

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Background: Empiric changes in infliximab (IFX) dose or regime for managing IFX-secondary failure and clinical disease relapse may not be the best strategy for children with inflammatory bowel disease (IBD). Therapeutic drug monitoring (TDM) with measuring serum IFX trough levels (ITLs) offers an attractive alternative for modifying IFX therapy and maintaining remission in those children. The clinical utility and the impact of measuring serum ITLs on decision-making in children with IBD are under-investigated. Our aim was to examine the impact of TDM on the clinical decision-making process in children with IBD on IFX.

Methods: Medical records of consecutive patients with IBD on IFX from two Canadian centers, who had ITLs between January 2013 and December 2015, were examined. Patients' demographics, diagnosis, indications for TDM, clinical and laboratory markers for disease activity and treatment changes before and after TDM were documented.

Results: A total of 73 children with IBD (51 with Crohn's disease and 22 with ulcerative colitis; mean age 15.2 ± 3.8 ; 40 boys) had 107 serum measurements of ITLs over the study period. While only 24 (22.4%) ITLs were requested because of clinical symptoms, 38 (35.5%) ITLs were considered suboptimal ($< 3.5 \mu\text{g/mL}$) by the managing physician. Out of 83 (77.6%) ITLs that were done as a part of routine patient care in the absence of clinical symptoms, 28 (33.7%) were suboptimal. Overall, 37 (34.6%) ITLs resulted in IFX dose changes with increasing IFX dose in 36 (33.6%) cases of IELTs and dose reduction in one case. On the other hand, 34 (32%) ITLs resulted in interval changes with 19 (17.8%) shortening of intervals and 15 (14%) lengthening of intervals. Adding or increasing the dose of immunomodulators took place as a result of 7 (6.5%) ITLs. Only four children (5.5%) had to be switched to adalimumab.

Conclusions: One-third of suboptimal ITLs happens in the absence of clinical symptoms and may need adjustment in children with IBD.

Therapeutic drug monitoring is a useful tool and is proven to be very helpful in the decision-making process for children with IBD on IFX.

Larger, prospective, well-designed studies with more objective disease markers and proper cost analysis are needed to confirm our conclusions.

712 INFLAMMATORY BOWEL DISEASE: DISHWASHING PRACTICES

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Background: Increasing rates of pediatric inflammatory bowel disease (IBD) have been attributed to fewer enteric infections and a more hygienic environment in modern industrialized countries.

Hypothesis: Early exposure to synthetic detergents may play a role in alterations of gut microbiome, predisposing children to the development of IBD.

Methods: Patients attending the pediatric IBD clinic were queried regarding ethnicity, place and mode of birth, use of plastic dish soaps, detergents and automatic dishwashing machines. Of 99 patients (53 males), 43 had Crohn's disease (CD) (24 male), 43 had ulcerative colitis (UC) (26 male), and 12 (9 males) had undifferentiated colitis (IBDU). The mean age was 13.2 years. Average disease duration was 6.0 years. 82.8% of the patients reported living in urban areas, of which 37 of these patients had CD and 34 had UC. 93% of the patients were born in Canada (no difference between the foreign-born group and native-born group in disease type). 79.8% of the sample were Caucasian, of which 38 had CD, 32 had UC and 9 had IBDU.

Results: The average duration of breast-feeding was 10 months. 83 patients used baby bottles with a nipple (CD: 32, UC: 39), 94 patients used plastic sippy cups (CD: 40 and UC: 42) and 45 individuals used a combination of glass and plastic dishes (CD: 20, UC: 20). 57 individuals used manual dishwashing at the age of 2 (CD: 27, UC: 21, IBDU: 8, N/A:1), 14 used only an automatic dishwasher (CD: 8, UC: 6), and 24 used both methods (CD: 8, UC: 16, IBDU: 3). Currently, 30 individuals use manual (CD: 10, UC: 15, IBDU: 4, N/A: 1), 25 individuals use an automatic dishwasher (CD: 14, UC: 9, IBDU: 2), and 44 use both methods (CD: 19, UC: 20, IBDU: 5). In a subgroup, 41 out of 55 patients were born vaginally. Among this population, 7 had CD and 5 had UC. 81.81% of the mothers were on no medication during their pregnancy, while 19 individuals among this population developed CD and 17 developed UC. The use of automatic dishwashers has increased over the past 30 years. Kenmore and Bosch dishwashers were the most commonly used. Cascade and Finish were the most common dishwasher detergents used. 35 individuals used rinse cycle agents in their dishwasher all the time and 11 used them occasionally. The average age of the dishwasher was 5.2 years. 41 individuals used Dawn and 31 used Palmolive detergent for manual dishwashing.

Conclusion: The patients studied are typical of our overall clinic population, in terms of age, ethnicity and disease classification. The observation that 74 out of the 99 patients (~77.78%) have been using automatic dishwashing detergent compared to 63% of the Canadian population, may well reflect other socio-economic factors important in the genesis of pediatric IBD. Further studies on the environmental contributors to pediatric IBD are presently being conducted through the CIDsCaNN children's IBD network.

713 ANTI TNF- α THERAPY FOR VERY EARLY-ONSET, INFLAMMATORY BOWEL DISEASE: A SINGLE-CENTER EXPERIENCE IN JAPAN

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Background: Very little research has been done on the safety and efficacy of anti-TNF- α therapy for very early-onset, inflammatory bowel disease (VEO-IBD).

Method: Eleven Japanese children (6 boys and 5 girls) with VEO-IBD were treated with anti-TNF- α therapy at a Japanese Children's hospital between December 2010 and March 2016. Ten of the patients received infliximab and 1 received adalimumab. The patients medical records were retrospectively reviewed for patient characteristics, therapeutic effects and adverse events.

Results: Of the 11 patients, 6 were diagnosed with Crohn's disease (CD), 1 with ulcerative colitis (UC) and 4 with IBD type unclassified (IBD-U). The mean age at diagnosis was 25.8 months (with a range of 6 - 62 months), and the mean time interval between diagnosis and the initiation of anti - TNF- α therapy was 15.8 months (with a range of 3 - 37 months). At the time of initiation of anti-TNF- α therapy, all of the patients were on azathioprine or 6-MP, 8 were on corticosteroids and 6 were on total parenteral nutrition (TPN).

One patient with IBD-U, who was suspected of having immunodeficiency, died of septic shock 3 months after the initiation of infliximab therapy. The other 10 patients remained on anti-TNF- α and had a mean follow-up period of 21.4 months (range 7 - 63 months). Seven patients were followed-up for 54 weeks or longer. After 10 weeks of anti-TNF- α therapy, 2 of the 10 patients (20%) achieved clinical remission. After 30 weeks, 3 of the 10 (30%) were in clinical remission. After 54 weeks of treatment, 3 of the 7 (42.9%) were in clinical remission. Of the 7 patients treated with corticosteroids, the dosage was reduced in 5 patients and corticosteroids were discontinued in 2 patients. Of the 5 patients receiving TPN, 3 remained on TPN. Two of the patients receiving infliximab developed infusion reactions, but infliximab therapy was continued using pre-medication with corticosteroids and a slower infusion rate. Other than the patient who died of sepsis, there were no serious infections or other adverse events that were likely associated with anti-TNF- α therapy.

Conclusion: Anti-TNF- α therapy appears to be relatively safe and effective for patients with VEO-IBD. Further evaluation in a multicenter setting would provide more insight about the proper use of anti-TNF- α in VEO-IBD.

714 THE CLINICAL CHARACTERISTICS OF VERY EARLY-ONSET, INFLAMMATORY BOWEL DISEASE IN A TERTIARY HOSPITAL IN CHIAN

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Background: The incidence of inflammatory bowel disease (IBD) in children has dramatically increased during the past ten years in China. Very early onset IBD (VEOIBD) demonstrates different clinical characteristics compared with adult onset IBD. Furthermore, VEOIBD has displayed a strong connection with monogenetic disease.

Method: We retrospectively studied 41 VEOIBD patients from November 2005 to February 2016.

Result: This study included 27 male and 14 female patients (Table 1). 78% (32/41) of VEOIBD was diagnosed during the last five years. The main symptoms were diarrhea (37/41), hematochezia (33/41) and abdominal pain (22/41). Common complications included malnutrition (11/41), perianal diseases (8/41), sepsis (6/41) and small intestinal perforation (3/41). The colonoscopy results included ulcers (23/41), ulcers with hyperplastic lesions (10/41), hyperplastic lesions (1/41) and non-specific inflammation (4/41). 13.6% (3/22) of patients found upper intestinal involvement. Capsule endoscopy found 72.7% (8/11) of small intestinal involvement. Six newly-diagnosed VEOIBD patients had been sent for whole exome sequencing. One patient was identified as harboring a new homozygous mutation in IL10RB (c.737G>A, p.W246X). Another patient harbored compound heterozygous mutations in TNFRSF13B. The rate of steroid therapy among these VEOIBD patients was as high as 78% (32/41) and the rate of enteral or para-enteral nutrition therapy was 75.6% (31/41). The rate of surgery was 19.5% (8/41). Six patients have died since being diagnosed.

Conclusion: The incidence of VEOIBD in our hospital has dramatically increased during the last five years. Whole exome sequencing would be helpful to diagnose rare monogenetic gene diseases for the neonatal and infant onset patients.

Table 1: Demographics of VEOIBD patients at diagnosis

Onset of disease	Diagnose	Number of patients
Onset \leq28D	CD	6 (14.6%)
(neonatal onset)	UC	1 (2.4%)
28D<Onset \leq2Y	CD	13 (31.7%)
(infant onset)	UC	1 (2.4%)
	IBDU	3 (7.3%)
2Y<Onset \leq6Y	CD	15 (36.6%)
	UC	2 (4.9%)

CD: Crohn's disease; UC: ulcerative colitis; IBDU: IBD unclassified

NEUROGASTROENTEROLOGY & MOTILITY

723 ANXIETY IN PEDIATRIC PATIENTS UNDERGOING HIGH-RESOLUTION ANORECTAL MANOMETRY: WHAT'S THE HARM?

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Introduction: Anxiety is easily provoked in children by invasive medical procedures. There are a variety of factors that contribute to this anxiety, including stranger anxiety, unfamiliarity with the procedural environment, decreased understanding, separation anxiety and fear of physical harm. Procedural anxiety has been studied in pediatric patients undergoing endoscopic procedures. High-resolution anorectal manometry represents relatively newer technology and little is known regarding its psychologic impact on pediatric patients. We hypothesized that high resolution anorectal manometry (HARM) is a significant source of distress and anxiety in pediatric patients.

Methods: Patients ages 8 years - 21 years, undergoing out-patient HARM for evaluation of chronic constipation, were prospectively enrolled in the study. Subjects were excluded from the study if they had a previous diagnosis of developmental delay, were on anti-anxiety medication, had previously undergone anorectal manometry or prior anorectal surgery, or required sedation for the procedure. Children aged eight years and older completed the state form of Spielberger State-Trait Anxiety Inventory (STAI-C). This is a standardized, validated questionnaire that measures anxiety in adults and children. Children undergoing upper endoscopy and colonoscopy were also prospectively enrolled and completed the state form of STAI-C just prior to undergoing endoscopic evaluation. All patients also completed the trait anxiety (STAI-C-T) inventory, which refers to differences in a child's underlying disposition.

Results: Fifteen patients (mean age: 12.4 years) undergoing HARM were enrolled, in addition to 21 patients undergoing upper endoscopy (mean age: 13.3 years) and 7 patients undergoing colonoscopy (mean age: 12.1 years). There were no significant differences in the STAI-C scores for children undergoing the varied evaluations. Patients undergoing HARM had an average STAI-C score of 46.1. Those undergoing upper endoscopy with biopsy had an average score of 33.8, while those undergoing colonoscopy had an average STAI-C score of 47.3. Anxiety scores for children undergoing HARM were similar to those undergoing colonoscopy ($p=0.92$). Anxiety scores were significantly higher in patients undergoing colonoscopy or HARM compared to those undergoing upper endoscopy ($p<0.001$).

Conclusions: Significant procedural anxiety is associated with high resolution anorectal manometry in pediatric patients. Anxiety levels are similar to those of children undergoing colonoscopy and are significantly higher than those of children undergoing upper endoscopy, which requires an IV, anesthesia and separation from a parent/guardian during the procedure. Consideration should be given to psychologic preparation and adequate procedural support during high resolution manometry procedures, as they are associated with significant anxiety.

724 STRATEGIES FOR MEDICAL MANAGEMENT OF PEDIATRIC EOSINOPHILIC ESOPHAGITIS: A SYSTEMATIC REVIEW OF RANDOMIZED, CONTROLLED TRIALS

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Background: Eosinophilic esophagitis (EoE) is associated with significant morbidity in children. Strategies for optimizing outcomes of EoE are hence essential.

Objective: To conduct a systematic review (SR) of strategies for medical management of EoE in children.

Methods: We conducted a SR of randomized, controlled trials (RCT) of medical interventions in children with EoE, using the Cochrane methodology. Databases, including PubMed, EMBASE, CINAHL, Cochrane Central Library and Google Scholar, were searched up to mid-March 2016. Primary outcomes were histological and symptomatic remission. Secondary outcomes were improvement in histological and endoscopic parameters and adverse effects.

Results: A total of 6 RCTs (n=497) with low-to-unclear risk of bias were included. The studied interventions included topical oral steroids, swallowed enteral steroids and anti-IL-5 agents. Pooling of data from all trials was not possible due to significant heterogeneity in interventions. A meta-analysis of data (n=141) from three RCTs (oral viscous budesonide: 2, fluticasone: 1) showed significant histological remission in the intervention vs. control group participants [RR: 10.32 (3.04, 35.03), $p=0.0002$]. Compared with anti-IL-5 agents, the studies assessing steroids reported high rates of clinical remission. Clinical remission did not correlate with histological improvement in all studies. Except for systemic corticosteroids, there were no significant adverse effects related to other interventions.

Conclusion: Limited, low-quality evidence exists on the effects of various interventions in children with EoE. Treatment with swallowed steroids showed beneficial effects in EoE. Large, well-designed RCTs are essential to confirm these findings.

Keywords: children, eosinophilic esophagitis, intervention, review, systematic

725 LONG-TERM FOLLOW-UP OF CHILDREN DIAGNOSED WITH FUNCTIONAL GASTROINTESTINAL DISORDERS BASED ON ROME III CRITERIA: A SINGLE PHYSICIAN EXPERIENCE FOLLOWING A BIOPSYCHOSOCIAL MODEL OF CARE

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Background: Functional gastrointestinal disorders (FGIDs) are one of the most common and challenging disorders in pediatrics. This study evaluated progression of ROME III-defined FGIDs in children treated in a biopsychosocial model of care on a long-term follow-up.

Methods: An open-label study, A retrospective chart review of all children aged 4 to 21 years who presented to gastrointestinal clinic and were diagnosed with ROME III criteria-based FGID; namely, functional abdominal pain (FAP), functional dyspepsia (FD), irritable bowel syndrome (IBS), abdominal migraine (AM) and cyclic vomiting syndrome (CVS). All patients were managed in a biopsychosocial model of care.

Demographics, investigations, treatment and FGID progression were reviewed. Responses were categorized as complete improvement (CIG) or partial improvement/no improvement (PIG/NIG). Statistics: continuous variables reported as mean, range and SD; categorical variables reported as N and %. Fisher's Chi-square/Student's t-test for data comparison between CIG and PIG/NIG with a statistical significance at $p\leq 0.05$.

Results: 260 of 310 patients were included (39 with no follow-up, 11 with organic diseases); mean age 10.5 years, 56% were female, mean number of encounters 3.32 visits (range 1 - 12 visits, SD 1.84). Diagnosis: FAP 44.6%, IBS 20.8%, multiple 13.1%, FD 12.7%, AM 8.1% and CVS 0.8%. Mean follow-up was 18.6 months (range 2 - 59, SD 15.7). Investigations: lab 93.5% (abnormal in 23.8%), imaging 45.4% (abnormal

in 5%) and endoscopy 43.1% (abnormal in 1.2%). 93.5% received some form of treatment: 91% received medication and 1.2% received surgery (all normal pathology). Progression: new FGID diagnosis 11.5%, evolution of FGID 10.4%, recurrence 35.8%, CIG 60.4%, PIG/NIG 39.6%. No statistical difference was seen between CIG and PIG/NIG regarding demographic data, labs, imaging performed and treatment received. PIG/NIG had more encounters (mean 3.63 vs. 3.11; $p=0.02$), more non-contributory abnormal lab results (34.4% vs. 19.7%; $p=0.02$), more endoscopies performed (52.4% vs. 36.9%; $p=0.02$), more treatment changes (mean 1.41 vs. 0.8; $p<0.01$) and more new FGID diagnoses (19.4% vs. 6.4%; $p<0.01$).

Conclusions: Patients with FGIDs in PIG/NIG tend to develop new FGID diagnoses, need more follow-ups, endoscopies, treatment changes, and have more non-contributory lab abnormalities compared to CIG. Since few FGID patients later developed organic disease, this supports the use of Rome III criteria. A biopsychosocial model of care is possibly beneficial in treating FGIDs. However, this needs to be validated in rigorous analytical studies.

Table: Demographics, investigations and treatments in 260 patients with comparisons between complete improvement and partial improvement/no improvement group

	Total N=260	CIG 157 (60.4%)	PIG/NIG 103 (39.6%)	<i>p value</i>
Mean age (years)	10.52	10.48	10.57	0.86
Female	145 (55.8%)	82/157 (52.2%)	63/103 (61.2%)	0.16
Caucasian	180 (69.2)	110/157 (70.1%)	70/103 (68%)	0.78
Mean duration of symptoms (months)	21.9	22.9	20.5	0.46
Family history of FGID	40 (15.4%)	24/157 (15.3%)	16/103 (15.5%)	1.00
Psychological disorder	81 (31.2%)	43/157 (27.4%)	38/103 (36.9%)	0.13
Mean number of initial FGID diagnoses	1.14	1.15	1.13	0.66
Mean number of encounters	3.32	3.11	3.63	0.02
Available follow up data (months)	18.6	17.4	20.5	0.12
Labs performed	243 (93.5%)	147/157 (93.6%)	96/103 (93.2%)	1.00
Abnormal lab results	62 (23.8%)	29/147 (19.7%)	33/96 (34.4%)	0.02
Imaging study performed	118 (43.4%)	66/157 (42%)	52/103 (50.5%)	0.20
Abnormal imaging study	13 (5%)	9/66 (13.6%)	4/52 (7.7%)	0.38
Endoscopy performed	112 (43.1%)	58/157 (36.9%)	54/103 (52.4%)	0.02
EGD performed	79 (30.4%)	41/157 (26.1%)	38/103 (36.9%)	0.07
EGD & colonoscopy performed	33 (12.7%)	17/157 (10.8%)	16/103 (15.5%)	0.34
Abnormal scope results	3 (1.2%)	0/157 (0%)	3/103 (2.9%)	0.11
Treatment received	247 (95.0%)	147/157 (93.6%)	100/103(97.1%)	0.26
Mean number of treatment changes	1.04	0.80	1.41	<0.01
Recurrence	93 (35.8%)	49/157 (31.2%)	44/103 (42.7%)	0.07
New FGID diagnosis	30 (11.5%)	10/157 (6.4%)	20/103 (19.4%)	<0.01
Mean total number of final FGID diagnoses	1.27	1.24	1.30	0.38
Mean duration from initial to final FGID diagnosis (month)	17.2	16.6	17.6	0.87

CIG: complete improvement group, PIG: partial improvement group, NIG: no improvement group, FGID: Functional Gastrointestinal Disorder. Bold numbers represent statistically significant values

726 RISK FACTORS ASSOCIATED WITH THE NEED FOR INPATIENT TREATMENT OF CHRONIC CONSTIPATION WITH FECAL IMPACTION IN CHILDREN

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Background: Chronic constipation is a common problem in childhood affecting up to 30% of children, and accounting for 3 - 5% of outpatient pediatric clinic visits. Fecal impaction is a state of severe constipation, usually requiring administration of high and/or frequent doses of laxatives. Typically, disimpaction is first attempted in the outpatient setting. However, there are children who fail outpatient treatments, perhaps, even repeatedly, and need to be treated as inpatients.

Objectives: We sought to study the prevalence of chronic constipation with fecal impaction requiring inpatient treatment, and investigate potential risk factors associated with the need for inpatient treatment in pediatric patients.

Methods: In a retrospective, cohort study, medical records of all patients under the age of 21 years with chronic constipation with fecal impaction, who visited or were referred to the pediatric gastroenterology clinic at MHMC between July 2012 and June 2014, were reviewed. Medical records were reviewed for patient demographics, medical and surgical history, symptoms of constipation according to Rome III criteria, duration of disease, potential associated risk factors and the treatment modality and history.

Results: During the study period, 188 patients met inclusion criteria and 30% (58/188) required inpatient treatment. Overall, patients were initially seen or referred to the pediatric gastroenterology clinic at an age of (mean \pm standard deviation) 8.8 ± 4.2 years, with 53% (99/188)

being females. The potential risk factors associated with the need for inpatient treatment were: age of onset ≤ 3 years of age [OR 1.94 (95% CI, 1.03-3.65); $p=0.03$], African-American ethnicity [2.15 (1.07-4.31); $p<0.001$], history of prematurity [2.39 (1.09-5.25); $p=0.02$], developmental delay [2.20 (1.12-4.33); $p=0.02$], encopresis [2.19 (1.09-4.39); $p=0.02$] and anorexia [2.02 (1.00-4.08); $p=0.046$].

Conclusion: Chronic constipation with fecal impaction requiring inpatient treatment is fairly prevalent in children and adolescents. Onset of constipation at a young age, African-American ethnicity, history of prematurity, developmental delay, encopresis and anorexia are potential risk factors associated with the need of inpatient treatment of fecal impaction. Identification of risk factors during a clinical encounter in a child with chronic constipation and fecal impaction will be helpful in anticipating timely institution of the most appropriate future intervention to relieve fecal impaction.

727 MEDIUM-TERM FOLLOW-UP OF ADOLESCENTS TREATED FOR RUMINATION SYNDROME IN AN INPATIENT SETTING

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Rumination syndrome is a functional GI disorder in which the individual repeatedly, involuntarily regurgitates food and fluid soon after eating. It has been demonstrated that behavioral approaches to treatment are effective in reducing rumination, at least in the short-term. While the benefit of treatment has been demonstrated in the short-term, little is known about patient progress after treatment. We embarked, in a medium-term, follow-up study, to add to our understanding of patient progress after completion of an in-patient rehabilitation treatment.

47 adolescent patients (mean age: 15.9 years), who had taken part in an inpatient treatment for rumination syndrome at our institution, completed follow-up questionnaires detailing changes in rumination since discharge from the program (mean time from discharge: 19.4 months). Adolescents also completed standardized reports of somatic complaints, health-related quality of life (HRQOL), repeat hospitalizations and provided information about the use of supplemental feeding tubes.

Improvements in rumination made during treatment were generally retained and further improvement was experienced by the majority of patients. Thirty-two percent of patients reported near or complete resolution of rumination. Patients also experienced improvements in their somatic symptoms ($p= .001$) as well as their HRQOL ($p= .001$). Rumination episodes continued for most patients, with 79% of patients having a period of time with no rumination. Within the group of patients who experienced a period of cessation of rumination, 73% experienced a relapse in symptoms, with 51% attributing the relapse to stress and 27% to intercurrent illnesses. Only 15% of patients had to return to the hospital or emergency room, mostly for dehydration. Four patients (9%), who were able to be off of enteral feeds by discharge, had recommenced use.

Our results suggest that intensive inpatient treatment for adolescents with rumination syndrome is beneficial in the medium-term and that improvements extend to improvements in quality of life. That said, patients continue to struggle with persistence of rumination, even after treatment, and continued therapeutic efforts, support and close monitoring are required during patients' recovery.

728 A POPULATION-BASED STUDY ON THE EPIDEMIOLOGY OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN YOUNG CHILDREN

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Functional gastrointestinal disorders (FGIDs) are common in children, but the epidemiology of FGIDs in infants and toddlers is largely unknown. Our aim is to perform a population-based study using Rome III criteria to describe the prevalence of FGIDs in children in Colombia. This is the largest study on FGIDs in infants and toddlers and the first study in Latin-America to examine the prevalence of FGIDs in this age group.

Methods: We conducted a multicity, cross-sectional study to investigate the epidemiology of FGIDs in infants, toddlers and children younger than four years of age using the Rome III criteria in Colombia. Local nurses at primary care clinics invited all consecutive parents of children 0 to 48 months of age of both genders (age group of infant/toddler version of the Rome III criteria) attending well-child visits to participate in this epidemiological study. Consenting parents received an explanation of the definitions and symptoms of FGIDs prior to completing the Spanish version of the Questionnaire on Pediatric Gastrointestinal Symptoms (QPGS-III-Spanish). Children with organic medical diseases were excluded. Parents provided demographic information and completed the QPGS-III-Spanish.

Results: Parents of 1207 subjects agreed to be included in the study. 24 children were excluded due to the presence of organic diseases and being more than 48 months of age. 480 children (40.5%) met at least one of the Rome III diagnostic criteria for an FGID (49% female, median age: 12 months). Functional constipation was the most commonly diagnosed disorder in infants and children aged 1 - 4 years (16.1% and 26.8%, respectively). Functional diarrhea was the least common FGID diagnosis in both infants and children aged 1 - 4 years (1.9% and 0.5%) (Table). There was an overlap between FGID diagnoses in 5% children. Of the children diagnosed with FGIDs, 95% of children qualified for one FGID diagnosis, 4.6% for two and 0.4% for three FGID diagnoses. The socio-demographic, familial, clinical and environmental variables of children with and without FGIDs were compared. Multiple regression analysis revealed that FGID prevalence was significantly higher in the only child in the family ($p 0.003$), first-born children ($p 0.007$) and children with divorced or separated parents. ($p 0.001$). Having a family history of FGIDs did not influence the prevalence in children ($p 0.8$).

Conclusion: Current findings suggest that FGIDs are common in children younger than 4 years of age. Functional constipation and infant colic were the most common FGIDs in infants, while functional constipation and rumination were the most common FGIDs in children 1 - 4 years of age. Large, prospective, longitudinal studies are needed to determine whether FGIDs in infants and toddlers persist into childhood, adolescence and adulthood. Further studies in children of different countries will be important to further elucidate the role of the different biopsychosocial factors in the pathogenesis of FGIDs.

Table. Prevalence of FGIDs in infants and toddlers (ages 1 - 48 months)

FGIDs	Age group (months)	Total children in the age groups	Diagnosed with FGID	% Prevalence
Total	1 - 48	1183		
FGIDs +			480	40.6
Regurgitation	1 - 6	341	38	11.1
	7 - 12	186	4	2.1
Rumination	1 - 12	527	38	7.2
	13 - 48	656	18	2.7
Cyclic Vomiting Syndrome	1 - 12	527	20	3.8
	13 - 48	656	40	6.1
Colic	1	69	9	13.0
	2 - 4	190	18	9.5
Functional Diarrhea	1 - 12	527	10	1.9
	13 - 48	656	3	0.5
Dyschezia	1	69	4	5.8
	2 - 5	237	17	7.1
Functional Constipation	1 - 12	527	85	16.1
	13 - 48	656	176	26.8

729 AN ANALYSIS OF THE ASSOCIATION BETWEEN RESPIRATION SYMPTOMS AND GASTROESOPHAGEAL REFLUX IN LOW-BIRTH-WEIGHT INFANTS USING MULTICHANNEL INTRALUMINAL IMPEDANCE pH MONITORING

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Background: Whether gastroesophageal reflux (GER) is related to respiratory symptoms, such as apnea and prolonged oxygen desaturation, in low-birth-weight infants is unclear. However, previous studies have conducted that pH monitoring suggests an insufficient correlation between apnea and GER. As infants show non-acid reflux more frequently than adults, 24-hour multichannel intraluminal impedance pH (MII-pH) monitoring is considered more useful for diagnosing GER disease (GERD) in pre-term infants. Therefore, we evaluated the correlation between respiratory symptoms and acid/non-acid reflux in these infants by using MII-pH monitoring.

Methods: This study enrolled 21 low-birth-weight infants (younger than 1 year) with prolonged symptoms, such as apnea, oxygen desaturation, or recurrent cough, who were admitted to the pediatric section of Gunma University between January 2010 and June 2014. MII-pH monitoring was performed in these infants and the results were analyzed in order to evaluate the relationship between symptoms and acid/non-acid reflux. We defined acidic GERD (AGERD) as a reflux index of >10% and non-acidic GERD (NAGERD) as a symptom association probability score of >95, or a symptom index of >50%. Furthermore, we compared the incidence of acid and non-acid reflux between the early and late phase after the milk-feeding period in all cases.

Results: Eleven (52.4%) of 21 infants had GERD. Of the 11 infants, only 5 (23.8%) had AGERD. The difference in the number of infants with acidic reflux was not significant between the AGERD and NAGERD groups, but the number of infants with non-acidic reflux was significantly higher in the NAGERD group. In the early phase after feeding, non-acidic reflux occurred more frequently than acidic reflux in both the AGERD and NAGERD groups. Both the AGERD and NAGERD groups showed acidic reflux more frequently in the late phase than in the early phase after feeding. Reflux duration was significantly longer in the AGERD group than in the NAGERD group, which suggests poorer clearance of regurgitated components in the AGERD group.

Conclusion: MII-pH monitoring is thought to be useful in the diagnosis of NAGERD, which cannot be detected by pH monitoring. MII-pH monitoring showed superiority in detecting non-acid reflux in infants, which occurs more often in the early phase after feeding.

***730 THE NR2F1 TRANSCRIPTION FACTOR PLAYS A KEY ROLE IN ENTERIC GLIOGENESIS**

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For a long time only considered passive support cells, enteric glial cells are now recognized as major players in the control of essential gastrointestinal functions, such as peristaltic movements and epithelial barrier function. Understanding the gene regulatory network that controls enteric gliogenesis is thus of primary importance but, surprisingly, almost nothing is known in this regard. We decided to address this problem using the Spot mouse line as a starting point. The Spot mouse line is a model of Waardenburg-Hirschsprung syndrome that we recently obtained through an insertional mutagenesis screen for genes involved in neural crest cell (NCC) development. Homozygous Spot mice at weaning age are depigmented and display spatial orientation defects and intestinal blockage, resulting respectively from a lack of NCC-derived melanocytes (in the skin and inner ear) and the enteric nervous system (in the colon). Detailed examination of developing intestines revealed that the Spot

mutation negatively impacts migration and proliferation of NCC-derived enteric neural progenitors, due to their premature differentiation towards the glial lineage. This phenotype results from transgene insertion-mediated perturbation of a silencer element that leads to NCC-specific upregulation of Nr2f1 and its overlapping lncRNA A830082K12Rik. Other data suggest that A830082K12Rik is involved in the activation of Nr2f1 transcription in cis and that NCC-directed overexpression of Nr2f1 alone is enough to phenocopy the Spot phenotype. Such an outcome is in total accordance with the fact that Nr2f1 and its paralogue Nr2f2 (which is also expressed in enteric neural progenitors) have both been previously implicated in the control of CNS gliogenesis. Interestingly, recent studies also suggest that some cases of Hirschsprung disease might be caused by premature glial differentiation induced by Sonic Hedgehog (Shh), whereas other studies have shown that Nr2f2 is a direct Shh target gene. Based on the fact that the main Shh effectors (Gli1/2/3, Ptch1, Boc, Gas1, Smo and Sufu) are unaffected in Spot enteric neural progenitors, we thus hypothesized that Shh-induced enteric glial differentiation is normally mediated by Nr2f1/Nr2f2 transcription factors. Preliminary data using embryonic gut explants cultured in the presence of Shh or cyclopamine (an inhibitor of the Shh receptor Smo) strongly support this possibility. In conclusion, our work suggests that a Shh-Nr2f1/Nr2f2 regulatory axis is at the head of the gene regulatory network controlling enteric gliogenesis.

731 MULTIDISCIPLINARY APPROACH IN CHILDREN AND ADOLESCENTS WITH FUNCTIONAL ABDOMINAL PAIN (FAP) OR IRRITABLE BOWEL SYNDROME (IBS) RESULTS IN IMPROVEMENT OF PAIN FUNCTIONING

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Methods: Retrospective review of 68 consecutive patients followed in the FAP program. Only severely disabled, intractable patients were accepted into the program. Measures collected included functional disability index (FDI), abdominal pain index (API) and measures of depression and anxiety.

Results: Clinical characteristics: 75% female with a mean age of 15.4 ± 3.1 years. Mean pain duration: 2.5 years. All patients were previously seen by a pediatric gastroenterologist, 74% by more than one physician (mean 2.34 ± 0.6). Prior work-up (%): EGD (86.8), colonoscopy (61.8), abdominal ultrasound (69.1), CT abdomen (41.2), MRI abdomen (20.3), UGI/SBFT (25), HIDA scan (15.7), motility studies (8.8) and capsule endoscopy (7.4). Therapies prior to presentation (%): previous surgery (29.4): appendectomy (14.7), cholecystectomy (7.4) or exploratory laparoscopy (1.5). Prescribed medications: antacids (67.6), antidepressants (61.8), laxatives (55.9), antibiotics (35.3), antispasmodics (38.2), probiotics (24), opioids (11.8) and gabapentin (14.7). 36.6% received CBT, relaxation techniques, hypnosis or biofeedback and 16.2% were seen in other pain clinics. Pain intensity: mean 6.28 ± 2.07 , maximum 7.94 ± 2.17 . Functional impairment: 76.9% missed a mean of 31.8 days in the previous school year and 10.8% a full year. FDI showed none/minimal disability in 28.8% of patients, moderate in 54.5% and severe in 16.7%. 11.3% were unable to participate in social activities. 26.4% rarely participated, 47.2% mostly participated and 15% participated normally. From previously-active patients, 16% were unable to exercise, 34.1% participated with some restriction and 24% normally. Interventions at FAP program (%): 93.7% were treated as outpatients, 4.1% in a partial day program and 2% as inpatients. At the first visit, 72.1% were prescribed additional medications, most frequently an antidepressant (32%), gabapentin (17.6%), PPI (26%), antibiotics (18%), laxatives (10.3%) or antispasmodics (8.8%). 76.5% were prescribed CBT, 55.9% individual psychological therapy and 53% biofeedback. Follow-up: 67.6% of patients returned for at least one visit (mean visits 3.13 ± 2.41) over 15.33 ± 12.1 months after the initial visit (up to 46 months). Outcomes (%): of patients returning, 68% reported subjective improvement in pain [asymptomatic (4.3%), much improved (42.6%), improved (21%), no change (28%), worsening (4.3%)]. Patients reported normal (23%), much improved (41%), improved (21%), unchanged (14%) or worse (2.3%) functioning.

Conclusion: A multidisciplinary approach, using the biopsychosocial model of disease, resulted in significant improvement of pain and functioning in a majority of patients with intractable, severe and disabling FAP/IBS.

732 BOWEL MOVEMENT FREQUENCY AND STOOL FORM IN CHILDREN WITH IRRITABLE BOWEL SYNDROME AS COMPARED TO HEALTHY CHILDREN

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Background: Children with irritable bowel syndrome (IBS) may be classified by their predominant stool form into one of four subtypes. These subtypes include: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with mixed stool type (IBS-M) and unsubtyped IBS (IBS-U). Though alterations in stool frequency/form are inherent in IBS, comparison of bowel movement frequency and stool characteristics with healthy children or among those with different IBS subtypes has not been reported.

Objectives: To compare both the form and frequency of bowel movements in children with IBS as compared with healthy controls (HC) and to compare IBS subtypes on form and frequency of bowel movements.

Methods: Children aged 7-12 years, with Rome III pediatric IBS and HC, were enrolled in studies evaluating functional gastrointestinal disorders. Subjects completed validated 2-week stool and pain diaries. The diaries captured the frequency of bowel movements and the number, occurrence and severity (0-10 Likert scale) of abdominal pain episodes. Subjects also rated stool form for each bowel movement using the Bristol Stool Form Scale.

Results: 206 children (HC: 68, IBS: 138) (mean age \pm SD: 9.7 ± 1.6 years) were enrolled; 113 (55%) were girls. There were no significant differences in demographic characteristics between the two groups. Children with IBS (as a group) had more frequent bowel movements than healthy children (Table). As a group, children with IBS did not differ from HC with respect to mean stool type (3.3 ± 0.8 vs. 3.1 ± 0.7 , $p=0.1$, respectively). As expected, there were significant differences in stool form between IBS subtypes (Table). There were no differences in abdominal pain frequency or pain severity between IBS subtypes. In addition, there were no differences in bowel movement frequency (Table) between the four IBS subtypes.

Conclusions: Children with IBS (as a group) have more frequent bowel movements, but do not have significant differences in stool form compared to healthy children. Stool form does differ predictably by IBS subtype; however, bowel movement frequency and pain (frequency and severity) do not differ significantly among those with different IBS subtypes.

733 IRRITABLE BOWEL SYNDROME SUBTYPES IN SCHOOLCHILDREN AND POSSIBLE ASSOCIATIONS

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Introduction: Prevalence of irritable bowel syndrome (IBS) in Colombian schoolchildren is 5.4%. Four IBS subtypes have been described: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M) and unsubtyped IBS (IBS-U).

Objective: To determine the prevalence of 4 subtypes of IBS in Colombian schoolchildren and possible associations.

Methods: We invited 222 schoolchildren, aged 8 - 18 years from 10 different Colombian cities. All children were diagnosed with IBS by the Rome III pediatric gastrointestinal symptoms survey in Spanish. Family, sociodemographic and clinical variables were obtained. Statistical analysis included estimation of the prevalence of IBS and its corresponding 95% CI, with other descriptive measures of interest and association estimated by multiple logistic regression analysis.

Results: 196 schoolchildren completed the study with a mean age (SD) of 11.5 (2.3) years, 53.6% were female, 39.3% were from the Andes region, 73.5% were from public schools, >90% were without intrafamily history of functional gastrointestinal disorders, were not an only child and were without altered height and >50% were without divorced parents, were not overweight/obese and had no history of dengue within the last year. The following IBS subtypes were presented: IBS-M 43.4%, IBS-C 26.0%, IBS-D 19.9% and IBS-N 10.7%. There was a predominance of IBS-C in different areas of the Andes (OR 2.03; 95% CI, 0.96-4.41; $p=0.0442$), of IBS-M with a history of dengue in the last year (OR 2.42; 95% CI, 1.00-6.07; $p=0.0293$) and IBS-N in males (OR 2.54; 95% CI, 0.90-7.79; $p=0.0491$). A possible risk factor for IBS-M was a history of dengue in the previous year (OR 3.21; 95% CI, 1.31-7.87; $p=0.010$).

Conclusion: The most common IBS subtypes in Colombian schoolchildren were IBS-M and IBS-E, with as a possible risk factor for IBS-M in children with a history of dengue in the previous year.

734 INTESTINAL TRANSIT IN ECUADORIAN CHILDREN UNDER 5 YEARS OF AGE ACCORDING TO THE BRISTOL SCALE

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Introduction: In Nicaraguan infants and toddlers, intestinal transit (IT) is slow in 1:5 children and accelerated in 1:3, according to the Bristol Scale (BS), with age as a possible risk factor.

Objective: To determine the prevalence of IT by using the BS in infants and toddlers in Quito, Ecuador and possible risk factors.

Methods: Prevalence study in 306 infants and toddlers in Quito, Ecuador. Family (parents separated/divorced, only child, eldest son) and sociodemographic variables (age and gender) were obtained. Statistical analysis included estimation of the prevalence of IT in infants and toddlers and their corresponding 95% CI, the estimation of other descriptive measures of interest and association analysis by multiple logistic regression.

Results: In this group of infants and toddlers, the mean age was 19.4 ± 15.4 months (between 1-60 months), 50.0% were female and male, respectively, 45.8% were only children and first-borns and 25.0% had divorced parents. The prevalence of normal IT was 59.5%, 8.8% was slow and accelerated was found in 31.7%. There was an opportunity for a higher chance of presenting with altered IT in infants (OR 4.51; 95% CI, 2.43-8.66; $p=0.0000$), with age being the only possible associated risk factor (OR 4.64; 95% CI, 2.23-9.63; $p=0.0000$).

Conclusion: According to the BS in Ecuadorian children under 5 years old, IT is slow in 1:11 children and accelerated in 1:3 children, with age as a possible risk factor.

735 FOLLOW-UP OF NAUSEAS IN COLOMBIAN SCHOOL CHILDREN AND ADOLESCENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS IN CALI, COLOMBIA

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Introduction: Nauseas have been reported in 28.0% of Latin-American school children and adolescents with functional gastrointestinal disorders (FGIDs).

Objective: To compare the prevalence of nausea in Colombian children with FGIDs in 2012 and 2016.

Methods: To identify the type of FGIDs and the presence of nausea in school children and adolescents in a public school in Cali, Colombia who were asked to complete the Rome III pediatric gastrointestinal symptoms survey in Spanish. Sociodemographic (age and gender) and family (only child, parents separated/divorced and FGIDs family history) variables were included. Statistical analysis included univariate and Chi-square analysis; $p<0.05$ was statistically significant.

Results: 544 (2012) and 631 (2016) school children and adolescents with a mean age of 12.5 ± 2.5 years (2012) and 13.0 ± 2.7 years (2016); 53.2% (2012) and 51.8% (2016) were male. A FGIDs prevalence of 21.5% (2012) and 23.5% (2016) ($p=0.234$) was found, with the most frequent FGIDs being functional constipation and irritable bowel syndrome. Prevalence of FGIDs in children with nausea was 18.8% in 2012 and 27.0% in 2016 ($p=0.077$).

Conclusion: In this group of Colombian school children and adolescents, an increase in prevalence of FGIDs and nausea between 2012 and 2016 was found, but it was not statistically significant ($p>0.05$)

736 SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF COLOMBIAN CHILDREN WITH IRRITABLE BOWEL SYNDROME

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Introduction: Four irritable bowel syndrome (IBS) subtypes have been described: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M) and unsubtyped IBS (IBS-U).

Objective: To determine the sociodemographic and clinical characteristics of four subtypes of IBS in Colombian schoolchildren.

Methods: Prevalence study in schoolchildren with IBS based on the Rome III pediatric gastrointestinal symptoms survey in Spanish. Family, sociodemographic and clinical variables were obtained. Statistical analysis included estimation of the prevalence of IBS in children and its corresponding 95% CI, estimating other descriptive measures of interest and Chi-square analysis, with $p<0.05$ representing statistical significance.

Results: 196 schoolchildren were included with a mean age of 11.5 ± 2.3 years; 53.6% were female, 39.3% were from the Andes region, 73.5% went to public school, 48.4 % had divorced parents, 8.9 % were singletons, 9.9% had a family history of functional gastrointestinal disorders, 31.4% were overweight/obese, 7.8 % had altered height and 15.4% had suffered dengue in the previous year. Among the 196 schoolchildren who met the Rome III criteria, 26.0% had IBS-C, 19.9% had IBS-D, 43.4% had IBS-M and 10.7% had IBS-U. Significant differences between the presence of supra-umbilical vs. infra-umbilical abdominal pain was found ($p=0.012$), specifically in IBS-M vs. IBS-C ($p=0.002$) and IBS-M vs. IBS-D ($p=0.010$) and in the presence of less frequent stools ($p=0.002$), in IBS-M vs. IBS-C ($p=0.002$), in IBS-M vs. IBS-D ($p=0.004$) and in IBS-M vs. IBS-N ($p=0.045$).

Conclusion: IBS-M was the most frequent subtype for IBS in Colombian schoolchildren. Supra-umbilical abdominal pain and the presence of less frequent stools were predominant.

737 CLINICAL PROFILE OF CONSTIPATED PEDIATRIC PATIENTS WITH DOLICHOCOLON

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Some intestinal pathologies leading to chronic constipation have not received much attention. In some cases, the excessive lengthening of the colon, known as dolichocolon, is underlying the constipation. Significance of this condition as a cause of chronic constipation remains unclear. The researcher noted several cases of constipated pediatric patients with dolichocolon; hence, further investigation on this condition was undertaken.

A review of records was conducted. The diagnosis of constipation was confirmed by abdominal radiograph. The following pertinent data were recorded: chief complaint or reason for consult, fulfillment of ROME III criteria for functional constipation, age of onset and duration of symptoms, medications received, dietary history and barium enema findings.

A total of 50 subjects were included in the study. The onset of symptoms in the majority of subjects was at 0 - 6 months old. The main reasons for consult were abdominal pain, constipation, vomiting and soiling. Most patients were treated for constipation and given laxatives. Some patients did not fulfill the Rome III criteria for functional constipation. The majority had inadequate fiber and fluid intake. The sigmoid colon was the most frequently affected part with redundancy (dolichosigma). Other barium enema findings present in some patients were suggestive of Hirschsprung disease and ischemic colitis. The majority of the patients had barium retention after 24 hours.

This study demonstrates that multiple factors contribute to constipation in pediatric patients and dolichocolon may play a significant role. Future studies are recommended to establish the causative relation of dolichocolon to constipation and its implications in management.

738 FIRST MULTICITY STUDY ON THE PREVALENCE OF FUNCTIONAL CONSTIPATION IN LATIN AMERICAN CHILDREN 2 - 4 YEARS OF AGE

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Background: Most children with functional constipation (FC) develop symptoms within the first 4 years of life. Rome III criteria for FC exist for children both < 4 years of age and ≥ 4 years of age. A nationwide study in the United States found a prevalence of FC of 9.4% among children 1 - 3 years of age. A previous survey study, based on the Rome III criteria for FC, found a prevalence of FC of 13% among children 8 - 15 years of age in Colombia. There are currently no data from any Latin-American country on the prevalence of FC in children less than 4 years of age. Furthermore, few studies exist on the prevalence of FC in this age group of children in any country. Based on published studies from Europe, 50% of children treated for FC continue to have problems after 10 years. As FC is multifactorial, and may be influenced by local factors, obtaining data from children of different ages and countries may help understand the pathophysiology of FC.

Objectives: To assess the prevalence of FC among Colombian children between 2 and 4 years of age.

Methods: We developed and validated a Spanish-language, parental questionnaire assessing the symptoms of the Rome III criteria for children up to 4 years of age. The questionnaire was given to parents of children between 2 and 4 years of age who were presenting for well-child visits in 3 different Colombian cities: Bogota, Cali and Florencia.

Results: Questionnaires were filled out by the parents of 204 children. 51% of these children were girls and the mean age was 2.6 years (SD 0.5). In total, 32 children (16%) fulfilled at least 2 Rome III criteria for FC. Of the 2-year-olds, 8 out of 73 (or 11%) met criteria for FC; of the 3-year-olds, 24 out of 131 (or 18%) met the criteria ($p=0.23$). The prevalence of FC was higher in boys than in girls (22% vs. 10%, $p=0.02$). In children with FC, painful defecation was the most frequently reported symptom (78%), followed by hard stools (63%), withholding behavior (59%), defecation frequency < 3 times per week (25%) and large-size stools (19%). Family factors, such as being an only child, being the firstborn child or having divorced or separated parents, were not associated with a significant difference in the prevalence of FC.

Conclusion: FC is a common problem among Colombian children between 2 and 4 years of age. The most commonly reported symptom in this age group was painful defecation. The overall prevalence of FC in young children found in this study is higher than reported in previous multicity studies in older children in Colombia.

739 FUNCTIONAL GASTROINTESTINAL DISORDERS IN JORDANIAN SCHOOL CHILDREN: AN EPIDEMIOLOGICAL STUDY

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Aim: Functional gastrointestinal disorders (FGIDs) are common in children. Data from our part of the world are scarce. Our aim was to perform a population-based study using Rome III criteria to estimate the prevalence of FGIDs in Jordanian children.

Methods: This was a cross-sectional study of school children covering the whole country. Children between 10 and 18 years were recruited. Children were asked to complete a two-part questionnaire: the first part was the Arabic version of the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III (QPGS-III); the second part included sociodemographic data of the child, the family and school stresses.

Results: A total of 815 children were recruited. Males comprised 46% of the population and the median age was 14.9 years (range 10 - 18 years). A total of 322 subjects (39.5%) met the criteria for an FGID. Abdominal pain-predominant FGIDs were the most common, affecting 18% of the children, followed by defecation disorders. Functional constipation was diagnosed in 15.3% of subjects.

Conclusion: FGIDs are common in Jordanian school children between 10 and 18 years of age. Abdominal pain-predominant FGIDs are the most common, followed by functional constipation.

740 PAIN MODULATION IN YOUTH WITH FUNCTIONAL GASTROINTESTINAL DISORDERS (FGID) MAY BE NORMAL: A ROLE FOR BASELINE NOREPINEPHRINE?

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Background: Children with FGID report pain complaints outside the gastrointestinal tract, suggesting abnormal descending noxious inhibitory control (DNIC). Catecholamines impact pain modulation in animals and are a logical target of investigation in humans.

Hypotheses: DNIC is reduced in children with FGID and correlates with functional disability measured through the Functional Disability Inventory (FDI). The DNIC response reflects circulating norepinephrine levels.

Methods: In this prospective, IRB-approved study, we compared DNIC (Chalaye *et al.*) in ascending and descending immersion of the arm up to the shoulder in 12-degree Celsius cold water, with a 45-min rest in between. Each of 4 segments (fingers, wrist, forearm and shoulder) was immersed for 2 min in cold water, with a rest period of 5 min between segments, and pain was reported by the subject on a 10-point numeric rating scale every 15 seconds during the immersion. DNIC was calculated by subtracting finger and wrist immersion during the ascending period (when DNIC was not activated) from the same report during the descending period (when DNIC was fully activated). Blood was obtained through an IV at baseline, at the end of ascending, prior to descending, and after descending was complete.

Results: We enrolled 11 FGID subjects (1 male; mean age 15.1 yrs, range 13 - 17 yrs). FDI ranged from 4 to 28, with a mean 18.6. DNIC could not be calculated in 2 FGIDs because they had no significant pain (<2 in NRS) when immersing their hand in cold water. The other 10 FGID subjects had a normal DNIC activation of a median of 3.1 points with a range of 2.8 - 10. Catecholamines and present DNIC were available in 7 subjects. DNIC activation correlated highly with baseline norepinephrine value (r 0.97; p <0.01). The FDI did not correlate with norepinephrine (r 0.36; p =0.42).

Conclusions: The DNIC is preserved in youth with FGID. Baseline norepinephrine correlated with the degree of DNIC activation, suggesting that norepinephrine levels contribute directly to pain modulation in some way.

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741 FUNCTIONAL DYSPEPSIA AND IRRITABLE BOWEL SYNDROME IN EARLY TEENAGERS: AN INTERNET SURVEY

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Background: Abdominal pain-related childhood functional gastrointestinal disorders (FGIDs), which are classified as functional dyspepsia (FD), irritable bowel syndrome (IBS), abdominal migraine, childhood functional abdominal pain and childhood functional abdominal pain syndrome, are common reasons for medical consultation in children. However, only a handful of surveys have investigated the epidemiology of childhood abdominal pain-related FGIDs based on the pediatric Rome III criteria, and consequently, the lifestyle characteristics of affected patients have not been fully clarified. On the other hand, orthostatic intolerance (OI) is a term used to describe symptoms associated with a maladaptive circulatory response to an upright posture. GI symptoms are reportedly common among early teens with OI. Chronic symptoms of OI also include headache and morning fatigue. The purpose of the present study was to determine the prevalence of FD and IBS in early teens and to evaluate the lifestyle characteristics of affected patients by focusing on OI symptoms and cephalalgia, as reported by their parents sampled from the general community.

Methods: The questionnaire survey, which was conducted over the internet with the co-operation of a research company, targeted adult members of the general public throughout Japan who lived with their children aged 10 - 15 years. We translated the Rome III childhood FGIDs diagnostic criteria into a series of questions about symptoms that would be easily understood by parents and used to screen for FD and IBS. The parents were further asked about their children, to describe the association of FD and IBS with daily life and other somatic symptoms.

Results: The prevalence of FD and IBS was 2.8% and 6.1%, respectively and 1.4% of the subjects met the criteria for both FD and IBS. The lifestyles of 155 subjects who met the criteria for FD, IBS, or both were compared with those of 1745 control subjects. In comparison with the control group, a significantly higher percentage of subjects with FD, IBS, or both, thought that their sleep was insufficient, that they ate meals irregularly, were susceptible to stress and to dizziness on standing, had difficulty in getting out of bed or felt sluggish in the morning, had a tendency for fainting when standing and suffered from migraine or chronic headache.

Conclusions: This study suggests that FD and IBS are common among Japanese children in their early teens and are associated with symptoms suggestive of OI and headache. Children with FD and IBS are susceptible to stress, have impaired sleep and eating habits and show more frequent symptoms of OI and headache as comorbidities. Cross-disciplinary evaluation and management of these comorbid complaints may help to improve the quality of life of children with FD and IBS.

742 EGFR-EXPRESSING ENTERIC GLIAL CELLS PRODUCE NEW NEURONS IN THE POST-NATAL GUT

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Introduction: The enteric nervous system (ENS) is a complex neuro-glial network that spans the length of the entire gastrointestinal tract. Throughout post-natal life, ENS neurons are subject to injury from a variety of insults, including inflammatory, toxic and surgical, as well as neuronal, loss due to aging. The loss of neurons would imply that, as in the central nervous system (CNS), post-natal neurogenesis would be necessary to maintain proper ENS function. Indeed, enteric neurogenesis has been extensively shown *in vitro* and, under specific conditions, *in vivo*. Recent evidence suggests that, as in the case of the CNS radial glia, in the ENS, glial cells may also be responsible for giving rise to new neurons. However, the identity of the ENS stem or neuronal progenitor is not known.

Objective: We aimed to find a purified population composed of the specific glial cell type responsible for neurosphere formation and the generation of new neurons.

Methods: We used a cell-sorting purification strategy isolating CD49b+, lin-(CD45-/TER119-/CD31-) and EGFRhigh glia, and then studied their ability to form neurospheres *in vitro*, as well as their mitogenic and neuronal differentiation potential. We then explored the *in vivo* neurogenic potential of the sorted glial cells using a transplant model into the E5 chick aneural hindgut.
Results: We show evidence that the CD49b+/EGFRhigh/CD45-/TER119-/CD31-gial cells are highly proliferative and form neurospheres which actively give rise to new neurons *in vitro* and *in vivo* when transplanted into the E5 chick aneural hindgut.
Conclusion: This knowledge will aid in finding the enteric glial population responsible for post-natal enteric neurogenesis.

743 VISCEROSENSORY PERCEPTION DURING DEFECACTION IN CHILDREN WITH CHRONIC CONSTIPATION WITH PALPABLE FECALOMA AND IN HEALTHY CHILDREN

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Introduction: As stool moves into the rectum, stretch receptors activate afferent pathways, sending information to the cortex resulting in the urge to defecate. Children with constipation often do not sense the urge to defecate. An adult viscerosensory questionnaire has been developed.
Aim: To develop a pediatric questionnaire and determine viscerosensory patterns in healthy and constipated children.
Methods: A pediatric version of the questionnaire was developed recording: presence/absence of sensation, location, quality, intensity of sensation and completeness of emptying (using a VAS scale 0-10) and type of stool (Bristol Stool Scale). Children reported every defecation for 2 weeks. Constipation group (CONS) had ≥ 2 yrs constipation, ≥ 6 months failed treatment and hard palpable fecaloma, confirmed by enlarged stool-filled rectum on x-ray.
Results: Forty-five CONS (6 – 18 yrs) and 20 healthy controls (HC) filled in diaries. Only 12/45 CONS had sensation at every defecation (27%), while 18/20 HC did (95.4 %, $p=0.0005$). Using a VAS scale, with 10 as strong sensation, HC had a higher mean strength of sensation than CONS (mean \pm SEM, HC 6.1 ± 0.4 , CONS 4.1 ± 0.4 , $p=0.003$). Sensation centered in the perianal or rectal region, with a similar size of sensation area on the anterior and posterior abdomen in HC. Anterior area was similar for HC and CONS (median [IQR], 6044 [4985-7544] vs. 4374 [2000-10267] pixels), while posteriorly, the HC had a larger area than the CONS (5924 [3433-7440] vs. 2202 [1273-3645] pixels, $p<0.0001$). HC felt more complete emptying than constipated patients (VAS, mean \pm SEM, HC 8.6 ± 0.4 , CONS 6.8 ± 0.3 , $p=0.002$).
Conclusion: Children with fecal impaction have sensations of defecation less often and, when present, the feeling is weaker, and emptying less complete, than in HC and the posterior area of sensation is reduced. This new questionnaire shows significant differences between constipated patients and HC.

744 A NOVEL APPROACH FOR THE TREATMENT OF REFRACTORY FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN: A RANDOMIZED, CONTROLLED TRIAL OF NEUROSTIMULATION

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Background: Pharmacological treatments are often inadequate for patients with functional gastrointestinal disorders (FGIDs) and psychological therapies are not always readily available. Newer, alternative therapies are needed in this population. IBstim (Innovative Health Solutions, IN, USA), an FDA-approved device, delivers percutaneous electrical stimulation (3.2V) with alternating frequencies to branches of cranial nerves (V, VII, IX and X) through the external ear. Preliminary studies in animals suggest that it alters neuronal activity in central nociceptive structures. This study aimed to evaluate the efficacy of IBstim in children with FGIDs who failed pharmacological therapy. We report an interim analysis of this ongoing trial.
Methods: In this prospective, double-blind, randomized, controlled trial, we enrolled 52 out of 100 intended subjects aged 11 - 18 years with FGIDs from an outpatient GI clinic. The IBstim device, which delivers stimulation on/off for 2-hour intervals, was applied to the external ear weekly for 5 days x 4 weeks. The control group had an inactive “sham” device. Patients were randomized by a computer-generated scheme. A Likert 0-10 scale assessed daily nausea and pain ratings. Baseline and weekly assessments included: 1) Pain-Frequency-Severity-Duration (PFSD) scale, 2) nausea profile with 3 subscales (somatic, GI and emotional distress) and 3) a 14-point validated Symptom Response Scale (SRS) (-7 “A very great deal worse”; 7 “A very great deal better”). A 1-point change on the SRS is considered clinically significant.
Results: 42/52 subjects (90% female) completed the trial. 92% had failed drug therapy with ≥ 1 neurally-active agent. Median age was higher in the sham group: [median (range) 16.6 (12.2 - 18.7) vs. 15.4 (10.8 - 18.4) years; $p=0.025$]. After 4 weeks, the group with IBstim treatment had a significant reduction in the worst pain intensity scores compared to sham (median): 8.0 to 5.0 vs. 7.0 to 7.0 ($p<0.05$). Similarly, those with the active device had improvement in overall symptoms compared to sham based on the SRS: [median (range): 3.0 (-3 to 6) vs. 1.0 (-4 to 6); $p=0.032$]. On this scale, 86% in the treatment group vs. 57% in the sham group showed a minimally important improvement with a change score ≥ 1 ($p=0.08$). Nausea profile scores (total and all subscales) decreased significantly over time in both groups, with a trend toward greater improvement in the treatment vs. sham group for the somatic distress ($p=0.064$) and emotional distress ($p=0.09$) subscales.
Conclusion: Our interim analyses show that percutaneous neurostimulation with IBstim offers a novel treatment approach for children and adolescents with refractory FGIDs. Further data on daily pain and nausea scores, physical functioning and health-related quality of life will be examined at the end of the trial.

745 NON-EROSIVE REFLUX DISEASE IN CHILDREN

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Introduction: Non-erosive reflux disease (NERD) is the most common presentation of gastroesophageal reflux disease (GERD) in adults, though less is known about NERD in children. Despite a recognition in the adult literature of reflux subtypes, such as NERD, hypersensitive esophagus and functional heartburn, there are no pediatric studies to determine the frequency of these subgroups or their responsiveness to proton pump inhibitor (PPI) therapy.
Methods: Children undergoing esophagogastroduodenoscopy (EGD) and multichannel intraluminal impedance testing (pH-MII) for evaluation of typical gastroesophageal reflux symptoms (pain, heartburn, chest pain, reflux, or regurgitation) between February 2004 and February 2016

were included in this study. All children underwent a minimum of an 8-week PPI trial prior to diagnostic studies, though all studies were performed off PPI therapy. Children with erosive reflux disease or eosinophilic esophagitis were excluded. Patients with abnormal esophageal acid exposure (pH <4 for >6% of the study) were classified as true NERD. Those with normal acid exposure, but a positive symptom index (SI) to either acid or non-acid reflux, were classified as acid or non-acid hypersensitive esophagus. Those with normal acid exposure and a negative SI were classified as functional heartburn.

Results: 50 pediatric patients reported symptoms during pH-MII monitoring (mean age 10.4 ± 5.2 years, 52% female). Reported symptoms included heartburn (36%) non-specific pain (50%), abdominal pain (26%), chest pain (4%), reflux (14%) and regurgitation (20%). 28% of children had abnormal esophageal acid exposure and were classified as true NERD. 32% of children were categorized as having hypersensitive esophagus (30% with a positive SI for acid events and 2% with a positive SI for non-acid events). The remaining 40% of patients had functional heartburn. Despite typical reflux symptoms, 40% of subjects did not respond to PPI therapy. 64% of NERD patients, 73% of acid hypersensitive esophagus patients, 0% of non-acid hypersensitive esophagus patients and 50% of functional heartburn patients had at least some symptomatic improvement with PPI use, though there were no significant differences between groups ($p = 0.32$). 20% of all patients had evidence of microscopic reflux esophagitis on histology. Among subtypes, 14% of NERD patients, 27% of patients with acid hypersensitive esophagus, 0% of those with non-acid hypersensitive esophagus and 20% with functional heartburn had microscopic esophagitis ($p = 0.86$).

Conclusions: There is an even distribution of NERD subtypes in pediatric patients. Correct diagnosis of patients is only possible with the use of pH-MII testing and is important to help guide future therapeutic options. While PPI responsiveness does not differ significantly between subgroups, many children do respond to PPIs and a trial is indicated in patients with typical reflux symptoms.

746 VNS IN INFLAMMATION: SYSTEMATIC REVIEW OF ANIMAL MODELS AND CLINICAL STUDIES

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Background: Vagus nerve stimulation (VNS) has been long used for treatment of drug-resistant epilepsy. More recently, an off-label use of this well-tolerated treatment modality has been explored in multiple animal experimental models and clinical trials for the treatment of a number of conditions involving the innate immune system in one way or another. The underlying premise has been the notion of the cholinergic anti-inflammatory pathway (CAP) mediated by the vagus nerves. While the macroanatomic substrate – the vagus nerve – is clear, the physiology of the pleiotropic VNS effects and the language of the vagus nerve-mediated, brain-body communication remain an enigma. Tackling this enigma is precisely the challenge for, and promise of, bioelectronic medicine.

Objectives: We review the state-of-the-art of this emerging field as it pertains to developing strategies to use the endogenous CAP for the treatment of inflammation and infection in various animal models and human clinical trials.

Methods: We included any studies listed on PubMed in the English language and meeting the search term criteria (vagus nerve stimulation [MeSH Terms]) AND inflammation [MeSH Terms]. All years up to March 28, 2016 were considered. All study designs were considered. We extracted data on animal model used, location and side of VNS, frequency, intensity, pulse and stimulation durations.

Results: We identified 288 records, of which 34 were deemed eligible and reviewed. We report the diverse profile of currently used VNS anti-inflammatory strategies in animal studies and human clinical trials. Apart from the successful use in refractory epilepsy in humans, the anti-inflammatory effects of VNS were not supported by the three human studies included in this review. Most studies were conducted in rodents: 19 in rats and 8 in mice. The overwhelming majority (23) of studies were done in male adult subjects and the left or right cervical vagus nerve was stimulated. We found a large variance in VNS settings in most of the studies not reporting the intensity of the stimulus. The majority of the studies (27) were designed as acute protocols (less than 24 hours' VNS treatment) and observed the inflammatory profile for less than 24 hours. All rodents VNS studies, except for one, resulted in a reduction of inflammation. All studies, except two, used VNS treatment prior to inducing inflammatory response, rather than after, to mimic a clinical scenario.

Conclusions and Implications of Key Findings: This review provides a foundation for more systematic and comparable VNS strategies in animal and human studies for the treatment of inflammation. Brain mapping initiatives are needed to decode vagus-carried, brain-body communication, before informed treatment approaches can be devised.

747 RELATIONSHIP BETWEEN ESOPHAGEAL ABNORMALITIES ON ESOPHAGRAM AND PULMONARY FUNCTION TESTING IN JUVENILE SYSTEMIC SCLEROSIS

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Background: Juvenile systemic sclerosis (JSSc) is an autoimmune disabling condition that affects multiple organs, most notably the gastrointestinal and pulmonary systems. Severe pulmonary involvement, including interstitial lung disease, pulmonary vascular disease and pulmonary hypertension, are associated with poor prognosis and significant morbidity and mortality. Pulmonary function tests (PFTs) are followed in adults and children to monitor for development and progression of restrictive lung disease. Esophageal abnormalities, including dysmotility, are frequently reported in children with JSSc. The role of esophageal abnormalities in the development and progression of pulmonary disease are conflicting in adults with systemic sclerosis. To our knowledge, the relationship between the pulmonary and the gastrointestinal systems in children with JSSc has not been described.

Aim: To describe the relationship between esophageal abnormalities on imaging [fluoroscopic esophagram and high-resolution chest CT (HRCT)] and PFT parameters.

Methods: Fluoroscopic upper gastrointestinal studies (UGIs) and PFTs of 19 children with JSSc were reviewed. Esophageal findings on UGI and HRCT were correlated with PFT parameters. Specific esophageal findings included: esophageal dilation, esophageal motility, primary or secondary peristaltic waves, bolus clearance, spontaneous gastroesophageal reflux (GER) and GER with provocation maneuvers. Esophageal abnormalities on HRCT included: dilated, patulous, or fluid-filled esophagus. Specific PFT parameters included: FEV₁ % predicted, FVC % predicted, FEV₁/FVC % predicted, FEF 25-75 % predicted, TLC % predicted, VC % predicted, DLCO adj. for Hgb % predicted, DLCO/VA adj. for Hgb % predicted and RV % predicted.

Results: 19 children (mean age, 143.9 ± 7.5 months, 4 male, 16 female) were retrospectively reviewed. There was a strong negative correlation between the presence of any esophageal abnormality on UGI and TLC % predicted ($r_s -0.585$, $p < 0.05$) and DLCO/VA adj. for Hgb % predicted

(rs -0.540, $p < 0.05$). A significant negative correlation was found between abnormal esophageal motility and FVC % predicted (rs -0.665, $p = 0.01$), DLCO/VA adj. for Hgb % predicted (rs -0.573, $p = 0.03$) and TLC % predicted (rs -0.587, $p < 0.05$). Abnormal bolus clearance correlated with lower FVC % predicted (rs -0.640, $p = 0.01$). There was no relationship between PFT parameters and GER on UGI, or between PFT parameters and esophageal abnormalities on HRCT ($p > 0.05$).

Conclusion: There was a significant correlation between esophageal abnormalities (abnormal esophageal motility and bolus clearance) and PFT parameters suggestive of restrictive lung disease and pulmonary function impairment. This is the first time a correlation between the pulmonary and gastrointestinal systems has been described in children with JSSc. Future studies are needed to demonstrate causality and establish the use of esophageal findings in predicting pulmonary function decline.

748 THE CORRELATION BETWEEN ELEVATED BREATH METHANE AND GASTROINTESTINAL SYMPTOMS IN CHILDREN: A RETROSPECTIVE STUDY

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Background: Recent studies in adults have shown that methane production on breath testing is significantly associated with slow transit constipation, as well as irritable bowel syndrome (IBS). Researchers advocate managing constipation by modulating the gut bacteria with antibiotics to decrease methane production. Studies in children are few, but they support higher methane production being related to slower colonic transit. However, there is still controversy over the utility of measuring methane and what is considered to be a positive value. We hypothesized that there would be a higher association of constipation symptoms with higher methane levels.

Methods: We evaluated 102 patients known to our pediatric gastroenterology clinic who were referred for lactulose breath testing for clinical suspicion of bacterial overgrowth. Data on methane values was collected at baseline and hourly during the test. Patients were all screened for constipation, bloating, dyspepsia, abdominal pain, encopresis and diarrhea. Details about constipation symptoms included bowel movements < 3 times a week, patient endorsing constipation at the time of test, retentive fecal incontinence, evidence of impaction within 3 months of test, bowel cleanout within 1 month of test, palpable abdominal mass on exam and history of constipation.

Results: Methane positivity was divided based on the most common definitions: methane ≥ 0 ppm anytime during the test ($n = 48$), methane ≥ 3 ppm anytime during the test ($n = 35$), methane ≥ 10 ppm anytime during the test ($n = 13$) and methane ≥ 3 ppm at baseline ($n = 17$). Since it is known that children do not reach adult levels of methane until at least age 10, we divided patients based on age into group 1 (< 10 years) and group 2 (> 10 years). We evaluated evidence of symptom association at different methane levels in both groups using the Fisher's test. At each of these methane cut-offs, no symptoms reached statistical significance. Symptoms also did not reach significance when patients under 10 years of age were excluded. A trend was noted between bloating and methane positivity. The odds ratio increased as the methane cut-off was set higher, though significance was not achieved. Bowel cleanout also seemed to be associated with lower methane values.

Conclusion: In this retrospective study, a trend between bloating and breath methane positivity was found. A prospective study on patients with bloating and constipation might determine the potential utility of methane breath testing in directing the management of children with such symptoms.

749 IMPLEMENTATION OF AN EVIDENCE-BASED GUIDELINE FOR DECREASING X-RAY USE IN PATIENTS BEING EVALUATED FOR FUNCTIONAL CONSTIPATION

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Introduction: Functional constipation (FC) is a common referral for outpatient gastroenterology consultation. A recently revised 2014 NASPGHAN guideline offered updated recommendations for the evaluation and treatment of FC in infants and children. As part of these revisions, the guidelines did not support the use of abdominal radiography (AX-rays) to diagnose FC. We developed a hospital-wide quality improvement Evidence-Based Guideline (EBG) initiative for standardizing clinical gastroenterology providers' approach to FC, with the aim of decreasing the routine use of AX-rays.

Methods: A retrospective review was conducted of all new outpatients ≥ 6 months of age being evaluated within the Division of Gastroenterology (GI) and Nutrition at Boston Children's Hospital with a primary diagnosis of FC (using International Classification of Disease, 9th or 10th edition) between February 2013 and December 2015. The EBG was implemented in January 2015. Therefore, baseline as well as post-guideline utilization of AX-ray was available. A primary outcome measure was defined as the change in the frequency of patients who underwent an AX-ray within 24 hours of their initial consultation before and after guideline implementation. Secondary outcomes included frequency of AX-ray use by individual GI providers, frequency of subsequent ED visits and hospitalization rates for constipation within 3 months of their initial GI visit. All primary and secondary outcomes, as well as average estimated X-ray costs (in 2016 US dollars), were compared before and after the guideline implementation in order to assess the guideline's effect on clinical care.

Results: 3377 outpatients within 13 clinics were seen for a new diagnosis of constipation; 1045 (30.9%) patients were seen at the main hospital. Mean age (SD) was 8.0 (5.1) years and 1609 (47.7%) were male. 544 (24.6%) patients presenting with constipation had an AX-ray performed before implementation of EBG versus 126 (11.4%) patients after EBG ($p < 0.05$, Figure 1). Three providers pre-EBG, versus only 1 provider post-EBG implementation, were found to be 3 standard deviations outside the expected use of AX-rays/visit. No changes in subsequent ED visits or hospitalization rates were seen after EBG implementation. The estimated cost of AX-ray use per patient decreased from approximately \$65/patient to \$29/patient following EBG implementation.

Discussion: Development of a hospital-wide quality improvement algorithm for FC was a useful tool for adopting NASPGHAN guidelines into our hospital's clinical practice. With this guideline implementation, we were able to decrease unwarranted use of AX-rays in the initial presentation of patients with FC. Further studies are needed to see if implementation of similar guidelines will impact constipation practice at other institutions. Additional quality interventions and monitoring may be needed to assess sustainability of this clinical practice improvement.

750 IMPROVED SELF-EFFICACY IN CHILDREN WITH FUNCTIONAL CONSTIPATION IS ASSOCIATED WITH TREATMENT SUCCESS
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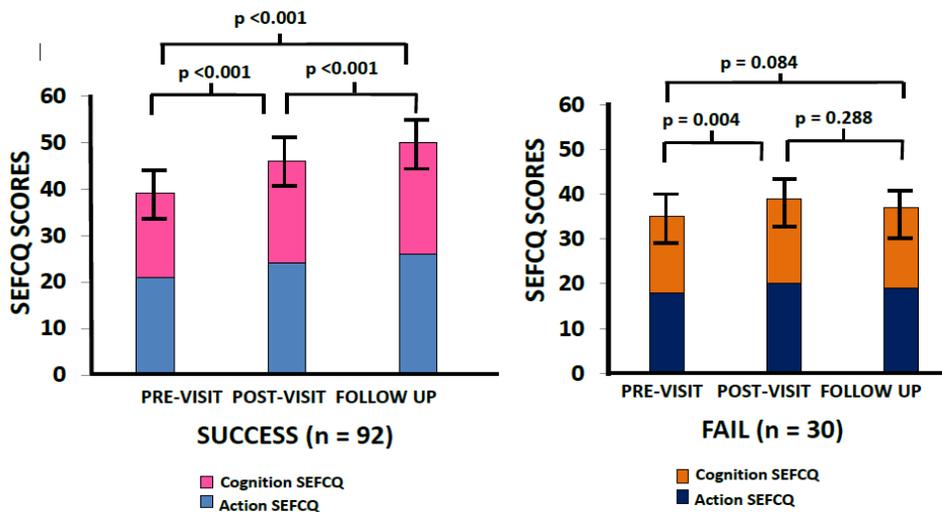
Background: Current clinical guidelines for treating pediatric functional constipation (FC) recommend education, disimpaction and maintenance of soft stools with non-stimulant laxatives, but only 50-60% of children enjoy treatment success. Self-efficacy is the belief that an individual can succeed at a goal. We hypothesized that, if children with constipation believe that they cannot defecate comfortably, this low self-efficacy prevents treatment success. Our aims were: 1) to develop and validate a self-efficacy for FC questionnaire (SEFCQ) and 2) to examine if self-efficacy predicts outcome.

Methods: We wrote 21 statements asking about ability to perform tasks needed for defecation and scored them on a 4 point scale. Subjects aged 8 – 16 years with FC and healthy controls completed the SEFCQ and 3 other questionnaires measuring related constructs to establish validity. Subjects completed the SEFCQ 3 times: before, immediately after and 3 weeks after the first clinic visit. We established treatment success as 3 or more bowel movements into the toilet and no fecal incontinence in the third treatment week.

Results: Aim 1 - Validity and reliability: The questionnaire was adjusted based on feedback from 10 children and 7 experts. We administered the SEFCQ to 130 subjects with FC (age 11 ± 3 years, 42% Caucasian, 45% African-American, 53% male, 43% with fecal incontinence) and 99 controls matched for age, gender and race. Factor analysis revealed two scales, a 7-item action scale and a 7-item cognition scale, with a moderate correlate (0.464). The internal consistency reliability for the action factor was 0.81 and 0.70 for the cognition factor. On the total of the 14 items, controls scored higher on the SEFCQ (53 ± 3 of a possible 56) than subjects (39 ± 7 ; $p < 0.001$). The SEFCQ correlated positively with general self-efficacy ($r 0.32$, $p < 0.001$) and quality of life ($r 0.20$; $p < 0.01$) and negatively with anxiety ($r -0.15$; $p < 0.05$). Aim 2 - Self-efficacy and treatment outcome: There was no difference in SEFCQ scores with age, race or gender ($p > 0.05$). Self-efficacy improved from before to immediately after the clinic visit regardless of treatment outcome ($p < 0.001$). Of the 122 subjects completing the study, 92 (75%) enjoyed treatment success. Total, action and cognition SEFCQ scores were higher in the Success group than the Fail group before, immediately after the clinic visit and at the 3-week follow-up ($p < 0.001$). Total, action and cognition SEFCQ scores improved at all time points in the Success group ($P < 0.001$). In the Fail group, total, action and cognition scores improved immediately after clinic visit ($p < 0.05$ for both) but did not change at the 3-week follow-up ($p > 0.05$).

Conclusions: We developed a questionnaire to measure self-efficacy for FC with high internal reliability and good initial validity. Improved self-efficacy is associated with treatment success in FC. We speculate that it might be desirable to find ways of enhancing self-efficacy in children with FC.

GRAPH 1. CHANGE IN SELF-EFFICACY OVER TIME



751 CONCERNS OF THAI PARENTS ABOUT FUNCTIONAL GASTROINTESTINAL SYMPTOMS IN INFANTS

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Background and Objective: Functional gastrointestinal symptoms (FGIS), especially infant regurgitation, infant colic and constipation, are common in infancy. Parental concerns may be one of the reasons for treatment, but parents in different cultures may react differently to these problems. We evaluated the concerns of Thai parents about FGIS among infants at two months of age and factors associated with the concerns and the symptoms.

Materials and Methods: A case-control study was performed at Phramongkutklao Hospital, Bangkok, Thailand. Infants about two months of age were enrolled into either a FGIS (case) group or a no-symptom (control) group, depending on their symptoms consistent with Rome III criteria. Their parents were interviewed and data on the symptoms (regurgitation, inconsolable crying and constipation) and associated factors were recorded in a questionnaire. Both groups of parents gave their concern score regarding FGIS (0 - 5, none to maximum).

Results: The study enrolled 51 infants in the case group and 63 in the control group. In the case group, the symptoms of regurgitation, colic and constipation were found in 82.4%, 17.6% and 7.8% of infants, respectively. There was no difference between the groups in terms of sex, age,

current weight, birth weight, breast- or bottle-feeding, parental age, marital status, income, smoking, number of caretakers and family history of FGIS. The case group had a higher percentage of infants being the first child of the family (odds ratio 2.7, 95% CI, 1.2 to 6.3). Infant colic was the most concerning symptom for parents of both groups, whereas infant regurgitation was the least concerning symptom (median concern score [P25, P75]: 5 [4,5] vs. 3 [2,3], $p < 0.001$). However, compared to the control group, the case group had a lower parental concern score for symptoms of regurgitation and colic (median [P25, P75]: 3 [2,3] vs. 3 [2,4], $p = 0.03$ and 4 [4,5] vs. 5 [4,5], $p = 0.029$). There was no difference in parental concern score for constipation. In the subgroup of infant regurgitation ($n = 42$), parents had a lower concern score for regurgitation compared to the control group (median [P25, P75]: 2 [2,3] vs. 3 [2,4], $p = 0.004$). No other factors were found to associate with parental concern scores.

Conclusions: Thai parents of infants having regurgitation could cope well with this symptom without much concern. However, infant colic was the most concerning symptom among the FGIS. Being the first child was the only factor associated with FGIS in this study.

752 FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN UNDER TWO YEARS OF AGE: PREVALENCE AND ASSOCIATED FACTORS IN A PRIMARY HEALTH SETTING IN BOGOTÁ

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Introduction: Functional gastrointestinal disorders (FGID) are chronic gastrointestinal manifestations anywhere in the digestive tract without evident structural or biochemical alterations; they can be classified according to Rome III criteria. Their prevalence in Latin American small children is not well known.

Objectives: To estimate the prevalence of FGID and each of its categories in children under 2 years of age and explore associated factors.

Methods: A cross-sectional study was carried out in a calculated, random sample of the population attending a primary health institution in Bogotá. Parents agreed to complete a written survey questionnaire based on Rome III criteria. Statistical analysis, performed with SPSS 21 software, included descriptive statistics and bivariate analysis; odds-ratio was calculated with a 95% CI. A University ethical committee reviewed and approved the protocol.

Results: A total of 323 children were enrolled. Prevalences were as follows: 22.1% for FGID; 14.6% for functional diarrhea, 12% for dyschezia, 9.2% for regurgitation, 3.3% for constipation, 2% for cyclic vomiting, 1.6% for infant colic; infant rumination was not found. Bottle feeds during neonatal hospital stay were associated with probable cyclic vomiting [OR 6 (1.076 - 33.447), $p = 0.021$]. Formula feeds during the first 6 months of life were associated with functional diarrhea [OR 0.348 (0.149 - 0.813), $p = 0.012$].

Conclusions: FGID constitute a relatively frequent cause of discomfort in children under 2 years. An initial description of local prevalences is presented. Infant feeding in the first months of life could facilitate some of these disorders. We suggest that frequency of FGID be studied in diverse settings and social conditions, as they may differ.

*753 PREVALENCE OF ROME IV FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN AND ADOLESCENTS IN THE USA
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Background: The new Rome IV criteria for functional gastrointestinal disorders (FGID) for children and adolescents have been refined to better reflect their prevalence and therefore include several changes to existing criteria and also introduce two new disorders: functional nausea and vomiting. It is unknown how these changes will impact the prevalence of FGIDs. The aim of the current study was to determine the prevalence of FGIDs in children and adolescents in a representative USA community sample.

Methods: A general population internet survey of mothers from all US states used stratified sampling to ensure equal child age distribution and adequate representation of Hispanic and African American children. To avoid biasing the sample, invitations to participate listed this as a health survey rather than a survey of GI symptoms. The Questionnaire on Pediatric Gastrointestinal Symptoms was updated for Rome IV criteria.

Results: Subjects were 1075 mothers of children and adolescents 4 - 18 years of age (mean 10.6 ± 4.5 years, 46% male, 77% white, 9% African American, 16% Hispanic). By maternal report, 24.4% of children and adolescents qualified for at least one FGID. Among those who qualified, 64% had one disorder, 24% had two disorders and 12% had 3 or more disorders. Overall, girls were not more likely to suffer from an FGID than boys. Gender differences were found only for functional abdominal pain-not otherwise specified (FAP-nos; 1.4% boys versus 3.2% girls, $p = 0.02$). Functional constipation (13%) was the most common FGID (Table 1), while no one qualified for rumination. The functional abdominal pain disorders (FAPD: IBS, functional dyspepsia, FAP-nos and abdominal migraine) accounted for 16.7% of the total. Compared to Rome III prevalence rates from a study using similar methodology, prevalence of abdominal migraine fell from 9.2% (Rome III) to 1.1% (Rome IV), while the other FAPDs saw slight increases (Table 1).

Conclusions: This large, community-based study is the first to show prevalence rates for the new Rome IV criteria. It suggests that almost 1 in 4 children and adolescents in the USA suffer from a FGID and this number is similar to the rate found with Rome III criteria. Abdominal migraine showed a large drop in prevalence, but this disorder was likely to have been overestimated with the Rome III survey questions. This study was funded by the AGA-Rome Foundation Functional Gastroenterology and Motility Disorders Pilot Research Award.

Prevalence of Rome III and IV FGIDs		
(percent of sample)		
	Rome III**	Rome IV
	N = 949	N = 1075
Any FGID	23.1	24.4
Functional Abdominal Pain-nos	0.8	2.7
Irritable Bowel Syndrome	2.8	5
Functional Dyspepsia	0.2	7.9
FD-PDS*	N/A	7.4
FD-EPS*	N/A	0.5
Abdominal Migraine	9.2	1.1
Functional Nausea	N/A	0.6
Functional Vomiting	N/A	1.3
Aerophagia	4.3	3
Cyclic Vomiting Syndrome	1.1	1.8
Rumination Syndrome	0	0
Functional Constipation	12.9	13.4
Non-Retentive Fecal Incontinence	1.8	0.2

Note: *FD-PDS = Functional Dyspepsia Postprandial Distress Syndrome; FD-EPS = Functional Dyspepsia Epigastric Pain Syndrome; nos = not otherwise specified; **Rome III data from van Tilburg MA, *et al.* Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents. *J Pediatr* 2016; May 4.

754 PSYCHOLOGICAL FACTORS AND PEDIATRIC FUNCTIONAL GASTROINTESTINAL DISORDERS: A SYSTEMATIC REVIEW

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Objective: Functional abdominal pain disorders (FAPD) are among the most common disorders experienced by pediatric patients. Although psychological factors are frequently described in pediatric patients with FAPD, a systematic review examining all pediatric FAPD and psychological factors has not been conducted in the past 20 years. The aim of this study was to systematically review published literature to better understand the relationship between pediatric FAPD and psychological factors.

Methods: A computer-assisted search of PubMed was performed for all publications from 2006 - 2016. Study selection criteria included: 1) common terms for pediatric FAPDs and 2) common terms for psychological factors. Four hundred and eighteen articles were compiled based on searches for FAPD with psychological factors in patients from birth to eighteen years of age. Eighty-eight publications were initially identified for inclusion in the systematic review.

Result: Thirty-five publications assessed patients in clinical settings and forty from subjects in population-based settings. Sixty-one publications evaluated patients in a cross-sectional manner and only four longitudinal publications were identified. Thirty-three articles examined functional abdominal pain, nineteen articles examined irritable bowel syndrome, and thirteen articles examined recurrent abdominal pain. Anxiety and depression were the most commonly studied psychological factors (48 out of 75 articles). Coping, especially catastrophizing, is an important factor addressed in psychological therapies for FAPD and was studied in fourteen papers. In eighteen publications, parental psychological factors, especially social learning and parental anxiety, depression and coping, was examined in FAPDs.

Conclusion: Pediatric FAPD are frequently present with comorbid psychological symptoms. These are suggested to play roles in the onset, exacerbation and maintenance of symptoms; however, more longitudinal research is needed to better understand the influence of psychological factors in patients with FAPDs.

755 SUBTYPE CLASSIFICATION OF CHRONIC FUNCTIONAL CHILDHOOD CONSTIPATION WITH A COLON TRANSIT TIME TEST: THERAPEUTIC PERSPECTIVE

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Purpose: To evaluate the usefulness of subtype classification of chronic functional childhood constipation with a colon transit time (CTT) test.

Methods: 190 out of 415 children were enrolled in this study, based on highly refined data collected from a defecation diary, medical records and a CTT test result (Metcalf protocol: capsules containing 20 radio-opaque markers were ingested on 3 consecutive days and supine plain X-rays were taken on the 4th and 7th day. 42 hours was the cut-off value of normal transit).

Results: As a whole, Forlax[®] (polyethylene glycol 4000) was prescribed in 51.1% (n=47/92) of normal transit type (NT) and in 91.8% (n=90/98) of abnormal transit type ($p<0.001$). In terms of subtype, in 51% (n=47/92) of NT, in 96.2% (n=25/26) of outlet obstruction type (OT) and in 90.3% (n=65/72) of slow transit type (ST), Forlax[®] was prescribed ($p<0.001$). In the encopresis group, 97.2% (n=35/36), and 66.2% (n=102/154) in the non-encopresis group, were on Forlax[®] ($p<0.001$). In the non-encopresis group, in terms of subtype, in 47.3% (n=40/84) of

NT, in 94.4% (n=17/18) of OT and in 86.5% (n=45/52) of ST, Forlax[®] was prescribed ($p<0.001$). In the encopresis group, in terms of subtype, in 87.5% (n=7/8) of NT, in 100% (n=8/8) of OT, in 100% (n=20/20) of ST, Forlax[®] was prescribed ($p=0.165$).

Conclusion: Subtype classification of chronic functional constipation in children based on a CTT test provides important therapeutic implications for drug choice.

756 ABDOMINAL X-RAY IMAGE AND INQUIRY SUGGEST PATHOPHYSIOLOGICAL DIFFERENCES IN FUNCTIONAL CONSTIPATION (FC) BETWEEN ADULTS AND CHILDREN IN JAPAN

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The prevalence of functional constipation (FC) among adults is 27% and ranges from 9.1% to 18.5% among children in Japan. Most adult FC was childhood-onset. Appropriate therapy of FC during childhood could have the potential to improve quality of life. As there is no pathognomonic diagnostic measurement for FC, the diagnosis relies on clinical symptoms and is only made after exclusion of organic diseases, especially in adults. We have reported on a non-sedative painless colonoscopy, "WATER NAVIGATION COLONOSCOPY 1". When colonoscopies are done only with a spasmolytic, persistent colonic movements are observed in approximately 10% of the patients and most of them have IBS or FC2. On the other hand, there are some IBS or FC patients without persistent colon movement and most of them have abnormal colon morphology, which makes colonoscopy difficult. From these findings, we also found that FC can be diagnosed into three pathophysiological types (anorectal type, abnormal colon morphology type, spastic type) even from abdominal x-ray images and inquiry. Aims and Methods: The present study was designed to evaluate pathophysiology of FC only with abdominal x-ray images and inquiry. 71 child (44 male, 27 female) and 99 adult (23 male, 74 female) patients were recruited. Diagnosis of FC was based on ROME III criteria. Colon morphology, such as sigmoid colon malrotation and mesocolon, was estimated based on the images of gas and stool on abdominal x-ray (supine and standing position). Anorectal type was diagnosed by fecal impaction at the rectum with no urge to defecate. Spastic type was diagnosed by colon spasm and symptom worsening with emotional stress.

Results: Age of onset of FC in male infants was $2.3 \pm 2.6^*$ years, 2.4 ± 4.4 years* in female infants (* $p=n.s.$), $41.3 \pm 24.8^{**}$ years in adult males and $25.5 \pm 20.2^{**}$ years in adult females (** $p<0.05$). 42.4% (26% male and 49% female) of adult FC cases were childhood-onset (under 16 years of age). Anorectal-type FC was found in 91%, 85%, 17% and 14% of cases (male infants, female infants, adult males, adult females, respectively). Abnormal colon morphology was found in 59%, 37%, 87% and 89%, respectively. Colon spasm was found in 2.2%, 0%, 22% and 16%, \pm . Age of onset of child anorectal type FC in male infants was $1.7 \pm 2.0^*$ years and in others it was $7.5 \pm 6.3^*$ years (* $p<0.05$).

Conclusions: Anorectal-type FC was dominant in children, not in adults. Age of onset of anorectal-type FC is younger than the other types of child FC. Although 42.4% of adult FC was childhood-onset, anorectal type FC was not dominant in childhood-onset adult FC. The pathophysiology of FC seemed to be significantly different between adults and children from abdominal X-ray in Japan.

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757 CYCLICAL VOMITING SYNDROME: A SINGLE UK CENTRE EXPERIENCE

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Objective: Cyclical vomiting syndrome (CVS) is a well-recognized progressive functional GI disorder associated with distressing symptoms of nausea and recurrent vomiting. There is no data available regarding the ethnicity prevalence of CVS. The aim of this study was to look at the ethnicity, disease progression and outcomes of children with an established diagnosis of CVS at 2-year follow-up referred to our University teaching hospital.

Methods: Retrospective analysis of case notes of patients referred with cyclical vomiting pattern.

Results: 110 patients were referred with cyclical vomiting pattern from 2004 - 2016. 50 of these patients were diagnosed with cyclical vomiting syndrome as per Rome III/NASPGHAN diagnostic criteria. 46 (92%) of these patients were Caucasians, 3 patients (6%) were of Asian origin and 1 patient was of mixed Afro-Caribbean origin. The reason for referral to our centre was recurrent vomiting in 47 patients (94%), chronic abdominal pain in 2 patients (4%) and recurrent respiratory tract infections in 1 patient. Associated symptoms included abdominal pain in 23 patients (46%) and headache in 16 patients (32%). Family history of migraine was present in 15 patients (30%). At 2 years of follow-up, 8 patients (16%) were symptom-free (7 on propranolol, 1 on amitriptyline). Of the remaining 42 patients, predominant symptoms included nausea with recurrent vomiting in 20 patients (47%), headaches in 15 (35%) and abdominal pain in 7 patients (16%).

Conclusions: Cyclical vomiting syndrome is common in the Caucasian population. As disease progresses, headache and/or abdominal pain are the predominant symptoms in at least half of these patients. Less than one fourth of these patients were completely symptom-free after the initiation of prophylactic pharmacotherapy.

NUTRITION & INTESTINAL REHABILITATION

763 MEASUREMENT OF BODY COMPOSITION BY AIR DISPLACEMENT PLETHYSMOGRAPHY IN PEDIATRIC INTESTINAL FAILURE PATIENTS

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Background: Children with intestinal failure (IF) require prolonged periods of parenteral nutrition (PN) for sustenance and growth until intestinal adaptation allows adequate enteral intake. The accrual and preservation of lean body mass is an important goal during this phase of nutritional rehabilitation. However, lean body mass is not accurately measured by currently available anthropometric techniques. Air displacement plethysmography (ADP) is a non-invasive measure of whole body composition and measures body mass and volume, with a calculation of percent body fat (%BF) using age- and sex-specific equations.

Objective: To determine, in children with IF, the correlation between %BF measurements using ADP, bioelectrical impedance analysis (BIA), and bedside anthropometric methods (sum of four-site skinfolds).

Methods: We are conducting a prospective cohort study in children recruited through the Center for Advanced Intestinal Rehabilitation (CAIR) program at the Boston Children's Hospital. Included are patients 2 - 17 years of age with IF (dependent on PN for more than 90 days). Spearman rank correlation and the method of Bland and Altman were used to compare ADP to both BIA and four-site skinfold anthropometry for %BF calculation. This study is part of a larger validation study correlating ADP with the gold standard technique of deuterium isotope dilution.

Results: Seven children with IF, median (IQR) age 8.3 (5.5 - 9.1) years, 5 (71%) female, were studied. Subjects had a median (IQR) residual bowel length of 40 (31 - 95) cm with all but one in continuity with their colon. Six subjects had their ileocecal valve (ICV) resected, one with unknown ICV status. Six children had surgical short bowel syndrome and one had chronic intestinal pseudo-obstruction. Median (IQR) energy intake was 88 (79 - 102) kcal/kg/day. Total energy intake was significantly correlated with BIA for %BF calculation (r 0.75, p = 0.05) and less strongly correlated with ADP (r 0.61, p = 0.15). Median %BF by sum of four-site skinfolds, BIA and ADP was 22.0, 26.0 and 20.8, respectively. %BF by ADP was unbiased in comparison to skinfold anthropometry (mean difference 0, r 0.32), and somewhat negatively biased in comparison to BIA (mean difference -7.4%, r 0.50).

Conclusion: In this preliminary report (7 subjects enrolled out of 25 planned), %BF by ADP was, on average, unbiased but poorly correlated with four-site skinfold anthropometry and somewhat biased, but moderately correlated, with BIA measurements. Future work will include validation of ADP via deuterium dilution, and estimation of 95% limits of agreement. If the feasibility and accuracy of ADP for body composition analysis can be demonstrated in our full cohort, this technique holds promise as a measure of nutritional status in children with intestinal failure.

764 MALNUTRITION SYNDROME: INSUFFICIENT OR EXCESSIVE INTAKE OF KEY NUTRIENTS IN MEXICAN OBESE CHILDREN: ROLE OF INDUSTRIALIZED SUPPLEMENTED FOODS

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Aim: To assess the intake of vitamins and inorganic nutrients in obese children.

Subjects and Methods: This case-control study was conducted in 6 to 11 year-old children of an elementary school during 2014. Subjects were classified as obese (BMI >2 SD, n=99) or as normal weight (BMI -2 SD to +1 SD, n=104). The intake of 18 micronutrients was assessed with two, 24-hour, recall surveys and an intake frequency survey. The data were transformed into quantitative variables with software for Mexican foods (Nutrikcal[®]). The results were compared with the NAC reference values.

Results: Intake of cereals and industrialized foods was excessive and the intake of fruits, vegetables and legumes was insufficient in both study groups. Vitamins: Intake of thiamin, riboflavin, niacin, pyridoxine, cyanocobalamin and ascorbic acid was higher in obese children and was associated with the ingestion of processed supplemented foods. All these nutrients exceeded the upper reference value for Mexican children. Intake of vitamins A and E were below the reference level in both groups. Inorganic nutrients: Ingestion of Fe, Zn, Ca and P were higher in the obese children, but were below the lower reference in both groups. Na and Mg intake was greatly increased in both groups.

Conclusions: The high intake of vitamins and minerals, including sodium, was associated with the ingestion of supplemented industrialized foods and not with natural nutritional sources. Intake of key nutrients, such as vitamins A, E; Fe, Zn and Ca, was deficient in both study groups, reflecting an overall inadequate diet.

765 UTILIZING TELEHEALTH FOR DIETICIAN CONSULTATIONS REDUCES SCHEDULING WAIT TIMES AND INCREASES REFERRAL FULFILLMENT

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Rationale: Outpatient nurses and dietitians spend a considerable amount of time coordinating referrals for nutrition consultations when a dietitian is not available at the time of the physician visit. This often results in delayed consultation due to scheduling constraints, or a dietitian consulting the family through non-billable means, such as a telephone encounter. Nutritional assessment is recommended by professional organizations in conjunction with the medical treatment of many disorders, including food allergy,¹ celiac disease² and inflammatory bowel disease.³

Objective: To expand the current clinical care model using a pilot of telehealth encounters with a registered dietitian, in order to reduce wait times for nutrition consultation and increase rates of consultation fulfillment, while increasing dietitian productivity and charging capability.

Methods: We developed a pilot program to improve access for registered dietitian consultations utilizing telemedicine technology to perform real-time consultations for outpatients in a satellite gastroenterology clinic. Our short-term goal was to design a pilot telehealth program for dietitian consultations. Longer-term measurable outcomes will include wait times for appointments and rates of fulfillment of real-time nutrition telehealth consultations compared with the standard referral process.

Results: Using a Plan-Do-Study-Act (PDSA) approach, we developed a series of interventions aimed at improving the process of telemedicine consultations. PDSAs centered on provider education, workflow streamlining, patient identification and communication between care team providers. We have completed 5 telehealth dietitian visits to date, replacing the need for after-visit phone call with a dietitian and utilizing clinic time more efficiently.

Conclusions: Future work will focus on measuring timeliness of visits and ability to expand dietitian productivity using this model.

Telemedicine serves as a modality to enhance seamless interdisciplinary clinical care delivery and improve patient experience and value by improving outcomes in a limited resource environment.

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***766 EFFECT OF THE DIETARY DELIVERY MATRIX ON VITAMIN D3 BIOAVAILABILITY AND BONE MINERALIZATION IN VITAMIN D3-DEFICIENT GROWING MALE RATS**

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Introduction: Vitamin D (VitD) plays a critical role in bone mineralization during growth phases of infancy and childhood. Recent population studies report a high prevalence of VitD deficiency and insufficiency due to many factors, including avoidance of sun exposure. Supplemented foods provide alternative sources of VitD, and for young children, milk provides an ideal vehicle. In our study, we tested the impact of dietary delivery matrix on the bioavailability of VitD3 and bone mineralization. Young, growing rats were fed solid diets sufficient or deficient in VitD3 or deficient diets supplemented with milks containing VitD3. Two solid diets and three different milks were compared in separate trials. **Methods:** Trial 1: Young male rats (n=8) were fed standard AIN93G (with casein) plus VitD3 (Group 1) or minus VitD3 (Group 2). Groups 3 and 4 were fed AIN93G minus VitD3 and supplemented with VitD3 in goat skim milk (SM) or cow SM, respectively. A control (Group 5) was fed a VitD3 sufficient grain-based Teklad Rodent diet. Trial 2: Young male rats (n=10) were fed modified AIN93G (with egg albumin) plus VitD3 (Group 1) or minus VitD3 (Group 2). Groups 3 and 4 were fed modified AIN93G minus VitD3 and supplemented with VitD3 in goat whole milk (WM) or goat SM, respectively. Rats were fed the diets from 4 to 8 weeks of age, euthanized and bloods and bones collected for analysis.

Results: All groups gained weight over the study period. In both trials, Group 2 (VitD3 deficient) was the lightest and had low/undetectable levels of serum 25(OH)D3. In trial 1, levels of serum 25(OH)D3 in milk-fed groups were similar or lower compared to groups fed VitD3 in their solid diet. In trial 2, milk-fed groups had similar or higher levels of serum 25(OH)D3 compared to Group 1 fed VitD3 in the solid diet. Ratios of serum 25(OH)D3 to dietary VitD3 intake were higher in milk-fed groups in both trials. Bone mineral content (BMC) and bone mineral density (BMD) were higher in all milk-fed groups compared to Groups 1 and 2. Groups 1 and 2 tended to have similar BMC and BMD values, except Group 1 had higher values for the lumbar spine. These values for Groups 1 and 2 from trial 2 with egg albumin as a protein source were lower than in trial 1 with casein.

Conclusion: Serum levels of 25(OH)D3 suggested the bioavailability of VitD3 was similar when supplemented in solid food or milk, although, when adjusted for dietary intake, animals offered milk had the highest ratios of serum VitD3 metabolite to intake. Modified AIN93G with egg albumin produced the lowest bone mineralization results. Standard AIN93G with casein also resulted in lower bone mineralization compared with the grain-based diet, but the reduction was less pronounced than with egg albumin. The effects of VitD3 deficiency in both solid diets were reversed by offering milks fortified with VitD3.

Trial	Group	Diet	Liquid	Serum 25(OH)D3 (nmol/L)	BMC Right Femur	BMC Lumbar spine	BMD Right Femur	BMD Lumbar spine
1	1	Std [#] AIN93G + VitD3	Water	33.6 ^{ab}	0.249 ^a	0.306 ^a	0.175 ^a	0.174 ^a
	2	Std AIN93G - VitD3	Water	01.1 ^c	0.258 ^a	0.294 ^a	0.173 ^a	0.166 ^b
	3	Std AIN93G - VitD3	Goat SM [*] + VitD3	28.6 ^{ad}	0.275 ^b	0.334 ^b	0.186 ^b	0.186 ^c
	4	Std AIN93G - VitD3	Cow SM + VitD3	25.6 ^d	0.275 ^b	0.339 ^b	0.187 ^b	0.187 ^c
	5	Teklad Rodent + VitD3	Water	36.0 ^b	0.276 ^b	0.327 ^b	0.196 ^c	0.196 ^c
2	1	Modif [§] AIN93G + VitD3	Water	23.0 ^a	0.092 ^a	0.145 ^a	0.124 ^a	0.120 ^a
	2	Modif AIN93G - VitD3	Water	00.0 ^b	0.112 ^a	0.096 ^b	0.117 ^a	0.110 ^b
	3	Modif AIN93G - VitD3	Goat [¥] WM + VitD3	25.9 ^a	0.243 ^b	0.263 ^c	0.173 ^b	0.164 ^c
	4	Modif AIN93G - VitD3	Goat SM + VitD3	31.0 ^c	0.258 ^b	0.283 ^c	0.179 ^b	0.169 ^c

AIN93G with casein protein § AIN93G with egg albumin * Skim milk ¥ Whole milk

767 EXPERIENCE WITH THE USE OF 70% ETHANOL LOCKS (ETL) IN POLYURETHANE-BASED AND SILICONE-BASED CENTRAL VENOUS ACCESS DEVICES (CVAD) IN PATIENTS WITH LONG-TERM HOME PARENTERAL NUTRITION: ARE POLYURETHANE CVAD SAFE TO USE WITH ETL?

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Introduction: Issues with vascular access are the most common complication in patients with intestinal failure that are dependent on home parenteral nutrition (HPN). Prophylactic ETL are used to reduce Central Line-Associated Blood Stream Infections (CLABSI) in this group of patients. In general, polyurethane CVAD are preferred, due to their robustness. However, due to *in vitro* studies demonstrating a fragility of polyurethane CVAD after being exposed to ethanol, most centers use silicone CVAD in patients with ETL. This has proven to be very limiting for our center, as the only silicone peripherally-inserted central catheter (PICC) available was frequently having mechanical complications resulting in CVAD replacement, regardless of ETL use. As of May 2011, fearing an increase in CLABSI rates due to frequent breakage, our infectious control department recommended to stop using these catheters and revert to the polyurethane PICC.

Aim: The purpose of this study was to compare the CLABSI and mechanical complication rates of silicone and polyurethane CVAD in our HPN population using ETL.

Method: We did a retrospective chart review of our HPN patients between May 2011 and May 2015 to identify all the CVADs that had received ETL during this period. We compared incidence rates of CLABSI and complications (breakage, replacement and use of tissue plasminogen activator) between silicone and polyurethane CVAD. Statistical analysis was performed with STAT 12.0.

Results: In our study, 7 patients on HPN received ETL between May 2011 and May 2015. A total of 3147 catheter days were analyzed from 29 CVADs. The reason for intestinal failure were short bowel syndrome (n=4), feeding intolerance NYD (n=2) and functional short gut (n=1). The mean age at the start of the study was 3.14 years \pm 1.7. We found that the mean number of CLABSI per 1000 catheter days was similar in both types of catheters: 2.4 per 1000 catheter days in silicone and 3.3 per 1000 catheter days in polyurethane CVAD (95% CI, -0.01 to 0.01). The rate of breakage was 4.9 per 1000 catheter days in silicone and 6.7 per 1000 catheter days in polyurethane CVAD (95% CI, -0.01 to 0.01). There was an increase in the complications and replacement rate in the polyurethane group, without reaching statistical significance.

Conclusion: In our population at the Montreal Children's hospital, we found that the use of polyurethane CVAD was linked to a similar incidence of CLABSI, without significantly increasing the number of complications and replacement. The use of polyurethane CVAD can be a safe alternative for the HPN population using ETL.

768 EFFECT OF CYPROHEPTADINE ON GROWTH VELOCITY IN CHILDREN WITH SILVER-RUSSELL SYNDROME

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Introduction: Russell-Silver syndrome (RSS) is characterized by at least 4 of the following criteria: intrauterine growth restriction or failure to thrive below -2 SDS, relative macrocephaly, hemi-body asymmetry, feeding difficulties, body mass index (BMI) below -2 SDS, or prominent forehead. Nutritional care is crucial during the first years of life before initiation of growth hormone (GH) treatment, because patients with RSS are often malnourished and risk hypoglycemia, sometimes requiring enteral nutrition. Cyproheptadine (CYP) was previously described for its orexigenic effect in diseases such as cystic fibrosis or AIDS, but its effect in RSS patients has not been studied. Our study aimed to evaluate the effect of CYP on weight and height evolution of RSS patients.

Methods: Anthropometric parameters (weight [W], height [H], W/expected W for H [W/H] and BMI) of 34 children with RSS were recorded at baseline (M0-CYP) and at 3, 6, 9 and 12 months (M3 to M12-CYP) after CYP beginning. We described 2 groups: group 1 included children treated with CYP only (n=23) and group 2, children treated by CYP in addition to previously introduced enteral nutrition (EN) and/or GH (n=11).

Results: At M0-CYP, median parameters of RSS children were as follows: age of 2.0 years, weight of 7.5 kg (-4.7 SDS), height of 75.6 cm (-3.2 SDS), W/H of 77.3 \pm 8.3% and BMI Z-score of -2.8 \pm 1.4 SDS. At T0, in group 1, children were significantly shorter and thinner when compared to group 2 (weight: -5.72 \pm 1.5 SDS vs. -3.55 \pm 2.0 SDS, $p=0.015$; height: -3.6 \pm 1.2 SDS vs. -2.86 \pm 1.0 SDS, $p=0.034$), with a marked weight stagnation during the months preceding CYP initiation. Weight and height were significantly different from M0-CYP to all other times (M3 to M12-CYP) and this without significant differences between groups 1 and 2. After one year of treatment, overall size and weight gains were significant (weight: +1.06 SDS, $p<0.0001$; height: +0.31 SDS, $p=0.027$) as soon as after 3 months of treatment. At M3, significant improvement of W/H and BMI were also noticed (group 1: W/H 74.9% vs. 79.3%, $p=0.016$; BMI Z-score: -3.4 vs. -2.4 SDS, $p=0.006$; group 2: W/H 79.3% vs. 88.9%, $p=0.032$). 58.1% of the patients were classified as responders or partial responders to CYP, defined as weight gain of at least 1 SDS over the evaluation period. When compared to non-responders, responders were significantly thinner (weight: -5.63 \pm 1.3 SDS vs. -3.55 \pm 2.1 SDS, $p=0.019$) and younger (1.9 \pm 2.3 years vs. 2.5 \pm 2.3 years, $p=0.04$) and gained +1.5 SDS of weight over the one-year period. EN had no influence on CYP effect.

Conclusion: In our cohort, CYP was effective in approximately 60% of RSS patients and associated with significant improvement of growth velocity and nutritional status before GH treatment. Our results suggest that CYP can be used for nutritional management of children with RSS. Further studies are necessary to confirm these results, especially with a double-blind, controlled design.

769 COMPARATIVE TOLERANCE, EFFICACY AND SAFETY EVALUATION OF DIFFERENT INTRAVENOUS LIPID EMULSIONS IN LONG-TERM PARENTERAL NUTRITION OF CHILDREN WITH PRIMARY INTESTINAL FAILURE

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Introduction: Intravenous lipid emulsions (ILEs) are an essential component of parenteral nutrition (PN) regimens, representing a major source of energy and essential fatty acids (EFAs). Different generations of lipid formulations have been used in clinical practice to improve safety, tolerance and efficacy outcomes. In addition, Intestinal Failure-Associated Liver Disease (IFALD), a major complication in children on PN, is usually linked with intravenous lipid intake.

Objectives: To evaluate tolerance, efficacy and safety of different generations of ILEs in three different groups of patients on long-term PN seen in the last 15 years for primary IF. The follow-up period for each group was approximately 5 years.

Method: Children on long-term PN (>6 months), who had been attending the Reference Center for Paediatrics Artificial Nutrition of University "Federico II" of Naples since January 2000 to January 2016, were retrospectively enrolled according to very strict inclusion criteria. Our sample (n=14) was distributed in three groups and each received a different ILE: Intralipid[®], Clinoleic[®] or SMOFlipid[®]. Safety, tolerance and efficacy parameters were recorded and analyzed during the examination period for each group, which lasted approximately 5 years. The following parameters, expressed as SD-scores, were collected: serum triglycerides (TG) concentration, International Normalized Ratio (INR) for coagulation, platelet (PLT) count, serum liver enzymes and total bilirubin (TB).

Results: Fourteen children, who met the inclusion criteria, were distributed in three groups. The first group (n=5, 4 males, age 160.2 \pm 23.82 months) received a soybean-based formula, Intralipid[®], for a period of 36 \pm 33.94 months. The second group (n=6, 4 males age 133 \pm 68.66 months) received an olive oil-based formula, Clinoleic[®], for 40.8 \pm 18 months. The third group (n=10, 8 males, age 88.44 \pm 50.9 months) received SMOFlipid[®], a lipid emulsion containing a physical mixture of soybean oil, MCT, olive oil and fish oil and is enriched in vitamin E. Safety and tolerance outcomes, TG serum levels, INR and platelet counts remained normal over time in all children. We observed a progressive decrease in TG levels, but it was not statically significant, probably due to the small number of patients. Efficacy outcomes, TB serum levels, GT and ALT significantly decreased from the first to the third group ($p<0.05$).

Conclusions: Over the past 15 years, thanks to the continuous innovation in the ILE field, the management of PN has been improved, leading to successful results in growth and decreasing incidence of ILE-related side effects, IFALD firstly. An optimal PN, with the absence of liver complications, can significantly improve the growth of children with IF.

770 MATERNAL VITAMIN D SUPPLEMENTATION AMONG LACTATING MOTHERS IN THE PREVENTION OF VITAMIN D DEFICIENCY AMONG BREASTFED TERM INFANTS: A META ANALYSIS

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Background: Exclusively breastfed infants, pregnant and lactating mothers have been identified as a population in need of special requirements of vitamin D. While breast milk is a nutritionally complete food, studies reporting that it is low in vitamin D may place exclusively breastfed infants at risk for vitamin D deficiency.

Objective: To determine the optimal dose of maternal vitamin D supplementation in lactating mothers to achieve maternal vitamin D adequacy and to prevent vitamin D deficiency in fully breastfed term infants.

Methodology: An electronic search of literature to identify all prospective, randomized, controlled trials that evaluated the vitamin D level of exclusively breastfed infants supplemented through their mothers via milk transfer published in PubMed, Cochrane Collaboration, Science Direct and Google Scholar from 1999 to 2014 was done.

Data Analysis: Review Manager version 5.3 was utilized to determine the risk ratio for dichotomous data and weighted mean differences for continuous data. Heterogeneity and overall effect were analyzed. The corresponding 95% CI for both outcomes was determined.

Results: Three studies were included, in which a total of 170 participants were enrolled, but only 83 were included in the results. They were supplemented with vitamin D as follows: 12 participants with 2000 IU/day vs. 13 participants with 4000 IU/day for 3 months (Basile *et al.*, 2006), 9 participants with 2000 IU/day vs. 9 participants with ,000 IU/day for 3 months (Hollis and Wagner 2004) and 20 participants with 150,000 IU once vs. 20 participants with 5000 IU/day for 28 days (Oberhelman *et al.*, 2013). The three studies' results favored supplementation with 2000 IU of vitamin D and a 150,000 IU of vitamin D one-time supplementation for better improvement of the vitamin levels in the maternal blood. The overall effect of the 2000 IU and 150,000 IU supplementation was statistically significant at 0.0003. The meta-analysis performed on the infant levels of vitamin D after maternal supplementation showed that the two dosages did not have any significant differences (computed overall effect 0.071). The p-value for heterogeneity was above 0.045, indicating the studies were statistically similar.

Conclusion: A maternal vitamin D supplementation of 2000 IU and a single dose of 150,000 IU can improve maternal vitamin D levels. These doses had an effect on infant vitamin D level; however, this failed to demonstrate a significant difference to favor of one dose over another. Supplementing infants with vitamin D via milk transfer shows potential, but further studies in the form of randomized, controlled trials are required to determine the optimal doses of vitamin D supplementation during lactation for maintaining vitamin D adequacy in breastfed infants.

771 IRON DEFICIENCY IN HEALTHY 18-MONTH-OLD DANISH CHILDREN: PREVALENCE AND ASSOCIATED FACTORS: A SUBPROJECT IN THE ODENSE CHILD COHORT

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Background: Iron deficiency (ID), defined by plasma-ferritin <12 µg/L, is associated with delayed cognitive development, as well as an increased propensity for infections and failure-to-thrive. The aim of this study was to determine the prevalence of ID and to describe associated factors with ID in a population of healthy Danish 18-month-olds.

Materials and Methods: Blood samples and anthropometric measurements were obtained from 1150 18-month-old children in the Odense Child Cohort (OCC), a birth cohort of 2549 children. Plasma-ferritin and CRP were analyzed in 449 randomly selected samples. We excluded 79 children because of chronic disease, acute infection within 7 days, CRP level >10 mg/L, twin birth, or prematurity, leaving 370 children as the study population. Parents provided questionnaire data on the childrens' current diet and intake of oral iron supplements and breastfeeding in infancy. The associations with ID were analyzed with a logistic regression model adjusting for maternal educational level, gestational age, growth in weight and length and exact age at blood sampling.

Results: The prevalence of ID was 15.1% (56/370, Wilson CI, 11.8% to 19.1%). Gender, gestational age, birth weight and length, age at blood sampling, maternal smoking and ethnicity did not differ between children with or without ID. Mothers of children with ID were more often educated at the high school level plus at least 4 years of education (44.8%) than mothers of children without ID (20.5%). However, this high level of education was no longer significantly associated to ID when it was adjusted in the logistic regression model (OR 1.77 [0.44 to 7.17]). No intake of oral iron supplements from 6 - 12 months was associated with an increased risk of ID compared to intake of oral iron supplements (OR 4.63, 95% CI, 1.12 to 19.05). Exclusive breastfeeding beyond 4 months was also associated with increased risk of ID (OR 7.55, 95% CI, 1.54 to 37.08). Duration of partial breastfeeding and current intake of unmodified cow's milk, fish and meat were not significantly associated with ID.

Discussion: We lack quantitative data on intake of iron-fortified formula, which was recommended interchangeably (>400 mL/day) with oral iron supplements in Denmark. Thus, the association between no iron supplements and ID may be even stronger than reported. In conclusion, the prevalence of ID was 15.1% in this cohort of healthy Danish 18-month-old children. ID was associated with no intake of oral iron supplements at the age of 6 - 12 months and exclusive breastfeeding beyond 4 months, but it was not significantly associated to current diet. Further analyses will be done to confirm these preliminary results and to explore the association between exclusive breastfeeding beyond 4 months and ID, considering the many benefits of exclusive breastfeeding for 6 months as recommended by the WHO.

Table 1. Basic characteristics of the 370 participants

Characteristics	Non-ID (n=314) Number (percent)	ID (n=56) Number (percent)
Sex		
Male	168 (50)	34 (58.6)
female	146 (43.5)	22 (37.9)
Birthweight		
≤2999 g	32 (9.5)	7 (12.1)
3000 - 3999 g	221 (65.8)	37 (63.8)
≥4000 g	58 (17.3)	10 (17.2)
Missing	3 (0.9)	2 (3.4)
Birth length		
≤50 cm	62 (18.5)	11 (19)
51 - 54 cm	200 (59.5)	38 (65.5)
≥55 cm	43 (12.8)	5 (8.6)
Missing	9 (2.7)	2 (3.4)
Gestational age		
37 - 39 weeks	125 (37.2)	24 (41.4)
40 - 42 weeks	189 (56.3)	31 (53.4)
Missing	0 (0)	1 (1.7)
Maternal smoking		
No	298 (88.7)	51 (87.9)
Yes	13 (3.9)	3 (5.2)
Missing	3 (0.9)	2 (3.4)
Maternal education		
Lower. High school or less	61 (18.2)	12 (20.7)
Intermediate. HS + 1 - 3 years	93 (27.7)	8 (13.8)
Higher. HS + 4 years or more	69 (20.5)	26 (44.8)
Missing	91 (27.1)	10 (17.2)
Maternal ethnic background		
Danish	298 (88.7)	50 (86.2)
Western	9 (2.7)	4 (6.9)
Non-Western	7 (2.1)	2 (3.4)
Missing	0 (0)	0 (0)
Age at blood sample and questionnaire		
17 - 19 months	122 (36.3)	22 (37.9)
20 - 23 months	154 (45.8)	27 (46.6)
Missing	38 (11.3)	7 (12.1)

772 VITAMIN E DEFICIENCY IN CHILDREN WITH CYSTIC FIBROSIS AND CHOLESTATIC LIVER DISEASES

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Introduction: Vitamin E is an important fat-soluble vitamin that acts as an antioxidant and also plays an essential role in stabilization of cell membranes. Thus, its deficiency results not only in hemolytic anemia, but also different neurological presentations. Vitamin E deficiency occurs in a variety of conditions causing fat malabsorption. Cholestatic liver disease and cystic fibrosis (CF) are two of them that result in vitamin E deficiency, but neurological manifestations are not commonly reported in these groups of children. The aim of this study was to observe the various neurological presentations of vitamin E deficiency among children with cystic fibrosis and hepatobiliary diseases and their response to vitamin E therapy.

Methods: This was a retrospective study conducted at The Gastroenterology Department of the King Khalid University Hospital, Riyadh, KSA. Children known to have cystic fibrosis or cholestatic liver disease, and found to have any neurological manifestation on follow-up over a period of 5 years, were enrolled in this study. Those included were less than 10 years old and diagnosis of cystic fibrosis and hepatobiliary diseases was based on clinical and laboratory findings along with radiology and histopathology evidence. Vitamin E levels were done for all patients followed by vitamin E supplementation to observe response.

Results: Ten cases, 6 with CF and 4 with hepatobiliary diseases, were seen with various neurological manifestations. Vitamin E levels were profoundly low, less than 1 micromole per mL in all of these patients. Overall, there were 7 males and 3 females with a mean age of 3.5 years

(range 1 - 5 years). Eighty percent had delayed motor milestones and generalized muscle weakness and 30% of those older than 2 years presented with excessive fatigue, difficulty in climbing stairs and difficulty in getting up with proximal myopathy. Two patients presented each with gaze apraxia, vertical paralysis, ophthalmoplegia, abnormal coordination, abnormal touch and vibration sensation and ataxic gait. One patient presented with dysarthria, hyporeflexia and hyperreflexia. All patients responded very well when put on parenteral vitamin E with total resolution of symptoms and normal levels at the 3- to 6-month follow-up.

Conclusion: Neurological manifestations due to vitamin E deficiency are common in children with CF and cholestatic liver diseases. Mode of presentation is diverse, ranging from spinocerebellar ataxia and myopathy to neuropathies and blindness. Early diagnosis and prompt treatment can make a difference in outcome in these patients.

773 VARIATIONS IN BODY COMPOSITION INDICES AND ANTHROPOMETRIC PARAMETERS OF HOSPITALIZED NICU INFANTS
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Background: In addition to weight gain, optimal fat and lean body mass are important predictors of long-term outcomes across the lifespan of neonates. Body composition may be altered in response to enteral and/or parenteral nutritional (PN) manipulations and metabolic factors. Newer and innovative methods like Air Displacement Plethysmography (ADP) are now available for safe and reliable measurement of body composition. Measuring body composition indices can help in the assessment of nutritional status and may provide further guidance to individualize nutritional therapy.

Aims: 1) To describe patterns of body composition change in non-syndromic, non-surgical, clinically-stable neonates in the Neonatal Intensive Care Unit (NICU) across maturation; 2) to identify an ideal time interval between consecutive body composition measurements by ADP that can detect a significant change; 3) to examine correlation between change in proportion of body fat (%BF) and change in anthropometric measurements; 4) to examine the effect of PN on %BF.

Methods: Hospitalized NICU infants underwent body composition measurements by air displacement plethysmography (ADP) via PEAPOD® at 37.5 ± 0.7 weeks (Time-1) and 41.0 ± 0.7 weeks (Time-2) corrected gestational age. Concurrent anthropometric measurements (skinfold thickness, abdominal girth, mid-arm circumference, cm) were obtained. Nutritional data (PN frequency) were recorded from chart review. Data were analyzed using paired t-tests and linear regression models, presented as mean ± SEM, median (IQR), or %.

RESULTS: 22 neonates (54% males, 32.2 ± 0.9 weeks gestation) were evaluated at Time 1 corresponding to 37.5 ± 0.7 weeks post-menstrual age (PMA) and Time 2 at 41.0 ± 0.7 PMA with median interval of 3.6 (2.9-4.0) weeks between studies. Maturation effect on body composition parameters and anthropometric measures are shown which demonstrates that weight and %BF increased significantly; % fat free mass (FFM) decreased significantly (Table 1). There was no significant difference between mean weight and mean % BF between study subjects and normal references. No relationships between change in %BF and change in anthropometric measures were observed (P >0.05). % BF of neonates who received PN was 10.6 ± 1.9 at increase at Time-1 vs. 11.9 ± 1.5 at Time-2 (P=0.4). %BF of neonates who did not receive PN was 11.7 ± 2.2 at Time-1 vs. 15.9 ± 2.4 at Time-2 (P=0.07).

Conclusion: An interval of 3.6 weeks between measurements can detect significant changes in weight, %BF and %FFM by ADP and anthropometric measures. There was no correlation between ADP and anthropometric measurements. Current nutritional practices in the NICU are adequate for catch-up growth. There was no significant difference between body composition parameters among patients on PN versus those who did not receive PN. This study provides a basis for further research related to factors responsible for variable body composition of NICU infants.

CHARACTERISTIC	TIME 1 (T1)	TIME 2 (T2)	P-VALUE
Weight, kg	2.5 (2.0-3.5)	3.2 (2.9-4.2)	<0.01
% Body Fat	11.8 ± 1.4	14.6 ± 1.2	<0.01
% Fat Free Mass	88.2 ± 1.4	85.5 ± 1.2	<0.01
Triceps Skinfold thickness, cm	4.7 (4 – 5.6)	6 (5.2 – 7.3)	<0.01
Biceps Skinfold thickness, cm	4 (3.4 – 4.5)	4.8 (4 – 5.5)	0.045
Sub-scapular Skinfold thickness, cm	4 (3.6 – 5.2)	5.4 (4.6 – 6.4)	<0.01
Supra-iliac Skinfold thickness, cm	3.1 (2.6 – 3.7)	4 (3.5 – 5)	<0.01
Abdominal Girth, cm	31.1 ± 0.8	34 ± 0.8	<0.01
Mid-arm circumference, cm	10 (9.6 – 12)	9 (8.5 – 10.5)	<0.01

774 DAILY ETHANOL LOCK THERAPY REDUCES CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS IN HIGH-RISK HOME PARENTERAL NUTRITION PATIENTS

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Background: Ethanol locks therapy (ELT) is widely used to prevent central line-associated bloodstream infections (CLABSI) in home parenteral nutrition (HPN) patients. Some authors report association between ELT and central venous catheter (CVC) integrity compromise. Anecdotal evidence suggests that a subset of HPN patients continue with persistently high CLABSI rates despite using ELT and other CLABSI prevention strategies.

Objective: To evaluate the effect of an increased intensity ELT regimen on CLABSI and CVC fracture rates for high-risk HPN patients.

Design: Prospective, case-control, open-label, quality improvement project.

Setting: Multi-disciplinary HPN program.

Patients: Cases were 15 high-risk HPN patients (CLABSI rate >4 times program average). Controls were 215 standard-risk HPN patients (CLABSI rate <4 times program average, which is 1.9 per 1000 line-days). Eligible patients for ELT had history of at least 1 CLABSI, age ≥ 6 months and silicone (not polyurethane) CVC. Intervention: ELT (dwell of 70% ethanol ≥ 4 h, withdrawing using 10 mL syringe) frequency increased from 3 to 7 days per week.

Measurement: CLABSI and CVC fracture rates compared pre- and post-intervention periods (March 2014 - February 2015 vs. March 2015 - February 2016). Data presented as N (%) or median (IQR).

Results: HPN patients treated with daily ELT had a significant reduction in CLABSI prevalence (5.2 to 2.7 per 1000 line-days) compared with the control group (1.5 to 1.9 per 1000 line-days), representing 57% (-80% to -4%) reduction relative to control (p 0.04). For CVC fracture prevalence, for the daily ELT group (13.8 to 6.4 per 1000 line-days) compared with the control group (1.9 to 0.8 per 1000 line-days), there was no differential effect of intervention (p 0.87). Both groups experienced 56% (-74% to -26%) reductions between pre- and post-intervention periods.

Limitations: There are numerous factors affecting CVC care in community. HPN program efforts to reduce CVC fractures may have impacted outcomes.

Conclusions: For high-risk HPN patients, daily ELT was associated with a significant reduction in CLABSI rates without increased fracture rate when compared with standard ELT protocol.

775 DO PEDIATRIC GASTROENTEROLOGISTS ACKNOWLEDGE AND ADDRESS OBESITY AT OUTPATIENT VISITS?

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Background: Childhood obesity is a major health issue in the U.S. Many consider obesity management a component of pediatric gastroenterology practice; however, it is unknown how often obesity is actually acknowledged and addressed at pediatric gastroenterology outpatient visits.

Aim: To assess how often obesity is acknowledged and addressed at pediatric gastroenterology outpatient visits and to determine factors associated with obesity being recognized.

Methods: A retrospective chart review of electronic medical records identified 132 obese children (BMI $\geq 95^{\text{th}}$ percentile for age and sex), aged 3 - 20 years, seen as new visits by a pediatric gastroenterology practice over a 1-year period of time. Data recorded included demographics, obesity comorbidities, reason for referral, whether diagnosis of obesity was given at the visit and whether a plan to address obesity was given. Chi-squared or Fischer's exact tests were used, as appropriate, to examine statistical associations between the factors examined.

Results: Only 49% of obese children were given a diagnosis of obesity at their visit; in 58% of children, being overweight or obese was acknowledged in their assessment. Moreover, only 52% of children were given a plan to address reducing their BMI. A diagnosis of obesity was more likely to be given in younger children (3 - 5 years: 100% diagnosed, 6 - 8 years: 50% diagnosed, 9 - 11 years: 74% diagnosed, 11 - 15 years: 47% diagnosed, 16 - 20 years: 33% diagnosed, $p=0.02$) and in males (females: 38% diagnosed vs. males: 58% diagnosed, $p=0.02$), but was not affected by ethnicity or race. Those with severe obesity (BMI $\geq 99^{\text{th}}$ percentile) were not more likely to be given a diagnosis of obesity. A diagnosis of obesity was more likely to be given in those with obesity related comorbidities, such as non-alcoholic fatty liver disease (those with comorbidities: 75% diagnosed vs. those without comorbidities: 40% diagnosed, $p=0.0004$) and also if the patient was referred for obesity or an obesity correlated morbidity as opposed to other referrals, such as abdominal pain (referred for obesity or comorbidity: 79% diagnosed vs. other reason for referral: 38% diagnosed, p 0.01). Giving a diagnosis of obesity was highly provider-specific among the 12 providers in the practice (p 0.0005). Importantly, those given a diagnosis of obesity were more likely to receive a plan to reduce their BMI at the clinic visit (74% vs. 22%, $p<0.0001$).

Conclusions: Pediatric gastroenterology outpatient visits offer an opportunity to acknowledge and address childhood obesity by specialists; however, obesity is diagnosed in only about 50% of obese children seen, with an increasing likelihood of diagnosis in younger children and in those with obesity correlated morbidities. Further investigation into barriers against addressing obesity at pediatric gastroenterology outpatient visits and education of providers is needed in order to prevent missing an opportunity to address, and potentially decrease, childhood obesity.

776 CORRELATION BETWEEN WAIST CIRCUMFERENCE, BODY MASS INDEX AND HEIGHT FOR AGE IN SCHOOLCHILDREN AND ADOLESCENTS IN CALI, COLOMBIA

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Introduction: The anthropometric nutritional state of children can be objectively obtained with the determinations of weight (W), height (H) and waist circumference (WC).

Objective: To determine the correlation between WC, body mass index (BMI) and height for age (H/A) according to the World Health Organization (WHO), in children aged 8 - 18.

Methods: This prevalence study included schoolchildren ($n=252$) and adolescents ($n=365$) from a public school in Cali, Colombia.

Sociodemographic (age, gender), familial (only child, first-born, marital state of parents) and clinical (W, H, WC) variables were obtained. BMI and H/A were calculated according to the WHO. Univariate and bivariate analyses were performed and the R Pearson to identify the correlation. Results: 617 children (aged 12.9 ± 2.7 years, 51.4% male) were analyzed, with an average W, H and WC of 49.4 ± 15.0 kg, 154.6 ± 14.6 cm and 70.0 ± 9.7 cm, respectively. 27.9% presented with overweight and obesity, 3.2% with a low H/A. There was a higher chance of an increased BMI in schoolchildren (OR 1.94, 95% CI, 1.34 - 2.79, p 0.0002) and children who were an only child (OR 1.75, 95% CI, 0.99 - 3.06, p 0.0345). The correlation between WC and BMI was positive and statistically significant (R^2 0.4236, p 0.0000), especially in overweight and obese (R^2 0.2750, p 0.0000) and eutrophic (R^2 0.1805, p 0.0000) children. Correlation between WC and H/A was positive and statistically significant as well (R^2 0.0336, p 0.0000), especially in eutrophic children (R^2 0.0382, p 0.0000).

Conclusion: In this group of schoolchildren and adolescents, WC was, despite a weak correlation with the BMI and H/A, statistically significant and should be considered in all pediatric anthropometric nutritional assessments.

777 ANTHROPOMETRIC NUTRITIONAL STATUS IN ECUADORIAN INFANTS AND TODDLERS AND POSSIBLE ASSOCIATIONS

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Introduction: There is not much literature on the prevalence of malnutrition (overweight, obesity, malnutrition and altered height) in Ecuadorian infants and toddlers.

Objective: To determine, through body mass index (BMI) and height for age (H/A) according to World Health Organization (WHO), anthropometric nutritional status of healthy infants and toddlers in Quito, Ecuador during 2016 and possible risk factors.

Methods: Prevalence study in infants and toddlers. Sociodemographic data (age, gender), weight (kg) and height (cm) were included. Data were analyzed in Anthro and Anthroplus WHO, being classified by BMI in obesity, overweight, overweight risk, severe malnutrition, malnutrition and eutrophic and according to H/A in tall, low, severe low height and eutrophic.

Results: We acquired data from 229 subjects, with a mean (SD) age of 24.5 (17.2) months, 52.0% were male, mean (SD) weight was 11.0 (3.9) kg and mean (SD) height was 80.9 (15.0) cm. The prevalence of malnutrition was 36.2% and 21.8% had an altered height. There was a predominance of low height in females (OR 2.09, 95% CI, 1.04 - 4.31, p 0.0247), which was a possible risk factor for low height (OR 2.18, 95% CI, 1.13 - 4.23, p 0.020).

Conclusion: Nutritional status alteration was found in Ecuadorian infants and toddlers according to BMI: 11.0% were overweight or obese, 16.6% were at risk for overweight and 4.4% had malnutrition. According to H/A, 18.9% had low height and being female was a predominant and possible risk factor for low height.

778 INSULIN RESISTANCE AND VITAMIN D IN OBESE MEXICAN SCHOOL-AGED CHILDREN

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Introduction: Recent studies suggest that vitamin D plays an important role in insulin sensitivity and have described that obese children are likely to have low 25-hydroxyvitamin-D (25OHD) levels. In Mexico, around 35% of school-aged children are overweight or obese.

Aim: To determine the association between insulin resistance and serum levels of vitamin D in Mexican obese children.

Methods: Cross-sectional design that included 96 randomly (6 - 8 years) obese (z -score $>+2$ SD of BMI/age) in whom we analyzed serum levels of 25OHD, measured by means of the competitive enzyme-linked immunosorbent assay, and insulin resistance was estimated from fasting plasma measurements using the HOMA-IR. The statistical analysis included means and SD, as well as Pearson correlation and significance was set at a p -value of <0.05 .

Results: The mean serum level of vitamin D was 27.25 ng/mL, of which 56.3% of subjects presented with vitamin D insufficiency (20 - 29 ng/mL), 25% were deficient (<20 ng/mL) and only 18.8% were sufficient (>29 ng/mL). The mean HOMA-IR was 2.43, of which 72.9% had insulin resistance. No significant correlation was identified between vitamin D and HOMA-IR (r -0.29, $p=0.89$). When comparing girls with boys, we found that the levels of insulin were significant higher in girls (11.4 ± 8.0 μ UI/mL) than boys (9.2 ± 5.6 μ UI/mL) (p 0.09) and the levels of vitamin D were significant lower in girls (25.7 ± 8.0 ng/mL) than boys (25.7 ± 8.0 ng/mL) (p 0.03). No differences were found in glucose and insulin between genders.

Conclusion: A significantly high percent of school-aged obese children did not had the optimal values of vitamin D and had insulin resistance; however, no correlation was found between HOMA-IR and vitamin D levels in obese Mexican children. When comparing girls to boys, the girls had significantly higher levels of insulin and lower levels of vitamin D.

Table 1. Biochemical variables in obese girls and boys

Variables	Girls (n=45)	Boys (n=51)	p
Glucose (mg/dl)	96.4 \pm 5.6	94.2 \pm 7.36	0.32
Insulin (μ UI/mL)	9.2 \pm 5.6	11.4 \pm 8.0	0.09
HOMA-IR	2.2 \pm 1.4	2.7 \pm 1.9	0.16
25OHD (ng/mL)	25.7 \pm 8.0	28.6 \pm 17.3	0.03

779 GASTRIC RESIDUALS AND TIME TO REACH FULL FEEDINGS IN EXTREMELY PRE-TERM INFANTS

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Background: There is little consensus on the definition, management and overall significance of gastric residual volumes (GRV) in tube-fed, extremely pre-term (EP) infants. Many institutions assess GRV prior to feeds, yet there is little evidence to support decisions to discard/refeed GRVs, or withhold feedings, in the presence of a normal abdominal exam. Indeed, a recent survey of clinicians indicated wide variability in their management of GRVs.

Objective: We hypothesized that the time to reach full tube-feedings is not associated with the presence of GRVs in EP infants.

Design/Methods: We conducted a retrospective review of EP infants (birth weight <1000 g) consecutively admitted to our two NICUs who were 23 to 30 weeks' gestation inborn or transferred within 24 hrs of birth. Data were collected on the number, volume and quality (green, blood-tinged, or milky) of GRVs from birth to the time of full tube-feeding (no further intravenous nutrition). Data were analyzed by univariate and multivariable regression analysis.

Results: We evaluated 76 infants (birth weight 789 ± 118 g, gestational age 26 ± 1.8 weeks, mean \pm SD) who began feeding on day 4 ± 3 and achieved full tube feedings on day 21 ± 12 . GRVs were present in 76% of infants, large GRVs (50% of 3 h feeding and 30% of 3 h feeding) were present in 62% and 68%, green GRV in 47%, GRV 2 mL/kg in 63%, blood-tinged GRV in 18%, and milky GRV in 74%, respectively. Feedings were withheld in 55% of infants. The time to full feeding correlated inversely with gestational age (r -0.48 and $p<0.001$) and birth

weight ($r -0.37, p < 0.001$) and positively with the number of feedings withheld each day ($r 0.50, p < 0.001$). There were no relationships between the time to full feedings and daily number of GRVs, or the presence of bilious, bloody, or milky residuals by univariate analyses. When gestational age was included in the multivariable model, relationships between time to full feedings and number of large GRV/day were significant ($R^2 27\%, p < 0.001$), but the number of any GRV, green, blood-tinged, or milky GRVs were not significant. The number of feedings withheld directly correlated with the presence of GRVs: any ($r 0.32, p 0.006$), large ($r 0.36, p 0.001$), green ($r 0.25, p 0.03$) and milky ($r 0.30, p 0.01$).

Conclusions: We found a wide variability in time to full feedings in tube-fed EP infants, which was minimally explained by GRV as a measure of feeding tolerance. The types of GRV did not affect the time to full feedings but did relate to feedings being withheld. Further investigation on how clinicians manage GR, and reasons for withholding specific feedings, is warranted. These data support the need for education on management of feeding tolerance in EP infants.

780 ASSOCIATION BETWEEN ALTERATIONS IN THE GUT MICROBIOTA AND FOOD SENSITIZATION IN THE EARLY LIFE OF CHILDREN

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Background: We hypothesized that food sensitization (FS) in children could be linked to specific gut microbiota. The purpose of the present study was to identify differences in the intestinal microbiota between healthy children and children with FS. We attempted to identify specific microbiota signatures of FS and their relationships with clinical measures using feces as a proxy for the intestinal microbiota and targeting the 16S rRNA gene.

Methods: A case-control study of 23 children with FS and 22 healthy children was performed. These 45 younger children (age from 6 months to 24 months of age) had undergone complete screening of the fecal microbiota and determination of serum total IgE and specific IgE levels. Individual microbial diversity and composition were analyzed via parallel barcoded 454 pyrosequencing targeting the 16S rRNA gene hypervariable V3-V5 regions.

Results: A comparison of the taxonomic data revealed that the children with FS exhibited relatively high abundances of *Firmicutes*, *Actinobacteria* and *Proteobacteria* at the phylum level and a relative under-representation of the phylum *Bacteroidetes*. At the order level, the relative abundance of *Bacteroidales* ($p < 0.01$) was lower in the children with FS compared with the healthy controls. In contrast, the relative abundance of *Clostridiales* ($p < 0.01$), belonging to the phylum *Firmicutes*, was higher in the children with FS. At the genus level, we observed significant increases in the numbers of *Sphingomonas*, *Sutterella*, *Bifidobacterium*, *Collinsella*, *Clostridium sensu stricto*, *Clostridium IV*, *Enterococcus*, *Lactobacillus*, *Roseburia*, *Faecalibacterium*, *Ruminococcus*, *Subdoligranulum* and *Akkermansia* in the FS group. We also found significant decreases in the numbers of *Bacteroides*, *Parabacteroides*, *Prevotella*, *Alistipes*, *Streptococcus* and *Veillonella* in this group. Using the linear discriminant analysis (LDA), coupled with effect size measurements method, we found that *Clostridium* and *Subdoligranulum* sequences were significantly enriched in the children with FS, and sequences from other taxa were enriched in the healthy controls, such as *Bacteroides* and *Veillonella*, which could be used to identify FS.

Conclusions and Discussion: Our results showed that food sensitization is associated with compositional changes in the gut microbiota and the results support the hypothesis that microbial dysbiosis is associated with an increased risk of allergic disorders. These findings could be useful for developing strategies (e.g., consumption of human milk glycan, inulin and fructooligosaccharides, insoluble complex carbohydrates and protein-rich diets to enhance the growth of *Bacteroides*) to modify the gut microbiota, or medical applications (e.g., probiotics or healthy microbe preparations) involving beneficial microorganisms to control the development of FS and atopic disorders.

781 THE EFFECTIVENESS OF THE IDENTIFICATION AND MANAGEMENT OF FEEDING DIFFICULTIES FOR CHILDREN (IMFED) PROTOCOL ON IMPROVING FEEDING DIFFICULTIES IN CHILDREN SEEN AT THE MEDICAL CITY CENTER FOR DEVELOPMENTAL PEDIATRICS FEEDING CLINIC

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Background: Feeding difficulties are noted in approximately 20 - 50% of normally developing children and 70 - 89% of children with developmental disabilities. A standardized feeding protocol involving effective behavioral interventions will guide pediatricians in the diagnosis and management of feeding difficulties encountered in clinical practice.

Objective: This study aims to determine if the Identification and Management of Feeding Difficulties for children (IMFeD)-based feeding intervention improves feeding difficulties in patients in terms of weight, food variety, compliance and parental satisfaction.

Design and Methodology: In this retrospective study, charts of all patients who had undergone the feeding intervention from April 2012 to May 2014 were reviewed. Baseline demographics, weight and variety of food intake were obtained. Structured interviews via telephone call compared pre- and post-intervention weight and variety of food intake. Compliance to feeding guidelines and parental satisfaction were also measured.

Subjects: One hundred thirty-one (131) patients who had undergone the feeding intervention were enrolled. Thirty-three (33) caregivers participated in the follow-up interview.

Statistical Analysis: Paired t-test, Chi-square, means.

Results: A statistically significant increase in weight was noted post-intervention ($p < 0.001$). Food variety increased in the majority of patients, but the increase was significantly lower in vegetables than in grains ($p < 0.001, x^2 17.2$) and meat ($p 0.002, x^2 22.7$). All caregivers reported moderate-to-high compliance with the feeding guidelines, with significantly better compliance in children > 2 years of age compared to infants aged 5 months to 2 years ($p 0.025, x^2 4.991$). Parental satisfaction was reported at 66.7%.

Conclusion: The findings of this study support the use of the IMFeD-based intervention in the improvement of feeding difficulties in patients seen at the feeding clinic.

Key words: feeding difficulty, IMFeD, food variety.

782 EFFECTS OF PROBIOTIC SUPPLEMENTATION ON AMELIORATION OF BODY FAT ACCUMULATION AND WEIGHT GAIN: A POTENTIAL STRATEGY TO REDUCE OBESITY IN THE FUTURE

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Introduction: Obesity predisposes individuals to an increased risk of developing metabolic disorders, including diabetes, hyperlipidemia, non-alcoholic fatty liver disease and metabolism-mediated carcinogenesis. Recent studies in humans and animal models have revealed that obesity is associated with chronic inflammation and a changing pattern of gut microbiota *Firmicutes/Bacteroidetes* (F/B) ratio. One of the key molecules implicated in chronic systemic inflammation is lipopolysaccharide (LPS). Anti-inflammatory benefits of *Lactobacillus* may improve metabolic disorders. Probiotic supplementation is considered to affect F/B ratio. The aim of this study is to evaluate the effect of *Lactobacillus* on body weight gain and fat accumulation in obese mice.

Methods: Adult male C57BL/6J mice were fed a high-fat diet (HFD) or normal diet (ND). The mice were then fed with or without a suspension of probiotic (*Lactobacillus casei* variety rhamnosus, Lcr35) for 12 weeks. Body weight (BW) was recorded and plasma biochemical values were analyzed. Visceral fat weight (VFW) was measured and specimens were analyzed histologically. Visceral fat percentage (VFP) was calculated (VFW divided by BW). Inflammation severity was determined by serum LPS level. F/B ratio was analyzed by real-time PCR.

Results: After 12 weeks, the HFD group gained more BW and VFW with increased serum cholesterol, triglyceride (TG), glucose, VFP and LPS levels when compared with the ND group. Supplementation with probiotic Lcr35 significantly inhibited weight gain, lowered TG and LPS levels in the HFD group. However, the VFW and VFP values were not affected much: VFW: ND 0.5 g, ND with Lcr35 0.6 g, HFD 2.1 g, HFD with Lcr 35 1.8 g; VFP: ND 1.7%, ND with Lcr35 1.9%, HFD 5.1%, HFD with Lcr35 4.9%. Additionally, the F/B ratio was significantly higher in the HFD group than in the ND group. However, no obvious difference was found after Lcr35 supplementation.

Conclusions: HFD-induced obesity obviously resulted in visceral fat accumulation in this study. We demonstrate that probiotic treatment appears to attenuate inflammation and inhibit steatosis in obese mice. Probiotic supplementation can ameliorate weight gain, but not visceral fat accumulation. We conclude that probiotics show protective potential in metabolic disorders. It may play an important role in providing a novel opportunity in anti-NAFLD performance and probiotic administration may become a potential strategy to reduce obesity in the future.

783 AMINO ACID COMPOSITION OF BREAST MILK FROM URBAN CHINESE MOTHERS

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Background: The amino acid composition of breast milk may vary depending on geographical location. Data from China is very limited. This study aimed to compare the levels of free (FAA) and total (TAA) amino acids in milk secreted during the different stages of lactation in a large cohort of urban Chinese mothers.

Methods: This was a cross-sectional study in which breast milk was collected in 3 Chinese cities from lactating mothers who had given birth to healthy, term infants. Four hundred and fifty milk samples from 5 postpartum periods (i.e., 5 to 11 and 12 to 30 days and 1 - 2, 2 - 4 and 4 - 8 months, n=90 each) were analyzed for TAA and FAA content by using the OPA/FMOC procedure.

Results: Both the sum and individual values of TAA in milk significantly decreased during the first periods of lactation until 2 - 4 months and then generally leveled off. Leucine and methionine were the most and the least abundant indispensable amino acids (IAA), respectively, across all the lactation stages, whereas glutamic acid + glutamine (Glx) was the most, and cystine the least, abundant dispensable amino acids (DAA). The contribution of FAA to TAA levels was less than 2% for most amino acids studied, except for free Glx, which was the most abundant FAA and contributed up to more than 10% of total Glx values in the latest lactation period. Contrary to TAA, FAA levels were globally lower in early than in late lactation stages.

Conclusions: The amino acid composition of the milk from our large cohort of urban Chinese mothers was comparable with human milk data from other parts of the world, suggesting that this is an evolutionary-conserved trait largely independent of geographical, ethnic or dietary factors.

784 A SIMPLE CLINICAL-BASED EQUATION TO PREDICT TOTAL BODY FAT MASS FOR THE EVALUATION OF NUTRITIONAL STATUS IN CHILDREN

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Childhood malnutrition is a pathological condition representing a health emergency in developing countries and an increasingly reported complication in hospitalized children in developed countries. To prevent and cure malnutrition, it is crucial that children at risk for nutritional deficiency are identified by means of simple and reliable indicators of nutritional status.

The aims of our study were to verify the correlation between the assessment of nutritional status by simple anthropometric indicators and the evaluation of the body composition by bioelectrical impedance analysis (BIA), which, estimating fluid content, allows body fat calculation and to elaborate a simple clinical-based equation to predict total body fat mass.

We analyzed two populations: the first consisted of 398 subjects (5 - 18 years of age) hospitalized for various diseases and the second of 193 age-matched controls attending a secondary school. All children had been evaluated with anthropometric measurements (weight, height, BMI, waist circumference, skinfold plicometry) and body fat mass was determined by the BI analyzer Tanita BC-601. We looked for correlation (Pearson test) between anthropometric variables and bioelectrical measurement of fat mass (FM). Multiple regression analysis was performed having FM as a dependent variable and the other measured covariates as independent values (software: SPSS 22). BMI, waist circumference, gender, age, tricep and subscapular skinfolds showed a significant correlation with the percentage of total FM, the dependent variable. In particular, BMI, waist circumference, tricep and subscapular skinfolds showed a direct correlation, while age showed an inverse correlation. Among the anthropometric variables, tricep and subscapular skinfolds showed the highest correlation with the total fat mass (Table 1). To evaluate the consistency between the BIA results and the equation proposed to estimate body fat percentage, we used the Bland-Altman

dispersion plot test. The multiregression equation we obtained was based on BMI, waist circumference (WC), gender (G 0 for female, 1 for male) and age (A) for prediction of total FM%, including the other measured variables which did not influence the validity of the equation (R2): % FM $7.676 + 0.722 \cdot \text{BMI} + 0.281 \cdot \text{WC} - 4.7 \cdot \text{G} - 0.004 \cdot \text{A}$. (The value of the coefficient of correlation r indicates that there was a highly significant correlation ($p < 0.0001$.) Bland Altman analysis between the values of fat mass obtained with the reference method - that is, the BIA and the multilinear regression equation developed by us - showed both methods to be equivalent. In conclusion, this study shows that, in children, the evaluation of nutritional status can be obtained with a simple and affordable method to obtain a reliable estimation of the body total fat mass without the use of any instrumentation.

Table 1. Relationship between anthropometric variables and total fat mass, as measured by BIA

Variable	Pearson r
BMI	0.628**
WC	0.480**
Age	-0.065
Tricipital fold	0.768**
Subscapular fold	0.729**

** $p < 0.01$

785 MATERNAL, INFANT AND EARLY GROWTH FACTORS ASSOCIATED WITH DYSLIPIDEMIA IN SCHOOLCHILDREN

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Introduction: Maternal, infant and early growth factors have been associated with posterior development of dyslipidemia. Associations found between specific factors and dyslipidemia in schoolchildren are variable. Screening of dyslipidemia before the age of 9 is recommended for children with specific risk factors.

Objective: The aim of this study is to identify maternal, infant and early growth factors associated with dyslipidemia in schoolchildren at age 7, in order to suggest specific factors to be included in an earlier screening of dyslipidemia.

Methods: We studied the association between maternal, infant and early growth factors with dyslipidemia at age 7 in a nested, case-control study of 1020 children selected from the Growth and Obesity Cohort Study. Birth weight and length data were obtained from obstetrics' records. A survey was applied to all parents to obtain social and anthropometric data, maternal medical history during pregnancy and early infant feeding patterns. Annual anthropometric measurements were performed and a blood sample was obtained at age 7 to identify dyslipidemia.

Results: Prevalence of dyslipidemia in schoolchildren was 53.6%. Maternal obesity, gestational smoking, gestational diabetes and obesity at age 7 were associated with dyslipidemia in schoolchildren. After multivariable regression analysis, adjusted by confoundable variables, gestational diabetes remained significantly associated with dyslipidemia with an OR of 1.99 (95% CI, 1.09 - 3.64), gestational smoking was significantly associated with an OR of 1.41 (95% CI, 1.03 - 1.94) and obesity at 7 years was strongly associated with an OR of 2.15 (95% CI, 1.09 - 3.64).

Conclusions: Maternal obesity, gestational smoking, gestational diabetes and obesity at age 7 were associated with dyslipidemia in schoolchildren. These findings support the current recommendation of screening obese schoolchildren before age 9 for dyslipidemia and suggest including a history of maternal overweight or obesity, gestational smoking and gestational diabetes as additional risk factors.

786 SELECTIVE HOME-MANAGEMENT OF FEVER AND CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION IN PEDIATRIC PATIENTS WITH INTESTINAL FAILURE

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Background: Pediatric patients with intestinal failure (IF) are at risk of central line-associated blood stream infections (CLABSI). Febrile illnesses often result in frequent hospitalization for at least 48 hours of empiric intravenous (IV) antibiotics while awaiting blood culture results, which can be a tremendous burden on the quality of life for the patient and their family, as well as a burden on healthcare resources.

Hospitalization may be unnecessary if appropriate therapy can be initiated at home. The purpose of this study is to describe our algorithm for home-management of fever and CLABSI in select patients who meet specific criteria and to report our outcomes using this algorithm.

Materials and Methods: A retrospective cohort of IF patients <21 years of age who were on home parenteral nutrition from 2010 - 2015 was analyzed to determine frequency of fever, CLABSI and hospitalization. To qualify for home-management, resources for expedient blood culture and delivery of home antibiotics must be available, the family must maintain frequent communication with our team and have experience with home antibiotics, and "red flag" signs and symptoms must be absent.

Results: 31 patients contributed 22,576 catheter days. There were 245 potential CLABSI events (fever or change in clinical status), with a CLABSI rate of 6.7/1000 catheter days (61% of potential events) and a rate of culture-negative febrile illness of 4.2/1000 catheter days. Of the 150 CLABSI events, 63% were treated without hospitalization. The most common pathogen requiring admission to both the hospital and intensive care unit was yeast.

Conclusion: Home-management of fever and CLABSI may be safely accomplished in select IF patients if the appropriate resources are available for close follow-up and to expeditiously obtain a culture and begin IV antibiotics at home. The presence of "red flag" symptoms or yeast are general indications for admission.

787 PSYCHOSOCIAL FUNCTIONING IN PEDIATRIC PATIENTS WITH INTESTINAL FAILURE: CONSIDERATIONS FOR PSYCHOLOGY INVOLVEMENT

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Pediatric intestinal failure (IF) is defined as the inability of the intestinal tract to function properly due to decreased length, resulting in the need for parenteral nutrition, medication and surgical intervention. Much is known about the medical complications and sequelae of IF; however, little is known about the psychosocial impact for children and their families. The purpose of this study was to further investigate psychosocial

factors, including health-related quality of life (HRQoL) and behavior problems within this population, in order to identify concerns and determine the need for psychology intervention.

Parents and patients (aged 8 and older) completed questionnaires at their GI clinic visit measuring HRQoL (for patient, parent and family) and behavior concerns. Questionnaires were scored and interpreted by a psychology fellow. The 40 patients were aged 2 - 12 and 68% were diagnosed with short bowel syndrome (SBS).

Mean scores for patient and parent/family HRQoL were generally within the normal range, with the exception of school functioning, which was considered at-risk. Twenty-five percent of parents reported clinically significant behavior problems in their children.

The data collected through this study provide further examination of psychosocial functioning within the pediatric IF population. Results of this study replicate previous studies in the literature and expand on what is known by providing information about behavioral functioning. Given concerns identified by parents and at-risk functioning in the school domain, patients and families may benefit from psychology consultation for support and connection to intervention.

788 PREDICTING OUTCOME OF NEONATAL SHORT BOWEL SYNDROME

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Background: The treatment of short bowel syndrome (SBS) has improved rapidly in developed countries. The situation in ASEAN countries is different where the population of children is high and the care of SBS may not be at par with other developed countries. Singapore (SG) is fortunate to have advanced medical care. We tried to look at the outcomes of SBS in SG and determine where we stand in relation to other developed countries.

Objective: To determine predictors of outcome in neonatal SBS patients in our population of children.

Methods: A retrospective medical record review at a single institution was conducted. Neonates with less than 100 cm of small bowel length (SBL), at a corrected gestational age (CGA) of not more than 30 days, who were diagnosed with a surgical gastrointestinal disease or parenteral nutrition (PN) dependence for at least 60 days, were included in the study. Data were collected from June 2007 to June 2015. Primary outcome was survival and secondary outcomes were the ability to wean PN, central line-associated bloodstream infection (CLABSI) and cholestasis. Intestinal motility disorders were included, but analyzed separately, as they had normal intestinal lengths.

Results: A total of 29 patients were included in the study and followed for a median of 1.2 (0.1 - 8.5) years. Median gestational age was 31 weeks (24 - 42) and birth weight was 1700 g (425 - 3965). The most common diagnoses resulting in SBS were necrotizing enterocolitis (14 [48%]), malrotation (4 [14%]), bowel dysmotility with normal intestinal lengths (4 [14%]), meconium peritonitis (3 [10%]), ileal atresia (2 [7%]) and bowel ischemia (2 [7%]). Median residual small intestinal length was 66 cm (18 - 98) and percentage of predicted small intestinal length was 37.3% (7.1% - 100%). The ileocecal valve was resected in 8 patients (27.5%) during the study period. The median duration of PN was 10.3 months (0.5 - 92.3). Fifteen (51%) received SMOFlipid emulsion. Twenty-four (83%) were weaned from PN while 5 (17%) remained PN-dependent. Of the 5 patients who remained PN-dependent, 4 (80%) have intestinal dysmotility disorder and are on home PN care. Nineteen (66%) had less than 50% of residual small intestinal length of expected normal bowel length based on published guidelines. Small intestinal length was found to be the primary predictor of wean and patients with motility disorder will be PN-dependent. Cholestasis (conjugated bilirubin >34 µmol/L) was observed in 23 (79%) patients, but none of them progressed to liver failure. Only 5 (17%) had CLABSI. Twenty-seven (93%) survived and 2 (7%) died due to RSV pneumonia and pulmonary hypertension.

Conclusions: Our results are encouraging, as we had a low mortality rate and low central line-associated bloodstream infection. They also showed that a majority of patients will be weaned from PN, despite short intestinal length, as a result of new hepatoprotective strategies combined with a multidisciplinary team approach.

789 THE EFFECT OF BETWEEN-BREAST DIFFERENCES ON HUMAN MILK MACRONUTRIENT CONTENT

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Objective: Little is known about the effect of maternal handedness and preferential side of breastfeeding on macronutrient concentration in human milk (HM). We aimed to compare macronutrient content of HM from both breasts, taking into account the self-reported preferential feeding (dominant) breast, breast size and handedness (right versus left). We tested the null hypothesis that macronutrient content of HM is not affected by breast dominance, breast size or maternal handedness.

Design: Fifty-seven lactating mothers were recruited. HM macronutrients were measured after mid-manual expression using infrared transmission spectroscopy.

Results: Out of the 57 mothers recruited, 12 were excluded from the analyses because they brought in insufficient samples. Among the 22 who reported a size difference, 16 (73%) had a larger left breast ($p < 0.001$). Approximately a third of women reported no breastfeeding side dominance, a third reported a right dominance and another third reported a left dominance. Breastfeeding side dominance was unaffected by handedness or breast size. When size asymmetry was reported ($n = 22$), the dominant side was also the larger breast in 16 (73%) women, the smaller breast in 2 (9%) women, while 4 (18%) additional women with asymmetry had no preferential breastfeeding side. There were no statistically significant differences in macronutrients between the right and left breasts. In multiple, step-wise, backward regression analysis, fat, carbohydrate, protein and energy contents were unaffected by maternal handedness, breast side dominance, or breast size asymmetry.

Conclusions: Macronutrient content of mid-expression HM is unaffected by maternal handedness, breast size, or breast side dominance.

790 BONE HEALTH AND GROWTH OF CHILDREN RECEIVING LONG-TERM PARENTERAL NUTRITION

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Rationale: Children receiving long-term parenteral nutrition (PN) are at increased risk of 25-hydroxyvitamin D3 (25-OH D3) deficiency, suboptimal growth and decreased bone mineral density (BMD). The factors associated with these negative outcomes are not well known.

Methods: Children receiving PN for more than 2 years were included. Blood and urine analyses and dual X-ray absorptiometry were performed during outpatient clinics.

Results: Forty-one children were assessed at 14.1 ± 4.0 years of age. Mean age at PN start was 2.0 ± 1.8 (median 0.5). The indications for PN were short bowel syndrome (SBS, n=24), chronic intestinal pseudo-obstruction syndrome (CIPOS, n=9) and congenital enteropathies (CE, n=8). The mean number of PN perfusions was 5.8 ± 1.2 /week. The ratio of non-protein energy intake to resting energy expenditure (NPEI/REE), an index for PN dependency, was 1.1 ± 0.3 . Six children (15%) received steroids for a period exceeding 4 weeks. The mean concentrations of calcium and phosphorus in serum were 2.31 ± 0.11 and 1.41 ± 0.28 mmol/L, with mean intakes from PN of 0.4 ± 0.1 and 0.6 ± 0.3 mg/kg/day, respectively. The mean serum level of 25-OH D3 was 28.1 ± 8.9 ng/mL (normal: 30 - 60) with a mean intake from PN of 8.2 ± 2.7 IU/kg/day. The average parathyroid hormone (PTH) serum concentration was 39 ± 19 pg/mL (normal: 10 - 55 pg/mL). Five children had PTH levels above normal (1.3 upper limit of normal) with low 25-OH D3 in serum. The mean ratio of phosphorus to calcium in urine was 10.2 ± 16.9 (median 3.0). Only 16 children (39%) had a normal value of 25-OH D3. There were no differences in serum 25-OH D3 levels between children living in northern (sunlight exposure <2250 hrs/yr; n=12; 27.2 ± 9.1 ng/mL) and southern France (≥ 2250 hrs/yr, n=29; 31.1 ± 7.5 ng/mL, $p=0.6$). The levels of 25-OH D3 in winter/spring (n=23; 28.6 ± 9.4 ng/mL) and summer/autumn (n=18; 28.4 ± 8.4 ng/mL) were not different ($p=0.62$). Indication for PN, presence of stoma, residual bowel length, absence of ileocecal valve, colon resection, intestinal failure-associated liver disease and PN duration above 10 yrs had no effect on 25-OH D3 levels. The mean weight and height Z-scores were -0.4 ± 1.0 and -0.6 ± 1.2 , respectively. The height was lower than predicted on the basis of parents' stature (which was 0.9 ± 1.0 , $p<0.001$). Six children had insulin-like growth factor-1 below normal for their age (15%). The average body mass index was 18.1 ± 3.2 kg/m². The mean non-protein kcalorie to nitrogen ratio was 185.4 ± 29.5 . Children with CIPOS and CE were shorter than those with SBS ($p=0.02$). The BMD Z-scores of the spine, the left femur and the whole body were -1.3 ± 1.4 , -0.9 ± 1.1 and -1.0 ± 1.5 , respectively. Also, they were lower in children with CE ($p=0.02$, 0.02 and 0.04, respectively). Two children had bone fractures after a mild trauma (5%).

Conclusion: All children on long-term PN, and particularly those with CE, are at risk of 25-OH D3 deficiency, suboptimal growth and osteopenia. PN-related bone fractures are rare. Close follow-up remains mandatory.

791 FECAL MICROBIOTA ANALYSIS IN CHILDREN RECEIVING SACCHAROMYCES BOULARDII CNCM I-745 DUE TO ACUTE ROTAVIRAL INFECTIOUS DIARRHEA (FACID STUDY): A NEW MECHANISM OF ACTION FOR PROBIOTICS

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Background: Acute infectious diarrhea is one of the leading causes of mortality and morbidity in children worldwide. Probiotics have been recommended for the treatment of acute infectious diarrhea in children and the effects are strain-specific. There have been reported mechanisms of action about the effects of probiotics on diarrhea. The aim of this study was to evaluate potential effects of *Saccharomyces boulardii* CNCM I-745 on fecal microbiota composition in children with acute infectious diarrhea caused by rotavirus.

Methods: The subjects of the experiment were ten children within the first 48 hours of acute infectious diarrhea due to rotavirus and six healthy children who were without any complaints during the study period aged 3 - 4 years. In the study group with rotavirus diarrhea, all children received *Saccharomyces boulardii* CNCM I-745, 250 mg twice daily for 5 days. Fecal samples (n=80) were collected from each subject at days 0, 3, 5, 10 and 30. Microbiota composition were characterized by 16S ribosomal RNA gene sequencing and analyzed with bioinformatic tools. Results: In the rotavirus diarrhea group, all children had no diarrhea by the third day of intervention. The abundance of genera was different between the patient and control groups at days 0, 3 and 5. The Shannon index was significantly different between patients and controls at days 0, 3 and 5, whereas no significant difference was found at days 10 and 30. We compared the UniFrac distances between all times of every child, and concluded that the average temporal variability of the patients was significantly different from controls ($p<0.05$). In the control group, there were no differences in fecal analysis between days 0, 3, 5, 10 and 30, showing that microbiota had a stable composition in healthy children. Canonical correspondence analysis showed that diarrhea in each patient was located in a restricted space. There was some individuality in each person due to microbial composition.

Discussion: This is the first time we showed that disease improvement with probiotics might be associated with modified/restored fecal microbiota composition in children with acute rotavirus diarrhea.

*792 DECREASING TIME TO ANTIBIOTICS IN SHORT BOWEL SYNDROME PATIENTS WITH CENTRAL LINE AND FEVER IN THE EMERGENCY DEPARTMENT

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Background: Short bowel syndrome (SBS) patients have a higher rate of central line-associated bloodstream infection (CLABSI) than patients without intestinal failure (7.8 vs. 1.3 per 1000 catheter days). SBS patients have a high incidence of Gram-negative bacteremia, which is known to carry a high rate of morbidity and mortality. Prompt administration of antibiotics is crucial for the successful management of patients with central line and fever.

Aim: To decrease the time to antibiotics in SBS patients with central line and fever in the emergency department (ED) by 50% by December 2016.

Methods: The setting was an academic ED at an urban quaternary center that sees ~60,000 children annually. We did a retrospective chart review of all SBS patients with central lines between April 2014 and July 2015 and collected demographic data, time to antibiotics when presenting to the ED with a fever and blood culture results. In August 2015, we assembled a multidisciplinary quality improvement (QI) team, determined key drivers and intervention steps and implemented changes to decrease the time to antibiotics in SBS patients with central line and fever in the ED. Interventions included education of ED staff, creation of "Fast Pass" wallet cards for families and communication with pharmacy. Monthly average time to antibiotics was tracked and outcomes were presented using a run chart with pre-intervention and post-intervention data. The median time to antibiotics in the pre- and post-intervention periods was analyzed using a Wilcoxon Rank Sum Test. **Results:** In total, there were 41 admissions for fever in 11 SBS patients with central lines (19 admissions in the pre-intervention period and 22 admissions in the post-intervention period). In the pre-intervention period, 32% of blood cultures were positive, of which 50% were due to Gram-negative bacteria. In the post-intervention period, 50% of blood cultures were positive, of which 63% were due to Gram-negative bacteria. The median time to antibiotics decreased by 38% following implementation of a QI team from 213 minutes (IQR: 159 - 239 mins) pre-intervention to 131 minutes (IQR: 110 - 195 mins) post-intervention ($p=0.04$).

Conclusions: Forming a multidisciplinary QI team led to a 38% reduction in time to antibiotics for SBS patients with central line and fever. Efforts continue to drive the time to antibiotics lower and assess the sustainability of these changes. Future studies are needed to determine whether the improvement in time to antibiotics will lead to fewer admissions to the intensive care unit, shorter hospitalizations and decreased rates of central line removal.

793 IMPROVED ADHERENCE TO SURVIVING SEPSIS: USE OF A GUIDELINE FOR PATIENTS WITH PEDIATRIC INTESTINAL FAILURE, FEVER AND A CENTRAL LINE

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Children with intestinal failure are dependent upon daily use of a central venous catheter for nutrition and hydration. Recent reports indicate the high rate of central line-associated blood stream infection of 8.9 infections per 1000 catheter days, putting this population at great risk for sepsis and death. Among adult patients with septic shock, the administration of antibiotics within one hour of documented hypotension improved outcomes, while delays resulted in increased mortality.

We evaluated over 3 years of emergency room encounters for fever in the setting of a central line among children with intestinal failure. We began by retrospectively reviewing 1 year of cases. We then instituted a protocol for emergency medicine triage, treatment and admission using a successful existing process for oncology patients, with fever as a template. Parents phoned the GI team to report a fever. The GI provider then called the emergency medicine physician to activate a pre-arrival referral process, including a standard order set in the electronic medical record for laboratories and empiric, broad spectrum antibiotics that would be awaiting the patient on arrival in the ED. A room in the emergency department was then saved for the patient. Antibiotic administration in less than 60 minutes from arrival was considered a "success". Continuous variables were evaluated by t-test and categorical variables by Fisher's exact test.

We observed all 210 encounters involving 54 children with intestinal failure presenting to our emergency room with a fever in the setting of a central line between November 5, 2012 and December 31, 2015. The median number of encounters per child was 2.5 (range 1 to 13). Median time to antibiotics was 53 minutes and ranged from 15 minutes to 5 ½ hours. There was no difference in time to antibiotic administration with initiation of our protocol; however, there was a significant increase in the proportion of "success" encounters ($p=0.043$). The largest barrier to successful antibiotic administration was lack of parental notification prior to arrival. There was no difference in ED or hospital length of stay. There was no difference in the rate of admission to the intensive care unit. Seventy-one encounters (34%) were associated with a positive blood culture drawn at the time of presentation.

The implementation of a standardized triage and treatment procedure for children with intestinal failure and fever resulted in significantly more "success" encounters, defined as the provision of empiric antimicrobial coverage within 60 minutes of presentation. Further, the rate of bacteremia in children with intestinal failure presenting with fever was 34%, supporting a culture of rapid and aggressive evaluation and treatment of this vulnerable population. Further work targeting reductions in hospital and emergency department length of stay may not only improve patient satisfaction, but also improve system performance and efficiency.

794 COMPARISON OF MACRONUTRIENT CONTENT OF MATERNAL AND DONOR HUMAN MILK USING A HUMAN MILK ANALYZER

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Background: Growth failure in Very Low Birth Weight (VLBW, <1500 grams) infants is common in the neonatal intensive care unit and is associated with poorer outcomes. It is well established that human milk is ideal for enteral feeding and donor milk (DBM) is used when mother's own milk (MOM) is not available. However, neither has a nutrient composition to meet the requirements for growing premature infants. DBM is associated with poorer growth and is hypothesized to have nutritional content below that of MOM. Various strategies are available to increase the macronutrient content of human milk; however, the baseline nutritional content is unknown therefore it is not possible to determine if added fortifiers help in reaching the target goals.

Objective: To determine the macronutrient content of MOM compared to DBM before fortifiers are added.

Methods: This is a prospective, observational study in 31 VLBW infants, completed gestational age ≤ 32 weeks with birth weight $>3^{\text{rd}}$ percentile on the Fenton growth curve receiving MOM and/or DM. Subjects were enrolled in a study evaluating the tolerance and outcomes of a new liquid protein fortifier (LP). Human milk was analyzed using the Calais Human Milk Analyzer at baseline (prior to fortification with LP) then twice-weekly until study completion. All statistical tests were two-sided and a p -value <0.05 was considered statistically significant.

Results: A total of 267 milk samples (145 MOM and 122 DM) from 31 subjects had nutritional analysis completed. There was a statistically significant difference between the calorie, fat and protein content between MOM and DM (Table 1). The calories/ounce was higher in MOM (18.68 ± 3.21) compared to DM (17.96 ± 1.73), $p=0.021$ while the mean fat content was also significantly higher 3.69 ± 1.25 (MOM) vs. 3.42 ± 0.56 (DBM), $p=0.02$. The total and true protein results were consistent with these results, 1.07 ± 0.04 (MOM) vs. 1.05 ± 0.08 (DBM) for total

protein, $p=0.014$ and 0.88 ± 0.11 (MOM) vs. 0.77 ± 0.06 (DBM) for true protein, $p<0.0001$. There was no significant difference between the groups for lactose.

Conclusions: DM was significantly lower in calories, fat and protein when compared to MOM. The mean calorie content was lower for both groups than the reference standard of 20 Cal/oz, indicating that the current practice of standard human milk fortification may fail to meet the goals for nutritional content that will support normal growth and development. Targeted fortification using milk analysis may help meet the increased calorie and protein needs of VLBW infants.

Table 1:

	MOM (n=145)	DBM (n=122)	Mean difference (95% CI)	P
	Mean± SD	Mean± SD		
Fat (g/100mL)	3.69 ± 1.25	3.42 ± 0.56	0.28 (0.03, 0.52)	0.02
Total Protein (g/100mL)	1.07 ± 0.04	1.05 ± 0.08	0.02 (0.00, 0.03)	0.014
True Protein (g/100mL)	0.88 ± 0.11	0.77 ± 0.06	0.11 (0.09, 0.13)	<0.0001
Lactose (g/100mL)	6.45 ± 0.29	6.44 ± 0.40	0.01 (-0.07, 0.9)	0.83
Cal/Oz	18.68 ± 3.21	17.96 ± 1.73	0.70 (0.07,1.35)	0.021

795 PERINATAL AND NUTRITIONAL FACTORS ASSOCIATED WITH PROTEIN TOLERANCE RECOVERY IN IGE-MEDIATED COW MILK ALLERGY

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Introduction and Objectives: IgE-mediated Cow Milk Allergy (CMA) is the most frequent food allergy in the first year of life. The majority of patients recover tolerance during the first few years of life, but some may take several years to do so, while others may never recover it at all. Patients and Methods: We analyzed 202 patients with IgE-mediated CMA. The analyzed variables were tolerance in pregnancy, mode of delivery, commencement and duration of breast-feeding, incidence of occasional intake of artificial formula while in maternity and type of special formula indicated (Nutramigen®, Pregestimil®, Nutramigen LGG®, hydrolyzed rice, elemental and soy formula.). Follow-up and provocation test protocols were the same in all cases. We considered, as tolerance recovery, the time in months between diagnosis and the patient tolerating cow milk protein for the first time in a provocation test. Patients who had not recovered tolerance by October 2015 were considered under the conditions of the study to be intolerant. We used the SPSS 17.0 statistical package to analyze data. We plotted survival curves and considered, as censored occurrences, the dates when patients recovered tolerance. (We will display the significant survival curves in the poster.)

Results: (included in the table).

Conclusions: The main perinatal factor related with late tolerance recovery was Caesarean delivery. However, the type of special formula given to the patients also influenced tolerance recovery, with patients fed hydrolyzed casein (Pregestimil®, Nutramigen® and Nutramigen LGG®) recovering sooner than those fed other formulas. When we compared the group fed with Pregestimil® or Nutramigen® against that fed with Nutramigen LGG®, patients in the Nutramigen LGG® group recovered earlier.

Survival curve results		
	Long-Rank (Mantel-Cox)	p
Pregnancy Tolerance (Poorly tolerated/Well tolerated)	0,19	NS
Mode of delivery (Caesarian/normal birth)	4,843	0,028
Breast-feeding start (Yes/ No)	0,065	NS
Breast-feeding duration > 6 months (Yes/ No)	0,188	NS
Occasional contact with Artificial Formula (Yes/ No)	0,83	NS
Special Formulas (All Formulas))	10,34	0,035
Comparison of PREGESTIMIL+NUTRAMIGEN vs NUTRAMIGEN LGG	7,551	0.006

796 USE OF A NOVEL AUTOMATIC BREATH TEST TECHNOLOGY FOR HYDROGEN BREATH TESTING IN NEWBORNS AND SMALL CHILDREN

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Background: The clinical utility of H₂ breath tests in diagnosing GI disorders is well documented, but limited to use in patients old enough to comply with instructions. Breath analyses diagnose a wide range of disorders (e.g., lactose intolerance, small intestinal bacterial overgrowth, fructose intolerance, sucrose intolerance, irritable bowel syndrome). However, current methods require a forced-exhalation after breath hold, which cannot be reliably performed by infants or young children, or require a breathing mask, which may not be well tolerated. Hence, invasive diagnostic procedures or protracted dietary modifications may result. A new technology (Sensalyze™ Technology Platform, Capnia) includes an automatic sampling system via an unobtrusive nasal cannula and does not require a breathing maneuver by the patient. This microfluidic technology automatically detects a valid breath sample and segments the alveolar gas, representative of the blood level of the analyte, which is then measured. The first product using this technology (CoSense® End-Tidal Carbon Monoxide [ETCO] Monitor) accurately measures ETCO levels in neonates, despite erratic, fast, episodic and low tidal volume breathing. It is hypothesized that the Sensalyze technology can be adapted to measure end-tidal H₂ (ETH₂) and end-tidal methane (ETCH₄) for the purpose of diagnosing GI disorders, thus filling an unmet need in infants and young children.

Objective: To determine if a new breath-sensing technology is capable of accurately measuring ETH₂ by using a bench model that imitates infant breathing patterns.

Materials and Methods: A prototype device was developed with an electrochemical sensor designed to measure H₂ gas. A custom calibration method and equation were developed to calibrate the sensor using known concentrations of H₂. Additional equations and algorithms were developed to measure ETH₂ in a breath sample of unknown H₂ concentration, using the calibration values. A bench model was used to imitate infant and young child breathing patterns. Breath test simulations were performed and resultant ETH₂ measurements compared to known H₂ concentrations. A range of conditions was tested to challenge the robustness of the prototype device.

Results: At respiratory rates of 20 - 50 bpm, accuracy ranged from a mean of -1.2% to ± 2.5% at 31, 48 and 98 ppm H₂, all clinically relevant H₂ levels (see Table).

Conclusions: This new technology is capable of accurately measuring ETH₂ in simulated infant breathing. Measurements are repeatable and robust under a wide range of conditions (RR, H₂ concentration). A product using Sensalyze Technology could be beneficial in diagnosing GI disorders, in which there is currently a need for a rapid, non-invasive, point-of-care test for infants and young children. Such an ETH₂/ETCH₄ monitor could open up new areas of research and clinical care, and is currently in development.

Hydrogen Measurement Accuracy															
Actual Gas Concentration→	31 ppm H ₂					48 ppm H ₂					98 ppm H ₂				
	Breath Rate(bpm)	20	30	40	50	20-50	20	30	40	50	20-50	20	30	40	50
N	6	6	6	6	24	6	6	6	6	24	6	6	6	6	24
Mean ETH ₂ (ppm)	29.5	31.2	30.3	30.3	30.3	49.1	49.2	49.3	49.9	49.4	100.0	100.0	100.2	98.2	99.6
Std Dev	1.6	0.9	1.5	1.2	1.4	1.7	1.1	2.1	2.0	1.7	2.48	0.88	1.76	1.43	1.8
Mean % accuracy	-4%	2%	-1%	-1%	-1.2%	2%	2%	2%	4%	2.5%	2%	2%	2%	0%	1.6%

797 AN INNOVATIVE APPROACH FOR THE SELF-MANAGEMENT OF CYSTIC FIBROSIS PATIENTS IN EUROPE: DEVELOPMENT, VALIDATION AND IMPLEMENTATION OF A NEW EHEALTH TOOL: THE MYCYFAPP PROJECT

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An accurate pancreatic enzyme replacement therapy (PERT) and close nutritional monitoring to achieve optimal nutritional status are the main pillars for the treatment of children with cystic fibrosis (CF) and may result in a better disease prognosis. Currently, there is a lack of evidence-based methods to adjust PERT dosing and no practical tools or resources are available to promote nutritional recommendations and guidance for patients to follow a balanced and adapted diet.

The MyCycFAPP Project (www.mycyfapp.eu) addresses this challenge through the development of a new mobile APP to empower patients and their families to self-manage these aspects of their day-to-day treatment, to guarantee patient adherence and to obtain the most optimal outcomes from the nutritional intervention. This app will allow an easy intercommunication between patients and health professionals and real-time follow-up and monitoring of patients' progress.

The main tailored and evidence-based features that are being developed as part of the new app are the following: 1) a nutritional recommendation guideline for the patient that is based on current national nutritional imbalances, as identified through an elaborate survey on dietary habits in five European countries; 2) an *in vitro* digestion model to study nutrient behaviour under CF gastrointestinal conditions; 3) a mathematical predictive algorithm to estimate the individual optimal dose of enzymes for each meal, identified by an *in vitro* digestion model to study nutrient digestion under CF gastrointestinal conditions; 4) various educational games and interactive resources to promote the patients' knowledge and empowerment.

In order to make the new eHealth tool a success, we have set up an international multidisciplinary consortium, in which different and complementary areas of knowledge have joined, including nutrition, gastroenterology, food science and engineering, psychology, eHealth software development and serious games' design. Furthermore, end-users (i.e., patients and health professionals) have been constantly involved into the developmental process, to ensure the integration of the ICT tool into the regular CF therapy and a real added value of the product as a prerequisite of its usage.

The implementation of the app as a key decision support system aims to accomplish the ultimate goals of the project: improved health status and quality of life, as well as economic savings both for national health systems and for the patients' families.

798 EARLY LIFE INFLUENCES ON THE INTESTINAL MICROBIOME AND GROWTH TRAJECTORIES OF CHILDREN

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Aims: To investigate the complex inter-relationships of early life diet quality and antibiotic exposure with the developing intestinal microbiome and the growth trajectories of children between 0 - 24 months of age. We hypothesize that poor diet quality (particularly early introduction to refined sugars and processed foods) will lead to adverse growth trajectories from 0 - 24 months and to significant changes in the intestinal

microbiome. We also hypothesize that early exposure to antibiotics, in combination with poor diet quality, will lead to greater weight gain than poor diet quality or antibiotic exposure alone.

Methods: The MGH Healthy Infant Study is a cohort of 115 children, enrolled as infants (median age: 3 months) and now followed to the age of 2 years. Stool microbiome was obtained at enrollment and then again at the 2-year, well-child visit. Diet history was obtained at enrollment and at the 2-year, well-child visit. Electronic health records provided serial weight and length measurements, as well as medical problems and medication history.

Results: Data collection is ongoing but should be complete by July 2016. At present, we have interview and medical record data from 92 children (80%) and stool samples from 82 (73%). Preliminary analyses of 57 of the children enrolled have revealed 33% of children have a history of antibiotic use and a mean BMI percentile of 42% at their 2-year, well-child visit with a standard deviation of 28. At the World Congress for Pediatric Gastroenterology, Hepatology and Nutrition (October 2016), we will describe results from the questionnaires that address prenatal and perinatal care, birthing delivery mode, dietary regimen, infection, antibiotic use, household and social environment. We also anticipate having our microbiota analysis complete this summer and will address the following scientific questions: 1) What is the association of exposure to antibiotics and birth – 2 year growth trajectories: does the intestinal microbiome mediate this relationship? 2) Does poor diet quality alter infant growth trajectories or the intestinal microbiome from infancy to 2 years of age?

Discussion: With these longitudinal data, we anticipate that the MGH Healthy Infant cohort study can help to identify factors that may modify an infant's risk of an adverse growth trajectory and obesity. We hope this study will inform the development of a much larger cohort and, eventually, the implementation of evidence-based strategies to prevent childhood obesity.

*799 A NEW RED BLOOD CELL FATTY ACID PROFILE IN CHILDREN RECEIVING INTRAVENOUS FAT EMULSION CONTAINING 15% FISH OIL

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Intravenous lipid emulsion (ILE) rich in n-3 fatty acids, containing soybean (30%), medium chain triglycerides (MCT) (30%), olive (25%) and fish (15%) oil (SMOFlipid[®]) is now widely used in premature infants, newborns and children on parenteral nutrition (PN), especially for preventing intestinal failure associated liver disease (IFALD). Long-term use is not documented in home-PN (HPN) children.

Aim: To assess the fatty acid (FA) profile of such HPN children.

Population: 31 children with chronic intestinal failure (CIF) were assessed (ultra-short bowel syndrome 16, congenital enteropathy 7, total aganglionosis 5, chronic intestinal pseudo-obstruction 3) aged 6 months to 16 years on HPN for 5 months to 16 years, all highly dependent on PN, as supported by the disease causing CIF, low plasma citrulline levels and high PN intake. All received SMOFlipid[®] as the sole source of ILE from 6 to 38 months at the dose of 2.1 ± 0.39 g/kg/day, 6.7 ± 0.7 days per week.

Methods: Sampling was performed after ≥ 24 hr, fat-free PN and 6 – 8 hrs after PN discontinuation. After red blood cell (RBC) NaCl 9/1000 washing, RBC-FA profiles were established by using gas-chromatography. Citrulline plasma levels, ratio PN-intake/resting energy expenditure (REE), using Schofield equation, growth expressed in standard deviation (SD) and total plasma bilirubin were assessed in all children. FA profiles were compared to those obtained from a former randomly controlled trial comparing soybean-oil-based lipid emulsion (Intralipid[®]) and SMOFlipid[®] for 4 weeks (JPEN 2010).

Results: Plasma citrulline mean was 6.1 ± 6.3 $\mu\text{mol/L}$ (median: 4); PN/REE ratio was $130 \pm 20\%$, (med: 130); total bilirubin was 12.2 ± 8.5 & $\mu\text{mol/L}$ (med: 9). Growth was within normal range: body weight: $+0.1 \pm 1.8$ SD (med: 0); height: -0.1 ± 1.4 SD (med: 0). RBC-FA profiles are expressed in percentage and compared (t-tests) with reference data after 4 weeks of SMOF[®].

C16: 0 Palmitic Ac	23.8 ± 3.0	$p=0.18$
C18: 1n-9 Oleic Ac	14.1 ± 1.5	$p=0.73$
C18: 2 n-6 Linoleic Ac	6.1 ± 1.2	$p<0.001$
C20: 4 n-6 Arachidonic Ac	6.2 ± 1.5	$p=0.27$
C20: 5 n-3 EPA	9.3 ± 2.2	$p <0.001$
C22: 6 n-3 DHA	12.5 ± 1.8	$p=0.02$

Conclusion: Long-term administration of an ILE rich in fish oil (15%) in highly PN-dependent children (PN/REE: $130 \pm 20\%$) was well tolerated. Despite very long-term PN, bilirubin plasma levels remained low and growth was normal. The RBC-FA profile, that did not change in the short-term (4 weeks), is different over the long-term for C18:2n-6, C20:5n-3 and C22:6n-3 without significant change in C20:4n-6 (arachidonic acid). It reflects the n-3/n-6 FA acid composition of this new fish oil-rich ILE. This "unusual" RBC-FA profile, followed over the long-term, is not accompanied by any harmful effect and can be considered as safe and probably beneficial for preventing IFALD.

800 FOOD INDICATORS AND NUTRITION STATUS EVALUATION OF 221 NEWBORNS AND INFANTS LIVING IN SUBURBAN DAKAR

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Infant and Young Child Feeding (IYCF)'s strategy, adopted since 2003 by several developing countries including Senegal, aims at promoting newborns' and infants' diet. Its evaluation is based on 8 basic indicators and 7 complementary indicators. To evaluate the IYCF indicators in suburban Dakar, we surveyed the mothers of 221 healthy-looking children aged 0 - 23 months from September 27 to November 3 who had come for vaccination. A questionnaire was given to them, enabling us to evaluate those childrens' dietary practices. All the children were weighed and measured, which helped evaluate their nutrition status using the WHO standards.

The basic IYCF indicators studied revealed a number of results. Early initiation to breastfeeding before the first hour was low, estimated at 1.8%, but 92.8% of the newborns had been breastfed in the first 24 hours following birth. Exclusive breastfeeding was practiced among 44.4% of the infants under 6 months old. Continuous breastfeeding was the norm among 95.8% of the children aged 12 to 15 months, showing the quasi-universal nature of breastfeeding until that age. The introduction of solid, semi-solid or tender food was done among 76% of the 6-to-8-month-old children. The minimum rate of dietary diversification was 49.5% among 6-to-23-month-old breastfed children and 82.4% of the non-breastfed children of the same age. The minimal number of meals was complied with among 20% of the 6-23-month-old infants as compared to

5.9% of the non-breastfed infants. The minimal dietary intake among 6-23-month-old infants was only acceptable among 8.6% of the breastfed infants as compared to nearly zero among the non-breastfed. The consumption of iron-rich or iron-fortified food was observed among 85.1% of the 6-23-month-old infants. The two main complementary indicators were: breastfeeding median duration was 17.3 months among non-breastfed infants; bottle-feeding was practiced among 32% of the infants aged 0 to 23 months. Nutrition status: We have observed wasting among less than one infant in ten (8.6%). Stunting was observed among 9.5% of the infants and, paradoxically, the lack of an acceptable minimum dietary intake among 6-to-23-month-olds has not significantly influenced their nutrition status.

In conclusion, we have observed that breastfeeding is quasi-universal in contrast with the poor quality of food diversification, as shown by the number of minimum meals and minimum food intake among 6 to 23 month-old infants. But malnutrition, as observed in this work, has in this context other determinants that deserve to be better studied so as to include them in the care provision strategies for greater efficiency.

801 FOOD, NUTRITION AND HEALTH AMONG SENEGALESE CHILDREN

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Thanks to such programs as vaccination and vitamin A supplementation, child mortality has decreased considerably over the last few years in Senegal. Because of their frequent occurrence, malnutrition and micronutrient deficiencies have greatly contributed to these childrens' deaths. From September 1, 2012 to October 31, 2012, a review of the literature and interviews of 24 leading experts in nutrition helped us to identify among Senegalese children some key health indicators, including mortality and survival programs, food habits, nutritional status and various micronutrient deficiencies. Data from the literature were compared to the experts' opinions before their validation.

Despite a significant decrease over the past few years, Senegal is characterized by strong child (72%) neonatal (29%) mortality. Good vaccine coverage and a vitamin A supplementation rate over 80% have helped reduce deaths. Breastfeeding is characterized by sometimes late beginnings, with an average rate of exclusive breastfeeding of 39%. Weaning, which is the hard part in Senegalese newborn babies' diet, is still characterized by a heavy consumption of cereals in combination with a poor intake of meat, fish, vegetables and fruit. Milk and dairy product consumption is still low among the children. The mothers' ignorance, illiteracy and lack of nutritional education apparently play a more important role than poverty, according to the nutrition experts.

The quality of the food explains the high incidence of malnutrition and micronutrient deficiencies. Despite the various health and malnutrition-fighting programs, the childrens' nutritional status is still precarious. Slow growth or chronic malnutrition rose from 23.2% in 1986 to 26.5% in 2010. Acute malnutrition increased between 1986 (5.8%) and 2010 (10.1%), showing a serious nutrition status. Child obesity, on a steady rise, especially in the city and among upper class people, have not yet been provided with any programs to combat it.

Anemia, often due to iron deficiency, is specifically frequent (86.5%), even among healthy-looking newborn babies and is today a major nutritional challenge. Vitamin A deficiency which affects 17.1% of the children has a supplementation program that covers over 80% of the children. Zinc deficiency (49.7%), although very frequent throughout the country, is still neglected.

In summary, the high child mortality can largely be explained by several factors, including malnutrition and various micronutrient deficiencies. Improving childrens' health and nutrition status requires a good communication policy for real behavior change, especially with respect to weaning.

802 CHILD FEEDING BEHAVIORS AND FACTORS AFFECTING PARENTAL PERCEPTION OF FEEDING CONCERNS IN CHILDREN

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Objectives: To describe child feeding behaviors and impact of parental perception of feeding problems in children, particularly in those born premature or with a low birth weight (LBW).

Methods: Children aged 12 - 35 months attending routine general pediatric outpatient clinics were invited to participate. An anonymous survey of demographics, feeding information, the Behaviour Pediatrics Feeding Assessment (BPFA) and Caregiver's Feeding Styles Questionnaire (CFSQ) was completed by parents. On the BPFA child behavior frequency component, parents rate each behavior as never/sometimes/always. Scores higher than cut-offs on the BPFA are considered to suggest feeding difficulties.

Results: One hundred children (49 male) were recruited. Age at survey: 12 - 17 months (33%), 18 - 23 months (26%), 24 - 29 months (26%) and 30 - 35 months (15%). Twenty-four were born pre-term, with median (range) gestational age of 32 to <35 weeks and median (range) birth weight of 2 - 2.49 kg. 22 had LBW (<2.5 kg), 13 of whom were termed small for gestational age (SGA). Parents of children with LBW are more likely to have concerns about their child's feeding (38% vs. 28%, $p < 0.0005$). Gender, race, prematurity, medical conditions and being tube fed were not confounding factors. However, parental feeding style (CFSQ) was a confounding factor for this association ($p = 0.006$). After correcting for parental feeding style, there was no longer a statistically significant relationship between LBW and parental concerns about their child's feeding ($p = 0.3$). 59% of parents reported that their child had more than one problem symptom during feeding, the top 3 being: difficulty staying long enough to complete the meal (40%), selective eating (37%) and holding food in the mouth (34%). Those who had LBW (40%) were more likely than those with normal birth weight (11%) ($p = 0.01$) to have vomiting during eating or drinking, even after correcting for gender, race, prematurity, medical conditions and parental feeding style. Parents of toddlers who had difficulty weaning were more likely to have concerns about their child's feeding (81% vs. 22%, $p < 0.0005$). However, weaning difficulties were not associated with prematurity or LBW. Premature or LBW infants were also not more likely to score positively on the BPFA. Top feeding behaviors that occurred at least sometimes on BPFA were: longer than 20 minutes to finish meal (67%), getting up during meals (57%), spitting out food (49%) and holding food in mouth (41%). This corresponded to the behaviors viewed as problems by parents. However, no association was seen between LBW or prematurity and parent report of their own problematic responses to the feeding difficulties.

Conclusions: Long meal duration was the most common symptom reported by parents of young children, irrespective of BW or gestational age. Parents of LBW children are more likely to report concerns about their child's feeding. There was no apparent association between prematurity and problem symptoms during meals.

803 CONTINUOUS PHYSICAL EXERCISE IN TEENAGERS MAY MODIFY THE DISRUPTION OF EARLY-LIFE GUT MICROBIOTA ASSOCIATED WITH CAESAREAN DELIVERY

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Intestinal microbiota development commences immediately after birth. The frequency of Caesarean delivery is increasing worldwide. Caesarean-born infants harbor a different microbiota as compared to vaginally-born infants, mainly due to evaded contact with maternal vaginal/fecal microbiota and an extended stay in the hospital. Such differences may influence whole-of-life health, but it is unclear how long-lasting these differences in the microbiota can be. In this context, we aimed to assess the intestinal microbiota of healthy young adults (n=165; male 114; female 51; age: 18.8 ± 0.9 years [range: 18 - 22 years]), profiled by the mode of delivery. Fecal samples (≈1.0 g) were collected into fecal collection tubes containing RNA later and an empty tube and were stored at 4°C until nucleic acid extraction. Bacterial groups, subgroups and genera were quantified by RT-qPCR. *C. perfringens* was quantified by qPCR targeting α-toxin and enterotoxin genes. Written informed consent was obtained from subjects and the study was approved by the ethics committee of the university.

Sixteen subjects had been delivered by C-section and 133 by vaginal delivery. We observed a significantly higher detection rate of *Bacteroides fragilis* group and *Lactobacillus sakei* subgroup in vaginally-delivered subjects compared with Caesarean-born subjects (p<0.05). The detection rate of fecal propionic acid was also significantly higher (p<0.05) in normally-delivered subjects compared to caesarean group. No differences were observed in the count or carriage rate of other fecal bacteria or organic acids, or in the physiological parameters such as body weight, BMI etc.

These results might suggest that the differences in the composition of gut microbiota and intestinal environment, in particular the carriage of *B. fragilis* group, *L. sakei* subgroup and fecal propionic acid, possibly as a result of C-section, might persist even beyond teen age. Given that these students belonged to the School of Sports Sciences, their disciplined physical training and active lifestyle might also have influenced the microbiota, as well as the physiological statistics. Hence, further studies should assess and validate these differences in different populations of different ages, as well as to decipher the association, if any, of these differences with any important aspect of host health and disease predisposition.

PANCREATOLOGY

811 PREVALENCE OF ISOLATED AMYLASE DEFICIENCY IN CHILDREN WITH SECRETIN PANCREATIC FUNCTION TEST

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Introduction: There are limited data on the prevalence of isolated amylase deficiency in children. Pancreatic amylase deficiency causes starch malabsorption with resulting symptoms of abdominal pain, bloating, loose stools, but unlikely failure to thrive if the other enzymes have normal activities. As per old reports, maturation of amylase activity typically occurs over time with levels approaching adult values by 9 months of age.

Methods: We performed endoscopic pancreatic function tests (ePFTs) with IV secretin on children 0 - 18 years of age who presented with symptoms suspicious for pancreatic exocrine insufficiency including diarrhea and poor weight gain. Improper sample collection was considered if the pH was 7 or less. After excluding these samples, we had 480 patients. In our practice, most of the specimens had a pH of 8 - 9.5. The cut-off for low amylase activity in our lab is <10.4 U.

Results: Table 1 summarizes the amylase activity by age in our ePFTs. As seen in the Table, there is a decrease in the prevalence of amylase deficiency by age. However, the finding of selective amylase deficiency is not unusual over 1 year of age. Generalized insufficiency was also noted more commonly in the first 3 years of life with a significant drop afterwards.

Discussion: Isolated amylase deficiency is present in children over 12 months of age. It can lead to clinical symptoms. The prevalence decreases by age. It should be noted that amylase activity, just like other digestive enzymes, depends on the substrate supply. Part of the low level may occur in children with low complex carbohydrate consumption.

Age group	N = 480	Amylase <3%		Part of a Generalized insufficiency	Prevalence of Isolated Amylase Deficiency	
		N	%		N	%
<6 months	8	7	87.5	0	7	87.5
6-12 months	46	31	67.3	3	28	60.8
1-3 years	192	57	29.6	9	48	25
3-10 years	157	36	22.9	2	34	21.6
>10 years	77	13	16.8	1	12	15.6

812 CLINICAL VALUE OF SERUM ANGIOGENIC GROWTH FACTORS IN CHILDREN WITH ACUTE PANCREATITIS TREATED WITH ENTERAL NUTRITION THERAPY

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Background: Enteral nutrition therapy (EN) is an effective method of treatment in acute pancreatitis (AP) in children. The mechanism of action of this method of treatment is not completely clear to date and it is not only related to improvement in the nutritional status of the patient, but also its strong anti-inflammatory activity. Angiogenic growth factors, such as transforming growth factor beta-1 (TGF-beta-1), vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), play an important role in the early stage of inflammation, stimulating angiogenesis and healing processes in the inflamed tissues.

Aim: The aim of our study was to assess the influence of EN on serum TGF-beta-1, VEGF and FGF concentrations in children with AP and their relation to the clinical course of the disease.

Materials and Methods: There were 15 children with AP (7 boys, 8 girls, mean age: 12.9 yrs, range: 5.5 – 17 yrs.) and 15 healthy controls (C) enrolled in the study. All AP patients were treated with EN carrying 100% of daily requirements, through a naso-gastric/duodenal tube, 24 hours a day for 4 weeks using a semi-elemental, fiber-free diet. Serum TGF-beta-1, VEGF and FGF concentrations were assessed at baseline and after 2 and 4 weeks of EN in the AP group and once in the C group, using ELISA immunoassays (R and D Systems, USA). Statistical analysis was performed with Statistica 10 software (StatSoft, USA) using the Mann-Whitney U test, Wilcoxon signed rank test and Spearman's correlation rank test. $P < 0.05$ was considered statistically significant.

Results: We found decreased serum TGF-beta-1 in the AP group at baseline compared to the C group (17.7 v. 27.8 ng/mL, respectively, $p < 0.05$), increased VEGF concentrations (512.8 v. 267.0 pg/mL, $p < 0.05$) and comparable FGF concentrations (254.4 v. 276.8 ng/mL, $p = \text{NS}$). After 2 and 4 weeks of EN, we observed an increase of serum TGF-beta-1 (26.6 and 27.2 ng/mL, respectively, $p < 0.05$), maintained increased in VEGF concentrations (592.8 and 467.5 pg/mL, $p < 0.05$) and a decrease of FGF (142.7 and 71.7 ng/mL, $p < 0.05$). During the entire 4-week period, VEGF correlated with serum amylase (R -0.9, $p < 0.05$), but not to CRP and clinical symptoms. TGF-beta-1 and VEGF correlated with ultrasound severity of inflammatory lesions (R 0.82, $p < 0.05$), but not to CT severity index (Balthazar score) after 4 weeks of EN.

Conclusions: Differences among serum TGF-beta-1, VEGF and FGF concentrations during EN in children with AP reflect different influences of EN on angiogenic growth factor secretion. Correlation of TGF-beta-1 and VEGF with amylase levels and ultrasound scores may indicate their contribution in healing processes in AP and potentially may be used in clinical practice.

813 FREQUENCY OF INTOLERANCE TO CARBOHYDRATES AND DIABETES MELLITUS IN PATIENTS WITH CYSTIC FIBROSIS SEEN AT THE HOSPITAL DE PEDIATRIA CMNO IMSS

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Introduction: Cystic Fibrosis-Related Diabetes (CFRD) is a common comorbidity of this latter pathology and is associated with a higher mortality rate. Diagnosis is confirmed by a glucose tolerance curve. According to clinical practice guidelines, annual screening should begin at 10 years of age, while other authors suggest initiating screening at the age of 6 years.

Objectives: To determine the frequency of intolerance to carbohydrates and diabetes in patients with cystic fibrosis (CF) seen at the High-Specialty Medical Unit (UMAE) of the Mexican Institute of Social Security's Centro Médico Nacional de Occidente (IMSS CMNO) Pediatric Hospital.

Materials and Methods: Descriptive transversal study of patients aged >6 years with a diagnosis of CF. Weight and height measurements were taken, determining percentiles and Z-scores according to World Health Organization (WHO) criteria. Analysis of CFRD was carried out by means of a glucose tolerance curve.

Results: Thirty patients were studied, all with normal fasting glycemia. At 120 mins, one patient was found with carbohydrate intolerance (3.3%), in addition to two patients with a previous diagnosis of diabetes (6.7%). The three patients who exhibited alterations were >10 years of age. The nutritive state was evaluated, finding that 10% had moderate malnutrition and 5% severe malnutrition. On comparing the nutritive state of patients with alterations in carbohydrates with patients demonstrating normal glucose tolerance curves, it was found that the nutritive state is not a statistical variable that intervenes in the behavior of the glucose.

Conclusions: Ten percent prevalence was found of CFRD, coinciding with that reported in the international literature in which numbers ranging from 3 - 9% were reported, as well as its increase according to age. Scrutiny should be used to discard CFRD in all patients with cystic fibrosis.

814 PROFILE OF ACUTE PANCREATITIS IN CHILDREN IN A TERTIARY CARE CENTER IN BANGLADESH

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Background: Acute pancreatitis (AP) is an acute inflammatory condition of the pancreas that may extend to local and distant extrapancreatic tissues. The incidence of AP in children has increased significantly over the past two decades. It should be considered in every child with unexplained acute abdominal pain.

Objectives: To observe the clinical, biochemical and imaging profiles of AP in children.

Methods: This was a cross-sectional study conducted at the Department of Pediatric Gastroenterology & Nutrition of Bangabandhu Sheikh Mujib Medical University, Dhaka, from January 2014 through June 2015. A total of 50 cases of AP were included in this study. The diagnosis of AP was based on diagnostic criteria made by the INSPPIRE group (i.e., if a child has any 2 of the 3 criteria: abdominal pain compatible with AP, elevated serum amylase and/or lipase level more than three times the upper limit of normal, or imaging findings compatible with AP). Clinical characteristics, laboratory and imaging profile of the cases, etiologies, complications and hospital management were studied.

Results: Among 50 cases, 46% were males and the male:female ratio was 0.8:1. Mean age at presentation was 10.2 ± 3.2 years. Forty-eight (96%) patients had abdominal pain, which was severe agonizing in 81.3% of cases. Pain was commonly located in the epigastric region (77%) and radiating to the back in 22.9% of patients. Vomiting was present in 72% of patients followed by fever (30%). Two (4%) patients had jaundice, ascites were noted in 12% of patients and abdominal mass in 6% of patients. The etiologies of AP in these children were idiopathic (82%), biliary sludge (6%), biliary ascariasis (4%), gallbladder stone (2%), choledochal cyst (2%) and Wilson disease (4%). Laboratory tests revealed high serum amylase and lipase levels in 56% and 58% of patients, respectively. Moderate negative correlation was observed between serum amylase level and day of presentation, but in the case of serum lipase level, moderate positive correlation was found from the 1st to 5th day of presentation and then from the 6th to 14th day of presentation, strong negative correlation was found. Positive findings in ultrasonogram was present in 66% patients. In the present study, hypocalcemia was found in 38% of patients, SIRS in 28%, pseudocyst in 6% and pancreatic necrosis in 2%. Mean duration of hospital stay was 7.92 ± 4.6 days.

Conclusion: In the present study, abdominal pain was the most common clinical presentation in children with AP and the common location of pain was the epigastric region. The cause of AP was unknown in most cases. For confirmation of clinically diagnosed pancreatitis, both serum amylase, lipase level and abdominal ultrasound were found to be useful tools. In the study, only a small percentage of patients developed complications.

815 ROLE OF ENDOSCOPIC ULTRASOUND IN IDIOPATHIC ACUTE PANCREATITIS IN CHILDREN

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Acute pancreatitis (AP) is a result of inflammation of the pancreas without any previous morphological changes on imaging studies. Alcohol and gallstone disease are the most common causes of AP in adults. Other etiologic factors should be considered in children, including trauma, infections, genetic mutations, medications and congenital anomalies. Trans-abdominal ultrasound (US), contrast-enhanced computed tomography scan (CECT) of the abdomen and magnetic resonance cholangiopancreatography (MRCP) are the routinely-used imaging studies in the evaluation of severity and cause of AP. Despite a thorough diagnostic work-up, in a variable proportion of patients (2 - 30%) a definitive cause cannot be established and they are considered as idiopathic acute pancreatitis (IAP). The ease to image the pancreas in close proximity to the probe, non-interference of the intestinal gases with image acquisition and availability of high frequency US probes makes endoscopic ultrasound (EUS) a very useful modality to investigate children with IAP. The aim of our study was to retrospectively report our experience with EUS in investigating children with IAP.

Forty patients (27 males; age range: 9 - 19 years) of IAP with no underlying cause identified after work-up that included labs, genetic work-up and radiology, including US, CECT and MRCP, were studied. Twenty-one (52.5%) of the patients had biliary tract disease (cholelithiasis in 3, gallbladder sludge in 13 [with microlithiasis in 8], choledocholithiasis in 1 and common bile duct sludge in 3 patients) and one had an 8-mm tumor (pseudopapillary tumor) in the head of pancreas and pancreas divisum. No underlying cause could be found in 13 (32.5%) patients. Five patients had features of chronic pancreatitis (CP) and the remaining had a normal pancreas. Of the patients who had biliary tract disease (cholelithiasis in 3, gallbladder sludge in 13, choledocholithiasis in 1 and common bile duct sludge in 3 patients). One each had an 8-mm tumor in the head of pancreas and pancreas divisum. No underlying cause could be found in 18 (45%) patients. Nine patients had features of chronic pancreatitis (CP) and the remaining had a normal pancreas.

Occult biliary pathology is the predominant cause of IAP. 9 (22.5%) of the cases without identified etiology already had underlying CP. EUS is a very important tool in evaluating children with IAP and less invasive than ERCP.

816 PANCREAS DIVISUM IN PEDIATRIC ACUTE RECURRENT AND CHRONIC PANCREATITIS

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Introduction: Pancreas divisum (PD) is the most common congenital anomaly of the pancreas (5 - 10% of autopsy studies). The clinical significance of PD is debated, but a higher frequency of PD in adults with idiopathic pancreatitis (up to 40%) suggests a potential association. No large pediatric studies have evaluated the significance of PD in children associated with pancreatitis.

Objective: To determine the frequency and association of PD and patient characteristics in the well-phenotyped INSPPIRE (International Study group of Pediatric Pancreatitis: In search for a cuRE) cohort.

Methods: Demographic and clinical information of children with acute recurrent pancreatitis (ARP) and chronic pancreatitis (CP) 19 years of age at the time of enrollment were entered into the REDCap database at sixteen pediatric centers. Presence of PD was confirmed with magnetic retrograde cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), or both. Differences between children with or without PD were analyzed using two-sample t-tests or Wilcoxon rank sum test for the continuous variables, and Pearson Chi-square or Fisher's exact test for categorical variables.

Results: Of 288 registry subjects, PD was found in 39 (13.5%). Females were more likely to have PD (72% with PD v. 53% without PD, $p=0.025$). Children with PD were not different in ethnicity, age at first presentation of acute pancreatitis (AP) or CP, or time from the diagnosis of first AP to CP. Medical, endoscopic and surgical interventions were similar between children with or without PD. The frequency of PD was not different in those with SPINK1, CFTR, or CTRC mutations or with other obstructive, and/or toxic-metabolic risk factors. INSPPIRE children with PD were less likely to have a family history of pancreatitis ($p<0.05$) and had a lower rate of PRSS1 mutations (10% with PD v. 36% without PD; $p=0.004$). Although PD did not have any impact on the frequency or pattern of the abdominal pain or school attendance, children with PD reported a higher number of lifelong emergency room visits and hospitalizations ($p=0.042$ and 0.021 , respectively) compared with non-PD. Finally, children with PD were less likely to be exocrine pancreatic insufficient ($p=0.032$).

Conclusion: The frequency of PD was only slightly higher in the INSPPIRE cohort compared with reported rates in the general population. Presence of PD did not seem to be associated with genetic mutations to influence the risk of pediatric pancreatic disease. Even though children in our cohort with ARP and CP with PD had more ER visits and hospitalizations over their lifetime than children without PD, PD did not appear to have a major impact on the risk for pancreatitis or disease progression in childhood.

Friday, October 7, 2016

CONCURRENT SESSION IV 2:00 PM

INFLAMMATORY BOWEL DISEASE

817 TRENDS IN EPIDEMIOLOGY OF PEDIATRIC INFLAMMATORY BOWEL DISEASE IN CANADA: DISTRIBUTED NETWORK ANALYSIS OF MULTIPLE POPULATION-BASED PROVINCIAL HEALTH ADMINISTRATIVE DATABASES: THE CANADIAN GASTROINTESTINAL EPIDEMIOLOGY CONSORTIUM (CANGIEC)

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Background: The incidence of pediatric inflammatory bowel disease (PIBD) is increasing worldwide, and Canada has among the highest rates. Provincial, population-based, health administrative data can be used to determine national Canadian disease rates and compare regional trends in epidemiology.

Aims: To determine the incidence and prevalence of PIBD in Canada and assess trends over time.

Methods: We used validated algorithms to identify children <16 years diagnosed with IBD from administrative data in 5 provinces: Alberta (AB) 1999 - 2008, Manitoba (MB) 1999 - 2010, Nova Scotia (NS) 2000 - 2008, Ontario (ON) 1999 - 2010 and Quebec (QC) 1999 - 2008.

These algorithms consisted of combinations of outpatient, hospitalization and procedural codes to accurately distinguish IBD cases from the rest of the population. A distributed network analysis using standardized methodology was applied to each Canadian province's health administrative data to produce estimates of incidence and prevalence in each province. Sex- and age-standardized annual prevalence and incidence per 100,000 population were determined for each province in which data were available, with corresponding 95% confidence intervals (CI) based on Gamma distribution and reported as annual percentage change (APC). To produce national estimates of incidence and prevalence, standardized estimates and trends were then combined by meta-analysis using random-effects models' analysis to account for heterogeneity.

Results: A total of 5214 incident cases and 6554 prevalent cases were included in the study. For the full study period, the overall standardized incidence for all provinces was 9.7 (95% CI, 9.1 to 10.2) per 100,000. Overall pooled incidence per 100,000 children changed from 7.9 (95% CI, 6.4 to 9.4) in 1999 to 10.6 (95% CI, 8.5 to 12.6) in 2008. While all age groups demonstrated positive incidence rate change, the only statistically significant finding was an increased overall incidence in children 6 months to 5 yrs (APC +7.2%; 95% CI, 2.8 to 11.6%) with no significant heterogeneity among provinces. In this youngest group, incidence did not rise significantly when stratified by CD (APC +3.2%; 95% CI, -3.2 to 9.7%) and UC (APC +5.5%; 95% CI, -0.3% to 11.4%). The overall standardized prevalence for all provinces was 38.2 (95% CI, 35.8 to 40.7) per 100,000 children. IBD prevalence increased by 4.6% (95% CI, 3.7 to 5.4%) per year, CD prevalence increased by 3.9% (95% CI, 1.9 to 5.9%) per year, and UC prevalence increased by 4.4% (95% CI, 1.8 to 6.9%) per year. Time trends analysis demonstrated statistically significantly increased prevalence in all age groups, except adolescents aged 14 - 15.9 yrs.

Conclusions: Canada has among the highest incidence of PIBD in the world. While the incidence of IBD has stabilized in children over the age of 5 years, the incidence is rising rapidly in children under 5 years old. The increasingly early age of onset implies early life environmental triggers in at-risk patients.

Table 1. Standardized incidence and prevalence over the full study period based on pooled meta-analysis of annual estimates

	Alberta	Manitoba	Nova Scotia	Ontario	Quebec	Pooled All Provinces
Incidence						
IBD						
Number of cases	655	221	236	2656	1437	5214
Incidence per 100,000 (95% CI)	9.71 (8.81 to 10.62)	7.22 (6.18 to 8.26)	15.18 (13.1 to 17.25)	9.28 (8.22 to 10.34)	10.26 (9.50 to 11.02)	9.68 (9.11 to 10.25)
CD						
Number of cases	386	129	149	1570	1228	3462
Incidence per 100,000 (95% CI)	5.89 (5.30 to 6.48)	4.17 (3.36 to 4.97)	9.34 (7.69 to 11.00)	5.48 (4.91 to 6.04)	8.8 (8.15 to 9.45)	6.47 (5.91 to 7.04)
UC						
Number of cases	192	92	73	902	123	1382
Incidence per 100,000 (95% CI)	2.67 (2.13 to 3.21)	2.77 (2.02 to 3.51)	4.22 (3.03 to 5.41)	3.11 (2.66 to 3.56)	0.99 (0.92 to 1.06)	2.35 (2.09 to 2.61)

	Alberta	Manitoba	Nova Scotia	Ontario	Quebec	Pooled
Prevalence						All Provinces
IBD						
Number of cases (in final year of study period)	360	63	99	1025	547	2088
Prevalence per 100,000 (95% CI)	44.48 (40.87 to 48.08)	24.74 (22.86 to 26.61)	53.79 (49.63 to 57.95)	31.8 (29.18 to 34.42)	44.06 (39.00 to 49.12)	38.25 (35.78 to 40.73)
CD						
Number of cases (in final year of study period)	185	39	62	554	476	1316
Prevalence per 100,000 (95% CI)	26.18 (24.97 to 27.39)	14.05 (12.62 to 15.48)	37.85 (34.66 to 41.05)	17.67 (16.27 to 19.07)	37.5 (33.19 to 41.81)	25.47 (22.85 to 28.09)
UC						
Number of cases (in final year of study period)	110	24	32	380	58	604
Prevalence per 100,000 (95% CI)	12.92 (10.86 to 14.97)	10.58 (9.33 to 11.83)	13.59 (10.63 to 16.55)	12.04 (11.04 to 13.03)	6.22 (5.49 to 6.95)	10.7 (9.84 to 11.56)

818 COMPLEX AND DEFINED BACTERIOTHERAPY CAN INHIBIT ACUTE COLITIS IN MICE

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Introduction: Inflammatory bowel disease (IBD) is thought to develop secondary to an uncontrolled immune response against the gut microbiome. Therefore, the disruption of the healthy microbiome may be an important element in disease development. It is hypothesized that the restoration of normal microbiome via fecal microbiota transplantation (FMT) may be therapeutic for IBD. However, the fecal microbiome is highly complex and dynamic, leading to substantial difficulties in deciphering the key therapeutic attributes of FMT. The identification of stable bacterial communities that carry the therapeutic effects of FMT could provide a more consistent and testable bacteriotherapy for IBD.

Importantly, a bacterial preparation with 10 species has been shown to effectively treat *C. difficile* colitis. Key species in this combination belonged to the *Bacteroides* genus. Our goal was to compare the anti-colitic effects of delivery of a triple-*Bacteroides* combination (*B. ovatus* [BO], *B. vulgatus* [BV], *B. thetaiotaomicron* [BT]), individual strains of *Bacteroides* and FMT in a murine model of acute colitis.

Methods: Experimental colitis was induced in 8 to 12-week old C57BL/6 mice using 3% dextran sulfate sodium (DSS). The mice were simultaneously treated by oral gavage with a 3-*Bacteroides* combination, FMT using stool from healthy donor mice, or autologous FMT (control group). This experiment was then repeated comparing mice treated with 3-*Bacteroides* combination, individual *Bacteroides* species and autologous FMT. Weight loss was monitored as a marker of colitis severity and 16S rRNA gene profiling of fecal and mucosal microbiomes were conducted.

Results: Survival was significantly lower ($p < 0.05$) in the control group (40%) than in the FMT (73%) and 3-*Bacteroides* (100%) groups. Mice receiving 3-*Bacteroides* therapy lost 3.5% of their body weight, significantly less than the control (17.4%, $p < 0.001$) and FMT (9.1%, $p = 0.03$) groups. FMT and control group microbiomes more closely resembled pre-treatment composition than the 3-*Bacteroides* group, with FMT restoring richness and diversity to near-healthy levels. The 3-*Bacteroides* group had the least rich/diverse microbiome. In the 3-*Bacteroides* and

individual strain experiment, all mice receiving bacteriotherapy survived (100%), as compared to only 42% of controls. Mice receiving *B. ovatus* lost 2.7% of their body weight, significantly less ($p < 0.05$) than all other groups (BV 7.8%, BT 6.1%, 3-*Bacteroides* 10%, control 11.2%). Conclusion: FMT from healthy donors, 3-*Bacteroides* combination, and individual strains of *Bacteroides* can reduce weight loss and improve survival during acute colitis in mice. *B. ovatus* therapy was significantly more effective than all other bacteriotherapy in this respect. Restoration of microbial diversity and microbiome structure was not key in conferring survival advantage during chemically-induced colitis. Our findings may have readily applicable relevance for human IBD treatment.

820 EARLY CHANGES IN MICROBIAL COMMUNITY STRUCTURE ARE ASSOCIATED WITH SUSTAINED REMISSION FOLLOWING NUTRITIONAL TREATMENT OF PEDIATRIC CROHN'S DISEASE

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Background: Clinical remission of pediatric Crohn's disease (CD) is achieved in about 80% of children after a 6 - 12-week course of exclusive enteral nutrition (EEN). EEN is associated with marked microbiome changes. After resuming their normal oral diet, 50% of patients experience a disease flare, requiring anti-inflammatory treatment escalation. In this prospective study of EEN, we employ a hierarchical model of microbial community structure to distinguish between pediatric CD patients who achieved sustained remission (SR) and those who relapsed early (non-SR), after restarting a normal diet.

Methods: Fecal samples were obtained from 10 patients (age 10 - 16) and from 5 healthy sibling controls (age 9 - 14). All patients had CD involving the ileum and 8 were newly diagnosed. The microbiota was assessed via 16S rRNA sequencing. In addition to standard measures of microbial biodiversity, we employed Bayesian methods to characterize the hierarchical community structure. Community structure between patients who sustained remission (wPCDAI <12.5) up to their 24-week follow-up (SR) was compared to patients that had not sustained remission (non-SR).

Results: Nine of the ten patients achieved clinical remission by week 12 of EEN therapy, as determined by wPCDAI scores (wPCDAI <12.5). Four of the nine patients who achieved remission experienced a clinical relapse of disease by week 24. Microbial diversity was lower in CD patients relative to controls, and lowest in patients who did not achieve SR. SR patients differed from non-SR patients in terms of the structure and prevalence of their microbial communities. Species diversity decreased among SR samples, whereas it increased among the non-SR samples over the course of EEN treatment. The taxonomic composition of the SR gut microbiota was much more similar to the sibling controls than the non-SR. The SR prevalent community contained a number of strains of *Akkermansia muciniphila* and *Bacteroides* and was limited in *Proteobacteria*, while the non-SR prevalent community had a large *Proteobacteria* component which increased in prevalence over the course of EEN. Their communities were so different that a model, trained to discriminate SR and non-SR, had 80% classification accuracy, already at baseline sampling.

Conclusions: Microbial community structure differs between healthy controls, patients who have an enduring response to EEN and those who relapse early upon introduction of normal diet. Our novel Bayesian approach to these differences is able to predict sustained remission following EEN.

821 VITAMIN D STATUS IN NEWLY DIAGNOSED PEDIATRIC ULCERATIVE COLITIS AND RACIAL DIFFERENCES DETERMINED BY GENETIC POLYMORPHISMS: RESULTS FROM THE PROTECT STUDY

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Background: Vitamin D has been demonstrated to affect epithelial tight junctions in the gut and to play an important role in both innate and adaptive immunity. Vitamin D deficiency is commonly observed in patients with ulcerative colitis (UC), especially African Americans (AA), and commonly leads to oral vitamin D supplementation. Total vitamin D includes albumin-bound, vitamin D-binding protein (VDBP), bound, and free vitamin D, with the albumin-bound and free fractions considered bioavailable to target tissues. Low vitamin D in UC may be in part due to protein loss, including albumin and VDBP. Racial differences in vitamin D may be related to low VDBP associated with specific genetic polymorphisms. AA patients typically have lower total vitamin D and lower VDBP; however, a recent report using calculated values suggested that free vitamin D levels are comparable in healthy adult Caucasians and AAs.

Aim: To examine the relationship of directly measured total and free vitamin D levels, VDBP and its genetic polymorphisms in children newly diagnosed with UC.

Methods: The PROTECT (Predicting Response to Standardized Pediatric Colitis Therapy) study enrolled children ≤ 17 years newly diagnosed with UC by standardized criteria. Total 25-OH vitamin D, free vitamin D, and VDBP were measured on stored serum. Two known genetic polymorphisms (rs7041, rs4588) were measured by the UK Biobank Axiom Array.

Results: Data were available for 350 subjects, mean age 12.9 years, 49% female, 8% AA, 83% extensive/pancolitis. The median (IQR) total vitamin D was 28.8 (24.2 - 35.3) ng/mL. The prevalence of vitamin D deficiency (<20 ng/mL) was 10% while the prevalence of vitamin D insufficiency (20 ng/mL - 30 ng/mL) was 44%. Comparing AA (n=27) subjects to Caucasian subjects (n=323), median (IQR) total 25-OH vitamin D was lower in AA subjects at 23.9 (20.0 - 28.4) ng/mL compared to Caucasian subjects with a median (IQR) total vitamin D of 29.4 (24.8 - 35.6) ng/mL. Free vitamin D was also significantly lower in AA subjects compared to Caucasians (3.1 [2.0 - 3.5] pg/mL vs. 4.3 [3.1 - 6.1] pg/mL, $p=0.001$). VDBP was lower in AA subjects than Caucasian subjects. Analysis of 2 known single nucleotide polymorphisms in vitamin D binding protein demonstrated a significant difference between Caucasian and AAs in VDBP genotype and VDBP genotype correlated

with measured VDBP. AAs were more likely to demonstrate Gc1F VDBP phenotype while Caucasians were more likely to demonstrate Gc1S VDBP phenotype.

Conclusions: Vitamin D deficiency and insufficiency are highly prevalent in children with newly diagnosed ulcerative colitis. VDBP concentration was driven by two well-known, single nucleotide polymorphisms and these polymorphisms and VDBP phenotype differed according to race, as has been described in the literature. AA subjects demonstrated a lower total 25-OH vitamin D and a lower vitamin D binding protein and a lower free vitamin D when compared to Caucasians.

Characteristic	Total Population ^a (n=350)	Caucasian (n=323)	African American (n=27)	P-value ^b
Age (years), Mean ± SD	12.9 ± 3.2	13.0 ± 3.2	12.7 ± 3.3	0.7
Female, N (%)	172 (49%)	159 (49%)	13 (48%)	0.91
Disease Location, N (%)				0.06
Proctosigmoiditis	20 (6%)	20 (6%)	0 (0%)	
Left-sided colitis	40 (11%)	39 (12%)	1 (4%)	
Extensive/Pancolitis/ Unassessable	290 (83%)	264 (82%)	26 (96%)	
Albumin (g/dL)	348	321	27	
Median (IQR)	3.8 (3.2, 4.2)	3.8 (3.2, 4.2)	3.5 (3.2, 3.9)	0.05
≥3.5 g/dL	232 (67%)	217 (68%)	15 (56%)	0.2
Total Vitamin D (ng/mL)				
Median (IQR)	28.8 (24.2, 35.3)	29.4 (24.8, 35.6)	23.9 (20.0, 28.4)	0.001
Vitamin D <20	36 (10%)	31 (10%)	5 (19%)	0.01
Vitamin D 20 - <30	155 (44%)	139 (43%)	16 (59%)	
Vitamin D ≥30	159 (45%)	153 (47%)	6 (22%)	
Vitamin D Binding Protein(µg/mL)	335	309	26	
Median (IQR)	176.2 (131.5, 228.4)	181.7 (144.1, 239.5)	70 (51.1, 105.8)	<.001
Free Vitamin D (pg/mL)	339	314	25	
Median (IQR)	4.2 (3.0, 5.9)	4.3 (3.1, 6.1)	3.1 (2.0, 3.5)	0.001
VDBP Genotype (Phenotype) (rs7041/rs4588)	345	320	25	<.001
TT/CC (Gc1F)	18 (5%)	6 (2%)	12 (48%)	
GT/AA	60 (17%)	53 (17%)	7 (28%)	
GG/CC (Gc1S)	101 (29%)	101 (32%)	0 (0%)	
TT/CA	33 (10%)	27 (8%)	6 (24%)	
GT/CA	110 (32%)	110 (34%)	0 (0%)	
TT/AA (Gc2)	23 (7%)	23 (7%)	0 (0%)	

^a There were 350 participants who were Caucasian or African American with a measured vitamin D

822 NOD2 PROTECTS THE INTESTINE REMOTE FROM LOCAL GUT INJURY

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Background/Aims: NOD2 mutations are risk factors for Crohn's disease (CD). Nod2 plays a crucial role in intestinal mucosa homeostasis by controlling the innate and adaptive immunities and gut epithelial permeability, but its role in non-inflammatory areas remains poorly understood.

Methods: Nod2 expression was determined in uninflamed areas from CD patients. Trinitrobenzene sulfate (TNBS)-induced proctitis was performed in wild-type and Nod2 deficient mice to determine the impact of Nod2 remote to gut injury. Bone marrow transplantation experiments were used to dissect the role of Nod2 in hematopoietic and epithelial compartments.

Results: In CD patients, NOD2 over-expression was observed in epithelial cells far away from inflamed areas. Nod2 expression was also increased in the small bowel of wild-type mice with proctitis. Nod2 overexpression was associated with higher cytokine levels and paracellular permeability remote to gut injury. CD4+ T-cell depletion or MLCK inhibition reduced this effect. In contrast to wild-type controls, Nod2 knock-out/mutated mice developed a duodenitis and an ileitis after TNBS-induced proctitis. The development of inflammatory lesions remote to gut

injury was related to Nod2 deficiency in the hematopoietic compartment, but Nod2 stimulation of non-hematopoietic cells reduced the increase of permeability, despite high cytokine levels in the small bowel.

Conclusions: Nod2 is a gatekeeper of inflammation all along the digestive tract and Nod2 deficiency may explain the extension of skip inflammatory lesions far from the initial mucosal injury in CD.

Friday, October 7, 2016

CONCURRENT SESSION IV

2:00 PM

PANCREATOLOGY AND CYSTIC FIBROSIS

PANCREAS PRIZE

823 IMPACT OF OBESITY ON PEDIATRIC ACUTE RECURRENT AND CHRONIC PANCREATITIS

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Introduction: Obesity is associated with a heightened inflammatory response in acute pancreatitis and serves as a prognostic factor for disease severity and outcome in adults. It is not known whether obesity has an impact on the progression and severity of pediatric pancreatitis.

Objective: To study the impact of obesity on pediatric pancreatic disease characteristics in the well-phenotyped INSPPIRE (INternational Study group of Pediatric Pancreatitis: In search for a cuRE) cohort.

Methods: Demographic and clinical information from children with acute recurrent pancreatitis (ARP, n=186) and chronic pancreatitis (CP, n=187) ≤19 years of age at the time of enrollment were entered into REDCap database at sixteen pediatric centers. CDC growth charts and pediatric age- and gender-specific BMI were used to determine children who were underweight (<5th percentile), of normal weight (5th - <85th percentile), overweight (85th - <95th percentile), or obese (>95th percentile). Categorical variables were analyzed using the Cochran-Armitage trend test to examine whether prevalence of findings increased/decreased with BMI. The Jonckheere-Terpstra test was used to assess the association between BMI and levels of pain and missed school days.

Results: Of 373 registry subjects, 17 (4.5%) were underweight, 221 normal weight (66%), 57 (15%) overweight and 78 obese (23%). The groups were not different in gender, race, age at first presentation of acute pancreatitis (AP) or CP, or time from the diagnosis of first AP to CP. Obese children were more likely to be of Hispanic ethnicity (p 0.004) and less likely to have CP (p 0.028), with imaging studies showing acute inflammatory changes (p <0.0001) rather than chronic duct damage (p 0.038). Genetic, obstructive and toxic metabolic risk factors were distributed equally among the groups, except SPINK1 mutations were less common and hypertriglyceridemia was found almost exclusively in overweight and obese patients (p 0.013 and p =0.021, respectively). BMI had no impact on the frequency or pattern of abdominal pain, school attendance, emergency room visits, or hospitalizations. Obese children were less likely to undergo medical or endoscopic interventions and total pancreatectomy and islet autotransplantation compared to other groups (p 0.012, 0.022 and 0.012, respectively). Finally, overweight and obese children were less likely to be exocrine pancreatic-insufficient (p 0.004).

Conclusion: Obese children with recurrent pancreatitis seem to have a proinflammatory rather than a profibrotic phenotype. The impact of obesity as risk factor on pediatric disease progression and severity needs to be further investigated.

Supported by NIH R21 DK096327, U01 DK108334, CTSA 2UL1 TR000442 and REDCap

824 PROGRESSION OF ACUTE PANCREATITIS TO ACUTE RECURRENT PANCREATITIS IN THE PEDIATRIC POPULATION: A SINGLE-CENTER. PROSPECTIVE DATABASE REPORT

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Background: Acute pancreatitis (AP) in the pediatric population remains poorly understood with a rising incidence to a rate of 1/10,000. Research is lacking on AP natural history and factors influencing progression of disease. Previous studies in AP are single-centered and retrospective in nature. Therefore, it is difficult to predict which AP patients are at greater risk for advancement to acute recurrent pancreatitis (ARP). We designed a novel database and registry to prospectively study initial and recurrent AP attacks to gain better insight into pediatric AP.

Objective: We aimed to study the progression from AP as a first episode to ARP using our comprehensive prospective database.

Methods: Patients admitted to Cincinnati Children's Hospital Medical Center with AP or evaluated at our outpatient Pancreas Care Center for pancreatitis were identified and consented for inclusion in our IRB-approved database. We have thus far enrolled 85 patients beginning from May 2013. A total of 83 patients had a minimum of 3 months' follow-up. Physician surveys were entered in REDCap (Research Electronic Data Capture). Data entered included laboratory and imaging findings, family history, risk factors, management and interventions, as well as the clinical course and outcomes. Data from patients who developed ARP (a second attack at least one month after the first with resolution of symptoms in between) during follow-up were entered in a separate database to assess factors, such as time to ARP diagnosis, genetic testing, and chronic symptoms.

Results: As of April 2016, 17 of the 85 (20%) AP patients have been diagnosed with ARP. The most common etiologies for the first AP attack were unknown (33%), toxic/drug (19%), viral/systemic (18%), gallstone/biliary (18%) and trauma (9%). Thirteen of 17 patients with ARP (76%) had their second AP attack within five months and 11 of 17 (65%) patients with ARP had their second attack within three months of the first attack. To identify factors associated with rapid recurrence, patients who progressed to ARP within 3 months (n=11) were compared to patients who had only a single attack with at least 3 months of follow-up (n=72). A univariate analysis of clinical and laboratory characteristics between the two groups showed that the weight percentile for age was significantly higher in the rapid progression group (p =0.03). The presence of pancreatic necrosis during the first AP attack significantly differed between the two groups, 2/11 cases (18%) in the rapid progression versus no cases in the no progression group (p =0.02).

Conclusions: From 2013, our institutional database contains information on the initial presentation and outcomes of pediatric AP and progression to ARP. A higher weight percentile for age and the occurrence of pancreatic necrosis during the first AP attack were associated with a rapid progression to ARP within 3 months. Future studies are needed to better understand factors that lead to pediatric ARP progression.

825 CLINICAL PROFILE AND LONG-TERM OUTCOME OF ACUTE, RECURRENT PANCREATITIS IN CHILDREN: SINGLE-CENTER EXPERIENCE OF 93 CASES

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Background/Aims: Overall, there is scarcity of published data on acute recurrent pancreatitis (ARP) in children and not much information available about its long-term outcome. Hence, we analyzed our experience of ARP to look at its clinical profile and long-term outcome.

Methods: From January 2003 to December 2015, consecutive children (≤ 18 years of age) diagnosed with ARP were included in this study. ARP was defined as two or more distinct episodes of acute pancreatitis (AP) along with complete resolution of pain (≥ 1 -month pain-free interval between the diagnosis of AP) or complete normalization of serum pancreatic enzyme levels along with complete resolution of pain irrespective of specific time interval between AP episodes. Baseline magnetic resonance cholangiopancreatography (MRCP) was done in all cases to detect structural causes of ARP and also to rule out the presence of chronic pancreatitis (CP). Serum calcium, lipid profile, blood sugar and stool fat (Sudan stain) were done in all cases. Follow-up repeat MRCP was done if there was persistence or recurrence of symptoms to detect changes of CP. Genetic markers (PRSS1, SPINK1 and CFTR) were studied in a group of 22 idiopathic ARP cases.

Results: During the study period, a total of 373 cases of pancreatitis were managed in our center; 169 (45%) were AP, 111 (30%) CP and 93 (25%) ARP. The median age of ARP cases was 13 (range, 4 - 18) years with a male:female ratio of 53:40. The median number of episodes prior to presentation was 3 (range, 2 - 12) and the duration of symptoms was 12 (range, 1 - 132) months. The etiology included biliary 14 (15%; choledochal cyst 11, gallstones 3), pancreas divisum 6 (7%), other 3 (3.5%; hereditary 1, duodenal diverticulum 1, drug 1) and the remaining 70 (75%) were idiopathic. Heterozygous SPINK1 mutation was found in 10 of 22 (45%) cases of idiopathic ARP and none were found to have PRSS1 or CFTR mutations. Five children were lost to follow-up and over a median follow-up period of 30 (range, 3 - 144) months, 37 of 88 (42%) developed CP. On multivariate analysis, idiopathic etiology (34 of 70 vs. 3 of 23, $p < 0.03$), presence of SPINK1 mutations ($p < 0.01$) and longer duration of follow-up (51.4 ± 31.2 vs. 20.7 ± 22.0 months, $p < 0.001$) were found to be associated with progression from ARP to CP.

Conclusions: A quarter of all pancreatitis in children is due to ARP. Though the majority are due to idiopathic causes, structural causes need to be ruled out in all cases as they are responsible for the bulk of known causes of ARP. On follow-up, almost half of them progress to CP.

Idiopathic etiology, presence of genetic mutations and longer follow-up duration are associated with progression. Hence, all ARP, especially idiopathic should be kept on follow-up to detect CP.

826 STUDY ON GENETIC SUSCEPTIBILITY AND CLINICAL FEATURES IN CHINESE CHILDREN WITH CHRONIC PANCREATITIS

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Objectives: To date, there are few studies in pediatric chronic pancreatitis (CP) in China. It is necessary to discover clinical features and genetic variations in Chinese children with CP, because of the differences in race, geography and culture between foreigners and the Chinese. In addition, endoscopic retrograde cholangiopancreatography (ERCP) was applied in children with CP. The outcomes of ERCP on pediatric CP still need further study.

Methods: We did a retrospective study on clinical features in 94 CP children. Additionally, genomic DNA was extracted from peripheral white blood cells in 56 CP and 13 recurrent acute pancreatitis (RAP) children. We used Illumina Miseq platform and sequenced exons and flanking sequences of the following 11 genes: PRSS1, SPINK1, CFTR, CTSC, PRSS2, CASR, CTSB, KRT8, CLDN2, CPA1 and ATP8B1. Finally, we did an analysis of types of operation, findings of ERCP and complications in patients who have received ERCP.

Results: Among 94 children with CP, the main etiological factors were idiopathic (61) and anomalies in anatomy (25). Of the patients, 93 had suffered abdominal pain, most pain attacks (93.3%) were moderate-to-severe. In the last 6 months, the median number of emergency department visits was 2, the median duration of hospitalization was 29 days, the median duration absenteeism was 30 days and the median of duration of symptoms prior to diagnosis was 6 months. Weight standard score (SDS), BMI SDS and insulin-like growth factor 1 SDS in children with CP were lower than normal. After applying NGS among 69 patients with CP and RAP, there were 45 children harboring pathological SNVs associated with pancreatitis in the following genes: PRSS1, SPINK1, CFTR, CASR, CTSB, CTSC and KRT8. Mutations in SPINK1 could increase the risk of pancreatic intraductal stones (OR 11.07, $p = 0.003$). 204 ERCPs were performed on 129 pediatric patients older than 1 year of age. The success rate of ERCPs in our center was 99.5%. There were 157 ERCPs in 84 pediatric CP. Common complications of ERCP were hyperamylasemia (58 cases) and post-operation pancreatitis (35 cases). However, 5 patients suffered gastrointestinal bleeding. When hyperamylasemia was excluded, the total complication rate was 31.7%. There was a lower risk of post-operation pancreatitis in patients who had two or more ERCPs (OR 0.171, $p = 0.001$).

Conclusions: The common etiological factors in Chinese pediatric CP were idiopathic and anomalies in anatomy. When compared to normal children, CP patients had a lower weight SDS and BMI SDS. Mutations in PRSS1, SPINK1 and CFTR were common causes in idiopathic CP. Mutations in SPINK1 could increase the risk of pancreatic duct stones. There was a high success rate of ERCP in pediatric patients older than 1 year of age. ERCP was a good fit for CP treatment. After ERCP, a higher complication rate was observed, especially in pancreatitis.

Friday, October 7, 2016

**CONCURRENT SESSION IV
2:00 PM**

TRANSPLANTATION

827 CHANGES IN GUT MICROBIOTA IN RECIPIENTS OF SMALL BOWEL TRANSPLANT

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Objectives: Small bowel transplantation (SBT) is a life-saving procedure for patients without sufficient bowel length to absorb enough nutrients to survive. However, the role of the microbiota in these severely immune-suppressed individuals is unknown. The aim of this study was to investigate the changes of gut microbiota in SBT patients.

Materials and Methods: SBT patients without obvious sepsis, weaning from parenteral nutrition (PN) and with normal oral intake were enrolled in this study. These SBT patients received oral probiotics (*Clostridium butyricum* MIYAIRI 588, 1.5×10^9 CFU/day) for 1 month. Fecal samples were collected for analysis of microbiota before, 1 week and 1 month after oral probiotic therapy. DNA was isolated from fecal samples. After DNA isolation, 16S rRNA genes were amplified by PCR using primers for region V1-V3. Next-generation sequencing (NGS) methods were used to analyze the microbiota. We used linear mixed model to compare the changes of microbiota before and after probiotic treatment.

Results: Eighteen samples were obtained from 6 SBT recipients before and after probiotic treatment. These SBT patients had no obvious sepsis and no rejection during this period. Upon analysis based on the family level, SBT patients before probiotic treatment had a higher proportion of *Enterobacteriaceae* (mean proportion 63.57%). After probiotic treatment, the proportions of family *Bifidobacteriaceae*, *Bacteroidaceae*, *Lactobacillaceae* and *Clostridiaceae* were significantly increased ($p < 0.001$), while those of the family *Enterobacteriaceae* were significantly decreased ($p < 0.001$).

Conclusions: In conclusion, the findings obtained during this study suggest that probiotic (*Clostridium butyricum* MIYAIRI 588) treatment is associated with changes of the microbial populations in SBT patients. Therapy with probiotics by replenishing bacterial groups could potentially be used to correct specific deficiencies of protective bacteria in SBT patients.

828 HEPATOCYTE-LIKE CELLS OF STEM CELLS FROM HUMAN EXFOLIATED DECIDUOUS TEETH INDUCED LIVER REGENERATION IN LIVER FIBROSIS MODEL MICE

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Background: Stem cells from human exfoliated deciduous teeth (SHED) have been identified as a novel population of mesenchymal stem cells (MSCs) with self-renewal and high proliferation. In our previous study, we showed trans-differentiation capability of SHED into hepatocyte-like cells (SHED-HLC) *in vivo* and their therapeutic potential for liver fibrosis. In this study, we investigated the capability of SHED and SHED-HLC in accelerating liver regeneration in liver fibrosis model mice.

Methods: SHED was cultured under a hepatic differentiation condition stimulated with hepatocyte growth factor, dexamethasone, insulin-transferrin-selenium and oncostatin M for 28 days. C57BL/6J mice were injected by CCl₄ to generate liver fibrosis before transplanted by SHED and SHED-HLC. After transplantation, the transplanted cells were analyzed *in vivo* for their homing at 8 weeks. In addition, we also analyzed CCl₄-injected mice without transplantation and healthy mice as a control group. Mice were sacrificed at 8 weeks and 12 weeks after fibrosis induction and their livers were harvested. To characterize the hepatocytic properties, liver tissue was analyzed by histology, immunohistochemistry using human leukocyte antigen-ABC (HLA-ABC) to evaluate homing of cells, alpha-smooth muscle actin (α -SMA) antibody to evaluate hepatic stellate cell proliferation and proliferating cell nuclear antigen (PCNA) and Ki-67 antibody to evaluate continuing liver regeneration process.

Results: *In vitro* study of SHED hepatic differentiation showed that, at day 28 of induction, SHED cultured showed polygonal and parenchymal-like cells resembling hepatocytes. RT-PCR analysis demonstrated that these cells expressed hepatocyte-specific genes. *In vivo* study showed that transplanted SHED and SHED-HLC homed to recipient liver. Histological analyses at 8 weeks showed PCNA-positive areas were higher in SHED group ($1.0 \pm 0.87\%$; cell count 27.4 ± 14.1 cells/field) and SHED-HLC group ($2.09 \pm 1.6\%$; cell count 94.0 ± 56.4 cells/field), compared to the CCl₄ group ($0.19 \pm 0.27\%$; cell count 6.2 ± 6.4 cells/field) and control groups ($0.23 \pm 0.17\%$; cell count 27.4 ± 14.1 cells/field) and CCl₄ ($1.0 \pm 0.87\%$; cell count 6.0 ± 5.1 cells/field); $p = 0.0006$ (% area) and $p < 0.0001$ (cell count). At 12 weeks, although less PCNA-positive area was shown than at 8 weeks, PCNA-positive area was also found to be higher in SHED and SHED-HLC groups compared to control and CCl₄ groups; $p = 0.021$ (% area) and $p = 0.0002$ (cell count). These findings were supported by Ki-67 analysis, which also showed higher positivity area in SHED and SHED-HLC groups. In addition, transplantation of SHED also showed suppressed liver injury.

Conclusion: This study indicates that transplanted SHED and SHED-HLC in liver fibrosis model mice accelerate liver regeneration and improve hepatic dysfunction, suggesting that SHED might be a promising source for liver regeneration.

Keywords: hepatocyte-like cells, stem cells from human exfoliated deciduous teeth, liver regeneration

829 OUTCOMES OF TOTAL PANCREATECTOMY AND ISLET AUTO TRANSPLANTATION FOR PAINFUL REFRACTORY CHRONIC PANCREATITIS IN YOUNGER CHILDREN

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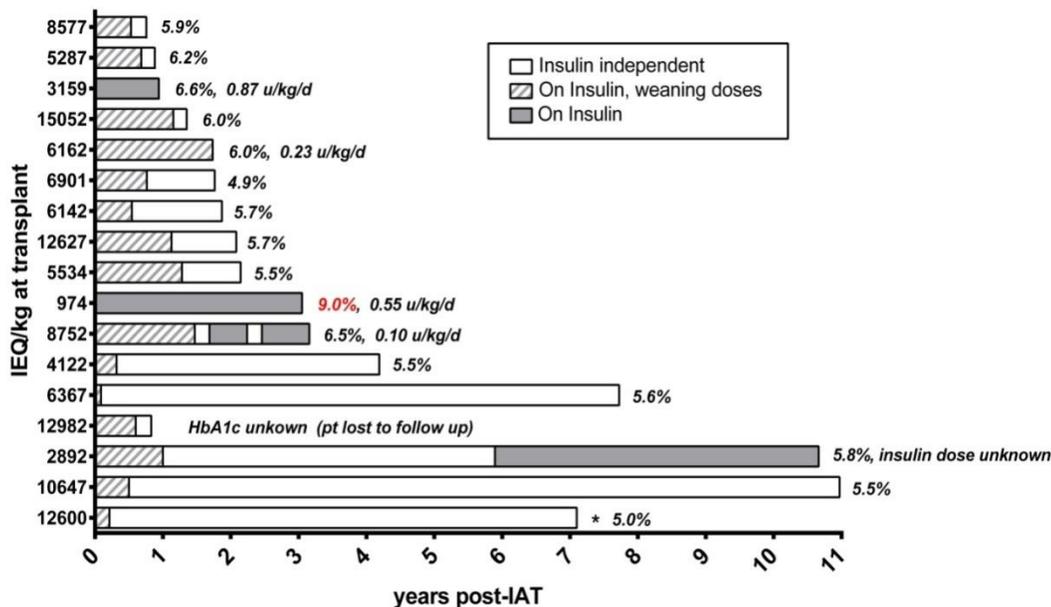
Purpose: Total pancreatectomy and islet auto transplantation (TP-IAT) are increasingly used for treatment of childhood pancreatitis that fails medical, endoscopic and surgical drainage/resection procedures. However, since most of the published case series are in teenagers, centers are often reluctant to offer surgery to younger children due to unknown outcomes. Fear of diabetes and major surgery may prohibit referral of young

children severely impacted by pancreatitis for total pancreatectomy and TP-IAT. With ongoing pain, these children can become narcotic-dependent, miss school and have poor quality of life. Some become TPN- or tube-feed-dependent to prevent precipitation of pancreatitis attacks. We evaluated outcomes in our youngest TP-IAT recipients, aged 3 - 8 years at surgery.

Methods: Among all 106 pediatric TP-IAT recipients at our center, 17 children (9 female), met inclusion criteria of age <8 years at time of surgery. Procedures were performed from 2000 - 2014. Pancreatitis was attributed to genetic mutations in 14/17. TP-IAT recipients were followed prospectively with quality of health questionnaires, including assessments of pain and narcotic use, and laboratory evaluations, including HbA1c and mixed-meal tolerance tests, both preoperatively and at regular intervals thereafter. Median follow-up was 2.2 years (IQR 1.5 - 4.3).

Results: The indication for TP-IAT in all children was painful recurrent or chronic pancreatitis, necessitating daily or intermittent narcotic therapy and repeated hospitalizations, with a median of 14 hospitalizations/patient (IQR 4 - 20). All 17 children had previously documented recurrent acute pancreatitis and all children with imaging available for review had imaging changes of chronic pancreatitis (11/11 with MRCP, 1/1 with endoscopic ultrasound) and histopathology showed chronic pancreatitis in 12/12 cases (pathology not done or inadequate specimen obtained in 5). Median patient weight before surgery was 25.6 kg (IQR 21.1 - 32.0, smallest 15.2 kg). There was no perioperative mortality. Surgical complications requiring re-operation occurred in 4 patients for bowel obstruction (n=2), intraabdominal abscess (n=1) and bile leak (n=1). All had relief of pain and were off narcotics by 6 months post-surgery. Islet graft function is shown in Figure 1. Thirteen (76%) achieved insulin independence (versus 41% in older patients) ($p=0.004$). Median HbA1c after TP-IAT was 5.9% (IQR 5.6 - 6.3%). Quality of life improved in all patients.

Conclusions: Very young children with severe refractory chronic pancreatitis may be good candidates for total pancreatectomy and islet auto transplantation. The majority of these patients experience high rates of pain relief and insulin independence with excellent glycemic control. For young children severely impacted by pancreatitis, early referral for total pancreatectomy and islet autotransplantation should be considered.



830 CHANGES IN HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN PEDIATRIC LIVER TRANSPLANT (LT) RECIPIENTS DURING PROTOCOLIZED IMMUNOSUPPRESSION WITHDRAWAL (ISW): THE iWITH TRIAL

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Chronic immunosuppression is associated with complications which impact quality of life. We hypothesize that HRQOL improves with ISW. To test our hypothesis, we conducted a prospective cohort study of HRQOL in pediatric LT recipients undergoing ISW as part of iWITH (NCT101638559).

Methods: 88 recipients (39 M/49 F; 31/57 living/deceased grafts) at 12 centers met clinical, biochemical and histological eligibility criteria. ISW occurred in 8 steps over 36 - 48 weeks. Tolerance was defined by stable ALT, GGT and histology 1 year after last IS dose, compared to study entry (2 years earlier). HRQOL was measured over 19 subscales using parent proxy and self-reports of the PedsQL™4.0 Generic Core (6 subscales) Scale, Multi-dimensional Fatigue (4 subscales), and transplant module (9 subscales) at baseline (BL) and every 6 months thereafter up to 2 years after initiating ISW. 78 patients attained the two-year point and surveys were received for 72.(92% response). Responses were analyzed using mixed modelling for trends over 24 months. Mean HRQOL scores by tolerance status (29 tolerant; 43 non-tolerant) at 24 months were compared to BL by two-sided t-test with Bonferroni correction.

Results: Over 24 months, of the 38 self- and parent-reported subscales from the entire cohort, seven significantly improved, an additional 25 improved, while none significantly worsened compared to BL. There were six self-reported subscale improvements: total score ($p<0.01$), medication I ($p<0.01$), communication ($p<0.01$), treatment anxiety ($p=0.03$) and worry ($p=0.02$) subscales of the transplant module and the

social functioning subscale of the generic core ($p=0.01$). The only parent-reported subscale to significantly improve was my transplant and others subscale of the transplant module ($p=0.03$). Parent- and self-reported scores did not differ significantly by tolerance status. However, tolerant subjects demonstrated a trend towards improved self- and parent-reported scores from BL in select subscales with moderate effect sizes (≥ 0.50) (Table).

Conclusions: In this preliminary report, pediatric LT recipients undergoing ISW had modest longitudinal improvements in overall HRQOL over the first two years. Tolerant compared to non-tolerant subjects demonstrated a trend towards greater improvement in self- and parent-reported HRQOL scores in several generic and transplant-specific domains. The magnitude and durability of these outcomes requires extended follow-up.

	Sub-Scale		Tolerant (n=29)		Non-Tolerant (n=43)		Effect Size
			Mean \pm SD	Δ from BL	Mean \pm SD	Δ from BL	
Generic Core	Parent	Physical Functioning	92.7 \pm 13.0	6.9	83.3 \pm 19.4	-0.6	0.55
		Social Functioning	90.9 \pm 13.4	5.6	82.0 \pm 18.8	-1.9	0.53
Multi-dimensional Fatigue	Parent	General Fatigue	90.6 \pm 13.0	7.2	79.2 \pm 18.6	0.2	0.69
Transplant	Self	My Transplant and Others	89.4 \pm 11.2	6.1	81.5 \pm 16.6	-0.6	0.54
	Parent		90.0 \pm 15.6	8.7	81.5 \pm 14.9	1.8	0.56

831 A MULTICENTER, PROSPECTIVE STUDY OF FRAILTY IN CHILDREN WITH LIVER DISEASE

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Background: Frailty is a biologic syndrome of decreased physiologic reserve associated with adverse health outcomes in adults, composed of five criteria: shrinkage, fatigue, weakness, slow walking speed and low physical activity. Frailty has been shown to predict mortality in adult liver transplant (LT) candidates independent of severity of liver disease scores. Frailty has not been previously investigated in children. The aim of this study was to adapt the assessment of the 5 classic frailty criteria to evaluate frailty in children with liver disease. We hypothesized that children listed for LT are frail.

Methods: Children aged 5 - 17 years with liver disease underwent frailty assessments at one of 19 participating North American pediatric LT centers. Validated pediatric tools were used to evaluate shrinkage (triceps skinfolds), fatigue (PedsQL 4.0™ Multidimensional Fatigue Scale) and physical activity (modified Physical Activity Questionnaire, PAQ). Grip strength and the 6-minute walk test were used to evaluate weakness and walk speed, respectively, as in adult evaluations. Each item result was compared to age- and gender-norms, and scored 0 (Z-score >-1SD), 1 (Z-score -1 to -2 SD) or 2 (Z-score <-2SD). Higher summed scores (max 10) reflected greater frailty. A subgroup analysis was performed and frailty scores compared between children listed for LT and controls with compensated chronic liver disease.

Results: A total of 71 (35 listed, 36 controls) subjects were included in the analysis. Patient demographics were similar. The most frequent underlying diagnoses were biliary atresia 28% (33% in the listed group) and autoimmune hepatitis 26% (44% in the control group). The median frailty score was 4 (IQR 3 - 3.75). Frailty scores were significantly higher in the listed group with a median of 5 (IQR 4 - 7) than in controls ($p<0.0001$). Frailty scores were a good discriminator between the two groups (AUC 0.82). In a preliminary subgroup analysis of the 34 listed children, for whom PELD (n=19) or MELD-Na (n=16) scores were available, no correlation of frailty scores with MELD-Na (r 0.1748; CI, -0.3654 to 0.6269) or PELD scores (r 0.1759; CI, -0.3156 to 0.5929) was seen. The median time to completion of a full assessment was 60 minutes per patient.

Conclusion: This is the first study describing the frailty phenotype in children. Children with end-stage liver disease listed for LT had significantly higher frailty scores than children with compensated liver disease. Frailty was a good test to discriminate between the two groups. Of note, frailty scores did not correlate with MELD-Na scores, indicating that the frailty evaluation is assessing additional components of ill-health in these children not captured by standard laboratory assessments. Future studies are needed to evaluate frailty in larger cohorts of children with liver disease to identify opportunities for pre-habilitation and to assess the association of frailty with post-LT outcomes.

832 SINGLE-CENTER EXPERIENCE IN PEDIATRIC INTESTINAL TRANSPLANTATION

Cal Matsumoto, Nada Yazgi, Khalid Khan, Stuart Kaufman, Georgetown University Transplant Institute, Washington, DC, USA

The results of intestinal transplantation (ITx) have improved over the last decade. Adult and pediatric ITx was first initiated at our center in November 2003. We retrospectively reviewed our experience with ITx. Primary immunosuppression consisted of IL-2 receptor blockade

induction with maintenance steroids, tacrolimus and sirolimus. Sensitized recipients, or recipients with a positive cytotoxic cross-match, received thymoglobulin induction. 109 pediatric (≤ 18 years) ITx have been performed in 108 patients from November 2003 to March 2016. Median follow-up time was 69 months. Overall average age was 3.3 ± 3.9 years. Grafts comprised of 42 isolated intestines (iITx), 53 liver-intestine (LI) and 14 multivisceral (MVTx) grafts. 51 recipients received an en-bloc colon graft with the intestine. The most common indications in pediatric recipients were gastroschisis (26), necrotizing enterocolitis (22) and pseudoobstruction (16). Operative time was $7:07 \pm 2:05$ hours. Postoperative ventilated days were 10.3 ± 15.7 . Mean length of stay was 50.7 ± 45.0 days. Mean time to enteral independence after transplant was 29.7 ± 21.8 days. Mean time to temporary stoma being removed was 229.2 ± 232.2 days after transplant. Overall, 1- and 3-year patient survival are 86.9% and 77.5 %, respectively. Survival by Era: Era 1 (2003 - 2010, n=64) was 84.5% and Era 2 (2011 - 2015, n=50) was 93.9%, ($p=0.26$). 1 year iITx, LI and MVTx patient survival was 89.7%, 90.0% and 67.7%. Overall cellular rejection occurred in 36.9% of patients. Overall, 1- and 3-year freedom from rejection (FFR) was 81.1% and 75.4%. FFR in adult and pediatric recipients was 57.4% and 75.4%, respectively ($p=0.039$). Early experience with CMV infection had a 25.1% incidence, whereas the latter experience was significantly less due to more optimal donor-recipient matching. Overall incidence of PTLD was 8.7%.

These data reflect a cumulative experience of pediatric intestinal transplantation at a single institution with extensive pediatric and adult intestinal transplant experience. Excellent outcomes can be achieved at high volume pediatric centers in those infants and children suffering from the complications of parenteral nutrition. Cellular rejection and opportunistic infections are manageable complications after intestinal transplantation.

Saturday, October 8, 2016

PLENARY SESSION V
8:00 AM

833 PROSPECTIVE INCIDENCE, EARLY LIFE RISK FACTORS AND THE ROLE OF THE MICROBIOME IN ALLERGIC PROCTOCOLITIS: THE GMAP STUDY

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Introduction: Allergic diseases are dramatically rising in the United States. Allergic proctocolitis (AP) is an early, common and generally benign manifestation of food allergy. Yet, its true incidence, risk factors, pathophysiology and relationship to other manifestations within a spectrum of IgE- and non-IgE-mediated food allergy remain poorly understood. Our primary hypothesis was that Caesarean mode of birth would increase the risk of AP by adversely affecting the infant microbiome.

Methods: GMAP (the Gastrointestinal Microbiome and Allergic Proctocolitis study) is an ongoing, prospective, observational, cohort study designed to study the development of AP among healthy newborn infants from a single pediatric primary care office. We serially enrolled 700 infants at their initial well-visit (median age 8 days) and collected stool and comprehensive data on pregnancy, family, medical history, environment, feeding practices and symptoms at every subsequent standard, well-child visit (0.5, 1, 2, 4, 6, 9, 12 months) as well as unscheduled sick visits over the first year of life (median age 390 days). AP case inclusion criteria were physician clinical diagnosis with documented and otherwise unexplained guaiac positive or grossly bloody stool. Stool DNA was extracted and the V4 region of 16S rRNA was sequenced for taxonomic analysis using phyloseq. Disease and exposure associations were analyzed using the MaAsLin pipeline.

Results: Of the 700 infants enrolled, 97 cases met the pre-defined inclusion criteria, giving a cumulative incidence of AP of 14% over two years. 51% of cases were male and the median age at diagnosis was 33 days (range 5 - 163 days). Caesarian delivery was not associated with the development of AP. However, infants who were never breastfed were significantly more likely to develop AP (24%) than those who were ever breastfed (13%, $p=0.009$). In an exploratory stool microbiome pilot ($n=47$, 24 cases and 23 age-matched controls), there was a significantly lower abundance of *Bifidobacterium* ($p<0.001$) and higher abundance of *Enterobacteriaceae* ($p 0.004$) in cases of AP when compared to healthy controls at 4 months (both below predefined FDR of 0.25). We also observed longitudinal assemblage of several important healthy taxa in the overall cohort, driven by the healthy controls, which were notably absent in infants who developed AP.

Conclusions: This is the largest prospective, observational cohort designed to study AP. The incidence of AP in this suburban population is strikingly higher than most estimates. Consistent with retrospective data, breastfeeding appears to be protective against the development of AP. The markedly lower abundance of *Bifidobacterium* and increase in facultative anaerobes among cases suggests that early dysbiosis in these infants plays a role in pathogenesis and warrants further study.

834 WHEN 5-AMINOSALICYLATES FAIL, ARE GUT MICROBES PART OF THE REASON?

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Introduction: Individuals vary widely in drug response. Interpersonal variation in gut microbial composition may contribute to this unpredictability. Here, we investigate this relationship for 5-aminosalicylate (5-ASA) drugs that are widely used for the treatment of inflammatory bowel disease, but carry a 35% failure rate. Prior research has established that the presence of gut microbes is required for activation of many 5-ASA prodrugs, and that some bacterial species can inactivate these drugs *in vitro*. However, the relationship between gut microbial community composition and 5-ASA metabolism is unknown.

Methods: We established a mouse model for 5-ASA pharmacokinetics by transplanting human gut microbial communities from healthy donors into germ-free mice (that have no microbes of their own) treated with the 5-ASA prodrug sulfasalazine or 5-ASA enemas. We have also anaerobically incubated the drugs with single bacteria and whole stool microbial communities. We used 16S sequencing to monitor community composition and HPLC and mass spectrometry to quantify drug metabolism.

Results: Transplantation of human gut communities into germ-free mice successfully established a model of interpersonal microbial variation that controls for host genotype and environment. We measured drug metabolism in groups of mice carrying gut microbiomes from six unrelated donors and germ-free controls. 5-ASA activation: In the absence of a gut microbiome, germ-free mice were unable to metabolize the prodrug as expected. In contrast, mice carrying microbiomes from different human donors exhibited significantly different proportions of active and inactive drug in multiple gut locations in a donor-specific manner. *In vitro* studies had identified significant differences between gut microbes in their ability to activate the prodrug and the rate of activation. 5-ASA inactivation: While germ-free mice had higher expression of the host enzyme that inactivates 5-ASA (mNAT2), they had significantly lower inactivation activity compared to conventionalized mice carrying a complete microbiota.

Discussion: Gnotobiotic mice carrying human gut microbial communities allow separation of human and microbial variation and provide a tractable model for dissecting microbiota drug interaction. By applying this model to understand variability in 5-ASA metabolism, we demonstrate that individual human microbiomes can impact active drug levels in genetically identical hosts. These results further suggest a new role for gut microbes in 5-ASA inactivation *in vivo*.

WILLIAM F. BALISTRERI PRIZE

836 EPITHELIAL BARRIER FUNCTION IN EOSINOPHILIC ESOPHAGITIS IS REGULATED BY A HIF-1 α -CLAUDIN-1 AXIS

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Background: Dysregulated tight junction integrity and altered barrier function is implicated in EoE pathophysiology, however the cellular mechanism(s) remain poorly defined. Hypoxia inducible factor (HIF) signaling has previously been associated with maintaining mucosal barrier

function and we hypothesized that chronic inflammation during EoE may result in dysregulated HIF signaling and diminished epithelial barrier function. We sought to define the mechanism(s) by which chronic hypoxia regulates epithelial barrier.

Methods & Results: An array of biopsies from patients with active EoE identified a significant decrease in both the mRNA and protein of the tight junction molecule, claudin-1 (CLDN1) (80% decrease, $P<0.01$) and in the L2-IL-5^{OXA} mouse model of EoE (30% decrease, $P<0.05$). Molecular analysis of active EoE biopsies revealed a concomitant decrease in HIF-1a protein (50% decrease, $P<0.001$) and the HIF-1a responsive gene, GLUT1 (85% decrease, $P<0.001$). Similarly, downregulated HIF-1a (30% decrease, $P<0.05$) and GLUT1 (45% decrease, $P<0.01$) expression was evident in the L2-IL-5^{OXA}-EoE mice. We used chromatin-immunoprecipitation and promoter-mutagenesis luciferase studies to confirm direct HIF-1a binding and activation of the CLDN1 promoter in esophageal epithelial cells (EPC2-hTERT). Of note, chronic exposure to experimental hypoxia *in vitro* (1% O₂) significantly decreased HIF-1a protein expression in EPC2 cells (66% decrease; $P<0.05$). Aligned with this, we determined that human peripheral eosinophils rapidly consume oxygen once activated *in vitro*, and that L2-IL-5^{OXA}-EoE mice have increased areas of epithelial hypoxia that co-localized with eosinophils. To define a functional effect for a HIF-1a-CLDN1 axis in barrier function HIF-1a-knock-down (HIF-1a-KD) EPC2 cells were utilized in a 3-dimensional air-liquid interface model *in vitro*. HIF-1a-KD resulted in decreased TEER barrier (22% decrease, $P<0.05$), increased FITC-Flux permeability (1.3-fold increase, $P<0.05$) and repressed claudin-1 expression (69% decrease; $P<0.001$). We generated a triple transgenic mouse that overexpresses HIF-1a specifically within the esophageal epithelium (L2-IL5^{Oxa}/K14Cre/LSL-HIF1a: Triple-TG) to test the hypothesis that epithelial specific HIF-1a stability is protective to barrier function via CLDN1 expression and ultimately leads to decreased esophageal eosinophilia. Triple-TG mice demonstrated a marked improvement in epithelial histological activity following experimental EoE (3.6 vs 11.9, Triple vs Ctrl, $P<0.05$), in addition to decreased eosinophilia (26 vs 67, Triple vs Ctrl, $P<0.001$). This improvement was congruent with increased CLDN1 mRNA (1.7-fold, $P<0.05$) and protein expression (1.5-fold, $P<0.01$).

Conclusion: Collectively, these studies reveal that HIF-1a plays a critical role in maintaining esophageal epithelial barrier integrity and highlights stabilization of the HIF-1a-CLDN1 axis as a novel therapeutic target for mucosal healing in EoE.

ENDOSCOPY PRIZE

837 A SIMULATION-BASED TRAINING CURRICULUM OF PROGRESSIVE FIDELITY AND COMPLEXITY IMPROVES CLINICAL COLONOSCOPY PERFORMANCE: A BLINDED, RANDOMIZED TRIAL

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Introduction: Graded delivery of simulation-based training (SBT) in endoscopy may improve initial clinical performance. Studies for simpler procedures demonstrate that a progression from low- to high-fidelity simulator training results in superior skill transfer, compared to either low- or high-fidelity simulation alone.

Aims: To determine whether an SBT curriculum of progressive fidelity and task complexity improves colonoscopy skill acquisition and transfer to the clinical setting, compared to a curriculum utilizing high-fidelity simulation in isolation.

Methods: 37 novice endoscopists were randomized to 2 groups. The progressive group received 6 hours of simulation training, with the first hour on a bench-top simulator (low-fidelity) and 5 hours on a virtual reality (VR) simulator (high-fidelity), performing tasks of sequentially increasing complexity. The high-fidelity group received 6 hours of training on the VR simulator, with tasks arranged in random order of complexity. Both groups received feedback from an expert endoscopist and 4 hours of lectures. The primary outcome measure was performance during participants' first 2 clinical colonoscopies (performed 4 - 6 weeks after training), assessed by blinded video review of the procedures using the JAG DOPS scale, a task-specific colonoscopy assessment tool. Secondary outcome measures were differences in: 1) procedural knowledge, evaluated using a multiple-choice test; 2) performance on a VR simulator task (immediately and 4 - 6 weeks after training), measured by a modified JAG DOPS scale; 3) performance during an integrated scenario (where participants perform a VR colonoscopy while interacting with a standardized patient 4 - 6 weeks after training), measured by JAG DOPS and validated communication and global rating scales.

Results: At baseline, there were no significant differences between groups in demographics, VR performance or procedural knowledge ($p>0.05$). The progressive group demonstrated superior performance compared to the high-fidelity group on the first (progressive: 72.1 ± 12.1 vs. control: 58.3 ± 8.3 , $p<0.001$) and second (progressive: 72.3 ± 11.1 vs. control: 58.2 ± 13.4 , $p=0.001$) clinical colonoscopies. The progressive group displayed superior technical skills on the VR simulator at the delayed post-test ($p<0.05$) and performed significantly better during the integrated scenario in terms of communication, global performance and colonoscopy-specific performance ($p<0.05$). There was no difference in knowledge acquisition between groups ($p>0.05$).

Conclusion: An SBT curriculum in colonoscopy incorporating progressive fidelity and increasing task complexity is associated with improved skill retention and transfer to the clinical setting, as compared to high-fidelity training alone. This finding is commensurate with challenge point theory and suggests that SBT is likely most effective when trainees are exposed to endoscopy in a graded fashion. (Clinicaltrials.gov ID NCT02000180)

Saturday, October 8, 2016

CONCURRENT SESSION V 10:00 AM

INFLAMMATORY BOWEL DISEASE

838 LONGITUDINAL CHANGES IN GUT MICROBIOTA IN PEDIATRIC CROHN'S DISEASE (CD)

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Introduction: There is limited knowledge on changes in the gut microbiome in response to treatment, during periods of remission and relapse in CD. The aim of this study was to analyze the longitudinal variation in gut microbiome in pediatric CD from diagnosis and correlate it to clinical and environmental features.

Methods: This prospective, longitudinal, cohort study was conducted at the Murdoch Children's Research Institute, Melbourne, Australia. Gut biopsies were obtained at initial diagnosis and during follow-up examinations, 6 - 18 months after diagnosis. The bacterial V2 16S gene was amplified by PCR and sequenced by Illumina MiSeq. Bioinformatics analyses were performed using MOTHUR and oligotyping. Environmental data were obtained via a questionnaire filled out by families at diagnosis. Statistics were performed using R environment and statistic package PAST3.

Results: 128 CD patients and 68 controls were enrolled, from which 345 biopsies (179 ileum; 166 colonic) were used for bacterial 16S analyses. The cohort was comprised of 83 females and 123 males with an average age of 12.12 years (3.4 - 18 years). Longitudinal biopsies (n=105) were available from 53 patients 2 - 180 months from diagnosis. The five most abundant oligotype species were *Bacteroides vulgatus* (21.48%), *Bacteroides dorei* (4.38%), *Faecalibacterium prausnitzii* (3.25%), *Prevotella copri* (3.07%) and *Bacteroides dorei* (2.46%) in the entire cohort. PERMANOVA statistics revealed distinct microbial profiles in CD patients and controls ($p=0.0001$), which differed on the basis of gender ($p=0.0002$), ASCA status ($p=0.0168$), mode of delivery ($p=0.0036$) and stress ($p=0.0217$). We also observed a different microbial profile in the young CD group (1 - 10 years) compared to the older group (11 - 18 years) ($p=0.0218$). Analyses of longitudinal biopsies revealed a distinct microbial profile between patients in remission and relapse ($p=0.0038$). The distinct bacterial profiles between groups observed by PERMANOVA analyses were confirmed by supervised ordination using discriminant analysis of principal components (DAPC) using the R package Adegenet 2.0.0. ANOVA analyses revealed 23 OTP species at higher abundance in the control group. The most frequent OTP species associated with CD was *Veillonella atypica*. *Ruminococcus torques* and *Bacterium* YE61 were detected at a significantly higher rate in the ASCA-positive CD group (FDR<0.05). *Bacteroides fragilis*, *Pseudoflavonifractor capillosus* and *Ruminococcus gnavus* were significantly underrepresented in the relapsed CD group (FDR<0.05).

Conclusion: Significant differences in microbial population were noted between CD patients and controls. Longitudinal analyses revealed different microbiome profiles between patients in relapse and remission.

839 MUCOSAL HEALING IN PEDIATRIC PATIENTS WITH MODERATE-TO-SEVERE LUMINAL CROHN'S DISEASE UNDER COMBINED IMMUNOSUPPRESSION: ESCALATION VERSUS EARLY TREATMENT

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Background: The early introduction of biologics during the disease course in Crohn's disease yields superior results compared to a 'step-up' strategy. We aimed to compare the efficacy of combined immunosuppression in terms of mucosal healing in pediatric patients with moderate-to-severe luminal Crohn's disease receiving infliximab according to either an 'escalated combined immunosuppression' or an 'early combined immunosuppression' strategy.

Methods: In this prospective, observational study, the efficacy of combined immunosuppression was evaluated in terms of mucosal healing at weeks 14 and 54 from baseline infliximab infusion. Comparison was performed between the escalated, combined immunosuppression group (group A) and the early, combined immunosuppression group (group B). Factors associated with mucosal healing at weeks 14 and 54 from baseline infliximab infusion were also investigated.

Results: Seventy-six patients initiated infliximab with concomitant azathioprine (group A 28; group B 48). Comparison of baseline characteristics revealed a significantly longer duration from initial diagnosis to infliximab infusion in group A (median 8.1 vs. 0.7 months; $p<0.001$). Mucosal healing was achieved in 32% of patients in group A and 51% in group B at week 14 ($p=0.121$), and in 42% in group A and 74% in group B at week 54 ($p=0.007$). Group B was also positively associated with mucosal healing at week 54 on multivariate logistic regression (odds ratio 6.216, 95% CI, 1.782 - 21.686, $p=0.004$).

Conclusions: Mucosal healing during combined immunosuppression is more effectively achieved by treatment with an early combined immunosuppression strategy without corticosteroid induction administered within 1 month, rather than escalating to receive combination therapy later during the course. The therapeutic window of opportunity in early Crohn's disease may be shorter than generally thought, especially in children.

840 A NOVEL PERSONALIZED DOSING CALCULATOR FOR OPTIMIZED INFLIXIMAB THERAPY IN INFLAMMATORY BOWEL DISEASE

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Background and Objective: Infliximab dosing in pediatric inflammatory bowel disease (IBD) is evolving from a one-size-fits-all approach to include the use of escalated dosing strategies to improve treatment responsiveness and durability. Although there is general acceptance for the importance of optimizing anti-TNF dosing, a knowledge gap exists between the clinical research and the implementation of a personalized dosing strategy in real-world practice settings, particularly at the time of infliximab administration. We aimed to: 1) develop a personalized infliximab dosing calculator using published pharmacokinetics (PK), as well as clinical markers of disease severity and outcomes; and 2) describe the clinical impact of its use in the setting of an outpatient infusion unit.

Methods: We set out to create a web-based, mobile-friendly, personalized dosing calculator that would take into account clinical markers that are known to be associated with disease severity and treatment outcome. Calculator input also included markers with known effect on drug clearance from published PK modeling data. Input variables to the calculator were CRP, albumin, patient weight, calprotectin, disease symptom scoring and drug level. We next implemented a quality improvement initiative whereby all patients receiving infliximab had routine therapeutic drug monitoring (at 10 - 15 weeks and at 6-month intervals) and calculator-generated dosing recommendations (dose escalation or current dose) given to the treating gastroenterologist. Final dosing decisions were made by the gastroenterologist and all treatment decisions were recorded longitudinally.

Results: 48 IBD patients (mean age 15.3 years, mean weight 52.8 kg) on infliximab therapy were evaluated. 42 of the 48 patients were receiving maintenance regimens at the start of the calculator-generated dosing initiative. 36 of 48 and 14 of 48 had dosing regimens exceeding 5 mg/kg every 8 weeks and 5 mg/kg every 6 weeks, respectively, before calculator implementation. Calculator-generated dosing recommendations were followed for 81/105 (77%) infusion events. Comparing calculator-generated, dose-adherent versus non-adherent groups, subsequent target therapeutic infliximab trough levels ($>5 \mu\text{g/mL}$) were achieved in 90% of the events in the adherent group compared to 40% in the non-adherent group ($p=0.01$). Mean drug trough was $14.5 \mu\text{g/mL}$ and $6.2 \mu\text{g/mL}$ for adherent versus non-adherent groups, respectively. Comparing secondary measures of calprotectin and CRP among adherent and non-adherent groups, mean calprotectin levels were $428 \mu\text{g/g}$ and $892 \mu\text{g/g}$ ($p<0.02$) and mean CRP levels were 5.1 mg/L and 9.8 mg/L ($p<0.01$), respectively.

Conclusions: We show the feasibility of a novel, personalized dosing calculator for infliximab dosing in IBD. Early efficacy data indicate that adherence to the calculator-generated dosing strategy improves the probability of adequate anti-TNF exposure and reduces biochemical evidence of inflammatory disease burden.

841 INCREASED MUCOSAL TYPE 2 AND TYPE 17 GENE EXPRESSION DISTINGUISHES ULCERATIVE COLITIS FROM COLITIS-ONLY CROHN'S DISEASE IN TREATMENT-NAÏVE PEDIATRIC PATIENTS

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Background: The role of type 2 inflammation, characterized by the cytokines IL-4, IL-5 and IL-13, in the pathogenesis of ulcerative colitis (UC) remains controversial. Evidence from treatment-naïve and pediatric patients is lacking. The aim of this study was to determine whether mucosal expression of genes associated with type 2 inflammation is upregulated in treatment-naïve pediatric UC compared to Crohn's colitis.

Methods: Rectal mucosal RNA from 184 treatment-naïve, pediatric IBD patients (49 UC, 40 colitis-only CD [CDc], 46 CD ileocolitis [CDic]) with macroscopic rectal disease and non-IBD controls ($n=49$) enrolled in the CCFA RISK study were analyzed by real-time PCR array for expression of 24 genes associated with type 1, 2 and 17 inflammation. A false discovery rate-corrected P -value of ≤ 0.05 was deemed significant. Results were validated by real-time PCR of RNA from involved rectum of 52 patients (17 UC, 20 CD, 15 non-IBD) enrolled in an independent Cincinnati cohort. Immunohistochemical (IHC) staining for IL-13 receptor alpha-2 (IL-13R α 2) was performed on a subset of Cincinnati patients.

Results: RISK cohort differential colon mucosal gene expression is detailed in the Table. While CDic exhibited primarily increased IFNG expression, both UC and CDc exhibited significantly increased expression of type 1 (INFG, TBX21), type 2 (CCL11, IL13, IL1RL1) and type 17 (IL17A, IL23A) genes compared to non-IBD. Only UC exhibited increased expression of the type 2 genes, IL13RA2, IL33 and ICOS.

Furthermore, when comparing UC to CDc, UC exhibited significantly increased expression of IL13, IL13RA2, IL17A, IL23 and S100A8. In a diagnosis-unbiased analysis, hierarchical clustering separated patients into 4 gene-expression clusters with an unequal distribution of clinical phenotypes ($p<0.001$). Age, sex and physician's global assessment were similar between clusters. Clusters 1 and 2 contained 73% of the IBD patients and exhibited increased expression of multiple inflammatory genes compared to clusters 3 and 4, which contained 85% of the non-IBD patients. Cluster 1, which was 59% UC, was distinguished from cluster 2 (23% UC) by high expression of the type 2 genes IL13, IL13RA2 and IL5. In the Cincinnati cohort, UC patients also exhibited significantly increased expression of IL13RA2, IL13, IL17A and IL23 compared to non-IBD and CD, thereby validating findings from the RISK cohort. IHC revealed increased IL-13R α 2 in rectal lamina propria immune cells of UC ($p 0.004$) and CD ($p 0.02$) compared to non-IBD. IL-13R α 2 staining was correlated to Mayo endoscopic score in UC patients ($r 0.61$, $p=0.02$).

Conclusions: Mucosal gene expression in treatment-naïve pediatric colitis suggests augmented type 2 and type 17 inflammation in UC compared to colon-only CD. A molecularly-defined colitis patient subpopulation is distinguished by increased type 2 gene expression. Future analyses will determine whether type 2 gene expression is associated with treatment outcomes.

Table. Differential colon mucosal gene expression by real-time PCR array between medication-naïve UC and Crohn's colitis phenotypes and non-IBD controls

Gene*	CDc vs. Non-IBD		CDic vs. Non-IBD		UC vs. Non-IBD		UC vs. CDc		UC vs. CDic	
	Fold Change	FDR P-value	Fold Change	FDR P-value	Fold Change	FDR P-value	Fold Change	FDR P-value	Fold Change	FDR P-value
<i>CCL11</i>	3.8	0.000	1.7	0.125	5.2	0.000	1.4	0.087	3.0	0.000
<i>CHI3L1</i>	16.1	0.000	6.7	0.001	32.1	0.000	2.0	0.138	4.8	0.005
<i>GATA3</i>	-1.2	0.834	-1.3	0.601	-1.2	0.431	1.0	0.669	1.1	0.843
<i>ICOS</i>	1.4	0.098	1.2	0.615	1.9	0.002	1.3	0.352	1.5	0.016
<i>IFNG</i>	5.4	0.000	3.5	0.001	6.4	0.000	1.2	0.777	1.8	0.088
<i>IL13</i>	8.1	0.010	12.1	0.125	37.5	0.000	4.6	0.014	3.1	0.000
<i>IL13RA2</i>	3.5	0.281	1.9	0.174	8.1	0.000	2.3	0.044	4.3	0.023
<i>IL17A</i>	4.9	0.001	1.5	0.228	16.9	0.000	3.4	0.009	11.4	0.000
<i>IL1RL1_95</i>	-1.3	0.281	-1.2	0.615	1.1	0.277	1.4	0.044	1.3	0.051
<i>IL1RL1_97</i>	1.5	0.013	1.4	0.174	3.2	0.000	2.0	0.081	2.2	0.003
<i>IL22</i>	4.6	0.046	4.8	0.068	6.0	0.006	1.3	0.633	1.3	0.454
<i>IL23A</i>	1.9	0.030	1.2	0.469	3.4	0.000	1.8	0.031	2.9	0.000
<i>IL33</i>	1.0	0.417	1.0	0.897	1.2	0.011	1.2	0.235	1.2	0.023
<i>IL5</i>	2.6	0.677	11.0	0.693	113.1	0.003	43.6	0.083	10.3	0.023
<i>RORC</i>	-1.5	0.000	-1.3	0.068	-2.0	0.000	-1.4	0.087	-1.5	0.000
<i>S100A8</i>	12.8	0.000	9.1	0.001	60.5	0.000	4.7	0.026	6.7	0.000
<i>TBX21</i>	1.6	0.003	1.3	0.134	1.5	0.001	-1.0	0.884	1.2	0.148
<i>TGFB1</i>	1.0	0.980	-1.1	0.487	1.1	0.235	1.0	0.244	1.2	0.026

* No significant difference between any two groups for *IL10*, *RORA* and *IL4* (data not shown)

CDc, colitis-only Crohn's disease; CDic, ileocolonic Crohn's disease; FDR, false discovery rate; UC, ulcerative colitis; *IL1RL1_95*, transcript for membrane-bound IL-33 receptor; *IL1RL1_97*, transcript for the soluble IL-33 receptor

842 MULTI-CENTER EXPERIENCE OF VEDOLIZUMAB EFFECTIVENESS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Background: Though vedolizumab has received regulatory approval for the treatment of Crohn's disease (CD) and ulcerative colitis (UC) in adults, there is increasing off-label use in children.

Aims: To describe the experience with vedolizumab in pediatric IBD patients at three tertiary IBD centers and examine predictors of remission.

Methods: A retrospective review identified pediatric IBD patients (age <18 years) receiving vedolizumab. Data on demographics, disease behavior, location, activity and previous treatments/surgeries were collected. Disease activity was assessed using the weighted pediatric CD activity index (wPCDAI) or pediatric UC activity index (PUCAI). Primary outcome was week 14 remission, defined as PUCAI <10 or wPCDAI <12.5. Descriptive statistics and univariate analyses were performed to examine associations of clinical characteristics with efficacy.

Results: Fifty-two patients, 58% CD and 42% UC, initiated vedolizumab between June 2014 and August 2015. Median age at vedolizumab initiation was 14.9 (range 7 - 17) years. Ninety percent had failed ≥1 anti-TNF agent. Week 14 remission rates for UC and CD were 76% and 42%, respectively ($p < 0.05$). Eighty percent of anti-TNF-naïve patients experienced week 14 remission. At week 22, anti-TNF-naïve patients had higher remission rates than TNF-exposed patients (100% vs. 45%, $p = 0.04$). There were no infusion reactions or serious adverse events/infections.

Conclusions: Our results suggest that vedolizumab is efficacious and safe in pediatric IBD patients, with UC patients experiencing earlier and higher rates of remission than CD patients. Anti-TNF-naïve patients experienced higher remission rates than those with anti-TNF exposure. Controlled clinical trial data are needed to confirm these observations.

843 EFFICACY OF THALIDOMIDE THERAPY AND ITS EFFECT ON MUCOSAL ANGIOGENESIS IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE

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Background and Aims: Thalidomide is emerging as a treatment for various diseases. However, its mechanism has not been well understood. Our study was aimed to assess the efficacy of thalidomide therapy in pediatric Crohn's disease (CD) patients who were corticosteroid-dependent, corticosteroid-resistant, or those with concomitant tuberculosis and investigated its effect on angiogenesis in intestinal mucosa.

Methods: An open-label, observational study was performed in pediatric CD with thalidomide treatment. Clinical response and remission were assessed by the Pediatric Crohn's Disease Activity Index (PCDAI). Laboratory evaluations, weight-for-age Z-score and corticosteroid discontinuation were recorded. Vascular endothelial growth factor (VEGF) and CD31 in mucosal tissues were measured by immunohistochemistry. The local expression of VEGF was also evaluated with Western blot.

Results: 17 patients enrolled in this study, 8 were corticosteroid-resistant, 5 corticosteroid-dependent and 4 with tuberculosis. The overall remission rate (PCDAI \leq 10) at 12 months was 88.2% (15/17). 11 of 12 patients suspended corticosteroids. Laboratory parameters were improved and a significant increase observed in weight-for-age Z-score. Immunohistochemical expressions of VEGF and CD31 in CD were higher than healthy controls ($p < 0.001$) and the levels were reduced after thalidomide therapy ($p < 0.05$). The VEGF levels from intestinal mucosa were down-regulated after treatment by Western blot evaluation ($p < 0.05$).

Conclusions: Thalidomide appears to be an alternative treatment for pediatric CD patients with corticosteroid dependence, corticosteroid resistance, or those with concomitant tuberculosis. The mechanism of action of thalidomide might be associated with inhibition of VEGF expression in intestinal mucosa.

Saturday, October 8, 2016

**POSTER SESSION III
12:00 – 2:00 PM**

*** Poster of Distinction**

CELIAC AND OTHER LUMINAL DISORDERS

857 FECAL GLUTEN IMMUNOGENIC PEPTIDES (GIP) REVEAL LIMITATIONS OF SEROLOGICAL TESTS AND FOOD QUESTIONNAIRES FOR MONITORING A GLUTEN-FREE DIET IN CELIAC DISEASE PATIENTS

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Introduction: Treatment for celiac disease (CD) is a lifelong strict gluten-free diet (GFD). Patients should be followed-up with dietary interviews and serology as CD markers to ensure adherence to the diet. However, none of these methods offer a flawless measure of dietary compliance.

Objectives: To evaluate measurement of gluten immunogenic peptides (GIP) in stools as a marker of GFD compliance in CD patients and compare it with traditional methods of GFD monitoring, serology and dietetic records.

Methods: We performed a prospective, non-randomized, multicenter study including 188 CD patients on GFD and 84 healthy controls. Subjects were given a dietary questionnaire and fecal GIP quantified by ELISA. Serological anti-tissue transglutaminase (anti-tTG), IgA and anti-deamidated gliadin peptide (anti-DGP) IgA antibodies were measured simultaneously.

Results: Of 188 celiac patients, 56 (29.8%) had detectable GIP levels in stools. There was a significant association between age and GIP in stools that revealed increasing dietary transgressions with advancing age (39.2% in subjects older than 13 years age) and with gender in certain age groups (60% in men older than 13 years age). No association was found between fecal GIP and dietary questionnaire or anti-tTG antibodies. However, an association was detected between GIP and anti-DGP antibodies, although 46 of the 53 GIP-stool-positive patients were negative for anti-DGP.

Conclusions: Detection of gluten peptides in stools reveals limitations of traditional method for monitoring GFD in celiac patients. The GIP-ELISA enables direct and quantitative early assessment of gluten exposure after ingestion. It could aid in the diagnosis and clinical management of non-responsive CD and refractory CD.

Financial support: This work was supported by grants from Ministerio de Ciencia e Innovación and FEDER funds (DELIAC, IPT-2011-0952-900000), and Corporación Tecnológica de Andalucía (SINGLUCHECK, 1737/0118). We also thank the generous volunteer subjects who enrolled in the study.

858 ANTHROPOMETRIC MEASURES AND PREVALENCE TRENDS IN ADOLESCENTS WITH CELIAC DISEASE: A POPULATION-BASED CROSS-SECTIONAL STUDY

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Background: Celiac disease (CD) occurs in about 1-3% of the population in most countries, with a recently reported increase in prevalence. Data regarding anthropometric measures in adolescents with CD, particularly final adult height, is inconclusive and mostly relies on relatively small cohorts. We aimed to investigate anthropometric measures including height at late adolescence in a large national cohort. In addition, we assessed trends in the prevalence of diagnosed CD over time and impact of socio-demographic factors.

Methods: Between 1988 and 2015, most of the Jewish population of Israeli adolescents (n=2,001,353) underwent a general health examination at a median age of 17.1 (16.9 - 17.4) years. A definite diagnosis of CD was based on accepted criteria. Covariate data included demographic and anthropometric measures.

Results: Overall, 10,566 CD cases were identified and analyzed. Multivariate analysis demonstrated that males with CD are leaner (BMI 21.2 \pm 3.7 vs. 21.7 \pm 3.8, $p=0.02$) while females with CD were shorter (161.5 \pm 6 vs. 162.1 \pm 6, $p=0.017$) than the general population. The prevalence

of diagnosed CD increased from 0.5% to 1.1% in the last 20 years with a female predominance (0.64% vs. 0.46%). CD prevalence was significantly lower in subjects of lower socioeconomic status and those of African, Asian and former Soviet Union origin ($p < 0.0001$). Conclusion: Adolescent males with CD are leaner and females with CD are shorter compared with the general population. However, the clinical relevance of the small differences suggests that when CD is diagnosed during childhood, final weight and height are not severely impaired. Our cohort reinforces the observed increase in diagnosed CD.

***859 HAPTOGLOBIN-2 GENE EXPRESSION IN CELIAC DISEASE, NON-CELIAC GLUTEN SENSITIVITY AND TYPE 1 DIABETIC PATIENTS**

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Background: Haptoglobin (HP) function has long been known as a scavenger for hemoglobin, used as a marker for general inflammation before the discovery of C-reactive protein (Asleh *et al.*, 2003). Human HP appears in three different genotypes: Hp1-1, Hp2-1 and Hp2-2 (Maeda *et al.*, 1984) and many studies have shown an association between diseases and the HP phenotype/genotype (Quaye 2008). The HP2-2 phenotype has been associated with worse prognosis of several infectious diseases (Delanghe *et al.*, 1998; Kasvosve *et al.*, 2000), autoimmune disorders such as celiac disease (Tripathi *et al.*, 2009) and neurological disorders (Gloria-Bottini *et al.*, 2008; Maes *et al.*, 2001). Recently, our group has discovered the precursor of haptoglobin-2 (pHP2) is active as zonulin (Tripathi *et al.*, 2009). Zonulin is a protein able to regulate intestinal permeability by reversible disassembly of intercellular tight junctions and has been associated with some autoimmune disorders, diseases of the nervous system, and neoplastic conditions (Fasano 2011). Therefore, our hypothesis is that people with one or two copies of the HP2 gene (HP2-1 or HP2-2 genotype) produce more zonulin leading to increased intestinal permeability and will develop a more severe clinical outcome.

Aim: To determine the genotype/phenotype distribution of haptoglobin in celiac disease (CD), non-celiac gluten sensitivity (NCGS), type 1 diabetes (T1D) and first-degree relatives of T1D (T1DR).

Material and Methods: Samples were obtained retrospectively using biorepository material. HP genotype was done with specific primers designed in exon 2 and exon 5 of HP1 corresponding to exons 2 and 7 of HP2 amplified by high-fidelity PCR system. After PCR, the amplicons were run on a 1% agarose gel and read under a UV bulb. The size difference allowed differentiation of the two genotypes (HP1: 2.5 kb and HP2: 5.3 kb). When blood was not available, serum was used to phenotype the individuals by western blot. Serum total proteins were denatured, separated by size in an electrophoresis gel and then transferred to a PVDF membrane. Immunoblotting was performed using an anti-zonulin antibody.

Results: 1210 individuals were genotyped or phenotyped. HP distribution was statistically different ($p < 0.01$) in all of the analyzed population compared to the control group ($n=99$) and the frequency was 20.2, 51.5 and 28.3% for HP1-1, HP2-1 and HP2-2, respectively. We observed a decrease in HP1-1 frequency (NCGS 10.6, CD 13.4, T1D 41.3 and T1DR 16.3) and an increase in HP2-2 frequency (NCGS 47.1, CD 44.6, T1D 38.4 and T1DR 43.2).

Conclusion: Our data reported for the first time an increased frequency of HP2 genes among celiac disease, NCGS, T1D and first-degree relatives of T1D individuals. Interestingly, NCGS showed a higher frequency of HP 2-2 compared to the other diseases, which could play a role in the pathogenesis of this controversial clinical entity.

860 PREVALENCE OF CELIAC DISEASE AND USE OF ANTI-TISSUE TRANSGLUTAMINASE (TTG) ANTIBODIES AMONG CHILDREN WITH IBD

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Introduction: Celiac disease and inflammatory bowel disease (IBD) are immune-mediated chronic gastrointestinal disorders, which present with similar symptoms, such as abdominal pain, diarrhea and growth failure. Moreover, both conditions can be associated with duodenitis. In adults, some studies show increased prevalence of celiac disease in patients with IBD while other studies have not confirmed it. To the best of our knowledge, there are no data in children. We aim to investigate the prevalence of celiac disease and anti-tissue transglutaminase (tTG) antibodies among children with IBD.

Methods: We performed a retrospective chart review of children with IBD, who have been followed routinely in our clinic over the last 4 years. These children were matched with a non-IBD control group of children presenting with gastrointestinal symptoms to gastroenterology clinics. All children were routinely screened for celiac disease with tTG-IgA and total IgA. Clinical, pathological and laboratory data were collected in all children. Abnormal tTG was defined as >30 U/mL.

Results: The study population included 129 children with IBD and 257 in the control group. TTG values were obtained in 200 and 285 encounters with these children, respectively. The mean age of the children was 14.6 ± 3 years and 58% were males. The IBD group included 74 children with Crohn's disease and 55 with ulcerative colitis. Abnormal tTG levels were found in 6 patients in the IBD group and 20 patients in the control group (4.6% vs. 7.8%, $p=0.24$). Further evaluation of these children, including anti endomysial antibodies and duodenal histology, led to celiac diagnosis in one patient with IBD and in 12 patients in the control group. Celiac disease prevalence was lower among children with IBD compared with the control group (0.8% vs. 4.7%, $p=0.07$). False positive rates were 3.9% and 3.3% for the IBD and the control groups, respectively.

Discussion: Children with IBD do not have higher prevalence of celiac disease compared to other children who present with gastrointestinal symptoms to a gastroenterology clinic. Prevalence of celiac disease in children with IBD (0.8%) is similar to that of reported prevalence (1%) in the general population. Rates of false positive tTG antibodies are similar in children with IBD and the control group. Routine screening for celiac disease in children with IBD is not warranted.

***861 A COMBINED GENETIC-EPIGENETIC STRATEGY FOR IDENTIFYING CELIAC DISEASE SUSCEPTIBILITY LOCI**

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Background: An immune-mediated, gluten-sensitive enteropathy that affects approximately 1% of the population worldwide, celiac disease has complex biology and genetics. Genome-wide association studies (GWAS) have identified susceptibility loci, but many of the interesting statistical signals are sub-threshold, and even for the supra-threshold peaks, the causal nucleotide changes and biologic mechanisms remain poorly understood. Mapping haplotype-dependent, allele-specific methylation (hap-ASM) and overlapping the resulting maps with GWAS data is a useful approach to hone in on the critical DNA regulatory sequences that underlie supra- and sub-threshold GWAS signals and thereby to identify transcription factors and biological pathways that converge on these genetically polymorphic DNA sequences.

Objective: To identify regulatory DNA sequences underlying celiac disease and Crohn's disease susceptibility, we are mapping hap-ASM around a set of celiac disease and Crohn's disease GWAS peaks. In this "post-GWAS" approach, bona fide regulatory haplotypes reveal their presence by conferring methylation asymmetry between the two alleles.

Methods: In the first step, Illumina 450K methylation BeadChip microarrays and Nextgen bisulfite sequencing (Methyl-Seq) were performed to map genome-wide hap-ASM in human T-cell lymphocytes. GWAS peaks for celiac disease and Crohn's disease were scrutinized for hap-ASM and methylation quantitative trait loci (mQTLs). Top ranked regions were then selected for fine-mapping of hap-ASM by bisulfite sequencing using a Fluidigm AccessArray-MiSeq pipeline.

Results: Our study examined a group of T lymphocyte DNA samples from 48 individuals, including both normal controls and patients with celiac disease. We have mapped hap-ASM in the PSMD5-PHF19-FBXW2 region containing a celiac GWAS signal and our methylation mapping has also revealed hap-ASM near a GWAS variant in the IRF1 gene, associated with Crohn's disease. Hap-ASM mapping in several additional chromosomal regions associated with celiac disease and Crohn's disease is in progress.

Conclusions: Our genetic-epigenetic mapping approach applied to T lymphocytes is providing novel insights into celiac disease by identifying critical DNA regulatory sequences that underlie GWAS signals for this important immunologically-mediated human disease.

862 HLA TYPING IN HEALTHY AND DIABETIC CHILDREN WITH CELIAC DISEASE IN CALI, COLOMBIA

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Introduction: Children with diabetes mellitus type 1 (DM1) have increased risk of celiac disease (CD). The HLA haplotype DR3-DQ2 or DR4-DQ8 is associated with increased risk for CD.

Objective: To determine the HLA in children with DM1 from the University Hospital of Valle in Cali, Colombia and healthy children from public schools in the cities of Cali, Sotavento and La Union, Colombia.

Methods: 142 children with DM1 and 304 healthy children aged 10.8 ± 3.6 years, 54.9% female, underwent screening with IgA anti-transglutaminase for CD (Biocardtest[®]), which was positive in 13/142 in the DM1 group (9.2%) and 4/304 (1.3%) in the healthy control group. CD was considered present when immunohistochemistry and/or HLA DQ2/DQ8 were positive.

Results: CD was presented in 12/142 children with DM1 (8.5%) and 3/304 healthy children (1.0%). In children with DM1, the most common HLA DQ2 genotype was DQ8 (85.7%) and healthy children were carriers of HLA DQ2 and/or HLA DQ8, with the most frequent genotype being HLA DQ2. The incidence of allele presentation in children with DM1 was A1 * 0201 / B1 * 0201 (DQ2.2) in 85.6% and A1 * 0501 / B1 * 0201 (DQ2.5) in 14.4%.

Conclusion: The presence of DQ2 in the group of Colombian children with CD is consistent with that reported in the literature. However, most frequently found alleles differ with other populations. These results suggest that, although the clinical presentation of CD in different populations is similar, there are genetic differences that may have an impact on different aspects, which requires further investigation.

*863 EARLY GROWTH IN CHILDREN WITH CELIAC DISEASE: A PROSPECTIVE COHORT STUDY

Christian Riddervold Kahrs¹, Maria C. Magnus², Knut E. A. Lundin³, Ketil Størda², ¹Østfold Hospital Trust, Grålum, Norway, ²Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway, ³Oslo University Hospital Rikshospitalet, Oslo, Norway & Centre for Immune Regulation, University of Oslo, Oslo, Norway

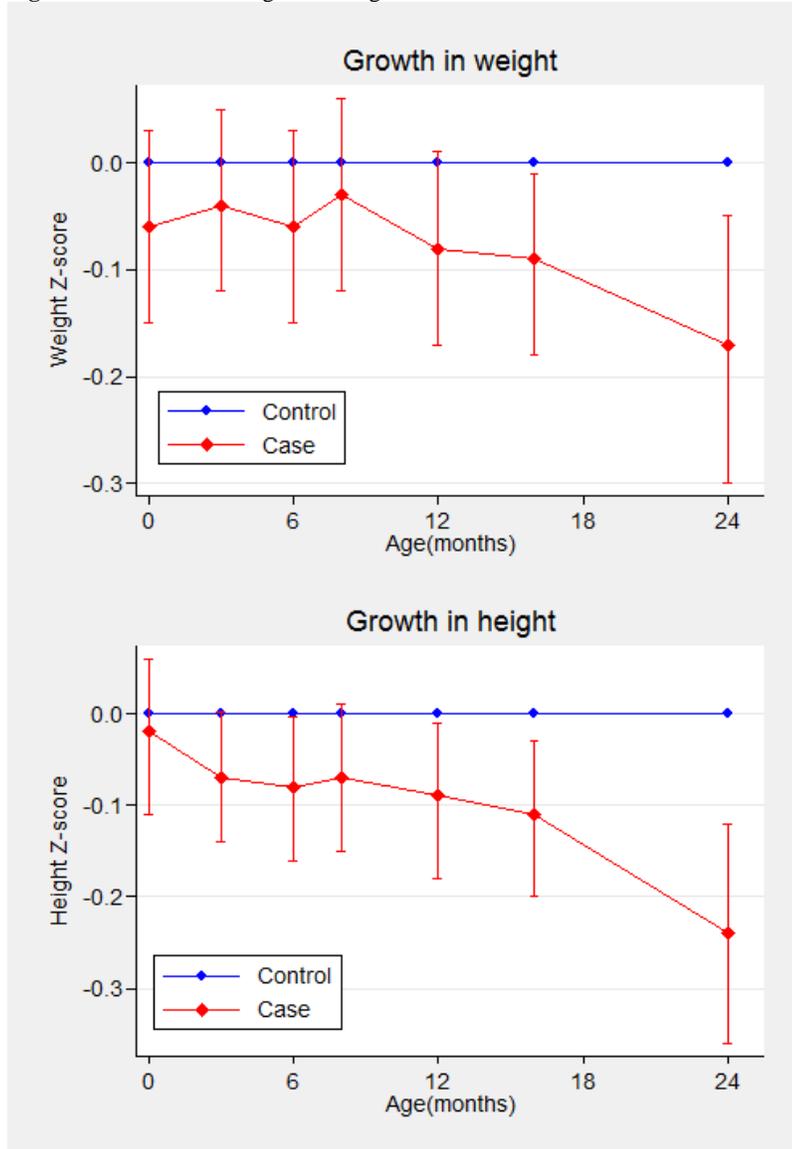
Objectives: Impaired growth is an early and common feature in patients with celiac disease, but little is known about when growth faltering starts. We aimed to compare growth data from birth to 24 months in children later diagnosed with celiac disease and healthy controls in a large birth cohort.

Methods: This study is based on the Norwegian Mother and Child Cohort Study (MoBa) and includes 58,675 children born from 2000 - 2009 with prospectively-collected growth data as measured at birth and at the child's health center at 3, 6, 8, 12, 15 - 18 and 24 months of age. When studying growth, we used Z-scores calculated from the studied population. Celiac disease was identified through combined data from questionnaires and the Norwegian Patient Register. Multivariable linear regression was used.

Results: During a median follow-up of 8.6 years, 440 children (0.8%) were diagnosed with celiac disease. Mean age at celiac disease diagnosis was 4.4 years (range 1.5 - 8.5). Children later diagnosed with celiac disease had significantly lower Z-scores for height from 12 months (-0.09, 95% CI, -0.18 to -0.01) and weight from 15 - 18 months of life (-0.09, 95% CI, -0.18 to -0.01). At 24 months of age, the difference was further increased to -0.24 (95% CI, -0.36 to -0.12) and -0.17 (95% CI, -0.30 to -0.05), respectively (see Figure). This corresponds to 250 g and 0.8 cm at age 24 months. Excluding children diagnosed before 2 years of age yielded similar results.

Conclusion: This study indicates, as a novel finding, that children later diagnosed with celiac disease had lower growth as early as 12 months of age. This highlights the importance of diagnosing celiac disease as early as possible and starting treatment. In future studies, screening growth before seroconversion warrants attention.

Figure. Differences in weight and height Z-scores between celiac children and controls from birth to 24 months



NOTE: Values are based on multivariable linear regression models and reflect differences in height and weight Z-scores between celiac children and controls. The model was adjusted for birth weight/height, maternal CD, parental weight/height, maternal education, maternal smoking during pregnancy, pre-term birth (<37 weeks), breastfeeding and childhood infections.

864 HOW WELL ARE PEDIATRIC CELIAC PATIENTS FOLLOWED? A RETROSPECTIVE LOOK AT A LARGE PEDIATRIC CELIAC DISEASE CENTER

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Background: Factors that influence compliance of routine follow-up and gluten-free diet (GFD) are poorly understood in pediatric patients with celiac disease. The University of Chicago's Celiac Disease Center (UCCDC) database includes 898 adult and pediatric patients evaluated for celiac disease (CD) or concern for CD. The UCCDC database includes 359 patients who have been seen as children at the UCCDC since the center started in 2001. Data was retrospectively collected from patients and chart review.

Objective: To assess predictors of adherence to follow-up and GFD at a large celiac referral center.

Methods: Retrospective analysis using Statistical Software R was completed by Random Forest, linear regression and recursive partitioning, evaluating management and follow-up of patients at the UCCDC. Analysis was completed on pediatric patients (0 - 18 years old) whose initial visit or date of diagnosis was in 2001 - 2013. Patients were also included based on diagnosis of CD at the UCCDC, or by an outside physician, and were excluded if CD was not yet determined, if CD diagnosis was excluded, or found to have gluten intolerance/sensitivity. This left 331 patients in the cohort analysis. We specifically analyzed documented follow-up visits, completion of upper endoscopy (EGD), adherence to GFD and repeat serologic testing.

Results: Please see Table 1 for descriptive data. Greater than 75% of patients were seen within 7 months after their initial encounter, and within 14 months thereafter, for their yearly visit. By the first follow-up visit, nearly half of patients (47%) reported strict adherence to GFD. Biopsy

was obtained for 290 (88%) of the patients. For the 41 patients in whom biopsy was not obtained, 33 patients had positive EMA and TTG Iga greater than 10 times the upper limit of normal. Neither gender, age, race, GI symptoms prior to presentation, nor failure to thrive predicted at initial follow-up by 7 months, was statistically significant. These variables are not predictors for GFD compliance by 36 months. There is a statistically significant correlation between obtaining biopsy and having the patient followed-up three times by 30, as well as how quickly the patient began GFD (R-squared 0.30, $p < 0.01$).

Discussion: The UCCDC is a large referral center and demonstrates robust follow-up, GFD adherence and completion of EGD. It is likely that compliance with follow-up and strict GFD are higher than what our center is able to capture. A possible limitation of the data is the inability to track patients' follow-ups with primary care providers, as well as outside hospital labs or EGD. Follow-up is important, as it is shown to correlate with compliance to a GFD, which is the best way to prevent symptoms of celiac disease. Determining predictors for patients who will likely follow-up and follow strict GFD will help physicians stratify patients who are at risk of being lost to follow-up or at risk of struggling with strict GFD.

Retrospective Analysis at UCCDC		
	Patients	% of 331 Patients
Total Patients Seen Initially Between 2001-2013	331	
Diagnosis		
Atypical CD (predominant extra-intestinal manifestations)	10	3
Diagnosis of CD with GI symptoms, abnormal serology, and biopsy pathology available	234	71
Diagnosis of CD with positive serology and GI symptoms, no biopsy initially performed	47	14
9 of these patients ended up undergoing EGD	9 of 47	
Silent CD (abnormal biopsy, positive serology, no symptoms)	11	3
Potential CD (normal biopsy [Marsh 0-I], positive serology, +/- symptoms)	18	5
Uncertain CD (diagnosed with outside provider and on GFD prior to being followed at UCCDC)	6	2
Latent disease (normal biopsy [Marsh 0-I], fluctuating serology and symptoms, previous gluten enteropathy)	4	1
Other (Positive Biopsy, symptomatic, normal serology)	1	0
Adherence to follow up frequency		
Second Encounter within 7 months after initial encounter	251	76
Third Encounter within 14 months after second encounter	257	78
Fourth Encounter within 14 months after third encounter	185	56
Fifth Encounter within 14 months after fourth encounter	137	41
Sixth Encounter within 14 months after fifth encounter	95	29
Biopsy Obtained	290	88
No Biopsy Obtained (initially)	41	12
Of These Patients, TTg Iga was greater than 10 times the Upper Limit of Normal	37 (90% of 41)	
Of These Patients, TTg Iga was greater than 10 times the Upper Limit of Normal and Positive EMA	33 (80% of 41)	
Reported Adherence at least once to Strict GFD		
By First Follow Up Visit (<7 months from initial encounter)	154	47
Within 12 Months	191	58
Within 18 Months	222	67
Within 24 Months	237	72
Within 30 Months	251	76
Within 36 Months	237	72
Reported Strict GFD Within 96 months	285	86

865 WATERMELON JUICE: NOVEL METHOD OF PREVENTING SMALL BOWEL MICROBIAL OVERGROWTH IN PATIENTS WITH LONG-TERM GASTROJEJUNAL TUBES

Bijal Mehta¹, Chirajyoti Deb², Elizabeth Felix², Karoly Horvath², ¹Winter Park High School, Orlando, FL, USA, ²Arnold Palmer Hospital for Children, Orlando, FL, USA

Introduction: Gastrojejunal (GJ) tubes lead to bacterial overgrowth around and in the lumen of the GJ tube as well as the small bowel and lead to malabsorptive symptoms, as well as dysfunction of the GJ tube. Antibacterial medications may help in the short-term, but may lead to resistance and risk of *C. difficile* infection. We report successful use of watermelon juice and present data supportive of its antimicrobial effect.

Materials and Methods: Case reports: Caregivers of 2 patients (14 yrs and 11 yrs), both with MRCP and GJ, had recurrent overgrowth around their GJ tubes for 3 and 4 years, with a rate of GJ tube change every 6 to 9 months. Feeding intolerance, abdominal distension and halitosis occurred at least 4 days per month. After initiating 4 to 5 ounces of watermelon juice daily over 2 to 3 hours, symptoms typical of overgrowth diminished to once every 3 to 4 months, with a follow-up of 3 years for both. GJ changes, made annually by protocol, showed clean outsides and patent lumen. Red flesh rind and green rind extracts as well as organic extracts of ethanol and methanol + chloroform were studied and compared with control. Listerine™ was used as a positive control against *B. fragilis*, *E. coli*, *P. aeruginosa*, *S. pyogenes*, *mitis*, and *S. aureus*.

Results: Watermelon juice, even when concentrated, had minimal or no antibacterial effect in our model. However, red rind, after ethanol or chloroform extraction, had significant inhibition of growth of almost all bacteria. Likewise, Listerine inhibited all bacteria tested. The green rind was partially effective.

Discussion: Antibacterial effect of watermelon juice, though only seen in our model after organic extraction, may explain efficacy with GJ tubes reported by patients. Antimicrobial activities of foods, such as watermelon, provide a novel approach to averting overgrowth.

866 DO HISPANIC CHILDREN WITH CELIAC DISEASE PRESENT DIFFERENTLY THAN NON-HISPANIC CHILDREN WITH CELIAC DISEASE?

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Background: Celiac disease (CD) is an immune-mediated disease characterized by villous atrophy at the level of the small intestine triggered by the ingestion of gluten-containing grains in genetically-susceptible individuals. CD has a highly variable clinical picture that leads to a large

number of patients remaining undiagnosed. To the best of our knowledge, there is a limited available evidence in Hispanic patients with CD and if any difference exists with non-Hispanic patients with CD.

Objective: To determine if any difference exists between Hispanic CD patients (HCD) vs. non-Hispanic CD (nHCD) patients.

Methods: We performed an IRB-approved chart review of all patients with CD at the Pediatric Gastroenterology outpatient clinic from February 2012 to October 2015. Demographic data, celiac serology levels, duodenal biopsy results, gastrointestinal symptoms, extra-intestinal symptoms, gluten-free (GF) diet compliance and symptomatic improvements with GF diet were recorded. We excluded all patients with negative celiac serology (with the exception of selective IgA deficiency), absence of duodenal biopsy results, or with a duodenal biopsy score of Marsh 2 or less. Patients were divided into HCD and nHCD groups.

Results: A total of 96 charts were reviewed and 54 patients were included in our study. There were 34 patients in the HCD group vs. 20 patients in the nHCD group. There was no difference between the groups regarding the age of diagnosis, BMI and gender ($p=0.27$). Although not statistically significant, HCD were diagnosed 2 years later compared to nHCD (8.47 vs. 6.23 years). There was no difference in the celiac serology testing in both groups with TTG IgA as the most common positive test (46% vs. 47%; $p=0.72$). There was no difference in the diagnosis of selective IgA deficiency and CD between both groups (53% vs. 58%; $p=0.48$). Regarding intestinal symptoms, there was no statistical significance for abdominal pain, bowel habits, or abdominal distention when comparing both groups ($p=0.49$). Short stature in association with CD was exclusively seen in HCD ($p<0.05$). Diabetes mellitus and CD was present in 8 patients with an increased incidence in HCD vs. nHCD (75% vs. 25%, $p=0.04$). Regarding GF diet compliance, there was no statistical significance between groups (46% vs. 52.9%, $p=0.76$). In both groups, there was symptomatic improvement after GF diet was initiated (83% vs. 76.4%, $p=0.71$). Regarding other syndromes associated with CD, there was no difference among the groups ($p=0.76$).

Conclusions: There was no difference in patients with HCD vs. nHCD in regards to the demographics, diagnosis and GF diet compliance. Both groups had a favorable clinical response with dietary restrictions to gluten. Patients with HCD had a higher association with diabetes mellitus and short stature compared to nHCD. Hispanic children with diabetes mellitus or short stature, or suspected symptoms, should be screened for celiac disease in the appropriate clinical setting.

867 OATS IN THE DIET OF CHILDREN WITH CELIAC DISEASE: A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, MULTICENTER STUDY

Elena Lionetti, Simona Gatti, Nicole Caporelli, Tiziana Galeazzi, Ruggiero Francavilla, Maria Barbato, Paola Roggero, Basilio Malamisura, Giuseppe Iacono, Andrea Budelli, Rosaria Gesuita, Carlo Catassi, Marche Polytechnic University, Ancona, Italy

Objectives and Study: The inclusion of oats in the gluten-free diet (GFD) for treatment of celiac disease (CD) is controversial. We aimed to evaluate, in a 15-month, randomized, double-blind, placebo-controlled, multicenter trial, clinical, serological and mucosal safety of a variety of pure oats in the treatment of pediatric patients with CD.

Methods: This is a non-inferiority clinical trial with a crossover design. Sample size was estimated using intestinal permeability test (IPT) as a primary response variable and considering a clinical difference between the two diets of 0.01 as maximum. We randomly assigned 306 children with a biopsy-proven diagnosis of CD to a GFD for at least 2 years, to receive a treatment AB (6 months of diet "A", 3 months of standard GFD, 6 months of diet "B"), or BA (6 months of diet "B", 3 months of standard GFD, 6 months of diet "A"). A and B diets included gluten-free products (flour, pasta, biscuits, cakes and crisp toasts) with either purified oats or placebo. The intake of oats was. Clinical [body mass index (BMI), class of BMI, Gastrointestinal Symptoms Rate Scale (GSRs) score], serological [IgA anti-transglutaminase antibodies (TGA), IgA and IgG anti-deamidated gliadin peptides (AGA) and IgA anti-avenin] and TPI data were measured at baseline (B1) and after six months of diet in the first period (T6), after three months of washout at the beginning of the second period to obtain measurements at the second basal (B2), and after six months of diet (T15). First- and second-order carry-over effect (θ , λ) and direct treatment effect were evaluated (τ) by a non-parametric approach using medians as summary statistics.

Results: After the exclusion of 129 patients who dropped out, the cohort included 177 children (79 in group A and 98 in group B). There were 124 girls (70%), and the median age of the cohort was 8.9 years (range, 6.9 to 11.2). Differences in treatment carry-over at the time of the second baseline measurement, differences in treatment carry-over at the time of the second treatment measurement (second-order carry-over or direct by period interaction), and direct treatment effect were not found to be statistically significant for all clinical, serological and mucosal variables studied. The upper limit of the 95% confidence interval of TPI direct treatment effect was found to be lower than the highest difference considered clinically relevant. Results from the crossover analysis are shown in the Table.

Conclusion: Pure oats are safe in the treatment of children with CD.

Table. First order carry-over effect, direct-by-period interaction, direct treatment effect according to the sequences AB, BA. Differences are 15 vs. 6 months' measurements

	θ	λ	τ
Median (1- α /2 % CI)	1st-order carry-over effect	Direct-by-period interaction	Direct treatment effect
BMI	0.084 (-0.05; 0.20)	0.05 (-0.15; 0.20)	-0.5 (-0.12; 0)
BMI Class	0.50 (-1.0; 1.50)	0.50 (-1.0; 2.0)	-0.25 (-1.0; 0.25)
GRSR Score	0 (0; 0)	0 (-0.5; 0)	0 (-2.5; 0)
IgA Aga	0.29 (-0.35; 0.90)	0.14 (-0.70; 1.05)	-0.15 (-0.50; 0.25)
IgG Aga	0.29 (-0.35; 0.90)	0.15 (-0.70; 1.05)	-0.15 (-0.50; 0.25)
TGA	0.4 (-0.05; 0.95)	0.30 (-0.25; 0.80)	-0.02 (-0.25; 0.23)
TPI	0.001 (-0.01; 0.01)	-0.003 (-0.014; 0.007)	0.004 (-0.0002; 0.0089)
IgA Anti-avenin	0.0005 (-0.0005; 0.0014)	-0.0005 (-0.0019; 0.0005)	-0.0002 (-0.0007; 0.0003)

868 CELIAC DISEASE SCREENING IN ASYMPTOMATIC TYPE 1 DIABETES MELLITUS PATIENTS ACROSS NORTH AMERICA AND EUROPE

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Objective: Many medical associations recommend screening for celiac disease (CD) in at-risk groups, as type 1 diabetes mellitus (T1DM).

There is a lack of consensus among guidelines on who and how to screen, specifically concerning asymptomatic patients. We aim to evaluate current practices and factors influencing and limiting the screening of CD in asymptomatic T1DM patients across North America and Europe. We also compared the screening habits of different countries.

Methods: A web-based survey was sent to pediatric endocrinologists and pediatricians with an expertise in T1DM in Canada, the United States and Europe between February 2014 and December 2015. Physicians were contacted through the following associations: Pediatric Endocrine Society (PES), International Society for Pediatric and Adolescent Diabetes (ISPAD) and European Society of Pediatric Endocrinology (ESPE). **Results:** A total of 381 participants responded to our survey. Two hundred and twenty-nine (60.1%) were from the United States, 90 (23.6%) from Europe, 48 (12.6%) from Canada and 14 (3.7%) from other countries. Almost 21% of Canadians claimed to never screen asymptomatic T1DM patients for CD, compared to 0.4% of Americans ($p<0.001$) and 0.0% of Europeans ($p<0.001$). When asked about the possible consequences of not treating asymptomatic CD patients, 22.2% of Canadians reported no possible consequence compared to 5.7% of Americans ($p<0.001$) and 5.6% of Europeans ($p=0.01$). 37.5% of Canadians do not agree that screening for CD in asymptomatic patients with T1DM can reduce their morbidity, compared to 12.0% of Americans ($p<0.001$) and 14.4% of Europeans ($p=0.06$). There is a difference in association guidelines used across countries for screening for CD in asymptomatic patients with T1DM. Canadians are mostly familiar with the Canadian Diabetes Association recommendations (87.5%, $p<0.001$), while Americans are more familiar with the American Diabetes Association (79.3%, $p<0.001$) and European with ISPAD (82.2%, $p<0.001$) and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (56.7%, $p<0.001$). Less than 15% of Canadians and Americans are familiar with the North American Society for Pediatric Gastroenterology Hepatology and Nutrition guidelines. 56.3% of Canadians think that the recommendations from their endocrine associations are unclear regarding screening for CD in asymptomatic patients with T1DM, compared to 34.5% of Americans ($p=0.01$) and 19.8% of Europeans ($p<0.001$).

Conclusions: We noted a clear difference in practices, mostly between Canadians and other responders. This difference could be explained by the discordance existing between current guidelines. A unification of guidelines would be needed to clarify practice, mostly in Canada. To help achieve this goal, more studies would be helpful concerning the possible consequences of screening, or not screening, asymptomatic T1DM patients for CD.

869 DESCRIPTIVE POPULATION-BASED STUDY OF CELIAC DISEASE IN A NORTH AMERICAN PEDIATRIC POPULATION

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Background: Celiac disease (CD) is common immune-mediated disorder that affects up to 1% of the general population. Consuming gluten in genetically-susceptible subjects results in small bowel mucosal damage. Recent reports suggest that incidence of CD has reached a plateau in many countries.

Methods: Using the unified record of Rochester Epidemiology Project, we retrospectively reviewed Mayo Clinic and Olmsted Medical Center medical, pathological and laboratory records from January 1994 to December 2014 to identify all CD cases in Olmsted County in subjects aged 18 or younger at the time of diagnosis. Incidence rates were calculated by adjusting for age, sex and calendar year and standardizing to the 2010 US white population.

Results: We identified 100 CD patients who met our inclusion criteria. Incidence of CD has increased from 8.1 per 100,000 per year from 2000 - 2002 to 21.5 per 100,000 per year from 2011 - 2014. There was an increase in CD prevalence in children from 0.10% in 2010 to 0.17% in 2014. Thirty-four patients (34%) presented with classical CD symptoms, whereas 43 patients (43%) had non-classical CD and 23 patients (23%) were diagnosed by screening asymptomatic, high-risk patients. Thirty-six patients had complete atrophy on small bowel biopsy, 51 had partial atrophy, 11 had intraepithelial lymphocytosis and 2 were diagnosed without biopsy. Most patients had normal BMI, 17% were overweight/obese and only 9% were underweight.

Conclusion: Despite the reports that CD occurrence had reached a plateau in some European countries, both incidence and prevalence continued to increase in children over the last 15 years in Olmsted County. The clinical and pathological manifestations of CD are changing over time. More non-classical and asymptomatic cases are being diagnosed.

870 FREQUENCY OF CELIAC DISEASE IN CHILDREN PRESENTING WITH LIVER DISEASE AT A TERTIARY CARE CENTER

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Background: Celiac disease (CD) is a genetically-determined, chronic inflammatory disease induced by an environmental precipitant. It is a multisystem disease and can develop at any point of time during life in genetically-susceptible individuals upon ingestion of wheat gluten and related cereal proteins. The onset of symptoms in the atypical form generally occurs between 4 and 15 years of age. The common presentations are short stature and refractory anemia. Diagnosis of CD with extra-intestinal manifestations is frequently missed, as it presents without diarrhea.

Objective: To observe the frequency of celiac disease in children with liver disease attending at the Pediatric Gastroenterology and Nutrition department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Method: This cross-sectional study was conducted at BSMMU from January 2014 through June 2015. A total of 59 children (aged 18 months to 16 years) with clinical and biochemical features of liver disease were initially enrolled in the study. Their clinical history, examination findings and investigation reports were recorded on a self-developed data collection sheet and informed consent was obtained from parents. Routine investigations, liver function tests, tTG (IgA), total IgA, etcetera, were done. After exclusion of other causes of liver disease, endoscopy of upper gastrointestinal tract (GIT) was done on patients who were tTG-positive (titer more than 50 U/mL). Patients who were tTG-negative,

but found IgA-deficient (1 patient), were also selected for upper GI endoscopy and biopsy fragments which were taken from duodenum (D2) and sent for histopathology.

Result: Mean age of studied children was 8.33 ± 3.64 years. Out of 59 children with liver disease, 32.2% were tTG-positive, of whom 8 (13.6%) were female and 11 (18.6%) male. Mean age at diagnosis of all patients in the tTG-positive group was 8.24 ± 2.78 (range 4 - 12) years. Among 19 sero-positive patients, short stature was found in 57.9% children. Mean Hb level in the tTG-positive group was 8.83 ± 2.64 gm/dL and 10.27 ± 1.74 gm/dL in the tTG-negative group. Sixteen (84.2%) out of 19 tTG-positive patients had raised S. ALT. Out of 19 tTG-positive children, endoscopy was done in 15 cases (endoscopy could not be done in 4 patients due to persistently raised PT) along with 1 patient who was IgA-deficient. Endoscopic changes were mosaic and scalloping of D2 mucosa in 1 and 2 cases, respectively. Histological changes compatible with CD were found in 5 (31.3%) patients. Marsh 3a category was found in 2 (12.5%) cases and 3b in 3 (18.8%) cases.

Conclusions: In the present study, 32.2% of liver disease cases were found to be tTG-positive. Histological changes compatible with CD were found in 31.3% of cases. Screening for celiac disease may be included in the diagnostic tests for evaluation of liver disease in children.

871 NEW PATHOLOGICAL CONSIDERATIONS FOR CELIAC DISEASE

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Objectives: Celiac disease (CD) currently affects 1% of the general population. Sampling duodenal biopsies characterized by villous atrophy (VA) and increased intraepithelial lymphocytes (IEL) remains the gold standard confirming diagnosis. However, there are cases where diagnosis remains difficult, because the histological criteria are not fully met: either the number of IEL is not increased, or VA is incomplete. In addition, an increase in IEL can occur in other digestive disorders (DD). The aim of this study was to refine histological diagnostic criteria of CD.

Methods: This study includes 175 duodenal bulb D1 (n=79) and duodenal D2 (n=96) biopsies from 96 CD patients (58 females; mean age 7 yrs), 135 normal D2 biopsies (69 females; mean age 12 yrs) and 64 D2 biopsies of other DD (39 females; mean age 13 yrs), such as Crohn's disease, *Helicobacter pylori*-gastritis, or eosinophilic oesophagitis. Biopsies were obtained from children over a period of 4 years for histological review by 2 pathologists (N.P. and D.D.S).

Results: Inter-observer agreement was greater for the classification of Corazza-Villanacci, when compared to Marsh-Oberhuber's ($\kappa 0.812$ vs. $\kappa 0.409$, respectively). A threshold of 25 IELs/100 epithelial cells (EC) allowed for discrimination between normal and celiac cases. When the IEL count ranged from 40 and 70 IELs/100 EC, 32% of patients were CD, whereas 50% had other DD. When IEL count was above 70 IELs/100 EC, 53% were CD and only 6% had other DD. In CD, IELs were significantly located above EC nuclei compared to other DD, (12 IELs/100 EC vs. 2, respectively). In 21% of CD cases, D2 were normal and the diagnosis could only be made on biopsies in D1. Finally, 6% of CD cases showed isolated increase in IELs in D1 without architectural modification.

Conclusions: The duodenal bulb D1 allowed diagnosis of CD in 21% of cases. Moreover, our work demonstrated that, in 6% of D1 celiac cases, increased IEL may be the sole abnormality. An intraepithelial count >70 IELs/100 EC strongly evokes CD, as only 6% of patients with other DD fell within this range. Between 40 and 70 IELs/100 EC, CD is very likely, but other DD must be considered. For villous architecture gradation, Corazza-Villanacci's classification reported best inter-observer reproducibility. Finally, the preferential localization of IELs above EC nuclei favours CD.

872 SERUM AUTO-ANTIBODIES FOR CELIAC DISEASE MONITORING IN CHILDREN

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Objective. Our aim was to evaluate the utility of different serological tests in celiac disease (CD) monitoring. At present, these tests are mostly used for diagnosing CD.

Methods: 63 newly CD-diagnosed children were included in the study. The children were diagnosed at the National Institute for Mother and Child Health according to current ESPGHAN CD diagnosis guidelines. Data regarding gender, age, investigations at diagnosis, compliance with a regular follow-up and adherence to a gluten-free diet (GFD) were collected for all. Quantitative determination of serum celiac-specific auto-antibodies: IgA-antitransglutaminase2 (tTG2-IgA, positive cut-off 20 U) and antiendomysium (EMA, positive cut-off at serum dilution of 1:5) were done at their regular follow-up visits.

Results: Median age at diagnosis was 5 years with a girl:boy ratio of 1.86. Nineteen children did not require small-bowel biopsy for CD confirmation according to ESPGHAN criteria. Mean period of compliance for the regular follow-up was 2 years. Transgressions from the GFD were declared by 8 children. Both tTG-IgA and EMA antibodies showed positivity 18 months after the diagnosis in up to 29% children declaring strict avoidance of gluten. The percentage of children with negative seroconversion was significantly higher in biopsy-proven rather than in serology-based diagnosed children. After two years of GFD, only 31 (49%) children showed negative seroconversion of tTG2-IgA and 47 (74%) EMA, respectively.

Conclusions: Children with only serology-based diagnosis seem to be less adherent to the GFD and to regular follow-up. EMA is the first antibody to react to GFD, with tTg-IgA being the last to seroconvert. The high proportion of patients with still positive antibodies after 2 years on GFD suggests the necessity of a frequent and regular follow-up. The discrepancy between the number of children that reported adherence to GFD, and the number of children that became seronegative, indicate the utility of the serological tests in long-term follow-up of CD.

873 ASSOCIATION BETWEEN CYP2C19 EXTENSIVE METABOLIZER PHENOTYPE AND pH PROBE-TESTING ACID EXPOSURE OUTCOMES IN CHILDREN TAKING PROTON PUMP INHIBITOR MEDICATIONS

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Esophageal pH probe testing is commonly performed in children to assess the efficacy of proton pump inhibitor (PPI) medication therapy for gastroesophageal reflux disease (GERD). PPI medications are metabolized by the CYP2C19 enzyme, which is encoded by the CYP2C19 gene, variants of which give rise to extensive, normal and poor metabolizer (EM, NM, PM) phenotypes. We hypothesized that the CYP2C19 enzyme

EM phenotype among children who have undergone esophageal pH probe testing while on PPI therapy would be associated with pH probe acid exposure outcomes. Across the Nemours Health System between 2000 - 2014, we identified a retrospective cohort of 74 children >2 years of age who had stored endoscopic tissue samples available and had previously undergone esophageal pH testing on PPI therapy. CYP2C19 SNPs were genotyped by TaqMan (rs4244285, *2; rs4986893, *3, rs41291556, *8; rs17884712, *9; and rs12248560, *17) and patients were classified as PM, NM and EM phenotypes. Basic demographics and pH probe acid exposure outcomes were compared among 21 EM vs. 53 NM + PM and are shown in the table below. PPI CYP2C19 EM phenotype was significantly associated with higher acid exposure outcomes compared to NM + PM phenotypes. In conclusion, PPI medication therapy in children may be better optimized with genotype-guided dosing prior to pH probe testing.

pH PROBE OUTCOMES MEAN (SD)	CYP2C19 METABOLIZER PHENOTYPE		
	PM+NM (N = 53)	EM (N = 21)	p value
Caucasian % (n)	69.8% (37)	76.2% (16)	0.82
Male % (n)	62.3% (33)	66.7% (14)	0.86
Age at pH probe, years	8.3 (4.9)	8.6 (4.8)	0.41
PPI dose, mg/kg	1.10 (0.62)	1.26 (0.45)	0.33
Test duration, minutes	1463 (590)	1225 (260)	0.16
Number of reflux events	48.5 (37.1)	62.8 (46.2)	0.07
Duration of longest reflux event, minutes	10.1 (17.4)	23.4 (45.0)	0.05
Number of episodes > 5 minutes	1.5 (2.6)	2.9 (3.6)	0.08
Time pH < 4.0, minutes	33.5 (48.2)	76.5 (121)	0.01
Percent of time pH < 4.0	2.67 (3.85)	5.71 (8.50)	0.01
Acid clearance, seconds	109 (159)	181 (278)	0.04

874 CELIAC DISEASE SCREENING IN THE ASYMPTOMATIC PEDIATRIC POPULATION: PARENTS' AND ADOLESCENTS' PERSPECTIVES

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Objectives: Celiac disease (CD) mass screening in the pediatric population is still controversial. The purpose of this study is to investigate the opinion of parents and adolescents about CD screening in asymptomatic pediatric population and to assess their knowledge of the disease.

Methods: This cross-sectional, descriptive study was conducted between November and December 2015. An anonymous self-administered questionnaire, developed after a careful literature review and tested previously by volunteer adolescents (aged 14 - 17 years) and parents, was administered to adolescents and parents of children without symptoms or a diagnosis of CD when they were presenting to the pediatric outpatient clinic at the Centre Hospitalier Universitaire de Sherbrooke, Québec, Canada. The questionnaire consisted of 3 parts. The first part focused on the participants' knowledge of CD. The second part evaluated the level of agreement of respondents on different arguments in favor of, or against, CD screening. The seven selected arguments can be summarized by "right to know", "resolution of health problems", "long-term benefits", "pain associated", "unnecessary gastroscopy", "lack of long-term benefits" and "life-long, gluten-free diet". The participant's opinion on CD screening was asked after mentioning different prevalences of the disease. The last part consisted of demographic information.

Results: Overall, 76 adolescents and 151 parents of children without symptoms or a diagnosis of CD responded to our questionnaire. Among respondents, only 46.1% were in favor of the screening, without differences between the adolescent and the parent group. However, after respondents were informed of a hypothetical prevalence of CD similar to those having a high-risk condition (10%), 82.4% presented a positive attitude toward screening. Arguments that were most predictive of a favorable opinion were the patients' right to know if they had CD (OR 1.66, $p=0.004$) and the resolution of unrecognized health problems (OR 1.75, $p=0.006$). Participants' mean knowledge score was 62.1%. A higher knowledge score and the presence of a high-risk condition in adolescents or children were both factors that were linked to a favorable opinion on screening.

Conclusion: Mass screening doesn't seem to be acceptable to the majority of participants. However, a large proportion of them were in favor of screening when they were confronted with a prevalence of CD of 10%, similar to those with a high-risk condition. This result is in accordance with the current trend of recommendations to screen for CD in high-risk groups.

875 DEVELOPMENT OF THE STANDARDIZED DIETICIAN-INTEGRATED EVALUATION TOOL FOR GLUTEN-FREE DIETS (DIET-GFD)

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Background: Celiac disease is a chronic immune disorder for which the primary treatment is a gluten-free diet. Assessment of dietary adherence by a dietician is the best available non-invasive method to monitor patients with celiac disease, yet neither the process, nor the content of this assessment, have been standardized.

Aims: To develop a standardized reporting tool for dieticians evaluating gluten-free diet adherence by patients with celiac disease.

Methods: A literature review guided initial content for the scale, with consideration of the elements required to evaluate adherence to a gluten-free diet as a behavior, as well as an outcome. Using a consensus process, an expert panel composed of gastroenterologists, dieticians with expertise in monitoring patients on gluten-free diets, psychologists and persons with celiac disease developed a ten-point ordinal descriptive scale for dietary adherence, ranging from poor adherence and no precautions to avoid gluten to strict adherence and strict precautions to avoid gluten. The dieticians then performed duplicate assessments of 10 patients and the scale was further revised following panel discussions of the cases, where the dietician ratings were discordant, or they were uncertain which rating to apply. The revised scale was used for duplicate assessments of 23 additional patients by the same dieticians. These assessments were used to determine the intraclass correlation coefficient.

Results: The Dietician Integrated Evaluation Tool for Gluten-Free Diets (DIET-GFD) includes features related to frequency and quantity of gluten ingestion based on self-report and food frequency evaluation, shopping and dining habits, how food is prepared and consumed, eating behaviors, locations where food is prepared and consumed and label reading skills. For example a score of 1 was assigned if there was gluten in the kitchen and no precautions with food preparation, or greater than 5 gluten-containing foods on a food frequency questionnaire, or consumption of gluten as a major ingredient >1/week and consumption of gluten when eating out. The assigned global scores ranged from 1 - 10 (mean 7.2, SD 1.7, median 8, IQR 7 - 8). The interrater agreement was good with an intraclass correlation coefficient of 0.804.

Conclusions: The DIET-GFD is a descriptive reporting tool for dietician assessment of patient adherence to a gluten-free diet. The level of agreement between two expert dieticians was good. Use of a standardized tool facilitates comparison of ratings by different dieticians and serial ratings in a single individual over time. Further studies are needed to evaluate reliability and validity and to determine how this scale can be applied across institutions and cultures.

*876 A CELIAC GENETIC RISK SCORE IS A HIGHLY DISCRIMINATIVE "RULE OUT" DIAGNOSTIC TEST

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Background: Celiac disease is a common autoimmune gastrointestinal disorder and its incidence is rising. Clinical diagnosis can be difficult, particularly when patients eliminate gluten from their diet, as this reduces the sensitivity of TTG antibodies (aTTG) and of biopsy. There is strong genetic predisposition for celiac disease that can be measured by Single Nucleotide Polymorphism (SNP) genotyping which is rapid, inexpensive (10c/SNP) and stable over time. Importantly, SNPs can very accurately tag the HLA alleles known to be critical for susceptibility to celiac disease.

Aim: To determine whether a celiac genetic risk score (CGRS) generated from SNPs could be used as a diagnostic test to rule out celiac disease.

Methods: We developed a CGRS from 46 published celiac-associated SNPs. This included 6 SNPs to tag classical HLA-DQ haplotypes, 6 SNPs to tag additional HLA risk and 34 non-HLA celiac associated SNPs. The GRS was generated by summing genetic contribution of each SNP weighted by published odd ratio (Oram *et al*, *Diabetes Care* 2016; PMID: 26577414). We tested the ability of the score to discriminate celiac disease diagnosis in two cohorts: 1) In a population-based study, we included 120,000 people from UK Biobank who were genotyped with the UK Biobank Axiom Array. We identified patients with celiac disease (n=312) based on electronically-linked hospital diagnoses. 2) A local cohort of 67 children referred to a specialist pediatric celiac disease clinic were assessed using endoscopy (n=42) or serial aTTG testing (n=25); 55 had celiac disease diagnosed by either endoscopic biopsy or serology.

Results: The CGRS was highly discriminative of celiac disease in the UK Biobank (ROC-AUC 0.89, $p < 0.0001$). Median (IQR) CGRS in non-celiac disease vs. celiac disease was 1.4 (-0.1 - 4.1) vs. 5.5 (4.6 - 6.2), $p < 0.0001$. The predictive power of the CGRS was almost entirely due to the 12 HLA SNPs (ROC-AUC 0.88, $p < 0.0001$) with little contribution from the 34 non-HLA SNPs (ROC-AUC 0.60, $p < 0.0001$). A low score effectively excluded celiac disease (GRS > 0.24 , 60% specific, 96% sensitive) and a high score was indicative of celiac disease (GRS $> 0.5.8$, 95% specific, 44% sensitive for celiac disease). In the local pediatric cohort, the GRS was similarly able to exclude celiac disease (CGRS > 2.4 was 100% sensitive and 64% specific for celiac) disease. Not one proven celiac patient had a score below 2.4.

Conclusion: A CGRS is highly discriminative of celiac disease and a low score can be used to exclude a need for diagnostic endoscopy or repeated serological screening for celiac disease. Similarly, a high CGRS increases the likelihood of celiac disease as a diagnosis. The CGRS is very cheap (<\$5), more predictive than HLA typing alone and could improve clinical diagnosis of celiac disease. CGRS could prove superior for serological diagnosis and additionally be used to target high-risk individuals for future preventative studies.

877 CHARACTERIZING EPCAM GENE MUTATIONS CAUSING TUFTING ENTEROPATHY IN QATAR

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Introduction: Tufting enteropathy (TE) is a rare, autosomal, recessive disease that causes early-onset, severe, life-threatening diarrhea and malabsorption that leads to malnutrition and impaired growth. Most patients will require long-term total parenteral nutrition (TPN) and later, small bowel transplantation. Both interventions have significant morbidity and mortality. The estimated prevalence is around 1/50,000 to 100,000 live births in Western Europe, but it seems higher in areas with a high degree of consanguinity and in patients of Arabic origin.¹ Genetic studies have found the association of EPCAM² and SPINT2^{3,4} gene mutation in disease etiology. The present molecular genetics study was performed to identify the pathogenic variant in the EPCAM gene causing congenital TE in Qatari families.

Materials and Methods: Six consanguineous families with TE were ascertained from Qatar. The blood samples were collected from patients and normal family members after taking informed written consent. The DNA was isolated and the coding region of EPCAM gene was screened through sanger DNA sequencing for identification of pathogenic variant. The segregation analysis of the identified variant was also confirmed in whole family.

Results: The sequence analysis revealed a c.498_499insC mutation in exon 5 in the 6 families tested. This mutation truncates the protein synthesis (p.(Gln167Profs*21)). This predictably removes the C-terminal domain of EPCAM protein, which suggestively assists the EPCAM to anchor in the intracellular membrane.

Conclusions: The identified mutation, c.498_499insC, seems to be a founder mutation of Arab ethnicity, because it has already been reported in Qatari, Kuwaiti⁵ and Saudi⁶ families. The present molecular study has evidenced this mutation as a genetic hotspot and suggests formulating a molecular diagnostic test in Qatari families, affected with tufting TE, for genetic counseling. The test can also be added to the premarital screening tests done for Qataris.

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878 AN ANALYSIS OF GASTROINTESTINAL BLOOD FLOW WITH DOPPLER ULTRASONOGRAPHY IN CHILDREN WITH FOOD PROTEIN-INDUCED ENTEROPATHY

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Introduction: Reports of the image evaluation related to acute phase of gastrointestinal food protein-induced enteropathy (FPE) have been scarcely observed. The aim of this study is to compare the accuracy of diagnosis between ultrasonic findings and laboratory data, such as allergen-specific lymphocyte stimulation test (ALST), among 13 infants diagnosed as FPE.

Methods: Three groups consisting of 13 infants (3.7 ± 3.8 month-old) diagnosed as FPE with gastrointestinal symptoms, such as vomiting, bloody stool and failure to thrive, 15 infants (10.4 ± 2.4 month-old) diagnosed as acute infectious gastrointestinal enterocolitis (AGE) and 10 healthy controls (7.3 ± 3.5 month-old) were enrolled in this study. We investigated three examinations: 1) B-mode abdominal ultrasonic (US) findings in the FPE group, 2) laboratory data including ALST in the FPE group and 3) analyzing the power Doppler imagings of fasting intestinal blood flow signals with US and indirectly quantifying the intestinal blood flow with the method of vessel density (VD) which Epifanio *et al* reported previously.

Results: Thirteen patients with FPE were classified into two groups according to their clinical symptoms by Nomura *et al.* Six infants and seven infants were classified as cluster 2 and 3, from the chief complaints of vomiting and failure to thrive, respectively. In the B-mode US findings, wall thickness (13/13), poor peristalsis (13/13) and mesenteric thickness (12/13) of the small intestine were observed in both cluster 2 and 3. Colonic wall thickness was observed in a patient of cluster 3. Among the ALST against three types of cow's milk protein (β -lactoglobulin, lactoferrin and f β -casein), the positive rate against one or more antigens was 84.6% (11/13). While two cases were negative, each intestinal VD was more than 18.7%. Moreover, the sensitivity and specificity of intestinal VD in this study were 100% and 96.0%, respectively. Small intestinal VD in FPE was significantly enhanced than in that of AGE and healthy controls ($p < 0.01$). Meanwhile, no significant differences were observed between AGE and healthy controls.

Discussion: The involved site visualized by US substantially coincided with cluster classification, but cluster-overlapped cases were also seen. The accuracy of correct diagnosis rate was improved by the combination of ALST and VD. By comparing VD at the site of jejunum, ileum and colon among three groups, VD at the small intestine with FPE was enhanced significantly. In addition, there was a significant difference ($p < 0.01$) in VD between FPE and AGE, since there was no enhanced VD observed in AGE.

Conclusion: Abdominal Doppler ultrasonography and measuring intestinal VD could play a very important role in the diagnosis of FPE with severe symptoms of diarrhea and failure to thrive during infancy.

879 MATERNAL AND NEONATAL VITAMIN D STATUS IN RELATION TO CELIAC DISEASE

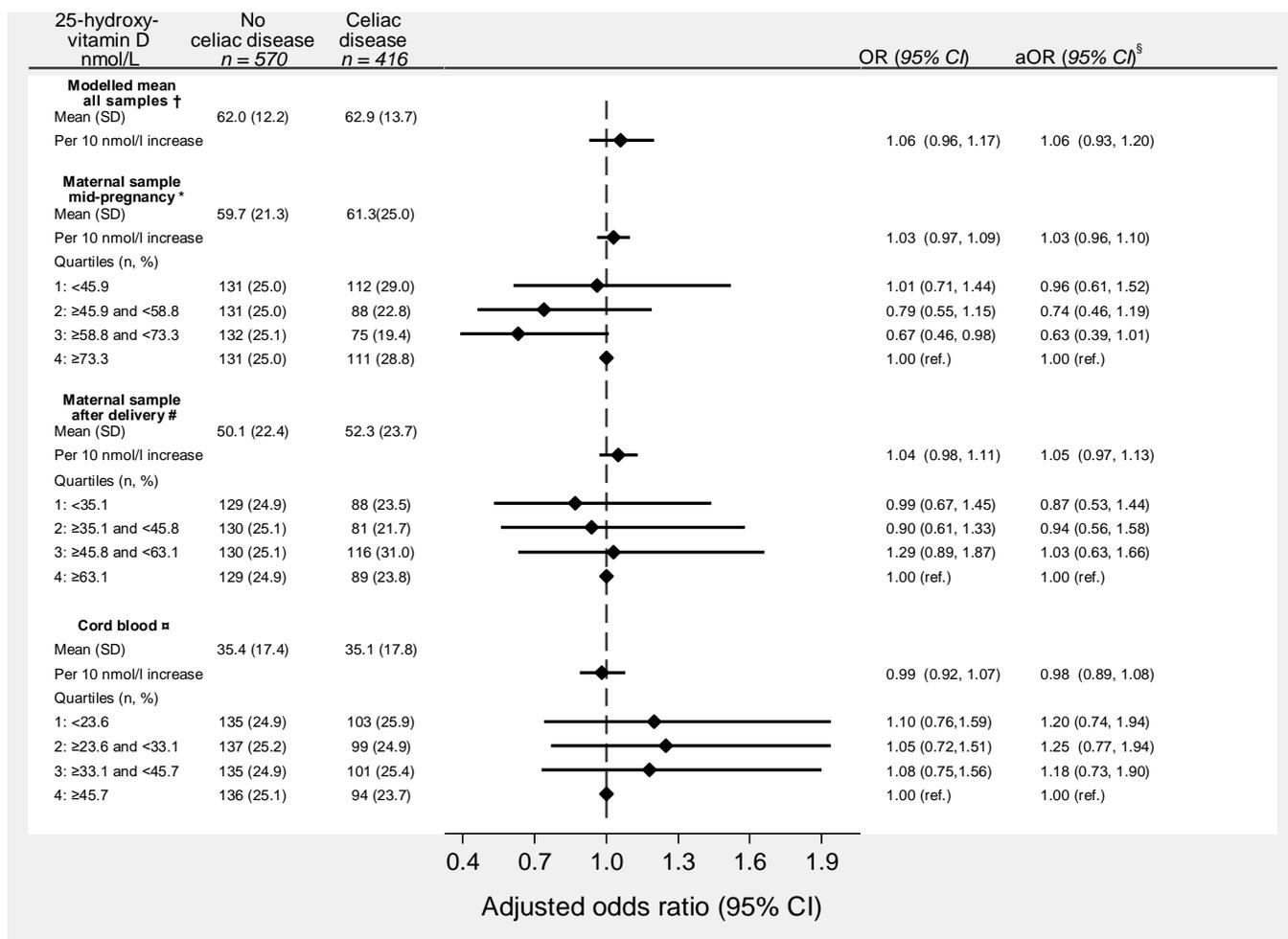
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Background: Low levels of 25-hydroxyvitamin D during pregnancy may, in addition to its role in skeletal health, contribute to the development of autoimmune disorders. Celiac disease is a prevalent immune-mediated disease with largely unidentified environmental risk factors, but with a higher prevalence for children born in spring. We therefore aimed to test whether low maternal and neonatal 25-hydroxyvitamin D predicted higher risk of childhood celiac disease.

Methods: We analyzed 25-hydroxyvitamin D in maternal blood from mid-pregnancy, at birth and in cord blood from 416 cases where the child was later diagnosed with celiac disease and 570 controls, nested within a large pregnancy cohort. Mothers and children were genotyped for established celiac disease and vitamin D metabolism variants. We used mixed linear regression models and logistic regression to study associations.

Results: Average 25-hydroxyvitamin D was 62.9 nmol/L in cases and 62.0 nmol/L in controls. The adjusted odds ratio for celiac disease per 10 nM increase was 1.06 (95% CI, 0.93 - 1.20), and concentrations were similar for all three samples separately. Vitamin D insufficiency genotype score was not associated with celiac disease (adjusted odds ratio 0.99, 95% CI, 0.57 to 1.70, for highest versus lowest child genotype quartile). Dietary vitamin D intake from food or supplements during pregnancy, or by the child postnatally, did also not predict celiac disease. Adjustment for HLA or other established genetic risk markers gave similar results.

Conclusions: We found no support for the hypothesis that maternal or neonatal vitamin D status is related to the risk of childhood celiac disease.



880 CELIAC DISEASE: NOT JUST DUODENAL DAMAGE AND LOW BMI

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Objective: Our aim was to analyze the clinical, serological and histological presentations of CD in children living in central Florida in the last decade.

Methods: We performed a retrospective study of all children who were diagnosed with celiac disease in the tertiary center of the Arnold Palmer Hospital for Children between 2005 and 2015. Patient records were reviewed to obtain information on demographic characteristics, symptom presentation, growth parameters and laboratory and histology results, including disaccharidases, associated diseases, treatment and its response. CD was defined as the presence of both typical histology and CD-positive antibodies.

Results: We identified 169 pediatric patients with CD. The female:male ratio of our sample was 1.8:1. Average age at presentation was 9.48 ± 4.39 years. The majority of patients were 5 - 15 years old at time of diagnosis. Abdominal pain was the most common presenting symptom in 44%, followed by diarrhea (18%) and constipation (16%). Short stature was the symptom in 15% of patients. Anemia was noted at presentation in 4.6% of the cases. Interestingly, failure to thrive was found on presentation in only 7% of the cases. Weight loss was noted in 8.6%. Body mass index (BMI) was below the 5th percentile on growth charts in only 5.5% of the case. However, 73% of the children had a BMI over the 50th percentile. Diabetes mellitus type 1 was associated with CD in 20% of the cases, while 5.7% had hypothyroidism and 3.4% had associated Down's syndrome. Two-third of the patients had a Marsh histology grade of 3 (37.1% grade 3A and 27.8% 3B). Severe histological changes with grade 3C were seen in 18.5% of the patients, while grade 1 and 2 was noted in 3.3% and 13.25%, respectively. There was a correlation between the Marsh scores and the level of tTG IgA elevation. Chronic gastritis was associated with CD at time of diagnosis in 52% of the cases, with only 2% being secondary to *Helicobacter pylori* infection. 19% of the patients had reflux esophagitis. Lactase deficiency was the most common associated disaccharidases abnormal activity (79.7%), followed almost equally by the rest of the disaccharidases (about 72% of patients). Generalized enzyme deficiency was present in 96.4% of cases with Marsh 3c damage. There was no immunity to HBV in 62.7% of the tested children. Duodenal culture was positive in 7 (28%) of the tested 25 patients.

Conclusions: The presentation of CD in children has changed in the past decade and non-specific abdominal pain became the most frequent symptom, replacing failure to thrive, chronic diarrhea and bloating. One-sixth of the children had constipation as the main symptom. The majority of children presented with BMI above the 50th percentile. Half of this population had chronic gastritis. Close to 80% of children had lactase deficiency and a temporary, lactose-free diet was beneficial in reducing their symptoms.

881 TRANSFORMING THE CARE OF CHILDREN WITH CELIAC DISEASE

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Celiac disease (CD) affects approximately 1% of the New Zealand population. New presentations of CD in children in the Auckland region have increased annually for the last decade. Diagnosis and long-term management was historically based at Starship Children's Hospital, meaning diagnosis was often delayed and follow-up clinics were over-subscribed. Care delivery was fragmented and lack of access to community pediatric dietitians meant service delivery remained at a tertiary specialist level. Factors such as delays to diagnosis, annual reviews without focus, travel times, inaccessible parking and lack of access to dietetic input outside of clinic appointments, were recognized by families as causes for dissatisfaction.

After review by a performance improvement team, a patient-centred, self-management care pathway was introduced. A collaborative process involving key stakeholders led to an evidence-based algorithm for diagnosis and management with tertiary services providing diagnostic endoscopy only. Thereafter care is delivered by primary healthcare and Coeliac New Zealand (NZ), a non-governmental organisation (NGO).

What this means for patients:

- Streamlined, more rapid diagnosis
- Consent for referral to Coeliac NZ prior to biopsy
- Long-term care coordinated by primary care
- Standardized nutrition information
- Community dietetic education
- Peer support from Coeliac NZ within three days of notification and 12 months' membership paid by the hospital.

What this means for primary healthcare:

- Electronic pathway to diagnostic service that is direct, instant and traceable
- Online guidance, resources and links to community services
- Dietitians and general practitioners receive complimentary membership to Coeliac NZ
- The current service model may struggle to deliver care within a standard appointment.

What this means for Starship Children's Hospital:

- Automatic acceptance of e-referrals for endoscopy
- Ongoing collaboration with key stakeholders
- Increased clinic capacity releasing more than 200 appointments annually and decreased waiting times for all patients.

Almost 100% of families consented to Coeliac NZ involvement. Some of those who did not, already had existing membership for other family members. Preliminary feedback of patient experience has been overwhelmingly positive. Patients have access to information they describe as helpful and reassuring, they feel better supported and value the peer support.

Subsidization of Coeliac NZ membership has been more than offset by cost savings in the tertiary sector of approximately NZ\$75,000 per year. This unique collaboration between primary and tertiary healthcare and an NGO has resulted in more effective use of tertiary resources and high family satisfaction. A program of consultation and resource development is planned to build longevity into the service. The pathway could be offered nationwide to achieve equitable care and an improved patient experience for all NZ children with CD.

*882 ENHANCED SURVIVAL FOLLOWING ORAL AND SYSTEMIC INFECTION WITH SALMONELLA TYPHIMURIUM INFECTION IN POLYMERIC IMMUNOGLOBULIN RECEPTOR KNOCKOUT MICE

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Background: The majority of IgA is produced in the intestinal lamina propria, where it is transported to the lumen as secretory IgA (sIgA) by the polymeric immunoglobulin receptor (pIgR). pIgR-mediated transport of sIgA is thought to play a crucial role in intestinal barrier function and protection from infection with *Salmonella typhimurium*. We conducted experiments to test the hypothesis that absence of sIgA impairs barrier function and resistance to *S. typhimurium*.

Methods: C57BL/6 or pIgR knockout mice (pIgR KO) were sacrificed at 6 - 10 weeks of age. Jejunal tissue was collected for Ussing chamber studies, mesenteric lymph nodes (mLN) were collected for aerobic bacterial counts and serum and stool were collected for antibody analysis. Separately, 6-to-10 week old C57BL/6 or pIgR knockout mice were inoculated either orally (10^{10} - 10^{13} CFU) or IV (3.2×10^2 CFU) with *S. typhimurium* SL1344 and followed for survival or sacrificed for tissue analysis.

Results: pIgR-KO mice displayed increased serum IgA, decreased stool IgA and proportion of IgA-coated fecal bacteria. pIgR KO mice exhibited decreased jejunal transepithelial resistance (TER), but no corresponding increase in FITC-dextran flux and decreased mLN bacterial growth. pIgR KO mice survived longer than C57BL/6 mice when challenged both orally ($p=0.01$) and IV ($p=0.005$) with *S. typhimurium*. C57BL/6 mice showed increased spleen weight and CFU counts in the cecum, mLN, spleen and liver 7 days following oral *S. typhimurium* infection.

Conclusions: pIgR promotes barrier function, but is not essential for protection against *S. typhimurium*. Importantly, mice lacking pIgR survive longer following both oral and IV infection, suggesting sub-epithelial immune factors are more critical for innate immunity to *S. typhimurium*. Further studies are needed to elucidate these factors to accelerate the development of effective interventions against this deadly pathogen.

883 OBSERVATIONAL STUDY ON THE CLINICAL OUTCOMES OF TREATMENT WITH AN EXTENSIVELY HYDROLYZED WHEY-BASED FORMULA IN INFANTS WITH COW'S MILK PROTEIN ALLERGY

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Background: Cow's milk protein allergy (CMA) is the most common food allergy in the first year of life. Infant growth and psychomotor development can be severely compromised without an adequate diagnosis and treatment. Current evidence on clinical response in children with CMA to an extensively hydrolyzed, whey-based formula is insufficient.

Objective: To determine the clinical outcomes (response, acceptance and cow's milk protein tolerance) in infants (<12 months old) diagnosed with CMA, who were fed an extensively hydrolyzed, whey-based formula (Nutrilon Pepti Junior®), assessed by resolution of the initial symptoms.

Methods: An observational, retrospective, case series study was conducted. Infants (<12 months old) who were referred for evaluation of CMA-related symptoms to a pediatric gastroenterology clinic, from January 2011 to October 2015, at Hospital Universitario Fundación Santa Fe de Bogotá (HU-FSFB) were included. Information on demographic characteristics, digestive manifestations, time from symptom onset, anthropometry and clinical response was abstracted by retrospective chart review. All calculations were performed using STATA 11.1 software. We considered a *p*-value < 0.05 to be statistically significant.

Results: 40 infants (42.5% male) were included, age 3.3 ± 2.4 months old, presenting with the following symptoms: vomit/regurgitation in 21 (52.5%), stomach cramps/irritability in 8 (20%) and blood in the stool in 4 (10%) patients. Family and perinatal history related to development of CMA was early introduction of cow's milk formula in the first week of life, 27 (67.5%); mother 30 years or older, 33 (82.5%); atopy in at least two family members (parents/siblings), 12 (30%); Caesarean delivery 30 (75%). 37 (92.5%) patients showed a positive clinical response to an extensively hydrolyzed, whey-based formula (Nutrilon Pepti Junior®), whereas 3 (7.5%) patients required a free amino acid-based formula. Z-scores for weight/age of -0.69 ± 1.03 and -0.79 ± 1.00 for weight/height from the first pediatric gastroenterology consult showed a significant improvement (*p*<0.05) on follow-up at age >12 months to -0.27 ± 0.98 for weight/age and -0.14 ± 0.98 for weight/height (Table 1). Follow-up was conducted for 10.1 ± 6.8 months, after which 19 (47.5%) patients developed tolerance to cow's milk between 12 and 18 months.

Conclusion: Nutritional recovery and tolerance to cow's milk were found in a large percentage of infants with CMA fed with an extensively hydrolyzed, whey-based formula.

Table 1. Nutritional status on first pediatric gastroenterology visit and on follow-up visit*

First visit (n=40)	Follow-up visit (n=24)	<i>p</i> -value
$-0,69 \pm 1,03$	$-0,27 \pm 0,98$	0,01
$-0,79 \pm 1,00$	$-0,14 \pm 0,98$	0,001

* Data for follow-up visit were included only if the patient was 12 months-old or older on last visit.

884 ASSESSMENT OF CELIAC SEROLOGY TESTING IN LOCAL CONNECTICUT LABORATORIES

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Introduction: Screening guidelines for celiac disease, an immune-mediated enteropathy caused by gluten, typically includes checking serology for tissue transglutaminase IgA (TTG IgA) and a total IgA. Additional serologies are available, though these tests are not usually required or necessary. Patients may undergo such testing based on physician request, or because of inclusion in available celiac panels in hematology laboratories. The aim of this study was to evaluate availability of celiac serology as individual tests and as part of panels at individual laboratories in screening for celiac disease.

Methods: We conducted a cross-sectional survey across local hematology labs throughout Connecticut. We created a standardized survey that was conducted via phone to each individual hematology lab. We asked questions about the availability of celiac testing as a send out test or performed locally including total IgA, TTG IgA/IgG, endomysial Ab IgA/IgG, deaminated gliadin peptide IgA/IgG, anti-gliadin IgA/IgG. We also assessed for the availability of celiac panels at each of the laboratories.

Study Results: A total of 25 hospitals and laboratories in the state of Connecticut were identified and surveyed. We collected information from 23 laboratories (92%), of which there were 20 unique hospital and clinical laboratories. 90% of the surveyed labs were hospital-based laboratories and the remainder were clinical laboratory companies. 90% utilized an outside laboratory for some, or all, of the celiac testing. Celiac panels were available at 85% of laboratories with only 2 labs requiring each specific test to be ordered individually by a healthcare provider. There were 16 unique celiac panels identified. 38% of celiac panels included deaminated gliadin IgA and/or IgG, 63% of panels included anti-gliadin IgA and/or IgG and 56% of panels included endomysial antibodies. Genetic testing for HLA DQ2 and DQ8 gene test was not included as part of any celiac panel, but available at 65% of laboratories as a send-out lab.

Discussion: ESPGHAN and ACG guidelines recommend screening for celiac disease to include total IgA and TTG IgA. In specific circumstances, additional testing may be needed, such as in children <2 years of age and in total IgA deficiency, where deaminated gliadin antibodies and IgG celiac serology are also important to check. Anti-gliadin antibodies lack specificity and have been replaced by deaminated gliadin antibodies. Anti-gliadin antibodies are still performed at 50% of labs and are part of 63% of bundles. Available celiac panels in the surveyed group included testing for serologic markers that are not required for evaluation of celiac disease. Extensive and unnecessary serology testing is a poor utilization of resources and false positive tests may lead to unnecessary diet changes, parental concern and further diagnostic testing. Standardizing available celiac lab bundles and panels may reduce over-utilization of unnecessary labs.

***885 THE CORRELATION BETWEEN THYMIC STROMAL LYMPHOPOIETIN RISK ALLELES AND FOOD ALLERGEN DISEASE TRIGGERS IN PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS**

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Background and Aims: Many patients with eosinophilic esophagitis (EoE) have an elevation in thymic stromal lymphopoietin (TSLP), which is a cytokine that is secreted by epithelial cells in response to stressors, such as infection, allergens, or stimulation of toll-like receptors. TSLP has been identified as a risk allele in the Caucasian population. To date, there are no large scale studies which analyze the number or type of EoE food allergen triggers in children with TSLP risk alleles, nor has there been study into the correlation of TSLP risk alleles and the presence of atopy in EoE pediatric patients. This study aimed to determine whether the presence of one or more TSLP risk alleles is correlated with having multiple EoE food allergen triggers and to define the atopy characteristics of these EoE pediatric patients with TSLP risk alleles.

Methods: A retrospective chart review was performed of all pediatric patients with EoE at the Children's Hospital of Philadelphia from 2008-2014. All patients that had TSLP genotyping were included. A food was identified as an EoE food allergen trigger if a patient was histologically diagnosed with EoE while eating the specific food, the food was removed from the diet and the number of esophageal eosinophils normalized once the food was removed. Atopy was defined as having at least one of the following features: asthma, allergic rhinitis, or atopic dermatitis. The number of patients that had at least one of these atopic features was compared with the number of patients that had no atopic features. IgE-mediated food allergy was also reviewed. The data were statistically analyzed using Chi-square analysis.

Results: We describe a population of 381 pediatric patients whose TSLP gene was genotyped. Fifty-seven patients were found to have homozygous protective TSLP alleles, whereas three hundred and twenty-four patients were found to be either heterozygous or homozygous for TSLP risk alleles. There was a statistically significant increase in the number of patients with 3 or more EoE food allergens among those who had one or more TSLP risk alleles compared to those with homozygous protective alleles ($p=0.01$). Table 1 shows the prevalence of various food allergen triggers compared to TSLP genotype.

There was also a statistically significant difference in the presence of atopy between those with homozygous protective TSLP alleles (81%) versus having at least 1 TSLP risk allele (90%, $p=0.03$). There was no significant difference in IgE-mediated food allergy or gender between the various genotypes.

Conclusions: The presence of the TSLP risk allele is associated with having multiple EoE food allergen triggers, as well as an increased prevalence of atopy in our patient cohort. This is a critical finding as, based on this evidence, we propose that the ideal treatment for these children with TSLP risk alleles may be medication-predominant rather than driven by food elimination diets.

Table 1. EoE Food Allergen Triggers. Food triggers not cited in this abbreviated table: fish (20% vs. 10%), rice (10% vs. 14%), oat (10% vs. 17%), barley (0% vs. 11%), seeds (0% vs. 4%)

	TSLP Homozygous Protective Allele, n (%)	At least 1 TSLP Risk Allele, n (%)
Total Number of Patients	57 (15%)	324 (85%)
3 or more EoE Food Allergen Triggers Identified*	10 (18%)	109 (34%)
Food Allergen Trigger:Milk	6 (60%)	70 (64%)
Food Allergen Trigger:Meat	5 (50%)	53 (49%)
Food Allergen Trigger:Vegetable	4 (40%)	49 (45%)
Food Allergen Trigger:Soy	6 (60%)	41 (38%)
Food Allergen Trigger:Egg	2 (20%)	39 (36%)
Food Allergen Trigger:Wheat	5 (50%)	38 (35%)
Food Allergen Trigger:Peanut	2 (20%)	33 (30%)
Food Allergen Trigger:Fruit	1 (10%)	26 (24%)
Food Allergen Trigger:Tree Nut	1(10%)	16 (15%)
Food Allergen Trigger:Shellfish	1 (10%)	11 (10%)

* One patient's specific food allergen triggers could not be identified due to limited medical records

886 SINGLE-CENTER EXPERIENCE WITH FRUCTOSE MALABSORPTION

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Background: The causes of abdominal pain can be multifactorial, chronic abdominal pain in children remains difficult to treat. Studies have shown that malabsorbed fructose may be a cause of abdominal pain in some patients previously labeled as functional. Other symptoms described in such group of patients include, but are not limited to, bloating, nausea, flatulence, diarrhea and emesis. Fructose is a naturally occurring monosaccharide, which is increasingly being used in the form of a high-fructose corn syrup as a cheap food additive. The aim of this study is to assess for a possible difference in presenting symptoms of patients who have fructose intolerance and those who do not have fructose intolerance diagnosed by a fructose breath hydrogen test (FBHT).

Methods: Institutional review board approval was granted by SUNY upstate medical university after review of the study protocol. This is a retrospective chart review study completed for children under the age of 21 years with the CPT code 91065 (breath hydrogen or methane test) seen in the pediatric gastroenterology clinic from March 2012 to September 2015. Data abstraction included demographic data, clinical characteristics upon first presentation and results from the FBHT X2 test was performed for statistical analysis of initial presenting symptoms among those patients who tested positive for FBHT and those who tested negative; significance was assigned at $p<0.05$.

Results: A total of 367 patients were identified (246 females and 121 males) with a mean age of 12.2 years. FBHT indicated fructose intolerance in 208 of 367 patients (133 females and 76 males) with a mean age of 11.5 years. A total of 159 of 367 patients (113 females and 45 males), with a mean age of 13.1 years, had a negative FBHT. Of the patients with positive FBHT, 206 had abdominal pain, 79 had diarrhea, 27 had constipation, 27 had emesis, 101 had nausea, 1 had foul breath, 45 had bloating and 11 had flatulence. Of the patients with negative FBHT, 158 had abdominal pain, 65 had diarrhea, 50 had constipation, 36 had emesis, 103 had nausea, 1 had foul breath, 23 had bloating and 7 had flatulence. Statistical significance between these two groups was reached for constipation, emesis and nausea with *P*-values of <0.001, 0.015 and 0.002, respectively.

Conclusions: Fructose malabsorption plays a role in the development of symptoms seen in patients with functional bowel syndrome. When fructose is not properly absorbed, it stays in the lumen drawing fluid and this may cause distention, producing pain and bloating. It is also fermented by colonic bacteria which produce gases. Fructose malabsorption has been described to present with different symptoms. In our study, we were able to demonstrate that patients who have fructose malabsorption are less likely to present with symptoms of constipation, emesis, or nausea compared to those who do not have fructose malabsorption upon initial evaluation.

887 ESOPHAGEAL DISTENSIBILITY AS A PREDICTOR OF CLINICAL PHENOTYPE IN PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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Background: The current practice for diagnosing and monitoring response to therapeutic interventions of eosinophilic esophagitis (EoE) is based on quantifying the number of eosinophils in esophageal mucosal biopsies. Studies have shown that EoE symptoms do not always correlate with the degree of eosinophilia shown on biopsy. Recent studies suggest the role of underlying esophageal fibrotic remodeling and poor distensibility in causing EoE symptoms, even in the absence of active mucosal inflammation. EndoFLIP is a new FDA-approved test that is able to assess the esophageal distensibility.

Methods: Pediatric patients who were referred to the Neurogastroenterology and Motility center at RCHSD for dysphagia were included in this study. Symptom severity was assessed using The Pediatric EE Symptom Score (PEESS). Each patient underwent UGI and concurrent EGD and EndoFLIP. Two biopsies were taken from each esophageal level: proximal, middle and distal. If EoE was diagnosed, a repeat EGD was done after an 8 - 16 week-course of PPI 1 mg/kg/day. EndoFLIP consists of a balloon catheter with 17 electrodes along its length. The catheter was placed with 2 sensors below the gastroesophageal junction (GEJ). The balloon was filled to a minimum volume of 30 cc and continued to fill until cross sectional areas (CSA) plateaued. We recorded the narrowest CSA along the esophagus (CSAmin) with maximal balloon distention.

Results: We enrolled three patients with dysphagia, age 7 - 12 yrs (2 M, 1F). Two were found to have newly diagnosed EoE and 1 of these had repeat endoscopy after a PPI course. Prior to therapy, CSAmin ranged from 162 to 198 mm², average eos/HPF 35 - 40, mean patient PEESS 0.9 to 2.25 (maximum score 4). On repeat endoscopy after PPI in patient (1), eosinophils/HPF (prox/mid/distal) improved from 18/100/24 to 0/58/32; PEESS was stable; CSAmin decreased from 198 to 150mm². Patient (3) had a history of food impaction and was scoped after 3 months of PPI. She was diagnosed with PPI-responsive esophageal eosinophilia (PPI-REE), with resolved mucosal eosinophilia at all esophageal levels. She had a CSAmin 191 mm², but GEJ diameter was narrow, suggesting need to evaluate the GEJ with manometry.

Conclusions: EndoFlip technique is a useful tool in identifying the etiology of dysphagia in children. In patients with EoE, CSAmin are <200 mm² as reported previously. EoE symptoms may correlate better with poor distensibility than with eosinophilia, as shown in patient (1). Symptomatic patients with PPI-REE may benefit from EndoFLIP, as seen in Patient (3).

888 TISSUE TRANSGLUTAMINASE AUTOANTIBODIES IN CHILDREN WITH NEWLY DIAGNOSED TYPE 1 DIABETES ARE RELATED TO HLA BUT NOT TO DIABETES AUTOANTIBODIES: A SWEDISH, NATIONWIDE, PROSPECTIVE, POPULATION-BASED COHORT STUDY

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Objectives: To study the association between tissue transglutaminase autoantibody (tTGA), a marker for celiac disease (CD) and high-risk human leucocyte antigen (HLA) genotypes and diabetes autoantibodies, or both, as well as possible variances by gender and age, in newly diagnosed type 1 diabetes mellitus (T1DM) children in Sweden.

Methods: Dried blood spots and serum samples were taken at diabetes diagnosis from children participating in a nationwide prospective cohort study for newly diagnosed T1DM children (0 - 18 years old) known as Better Diabetes Diagnosis. tTGA, HLA-DQ typing, GAD65, IA-2, insulin and three variants of inc transporter autoantibodies (ZnT8W, R, QA) were analyzed.

Results: Out of 2705 children with clinically diagnosed T1DM, 85 (3.1%) had tTGA and 63 (2.3%) had borderline values. The frequency of tTGA was higher in children with HLA genotype DQ2/2, DQ2/X or DQ2/8, compared to both DQ8/8 and DQ8/X and to DQX/X (*p*=0.0001) (see Table). The presence of tTGA was more common in girls (*p*=0.018) and no statistically significant difference was found between the age groups.

Conclusion: The high prevalence (5.5%) of tTGA at clinical onset of T1DM diagnosis was more common in girls and in children homozygous for DQ2/2, followed by children heterozygous for DQ2. No children lacking DQ2 and DQ8 were positive for tTGA. HLA-typing at diabetes diagnosis can be useful to decide who needs to be screened repeatedly for CD.

Abbreviations: 65 kDa isoform of glutamine acid decarboxylase autoantibodies, GAD65Ab; Insulinoma-associated protein 2 autoantibodies, IA-2Ab; Insulin autoantibodies, IAAb; Arginine 325 zinc transporter 8 autoantibody, ZnT8RA; Tryptophan 325 zinc transporter 8 autoantibody, ZnT8WA; Glutamine 325 zinc transporter 8 autoantibody, ZnT8QA; Zinc transporter 8 autoantibody to either one or all three amino acid variants at position 325, ZnT8Ab

Table. The distribution of HLA-DQ genotypes by tTGA results in 2526 newly diagnosed type 1 diabetes patients

HLA genetic markers	tTGA positive N (%)	tTGA borderline values N (%)	tTGA positive and borderline values N (%)	tTGA negative N (%)
DQ2/2, DQ2/X and DQ2.2/X <i>n</i> =503	22 (4.4)	17 (3.4)	39 (7.8) [†]	464 (92.2)
DQ2/2 <i>n</i> =172	10 (5.8)	8 (4.7)	18 (10.5)	154 (89.5)
DQ2/X <i>n</i> =284	12 (4.2)	8 (2.8)	20 (7.0)	264 (93.0)
DQ2.2/X <i>n</i> =47	0 (0)	1 (2.1)	1 (2.1)	46 (97.9)
DQ2/8 <i>n</i> =787	41 (5.2)	22 (2.8)	63 (8.0) [†]	724 (92.0)
DQ8/8 and DQ8/X <i>n</i> =1165	21 (1.8)	22 (1.9)	43 (3.7) [†]	1122 (96.3)
DQX/X <i>n</i> =216	0 (0)	0 (0)	0 (0)	216 (100)

DQ2 denotes (DQA1*05:01-DQB1*02:01); DQ8 (DQA1*03:01-DQB1*03:02);

DQ2.2 denotes (DQA1*02:01-DQB1*02:01); DQX is other haplotype than DQ2, DQ2.2 and DQ8.

[†]p-value DQ2/2 and DQ2/8 compare to DQ8/8 and DQ8/X <0.0001

889 CREATION OF CELIAC BENCHMARKS: THE FIRST STEP IN PRE-TRANSITION SELF-MANAGEMENT ASSESSMENT

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Background: Transition planning for children with chronic disease includes the development of independence in many self-management tasks. Conditions that depend on diet have distinct skill sets that are not well assessed by the traditional tools that assess transition readiness. For patients with diabetes and food allergies, there has been literature that describes age-appropriate skill acquisition. However, there are no age-appropriate benchmarks established for celiac disease (CD).

Methods: A multidisciplinary group of celiac experts (including SW, RD, MD, PNP, parents) collaborated on a list of tasks specific to CD self-management. A survey, based on this list, was developed asking patients what age he or she mastered a specific task and what age they thought other celiac patients mastered it. Parents had a parallel survey. IRB approved the study. Recruitment of patients ages 5 - 26 occurred in celiac clinics and through online announcements in a support group email. All surveys were anonymous and voluntary.

Results: Responses were collected from 83 parents and 57 patients. 59% of the patients were diagnosed with CD before age 7 and 93% were diagnosed before age 12. We developed a timeline for the acquisition of eighteen tasks based on the age at which 60% of participants reported that each self-management skill could be accomplished (Table 1). Parent- and patient-reported similar ages at which the patients were able to master each task. Parents, as compared to the patients, expected other children with CD to be able to master most tasks, particularly simpler tasks, at a slightly younger age. Conversely, for more complex tasks like traveling domestically or internationally, patients expected other children with CD to be able to master these more complex tasks at a slightly younger age than that reported by parents.

Conclusions: These preliminary results demonstrate that patient and parent surveys are effective instruments in assessing self-management skills in children with celiac disease, an important step in establishing age-appropriate and developmentally-relevant benchmarks for acquisition of CD self-management skills. These benchmarks, when developed, may provide valuable anticipatory guidance to children with CD, parents and medical clinicians to aid in transition planning as patients reach adulthood.

Table 1. Age by which 60% of participants reported that this self-management skill could be accomplished.

Skill	Patient		Parent	
	Self	Others	Child	Others
Age when washing hands <i>without</i> the help of an adult:	5	5	5	5
Age when asking if food was <i>safe</i> to eat:	8	8	8	6
Age when identifying that certain foods were <i>unsafe</i> to eat (bread, pizza):	8	8	8	6
Age when recognizing GF symbol as "Gluten-Free":	8	8	9	6
Age when able to eat safely (cleaning off table, wiping surfaces) in a shared space:	8	9	8	8
Age when recognizing and describing effects of eating gluten on their body:	10	9	9	8
Age when able to explain celiac disease <i>to a friend</i> :	10	9	9	8
Age when able to explain celiac disease <i>to an authority member</i> (teacher, friend's parent):	10	8	10	8
Age when able to explain celiac disease <i>to a stranger</i> (or family friend):	11	9	10	9
Age when taking vitamins on their own without adult supervision:	10	10	10	10
Age when able to plan their own gluten-free options to have at social gatherings:	12	11	10	10
Age when able to identify <i>safe</i> options for food and drink in <i>restaurant</i> :	11	11	11	10
Age when <i>able to ask</i> about food preparation in restaurants:	12	11	12	12
Age when able to identify that <i>vitamins</i> and/or <i>supplements</i> are gluten-free:	12	13	12	12
Age when able to identify that <i>medications</i> were gluten-free:	12	13	12	14
Age when able to negotiate <i>domestic</i> travel plans regarding their celiac condition:	13	13	14	14
Age when able to assess risk to their celiac condition during job opportunities (ex. working in a bakery, being a restaurateur):	15	16	15	16
Age when able to negotiate travel plans <i>internationally</i> regarding their celiac condition:	15	16	16	18

890 MANAGEMENT AND PRESENTATION OF CELIAC DISEASE IN A DISTRICT GENERAL HOSPITAL

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Background: Celiac disease (CD) is an immune-mediated enteropathy caused by a permanent sensitivity to gluten in genetically-susceptible individuals. In the UK, 1 in 100 people are affected by CD. Recent NICE guidelines set out the guidance for the diagnosis and management of CD. They recommend that all patients should be seen by a specialist, require dietician input and be annually reviewed. Children from the entire county of Lincolnshire are referred to Lincoln County Hospital (LCH) for their diagnosis and are managed by a single consultant pediatrician with an interest in gastroenterology. This gives a more accurate picture of presentation of CD in children from a local population when compared to the tertiary centre.

Aims: To compare our practice for the diagnosis and management of children with CD over a 5 year period from 2009 to 2014 with the current NICE guidelines and to look at any change in presentation/practice from the previous audit (1999 - 2005).

Methods: Retrospective review of the patients diagnosed with CD over a 5-year period from 2009 - 2014 in LCH was undertaken and compared with the previous audit (1999 - 2005). Age of presentation, duration of symptoms, clinical presentation, serology, biopsy findings, management, follow-up and sibling screening data were collected and compared. Patients diagnosed elsewhere and subsequently moved to Lincolnshire were excluded for analysis.

Results: 63 children (25 M, 38 F) were diagnosed with CD from 2009 - 2014 vs. 41 (19 M, 22 F) in the previous audit. Mean age of diagnosis was 8.1 yrs vs. 6.1 yrs, duration of symptoms was the same in both (6 - 8 months), 65% presented with gastrointestinal symptoms vs. 49%, iron deficiency anemia was 9% vs. 22%, IDDM 14% vs. 22%, associated disorder 5% vs. 7%, asymptomatic 7% vs. nil, latent celiac 8% vs. 12%, EMA and TtG 100% vs. 100% and 7% in the previous audit, HLA typing 14% vs. 4%, biopsy done in 97% in both audits, dietician reviewed 100% in both audits, siblings screened 100% vs. 55%, follow-up in celiac clinic 93% v.s 70% and first-degree relative 21% vs. 14% in the previous audit. Associated conditions included type-1DDM (9), Down's syndrome (2), Addison's disease (1) and skeletal dysplasia (1).

Conclusions: In our cohort of patients, we noted that there was a significant increase in the number of patients with CD and that they presented at a slightly older age. More patients had gastrointestinal symptoms. 7% were asymptomatic in the recent audit. The incidence of CD in a first-degree relative was high at 21%. Most patients are reviewed in annual celiac clinic and all siblings of patients are been screened. Overall, the audit shows that our practice is compliant with the NICE guidelines.

891 CELIAC DISEASE: EVOLUTION OF THE EPIDEMIOLOGICAL PROFILE OVER THE LAST DECADE

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Background: Celiac disease is a chronic, autoimmune enteropathy caused by gluten ingestion. We observed epidemiological changes over the last decade. Our objective was to study the epidemiological, clinical and evolutive characteristics of this disease, to seek changes in presentation in the last decade and to identify factors influencing this pathology.

Methods : We conducted a retrospective study of celiac children followed in the pediatric department of Mongi Slim Hospital La Marsa from January 1, 2004 until December 31, 2014. We studied the clinical, biological, endoscopic and evolutive characteristics of our patients and we compared the profile of the disease during 2 periods (2004 - 2009 vs. 2009 - 2014).

Results : Seventy-eight cases were recorded. The sex ratio was 0.41. The average age of gluten introduction was 6.26 months. The average period of breastfeeding was 6.1 months. The average age at onset of symptoms was 47.9 months. The average age at diagnosis was 82.4 months. The typical form was the most frequent (57.7% of cases). Beside chronic diarrhea, the most common clinical signs were: the break of the weight curve (48.7%), the break of the stature curve (42.3%) and abdominal distension (30.8%). The most common laboratory abnormalities were: hyposideremia (80%), hypocholesterolemia (66.6%), anemia (62%) and hypocalcemia (57.1%). At the intestinal biopsy, the villous atrophy was total or subtotal in 91% of cases. Compliance to a gluten-free diet was good in 68.2% of patients. A bone mineral density <-2 SD was noted in 5 children (15.6%). Serology was positive in those who were noncompliant to the gluten-free diet at 2 and 5 years of evolution ($p=0.000$). The comparison of the two groups identified the following independent factors: duration of breastfeeding ($p=0.039$), prophylaxis of vitamin D ($p=0.033$) and short stature in the initial examination ($p=0.004$).

Conclusion: The classic form (typical) remains the predominant form of celiac disease in Tunisia. Better awareness among pediatricians about atypical and asymptomatic forms is necessary to make an early diagnosis.

892 GASTROINTESTINAL AND EXTRA-INTESTINAL MANIFESTATIONS OF CELIAC DISEASE: EFFECTIVENESS OF THE GLUTEN-FREE DIET

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Background: Celiac disease (CD) is a complex autoimmune disease, triggered by the ingestion of gluten in genetically predisposed individuals, clinically leading to a wide range of gastrointestinal and extra-intestinal manifestations. The only effective treatment is a gluten-free diet (GFD). Objective: To evaluate the efficacy of the GFD in resolving gastrointestinal symptoms in pediatric and adult celiac populations at the University of Chicago (U of C) and how this compares to the resolution of extra-intestinal symptoms.

Methods: A retrospective chart review of the U of C Celiac Center clinic charts from January 2002 to May 2015 was performed. Demographics, serologic testing, intestinal biopsies and gastrointestinal symptoms at presentation, 12, 24, and >24 months were recorded. Gastrointestinal symptoms included abdominal pain, bloating, constipation, diarrhea, failure to thrive/weight loss, nausea, reflux and vomiting. Among extra-intestinal manifestations we analyzed: abnormal liver enzymes, arthralgia/arthritis, dermatitis herpetiformis, alopecia, fatigue, headache, anemia, stomatitis, myalgia, psychiatric disorders, seizures, neuropathy, short stature, delayed puberty, osteoporosis and infertility.

Results: From 827 celiac patients in our database at the May 2015 time point, 554 met inclusion criteria (biopsy confirmed CD or clinical symptoms consistent with CD plus TTG >10 ULN and positive EMA without biopsy); 277 pediatric (<18 years) and 277 adult patients. Gastrointestinal symptoms were reported by 80% of children and 91% of adults, while extra-intestinal symptoms by 59% of children and 67% of adults. Abdominal pain (52%), diarrhea (39%) and failure to thrive (37%) were the most commonly reported gastrointestinal symptoms at the time of diagnosis in children, while diarrhea (61%), bloating (56%) and abdominal pain (51%) were most common in adults. Short stature (33%), fatigue (28%) and headache (20%) were the most common extra-intestinal manifestations in children while iron deficiency anemia (48%), fatigue (37%) and headache/psychiatric disorders (24%) were the most common manifestations in adults. For pediatrics, the female-to-male ratio was 2:1 and the mean age at diagnosis was 8.8 years. Adults had a 3:1 female-to-male ratio and mean age at diagnosis was 39.3 years. Children had higher rates of both extra-intestinal as well as gastrointestinal symptom resolution compared to adults. Of note, improvement in gastrointestinal symptoms was greater than extra-intestinal symptoms recovery evaluated >24 months, in both children and adults, with a p-value of <0.0001.

Conclusions: Adults report less successful symptom resolution despite strict adherence to a gluten-free diet at >24 months compared to children, although the difference is not statistically significant. Both groups have significantly better gastrointestinal symptom recovery compared to the resolution of extra-intestinal symptoms after adhering to a gluten-free diet for >24 months.

893 IRON STATUS IN PEDIATRIC CELIAC DISEASE: A RETROSPECTIVE REVIEW

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Purpose: Proximal duodenal integrity is critical for dietary iron absorption. Celiac disease (CD) causes an autoimmune enteropathy that involves duodenal and jejunal villous damage. This suggests a potential role for serum iron studies in the diagnosis of CD. Current diagnostic standards only recommend measurement of serum IgA antibodies to tissue-transglutaminase (TTG-IgA) and histopathology assessment of villous damage from proximal duodenal biopsies (Marsh classification). The purpose of this study was to determine whether a relationship exists between serum ferritin levels, C-reactive protein (CRP), TTG-IgA and Marsh classification in a pediatric CD clinic population.

Methods: Patients 17 years or younger, who were followed by the pediatric CD clinic at McMaster Children's Hospital (Hamilton, Ontario, Canada) from 2007 to 2015 were included in the retrospective chart review. Charts were reviewed for measures of serum ferritin, TTG-IgA and duodenal biopsy-proven CD. Results were assessed by histopathology severity. Primary outcomes included correlation of serum ferritin with TTG-IgA and Marsh classification. Additional outcomes included change in ferritin levels after CD diagnosis, concurrent iron supplementation and correlation with other common intestinally-absorbed nutritional markers.

Results: 193 patients were identified from the retrospective chart review. 70 patients had serum ferritin levels performed prior to histopathology CD diagnosis (Marsh 1/2, 5 [7%]; Marsh 3A, 18 [26%]; Marsh 3B, 17 [24%]; Marsh 3C, 26 [37%]; Marsh 4, 4 [6%]). 653 paired ferritin/TTG-IgA levels were obtained and showed a significant, weak inverse correlation ($r = -0.114, p = 0.004$). There was a significant correlation between Marsh classification at diagnosis and ferritin levels [$F(4,65) 6.377, p = 0.0002$], as well as Marsh classification and TTG-IgA levels [$F(5,140) 2.412, p = 0.0393$]. Ferritin levels significantly rose after institution of a gluten-free diet (mean difference 8.685 $\mu\text{g/L}$, $p < 0.0001$). Patients receiving concurrent iron supplementation were excluded from analysis. No significant difference was found between 25-OH vitamin D and TTG-IgA, or CRP and TTG-IgA levels at diagnosis.

Conclusions: This retrospective review of iron status in pediatric CD demonstrates that serum ferritin levels correlate significantly with TTG-IgA levels in pediatric CD, but this relationship was weak and may have a limited role in diagnosis and disease monitoring. There was a strong, significant correlation between Marsh classification and both serum ferritin and TTG-IgA levels, as well as a significant increase in mean serum ferritin levels upon institution of a gluten-free diet. This study demonstrates that iron studies have a complementary role in the diagnosis and monitoring of pediatric CD patients. Prospective studies of additional nutritional markers may provide further insights into the diagnostic role for nutritional monitoring in celiac disease.

894 SHOULD WE ASSESS VITAMIN D STATUS IN PEDIATRIC PATIENTS WITH CELIAC DISEASE?

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Background: Celiac disease (CD) is an immune-mediated enteropathy caused by sensitivity to gluten in genetically susceptible individuals. Patients with CD have a variable degree of intestinal mucosal damage which places them at risk for nutrient malabsorption. Low bone mineral density has been strongly associated with both symptomatic and asymptomatic children with CD. However, there is no consensus on the vitamin D status of children and adolescents with newly diagnosed celiac disease.

Methods: Serum 25-OH D levels were drawn at the time of serologic screening or small bowel biopsy in children (3 - 18 years old) with suspected CD. Subjects with positive celiac serology and Marsh grade 3 changes were compared to controls with negative celiac screening. Patient demographics, the season when blood was collected and clinical symptoms were recorded. Daily intake of vitamin D was estimated based on average daily milk intake, as well as frequency and dose of multivitamin (MVI). Serum 25-OH D level was defined as deficient if <20 ng/dL and insufficient if <30 ng/dL but ≥ 20 ng/dL. Comparisons between the two groups were performed by two sample t-test or Mann-Whitney test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. Association between continuous factors and vitamin D levels were examined using Pearson correlation coefficient. Analysis of co-variance (ANCOVA) was used for multi-variable analysis. Summary statistics were reported as mean \pm standard deviation.

Results: 31 newly diagnosed CD patients (10.5 ± 3.1 years old, 52% F) and 77 controls (11.1 ± 4.2 years old, 57% F) were enrolled. Both groups were similar except for average estimated total daily vitamin D intake, which was significantly higher in CD patients ($304 \text{ IU/d} \pm 257$) vs. controls ($229 \text{ IU/d} \pm 273$), $p < 0.043$. MVI use was also higher in CD patients (52%) compared to controls (31%), $p \leq 0.047$, but vitamin D intake from MVI and milk separately was similar between the two groups. Mean 25-OH D level was similar in CD ($26.7 \text{ ng/mL} \pm 7.7$) and controls ($23.7 \text{ ng/mL} \pm 8.1$), $p \leq 0.076$. No significant correlation between 25-OH D level and demographic factors were noted except for age ($r = 0.234$; $p < 0.0148$) and daily vitamin D intake ($r = 0.427$; $p < 0.0001$). However, only the vitamin D intake was significantly associated with 25-OH D level ($p < 0.0001$) on multi-variable analysis.

Conclusions: There was no difference in the mean 25-OH D levels in newly diagnosed CD patients compared to non-CD controls, but for both groups the mean 25-OH D status was insufficient. 25-OH D levels were highly associated with the estimated vitamin D intake in both CD and control patients. These results emphasize the importance of dietary vitamin D intake and measurement of vitamin D status, which may still provide useful information in newly diagnosed children with CD.

895 A COMPARISON OF HEALTH-RELATED QUALITY OF LIFE IN YOUTH WITH CELIAC DISEASE VERSUS A GENERAL GI SAMPLE Rose Schroedl, Mary Shull, Tracy Ediger, MD, Nationwide Children's Hospital, Columbus, OH, USA

Celiac disease is an inherited autoimmune enteropathy of the small intestine characterized by permanent sensitivity to gluten which affects approximately 1% of the US population. Celiac disease is a chronic illness with significant treatment demands (i.e., implementation and adherence to a gluten-free diet); however, little is known about the psychosocial aspects of pediatric celiac disease, including health-related quality of life (HRQL). This study investigated the HRQL of youth with celiac disease prior to initiation of the gluten-free diet. The aims of this study were to: 1) compare parent-reported HRQL in youth with celiac disease with a general pediatric gastroenterology population, and 2) compare HRQL of youth with celiac disease to published data of HRQL in healthy youth.

Pediatric patients presenting for endoscopy for a variety of gastrointestinal symptoms (i.e., abdominal pain, diarrhea, constipation, or abnormal laboratory findings suggestive of celiac disease) were recruited to participate in this study. Parents completed the parent-version of the Pediatric Quality of Life Inventory 4.0 General Module (PedsQL), a measure of HRQL, which provides subscale scores in four domains of functioning (physical, emotional, social and school) and a total score (sum of the four subscales). Based on the results of the biopsy results from the endoscopy, patients were classified into two groups (celiac group and general GI group).

Of the 229 patients who participated in this study, 25% of patients were diagnosed with celiac disease. The celiac group was 75% female, with a mean age of 9.15 years (SD 4.6 years). The general GI group was 60% female, with a mean age of 12.2 years (SD 4.6 years). The celiac group and the general GI group did not differ on the PedsQL subscale or total scores. Patients with celiac disease reported poorer physical and school functioning compared to healthy youth ($p < 0.02$).

The current findings expand our knowledge about the HRQL of youth with celiac disease. Overall, patients with celiac disease report similar levels of HRQL as general GI patients, suggesting that youth newly diagnosed with celiac disease are not experiencing greater impairment in HRQL than youth with other GI conditions. However, celiac patients do appear to report poorer physical and school functioning than a sample of healthy youth. This study is the first to measure HRQL prior to starting a gluten-free diet. Further investigation is needed to understand the factors which impact HRQL in youth with celiac disease over time with initiation of a gluten-free diet.

896 DISEASE BURDEN OF EOSINOPHILIC ESOPHAGITIS: A SYSTEMATIC REVIEW OF THE EPIDEMIOLOGY AND HUMANISTIC AND ECONOMIC BURDEN IN CHILDREN AND ADOLESCENTS

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Background and Aims: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease characterized by esophageal inflammation and dysfunction. Little is known about the epidemiology and burden of the disease in children. A systematic review (SR) was conducted to evaluate the literature on the disease burden of EoE in children and adolescents.

Methods: Electronic databases (MEDLINE, Embase, Cochrane) and recent congresses were searched in February 2016 for English language publications describing the epidemiology and humanistic and economic burden of EoE in children and adolescents (aged ≤ 18 years). Publication screening was based on title and abstract and was conducted using a broad search strategy that included a mixture of free-text and medical subject headings terms.

Results: Of 1576 articles identified, 14 met inclusion criteria and were included in this analysis. The incidence of EoE in the EU ranged from 0.8 to 4.5/100,000. Prevalence estimates also varied widely, ranging from 7.3 to 50.5/100,000 across the USA, Australia and the EU. Prevalence increased over time from 0.5 to 8.9 per 100,000 between 1995 and 2004 in Australia, and from 9.9 to 43.0 per 100,000 between 2000 and 2003 in the USA. Only three small studies ($n=28, 42, 97$) assessed the impact of EoE on the health-related quality of life (HRQoL) of children or their families. The findings from one study showed that after 15 years of follow-up, HRQoL in children with EoE was poorer than in healthy controls ($p=0.002$). The second study assessed the longitudinal impact of EoE on children and families over 6 months and found that baseline HRQoL scores in children and their families were significantly correlated with symptom burden, atopic comorbidities and treatment type. Symptom burden remained correlated with HRQoL scores at follow-up points and, over the course of the treatment, HRQoL improved for children, with

the greatest improvements observed in children who had more severe symptoms at baseline. Finally, the results from a third study showed that children with EoE (aged 2-17 years) often experienced frustration, negative moods and anger as a result of diet, or social restrictions associated with EoE. Evidence relating to the economic burden of EoE was limited to two studies. Only one of these studies compared children with EoE (n=1761) with healthy controls (n=6864), reporting significantly higher costs relating to all-cause utilization of health-care services over a period of 2 years (US\$15,956 versus US\$2861, $p<0.001$).

Conclusion: There is an increasing prevalence of EoE, which may be due to increasing recognition and awareness of symptoms. Despite findings showing that EoE negatively impacts the HRQoL of families and children, the evidence is limited to a few studies with small sample sizes. Further research is needed to better understand the societal impact of EoE.

897 THE ASSOCIATION BETWEEN CELIAC DISEASE AND EOSINOPHILIC ESOPHAGITIS: MAYO CLINIC EXPERIENCE AND META-ANALYSIS OF THE LITERATURE

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Background: The association between eosinophilic esophagitis (EoE) and celiac disease (CD) has been the focus of multiple studies with variable results. Both EoE and CD are immune-mediated diseases with dietary triggers playing a role in pathogenesis. Eliminating food triggers can treat both EoE and/or CD. Despite the similarity in symptoms, immune-mediated pathogenesis and management with avoidance of food triggers, EoE and CD are two distinct diseases.

Objectives: To assess the magnitude of association and quality of supporting evidence between EoE and CD in children and report the characteristics and outcomes of children with both conditions.

Methods: We conducted a retrospective cohort study and a systematic review and meta-analysis of the literature. Electronic medical records (EMR) at the Mayo clinic were reviewed from January 1, 1998 through December 31, 2015 using key words: eosinophilic esophagitis, EoE, celiac disease and celiac sprue. Data were extracted from records of patients who have both EoE and CD. A systematic review and meta-analysis of multiple databases was conducted to include studies reporting on the same association. Random-effects model was used to report pooled odds ratio (OR) and 95% confidence interval (CI).

Results: In the cohort study, out of 10,201 patients who underwent at least 1 endoscopy, a total of 595 patients had EoE and 546 had CD. The risk of having EoE in patients with CD was not increased compared to those without CD (OR 0.29; 95% CI, 0.154 - 0.545). Meta-analysis of 23 studies showed similar results (OR 0.525; 95% CI, 0.364 - 0.797). A total of 45 cases in the literature had both CD and EOE (mean age of 10 years, 64% males, majority presenting with abdominal pain, vomiting and diarrhea). Data on treatment were available from the Mayo cohort with 9 out of 10 improving with a gluten-free diet, topical steroids and/or elimination diet. Evidence warranted low certainty.

Conclusion: Observational evidence suggests that a diagnosis of CD in children does not increase the risk of EoE.

898 HLA CLASS I AND II POLYMORPHISMS STUDY OF CELIAC DISEASE IN TUNISIAN CHILDREN

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Background: Celiac disease (CD) is an intestinal inflammatory disease due to gluten intake in genetically predisposed individuals. CD is strongly associated with HLA molecules DQ2 (~95%) and DQ8 (~5%) in most ethnic groups.

Aim: To evaluate the weight of HLA in CD predisposition in a Tunisian population.

Methods: Genomic DNA from 48 CD patients and 100 healthy controls, matched by sex and ethnic origin were analyzed for HLA class I and II polymorphisms by PCR-SSP.

Results: HLA-B*07, HLA-B*08 and HLA-DRB1*03 alleles were significantly more prevalent among CD patients than controls [($p=0.008$, OR [95% CI] 3.43 [1.19 - 10]), ($p=0.016$, OR [95% CI] 3.03 [1.08 - 8.53]) and ($p=0.018$, OR [95% CI] 2.23 [1.07 - 4.65]), respectively]. Besides, HLA-DQB1*0201 subtype was significantly associated with occurrence of CD, $p=0.0027$, OR (95% CI) 3.2 (1.37 - 7.51). We found a high linkage disequilibrium between B*08, DRB1*03 and DQB1*0201 alleles, Δ 0.23; $p=3.23$, E-11. Moreover, the DRB1*03/DQB1*0201 haplotype was significantly associated with CD, $p=2.19$, E-5, OR (95% CI) 5.9 (2.28 - 15.52). Analytical study did not show any association of the above alleles of susceptibility with any of the clinical and biological features of CD.

Conclusion: Our study revealed for the first time a predisposing HLA-DRB1*03/DQB1*0201 haplotype in a pediatric Tunisian population.

Nevertheless, given the high linkage disequilibrium, the part of each allele in CD predisposition remains to be evaluated.

899 SHOULD THE NEW ESPGHAN GUIDELINES ON DIAGNOSING CELIAC DISEASE BE MODIFIED TO APPLY TO ASYMPTOMATIC CHILDREN?

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Aims: In 2012, the ESPGHAN guidelines for diagnosing celiac disease (CD) were modified and recommend that in symptomatic patients a diagnosis of CD can be made without small-bowel biopsy by serological pathway, if anti-tissue transglutaminase antibody (TTG) titer is greater than 10 times upper limit of normal ($>10 \times$ ULN) and HLA-DQ2 and/or HLA-DQ8 is positive. The aim of this prospective study is to examine: 1) the relationship between TTG levels and histological grading in asymptomatic patients with newly diagnosed CD, and 2) to establish whether the recent CD guidelines could be reliably applied to these patients

Methods: Prospective data were collected at diagnosis on all asymptomatic children diagnosed with CD during March 2007 - May 2015. Our laboratory's ULN for TTG is <10 U/mL. The relationship between the modified Marsh criteria histological grading and contemporaneous TTG levels was analyzed. Data were also collected on the age of children and reason for initial serological screening. Cost benefit of extending the new diagnostic criteria to asymptomatic children with suspected CD was estimated based on biopsy pathway costing £1340.00 and serological pathway (TTG + HLA-DQ2/8) costing £65.00 per patient.

Results: 104 asymptomatic children were diagnosed with CD over the 8 years period. 70/104 children (67%) had TTG titers $>10 \times$ ULN and all these had small bowel enteropathy (sensitivity 100%). Table 1 shows the histological grading with contemporaneous TTG titers. 48/70 (68.5%) had TTG >200 U/L and this was associated with greater likelihood of total villous atrophy (Marsh 3c). The mean age at diagnosis was 9.1 years

(1.75 years - 17.25 years). Reasons for serological screening were: diabetes mellitus (n=34), family history of CD (n=23) and Down's syndrome (n=6). Estimated cost saving to the health service for each child was £1,275.

Conclusions: All 70 asymptomatic children with TTG>10 x ULN had biopsy-proven CD. 48/70 (68.5%) had TTG titers >200 U/mL and were more likely to have total villous atrophy (Marsh 3c). Our study suggests that the ESPGHAN criteria for diagnosing CD via the serological pathway should be extended to asymptomatic children with resultant cost benefit to the health service and convenience for the family.

Reference: 1. Husby S *et al. J Pediatr Gastroenterol Nutr.* 2012;54(1):136-60.

900 GENETIC PREDISPOSITION TO CELIAC DISEASE AND ORAL HEALTH: IS THERE AN ASSOCIATION? PRELIMINARY RESULTS OF A LARGE ITALIAN SCREENING IN CHILDREN

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Background: HLA DQ2 and DQ8 are extremely common in the general population, despite their close association with some diseases, particularly celiac disease. This has raised the question whether these genes could be protective towards other common conditions. Some limited data have shown a possible influence of HLA DQ2 towards the development of dental cavities.

Aims: To assess the prevalence of enamel defects, recurrent oral aphthous lesions and dental cavities in a large cohort of school-age children genetically predisposed to celiac disease (CD) in comparison with healthy controls (not predisposed) and children with CD.

Methods: Students aged 5 - 10 years were invited to participate. A rapid, single PCR reaction HLA test (Celiac Gene Screen, Biodiogene Italy) on a single blood drop was used to identify subjects susceptible to CD (both HLA DQ2 and DQ8). In a second step, serological tests were performed in HLA-positive patients (including serum anti-transglutaminase [TTG], anti-endomysium [EMA] and anti-deamidated gliadin peptides [DGP] antibodies). CD was diagnosed according to the ESPGHAN guidelines. A dental examination was performed in school settings, by the same examiner. For the assessment of cavities, the DMFT (decayed-missed-filled teeth) and dmft index were used, for permanent and deciduous teeth as appropriate. HLA-positive (group 1), HLA-negative (group 2) and celiac subjects (group 3) were compared.

Results: 1217 children have been enrolled and 1189 have been HLA screened so far (mean age: 8.06 years \pm 1.58). Four hundred and sixty-eight patients were HLA positive (40.06%), of these 362 underwent the serological evaluation. CD autoimmunity was found in 20 patients with 10 receiving a final diagnosis of CD. The overall prevalence of cavities was 43.6%, with no difference detected in the 3 groups. The mean dmft was 1.35 \pm 2.3, 1.2 \pm 2, 0.91 \pm 2 in groups 1, 2 and 3, respectively (p =NS). No statistical difference was found in the prevalence of reported oral aphthosis. The prevalence of enamel defects was similar in the 3 groups (group 1: 13.4%, group 2: 13.1%, group 3: 18%), with no difference in the severity of enamel hypoplasia.

Conclusions: Preliminary data show that genes predisposing to CD (HLA DQ2/DQ8) do not seem to be associated with susceptibility to dental cavities and other oral pathologies. Children with CD also did not show a particular risk of teeth and oral diseases compared to the other groups. Final results and analysis (multiple logistic regression) will further clarify these associations.

*901 MODE OF DELIVERY AND RISK OF CELIAC DISEASE: A NATIONAL REGISTER-BASED STUDY IN TWO COUNTRIES

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Background: Early environmental exposures contributing to the rapidly increasing prevalence of celiac disease (CD) are still to be identified. Concurrent with the increasing prevalence of CD, the prevalence of Caesarean section has increased dramatically. Caesarean section, especially before rupture of the membranes, has long-term consequences for the gut microbiota in early life. The gut microbiota in the first year of life may influence development of the immune system and is suggested to play an important role in CD. Studies have been inconsistent regarding the association between mode of delivery and risk of CD.

Materials and Methods: We included all children born in Norway between January 1, 2004 and December 31, 2012 and all children born in Denmark between January 1, 1995 and December 31, 2010. Diagnosed CD was defined as two or more registrations of CD in the National Patient Registers. Mode of delivery was registered in the National Medical Birth Registers. We categorized mode of delivery as vaginal delivery or Caesarean section and subsequently Caesarean section as before birth or during birth (before or after rupture of the membranes). We analyzed data with logistic regression and adjusted for birth year, because of different follow-up time. Furthermore, we adjusted for the potential confounders of gestational age, birthweight for gestational age, maternal age and educational level.

Results: From Denmark, we included 999,446 children after exclusions for missing data (n=55,978). CD was registered for 1247 children (0.12%). Caesarean section was registered for 187,741 children without CD (18.8%) and 256 children with CD (20.5%). Caesarean section was associated with CD (aOR 1.18, 95% CI, 1.02 - 1.36). Caesarean section during birth was not associated with CD (aOR 1.02, 95% CI 0.83 - 1.25), but Caesarean section before birth was (aOR 1.33, 95% CI, 1.11 - 1.58). From Norway, we included 512,412 children after exclusions for missing data (n=28,624). CD was registered for 1890 children (0.37%). Caesarean section was registered for 85,334 children without CD (16.7%) and for 285 children with CD (15.1%). Caesarean section was not associated with CD (aOR 0.89, 95% CI, 0.79 - 1.01), nor was Caesarean section before birth (aOR 0.92, 95% CI, 0.76 - 1.11) or during birth (aOR 0.88, 95% CI, 0.75 - 1.03).

Discussion: Caesarean section before birth was associated with an increased risk of diagnosed CD in Denmark. However, this association was not confirmed in Norway. The prevalence of CD and Caesarean section differs with the highest prevalence of CD and the lowest prevalence of Caesarean section in Norway. Our findings underline the necessity of conducting observational studies in various populations. Further studies of CD diagnosis in relation of age may modify these findings.

902 COW'S MILK ELIMINATION ALONE RESULTS IN SYMPTOM AND HISTOLOGIC IMPROVEMENT IN A MAJORITY OF CHILDREN WITH EOSINOPHILIC ESOPHAGITIS

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Introduction: One treatment modality for eosinophilic esophagitis (EoE) involves the removal of offending dietary antigens. The traditional six-food-elimination diet has long been considered a standard treatment. However, this approach has shown suboptimal effectiveness (72%) despite it being very restrictive and can negatively affect patients' quality of life. In 2012, Kagalwalla described an initial series of 17 patients who underwent cow's milk elimination (CME) with 65% achieving clinical and histological remission (<15 mean peak eosinophils per high power field [eos/hpf]). This outcome has been further supported by a 2015 study showing 64% (n=20) of patients achieving remission on a CME diet. **Objective:** To describe the clinical and histological response of study subjects who have undergone a CME diet as a primary intervention. **Methods:** This study was approved by The University of British Columbia/Children's and Women's Health Centre of British Columbia Research Ethics Board. A retrospective chart review was performed on EoE registry patients that were followed in a multidisciplinary EoE Clinic at BC Children's Hospital (BCCH), or seen in a GI clinic. Data on follow-up endoscopy and biopsy counts, symptoms as assessed at follow-up visits and skin prick test results were collected to measure the effectiveness of a CME diet. **Results:** Among 125 reviewed charts, 31 (25%) patients followed a CME diet. The majority (90%) of patients had high symptomatic improvement. Histologically, nearly three-quarters (74%) of patients on a CME diet had decreased eosinophil counts after the intervention. For both responders and non-responders, the mean average peak eosinophil count decreased by 26 (pre-treatment mean counts: 47.3 eos/hpf vs. post-treatment mean counts: 21.7 eos/hpf). Histologic remission (<15 eos/hpf) was achieved in 58% (18/31), with 16% (5/31) obtaining complete remission (0 eos/hpf). Patients who followed CME to a strict degree (i.e., reading labels and looking for hidden sources of milk protein) seem to have a higher chance of remission (63%, 14/22), compared to those who avoided only obvious sources of dairy (milk, cheese, yogurt, and creamy items) (44%, 4/9) ($p=0.39$). There was no differential response to CME for those with atopy versus those without ($p=0.38$). Skin-prick testing to milk was not predictive of response to CME among the 14 patients who underwent testing. **Conclusion:** Cow's milk elimination alone is an effective treatment to reduce symptoms and achieve histologic remission in the majority of EoE patients. This case series is the largest featuring patients undergoing CME alone. Further evaluation of CME as a first-line therapeutic intervention and comparison to more extensive elimination diets or medications is required.

903 MICRONUTRIENT DEFICIENCIES AT DIAGNOSIS IN CHILDREN NEWLY DIAGNOSED WITH CELIAC DISEASE

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Background: Celiac disease is an immune-mediated enteropathy triggered by gluten ingestion in genetically predisposed individuals. Children with untreated celiac disease may suffer from deficiencies of several micronutrients.

Objectives: To examine: the prevalence of micronutrient deficiencies at diagnosis, at 6 months and at 18 months following start of a gluten-free diet and any possible correlation between micronutrient deficiencies, serum tissue transglutaminase (TTG) IgA antibody titers and the degree of mucosal damage.

Methods: Children (<17 years) newly diagnosed with celiac disease had their serum vitamins, minerals, C-reactive protein (CRP) and anti-tissue transglutaminase (TTG) IgA antibodies measured at diagnosis, at 6 and 18 months after they were started on a gluten-free diet (GFD). Histopathological changes of duodenal biopsies at diagnosis were documented using modified MARSH classification. Regression analyses and Pearson correlation were performed to investigate any possible association between micronutrient deficiencies, anti-TTG titers and duodenal histopathology after adjusting for adherence to GFD, CRP and socio-economic status.

Results: A total of 131 children [mean age of 7.9 ± 3.9 years, 82 girls (62.6%)] were included. The serum micronutrient deficiencies are summarized in the Table. Twelve children (9.1%) were diagnosed with iron deficiency anemia at diagnosis. There was no correlation between serum of TTG IgA antibody titers or the degree of villous atrophy and micronutrient deficiencies at diagnosis. Serum levels of all measured micronutrients had normalized after 6 months of starting GFD, except for vitamin D and serum ferritin which improved, but remained subnormal at 18 months post-diagnosis in 12% of children.

Conclusions: At diagnosis, the degree of micronutrient deficiency in children with celiac disease does not correlate with the degree of villous atrophy or the serum titers of anti-TTG IgA antibodies. 30% of children with celiac disease had vitamin D deficiency at diagnosis. The majority of subnormal serum micronutrient levels normalized 6 months after starting on GFD and remained normal 12 months later. This poses the question as to whether routine annual monitoring of all serum micronutrient levels is necessary. Long-term, prospective, large-scale studies are needed to confirm our conclusions.

Serum Micronutrients	Number of patients with deficiencies (%)	Mean Serum Level (at diagnosis) \pm SD	Normal Range	P value
Serum Ferritin	30 (22.9%)	9.9 \pm 4.6	20-140 ug/L	p<0.05
Vitamin A	5 (3.8%)	0.76 \pm 0.04	0.9-1.5 umol/L	p<0.05
Vitamin E	3 (2.2%)	4.06 \pm 4.62	12-21 umol/L	p<0.05
Vitamin D	40 (30.5%)	56.2 \pm 10.32	75-250 nmol/L	p<0.05
Vitamin B ₁₂	5 (3.8%)	134.48 \pm 66.08	>180 pmol/L	p<0.05
Selenium	1 (0.76%)	1.14 \pm 0	1.22-1.82 umol/L	p<0.05
Zinc	7(5.3%)	9.14 \pm 0.72	10-20 umol/L	p<0.05
Copper	0 (0%)	0 \pm 0	11-25 umol/L	N.S

ENDOSCOPY

918 THE OUTCOMES OF USING FRESH PARENTAL STOOL VERSUS FROZEN ANONYMOUS-DONOR STOOL IN PEDIATRIC FECAL MICROBIOTA TRANSPLANT

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Introduction: Fecal microbiota transplant (FMT) has been well established for treating recurrent *Clostridium difficile* infection (CDI) and is increasingly used even in children down to age 1 yr. Our study attempts to identify 1) if the use of frozen anonymous donor stool in FMTs is equally effective as fresh parental stool, and 2) if Children aged 1 - 3 can be better assessed using inflammatory markers to identify which are truly infected versus carriers.

Methods: We prospectively enrolled children undergoing FMT for antibiotic resistant CDI. To assess outcomes of fresh and frozen FMT in different age groups, we compared Pediatric Ulcerative Colitis Activity Index (PUCAI) and Child Health Questionnaire (CHQ28) summary scores before and after FMT. We also compared stool calprotectin and lactoferrin levels, along with freezing samples for future microbiome analysis.

Results: 8 patients were enrolled and split into two groups: 1) A group of 1-3 year olds, 3/4 patients received frozen FMTs. Prior to FMT, all 4 patients had active PUCAI scores with normal levels of calprotectin and no lactoferrin in stools. Four to five months post-FMT, PUCAI scores were down to remission ranges in 3/4 patients. All stool results persisted to be within normal ranges in all patients. B) A group of 4- 18 year olds, 3/4 patients received frozen FMTs. Pre-FMT, lactoferrin was detected in stool with elevated levels of calprotectin in all 4 patients, with active PUCAI scores. Four to five months post-FMT, 2/4 patients had remission PUCAI scores. Persistence in stool lactoferrin and high levels of calprotectin were seen. The CHQ28 provides Physical and Psychosocial summary scores (PhS, PsS). PsS calculated before and after FMT showed significant improvement in 3 of 4 patients.

Discussion: Seven of eight children in this cohort had no recurrence of CDI during the 4-month follow-up. We also used PUCAI scoring to assess patients' condition before and after undergoing a FMT for CDI; 5/8 patients showed improvement, dropping down to remission scores. The other 3 persisted with active PUCAI scores; concomitant conditions at the time of follow-up could potentially explain their elevated PUCAI scores. The CHQ-28 is a validated survey instrument that provides scores for physical and psychosocial health. Our results showed no significant change in PhS post-FMT. However, PsS did improve in 3/4 patients (75%) post-FMT. The first age group (1 - 3 yrs) showed FMT was as effective at lowering PUCAI score/eliminating CDI as in the other age group, along with normal calprotectin and lactoferrin in stools before FMTs.

Conclusion: FMT using frozen anonymous donor stool is as effective as fresh parental donor stool at eradicating CDI in children. FMT and CDI eradication positively impact patients' psychosocial status. The levels of stool calprotectin and lactoferrin were not altered by FMT. These markers did not help identify truly infected cases from carrier states in children aged 1 - 3.

919 ENDOSCOPY FINDING IN CHILDREN WITH ACCIDENTAL EXPOSURE TO CONCENTRATED DETERGENT PODS: A RETROSPECTIVE REVIEW

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Background: Caustic ingestion is a common problem encountered in the pediatric population. The incidence of caustic ingestion with concentrated detergent pods (CDPs) in the pediatric population has been gradually increasing. Mechanism of injury and clinical manifestation vary and tend to be more severe in cases of exposure to CDPs compared to traditional detergents. There is insufficient literature about endoscopic findings in CDP ingestion and its correlation with the symptoms.

Objectives: The aim of this retrospective study is to review cases of children with exposure to CDPs from 2010 - 2015 at The Children's Hospital at University of Oklahoma Health Sciences Center (OUHSC) and to identify the possibility of a correlation between symptoms and the endoscopic findings.

Methods: This study is a single-center, retrospective study involving medical records of children ages 0 - 18 years with accidental caustic exposure and specifically with exposure to CDPs between January 2010 and December 2015. Patients with prior history of histologically-confirmed esophagitis were excluded. The data extracted from the medical records included: demographics, type of exposure, clinical symptoms, physical exam, details of the emergency department and hospital course, including laboratory, radiology data and any specific management. Esophago-gastro-duodenoscopy (EGD) findings (edema, congestion, erythema, erosions, ulcerations, stricture, were considered positive) and direct laryngoscopy-bronchoscopy (DLB) findings (epiglottitis, tracheal edema, secretions, ulcerations, collapse, or compression were considered positive) were also noted.

Results: There were 63 cases of caustic ingestion between January 2010 and December 2015. 19/63 (30%) were due to CDPs. There has been an increase in incidence of caustic ingestion secondary to CDPs in the last 3 years, since there were no cases identified in 2010 and 2011, but there were 19 cases between 2012 and 2015. The mean age was 1.9 years (SD 1.39) with a range of 7 months to 6 years. 73% of the patients were below 3 years of age. 12/19 (63%) of patients were males. These findings are comparable to the other studies on CDP ingestion. All 19 patients underwent EGD and 5/19 patients also had DLB done. 4/19 (21%) of patients had positive findings on the EGD. 4/5 (80%) patients had positive findings on DLB.

Conclusion: There is an increase in the incidence of caustic ingestion secondary to CDPs in the last 3 years (2012 - 2015). There is a male predominance. Only 21% patients undergoing EGD had positive findings secondary to CDP exposure. Number of cases is not sufficient to make a correlation between symptoms and endoscopic findings. Hence, it is reasonable to evaluate all cases of CDP exposure with endoscopy until further larger studies are conducted.

920 WHEN A COLONIC POLYP IS TOO LARGE FOR ENDOSCOPIC REMOVAL

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Background: Literature review reveals that endoscopic tattooing has been successfully performed in the adult population for many years. However, there is a paucity of evidence for its use in children. We present the case of a pediatric patient with juvenile polyposis syndrome in which endoscopic tattooing was utilized to help guide subsequent surgical intervention.

Case: A 7-year-old female presented to the office with a three-month history of painless rectal bleeding and intermittent abdominal pain. She had recently begun iron supplementation for microcytic anemia. During initial colonoscopy, eight polyps of various sizes were identified; all but three were small enough to be safely removed via polypectomy. Pathology confirmed juvenile polyps. Pediatric Surgery was consulted and recommended focal surgical resection of the remaining large polyps. In order to allow for their precise intraoperative identification, and thus minimize the amount of colon necessitating resection, a repeat colonoscopy with endoscopic tattooing was first performed. All three polyps were successfully labeled with SPOT tattoo dye via mucosal injection. Shortly thereafter, the patient underwent diagnostic laparoscopy with partial colectomies and recovered well. Surgical pathology confirmed juvenile polyps. Given the number of colonic polyps present in this patient, she was referred to Genetics and underwent testing for known mutations associated with juvenile polyposis syndrome (JPS). She tested negative, but met the clinical diagnosis of JPS based on the presence of more than five juvenile polyps in the colorectum. Therefore, she will continue to be followed closely in the GI clinic for appropriate monitoring.

Discussion: Endoscopic tattooing can result in improved outcomes in pediatric conditions like JPS. More studies are needed to support its utility, which was well-demonstrated in this case. We question whether the future practice of endoscopic tattooing will offer decreased recovery time and medical expense in the pediatric population.

921 A SINGLE-CENTER REVIEW OF PEDIATRIC COLONOSCOPY QUALITY INDICATORS

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Colonoscopy in pediatric patients is frequently done to evaluate for inflammatory bowel disease (IBD); therefore, intubation of the terminal ileum (TI) is essential. It is reported that up to 70% of pediatric patients have TI disease by histology, with or without colonic involvement at time of diagnosis or early in the disease course. A recognized quality indicator for pediatric colonoscopies is ileal intubation rate. The overall ileal intubation rate was recently reported as 69.4% in the Pediatric Endoscopy Database System-Clinical Outcomes Research Initiative (PEDS-CORI), a central registry analyzing over twenty-one thousand pediatric colonoscopies performed at 14 centers over 12 years. The primary aim was to identify our single-center ileal intubation success rate. A retrospective chart review of all colonoscopies performed by our department in 2015 was completed, identifying 458 procedures. These were performed by a staff provider alone or in conjunction with a fellow trainee. Sixty-seven patients were excluded for history of prior ileal or colonic surgical interventions and for limited procedures including planned ileoscopy, pouchoscopy and flexible sigmoidoscopy, resulting in 391 colonoscopies reviewed. The most frequent primary indications for colonoscopy included abdominal pain with "red flag" symptoms of hematochezia, diarrhea, weight loss, or anemia (35.5%), patients with known IBD (25.1%) and isolated abdominal pain (11.5%). Ileal intubation was achieved in 91% of all colonoscopies, with a cecal intubation rate of 94.4%. Failure of ileal intubation was a result of disease severity documented as significant inflammation or friability (1.4%), inadequate bowel preparation (1.4%), TI stricture (1.7%), the inability to identify or intubate the TI (1.7%), technically difficult procedure (1.7%), undocumented reason (1.7%) and one procedure (0.3%) electively not intubating the TI. Of the 35 colonoscopies without successful TI intubation, 20% were performed by staff provider alone. Colonoscopy time, designated as time from insertion to withdrawal of the colonoscope, was documented in 347 of 391 procedures. The mean colonoscopy time with successful TI intubation was 39 minutes and without TI intubation was 48.1 minutes. The overall mean colonoscopy time with staff provider alone was 33.6 minutes, compared to 41.8 minutes with a fellow trainee participating. Completion of colonoscopy to the TI is an essential part of a complete visual and histologic evaluation. Disease severity and stricturing disease accounted for inability to intubate the TI in 3.1% of patients in our series. Therefore, in approximately 5.9% of cases, there may be potential to increase TI intubation, and in 3.1%, a potential to increase cecal intubation by optimizing bowel preparation, or further refinement of endoscopic skills, which occurs with increased endoscopic procedure volume.

Primary Indication:	Number	Percent
Abdominal pain with "red flag" symptoms	139	35.5
Crohn's disease	82	21
Abdominal pain	45	11.5
Rectal bleeding	33	8.4
Ulcerative colitis	16	4.1
Diarrhea	21	5.1
Weight loss/failure to thrive	23	5.9
Anemia	10	2.6
Other	23	5.9
Total	391	
Colonoscopy Completion:	Number	Percent
Colonoscopy complete to the terminal ileum	356	91
<u>Reason for incomplete exam:</u>	35	9
Unknown/Unspecified	6	1.7
TI stricture	6	1.7
Inability to identify or intubate TI	6	1.7
Inadequate bowel preparation	5	1.4
Severity of disease	5	1.4
Technically difficult procedure	6	1.7
Electively did not intubate TI as colon appeared normal	1	0.3
Colonoscopy with cecal intubation	369	94.4
<u>Reason for incomplete exam:</u>	22	5.6
Unknown/Unspecified	6	1.7
Inadequate bowel preparation	5	1.4
Severity of disease	5	1.4
Technically difficulty procedure	6	1.7

922 ENDOSCOPIC MANAGEMENT OF ESOPHAGEAL STRICTURES IN CHILDREN WITH EPIDERMOLYSIS BULLOSA

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Background: Dysphagia due to esophageal strictures negatively impacts quality of life and nutritional status in children with epidermolysis bullosa (EB). Balloon dilation of esophageal strictures in patients with EB improves dysphagia symptoms and oral intake. Reported endoscopic dilation techniques in EB patients have varied in their approach. The aim of this study is to provide a comprehensive analysis of endoscopic esophageal dilation performed for patients with EB at an academic, tertiary, pediatric care center, including the frequency of adverse events (AE).

Methods: Retrospective chart review of EB patients who underwent esophageal dilation at Children's Hospital Colorado between January 2003 and April 2016. Procedural AE were defined as events occurring up to 72 hours post-procedure. Anesthesia was by an EB dedicated team. Dilation occurred via over the wire 5 or 8 cm long balloons just to elimination of waist (~5 - 15 seconds) with or without EGD from above or via G tube access.

Results: A total of 229 fluoroscopy-guided balloon dilation procedures (206 [90%] antegrade, 23 [10%] retrograde) of the esophagus were performed in 25 EB patients. EB patients were subtyped as 21 recessive dystrophic, 2 mixed dominant/recessive, 1 simplex, and 1 Kindler syndrome. Mean patient age at dilation was 9.4 years (SD 4.8). The median number of dilations per patient was 7 (range 1 - 32) and for those patients receiving repeat dilations the median interval between procedures was 169 days (range 5 - 1892). Strictures were more common in the proximal 1/3 of the esophagus with a mean stricture location of 13.9 cm from the lips (SD 4.5 cm). 74% of patients had a single stricture and 26% had multiple strictures dilated. During the years 2003 - 2012, only 4.1% of dilations were retrograde, whereas during 2013 - 2016, 20.2% of dilations were retrograde. AEs attributable to the dilation occurred in 10% of procedures. The most common AEs were fever, pain, and vomiting. No esophageal perforations or deaths occurred as a result of the procedure. Dilation approach (antegrade versus retrograde) did not impact the likelihood of AEs.

Conclusions: To our knowledge, we report the largest series of endoscopic balloon dilation procedures in patients with EB. The characteristic esophageal lesion in EB is a single, proximal esophageal stricture. Patients with EB can safely undergo repeat balloon dilations without risk for severe complication. In EB patients at our institution, we observed a trend towards increased use of an existing gastrostomy for retrograde endoscopic esophageal dilation.

923 PREDICTORS OF CHOLEDOCHOLITHIASIS AT ERCP IN PEDIATRIC PATIENTS: A REPORT FROM THE PEDIATRIC ERCP DATABASE (PEDI)

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Introduction: The American Society of Gastrointestinal Endoscopy (ASGE) has established guidelines for identifying common bile duct stones (CBDS) by ERCP in adults; however, these guidelines may not be wholly applicable for children. Recent data suggests that conjugated bilirubin in a pediatric population may have improved sensitivity for CBDS identification. Our study aim is to identify clinical characteristics that may improve patient selection for stone removal by ERCP.

Methods: Consecutive ERCPS on pediatric patients <19 years of age across 8 IRB-approved centers from May 1, 2014 through April 28, 2016 were entered prospectively into an electronic database (PEDI: Pediatric ERCP Database Initiative). Inclusion criteria for this analysis included successful cannulation of the CBD and completion of both the pre-procedural and procedural forms. Cases were excluded for patients with prior ERCPS or diagnosed with choledochal cyst or hemolytic disease. Patients were stratified upon the presence of CBDS at ERCP. Student's t-tests and Fisher's exact tests were used to compare continuous and categorical variables, respectively.

Results: Of 429 ERCPS, 139 had indications for suspected CBDS. Of these, 95 cases met inclusion criteria, were included for analysis and stratified between Group 1 (CBDS removed; n=69) and Group 2 (no CBDS removed; n=26). Sixteen percent of patients with CBDS at ERCP had a normal bilirubin. Significant predictors between groups were gallstone pancreatitis ($p<0.004$), conjugated and total bilirubin ($p<0.02$) (Table 1). 30% of patients with CBDS had a normal conjugated bilirubin, CBDS were identified by abdominal ultrasound in only 28% of cases (n=24; $p=1$ versus 74% (n=52) visualized by ERCP cholangiogram ($p<0.0001$). The very strong (VS) and strong (S) ASGE criteria were unable to predict CBDS within this multicenter pediatric population. Using lab indices taken within 24 hours of the endoscopy, a conjugated bilirubin of ≥ 0.5 yielded an odds ratio (OR) of 2.5 (0.9 - 6.4) of having a stone at endoscopy and a conjugated bilirubin of ≥ 2.3 had an OR of 8.3 (1.0 - 66.8).

Conclusions: Conjugated bilirubin is a strong indicator of identifying CBDS at time of ERCP; however, 30% of patients had a normal bilirubin. Current adult ASGE guidelines do not accurately predict CBDS in this multicenter series. Further research is needed to establish pediatric-specific factors to improve identification of CBDS prior to endoscopy.

Table 1: Patient, Laboratory and Imaging Characteristics

	Total (N=95)	Group 1 – CBDS removed at ERCP (69)	Group 2 – NO CBDS removed at ERCP (N=26)	p-value
Pt Characteristics				
Age, yrs (mean [IQR])	13.9 [8.7-15.5]	14.0 [12.8-16.0]	13.8 [13.0-16.4]	0.91
Female (n, %)	77 (81%)	58 (84%)	19 (73%)	0.25
Hispanic	66 (69%)	50 (72%)	16 (62%)	0.33
White	84 (88%)	62 (90%)	22 (85%)	0.49
African American	7 (7%)	3 (4%)	4 (15%)	0.09
Other	3 (3%)	3 (4%)	0 (0%)	0.56
Obese (n=92)*	(37%)	25 (37%)	13 (52%)	0.24
Gallstone pancreatitis	26 (27%)	13 (19%)	13 (50%)	0.004***
Cholangitis	3 (3)	2 (3%)	1 (4%)	1.00
Symptoms at ERCP				
RUQ pain at rest	54 (57%)	36(52%)	18 (69%)	0.17
RUQ pain with palp	66 (69%)	49 (71%)	17 (65%)	0.62
Jaundice	30 (32%)	22 (32%)	8 (31%)	1.00
Nausea	33 (35%)	23(33%)	10 (39%)	0.64
Imaging				
CBDS on ERCP cholangiogram (n=95)	70 (74%)	61 (88%)	9 (27%)	0.0001***
CBDS on AUS (n=86)	24 (28%)	18 (28%)	6 (27%)	1.00
CBDS on MRCP (n=20)	16 (80%)	13 (87%)	3 (60%)	0.25
CBDS on CT (n=16)	4 (25%)	1 (8%)	3 (75%)	0.03***
CBDS on IOC (n=6)**	6 (100%)	4 (100%)	2 (100%)	1.00
CBDS on EUS (n=7)	5 (71%)	5 (83%)	0 (0%)	0.29
CBDS on any pre-ERCP imaging modality (N=93)	47 (51%)	35 (52%)	12 (46%)	0.65
Peak CBD diameter any pre-ERCP modality, mm (mean [IQR]) (n=90)	9.0 [7.0-10.6]	9.2 [7.0-11.0]	8.7 [6.0-10.0]	0.69
ERCP CBD diameter, mm (n=93)	9.1 [7.9-10.3]	9.4 [8.0-11.0]	8.3 [7.1-9.0]	0.20
24 Hr Prior Labs				
Total bilirubin, mg/dL (n=90)	2.5 [0.7-3.4]	2.8 [0.9-3.6]	1.7 [0.5-2.7]	0.02****
Direct/Conjugated bilirubin, mg/dL (n=87)	1.3 [0.0-2.1]	1.5 [0.3-2.3]	0.7 [0.0-1.1]	0.02****
ALT, u/L (n=90)	332 [192-454]	320 [176-459]	360 [203-404]	0.81
AST, u/L (n=90)	199 [77-236]	192 [82-218]	214 [72-259]	0.97
GGT, u/L (n=83)	325 [182-385]	325 [155-381]	324 [213-378]	0.31
Alk Phos, u/L (n=86)	235 [133-267]	236 [123-245]	232 [146-294]	0.60
C/D Bili >2 (n=87)	22 (25%)	20 (32%)	2 (8%)	0.03***
C/D Bili <0.5 (n=87)	42 (48%)	26 (42%)	16 (64%)	0.10

* Obesity. Two were under two years of age, BMI doesn't apply (both in stone group). 1 patient did not have height recorded, thus BMI could not be calculated (in no stone group).

** CBDS on IOC defined as no duodenal filling of contrast with filling of CBD or identifying a fixed or mobile-filling defect in the CBD.

*** Significant by two tailed Fisher's exact test

**** Significant by paired Student's t-test

924 RATES OF ADVERSE EVENTS IN PEDIATRIC PATIENTS UNDERGOING DELAYED CHOLECYSTECTOMY FOR BILIARY COLIC
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Introduction: The optimal timing of cholecystectomies (early versus delayed) remains controversial in the pediatric patient population. Greater benefit has been demonstrated in the adult population with early cholecystectomies. However, there is only limited data regarding timing of cholecystectomy intervention in the pediatric population.

Aim: To compare the outcomes of undergoing early versus delayed cholecystectomy in pediatric patients presenting with biliary colic.

Methods: A pathology database was searched to identify all patients undergoing cholecystectomy between September 25, 2015 and December 31, 2015. Charts for these patients were subsequently reviewed retrospectively. Inclusion criteria: patients <19 years of age at cholecystectomy,

initial presentation consistent with biliary colic, underwent cholecystectomy. Exclusion criteria: age >19 years of age, cholecystectomies in conjunction with certain surgical procedures (liver transplantation or resections, choledochal cyst resection, Kasai procedures). Patients were divided into two groups. Group 1 included all patients who underwent cholecystectomy during their index encounter with a surgeon. Group 2 included all patients in whom cholecystectomy was delayed after initial encounter with a surgeon. The primary outcome measure was development of adverse events (AEs) between time of initial surgeon contact and date of surgery. AEs were defined as development of new pancreatitis, elevation in liver enzymes or dilation of common bile duct, choledocholithiasis, fever, or representation to a medical facility. Patient demographics, presenting characteristics, procedural outcomes and complications were also evaluated and reported.

Results: Thirty-five patients (30 female, 86%) met inclusion criteria. Ten were in group 1 and twenty-five were in group 2. The average age was 15.1 years old (range 8 - 18). The average BMI was 29.08 kg/m². Of the twenty-five children in group 2 who underwent a delayed cholecystectomy after initial encounter with a surgeon, 6 (24%) of them developed an AE while awaiting their surgery date compared to none in group 1 (*p*-value 0.15). AEs included presenting with abdominal pain to a medical facility in 6 patients (100%) and elevated liver enzymes in 2 patients (67%).

Conclusions: While not statistically significant in our small sample size, in pediatric patients undergoing cholecystectomies for biliary colic, the rate of AEs is higher in those who delay intervention compared to their early-intervention counterparts. Early cholecystectomy to treat biliary colic is safe in the pediatric population.

925 *HELICOBACTER PYLORI* DETECTION: ENDOSCOPIC AND HISTOLOGICAL FINDINGS IN CHILDREN WITH DYSPEPSIA

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Introduction: Dyspepsia stands among the most frequent symptoms in the study of chronic abdominal pain (CAP) in children and is a common reason for consultation. *Helicobacter pylori* (Hp) colonization up to 18 years of age occurs in 80% of the general population in low-income countries and its relationship with dyspeptic symptoms and endoscopic and histopathological findings are of debate.

Objectives: To describe the presence of Hp in a population of symptomatic children and its relationship with the endoscopic and histological findings.

Materials and Methods: Over 18 months, 138 patients who consecutively attended gastroenterology consultations for dyspepsia, for whom upper gastrointestinal endoscopy (UGIE) was indicated. Of these, with previous informed consent, 118 (89%) met the inclusion criteria and formed the definitive sample, with ages between 4 and 18 years. All patients underwent UGIE, the Rapid Urease Test (RUT) and histopathological study of the biopsies. Positivity was defined as the simultaneous identification of Hp both in the RUT and Geimsa stains. The demographic characteristics, and the endoscopic and histological findings are described, along with the relationship of the infection with these findings.

Results: Of the 118 patients, 2/3 (64.4%) were girls. The average age was 11.8 years (SD 3.25 years). 57% were eutrophic, 25% had some degree of malnutrition, and 5% were overweight. Hp was detected by UT in 66%, histology in 55% and by both methods simultaneously in 44%. Nausea and regurgitation presented in 36% of cases, accompanied by epigastralgia, a pivotal symptom for the definition of dyspepsia. In 90% of cases, endoscopic alterations were found, of which 53% corresponded to erythematous gastritis, followed by nodular gastritis in 33%. Histological changes were described in 93% of cases, with chronic gastritis being most frequent at 89%, in its active (23%), active follicular (29%), and inactive (38%) forms. Hp-positivity is correlated with the endoscopic findings, especially with nodular gastritis (*p*=0.001). The same is true, in a significant way, for the presence of Hp and the histological changes when chronic active gastritis is found (*p*=0.000). This correlation is maintained when there are no histological changes and Hp is not present (*p*=0.000).

Discussion: Hp was detected in 44% of cases, but endoscopic and histological alterations were found in 90% and 93% of cases, respectively.

The presence of Hp in children is significantly associated with nodular gastritis in endoscopy, and with chronic active gastritis, especially with active chronic follicular gastritis. This observation of activity and Hp positivity, to our knowledge, has not been previously reported in the literature.

926 PREVALENCE OF CLINICAL AND PATHOLOGIC FINDINGS IN FILIPINO CHILDREN UNDERGOING COLONOSCOPY

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Rationale: Colonoscopy has diagnostic and therapeutic roles in children with lower gastrointestinal complaints. There is no local report on the pathologic findings among children undergoing colonoscopy.

Objective: To determine the prevalence of a pathologic diagnosis based on colonoscopic and biopsy findings in children

Methods and Study Design: Retrospective-prospective, cross-sectional study.

Setting: Tertiary hospital.

Subjects: Patients 1 - 19 years old who underwent colonoscopy from 2010 - 2013 for the retrospective review and 2014 for the prospective part.

Outcomes Measured: Demographic data, indication for colonoscopy, anesthesia used, extent reached by colonoscopy, colonoscopic and biopsy findings and final diagnosis were collected. Data were reported as mean (SD) and number (percentages). Minimal sample size estimate was 92.

Results: A total of 129 colonoscopies on 121 patients were performed. Mean (SD) age at colonoscopy was 10.0 years (5.4) and 73 (56.5%) were males. The most common indications were lower gastrointestinal bleeding (76.7%) and suspected inflammatory bowel disease and its surveillance (12.4%). Seventy-three subjects (57%) had intravenous sedation and the rest had general anesthesia. The cecum was reached in 109 (84.5%) colonoscopies and ileal intubation in 89 (68.9%). Abnormal findings were seen in 120 (93.0%) colonoscopies. The most common colonoscopic findings were intestinal polyps (44.1%) and ileocolitis (34.8%). Biopsy was done in 86 colonoscopies with pathologic findings seen in 97.7%. Based on combined colonoscopic and biopsy findings, the prevalence of pathologic diagnosis was 93.8%. There were no major procedural complications. Four subjects had fever, resolving within 8 hours post-colonoscopy.

Conclusion: Colonoscopy in Filipino children with lower gastrointestinal complaints had a high prevalence of pathology and is a safe procedure. We recommend it as a diagnostic tool, especially in children with lower gastrointestinal bleeding.

Keywords: colonoscopy, children, biopsy

927 ENDOSCOPIC ENTEROCLYSIS IN THE DIAGNOSIS OF PARTIALLY OBSTRUCTIVE LESIONS

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Background: Children with partial or intermittent obstruction may have delayed diagnosis due to non-specific symptoms such as vomiting, abdominal pain and weight loss. Patients with these symptoms are likely to undergo endoscopy, which may reveal duodenal stenosis or otherwise abnormal intestinal anatomy. There has previously been one case reported of duodenal malrotation diagnosed with endoscopy after a fluoroscopic evaluation failed to demonstrate any abnormality. Here we review several children diagnosed with obstructive lesions during endoscopy with the use of concurrent fluoroscopy when prior studies had been normal.

Methods: We conducted an IRB-approved retrospective review of patients with partial obstruction diagnosed during endoscopy at our institution between November 1, 2005 and November 1, 2015. We reviewed presentation, endoscopic and fluoroscopic methods and findings, and outcomes of these patients.

Results: Six patients were identified with obstructive lesions noted endoscopically. Using contrast instilled via ERCP catheter, these lesions were confirmed with intra-operative fluoroscopy. In these patients, prior radiographic studies failed to identify a point of obstruction although 2/6 (33%) had delayed gastric emptying. All patients underwent surgical correction: 3/6 had duodenostomy, 2/6 had Ladd's procedure, and 1/6 had lysis of adhesions overlying duodenum. All but one had improvement in symptoms post-surgically, the one who continued with emesis was later diagnosed with foregut dysmotility on antroduodenal manometry.

Conclusion: Use of intra-operative fluoroscopy is often reserved for endoscopic instrumentation (dilation, motility catheter placement).

However, we have found intra-operative enteroclysis to be a valuable tool in evaluation of patients with obstructive symptoms. Correlating endoscopic visualization of the lumen with real-time radiography allows for a more detailed examination and can identify partially obstructive lesions that may otherwise be interpreted as normal variant or artifact.

928 SAFETY AND OUTCOMES OF EARLY NUTRITION FOLLOWING PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE PLACEMENT IN CHILDREN

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Background: In pediatric patients, it is common practice to wait up to 24 hours to begin enteral feedings through a newly placed percutaneous endoscopic gastrostomy (PEG) tube. This delay in feeding was believed to prevent post-procedural complications. Several studies report the safety and efficacy of initiating enteral nutrition as early as three to six hours after gastrostomy tube placement in adults. However, there are few studies that examine early feeding in the pediatric population.

Patients and Methods: An ongoing, IRB-approved, prospective, controlled trial beginning November 2015 initiating enteral nutrition four hours following PEG tube placement in children six months to 18 years of age. Outcomes measuring the safety and tolerability of early feedings, and hospital length of stay were recorded. Pain medication use and complications such as fever, vomiting and leakage around the stoma, in addition to adverse events, including peritonitis and aspiration were recorded. Results from the early feeding group will be compared to data collected from a historical control group whose feedings were initiated the first post-operative day.

Results: Seventeen participants were prospectively enrolled, consisting of 8 females and 9 males with a mean age of 6.2 ± 4.7 years. Most common indications for PEG tube placement included feeding difficulties (36%), failure to thrive (20%) and dysphagia (16%). Hospital length of stay was defined as the time on arrival to the inpatient unit following their procedure to time of hospital discharge. Participants who remained inpatients for reasons related to their primary diagnosis were excluded from the duration hospital of stay data. The mean duration of hospital stay for pediatric patients receiving enteral nutrition four hours following gastrostomy tube placement was 29.25 ± 7.68 hours.

Conclusion: Preliminary data suggests initiating enteral nutrition four hours following PEG tube placement is as safe as waiting until the first post-operative day in this pediatric cohort. There is no increase in reported adverse outcomes or events when comparing early feeding to patients who received nutrition the first post-operative day. Furthermore, initiating early nutrition following PEG tube placement in children may lead to a decrease length of hospital stay.

*929 ADVERSE EVENTS AND LONG-TERM OUTCOMES OF ENDOSCOPIC SPHINCTEROTOMY IN A PEDIATRIC POPULATION; A SINGLE-CENTER EXPERIENCE

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Objectives: The use of endoscopic sphincterotomy (EST) is increasing in the management of pancreaticobiliary disease in children. However, studies of adverse events and long-term outcomes of EST are limited in pediatric patients. The aim of this study was to evaluate the adverse events and long-term outcomes following EST in pediatric patients.

Methods: We retrospectively analyzed 203 pediatric patients who underwent ESTs at Asan Medical Center Children's Hospital between 1994 and 2013. The male-to-female ratio was 1:1.5 and the median age was 8.7 years old. We evaluated the indications, success, adverse events and long-term outcomes.

Results: Adverse events (<30 days) following 299 ESTs among 203 patients included 17 (5.7%) episodes of pancreatitis, 6 (2.0%) episodes of hemorrhage, 3 (1.0%) episodes of sepsis and 2 (0.7%) episodes of perforation. Long-term (>30 days) information was available in 198 patients with a median overall follow-up duration of 42 months (range, 1 - 232 months). Twelve patients (6.1%) developed late complications, including cholangitis with or without bile duct stone (n=7), and minor papilla stenosis (n=5). The cumulative incidence rates of late complications were 3.1%, 6.1%, 9.3% and 9.3%, at 1, 5, 10 and 15 years. There were no procedure-related pancreaticobiliary malignancies and deaths. All adverse events and long-term outcomes improved with appropriate managements.

Conclusions: Adverse events and long-term outcomes after EST in pediatric patients occurred with similar rates compared to those in adults and could be managed safely. This study suggested that EST is a reasonable method for treating pancreaticobiliary disease, even in pediatric patients.

930 ENDOSCOPIC FINDINGS IN CHILDREN WITH COW'S MILK ALLERGY

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Background: Cow's milk allergy (CMA) is a common problem in children that involves the gastrointestinal, respiratory tract and skin. It has an approximate prevalence of 2 to 7.5% in children under 1 year of age. Reactions may be mediated by IgE or other allergy mechanisms (non-IgE). Diagnostic methods in non-IgE-mediated are insufficient and endoscopy with biopsies may be an additional tool for diagnosis.

Objectives: To describe upper endoscopic and rectosigmoidoscopic findings in children with CMA.

Methodology: Retrospective, descriptive, cross-sectional, observational study.

We analyzed patients with confirmed CMA diagnosis by oral suppression and challenge test that underwent upper endoscopy and rectosigmoidoscopy with biopsies. Sex, age, upper endoscopy and rectosigmoidoscopic findings were obtained from the patients' records and we also obtained the histological findings from records of the Pathology Department of the National Institute of Pediatrics of Mexico City.

Results: We analyzed 24 patients. In the majority of patients, upper endoscopy was reported as normal, we found esophagitis only in 2 patients (8.3%), in 5 patients (21%) non-erosive gastropathy, in 1 patient (4.2%) duodenogastric reflux, in 8 patients (33.3%) nodular duodenitis and in 1 patient (4.2%) ulcerated duodenitis. At rectosigmoidoscopy, we found 75% patients as normal, in 12.5% (n=3) proctitis and in 8.3% (n=2) nodular proctitis.

Conclusions: In most patients diagnosed with CMA, panendoscopy and rectosigmoidoscopy were reported as normal.

931 GENERAL PEDIATRICIANS AND MANAGEMENT OF PATIENTS WITH GERD: LOW EXPECTATIONS FOR ENDOSCOPY

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Background: Optimal management of gastroesophageal reflux disease (GERD) in children may involve treatment by general pediatricians, as well as referral to pediatric endoscopists. Despite guidelines that address indications for both, recent European studies suggest pediatricians do not demonstrate best practices. Little is known about North American pediatricians' behaviors in managing GERD in children, as well as referral to pediatric GI.

Aim: To investigate the approach of pediatricians in New England when suspecting gastroesophageal reflux disease (GERD) in children, including their comfort with starting proton pump inhibitors (PPIs), as well as their expectations when referring to pediatric GI that endoscopy will be performed.

Methods: Pediatricians in two states (Connecticut and Massachusetts) were asked to complete an internet-based survey using case-based questions to describe their approach to newborns, older infants and adolescents when GERD is suspected. We used Likert scales (1 strongly disagree, 5 strongly agree) to assess pediatricians' likelihood of prescribing PPIs themselves vs. referral to pediatric GIs for management and for endoscopy.

Results: 51/96 (53%) of pediatricians surveyed responded. 44% reported being in practice for >10 years. There was no significant difference in pediatricians' reported likelihood of prescribing PPI when suspecting GERD in infant vs. adolescent patients. 55% reported that they agreed or strongly agreed that they frequently prescribe PPIs to infants 0 - 6 months of age, 51% to infants 6 - 12 months and 78% to adolescents, $p=.07$. Pediatricians were more likely to report referring older infants vs. newborns and adolescents to pediatric gastroenterologists (4% of 0 - 6 month-olds, 24% of 6 - 12 month-old infants vs. 4% of adolescents, $p=.030$). Pediatricians were most likely to report referring older infants, with the expectation that endoscopy would be performed (6% of 0 - 6 month-olds, 20% of 6 - 12-month-old infants, and 6% of adolescents, $p=.004$).

Conclusions: This pilot study suggests New England pediatricians vary in their approach to managing suspected GERD in accordance with patient age. By report, they are equally likely to prescribe PPIs to both infant and adolescent patients and are overall not likely to refer to pediatric gastroenterologists. On the other hand, they may be more likely to refer older infants with GERD symptoms, with the expectation that endoscopy will be performed. More studies are necessary to understand whether these behaviors are indicated and consistent with published guidelines and whether overall low expectations that endoscopy will be performed influence management approaches and referral patterns.

932 DISTAL/MID ESOPHAGEAL BIOPSIES ARE SUPERIOR TO PROXIMAL/DISTAL ESOPHAGEAL BIOPSIES FOR DETERMINING THE PRESENCE OF DISEASE: A PROSPECTIVE, PEDIATRIC, EOSINOPHILIC, ESOPHAGITIS STUDY

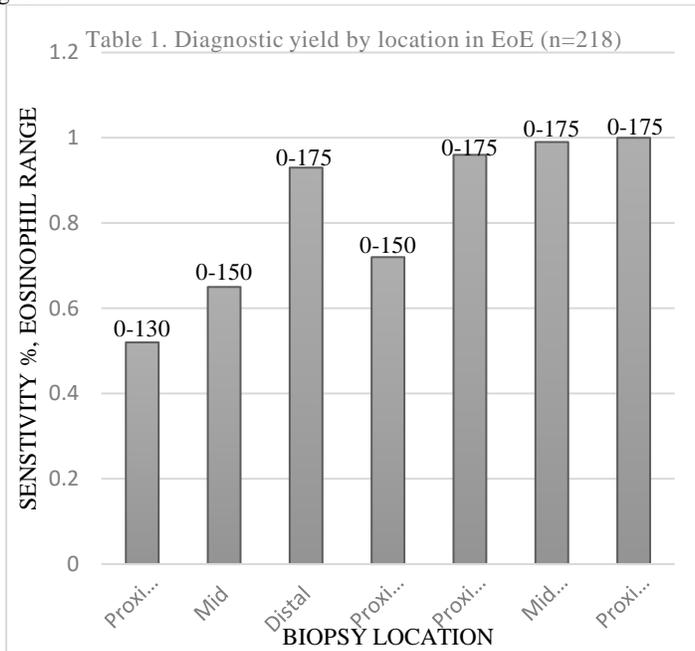
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Background: Esophageal biopsy is the gold standard for the diagnosis and follow-up evaluation of eosinophilic esophagitis (EoE), since there is significant histopathologic variability in EoE. To improve histopathologic yield, six biopsies from two locations (distal and proximal) are recommended to optimize diagnostic yield. There are no studies that compare eosinophil density of the proximal, mid and lower third of the esophagus, nor are there studies to determine which two sites offer the highest sensitivity for determining the presence of active disease. Our aim for this study was: 1) to determine if there is variability in eosinophilic density by location, and 2) to determine the best two locations to improve histologic sensitivity for detecting active disease, both for diagnosis and follow-up assessment after treatment intervention.

Methods: We performed a prospective study in 253 children undergoing a total of 472 diagnostic, surveillance, or post-intervention esophagogastroduodenoscopy (EGD) for EoE. All patients with EoE met the 2011 consensus guidelines' criteria. Measurements of the esophagus were obtained to confirm the location of the upper esophageal sphincter, proximal, mid, distal and GEJ. All the subjects had esophageal biopsies obtained from proximal, mid and distal esophagus.

Results: 253 children (76% males, mean age 9 years, 89% white) underwent 472 EGDs. 218 EGDs with active EoE were analyzed. The mean eosinophil count in distal, mid and proximal biopsies was 46 (range, 0 - 175), 37 (range, 0 - 150), and 24 eos/hpf (range, 0 - 130) ($p<0.0001$), respectively. 104 (48%) EGDs had <15 eos/hpf in the proximal esophageal biopsies and thus did not meet the threshold for diagnosis of EoE. 76 (35%) and 16 (7%), respectively, did not meet the diagnostic threshold if biopsies from the mid and distal were analyzed. 9 (4%) EGDs would not have met the threshold criteria if biopsies were taken both from proximal and distal sites, whereas 2 (1%) would have not met threshold criteria if biopsies were only taken from mid and distal sites.

Conclusion: Esophageal density is significantly higher in the distal and mid esophagus compared to proximal esophagus. All patients undergoing diagnostic endoscopy met criteria for EoE diagnosis without the need for proximal biopsies. Eosinophil density in the proximal esophagus is often below the diagnostic threshold criteria for active disease compared to the mid and distal, and does not appear to alter management.



933 IMPROVED ESOPHAGEAL FOREIGN BODY MANAGEMENT MAY INCREASE DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS: VANDERBILT EXPERIENCE

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Objective: Eosinophilic esophagitis (EoE) is an increasingly prevalent clinicopathological condition affecting approximately 1 per 10,000 children per year. The American Society for Gastrointestinal Endoscopy recommends that esophageal biopsies be obtained if there is a suspicion of EoE at the time of foreign body (FB) removal; however, many providers are unaware of these recommendations, or do not obtain biopsies based on normal esophageal appearance. The goal of our study was to assess how pediatric patients presenting with esophageal FB impaction are managed and determine if high-risk patients are being referred to pediatric gastroenterology for further work-up.

Methods: Retrospective chart review on 147 patients ages 1 - 18 who presented to Vanderbilt Children's Hospital Emergency Department in Nashville, TN, billed with the ICD-9 code 935.1 "foreign body in the esophagus" and ICD-10 code K22.2 "esophageal obstruction" from November 2009 - November 2015.

Results: Of 147 children, 116 (79%) required endoscopic removal and, of these, 31 (21%) had food impactions (FI). The remaining 31 (21%) cases did not require any endoscopic intervention. Pediatric Gastroenterology (Peds GI) performed 21 (18%) procedures, of which 11 (52%) were FIs, Pediatric Otolaryngology (ENT) performed 12 (10%) procedures, of which 1 (8%) were FIs, and Pediatric Surgery performed 83 (72%) procedures, of which 16 (19%) were FI. Of the 21 patients managed by Peds GI, 11 FIs and 2 non-FIs (61%) were biopsied and 12 (92%) had findings suggestive of EoE (100%). Of the 95 patients managed by ENT and surgery, excluding the 1 patient with a previous diagnosis of EoE, 4 patients (4%) were referred to Peds GI for further evaluation and all had histologic findings suggestive of EoE (100%). One of the 4 patients referred by surgery was biopsied by surgery at the time of FB disimpaction and had findings suggestive of EoE. Of the 22 patients diagnosed or suspected to have EoE, 19 (86%) presented with FIs and 3 (14%) presented with non-food FB. It is important to note that of the 31 patients that did not require endoscopic FB removal, 15 (48%) reported FI. There were 43 FIs without a prior diagnosis of EoE; 11 (26%) patients were biopsied and 10 (91%) had findings suggestive of EoE, while 1 patient was diagnosed with non-erosive reflux disease. The other 32 (74%) did not have GI follow-up or biopsies at the time of disimpaction, and therefore, were not fully evaluated for underlying esophageal disease.

Conclusions: Pediatric surgery performed the majority of FB removals in children presenting to the emergency department. A large discrepancy exists between Ped GI and surgery with regard to esophageal biopsy at time of foreign body removal. Our study shows 94% of pediatric patients underwent esophageal biopsies suggestive of EoE, particularly those presenting with FIs. High index of suspicion for EoE among providers caring for children presenting to ER with esophageal FB impaction is warranted.

934 ENDOSCOPIC BOUGIE DILATATION OF BENIGN ESOPHAGEAL STRICTURE IN INDIAN CHILDREN: A 5-YEAR EXPERIENCE

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Background: Benign esophageal stricture is a common indication for referral to pediatric gastrointestinal endoscopy units. However, there is a paucity of reported data on endoscopic dilatation methods and efficacy and safety in pediatric patients from India. This is a retrospective analysis of our experience of esophageal stricture dilatation using Savary-Gilliard bougies in Indian children.

Methods: From March 2011 to April 2016, all children referred to the pediatric gastrointestinal endoscopy unit of Chacha Nehru Bal Chikitsalaya, Delhi, for esophageal stricture dilatation were included in this study. Dilatations were done under ketamine sedation every 2 - 3 weeks initially until the esophageal lumen could be dilated to 11 mm in <1 year age, 13 mm in 1 - 5 years age and 15 mm in >5 years age. Subsequently, they were called every 6 weeks to 6 months, depending on symptoms.

Results: During this period, 102 children, aged 2 months to 12 years, were referred to our unit for dilatation. Their mean age at the time of referral was 5.3 ± 2.8 years and 68 (67%) were males. Twenty-three (22.5%) children had stricture resulting from accidental corrosive ingestion (acid 8, alkali 6, nature of corrosive not known 9). Non-corrosive strictures were consequent to surgical repair of congenital TEF (44), EST-induced (18), peptic (5) congenital (4), post-Nissen's fundoplication for GERD (3), post-esophageal foreign body impaction (1) and of unknown etiology (4). A total of 609 dilatations were performed with an average of 5.7 ± 3.9 dilatations per patient. Patients with post-corrosive strictures required significantly more sessions as compared to non-corrosive ones (8.2 ± 4.3 and 3.7 ± 1.9 respectively, $p < 0.05$). They also reported far more frequent dilatations on an "as needed" basis after achieving adequate luminal dilatation initially (5.7 ± 4.3 vs. 1.9 ± 2.2 , $p < 0.05$). We had a very low complication rate with no perforations. There were 2 cases of impacted guide wires, which had to be retrieved surgically. Both patients had uneventful recoveries and one came for subsequent dilatations as well. The other patient was lost to follow-up. Three patients did not respond favorably to endoscopic dilatation and were referred to pediatric surgery. All three had stricture following corrosive ingestion.

Conclusions: Post-operative esophageal stricture was the most common variety in this Indian series. The incidence of corrosive strictures was markedly less, as compared to older reported series. Savary-Gilliard bougie dilatation was found to be an effective and safe procedure in children as well as infants. All patients tolerated the procedure well and had marked improvement in feeding and nutritional status.

935 DIAGNOSTIC YIELD OF PEDIATRIC GASTROINTESTINAL ENDOSCOPY AT A TERTIARY CENTRE IN THE UK: RESULTS OF SERVICE EVALUATION

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Introduction: Endoscopy is integral to the diagnosis and management of many gastrointestinal problems in children. Recently, the number of endoscopic procedures performed has increased considerably worldwide, raising questions about their appropriateness and cost-efficacy. The aim of this service evaluation was to determine diagnostic yield (the likelihood that a procedure or test will provide information required to establish a diagnosis) of endoscopy in a pediatric population in a large, tertiary centre.

Methods: Over a 30-month period from April 2012 to October 2014, 3252 endoscopic procedures were performed on 2471 children. Out of these, non-consecutive 147 cases were randomly selected blinded to assessors. Indications for endoscopy, endoscopic and histopathological findings were collated and the endoscopic diagnostic yield and contribution to the management was evaluated. Notes were also reviewed for change in active management (any change in the treatment after endoscopy) and whether endoscopies contributed to the management.

Results: The mean age was 9.58 (0.5 - 16.5) years with a M:F ratio of 1:1.42. The positive diagnostic yield was 18.9% for esophagogastroduodenoscopy (OGD) alone, 32.6% for ileocolonoscopy (IC) alone and 39.2% when both occurred. The pre-test probability of making a positive diagnosis prior to endoscopy was 42.8%, with likelihood ratio of a positive test of 2.49. Using Fagan's likelihood ratio nomogram, a post-test probability of 65 is calculated, indicating a high degree of diagnostic contribution. In 45% of patients, the patients' management was actively changed due to endoscopy and histopathology findings and management contribution occurred in all patients.

Discussion: In children, a positive diagnosis is important, but significant negative findings may also be important in terms of patient management and reassurance. The relatively low positive diagnostic yield of OGD (18.9%) and IC (32.6%) in this cohort must be interpreted in this clinical context. Overall, endoscopic procedures had good sensitivity (71.4%) and specificity (71.4%) with an NPV of 76.9% and a PPV of 65.2% in our centre. Of course appropriate selection of patients contributes to this and judicious pre-procedural use of empirical therapy (e.g., PPI trial) and/or non-invasive tests (e.g., fecal calprotectin) may refine endoscopy use. Various studies have also suggested that the diagnostic yield of endoscopic procedures improve if indications and appropriateness are critically assessed with use of guidelines (e.g., ESPGHAN).

Conclusion: Adherence to well-established guidelines for appropriateness and indication of endoscopy in children improves the diagnostic yield of endoscopic procedures. A significant negative finding may be as important as a positive diagnosis for exclusion of suspected disorders with consequent reassurance and change in management. Further studies are required to analyze cost-effectiveness of endoscopic procedures.

936 EFFICACY OF ONE DAY POLYETHYLENE GLYCOL-BASED CLEANOUT AS COLONOSCOPY PREPARATION IN A PEDIATRIC POPULATION

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Background: The adequacy of cleanout is a critical determinant of the quality of colonoscopic exam in children, as in adults. There is currently no consensus on cleanout protocols in pediatrics and extrapolation from adult experience has several potential pitfalls. Focus has recently shifted to polyethylene glycol (PEG)-based cleanouts prescribed for two days, or in conjunction with a stimulant agent;¹ this, however, entails a greater disruption of daily activities, or the potential adverse effects of cramping, attendant to stimulant laxative, respectively. Herein we describe our experience with a one-day, PEG-only protocol.

Methods: This study is a retrospective review of a departmental quality improvement tool installed to monitor cleanout quality in a tertiary referral context. Consecutive pediatric patients (ages 2 - 21) who underwent colonoscopy in an ambulatory setting starting May 2015 were included. The protocol is described in *Table 1*. End metrics were reported by providers and ancillary staff at the time of the procedure and include: 1) procedure duration, 2) type of residual stool, 3) impact of residual stool on the timely completion of the procedure, 4) cecal and terminal ileum (TI) intubation and biopsy when indicated. Charts missing significant metrics were excluded.

Results: We analyzed 243 patients (11.8 ± 4.4 years; 99 male). The median number of standard PEG doses was 10 (range 1 - 17) in children 4 years and older. Stool residue was described as thin liquid in 149 (61.3%), thick liquid in 33 (13.6%) and solid matter in 18 (7.4%) of patients. The colon prep was reported to impair timely completion in 32 patients (13.2%). No significance difference in impairment was found for age and gender. The cecum was reached in 215 (88.5%) patients, TI biopsies were ordered in 217 (89.3%) of cases and, within that subset, 201 (92.6%) were able to successfully reach the TI. Mean (SD) procedure duration was 22.7 ± 11.5 minutes. Procedure time where faculty were assisted by fellow trainees was significantly longer (26.7 ± 14 min) when compared to unassisted procedures (21.3 ± 10 min; $p = 0.005$)

Conclusion: A one-day PEG 3350 prep is suitable to effect adequate cleanout that allows completion of the procedure in the vast majority of cases. A pragmatic strategy of assessing cleanout effectiveness by impact on completion rate is more suitable in pediatrics, as opposed to the adoption of adult-based standards that are intended, in the most part, to optimize adenoma detection rates, a concept and goal that is irrelevant to most pediatric colonoscopists.

Reference:1. Sahn B *et al.* Safety of a 1-day polyethylene glycol 3350 bowel preparation for colonoscopy in children. *J Pediatr Gastroenterol Nutr.* 2015 Dec 10.

937 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN JAPANESE CHILDREN: SINGLE-CENTER EXPERIENCE IN 2000

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Aim: To evaluate the utility of pediatric endoscopic retrograde cholangiopancreatography which were performed in the 2000s.

Methods: We retrospectively analyzed the ERCP examinations performed in patients with defined or suspicious pancreaticobiliary diseases which occurred before the age of 18 years. All ERCP procedures were performed at the Department of Pediatric Gastroenterology and Hepatology, Saiseikai Yokohama City Tobu Hospital between April 2007 and March 2016. Data regarding patient demographics, procedure indications, findings, interventions, adverse events and post-procedure course were abstracted from the electronic medical records and retrospectively analyzed.

Results: During the study period, 126 patients (64 male, 62 female) underwent 168 ERCP procedures. The median patient age at the time of ERCP was 10 years (range 0 - 27 years). Of 126 patients, 7 patients (14 procedures) were aged >18 years at the time of ERCP, but all of these 7 patients presented with initial symptoms before 15 years of age. Of the 168 ERCP procedures, 144 (85.7%) were primarily for biliary indications, 21 (12.5%) for pancreatic indications and 3 (1.8%) for unknown cause of abdominal pain. Ninety procedures were the therapeutic purpose. Of those patients, 4 (3.2%) were younger than 1 year, visualization of bile duct in all these cases was not accomplished. Their final diagnosis was biliary atresia. In biliary indication, 81 (48.2%) procedures were for the screening for sclerosing cholangitis (SC) and 37 (22.0%) received a diagnosis of SC. Twenty-six (15.5 %) were for follow-up of SC. Of these, 2 patients had normal ERCP findings with concentric laminar periductal fibrosis and received an initial diagnosis of small duct primary SC. However, follow-up ERCP in them showed the findings of typical large duct PSC. In pancreatic indication, 17 (10.1%) procedures were for investigating a cause of pancreatitis. Of these, 3 had pancreaticobiliary maljunction, 2 had dilation of the pancreatic duct caused by chronic pancreatitis, 2 had benign pancreatic duct stenosis and 7 had normal findings. The complication rate was 15.5 % (26/168) and post-ERCP pancreatitis occurred in 11 procedures (6.5%), including 6 mild and 5 moderate. Anesthesia-associated complications were observed in 8 procedures (4.8 %) and 3 laryngeal spasm associated with ketamine were included. No severe complications occurred in this study period. No complications occurred in children younger than 1 year.

Conclusion: Because of the development of imaging modalities, ERCP was mainly used for therapeutic purpose in adults. However, in children, ERCP still has an important role for diagnostic purposes. Although post-ERCP pancreatitis is a major complication, not only in adults but also in children, ERCP is useful for the evaluation for intrahepatic bile duct and pancreaticobiliary maljunction and especially the investigation of the cause of pancreatitis.

938 MEANINGFUL USE OF DISACCHARIDASE TESTING: A QUALITY IMPROVEMENT PROJECT

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Background: Disaccharidases are a group of membrane-bound proteins found within the microvilli of the small intestine. They assist in the digestion of disaccharides found in the human diet. A primary or secondary deficiency of disaccharidase enzymes can result in bloating, diarrhea, abdominal pain, or failure to thrive. Direct disaccharidase testing from intestinal biopsies can be used to help guide dietary management of symptoms. However, testing is expensive and is sometimes ordered with unclear indications by the provider.

Aim: In this quality improvement project, we describe a PDSA cycle with the primary aim of reducing the number of non-clinically indicated disaccharidase tests.

Methods: Initially, data were collected over several months to assess the number of total tests ordered, as well as to identify how many tests were clinically indicated (defined as diarrhea, bloating, gas, or abdominal pain, with at least one of the symptoms listed). Once baseline data were collected, an intervention was planned to help achieve our primary aim. Education materials were distributed to all of the nurse practitioners and physicians within the department who can order the testing and the electronic order was changed. Originally, when ordering an upper endoscopy, the default for disaccharidase testing was blank and the order could not be completed until this was answered, forcing providers to choose yes or no. For our intervention, the order was changed so that the default was "no", requiring the active change by the provider. Data was collected to analyze data over time and create a run chart.

Results: The total number of disaccharidase tests ordered decreased, despite a 40% increase in the volume of endoscopies. The number of disaccharidase tests ordered per month was 41 and 43 in the last two months prior to the change vs. 34 and 28 after the change took effect. Those same two months compared to the year before were significantly decreased as well (58 and 59 from the same two months in 2015 vs. 34 and 28 from 2016). The percentage of clinically indicated tests did not change significantly.

Discussion: It took two months before a change was noted, as most endoscopies are scheduled 1 - 2 months in advance. We believe that this provides a better experience for families, as the test is only ordered when providers think and plan for the test as opposed to selecting "yes" simply to obtain information which may not be indicated or useful. This also saves money; specifically, our hospital saves \$5,000 per month from costs to the reference lab and total patient savings is approximately \$21,500 per month. We believe that this represents an easy-to-perform change that encourages thoughtful ordering of this test. Further PDSA cycles will be performed to ensure sustainability and continued improvement.

	Total Disaccharidases	Indicated tests (%)	Abnormal tests (%)
June 2015	68	38 (56%)	36 (53%)
July 2015	39	20 (51%)	16 (41%)
August 2015	41	18 (44%)	22 (54%)
September 2015	43	17 (39%)	22 (51%)
Change made			
January 2016	43	24 (56%)	16 (37%)
February 2016	42	14 (33%)	24 (57%)
March 2016	34	20 (59%)	23 (68%)
April 2016	28	13 (46%)	13 (46%)

939 A PROSPECTIVE, RANDOMIZED, SINGLE-BLIND STUDY TO EVALUATE TWO DIFFERENT 1-DAY BOWEL PREPARATION REGIMENS IN CHILDREN AGES 8 - 21 YEARS UNDERGOING CAPSULE ENDOSCOPY

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Background: Video capsule endoscopy (VCE) is an established procedure for investigating small bowel and terminal ileal diseases in children. The success of a capsule endoscopy is largely dependent on adequate visualization of the small intestine mucosal lining. The ideal preparation should be not only effective in cleaning the bowel to allow for adequate visualization of the intestinal mucosa, but also safe, well-tolerated and short in duration. We prospectively examined the effectiveness, safety, efficacy and tolerance of a one-day polyethelene glycol (PEG) vs.. magnesium citrate (MC) bowel preparation in children undergoing VCE.

Methods: Patients who were scheduled for a VCE were approached to participate in the study. Patients were randomized to receive either PEG or MC for their cleanout. A patient/parent questionnaire examined pre-procedure experience with PEG/MC. Serum chemistries were measured prior to VCE in 14/15 patients and adverse events from the preparation reported. After the study was completed, three VCE trained pediatric gastroenterologists independently reviewed the VCE study and completed an evaluation form.

Results: A total of 15 patients (7 PEG and 8 MC) participated (mean age 14.8 years, 11 - 21 years, 53% males) and all patients had successful pan-VCE. Overall, small bowel preparation was rated as excellent or good in 95.3% cases in the PEG group and 83.3% in the MC group ($p=NS$). Small bowel visualization was >75% in 95% of patients in the PEG group vs. 67% in the MC group ($p=0.0247$). Small bowel transit time was 4.34 hours in the MC group vs. 3.13 hours in the PEG group ($p=NS$). Age or gender did not affect the prep quality. Serum electrolytes were not significantly different among groups, except phosphorus levels were more likely to be low in the MC group (71%) vs. the PEG group (50%). The most common complaints in both groups were dizziness, light-headedness followed by cramping and having clear liquids diet and no food.

Conclusions: A 1-day bowel preparation with PEG or MC is safe and effective. Base on this small sample size, the cleanout with PEG appears to give a better small bowel visualization, although MC is easier to administer and has a longer small bowel transit time.

GLOBAL HEALTH

940 GASTROINTESTINAL SOMATIZATION IN CHILDREN WITH DENGUE WITHOUT WARNING SIGNS IN THE UNIVERSITY HOSPITAL OF VALLE IN CALI, COLOMBIA

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Introduction: The presence of gastrointestinal signs and symptoms are alarm signals in dengue.

Objective: To determine, through the somatization inventory, the presence of gastrointestinal symptoms in children with dengue without alarm signs in the University Hospital of Valle in Cali, Colombia.

Methods: Through the somatization inventory, we asked for gastrointestinal symptoms like nausea, constipation, diarrhea, abdominal pain, dysphagia, vomiting, bloating and food intolerance in children diagnosed with dengue without alarm signs that consulted the emergency service at the University Hospital of Valle in Cali, Colombia. We include sociodemographic and clinical variables.

Results: Among 73 children, the mean age was 10.6 ± 1.9 years (range 8 - 14 years), 54.8% male, 37% with malnutrition and 28.8% with altered height. According to the somatization inventory, they presented with, in order of frequency, the following gastrointestinal symptoms: nausea 45.2%, abdominal pain 41.1%, vomiting 37.0%, abdominal distension 28.8%, diarrhea 27.8%, constipation 25.0%, dysphagia 21.9% and food intolerance 16.4%. There was more opportunity to suffer nausea in males (OR 3.11; 95% CI, 1.06 - 9.28; $p=0.0201$).

Conclusion: In this group of children at the University Hospital with dengue without alarm signs, 71.2% had some gastrointestinal symptoms in the somatization inventory, with nausea being the most frequent symptom in the male gender.

941 NUTRITIONAL STATUS AMONG HOSPITALIZED CHILDREN IN INDIA

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Background: Malnutrition is consistently associated with adverse clinical outcomes, including increased morbidity, mortality and increased length of hospital stay, as well as reduced quality of life. It is essential to identify malnourished children and children at increased risk of malnutrition, in order to devise a comprehensive nutrition care program. The present cross-sectional, observational study assessed the prevalence of malnutrition in hospitalized children as the first step in devising a comprehensive nutritional care program.

Method: The study period was January to December 2015, a sample of 999 children aged 0 - 18 years, regardless of gender, ethnicity, or reason for hospitalization, who were admitted to the hospital were included in the study. All patients were nutritionally screened followed by assessment of anthropometric measurement and BMI for age percentile using the WHO chart for 0 - 5 years and the MGRS (multicentric growth reference study) chart for 5 - 19 years.

Results: Of all children included, 575 were male and 424 were female. On classifying the subjects based on nutritional status, it was found that 382 (38.2%) were well nourished and the other 617 children (61.8%) were malnourished. Among the malnourished, 28.6% children drew closer to wasting, another 11% of them came under both wasting and stunting and a minimal percent of children (1.9%) were stunted in their growth. Among the over-nourished group, 9.8% were overweight and 10.4% were obese. 34.3% of the selected children were well nourished in the 1 - 3 years age group and wasting (45%) and severe malnourishment (30%) were common in the 0 - 6-month age group.

Conclusion: It is extremely important to identify the at-risk population to prevent its devastating effects on the patients and the possible impact on the healthcare system. Our study enumerated the problem of malnutrition in hospitalized patients. The prevalence of overweight and obesity are more common among the 4 - 9-year age group; this could be attributed to their unhealthy dietary practices and lack of physical activity.

This study shows malnutrition and over-nutrition rates remain high in children in a developing country like India. Therefore, special attention has to be given to their overall nutrition and identify the potential risk factors leading to this comorbidity. The onus is on the clinician, as well as the dietician, in picking up these cases and offering solutions pre-discharge and follow-up plans, which are both critical.

Conflict of Interest: None

Key Words: nutrition assessment, malnutrition

942 TRANSFORMING GROWTH FACTOR B1, TRANSFORMING GROWTH FACTOR B2 AND TOTAL IMMUNOGLOBULIN A LEVELS IN BREAST MILK IN RELATION TO INFANT ALLERGY IN A GERMAN COHORT

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Objectives: Breast milk not only supports infant growth, but also contains multiple immunological factors, such as cytokines and antibodies that can shape the newborn's immune system. In addition to providing protection against infection, a role of breast milk has also been described in allergy prevention. In particular, transforming growth factors beta 1 and 2 (TGFβ1 and TGFβ2) and total immunoglobulin A (IgA) in breast milk have previously been studied in relation to allergy risk, but results are conflicting. We aimed to measure TGFβ1, TGFβ2 and total IgA in breast milk samples of a mother-child cohort and to evaluate whether these immune factors are associated with allergy development in infants during the first year of life.

Methods: We have obtained breast milk samples from 155 mothers at 3 months after birth, as well as allergy data of infants of the LIFE Child cohort in Leipzig, Germany. Exclusive breastfeeding rate at this time point was 89%. Infants' allergy data were collected through parent-filled questionnaires during the first year of life and serum was analyzed for IgE levels. TGFβ1, TGFβ2 and IgA were quantified in breast milk samples by ELISA. Association of TGFβ1, TGFβ2, or total IgA levels and allergy manifestations in infants was assessed for each factor independently, taking into account relevant confounding factors.

Results: In line with previous reports, we found that higher total IgA levels in breast milk at 3 months were associated with reduced risk of developing atopic dermatitis or allergic sensitization, though this did not reach statistical significance (odds ratio 0.751, 95% CI, 0.546 - 0.970, $p=0.051$). On the contrary, TGFβ1 or TGFβ2 in 3-month breast milk samples did not appear to be directly linked to the appearance of allergic manifestations in the first year of life.

Conclusion: Our results support previous evidence on the role of immune factors present in breast milk and allergy development early in life. In order to draw stronger conclusions, broader and deeper analysis is warranted, including collecting breast milk at different time points after birth and monitoring allergy later in life.

943 RAPID MEASUREMENT OF FOLATE IN BREAST MILK USING A CLINICAL DIAGNOSTIC ASSAY REVEALS POSSIBLE GEOGRAPHICAL DIFFERENCES IN FOLATE CONTENT

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Background/Aim: Adequate maternal folate supply *in utero* is essential for an infant's health. Folate is derived from the diet or given as folic acid in supplements and, in some countries, in fortified grain flour. Folate comprises a group of several compounds differing in methylation, reduction and polyglutamylation and has hitherto been measured in breast milk with bacteriological growth assays or chromatography. These methods are time-consuming and resource hungry. Recently, diagnostic tools using folate-binding protein in competitive chemiluminescence assays have become available for blood analysis. We aimed to adapt such an assay for breast milk with the purpose of improving and facilitating milk folate measurement.

Methods: Milk was obtained from 10 volunteers around Lausanne (Switzerland) who donated on two separate occasions. Samples were also obtained from the LIFE-Child cohort in Germany (n=156) and from Lee Biosolutions Inc. in the USA (n=16). Swiss samples were obtained, on average, at 4 months of lactation, German samples at 3 months and time of sampling of the American samples was ≥ 4 weeks according to the supplier. For method development, a milk pool from 10 Swiss samples was used. Folate was measured with a Siemens Dimension EXL200 (FOLA assay).

Results: Reliable measurement required minimal sample pretreatment. Folate could be measured in a linear range from 8.4 - 298.1 nM (3.7 - 131.5 $\mu\text{g/L}$), with a CV of less than 10% at all levels, except near the lower level of quantification where it was $<15\%$. Recovery of 5-methyltetrahydrofolate spiked at 5 levels was 96 - 107%; measurement uncertainty was between 6 and 13%. Average values in German and Swiss samples were similar but, in both cases, significantly lower than in samples from the USA, where grain flour fortification is mandatory. Results of milk samples, including those with lowest and highest folate levels, correlated with values obtained by HPLC (sum of folic acid and 5-methyltetrahydrofolate; $R^2 0.81$). While this indicates the method's potential, geographical differences remain to be confirmed with samples obtained at identical timepoints since milk folate may increase during lactation.

Conclusion: Our findings suggest that folate levels in breast milk vary geographically, and that levels in breast milk may be higher in mothers from countries where grain flour is fortified. While this suggests that the maternal diet affects breast milk folate levels, it could have important public health and nutrition implications. The ease of this method may facilitate research on folate in mother-child cohorts.

944 SPECTRUM OF MUTATIONS AND CLINICAL PRESENTATION IN CYSTIC FIBROSIS

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Objective: We aimed to investigate genotype-phenotype and spectrums of clinical presentation in cystic fibrosis patients in the Azeri Turkish population.

Methods: A cross-sectional study was done at the Educational and Treatment Children's Hospital and Medical Genetic Laboratory in Tabriz, Iran from 2001 to 2015. Data of all patients was analyzed using the Chi-square test or Fisher's exact test and independent sample t-test using SPSS 21. Odds ratio with confidence intervals of 95% and $p \leq 0.05$ were considered significant.

Results: Of 331 patients, the risk of the appearance of gastrointestinal-nutritional disorders were higher in homozygous F508 Δ than homozygous 1677delT mutations (OR = 13 [95% CI, 2.11 - 79.95], $p=0.009$). The risk of appearance of sinopulmonary disease and gastrointestinal-nutritional disorders were higher in homozygous F508 Δ than homozygous G542X mutations (OR = 5.14 [95% CI, 1.03 - 26.6], $p=0.05$) and (OR = 9.75 [95% CI, 1.73 - 54.78], $p=0.01$), respectively. The occurrence of sinopulmonary disease and gastrointestinal-nutritional disorders were higher in homozygous F508 Δ than homozygous 2183 AA-G mutations (OR = 7.71 [95% CI, 1.71 - 34.64], $p=0.009$), (OR = 9.75 [95% CI, 1.94 - 48.82], $p=0.008$) and (OR = 8.95 [95% CI, 1 - 37.8], $p=0.02$), respectively. The rate of complications of bronchiectasis lung transplantation, digital clubbing, meconium ileus and fatty liver were further in the homozygous F508 Δ .

Conclusions: These results demonstrated that the homozygous F508 Δ have the most risk and the most appearance of this disease. Therefore, it is necessary that these aforementioned points should be considered by clinicians.

Keywords: cystic fibrosis; gastrointestinal; nutritional; mutations; sinopulmonary.

945 EPIDEMIOLOGICAL DATA FROM PATIENTS WHO UNDERWENT 24-HOUR ESOPHAGEAL pHMETRY STUDY

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Introduction: Esophageal pH monitoring is considered the gold standard for the diagnosis of gastroesophageal reflux disease because of the normal ranges across the pediatric age range. Twenty-four-hour esophageal pH monitoring measures the frequency and duration of acid reflux episodes. The main advantage of this test is its ability to quantify acid reflux and evaluate the correlation of symptoms with acid reflux. The purpose of the present study was to analyze pH studies from patients who underwent 24-hour pH-metry study in our department during the last 5 years. The majority of patients included presented with atypical clinical symptomatology.

Material and Methods: Charts of patients who underwent pH-study were reviewed. The sex, age of patients and their symptoms were recorded.

The pH-metry studies were analyzed. For the interpretation of pH studies, we estimated the reflux index, number of episodes of GER, the longest episode of acid GER and the numbers of GER episodes >5 minutes.

Results: From these 57 patients, 30 were boys and 27 were girls with a mean age of 2.4 years (1 month - 14.5 years). The most common symptoms were feeding refusal 8/57 (14%), regurgitation and vomiting 7/57 (12%), persistent wheezing 6/57 (10.5%), life-threatening episodes 8/57 (14%), recurrent respiratory infections 4/57 (7%), episodes of inspiration 4/57 (7%), episodes of apnea or cyanosis 4/57 (7%), cough in supine position 3/57 (5.3%), persistent cough 2/57 (3.5%), episodes of chest pain in supine position 2/57 (3.5%), sensation of clearing the pharynx 1/57 (1.7%), spasm of larynx 1/57 (1.7%), intermittent dystonic position of head/cervix 1/57 (1.7%), recurrent episodes of gastric bleeding 1/57 (1.7%).

34/57 (59.6%) of the studies made were negative for acid GER and 23/57(40.4%) were abnormal. In abnormal Ph-metry studies, the main symptoms were life-threatening event episodes in infants and respiratory system symptoms in older children.

Conclusions: The 24-hour pH study remains a principal investigation of GER, especially when the clinical picture is atypical.

946 CRITERION VALIDITY OF THE GASTROESOPHAGEAL REFLUX DISEASE SYMPTOM QUESTIONNAIRE AND REFLUX SYMPTOM INDEX AS DIAGNOSTIC TOOLS COMPARED WITH ESOPHAGEAL MULTICHANNEL INTRALUMINAL IMPEDANCE-pH MEASUREMENTS IN INFANTS

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Purpose of the study: Non-invasive methods to diagnose gastroesophageal reflux disease (GERD) through questionnaires have been pursued for decades. The GERD Symptom Questionnaire (GSQ) was validated and published by Deal *et al* in 2005. The Reflux Symptom Index (RSI) is one measurement derived from combined esophageal multiluminal impedance-pH (MII-pH) monitoring to evaluate for correlations between esophageal reflux and symptoms such as pain, cough, or regurgitation. The aim of this study is to determine whether the GSQ composite symptoms score (CSS), calculated as the sum of the individual symptoms scores (ISS), and the RSI correlate with outcomes in esophageal MII-pH monitoring.

Methods: Twenty-six infants with GERD-associated symptoms aged 0 - 2 years old who completed the esophageal MII-pH monitoring and the GSQ survey were included in the study. By using the Pearson correlation, we compared the results from the RSI score, the GSQ CSS results, and the ISS for regurgitation, cough-gag-choke and pain-fussiness with the number of occurrences (number of times parents recorded an event), the impedance score and reflux index score for all esophageal reflux, acid reflux and non-acid reflux events.

Results: Among 26 patients, a total of 2817 (1700 acid and 1117 non-acid) esophageal reflux episodes and 845 clinical reflux-associated behaviors were recorded. For all esophageal reflux events, there were significant correlations between the CSS and the impedance score (r^2 0.1414, $p=0.0152$), RSI regurgitation and impedance score (r^2 0.1735, $p=0.03828$), occurrences and ISS for regurgitation (r^2 0.8547, $p=4.1E-11$), occurrences and ISS for cough-gag-choke (r^2 0.7803, $p=4.9E-09$) and occurrences with ISS for pain-fussiness (r^2 0.9014, $p=4.63E-13$). For acid reflux events, there was a significant correlation between occurrences and ISS for regurgitation (r^2 0.8807, $p=4.18E-12$) and occurrences with ISS for pain-fussiness (r^2 0.8475, $p=7.14E-11$). For non-acid reflux events, there was significant correlation between occurrences and ISS for regurgitation (r^2 0.6544, $p=9.8E-07$), occurrences and ISS for cough-gag-choke (r^2 0.6887, $p=2.89E-07$), occurrences with ISS for pain-fussiness (r^2 0.4068, $p=0.00060$), RSI cough-gag-choke and impedance score (r^2 0.22.54, $p=0.016$) and RSI pain-fussiness with impedance score (r^2 0.5593, $p=1.7E-0.5$).

Conclusions: The number of times parents record an event (occurrences) was strongly correlated with the parent-reported ISS for all reflux, acid and non-acid reflux events. There were no significant correlations in our population with the parent-reported ISS versus the objectively

measured reflux index or impedance score. We conclude that the perception of reflux-associated symptoms reported by parents greatly influences GERD questionnaire scoring, which is a limitation in making a clinical diagnosis of GERD in this patient population.

947 IMPROVED IDENTIFICATION OF PEDIATRIC OBESITY RELATED COMORBIDITIES IN A DEDICATED WEIGHT MANAGEMENT PROGRAM COMPARED TO PEDIATRIC PRIMARY CARE

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Background: Select comorbidities related to pediatric obesity can be difficult to diagnose in primary care settings due to the need for blood work and invasive testing. Weight management programs (WMP) comprise a comprehensive multidisciplinary team of both primary care providers and specialists.

Purpose: To compare the rate of identification of comorbidities related to pediatric obesity in primary care versus a dedicated pediatric WMP. **Methods:** Patients were identified through the EPIC Pediatric Obesity Registry. All of the patients enrolled in WMP were included. Patients were randomly selected from primary practice sites and were matched by BMI, age and gender. Data is presented as mean \pm standard deviation or median [25th, 75th percentiles] for continuous variables and N (%) for categorical variables. All analyses were performed with 0.05 as the overall significance level.

Results: 884 patients were included in the study, 442 in each group with a mean age of 12.0 ± 4.9 years in the WMP group and 12.6 ± 3.8 in the ($p=0.073$). The mean number of comorbidities diagnosed in the WMP was greater than other sites (1.2 vs. 0.35 comorbidity per patient $p<0.001$). The WMP had a greater number of patients identified with acanthosis nigricans (1.8% vs. 5.4%, $p=0.004$), non-alcoholic fatty liver disease (NAFLD) (0.45% vs. 5.4%, $p<0.001$), hyperinsulinemia/pre-diabetes (3.9% vs. 6.8%, $p=0.031$), dyslipidemia (1.6% vs. 24.0%, $p<0.001$), obstructive sleep apnea (2.0% vs. 8.8%, $p<0.001$) and vitamin D deficiency (4.1% vs. 38.0%, $p<0.001$). There were similar rates of diagnosis of hypertension, asthma and depression in the two practice settings.

Conclusions: Weight related comorbidities are more likely to be diagnosed in patients being seen in WMP than in similar patients being seen in primary care.

***948 SERUM ANTI-FLAGELLIN AND ANTI-LIPOPOLYSACCHARIDE IMMUNOGLOBULINS AS PREDICTORS OF GROWTH IN PAKISTANI INFANTS AT RISK FOR ENVIRONMENTAL ENTERIC DYSFUNCTION**

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Background: Environmental enteric dysfunction (EED) is an acquired condition of the small intestine among children of low-income countries and has been linked to poor growth. Serum immunoglobulins to flagellin (FLA) and lipopolysaccharide (LPS) are hypothesized to be biomarkers of EED related to intestinal bacterial translocation and permeability. We aimed to assess the associations between FLA and LPS antibodies with child growth among young Pakistani children at risk of EE.

Design/Methods: A prospective, cohort study was conducted among 380 children from birth to 18 months of age in rural Sindh, Pakistan. Blood samples were obtained at age 6 and 9 months. Serum FLA- and LPS-specific immunoglobulins (IgA and IgG) were measured by ELISA.

Growth was measured monthly. Height-for-age (HAZ), weight-for-age (WAZ) and weight-for-height (WHZ) Z-scores were calculated according to WHO 2006 guidelines. Stunting was defined as height-for-age Z-score <-2 . Linear mixed effects models were used to examine longitudinal associations between FLA- and LPS-antibodies and changes in HAZ, WAZ and WHZ over time. Cox proportional hazard models were used to assess the associations between FLA- and LPS-antibody levels at 6 months and subsequent risk of stunting.

Results: At 6 months of age, higher LPS IgA levels were associated with a trend to greater decrease in HAZ scores over 18 months (comparing highest to lowest quartile, β change in HAZ score/year -0.29 , 95% CI, -0.05 to -0.54 , P -trend 0.009). Similarly, at 9 months of age, higher FLA IgA levels were associated with a trend to decrease in HAZ scores over 18 months (β -0.29 , 95% CI, -0.04 to -0.55 , P -trend 0.04); while higher FLA IgG levels were associated with a trend to decrease in HAZ scores over 18 months (β -0.27 , 95% CI, -0.01 to -0.53 , P -trend 0.07). LPS IgG and FLA IgG were primarily not associated with HAZ change. None of these biomarkers were associated with changes in WAZ or WHZ scores, except for the association of LPS IgG at 6 months, with increase in WHZ over 18 months (β 0.26, 95% CI, -0.04 to 0.56, P -trend 0.01).

Compared to children in the first quartile of LPS IgA level, those in the second (HR 1.57, 95% CI, 0.81 to 3.05) and third quartile (HR 2.23, 95% CI, 1.15 to 4.33) had an increased risk of stunting; however, this increased risk was not sustained in the highest quartile (HR 0.96, 95% CI, 0.48 to 1.91, P -trend 0.89).

Conclusions: EED, as measured by FLA- IgA and LPS-IgA antibodies at 6 and 9 months, is associated with declines in HAZ. Serum levels of FLA-IgA in early infancy are associated with stunting. The relationship between these growth markers and their biological significance with regards to EED require further study.

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Table 1: The Association of Anti-flagellin and Anti-Lipopolysaccharide Immunoglobulin Concentrations with Infant Growth

Linear mixed effects models examining annual ΔHAZ						COX proportional hazard models examining 6-month biomarkers and risk of stunting				
Association with 6-month biomarkers			Association with 9-month biomarkers			Events/N	Unadjusted HR (95% CI)	p-trend	Adjusted HR (95% CI) ¹	p-trend
β for annual ΔHAZ	SE	p-trend	β for annual ΔHAZ	SE	p-trend					
FLA IgA										
Q1	ref	-	ref	-		20/31	1		1	
Q2	0.289	0.124	-0.219	0.13	0.04	30/32	1.05 (0.57-1.96)	0.59	1.18 (0.63-2.20)	0.56
Q3	0.079	0.123	-0.253	0.128		20/32	1.05 (0.56-1.94)		1.18 (0.62-2.24)	
Q4	-0.051	0.124	-0.293	0.13		16/32	0.83 (0.43-1.61)		0.81 (0.41-1.60)	
FLA IgG										
Q1	ref	-	ref	-		18/31	1		1	
Q2	0.028	0.126	-0.063	0.131	0.07	20/32	1.35 (0.71-2.55)	0.93	1.43 (0.75-2.74)	0.95
Q3	0.098	0.125	-0.035	0.129		21/32	1.31 (0.70-2.46)		1.33 (0.70-2.53)	
Q4	-0.141	0.125	-0.269	0.131		17/32	1.06 (0.54-2.05)		1.06 (0.54-2.09)	
LPS IgA										
Q1	ref	-	ref	-		18/31	1		1	
Q2	0.014	0.124	-0.183	0.131	0.45	20/32	1.28 (0.68-2.43)	0.94	1.57 (0.81-3.05)	0.89
Q3	-0.036	0.125	-0.269	0.129		22/32	1.74 (0.93-3.24)		2.23 (1.15-4.33)	
Q4	-0.293	0.124	-0.142	0.131		16/32	0.96 (0.49-1.89)		0.96 (0.48-1.91)	
LPS IgG										
Q1	ref	-	ref	-		19/31	1		1	
Q2	-0.068	0.124	0.114	0.131	0.71	17/32	0.82 (0.43-1.59)	0.72	0.83 (0.42-1.64)	0.84
Q3	0.143	0.124	-0.053	0.131		23/32	1.33 (0.72-2.45)		1.43 (0.76-2.69)	
Q4	-0.104	0.124	0.093	0.132		17/32	0.78 (0.40-1.50)		0.82 (0.42-1.59)	

Note: ¹Adjusted for child sex (male/female), pre-term birth (yes/no), maternal age (≥30, <30 years), maternal education (illiterate, yes/no). Abbreviations: FLA=Flagellin; LPS=Lipopolysaccharide; IgA=Immunoglobulin A; IgG=Immunoglobulin G; ΔHAZ= change in Height-for-age Z scores

949 *HELICOBACTER PYLORI TIPα PROTEIN PROMOTES INFLAMMATION IN THE GASTRIC MUCOSA*

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Background and Aims: The bacterium *Helicobacter pylori* (*H. pylori*) colonizes the human stomach leading to chronic gastritis, peptic ulcers and gastric cancer. A combination of host, environmental and bacterial virulence factors contribute to disease development. *H. pylori*'s TNFα-inducing protein (Tipα) induces multiple inflammatory cytokines in addition to TNFα in epithelial cells *in vitro*. The goal of this study was to evaluate the role of Tipα in promoting inflammation in a model of gastric infection.

Methods: C57BL/6 mice were infected with either wild type *H. pylori* (HpSS1) or an isogenic Tipα knockout mutant (HpSS1:Tipα-) for either 1 or 4 months. Gastric tissue was evaluated for bacterial load by quantitative PCR and inflammation and hyperplasia by grading H and E stained histologic sections.

Results: The *H. pylori*-infected groups (HpSS1 and HpSS1:Tipα-) had comparable bacterial loads at 1 month. TNFα and IL-17 were significantly higher in the HpSS1 group compared to both naïve and HpSS1:Tipα- groups (5-fold and 10-fold higher, respectively; *p*<0.05) at 1 month and this differential increased by 4 months post-infection (*p*<0.0001). Mice infected with HpSS1 had significantly higher antral inflammation compared to HpSS1:Tipα- mice after 1 month, and by 4 months, significant inflammation was also observed in the corpus (*p*<0.0001). Similarly, acute and chronic inflammation scores were also significantly higher in the HpSS1 group compared to both HpSS1:Tipα- and naïve mice. Hyperplasia scores in HpSS1-infected mice at 4 months post-infection were significantly higher compared to HpSS1:Tipα- and naïve mice (*p*<0.05).

Conclusion: This data suggests Tipα plays an important role in *H. pylori*-induced inflammation. Further exploration of the role Tipα plays in pathogenesis would increase our knowledge of *H. pylori* virulence and provide insight bacterial pathogenesis and its treatments.

950 *CLINICAL FEATURES OF THE PERIANAL AREA IN CHILDREN WITH FUNCTIONAL CONSTIPATION*

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Objective: Painful defecation is a common chief complain in children with constipation. Inspection of the perianal region usually gives important information and leads the choice of an appropriate treatment. However, clinical features of possible perianal abnormalities have not

been well characterized yet. Our objective was to describe common findings in perianal area of children suffering from functional constipation for more than 3 months.

Methods: A total of 205 patients (3 - 10 yrs) with functional constipation were enrolled. Perianal area was examined at the first visit and was described as one of the following categories: anal fissure, localized erythema, perianal erosion with secretion, anal indurations, ragged perianal skin and normal appearance.

Results: Normal appearance was detected in 92 (44.8%) children. The remaining 113 (55.1%) subjects suffered from at least one dermatologic problem at the anal area including localized erythema (89, 43.4%), anal indurations with or without erythema (21, 10.2%), anal fissure (14, 6.8%), ragged perianal skin (3, 1.4%) and perianal erosion with secretion (1, 0.48%). Complex features were classified as "prominent lesion" except for indurations which were commonly with erythematous anal area.

Conclusion: Perianal skin lesions are frequently found in pediatric patients presenting with constipation and particularly painful defecation. We recommend careful examination of the perianal area which leads to better diagnosis and treatment in patients suffering from functional constipation.

951 SERUM INTERLEUKINS IN CHILDREN WITH FOOD ALLERGIES IN COLOMBIA

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Introduction: Interleukins (ILs) play an important role in the pathophysiology of food allergy (FA). Their measurement could be useful for a definitive diagnosis, especially in cases with nonspecific manifestations, as well as for monitoring and for avoiding invasive techniques such as endoscopies.

Objectives: To determine serum levels of EGF, eotaxin, GCSF, GMCSF, INF- α 2, IFN- γ -IL-10, IL-12p40, IL-12p70, IL-13, IL-15, IL-17, IL-1ra, IL-1 α , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IP-10, TNF- α , VEGF, IL-1 β , MPC-1, MIP-1 α , MIP-1 β and TNF- β in various clinical expressions of FA (IgE, non-IgE, or mixed) in patients \leq 18 years treated at the Gastroenterology, Hepatology and Nutrition Unit (Gastronutriped) at diagnosis of FA and after 3 months of medical and nutritional management, between June 2014 and April 2015.

Methods: Of 94 patients diagnosed with FA, the first sample was able to be taken in 14, and the second sample in 4 patients. The ILs were measured with MAP MILLIPLEX Human Cytokine/Chemokine Magnetic Bead Panel (Luminex) technology. The description of the continuous variables was done based on the average or the median, with their respective measure of dispersion, according to their distribution. Discrete variables were expressed as proportions. IL values in different groups (such as immune mechanism, clinical manifestation, baseline and follow-up) were compared, with the t-test for normally distributed variables and the Wilcoxon-Mann-Whitney test for variables that lacked normal distribution. A value of $p < 0.05$ was considered significant.

Results: The first sample was taken in 14 patients and 4 patients underwent control. In patients with allergic proctocolitis, significantly high IL-8 values were found. For allergic esophagitis, significant elevation of INF- α 2 was documented. In patients with atopic dermatitis, there was a significant increase in IP-10 and VEGF. There was no IL with a significantly different value in patients with allergic enteropathy. On assessing the values of ILs at diagnosis and at 3 months, no statistically significant differences were found, which could be related to the size of the sample.

Conclusions: The measurement of ILs associated with different mediator mechanisms of FA could be useful for diagnosis and monitoring and for establishing the right time for the food challenge. The levels of IL-8, INF- α , IP-10 and VEGF show statistically significant differences in patients with proctocolitis, esophagitis and allergic dermatitis. There should be further study of these ILs in order to determine their diagnostic usefulness in FA.

HEPATOLOGY

967 SYSTEMATIC REVIEW OF THE EPIDEMIOLOGY AND BURDEN OF DISEASE OF PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS (PFIC): A GENETIC DISEASE ASSOCIATED WITH LIVER FAILURE IN CHILDREN

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Introduction: Progressive familial intrahepatic cholestasis (PFIC) is a class of rare, inherited, cholestatic disorders associated with childhood liver disease and premature death. This systematic literature analysis aimed to summarize the epidemiology, natural history and burden of disease of PFIC and identify areas requiring further research.

Methods: Electronic databases (MEDLINE, In-Process & Other Non-Indexed Citations, Embase, Cochrane) and proceedings from key congresses were searched using PRISMA guidelines for data on the epidemiology, natural history, clinical features, economic burden and/or health-related quality of life (HRQoL) of PFIC; publications up to May 2015 were screened.

Results: Of 1113 screened abstracts, 20 publications reporting epidemiology (n=17) and/or humanistic burden (n= 5; two publications reported both) were included; of these, 6 reported data on PFIC occurrence among children and adolescents hospitalized with liver disease, 10 on PFIC subtype distribution and 7 on symptoms at presentation. The incidence of intrahepatic cholestasis was reported as 1:18,000 live births in one report; however, this study was carried out prior to the availability of genetic testing for PFIC. In studies in children hospitalized with cholestasis, acute liver failure or splenomegaly and which used genetic testing, PFIC incidences ranged from 9% to 51%. Among patients with genetically confirmed PFIC, PFIC2 was the most common PFIC subtype (43 - 91% of patients). Symptoms associated with PFIC generally appeared around 3 months of age and tended to appear earlier in PFIC2 than in PFIC1. Symptoms at presentation included jaundice, hepatomegaly, pruritus, splenomegaly, diarrhea and pancreatitis. Among patients receiving ursodeoxycholic acid, 10 - 42% required biliary diversion for pruritus and other cholestatic complications. Complications resulting from disease progression included liver failure and hepatocellular carcinoma. Liver transplantation was required in 20 - 83% of patients. The mortality rate of PFIC was 6 - 87% overall; this was reduced to 6 - 21% among patients receiving surgical or pharmacological treatment, with a mean age of death of 4 years. Two of five publications assessing the humanistic burden associated with PFIC focused on the impact of pruritus on HRQoL. Pruritus was reported by

patients to be often severe and associated with abrasions, cutaneous mutilation, hemorrhage and scarring, and resulted in a reduction in HRQoL compared with healthy peers. No assessment of the economic burden of PFIC has been published.

Conclusions: This first comprehensive literature review on PFIC confirms that the disorder is associated with debilitating symptoms and a poor prognosis despite surgical interventions. It also identifies important areas for further research including epidemiology and HRQoL, in order to inform the management of PFIC and the design of future therapeutic trials.

***968 LIVER INJURY ASSOCIATED WITH ANTI-TUMOUR NECROSIS FACTOR THERAPY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE**

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Background: The frequency of hepatotoxicity in children treated for IBD with anti-TNF has never been examined. The aim of this study is to characterize liver enzyme abnormalities and drug-induced liver injury (DILI) in a large cohort of pediatric IBD patients on anti-TNF.

Methods: All IBD patients treated with anti-TNF at SickKids Hospital (2000 - 2015) were linked electronically with laboratory data to identify ALT elevations (≥ 80 U/L). Patient characteristics and natural history of liver enzyme elevations were recorded; likelihood of causality was assessed using the Roussel Uclaf Causality Assessment Method.

Results: Of 672 pediatric IBD patients treated with anti-TNF, 65 (10%) developed 67 episodes of ALT elevation ≥ 80 U/L (25% female, 89% Crohn's disease [CD], 85% infliximab ([IFX/15% adalimumab). Median peak ALT was 117 U/L. The median time to ALT elevation was 5 weeks and the median duration of ALT elevation was 6.2 weeks. ALT normalized in 85% of cases. 40/65 received a concomitant immunomodulator. 15/672 patients (2%) had persistent ALT elevation (≥ 80 days) and at least a "possible" causal relationship with anti-TNF therapy. All had CD and 12/15 received IFX. In all cases, the pattern of injury was hepatocellular. 10/14 had ≥ 1 positive autoantibody. 4/15 underwent liver biopsy. The first, with peak ALT 401, met criteria for "definite" autoimmune hepatitis (AIH). IFX cessation was followed by liver enzyme normalization over 15 weeks. Causality in the second patient, with peak ALT 205 and GGT 102, is unclear. Focal periductal fibrosis and portal inflammation were seen on biopsy and mildly dilated ducts on imaging. However, liver enzymes normalized after IFX discontinuation and rose upon re-exposure, and ANA titer fluctuated with IFX exposure, suggesting the changes may be drug-induced. Anti-TNF therapy was discontinued in 2 additional patients, the first due to elevated transaminases and concurrent pancytopenia, with high titer ANA, and the second due to poor clinical response. ALT normalized after IFX discontinuation in both. The 2 other patients to undergo biopsy displayed non-specific findings (portal inflammation, pericholangitis, cholangiolar proliferation, focal periductal fibrosis), with normal cholangiograms. Both have remained on anti-TNF and failed to normalize ALT. Of the remaining patients who continued on anti-TNF, ALT remains elevated in 5/9 after follow-up of 36.7 to 78 weeks.

Conclusions: Significant ALT elevations occurred in 10% of children receiving anti-TNF therapy for IBD. The majority were transient but a small subset experienced marked and persistent elevations. Triggering of immune-mediated phenomena, such as AIH, can occur, in which case prompt anti-TNF cessation is indicated.

969 REGULATORY T CELLS MODULATE THE SCLEROSING CHOLANGITIS PHENOTYPE IN MDR2 -/- MICE AND ARE EXPANDED BY CYTOKINE AND ANTI-CHOLESTATIC THERAPY

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Background: Regulatory T cells (Tregs) are a subspecialized population of T lymphocytes, and their dysregulation is implicated in immune-mediated diseases including primary sclerosing cholangitis (PSC). Furthermore, mutation of IL2RA (CD25) abundantly expressed on Tregs is associated with PSC susceptibility. The *mdr2* -/- mouse displays a sclerosing cholangitis (SC) phenotype of sterile inflammation, cholestasis, and fibrosis which can be utilized to investigate the pathogenesis of fibrosing cholangiopathies such as PSC.

Hypothesis: We hypothesize that Tregs modulate the SC phenotype in *mdr2* -/- mice and are modulated by cytokine and anti-cholestatic therapy.

Methods: Hepatic lymphocyte composition was surveyed in juvenile *mdr2* -/- mice transgenic for FoxP3-GFP and correlated with SC phenotype. Treg lymphocytes were manipulated *in vivo* with a complex of IL-2/anti-IL2 (IL2c) and with the intestinal ASBT inhibitor SC-435. Single-cell RNA-seq utilizing the Fluidigm system was performed on FACS-sorted Tregs from *mdr2* -/- mice with SC-435 treatment vs. cholestatic conditions.

Results: The SC phenotype in *mdr2* -/- mice developed between day 14 - 30 with rising serum ALT and ALP levels accompanied by waning proportion of Tregs/CD8+ lymphocytes. Compared to age/gender-matched control *mdr2* -/- mice, IL2c treatment from day 7-30 increased the population of hepatic Tregs by 50%, decreased the frequency of hepatic CD8+ lymphocytes by 29% and restored the Treg/CD8+ ratio. IL2c treatment not only reduced cholestasis (mean ALP 174 vs. 185 IU/L in IL2c vs. PBS; $p=0.02$) but also diminished liver fibrosis on histopathology (% mean area fibrosis 3.3 vs. 4.9 in IL2c vs. PBS; $p<0.01$). Anti-cholestatic treatment with SC-435 between day 30 - 45 in *mdr2* -/- mice led to a 98% reduction in serum total bile acids and a more than 2-fold increase in hepatic Treg frequency (%Treg/CD3+ 7.0 vs. 3.1 in SC-435 vs. control; $p=0.03$). A total of 65 single-cells exhibiting Treg phenotype (31 from SC-435 treatment and 34 from controls) were available for RNA-seq studies. In a supervised analysis, SC-435 treatment was associated with upregulation of genes implicated in Treg suppressive function including Helios, GITR and ICOS, suggesting cholestasis causes decreased expression of genes critical for Treg-mediated modulation of inflammation. Interestingly, an unsupervised analysis comparing the gene ontologies of Tregs under both conditions identified a cluster comprised of only Tregs with SC-435 treatment (20% of total SC-435 treated Tregs) characterized by upregulation of genes in lymphocyte proliferation pathways and EB13, which encodes a subunit of the cytokines IL-35 and IL-27, which identify these as potential signaling pathways important in Treg homeostasis and suppressive functions in this model.

Conclusion: Tregs modulate effector T lymphocyte response and SC phenotype in murine fibrosing cholangiopathy and their homeostasis is susceptible to cytokine and anti-cholestatic therapy.

970 A SYSTEMATIC REVIEW OF ALAGILLE SYNDROME

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Background and Aims: Alagille syndrome (ALGS) is an inherited childhood disorder typically manifesting as cholestasis and potentially leading to end-stage liver disease and death. Misdiagnosis and consequent mismanagement are common, because the disease affects multiple systems; symptoms are heterogeneous and vary in severity. We performed the first comprehensive systematic review of ALGS, to identify studies reporting the epidemiology, natural history and disease burden, and aimed to better characterize the clinical profile of the disease.

Methods: Electronic databases (MEDLINE, In-Process & Other Non-Indexed Citations, Embase, Cochrane) and proceedings from major hepatology and gastroenterology congresses were searched, using PRISMA guidelines, for data on the epidemiology, natural history, economic burden and/or health-related quality of life (HRQoL) related to ALGS. Reports published up to March 2015 were screened.

Results: Of 525 screened publications, 20 met the inclusion criteria; 2 reported on epidemiology, 13 assessed the natural history and 5 described HRQoL. No publication presented economic data. Reported incidences of ALGS ranged between 1 in 30,000 - 70,000 live births; however, these data are not based on genetic diagnostics and are therefore likely underestimates. Liver-related symptoms included cholestasis (87% - 100% of patients), jaundice (66% - 85%) and cirrhosis (44% - 95%). Between 14% and 47% of patients underwent liver transplantation and 4% - 14% received partial biliary diversion. Other common symptoms included cardiovascular abnormalities, eye findings, kidney involvement, skeletal malformations and characteristic facial features. Most deaths were from vascular complications, including intracranial bleeding, and heart or liver problems. Pruritus affected the majority of patients (59 - 88%, of whom up to 45% had severe pruritus) and manifested during the first 10 years of life, resolving completely and permanently in a minority of patients between median ages of 10 and 13 years. For most patients, pruritus persisted with varying degrees of severity depending on the therapy received and their level of adherence. HRQoL was significantly impaired in patients compared with healthy children and those with other diseases. Itching was the symptom that most affected children with ALGS; treatment is frequently suboptimal and pruritus often persists.

Conclusion: ALGS is the most common inherited cause of cholestasis. This systematic review consolidates the current understanding of the clinical manifestations of ALGS and highlights the considerable gaps in knowledge in terms of economic data, epidemiologic data and its humanistic burden, especially regarding HRQoL data associated with pruritus. Pruritus is particularly burdensome for patients and is currently not well managed. Further research is needed to better evaluate patient symptoms and burden in order to inform future clinical trials of novel therapies for this serious disorder.

971 IMPACT OF THE HEPATIC COMPLICATION ON PEDIATRIC PATIENTS WITH CYSTIC FIBROSIS: ROLE OF TRANSPLANTATION IN THE TREATMENT

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Introduction The hepatic complications (HCF) in cystic fibrosis (CF) cause important morbi-mortality. On having improved the global life expectation in patients with CF, hepatic transplantation arises as a therapeutic alternative for those who present terminal hepatic failure or refractory disease to other therapeutics

Aims: To report HCF prevalence in a population of transplanted hepatic patients and evaluate characteristics and evolution.

Methods and Population: Descriptive, retrospective, observational, multicenter study. Information of patients was checked by HCF included in a transplant list and whole populations of 1253 hepatic pediatric patients were transplanted from 1990 to 2015. Complications, weight evolution and post-transplant survival was analyzed.

Results: Out of 1253 transplanted patients, 13 HCF acceded the waiting list and 10 were transplanted (0.7%). Median age for transplant was 10.6 years (IQR 6 - 18 years), 90% were males, the indication for transplant was cirrhosis with severe digestive hemorrhage in 6 patients, hepatic insufficiency with edematous-ascitic syndrome in 3, and severe hypersplenism in 1. Nine of them received cadaveric liver and one a living-related donor, her mother. The donor had a good evolution. The post-transplant weight evolution after first year showed an average increase of 9%. The patients had no pulmonary complications. The most important disease after transplant was diabetes in 5 (50%) and others were biliary stenosis, hepatitis secondary to citomegalovirus, acute rejection and severe osteoporosis in every one. The immunosuppression treatments included tacrolimus, methylprednisolone and basiliximab in 90% of the cases. This population showed 100% survival one year post-transplant and 90% survival after 5 years; a patient died of pulmonary infection after 3 years due to *Burkholderia cepacia*.

Conclusions: Hepatic complications in cystic fibrosis are a cause of high morbi-mortality and a clear indication of transplant in terminal stage. The prevalence of transplant in our population is less than in other series. Hepatic transplantation presented an excellent result in this population. Diabetes was the most frequent post-transplantation complication.

972 MODELING CYSTIC FIBROSIS LIVER DISEASE USING INDUCED PLURIPOTENT STEM CELL-DERIVED CHOLANGIOCYTES

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Background: As life expectancy of cystic fibrosis (CF) patients has increased, recognition of non-respiratory complications of CF have become more important. Cystic fibrosis liver disease (CFLD) is the third leading cause of mortality in patients with CF. CFLD is poorly characterized and affects cholangiocytes, the only cells in the liver that express cystic fibrosis transmembrane conductance regulator (CFTR) protein. With a lack of suitable models to study CFLD, rodent cholangiocytes, and immortalized human and rat cholangiocyte cell lines (typically derived from carcinomas) have been used to investigate electrophysiological and potential immunologic functions of cholangiocytes. Development of an *in vitro* model of human CFLD from patient cholangiocytes and liver tissue would be ideal, but access to such tissue with uniform genetics and controls in quantities appropriate for research is almost impossible. Using induced pluripotent stem cell (iPSC)-derived cholangiocytes (iChols) and hepatocytes (iHeps) from an affected patient containing the cystic fibrosis transmembrane conductance regulator (CFTR) mutation would provide a human *in vitro* model that could be dissected to investigate basic mechanisms of this disease, as well as a platform to develop therapeutic compounds.

Hypothesis: The chemical imbalance produced by the malfunction of the CFTR protein in cholangiocytes produces increased cellular stress in cholangiocytes and hepatocytes that results in chronic and inappropriately activated pathways, which drive hepatic fibrosis.

Methods: We obtained fibroblasts from a family affected with the $\Delta F508$ CFTR mutation (two affected siblings and their unaffected father as control). To differentiate fibroblasts into iPSCs, we used Yamanaka factors (reference PMID: 26439714). We then used recently published protocols (Sampaziotis *et al*, *Nat Biotechnol*. 2015 and Ogawa *et al*, *Nat Biotechnol*. 2015) to differentiate iPSCs into iChols and iHeps. We successfully obtained iPSCs and differentiated those into iChols and iHeps. We will evaluate iChols quantitatively by RNA sequencing and functionally by immunohistochemical staining. We will use iChols and iHeps to evaluate CFTR function by utilizing standard electrophysiological Ussing chamber studies and microfluidic techniques comparing CFTR $\Delta F508$ affected iChols to controls. Finally, we will characterize the effects of the CFTR $\Delta F508$ mutation in human iChols and iHeps on cellular stress pathways by assessing the expression of stress response pathways, apoptosis and TGF-beta signaling.

Anticipated Results: Our goal is to validate an experimental human *in vitro* model of CFLD that can be used to investigate basic mechanisms of disease within CFLD, as well as a platform for screening therapeutic compounds.

Mentors: Aras Mattis, MD, PhD and Phil Rosenthal, MD

973 RESOLVING MALNUTRITION WITH PARENTERAL NUTRITION PRE-TRANSPLANT IN PATIENTS WITH END-STAGE LIVER DISEASE

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Background: End-stage liver disease (ESLD) is the end result of many liver diseases and the most common indication for liver transplant in pediatrics. Malnutrition is a common complication due to anorexia with advanced liver disease, gastric compression from organomegaly and diarrhea from malabsorption. Malnutrition can persist with supplemental nasogastric (NG) feeds secondary to issues with vomiting, diarrhea and diaper dermatitis. NG feeds are not without risk with frequent displacement, difficult replacement and nasal or variceal bleeding. Previous studies show that malnutrition is associated with poor pre- and post-transplant outcomes, such as increased blood requirement during transplant, post-operative infections, longer ICU and hospital stays and increased costs. At Seattle Children's Hospital, experience with long-term parenteral nutrition (PN) in intestinal failure provides a foundation for expanding PN use to patients with ESLD with persistent malnutrition despite enteral feeds. Risks to using PN in this population include hepatotoxic effects of PN in an already diseased liver, fluid balance and electrolyte issues and central line-associated complications. The medical literature contains only a few single-center experiences describing the use of PN in children with ESLD.

Objective: The primary objective was to determine the effect of PN on malnutrition in children with ESLD. Secondary objectives included evaluation of complications associated with PN, such as central line infections, changes in MELD/PELD scores, labs, time admitted to the hospital, time from listing to transplant and ICU time post-transplant.

Design: Retrospective chart review was completed analyzing children at Seattle Children's Hospital with ESLD on PN who were transplanted January 1, 2010 – December 31, 2015. Patients with no anthropometric data collected between the start of PN and transplant were excluded. Baseline demographics were described, as well as the change in nutritional status and secondary outcomes over time from the start of PN to the time of transplant.

Results: 44 patients with ESLD were transplanted during the time frame. 18 (41%) received PN and anthropometric evaluation (median, 80 days; range, 22 - 320 days). All had biliary atresia with a median age at transplant of 10 months (range, 5 - 18 months). Mid-upper arm circumference and tricep skinfold thickness Z-scores showed complete resolution of malnutrition in 7 patients (39%) with normalization of one of the two measures in 4 more patients. Of the remaining patients, 6 had improved Z-scores and one had worsening malnutrition. There were no deaths in those patients receiving PN. Central line infection rates were 4.2/1000 catheter-days with 9 total central line infections occurring in 7 patients with a total of 2117 catheter-days.

Conclusions: Use of PN in children with ESLD has shown to improve and in many cases resolve malnutrition prior to transplant with the potential to improve surgical outcomes.

974 LIPOPROTEIN (A) LEVELS ARE FREQUENTLY ELEVATED IN CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Background: Elevated levels of lipoprotein(a) or Lp(a), a type of low density lipoprotein, may promote atherosclerosis and coronary artery disease. Non-alcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease in children and is associated with cardiovascular risk factors, including the presence of dyslipidemia, hypertension and metabolic syndrome. The aim of this study was to assess Lp(a) level, as a cardiovascular risk factor, in children with NAFLD and determine the prevalence of elevated Lp(a) in this population.

Methods: This was a cross-sectional study involving all consecutive patients with a body mass index (BMI) >85th percentile presenting with NAFLD confirmed with liver ultrasonography. Data including anthropometric measures, blood pressure, family and medical history, fasting lipid panels and Lp(a) level were collected on all the patients. Elevated Lp(a) level was defined as >30 mg/dL. High Lp(a) was modelled as the dependent variable and univariable and multivariable logistic regression analyses were performed.

Results: A total of 148 children with NAFLD were included in the study. The median age was 14 (12, 16) years, 65.5% male, 72% Caucasian, median BMI of 99.3%. The median Lp(a) for our cohort was 16.5 (6.0,41.5) and 35.8% had elevated Lp(a) level >30 mg/dL. On univariate analysis, African American ethnicity, asthma, total cholesterol and low density lipoprotein levels were associated with high LP(a). On multivariate analysis, male gender [OR (95% CI) 4.5 (1.5, 13.0), *p*-value 0.006], asthma (OR 2.9 (1.2, 7.2), *p*=0.022] and total cholesterol (OR 1.2 (1.06, 1.4), *p*=0.005] were significantly associated with high LP(a).

Conclusion: One-third of pediatric patients with NAFLD have elevated Lp(a) levels increasing their risk for atherosclerosis. Lp(a) levels correlated with male gender and the presence of high cholesterol and asthma. Further studies are needed to assess the correlation between Lp(a) levels and the histologic severity of NAFLD.

975 RETROSPECTIVE STUDY OF PEDIATRIC LIVER TRANSPLANT PATIENTS WITH POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE

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Background: Post-transplant lymphoproliferative disease (PTLD) can be a devastating complication of solid organ transplantation. This study aimed to determine the incidence and outcomes of pediatric liver transplant (LT) patients with PTLD at a single center.

Methods: A retrospective, observational, cohort study of pediatric patients who underwent LT between 2005 and 2015 was performed.

Systematic chart review was used to determine the incidence of biopsy-proven PTLD in these patients. The characteristics and outcomes of patients with PTLD were also described.

Results: During the 10-year study period, 158 children received a LT. Twenty-two out of these 158 patients (14%) were diagnosed with biopsy-proven PTLD. Of those with PTLD, median age at LT was 19 months (range 3 months - 13 years) and median length of follow-up from transplant was 53 months (range 11 months - 10 years). The top three indications for LT were biliary atresia (45%), genetic disorder (23%) and metabolic disease (18%). All donors and 9% of recipients had serologic evidence of past Epstein-Barr virus (EBV) infection. After LT, all patients were started on tacrolimus and prednisone for immune suppression. Mycophenolate was started in 27% of patients and azathioprine in 9% of patients. At least one rejection episode occurred in 59% of patients prior to diagnosis of PTLD with subsequent increase in immune suppression. Median age at PTLD diagnosis was 36 months (range 15 months - 13 years) and median time from LT to PTLD diagnosis was 10.5 months (range 2 months - 5 years). Biopsy proven sites of disease included 15 (68%) gastrointestinal, 6 (27%) lymph node, 3 (14%) lung and 2 (9%) liver. Pathology showed 50% early, 41% polymorphic and 9% monomorphic lesions. All patients had at least one positive EBV PCR from the blood between time of LT and PTLD diagnosis. The median time from first positive EBV PCR to PTLD diagnosis was 5.6 months (range 1 month - 3 years). Tacrolimus was stopped in 21 (95%) patients, 76% were started on sirolimus and 24% remained off immunosuppression completely. Chemotherapy was used in 13 (59%) patients. PTLD remission, defined as negative biopsy or resolution of EBV viremia, was achieved in 68% of patients. There were no deaths or patients who required repeat transplantation. However, 50% of patients suffered rejection after initiating PTLD management.

Conclusion: In this single-center, retrospective study, the 14% incidence of PTLD following pediatric LT is higher than previously published. Importantly, all patients with PTLD in this cohort had EBV detected by PCR prior to PTLD diagnosis, representing an opportunity to potentially intervene and prevent PTLD onset. A systematic approach to screening using EBV surveillance should be considered in LT patients with specific guidance on response to positive EBV PCR results. Efforts aimed at reducing PTLD incidence must be balanced against risk of organ rejection.

976 OPTIMIZATION OF METHODS TO INTERROGATE THE TRANSCRIPTOME IN FORMALIN-FIXED, PARAFFIN-EMBEDDED LIVER BIOPSIES

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Introduction: An infectious trigger in a genetically susceptible host has been proposed as etio-pathogenic in several pediatric liver diseases, including autoimmune hepatitis (AIH). Often, formalin-fixed, paraffin-embedded (FFPE) liver biopsies are the only hepatic tissues available, but retrieval of RNA from such small biopsies has been problematic. Our overall goal was to develop methods to obtain high quality RNA from FFPE liver biopsies in order to perform unbiased high throughput sequencing (HTPS) of transcriptomes to search for infectious pathogens.

Methods: Total RNA extracted from 45 FFPE liver biopsy samples [24 AIH type 1 patients (ages 9 - 30 years old) and 21 controls who had liver biopsies done for non-infectious indications (ages 4 to 25 years old)] was analyzed using RNAseq. RNA was extracted from two cored tissue samples (tissue ~1 mm diameter x 1-2 mm height) using the QIAGEN miRNeasy FFPE kit. After reverse transcription of RNA, cDNA libraries were constructed using the Illumina TruSeq Stranded Total RNA Sample Preparation Kit with Ribo-Zero Gold. Indexed paired-end sequencing of libraries was performed on an Illumina HiSeq2000. Initial quality control was performed using FastQC and then adapter sequences and bases with low quality were trimmed using Fqtrim. Preliminary metagenomic classification was performed using Kraken to assign taxonomic labels to metagenomic DNA sequences.

Results: TapeStation analyses of extracted RNAs revealed nucleotide lengths of around 200. Similar analyses of the resulting libraries revealed peaks at 220-314 base pairs (bp) (total bp insert size + 120 bp sequencing adapter/linkers). The average number of sequences obtained per library from HTPS was 55,136,519. FastQC of the sequences revealed that 5/45 samples had systematically poor quality for paired end read two extending over the entire length of the sequences. Trimming retained >95% of the original reads in most of the samples and Kraken was able to classify >90% of the reads in all samples except for those mentioned above. The fraction of human reads varied across samples (14 - 90%). The time of storage of the samples highly correlated with the number of human reads (p -value 1.98e-07), irrespective of co-variables such as the age or sex of the patient; the more recent the sample, the higher the yield of human reads.

Conclusions: We have optimized the methods for extraction and purification of RNA from FFPE liver biopsies stored for up to 20 years, as well as for subsequent library construction for use in HTPS and were able to classify >90% of the reads in samples that had been stored for less than ten years. These findings open up opportunities to analyze thousands of archived liver biopsies in hopes of shedding further light on the etiology of AIH and other inflammatory disorders of the liver.

*977 VERTICAL SLEEVE GASTRECTOMY (VSG) IN MORBIDLY OBESE ADOLESCENTS RESULTS IN INCREASED FIBROBLAST GROWTH FACTOR 21 (FGF21) THAT CORRELATES WITH WEIGHT LOSS

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Introduction: Vertical sleeve gastrectomy (VSG) results in elevated bile acids (BA) and fibroblast growth factor 19 (FGF19) levels. FGF21 shares essential co-factors with FGF19 and has been shown to be increased in energy-deficit states. We studied fasting and post-prandial changes in BA and FGF19/21 physiology in morbidly obese adolescents' post-VSG.

Methods: We enrolled 10 adolescents (age 17.4 ± 0.5 yrs and BMI 51.5 ± 2.5 kg/m²) that underwent VSG surgery. Fasting and post-meal challenge (100 mL Ensure™) blood samples were collected at 30-minute intervals (till 120 minutes) during 3 visits (Pre-G [V1], and at 1 [V2] and 3 months [V3] post-VSG) for analysis of BA, FGF 19 and FGF 21.

Results: 1 subject was excluded. As expected, post-VSG, subjects lost weight over time (V2 11.8 kg \pm 0.8; V3 21.9 kg \pm 1.7), while post-prandial BA (V2; 60 min $p=0.001$ and V3 60min $p=0.024$) and FGF19 (V2; 90 min $p=0.026$; V3; 90 min $p=0.085$) levels were increased. The surrogate marker for hepatic BA production, circulating C4, was lower post-VSG (V2; $p=0.029$). BA composition also changed post-VSG, with an increased share of chenodeoxycholic acid (CDCA) (V1 60 min 45.9% vs. V2 60 min 64.4%; $p=0.038$) and decreased deoxycholic acid (DCA) (V1 fasting 21.4% vs. V2 fasting 13.5%; $p=0.001$; V1 60 min 25.4% vs. V2 60 min 12.1%; $p=0.012$), (V3 fasting 19.4%; $p=0.039$; V3 60 min 15.5%; $p=0.052$ compared to V1). These BA composition changes resulted in an improved post-prandial hydrophobicity index (V3; 30 min, $p=0.030$ and 60 min $p=0.033$). We observed that post-VSG FGF21 levels initially increased (V2; fasting and 120 min, $p<0.01$), then returned towards pre-surgery levels at V3. There were positive correlations between the increase in postprandial BA and FGF 19 (V3; 90 min, $p=0.041$, r 0.774) and fasting BA and FGF21 (V2; $p=0.003$, r 0.894). Further, we observed a correlation between the rise in postprandial FGF19 and FGF21 (V2; 90 min $p=0.001$, r 0.920) but more interestingly between body weight lost (kg) and fasting FGF21 levels (V2; $p=0.012$, r 0.82).

Discussion / Conclusion: BA physiology is altered in obese adolescents' post-VSG with increased serum BA, FGF 19/21 levels, and an improved hydrophobicity index. Our study presents novel data regarding an increase in FGF21 that correlates with weight loss post-VSG. The role of FGF21 has not been studied extensively in bariatric surgery and warrants mechanistic investigation.

978 NEUROCOGNITIVE OUTCOMES IN CHILDREN WITH END-STAGE LIVER DISEASE: A BROADER SPECTRUM OF MORBIDITY IN DEVELOPING COUNTRIES

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Background: Concern has been expressed that infants and children with chronic disease such as chronic cholestasis suffering from end-stage liver disease could have a risk of neurological impairment injury resulting in poor school performance in the future. The purpose of our study is to evaluate neurocognitive development in children with end-stage liver disease waiting for liver transplantation in Indonesia.

Methods: All children age 3 months to 5 years with chronic cholestasis and end-stage liver disease coming to the outpatient clinic in our hospital were routinely evaluated for their growth and development, neurological function and nutritional status. Their body weight, body height, head circumference, arm circumference, development, nutritional status, neurological evaluation and comorbidities were recorded. Bayley Scales of Infant Development (BSID)-III Cognitive Composite score were used for assessing developmental delay and brain ultrasound and computed tomography scanning were used, if indicated. All data were evaluated for assessing their neurocognitive outcomes.

Results: Twenty-seven children with chronic cholestasis were evaluated. Their mean age was 18.83 (SD: 21.7) months, body weight was 7932.39 (SD: 3416.2) grams and poor nutritional status, as assessed by arm circumference (59.3% mild malnutrition and 25.9% severe malnutrition). High proportions of impairment in cognitive and psychomotor development were found in children with chronic cholestasis. In addition, high proportions of abnormal muscle tonicity, small head circumference and brain atrophic were also found in these children.

Conclusions: The most common neurodevelopment abnormalities were cognitive impairment, neuromuscular hypotonicity and psychomotor dysfunction, probably due to poor nutritional status and chronic morbidities related to end-stage liver disease. A prompt interdisciplinary evaluation and follow-up program should be designed to prevent neurodevelopmental delay due to chronic illness and comorbidities related to end-stage liver disease to provide better neurocognitive function after liver transplantation.

Keywords: end-stage liver disease, chronic cholestasis, neurocognitive, BSID-III

979 CHANGING PHENOTYPE OF PEDIATRIC AUTOIMMUNE LIVER DISEASE IN AN AUSTRALIAN COHORT

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Introduction: Autoimmune liver disease (AILD) incorporates those with primary sclerosing cholangitis (PSC), autoimmune hepatitis (AIH) and autoimmune sclerosing cholangitis (ASC), an overlap of AIH and PSC. AIH is characterized by histological evidence of interface hepatitis and positive autoantibodies. PSC is characterized by inflammation and progressive obliterative fibrosis of intrahepatic and/or extrahepatic bile ducts. Many children have AILD described in association with inflammatory bowel disease (IBD).

Aims: We describe a cohort of pediatric onset AILD to highlight long-term outcomes and prognostic indicators according to AILD type, as well as the change in diagnostic type with time and increasing use of magnetic resonance cholangio-pancreatography (MRCP).

Methods: A retrospective chart review was conducted from January 2000 to January 2016. Demographic and disease phenotypic data were collected at diagnosis and at any change in AILD type.

Results: Data were available in 75 children, 29 (38.6%) in 2000 - 2007 and 46 (61.4%) in 2008 - 2016. Presenting AILD type was AIH in 44 (58.6%), PSC in 13 (17.3%) and ASC in 9 (12%). The relative frequency of final diagnosis of PSC and ASC increased from 10 (34.4%) in 2000 - 2007 to 25 (54.3%) in 2008 - 2016. Of 44 presenting with AIH, 4 progressed to ASC, during a median follow-up of 3.2 years. PSC and ASC related to IBD also increased from 27.5% to 50%. Of the 32 with AILD-related IBD (28 ulcerative colitis, 2 Crohn's disease, 2 early onset IBD), 17 (53%) had PSC or ASC at diagnosis, 1 (3%) had AIH at diagnosis, 9 (28%) were diagnosed prior to PSC or ASC and 5 (16%) were diagnosed at least 3 months after PSC or ASC.

MRCP was performed in 34.4% (2000 - 2007) and 65.4% (2008 - 2016) of patients. Large duct disease was demonstrated in 60% and 68% in respective periods. Rate of colonoscopy in children with AILD increased from 55.1% (2000 - 2007) to 60.8% (2008 - 2016). 3 children with PSC and IBD required colectomy. 40.8% of all children with IBD had right-sided disease on colonoscopy. Portal hypertension was present at diagnosis in 47.5% of AIH and 20% of PSC and ASC patients. 53% of the total population presented with advanced fibrosis on biopsy. 5 (6.6%) progressed to liver transplant (3 ASC - IBD, 1 PSC - IBD and 1 AIH - all female) with a mean age of 7.8 years, 0.5 to 5 years after diagnosis. One patient died from pulmonary embolus secondary to recurrent PSC and active IBD.

Conclusion: In pediatric AILD, the relative proportion of PSC and ASC has increased in recent times, along with increasing association with IBD. This reflects change in performance of MRCP and colonoscopy. Females diagnosed with large duct ASC and PSC with IBD have the

greatest risk of liver transplant in those diagnosed with AILD. Children with large duct disease PSC in association with colitis are more likely to progress to colectomy. In children with PSC or ASC with IBD, full colonoscopy to the right colon is important for management and prognostication.

980 PARTIAL INTERNAL BILIARY DIVERSION IMPROVES CLINICAL, BIOCHEMICAL AND HISTOLOGICAL PARAMETERS IN PROGRESSIVE, FAMILIAL INTRAHEPATIC CHOLESTASIS: A STUDY OF 21 PATIENTS

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Progressive familial intrahepatic cholestasis (PFIC) is a heterogeneous group of autosomal recessive liver disorders characterized by early onset of cholestasis that progresses to end-stage liver disease before adulthood. Hallmarks of these disorders is pruritus and low -GT. PFIC was among the major indications for liver transplant. Facilitation of biliary salts' excretion and interruption of the enterohepatic circulation through surgical biliary diversion has yielded excellent clinical, biochemical and histologic response in patients of PFIC, provided there is no significant fibrosis on liver biopsy. The aim of this study is to report the clinical and biochemical outcomes of partial internal biliary diversion (PIBD) in a cohort of PFIC patients.

Patients and Methods: All patients with PFIC presenting at the Children Hospital and Institute of Child Health Lahore over 6 years (March 2010 to February 2016) were prospectively enrolled. Diagnosis of PFIC was made on family history, clinical manifestations, hematological investigations and liver histology. Specific tests were done to exclude other causes of cholestasis. All patients of PFIC who had significant pruritus and unsatisfactory response to medical therapy, having a liver histology of mild fibrosis, underwent PIBD using cholecystojejunocolonic anastomosis. Patients with advanced fibrosis on liver biopsy were excluded. The main outcome measure was clinical and biochemical remission. An additional outcome measure was improvement in liver histology. Morbidity data were recorded.

Results: During this period, 21 patients of PIBD were operated on (12 M, 9 F, median age 3 years, range 11 months - 16 years). All cases were products of consanguineous marriages, and 4 families had more than one child affected. Main clinical features, present in all patients, were jaundice, intractable itching, irritability and sleep disturbance. Five patients had history of large, foul-smelling, oily stools. After surgery, at follow-up of 2 and 4 months, 17 (81%) patients had dramatic resolution of pruritus, with complete clearance of jaundice in 16 patients. There was sound sleep and improved quality of life in all patients. Three patients showed only partial response with slightly reduced pruritus and incomplete resolution of jaundice, while one patient showed no response. There was significant improvement in serum bilirubin, ALT, AST and ALP (*p*-value <0.05) after surgery. Repeat liver biopsy, done on 4 patients during follow-up between 12 - 36 months, showed complete remission of cholestasis and reduced portal fibrosis. No major complications were noted during follow-up ranging from 2 months to 6 years.

Conclusion: PIBD is a highly effective procedure in a select group of PFIC patients with low -GT and mild or no fibrosis on biopsy. It improves the quality of life by reduction of pruritus and improved sleep. It may delay the progress of fibrosis preventing the onset of chronic liver disease and cirrhosis.

981 THE EPIDEMIOLOGY OF BILIARY ATRESIA FOCUSING ON THE CAUSAL RELATIONSHIP WITH ROTAVIRUS IN KOREA: A NATIONWIDE POPULATION-BASED STUDY

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Purpose: Biliary atresia (BA) is a rare disease of neonatal cholestasis and the major indication for pediatric liver transplantation. Although environmental factors, such as viral infection, have been proposed as the etiology of BA, it remains still unknown. The present study determines the incidence of BA and investigates the incidence trend associated with seasonal variation and the prevalence of rotaviral infection.

Methods: We analyzed the rare, intractable disease registration and Health Insurance Review and Assessment Services claims database, which includes information on every patient with BA diagnosed through uniform criteria from 2006 to 2013. Four hundred and three patients with BA newly diagnosed from 2006 and 2013 were traced for operation time and survival. The incidence trend of BA was compared with rotavirus infection prevalence and estimated rotavirus vaccination coverage rate.

Results: During the study period, incidence of BA was 1.09 cases per 10,000 live births (0.93 - 1.27 per 10,000 live births) without annual and seasonal variations. Three hundred and four patients (75.2%) underwent a Kasai portoenterostomy within 3 months of age. Five-year overall BA patient survival was 91.0%. After rotavirus vaccination coverage, the prevalence of rotavirus infection was reduced, but the incidence trend of BA remained constant.

Conclusion: Incidence of BA in Korea is similar with other East Asian countries. The change in prevalence of rotavirus infection has no effect on the incidence trend of BA.

982 CEREBROTENDINOUS XANTHOMATOSIS: AN OVERLOOKED CAUSE OF FATAL NEONATAL CHOLESTASIS

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Cerebrotendinous xanthomatosis (CTX), which usually presents with symptoms of nervous system involvement in adults or older children, is caused by mutations in CYP27A1. Reports on CTX presenting as neonatal cholestasis are very rare and the cholestasis is generally believed as transient. From January 2013 to September 2015, 5 patients, 1 male and 4 female, were referred for investigation of neonatal conjugated hyperbilirubinemia and finally diagnosed as CTX by homo- or compound heterozygous CYP27A1 mutations. All of them were born at term following an uneventful pregnancy from non-consanguineous parents. Four of them subsequently died due to liver failure. Urinary bile acid profiles determined by mass spectrometry in these fatal cases were atypical and the results were not consistent with that typically observed in patients with CTX patients. A predominance of sulfated bile alcohols appeared to be associated with a poor outcome. Their urinary bile acid profiles were not identical to adult CTX either. A male sibling of one live patient, who was suspected to be suffering from the disorder as well, also died from chronic neonatal cholestasis. Our result indicates that neonatal cholestasis in CTX might be overlooked by traditional biochemical markers and its outcome is not always benign. The biochemical diagnostic criteria and the best management of CTX which presents as severe cholestasis warrants further investigation.

983 INTERNATIONAL LYSOSOMAL ACID LIPASE DEFICIENCY REGISTRY

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The first global registry for lysosomal acid lipase deficiency (LAL-D) was recently established and is currently recruiting patients to collect data that will help improve understanding of the disease and the long-term safety and effectiveness of therapy (ClinicalTrials.gov NCT01633489). LAL-D is a rare, autosomal, recessive disorder that causes low-to-undetectable levels of LAL, the enzyme responsible for metabolizing cholesteryl esters and triglycerides in lysosomes. Typically fatal in infants, LAL-D is also associated with significant morbidity and mortality in children and adults due to liposomal accumulation of cholesteryl esters and triglycerides, which in turn leads to liver disease and accelerated cardiovascular disease. The objectives of the registry are to use uniform methodology to collect longitudinal data to further the understanding of LAL-D, including its progression and complications; evaluate the long-term effectiveness of therapeutic and supportive interventions; improve care of LAL-D patients through evidence-based management; and understand the relationship between access to care and LAL-D outcomes. In addition to other therapeutic and supportive interventions, the registry will collect data on long-term outcomes with sebelipase-alfa, a recombinant human LAL for treatment of LAL-D, including effects on liver function and hypersensitivity reactions. Participation is voluntary and open to any patient with confirmed LAL-D irrespective of age, gender, or treatment status or choice; clinical management will remain at the discretion of the treating physician. Carriers of LAL-D (i.e., individuals who have ≥ 1 mutation in the LIPA gene or have a parent or child with LAL-D) may also register. At enrollment, participating physicians enter demographic, socioeconomic, clinical and treatment data from patient medical records into a secure, web-based system. Such data are also being collected prospectively, along with quality-of-life questionnaire results, at least every 6 to 12 months through June 2029. Study progress reports with de-identified data will be issued annually. Data from all sebelipase-alfa-treated registrants will be analyzed, as well as data from subgroups of patients 2 - 4 years of age, adults >65 years, and women who are pregnant or lactating. The registry is being overseen by a scientific advisory board comprising international LAL-D experts who will work with the sponsor (Alexion) to facilitate analysis and dissemination of data via medical conferences and peer-reviewed publications. Limitations of this research include the potential for treatment selection bias, confounding factors, missing data, and loss to follow-up; however, the LAL-D registry has the advantage of providing long-term, real-world data on the natural history and treatment outcomes of this rare condition.

984 COMPARISON OF DIFFERENT DIAGNOSTIC METHODS FOR BILIARY ATRESIA

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Background: Biliary atresia is the main indication of liver transplantation among pediatric patients. Portoenterostomy is the only available treatment with better results when performed in the first two months of life, so early diagnosis is very important. Liver needle biopsy is the most accurate, but the most invasive, method among the various investigations for diagnosis of biliary atresia.

Objective: To evaluate the diagnostic accuracy of different diagnostic methods for diagnosis of biliary atresia (BA).

Methods: This cross-sectional study was conducted at the department of Pediatric Gastroenterology and Nutrition of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from August 2013 through July 2015 among purposively-sampled infants with neonatal cholestasis. A thorough history and physical examination were done and the liver enzymes were studied. Abdominal ultrasonography, hepatobiliary scintigraphy and percutaneous liver biopsy were done in all cases. The sensitivity, specificity and diagnostic accuracy of clinical parameters and investigations were calculated with liver biopsy as the gold standard for diagnosis of biliary atresia.

Results: A total of 86 neonatal cholestatic cases were studied, among them 38 (mean age, 81.5 ± 38.4 days) were diagnosed as BA and 48 (mean age, 88.7 ± 46.5 days) as INH. There were 67 (66.7%) male. The present study found that there was no significant difference between the subjects with BA and that of INH in terms of age at onset of jaundice, age at admission and sex. Term baby and good birth weight are significantly higher in BA cases. The presence of persistent pale-colored stool is significantly more in patients with BA ($p=0.000$). Liver size was found to be significantly larger (5.4 ± 1.2 cm vs. 4.3 ± 1.0 cm) in INH cases ($p=0.000$). GGT is the only liver enzyme that is found to be useful differentiating BA from INH at a cut-off value of ≥ 24 U/L or 9.5 times higher than upper limit normal ($p=0.000$) with sensitivity and specificity of 81.6% and 72.9%, respectively. In the present study, hepatobiliary scintigraphy was found to have a better sensitivity than ultrasonography (92.1% vs. 84.2%), but has a lower specificity (58.3%). The diagnostic accuracy of persistent pale-colored stool found to be highest (79.1 %).

Conclusion: The present study showed that persistent pale-colored stool and serum level of GGT with a cut-off value of ≥ 24 U/L or 9.5 times higher than upper limit of normal can be considered as predictive markers for a diagnosis of BA. The study found that negative results of USG and hepatobiliary scintigraphy can be used to exclude biliary atresia in infants with neonatal cholestasis. Further prospective studies with larger sample sizes may give higher sensitivity and specificity for diagnosis of biliary atresia if four of these parameters can be correlated.

*985 DXA BONE DENSITY DEFICITS DIFFER IN ALAGILLE SYNDROME AND CHRONIC INTRAHEPATIC CHOLESTASIS

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Osteopenia and bone fractures (fx) are significant causes of morbidity in children with cholestatic liver disease. We performed dual energy X-ray absorptiometry (DXA) analysis in a cohort of children with inherited cholestatic diseases and explored associations with anthropometrics, laboratory measurements and fx history.

Methods: Subjects were enrolled in the Longitudinal Study of Genetic Causes of Intrahepatic Cholestasis (LOGIC) in the NIDDK-funded Childhood Liver Disease Research Network (ChiLDReN). DXA was performed on subjects aged >5 years (with native liver), diagnosed with bile acid synthetic disorder (BAD; n=14), alpha-1 antitrypsin deficiency (A1AT; n=44), chronic intrahepatic cholestasis (CIC; n=41, 23 with genetically defined PFIC) and Alagille syndrome (ALGS; n=49). Pearson correlation coefficients were used to examine associations between subject reference and anthropometrically-adjusted DXA Z-scores and laboratory values [total bilirubin (TB), serum bile acids (SBA) and 25-OH vitamin D (vitD)] and fx history.

Results: There were significant differences among the four diagnosis groups for many anthropometric and lab parameters ($p<0.001$). Weight, height and BMI Z-scores were all lower in the CIC and ALGS groups. TB and SBA were highest in the ALGS group. Fx prevalence was higher in ALGS (40% with any fx; 21% in BAD; 20% in A1AT; 24% in CIC). Significant differences were found among disease groups in bone mineral density (BMD) and bone mineral content (BMC) DXA reference measures, with the lowest values in CIC followed by the ALGS group (total body minus head BMC, mean Z-score in BAD -0.08; A1AT 0.18; ALGS -1.23; CIC -1.8; $p<0.001$). After adjustment for height and weight, bone deficits persisted in the CIC group, but resolved in the ALGS group. In the ALGS cohort, height- and weight-adjusted total body minus head BMD and BMC Z-scores were negatively correlated with TB ($p<0.001$) and SBA ($p=0.02$), but not vitD. Anthropometrically-adjusted total body-head BMC Z-scores correlated negatively with TB in the CIC group ($p<0.03$). Mean height- and weight-adjusted total body-head BMD and BMC Z-scores were lower in ALGS subjects with a history vs. no history of fx (-0.7 vs. 0.7, $p=0.008$, and -0.6 vs. 0.4, $p=0.01$, respectively). Fracture history in CIC did not correlate with DXA measures.

Conclusions: BAD and A1AT patients did not have significant BMD/BMC abnormalities. CIC patients had significant bone deficits that persisted after adjustment for height and weight. In ALGS, low BMD and BMC reference Z-scores were explained by poor growth. Adjusted DXA measures in ALGS correlate with laboratory values and fx history; however, observed bone deficits were less than those generally associated with high fx risk. The divergent patterns of bone deficits in ALGS and CIC may be related to differences in underlying disease pathophysiology and possibly intrinsic abnormalities in bone composition caused by the genetic defect in Notch signaling in ALGS.

986 APPLICATION OF THE NHLBI DYSLIPIDEMIA GUIDELINES IN CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Objective: In children, non-alcoholic fatty liver disease (NAFLD) is associated with dyslipidemia, but it is not known how many children require lipid-specific intervention. Therefore, the study aim was to determine the percentage of children with NAFLD in whom intervention for low density lipoprotein-cholesterol (LDL-C) or triglycerides was indicated based upon National Heart, Lung, and Blood Institute (NHLBI) guidelines.

Methods: Children ages 9 - 18 years with NAFLD were enrolled in the NIDDK NASH Clinical Research Network and followed for one year. Branch tree analysis was applied to the dataset using the 2011 NHLBI Expert Panel Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. Outcomes included: 1) current use of anti-hyperlipidemic medications, 2) meeting criteria for lipid-lowering therapy in either a) the Target LDL-C Pathway, or b) the Target Triglycerides Pathway, and 3) achieving the age-specific lipid goal at 1 year of follow-up.

Results: Study cohort consisted of 623 children (443 males) with mean age 12.8 (SD 2.4) years and BMI 32.7 (SD 6.5) kg/m². Mean LDL-C was 100 (SD 30) mg/dL and mean triglyceride concentration was 151 (SD 87) mg/dL. At baseline, 2% (n=10) of children were taking antihyperlipidemic medications. An additional 15% (n 92) of participants, who had a mean LDL-C of 150 (SD 18) mg/dL, met criteria for intervention in the Target LDL-C Pathway. Of these 102 children, 94 had data at one year and based upon the Target LDL-C Pathway: 1) 20% (n=19) met criteria to begin statin therapy, 2) 28% (n=26) met criteria for enhanced dietary and lifestyle modifications, and 3) 52% (n=49) achieved the goal LDL-C level. Furthermore, at baseline, 51% (n=318) of children, with a mean triglyceride concentration of 198 (SD 66) mg/dL, met criteria for intervention in the Target Triglycerides Pathway. After one year, there were data for 315 of these children and based upon the Target Triglycerides Pathway: 1) 39% (n=122) met criteria to evaluate for antihyperlipidemic medication, 2) 38% (n=118) met criteria for enhanced dietary and lifestyle modifications, and 3) 24% (n=75) achieved the goal triglycerides level.

Conclusion: Over half of children with NAFLD met thresholds for clinical intervention for dyslipidemia. Referral to a registered dietician for nutritional counseling was the most common intervention indicated by the NHLBI guidelines. However, nearly one-quarter of children with NAFLD met criteria for the use of anti-hyperlipidemic medications. Thus, based upon the burden of clinically relevant dyslipidemia, screening of lipids in children with NAFLD is warranted and pediatric gastroenterologists caring for children with NAFLD should be trained in lipid management.

987 SPONTANEOUS SEROCONVERSION TO ANTI-HEPATITIS B e-ANTIBODY-POSITIVE STATUS IN CHILDREN WITH CHRONIC HEPATITIS B INFECTION

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Introduction: Spontaneous seroconversion of hepatitis B e-antigen (HBeAg) positive to hepatitis B e-antibody (anti-HBe) occurs during the immune active phase in children with vertically transmitted hepatitis B infection. The role of therapy in children with hepatitis B viral (HBV) infection is still unclear.

Methods: For documenting spontaneous seroconversion, a retrospective review of case records of children in KK Women's and Children's Hospital with HBV was carried out. The time interval between raised alanine transaminase (ALT), the peak ALT and clinical status were noted. Results: Ninety-one patients with hepatitis B were followed-up for an average of 14 years (± 6.8). Patients were routinely reviewed at a six-monthly interval unless they had raised ALT whereby they would be reviewed more frequently. Racial distribution of patients were 86/91 (95%)

Chinese, 2/91 (2%) Malay, 1/91 (1%) Indian, and 2/91 (2%) was Caucasian. There were 49/91 male (54%) and 42/91 female children (46%). Seroconversion from HBeAg positive to negative, with the development of anti-HBe occurred in 29/91 (32%) patients. Among the 29 who seroconverted, 18/29 (62%) were male and 11/29 (38%) were female. Mean age of conversion was 15 years (± 6.7). The largest numbers of children who seroconverted did so at the age of 12 years. Seven (7%) of those who seroconverted became HBsAg negative, including all the 6 children who seroconverted by the age of 3 years. Serum ALT levels of ≥ 57 U/L was predictive of HBeAg seroconversion. The median peak ALT for those who seroconverted was 111 U/L, interquartile range 39 - 266 U/L. Following peak ALT, seroconversion occurs in a mean of 2 years (± 1.3). One patient had elevated ALT of up to 1461 U/L which normalized spontaneously within a year without antiviral treatment. Following anti-HBe seroconversion, all the ALT levels returned to normal. HBV DNA load became undetectable in 10 patients, <97 IU/mL in 6, <479 IU/mL in 4 and one with a load of 1208 IU/mL. In 6 patients, viral load was not documented. Ultrasonography of the liver was normal in all the 29 patients. Unfortunately, none of the patients had liver biopsies, magnetic resonance imaging or fibroscans to assess liver fibrosis. Conclusion: Antiviral treatment will hasten HBeAg seroconversion and HBV DNA suppression. However, the effect of treatment in preventing serious sequelae, such as cirrhosis and hepatocellular carcinoma, in young adult life remains unproven. Our small study shows that in children, who are hepatitis B carriers, spontaneous seroconversion to anti-hepatitis B antibody does occur and under normal circumstances it is not mandatory to treat these children with antiviral therapy.

988 MORTALITY FROM NEONATAL INTRAHEPATIC CHOLESTASIS CAUSED BY CITRIN DEFICIENCY (NICCD): REPORT OF 8 CASES AND ANALYSES RISK FACTORS

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Background: Characteristics of already reported lethal or transplanted NICCD cases are poorly outlined and risk factors associated with poor outcome are unknown.

Objective: To report 8 cases of NICCD mortality, present clinical, laboratory and genetic features, and to explore associated risk factors.

Method: Between June 2003 and January 2012, SLC25A13 gene mutations were screened in patients who were referred to the Children's Hospital of Fudan University for investigation of conjugated hyperbilirubinemia with an age of onset before six months. Gender, birth weight, mutation type, referral age, biochemical data, blood coagulation profile, complete blood count (CBC), mass spectrometry data, genetic tests results and clinical management were compared between the deceased cases and survivors. STATA software was used for statistical analysis.

Results: 55 confirmed NICCD cases, including 47 cases with available data in the survival group, and 8 cases in the mortality group, were included in the final analysis. Age at referral in the mortality group was 6.52 ± 2.60 months and significantly higher when compared to the survival group (4.27 ± 3.24 months, $p=0.006$). Six out of eight children in the mortality group had infection, and the proportion with infection was significantly higher when compared to the survival group ($p=0.021$). 50.0% (4/8) patients in the mortality group did not receive lactose-free and/or MCT-enriched formula due to retrospective diagnosis, or failed to comply with the diet change, and this percentage was significantly higher than the survival group (12.8%, $p=0.029$). Platelet (PLT) count ($100.33 \pm 17.90 \times 10^9/L$) in the mortality group was significantly lower than that of the survival group ($407.93 \pm 169.74 \times 10^9/L$, $p=0.003$). Serum biochemistry parameters such as mean gamma-glutamyl transpeptidase (GGT), and total cholesterol levels were 87.43 ± 71.78 , and 2.12 ± 1.19 mmol/L and significantly lower in the mortality group when compared to the survival group (223.37 ± 125.91 IU/L and 3.47 ± 0.97 mmol/L) with p -values of 0.008 and 0.012, respectively.

Significantly more patients in the mortality group had TB levels greater than 273.6 $\mu\text{mol/L}$ (16 mg/dL) (2 out of 7) when compared to the survival group (0 out of 47, $p=0.015$). A significantly higher proportion (57%) of children in the mortality group had DB levels greater than 144.1 $\mu\text{mol/L}$ when compared to the survival group (11%, $p=0.011$). Mean level of citrulline (53.59 ± 18.11) was significantly lower in the mortality group compared to the survival group (139.32 ± 80.84 , $p=0.009$). On the other hand, mean level of tyrosine was significantly higher in the mortality group (195.58 ± 81.28) than that of the survival group (107.81 ± 44.37 , $p=0.010$).

Conclusion: Late referral, delayed treatment, low platelet count, low levels of GGT, total cholesterol, blood citrulline and high level of blood ammonia and tyrosine, were all associated with poor prognosis with NICCD.

989 INTERVENTIONS TREATMENT IN NON-ALCOHOLIC FATTY LIVER DISEASE IN OBESE ADOLESCENTS

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a clinicopathological entity with various evolutionary phases from hepatic steatosis to cirrhosis. Over the last years, NAFLD frequency has increased concomitantly with an increase in obesity. The objective of this work is to explore the effect of two interventions in 144 obese adolescents between 11 and 16 years (mean 13 years), of both sexes presenting NAFLD, who were followed by a pediatric gastroenterology consultation for four years.

Method: Two cohorts of patients (group 1 and 2) were studied. Group 1 ($n=74$) received treatment for lifestyle modification (diet 1500 - 1800 kcal/d and exercise) whereas group 2 ($n=70$) received a combined treatment, including the lifestyle modification treatment as well as vitamin therapy: vitamin E 400 mg/d, vitamin A 5000 IU/d, vitamin C 500 IU/d, omega 3 500 mg/d and metformin 500 mg 2 times/d. One year after starting treatment, we evaluated the effect of the aforementioned interventions in reducing BMI, improvement of hepatic steatosis by abdominal ultrasound and reduction of liver enzymes, such as alanino-aminotransferasa (ALAT), aspartate-aminotransferase (ASAT) and ganmaglutamyl transferase (GGT).

Results: 81% of patients in groupe 1 and 83% in group 2, who showed a decrease of 10% - 15% in BMI, improved their degree of hepatic steatosis. The liver enzymes decreased to normal levels in patients with reduced 10 - 15% BMI (74% of patients in group 1 and 77% of group 2). Patients who presented with a decrease less than 5% in BMI showed no change in hepatic steatosis by ultrasound or normalization of liver enzymes in either treatment group.

Conclusions: Vitamin treatment showed no evidence of overcoming the effect provided by the treatment with diet and exercise in improving NAFLD in obese adolescents.

990 PREVALENCE AND RISK FACTORS FOR TRANSIENT NEONATAL CHOLESTASIS IN A MOTHER AND CHILD TERTIARY UNIVERSITY HOSPITAL CENTER

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Background: Cholestasis of the newborn is defined as a decrease in bile flow in the first months of life. It has an incidence of approximately 1 in 2500 births and can be caused by a wide range of conditions. Transient neonatal cholestasis (TNC), usually included in the group of neonatal hepatitis, is characterized by an early-onset cholestasis, normalization of clinical and biochemical parameters at follow-up, and history of neonatal adverse event(s).

Aims: The primary objective of this study was to determine the prevalence of TNC in our mother and child tertiary university hospital center. The secondary objective was to determine the prevalence of risk factors for developing TNC, as compared to the group with cholestasis from other etiology.

Methods: This was a retrospective study that included all patients born between January 1, 2011 and December 31, 2013, who presented with cholestasis in the first 90 days of life. Cholestasis was defined as a direct bilirubin >17 $\mu\text{mol/L}$ (>1 mg/dL) if total bilirubin was <85 $\mu\text{mol/L}$ (<5 mg/dL) or >20% of the total bilirubin. All data were obtained from an electronic neonatal database and through medical chart review.

Results: One hundred and thirteen patients were diagnosed with neonatal cholestasis during the three-year study period. Of those, 75 (66%) had a diagnosis of transient neonatal cholestasis, 3 (3%) had an obstructive cause (biliary atresia, non-syndromic paucity of interlobular bile ducts), 9 (8%) had an infectious cause (TORCH, pyelonephritis), 3 (3%) had a metabolic cause (galactosemia, cystic fibrosis), 1 (1%) had an endocrine cause (panhypopituitarism), 1 (1%) had a tumoral cause (hepatic infiltration of juvenile myelomonocytic leukemia), 3 (3%) had inspissated bile syndrome from severe hemolysis and 18 (16%) died before the cholestasis was resolved, or before the etiologic evaluation was completed. The majority of patients with TNC had ≥ 2 risks factors (prematurity <32 weeks in 55% vs. 0% in the group with other etiology, parenteral nutrition >7 days in 81% vs. 20%, abdominal pathology or NEC in 62% vs. 15%, and sepsis in 49% vs. 15%, respectively). The mean maximal total and direct bilirubin was lower in the TNC group compared to the other etiology group at 130/72 $\mu\text{mol/L}$ vs. 227/104 $\mu\text{mol/L}$, respectively. The mean duration of cholestasis was 79.4 days (range 8 - 234 days) in the TNC group. In the other group, the duration was variable according to the etiology.

Conclusion: This study highlights that in a large mother and child hospital, the most likely etiology for cholestasis in infants under the age of 90 days, is transient neonatal cholestasis, despite advances in diagnostic techniques for metabolic and genetic disorders. This can be explained by the high-risk pregnancies being followed at this tertiary hospital, including prematurity, abdominal pathology requiring surgery and hemodynamically unstable newborns.

*991 CLINICAL, MOLECULAR AND GENETIC CHARACTERISTICS OF MITOCHONDRIAL HEPATOPATHY IN JAPAN

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Background: Mitochondrial hepatopathies are disorders, presenting as cholestasis, steatohepatitis and acute liver failure in early childhood, caused by mitochondrial dysfunction. Typically, multisystem involvement, such as neuromuscular symptoms, develops in their course. The aim of this study is to reveal clinical, molecular and genetic features of mitochondrial hepatopathies in Japan.

Methods and Results: Mitochondrial respiratory chain disorders (MRCs) were diagnosed by *in vitro* enzyme assay and BN-PAGE analysis. Subsequently, comprehensive genomic analyses were performed. We diagnosed 455 cases of MRCs since 2007. 58 cases (13%) were diagnosed with mitochondrial hepatopathy that showed liver abnormality as a prominent symptom. Among them, 19 cases were hepatocerebral, mitochondrial DNA depletion syndrome (MTDPS). Complex I deficiencies were the most frequent, the second was combined complex deficiency. The most common initial symptoms were failure to thrive, developmental delay and digestive symptoms, including poor oral intake and vomiting before liver dysfunction appeared. 14 cases (24%) were genetically diagnosed. 7 cases had mutations in MPV17, 3 had DGUOK mutations and 1 had POLG mutations in MTDPS cases. The other 3 cases had GFM1, MRPS23 as a novel causative gene and 6q24.3-q25.1 deletion, respectively. Six of our MPV17 cases had c.451dupC mutation. Liver transplantation was performed for 11 cases, but only 5 cases survived.

Discussion: MPV17 is the most frequent gene in mitochondrial hepatopathy and c.451dupC (MPV17) may be the hot spot in the Japanese population. Our study firstly demonstrates that MRPS23 encoding is a component of mitochondrial ribosome small subunit causes of mitochondrial hepatopathy.

992 IMMUNE RESPONSE TO SURFACE VARIANT PEPTIDES AFTER BOOSTER IN VACCINEES WITH WANING ANTIBODY

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Background: The most effective strategy to control HBV infection is through universal vaccination. Taiwan, the first country to launch this program, has provided powerful evidence in reduction of HBsAg carriage and HCC incidence. However, breakthrough infection was still noted in about 1% and vaccine-escape mutants were found in 30% of infected victims. Vaccine-induced antibody waned off naturally in half of vaccinees 5 - 20 years after neonatal immunization. Here we investigated the vaccine-induced immunity against HBsAg mutant *in vitro* by means of pre- and post-booster samples.

Methods: We recruited 142 individuals between 15 - 21 years old who had received complete HBV vaccination in infancy, but had negative anti-HBs, HBsAg and anti-HBc. Peripheral blood mononuclear cells and sera were collected. Recombinant HBsAg and synthetic peptides of wild type and mutants are used for *in vitro* assays, including proliferation assays, frequencies of cytokine-secreting T cell assay by ELISPOT before and after booster until serum antibody >100 mIU/mL or total 3 doses was given. Affinity assay of anti-HBs to mutant HBsAg will be checked by indirect ELISA method.

Results: Among the completely followed-up 140 subjects, 87 were 15 - 17 years old and 53 were 18 - 21 years old. After the first dose, 65 (46.4%) had anti-HBs >1000 mIU/mL, 42 (30%) 100 - 1000mIU/mL and 21 (15%) 10 - 100 mIU/mL, whereas 12 (8.6%) were anti-HBs negative. The anti-HBs titers (after 1st dose) were significantly different between those younger than 18 years old and older (GMT 357.8 vs. 117.6 mIU/mL, $p=0.012$, Mann-Whitney U test). Thirty-three subjects received a 2nd dose and 10 received a 3rd dose. Cumulatively, 139

(99.3%) had ant-HBs >10 mIU/mL after the 2nd dose and 140 (100%) after the 3rd dose. Cellular immunity assays showed presence of HBsAg-stimulated lymphocyte proliferation in 26/31(83.9%) before vaccine booster. There was no correlation between antibody response and the stimulation index. After booster, T-cell proliferation responses were enhanced both to the T- cell epitopes mutants (except 21W) and wild type. In sera with post-booster anti-HBs >1000 mIU/mL, the binding affinity only reduced in variant sP120A. ELISPOT analysis found lower INF- γ -secreting T cell frequency in epitope s16-33 mutants, but no difference of s213-226 mutation.

Conclusions: In 15 - 21 year-old adolescents who had lost protective antibodies, loss of immune memory was documented in around 10 - 20 % in terms of post-booster antibody response or pre-booster T-cell response. The booster response was better in younger vaccinees. T-cell response after booster could be mounted both to wild type and most variant T-cell epitopes. Although antibody binding affinity was reduced in sP120A mutants, and decreased INF- γ -secreting T-cell frequency toward epitope s16-33 mutations, the combined humoral and cellular immunity after booster of current vaccine should be able to protect against the surface antigen mutant.

993 PLASMA EXCHANGE IN PEDIATRIC FULMINANT HEPATIC FAILURE: ANALYSIS OF CLINICAL EFFICACY AND PROGNOSTIC PARAMETERS

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Background: Mortality of fulminant hepatic failure (FHF) is high in children. It is crucial to identify patients with poor prognosis for timely referral to liver transplantation. It has been suggested that plasma exchange may improve coagulopathy, remove various toxins from the systemic circulation and has been shown to be a bridging therapy to liver transplant or self-recovery. There are difficulties in determining whether the patient is able to recover with native liver or if liver transplant is needed.

Patients and Methods: This is a retrospective cohort study. The patients under 18 years of age who were admitted to National Taiwan University Hospital due to FHF from January 1, 2003 to December 31, 2015 were included. The plasma separator for children under 20 kg was unavailable in our institute before May 2008. Statistical analysis was performed to identify the efficacy of plasmapheresis and possible prognostic factors. Native liver recovery (NLR) was defined as survival with native liver.

Results: A total of 27 patients with FHF were found, 18 patients received plasma exchange, 4 patients received blood exchange, and 5 received neither. We analyzed 23 patients with plasma exchange or no plasma exchange/blood exchange. Age ranged from 3 days old to 15 years old, and the median age was 1.39 years old. The etiologies of FHF included infection (n=4), metabolic disease (n=2), immunological disease (n=2), drug toxicity (n=1) and idiopathic (n=14). 11 (48%) patients had NLR, 9 (39.1%) patients died without liver transplant, 1 (4.3%) subject died after liver transplant, and the other 2 (8.6%) subjects survived after liver transplant. In NLR group, there was less idiopathic cause (36.4% vs. 83.3%, $p=0.0361$) and the median time of plasma exchange was less (3 vs. 9, $p=0.0039$). There was no significant difference in peak bilirubin level and peak INR, but there was a lower peak in ammonia (148 vs. 302 $\mu\text{mol/L}$, $p=0.0006$) and higher initial AFP level (10.29 vs. 3.604 ng/mL in \log_{10} ratio, $p=0.0086$). Receiver operating characteristic (ROC) curve was calculated for total plasma exchange time, peak ammonia level and initial AFP level for outcome. The area under the curve was 0.818 - 0.924. For the best prediction of NLR, the cut-offs are ≤ 6 times, $<190 \mu\text{mol/L}$, >9.68 for plasma exchange, peak ammonia level and log initial AFP level, respectively. Survival analysis was also done using the cut-point calculated above, and significant difference was seen in all parameters (log rank test p -value: 0.002, <0.001 , 0.023).

Conclusion: Pediatric fulminant hepatic failure is a rare disease with high overall mortality. Idiopathic etiology, high peak ammonia level and low initial AFP level are associated with fewer NLR. Plasma exchange >6 times is also associated with fewer NLR, and further plasma exchange probably offers little benefit in patient survival if liver transplant is not promptly arranged.

994 NEWBORN SCREENING OF CHOLESTATIC JAUNDICE IN INFANCY: PRELIMINARY RESULTS

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Background: Cholestatic jaundice in infancy affects around 1 in every 2500 infants and has a wide number of causes. For some etiologies, such as biliary atresia (BA), early recognition to establish timely treatment is fundamental to ensure good prognosis. BA is responsible for the majority of cases and the results of its surgical treatment are superior when the procedure takes place in the first 60 days of life.

Objectives: The main objective of this study was to identify biomarkers of cholestatic jaundice in newborn screening. Clinical characteristics of infants with cholestatic jaundice included in the present study were also analyzed.

Methods: After informed consent was obtained, blood samples of 22 newborns stored since birth on filter paper were obtained. 8 of these who later developed neonatal cholestasis (Group I - cases), and 14 who did not (Group II - controls), were included in the study. The second group consisted of healthy children who required hospital admission for common childhood diseases, such as bronchiolitis, gastroenterocolitis, etc. These samples were originally from the national Neonatal Screening Program, drawn within neonatal hospitalization, just after 48 hours of life. The material was extracted and analyzed by high resolution mass spectrometry. The test was performed in triplicate, using mass range of 400 - 1200 m/z . Discriminant analysis of least squares guided the choice of biomarkers and online databases were consulted to select potential biomarkers with a smaller mass error of 2 ppm.

Results: For Group I cases, age at admission for evaluation of jaundice in a tertiary center varied from 11 to 90 days of life and age range for development of jaundice ranged from birth to 60 days of life, with a mean of 20 days (median - 15 days). The final etiology of jaundice in this group included: biliary atresia (4), cytomegalovirus infection (1), galactosemia (1), idiopathic (1) and multifactorial (1). Statistical analysis showed complete discrimination between the groups, with 100% sensitivity and 100% specificity to detect infants who developed cholestatic jaundice. The biomarkers found were bile acids and phospholipids. These compounds are known to be elevated in the plasma of infants with cholestatic jaundice, as a result of the reduction or blockage of bile flow.

Conclusions: Biomarkers of cholestatic jaundice – bile acids and phospholipids – are identifiable through screening tests performed in blood samples on filter paper, which can be obtained as early as in the first days of life. The biomarkers found to be of relevance included bile acids and phospholipids. This finding represents an important advance in early recognition of potential fatal diseases.

995 LIVING RELATED LIVER TRANSPLANTATION AS A CURE FOR METABOLIC DISORDERS WITH OR WITHOUT LIVER INJURY: ETIOLOGY, TIMING, SELECTION CRITERIA, SPECIFIC ISSUES AND OUTCOME

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Inherited metabolic disorders (IMD) that can be cured by living related liver transplantation (LRLT) include those with liver injury such as tyrosinemia (Tyr), Wilson's disease (WD), PFIC or those with no liver injury such as primary hyperoxaluria (PH), organic acidemia (OA) and urea cycle defects (UCD).

Aims: To analyze the etiology, selection criteria specific issues and outcome in children undergoing LRLT for IMD.

Materials and Methods: A retrospective analysis was done on pediatric patients undergoing LRLT from September 2004 to April 2016 for metabolic disorders. Etiology, timing of transplant, selection criteria, specific issues and outcome were analyzed. Except for Maple Syrup Urine Disease (MSUD), parents were accepted as donors.

Results: 197 children underwent LRLT, 63 (32%) had IMD. Mean age was 73 months (4 - 212), mean weight 23 kg (5 - 66) and 47 were males. 84% (n=53) had liver disease; WD 28 (44%, mean age 112 months), Tyr 11 (17%, mean age 17 months) and PFIC 7 (12%). Allagille syndrome 4, Prt. C & S deficiency leading to Budd Chiari Syndrome 2, and glycogen storage disease 1. IMD with no liver injury included citrulinemia 4, PH 2, MSUD 2, factor 7 deficiency 1, and Crigler-Najjar syndrome 1. 46% (n=29) of IMD had presented with ALF of which WD were 24 and Tyr 5. Non-affordability of NTBC and development of HCC on NTBC were other criteria for LT in Tyr. Both PH patients underwent combined liver kidney transplant. There were 3(4.7%) biliary strictures which were managed with PTBD/ERCP. No vascular complications were seen. The mean hospital stay was 23 days. 1-year survival was 95% with overall survival of 92% on a mean FU of 4.2 yrs. 2 WD patients died due to severe hemolysis and renal failure in the early post-transplant period while 1 died of PTLN after 2 years. 2 patients died due to sepsis. Donors were parents in 38 (mothers 28) and grandparents/close relatives in 15 (40%). Swap transplantation was done in 1 MSUD case. Both MSUD explant livers were used as domino grafts.

Conclusion: Identifying the etiology, multidisciplinary approach, right timing for LRLT before the onset of debilitating secondary complications, along with addressing specific disease-related issues and complications is important in the successful outcome of LT for IMD.

***996 PROMININ-1-EXPRESSING PROGENITORS TRANSDIFFERENTIATE INTO A SUBSET OF MYOFIBROBLASTS AND DUCTULAR REACTIVE CELLS WITHIN BILIARY FIBROSIS OF BILIARY ATRESIA**

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Biliary atresia (BA) is a congenital fibro-inflammatory obliterative disease of infants of the extrahepatic biliary tree. BA is the most common cause of end-stage liver failure in children and the leading indication for pediatric liver transplantation. The pathogenesis of the aggressive fibrosis associated with BA remains poorly understood. We previously demonstrated that the intrahepatic biliary fibrosis of BA is associated with the expansion of cells expressing the stem cell marker Prominin-1 (PROM1, CD133), both in the murine model of BA induced by rehesus rotavirus (RRV) as well as in human BA. These PROM1-expressing cells are phenotypically epithelial-mesenchymal progenitors with evidence of collagen-1 α expression in response to transforming growth factor- β (TGF β) stimulation. Thus, we hypothesized that Prom1-expressing progenitors transdifferentiate into biliary cells within proliferating ductular reactions as well as myofibroblasts. To test this hypothesis, we bred Prom1creERT2GFPlox-stop-lox, in order to lineage trace Prom1-expressing cells in experimental models of cholestasis/biliary fibrosis including RRV-induced BA, 3,5-diethoxycarbonyl-1, 4-dihydrocollidine (DDC) diet, and bile duct ligation (BDL) with pretreatment tamoxifen induction. In all three models (RRV, DDC, BDL), sham controls with tamoxifen induction demonstrated rare singular GFPpositive(pos) Cytokeratin-19 (CK19)pos cells within, or adjacent to, bile ducts. In comparison, there was an increased number of GFPposCK19pos cells comprising ductular reactions and GFPposVimentinpos cells and GFPposCollagen-1 α 1pos within surrounding periportal fibrosis two weeks after RRV inoculation and after 6 weeks on DDC diet. In contrast, GFP expression increased but was mostly restricted to CK19pos ductular reactions between 5 and 10 days following BDL. At later stages of DDC-induced cholestasis (6 weeks), GFP co-positivity with hepatocyte markers, albumin and hepatocyte nuclear factor-4 α was noted. Additionally, a significant fraction of periportal GFPpos cells co-express phospho-SMAD3, indicating evidence of TGF β signaling. These findings support potential trans-differentiation of Prom1-expressing progenitor cells to biliary cells within ductular reactions, some activated myofibroblasts, and hepatocytes in response to bile duct injury.

997 PEDIATRIC HEPATITIS B IN EAST LONDON

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Background and Aims: Childhood infection with hepatitis B is often asymptomatic; however, long-term complications of cirrhosis and hepatocellular carcinoma are of significant concern.¹ Our aims were to evaluate an East London population with confirmed hepatitis B who were diagnosed during childhood. We aimed to use HBsAg levels to determine whether the standard criterion of "inactive carrier" is applicable to pediatrics.

Method: An observational study of pediatric HBV. Data were obtained from medical notes, electronic healthcare records and CRS. HBsAg titers and HBV DNA levels were measured using Abbott architect and Roche Taqman, respectively.

Results: 48 patients were identified, 29 females. 1 patient moved out of area and 2 spontaneously cleared HBsAg. Data expressed as median (range). Age (years) at diagnosis 10 (1 - 18); follow-up 6.9 (0.3 - 14.0) years. 39/46 patients had HBsAg >1000 IU/mL, 11930.85 IU/mL (1466.41 - 174,935.30 IU/mL). 52.1% HBsAg >10,000 IU/mL. 17/21 inactive carriers (normal ALT, viral load <2000 IU/mL), 2 with HBsAg levels >1000 IU/mL identified; 9176.35 IU/mL (1466.41 to 34,929.55). 11/48 patients had an ALT >35, 25/48 if Prati criteria were applied.³ 6 patients (12.5%) had vaccine escape. All 6 were born in the UK. 9/48 patients could not be genotyped due to HBV DNA <100 IU/mL. Genotype D was most common: 43.1%, C 19.6%, A 8.7%, B 8.7%, E 2.2%. Genotype D was associated with a higher HBsAg and viral load.

Conclusion: The ethnic diversity is typical of an inner city population. 0.01 - 0.03% of chronic HBV carriers will develop HCC before adulthood.⁴ 25% will have disease progression with increased morbidity in adult life,⁵ a significant cost burden for the NHS. In adults a high HBsAg (>1000 IU/mL) indicates increased risk of disease progression to cirrhosis and HCC. Based on these results, we question whether the

same parameters should apply to pediatric HBV. Further research including detailed immune profiling is required to identify better markers to risk stratify pediatric disease progression in order to target effective earlier interventional treatments.

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998 ACUTE LIVER FAILURE IN MALAYSIAN CHILDREN

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Background: Little is known about the cause of acute liver failure among Malaysian children. We described the etiology and the outcome of acute liver failure among the children aged 0 - 18 years in Malaysia based on a single-centre experience.

Methods: Retrospective and prospective surveillance study on children with acute liver failure who were referred to the University of Malaya Medical Centre, a pediatric liver unit in Kuala Lumpur between 1996 and 2015. The demographics, clinical, laboratory and outcome data were collected and analyzed.

Results: There were a total of 60 patients (27 females and 33 males), with median age of 6 years old. They were from three main ethnic groups (37 Malays, 16 Chinese and 7 Indian). The identified causes of acute liver failure include dengue shock syndrome (20%), sepsis (9%), acetaminophen poisoning (9%), Wilson's disease (9%) and inborn error of metabolism (7%). Dengue fever was the most common identifiable etiology for acute liver failure, but the majority of the patients had indeterminate etiology (29%). Fifty-five percent of the patients had spontaneous recovery and 4% (n=2) survived after urgent liver transplantation. Up to 41% of the patients died without liver transplantation.

Conclusions: The etiologies of acute liver failure reported in our centre differs from the local adult population and children of other countries. The outcome of acute liver failure in Malaysian children remains unfavourable despite improved supportive care, mainly limited by the inavailability of liver transplant services.

999 PERCUTANEOUS CHOLANGIOGRAPHY AS AN ADJUNCT TO LIVER BIOPSY IN THE EVALUATION OF BILIARY ATRESIA

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Introduction: Infants with biliary atresia (BA) need to be identified quickly and receive early treatment in order to achieve the best outcomes. One common test to evaluate infants for BA is percutaneous liver biopsy. Liver biopsies typically show classic signs of extrahepatic obstruction, including bile plugging, duct proliferation and portal fibrosis. However, because these signs are not specific to BA, liver biopsies have a high false-positive rate and may lead to unnecessary, more invasive testing to exclude BA. In this study, we examine whether performing percutaneous cholangiography (PCC) at the time of liver biopsy can decrease the high false-positive rate of liver biopsies for BA.

Methods: Subjects were included if they underwent a combined PCC-liver biopsy procedure for evaluation of BA at our institution. Both PCC and liver biopsy were performed by interventional radiologists under ultrasound guidance. PCC images and liver biopsy samples were reviewed retrospectively. PCCs were abnormal if contrast did not fill the entire biliary system and pass into the liver and duodenum. Liver biopsies were considered abnormal if they showed any signs of obstruction, including bile plugging on hematoxylin and eosin staining, duct proliferation on cytokeratin 19 immunohistochemistry, or portal fibrosis on trichrome staining. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using standard techniques.

Results: There were 32 subjects, who had combined PCC-liver biopsy for evaluation of BA, with the average age at procedure of 60 ± 30 days. Liver biopsy alone resulted in seven false-positive cases (infants without BA whose histology showed obstructive signs). Liver biopsy alone had a sensitivity of 100%, specificity of 73%, PPV of 46% and NPV of 100% for BA. In contrast, a two-stage strategy of PCC first (test 1) followed by interpretation of liver biopsy (test 2) had only one false positive case. The two-stage strategy had a net sensitivity of 100%, net specificity of 96%, net PPV of 86%, and net NPV of 100% for BA. There were no serious adverse events associated with PCC or liver biopsy.

Conclusion: PCCs may be an effective way to improve the specificity of percutaneous liver biopsies for detecting infants with BA. PCCs have the added advantage of being performed at the same time as the liver biopsy, providing instantaneous results, and having few, if any, associated adverse events. Future investigations are needed to determine how well the two-stage strategy performs in larger, prospective studies. In addition, future investigations are needed to assess the technical challenges faced by interventional radiologists and pediatric gastroenterologists learning how to perform PCCs.

1000 UNMASKING ALAGILLE SYNDROME FROM BILIARY ATRESIA: A DIAGNOSTIC CHALLENGE

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Introduction: Alagille syndrome is a multisystem disease, primarily of autosomal dominant inheritance, but may also result from *de novo* mutations. Diagnosis requires meeting 3 of 5 criteria, including chronic cholestasis, congenital heart disease, abnormal facies, vertebral and ocular anomalies. However, diagnosis can be challenging when initial clinical presentation can mimic more common disorders such as biliary atresia, which can also manifest with extrahepatic findings involving the heart, spleen and intestines. Timing of intervention for biliary atresia also contributes to the challenges of diagnosis.

Case Description: Here we present an 8-week old full-term male with persistent jaundice and acholic stools. Initial labs were significant for direct hyperbilirubinemia, elevated liver enzymes, alkaline phosphatase and gamma-glutamyl transpeptidase (GGT). Liver and gallbladder ultrasound showed increased hepatic echogenicity and non-visualized gallbladder. Cholescintigraphy (HIDA) scan demonstrated lack of contrast excretion into the biliary system. Due to the patient's age, and the possible need for prompt intervention, he underwent intraoperative cholangiogram and liver biopsy for further evaluation. This revealed a contrast-filling defect into the proximal common hepatic duct, but preserved filling into the duodenum, findings consistent with biliary atresia and received a Kasai procedure. Final liver biopsy pathology reported histologic changes that were not suggestive of extrahepatic biliary obstruction and possible paucity of interlobular bile ducts. Post-

operatively, his course was complicated by acute ascending cholangitis with worsening direct hyperbilirubinemia and persistently elevated GGT, which warranted further investigation. This revealed multiple findings, including butterfly vertebrae, left ocular posterior embryotoxon, bilateral peripheral pulmonic stenosis, questionable renal cyst, and JAG1 mutation confirming the diagnosis of Alagille syndrome. Discussion: This case illustrates that Alagille syndrome can be a challenge to distinguish from other forms of cholestasis, such as biliary atresia, due to overlapping clinical and laboratory features. Due to the time-sensitive nature of appropriate diagnosis of biliary atresia, the decision was made to proceed with surgical intervention. Although appropriate initial evaluations were performed in this patient, this case highlights the importance of considering extrahepatic manifestations and to further pursue non-invasive screenings to evaluate for Alagille syndrome. Additionally, there are studies that show those with Alagille syndrome that undergo a Kasai procedure have a much higher mortality compared to those who do not. This demonstrates that further detailed evaluation is warranted for appropriate diagnosis given that the approach to management between the two diseases can be significantly different.

1001 USING TRANSIENT ELASTOGRAPHY FOR THE EVALUATION OF NON-ALCOHOLIC FATTY LIVER DISEASE IN OBESE CHILDREN AND YOUNG ADULTS

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Background and Aims: The application of transient elastography (Fibroscan) to evaluate liver steatosis and fibrosis is well studied in adults, but not in the pediatric group. Childhood obesity is a growing problem worldwide, which is frequently associated with pediatric fatty liver and further causes pediatric chronic hepatitis. By using Fibroscan, we sought characteristics of liver profiles in Taiwan obese and non-obese children and young adults.

Methods: Transient elastography (Fibroscan) was performed in subjects from 6 to 20 years old who visited General Veterans Hospital, Taipei. Liver steatosis, measured by controlled attenuation parameter (CAP), and liver fibrosis, evaluated as the liver stiffness measurement (LSM), were compared among overweight and obese subjects (BMI >85%) and non-obese health controls.

Results: Fibroscan were performed successfully in 32 subjects (12 of health controls and 20 of overweight and obese). CAP values were higher in the overweight and obese group compared with the health controls (245.1±61.6 dB/m vs. 186.3±43.2 dB/m, $p < 0.003$, < 0.05). LSM values were higher in the overweight and obese group compared with the health controls (5.5±2.4 vs. 4.4±0.8, $p = 0.08$). The resulting upper limit of normal CAP value (median plus 2 times standard deviation) was 229 and 8 subjects (40%) in the overweight and obese group had CAP values higher than the resulting upper limits, suggesting that these subjects have non-alcoholic fatty liver disease (NAFLD). 4 of these 8 subjects (50%) also have LSM values >8.0, suggesting that these 50% of NAFLD subjects have liver fibrosis.

Conclusion: Among those children and young adults with BMI > 85%, almost half of them have a liver steatosis problem. Also, in those having a liver steatosis condition, almost half of them was highly suspect to have liver fibrosis. The pediatric obesity problem is growing and cannot be ignored. Using transient elastography for liver steatosis and liver stiffness surveys in pediatric groups is practicable.

1002 EPIDEMIOLOGY OF BILIARY ATRESIA IN SAUDI ARABIA: TERTIARY CARE CENTER EXPERIENCE

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Background: Data from the West indicate that biliary atresia (BA) is the leading cause of end-stage liver disease in children and the most common indication for liver transplantation (LT) in the pediatric population. There are no local data on the incidence and epidemiology of BA in Saudi Arabia. The main objective of our study was to study the clinical, laboratory, treatment and outcome of BA in the Saudi population.

Methods: We retrospectively reviewed our database for cases of neonatal cholestasis that presented to our center in Riyadh city, the capital of Saudi Arabia, during the period from 2008 until 2015 and identified BA cases. Data on clinical, biochemical, imaging and histopathological characteristics were collected by chart review. Two main primary outcomes were studied: 1) successful Kasai operation, defined as resolution of jaundice and survival with native liver, and 2) failed Kasai operation and need for liver transplant (LT) or death before LT.

Results: Over the study period, we evaluated 450 cases of neonatal cholestasis. Twenty-one cases (11 males) were diagnosed with BA (4.7%). BA cases were first seen by a pediatric gastroenterologist at a median age of 8 weeks (range: 1 - 18 weeks). Kasai operation was performed in 12 cases at a median age of 10 weeks (range: 2 - 12 weeks). Successful Kasai surgery was achieved in 4 cases (33%). Of the remaining 8 cases, 5 had LT and 3 died before LT. Nine of the 21 BA cases were denied for Kasai operation and had LT at median 9 months of age.

Conclusion: In comparison to data from Western countries, BA is an uncommon cause of neonatal cholestasis in Saudi Arabia. Although our study sample size is small, it gives a snapshot of the epidemiology of BA in Saudi Arabia, which is characterized by late referral to pediatric gastroenterologists and poor outcome without LT during late infancy.

1003 SCLEROSING CHOLANGITIS WITH ASSOCIATED INFLAMMATORY BOWEL DISEASE IN SOUTH-EAST ASIAN CHILDREN

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Introduction: Sclerosing cholangitis (SC) is a chronic cholestatic disorder that can lead to progressive inflammation, fibro-obliterative bile duct damage and end-stage liver disease (ESLD). Its association with inflammatory bowel disease (IBD) is well recognized. Data regarding SC-IBD comorbidity in childhood is scarce and mainly from the West. We describe our experience in children with SC-IBD from three teaching hospitals in south-east Asia.

Method: Retrospective case-note review of children with SC-IBD from two centres in Singapore and one from Malaysia.

Results: 24 children (14 boys) were identified, median (inter-quartile range-IQ) age at SC diagnosis was 76 (52 - 108) months. Associated IBD was ulcerative colitis in 21, Crohn's disease in 1 and IBD-undifferentiated in 2. 7 children had acute or chronic hepatitis at presentation, 6 of whom were jaundiced. SC was incidentally diagnosed in 17 during follow-up for IBD. 15 (62%) had hepatomegaly, in whom 5 also had splenomegaly. Only 1 had pruritus. All had deranged liver function tests of varying severity with elevated GGT. Serum IgG levels were raised in 16 (67%). ANA titers >1:100 were seen in 16 (67%). 7 (29%) were positive for anti-smooth muscle antibodies. 19 underwent MRCP, 10 (53%) of whom showed cholangiographic abnormalities. Of the remaining 5, one had an ERCP while the rest had biliary tract abnormalities seen on ultrasonography. 23 (96%) had liver biopsy with reports available for 22. Histology revealed periductal fibrosis in 11 (50%), periductal

inflammation in 8 (36%), portal edema in 6 (27%), duct proliferation in 6 (27%), fibro-obliterative cholangitis and cholestasis in 1 each. 9 of 22 (41%) had evidence of interface hepatitis with histology suggestive of associated autoimmune hepatitis (AIH). All received ursodeoxycholic acid and varying degrees of immunosuppression for associated IBD and/or AIH. Median follow-up was 44 months (IQ range: 20 - 84). 3 (12.5%) achieved complete remission, 18 (75%) showed partial response while 3 (12.5%) had progressively worsening SC. 6 (25%) had portal hypertension, of whom 4 (17%) had evidence of synthetic liver dysfunction as well. One child with SC-AIH overlap and associated UC underwent LT with recurrence of AIH but no evidence of SC in the graft after 2 years. All survived.

Conclusions: Our experience describes the variable severity of SC in children with IBD, with the majority being incidentally diagnosed during follow-up for IBD. Most of the children in our study were relatively young, in contrast to the experience in Western populations. In most patients, only partial disease control was achieved, despite optimum treatment. This could potentially put them at risk of developing ESLD over time. This highlights the need for not only regular monitoring of liver function tests on a periodic basis in IBD patients, but also the importance of having a low threshold for utilizing imaging techniques to diagnose SC early and optimize clinical outcomes.

1004 METAGENOMICS OF THE LIVER: A PILOT STUDY

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Background: Metagenomics, the genomic analysis of a population of microorganisms, can be used with patient samples to characterize known and novel tissue-resident pathogens as well as the host response to those pathogens. Metagenomics studies have resulted in discovery of novel pathogens and identification of previously missed infections. We performed a pilot and feasibility study to detect known pathogens in fresh, frozen liver biopsy tissue by next-generation sequencing-based metagenomics. We sought to: 1) recover pathogen sequences from frozen infected liver where infection was known a priori, and 2) measure the ability of metagenomics to identify tissue-resident T-cell receptor sequences.

Methods: We used frozen liver samples obtained two controls, two HBV, two HCV, one pyogenic-cholangitis and two simple cysts. Total RNA and ribodepleted RNA were reverse transcribed, cDNA libraries were prepared with the Stranded RNA-Seq Library Prep Kit (KAPA Biosciences), and analyzed on a NextSeq500. Metagenomics data analysis was performed with Taxonomer (Flygare *et al.*, *Genome Biology*). To recover sequencing reads for the TCR complementary determining region-3 (CDR3), we used MiTCR (Bolotin *et al.*, *Nat Methods*).

Results: Known viral (HBV, HCV) and bacterial (pyogenic cholangitis) pathogen sequences were detected by RNA-seq and Taxonomer. As expected, ribodepletion generally improved pathogen detection. The number of CDR3 sequence reads recovered from infected livers was ~2-fold greater than from uninfected livers.

Conclusions: Metagenomics analysis of RNA from frozen liver tissue can be used for direct pathogen detection and T-cell receptor profiling providing a novel approach for studying the etiology and mechanism of heterogenous hepatic diseases.

1005 ANTIBODY-MEDIATED HEMOLYSIS AND ELEVATED NEONATAL CONJUGATED BILIRUBIN LEVELS

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Introduction: Plasma conjugated bilirubin (CB) is a promising biomarker in identifying patients with biliary atresia in the early neonatal period. However, the sensitivity of CB for biliary atresia is not well established and causes for elevated CB other than biliary atresia have not been well documented. While antibody-mediated hemolysis (AMH) is a common cause for elevated total bilirubin (TB), its effect on CB is not well recognized. In this study, we explore the association between AMH and CB in term or near-term neonates investigated for icterus.

Method: All outpatient term or near-term neonates in the Auckland region aged between 0 - 4 days investigated for clinically evident icterus were identified based on laboratory requests for TB. CB was performed on all these neonates as part of recently introduced reflex testing by the community laboratory and AMH is screened for by the direct antiglobulin test (DAT). In total, 516 complete sets of laboratory results were identified between April 2014 and September 2015.

Results: Conjugated bilirubin is positively associated with total bilirubin irrespective of AMH status ($r = 0.64$). Total bilirubin in neonates with AMH ($231.5 \pm 49.2 \mu\text{mol/L}$; mean \pm SD) was not significantly different from control neonates without hemolysis (231.4 ± 65.8 , $p = 0.99$). In contrast, conjugated bilirubin in neonates with AMH ($11.4 \pm 3.1 \mu\text{mol/L}$; mean \pm SD) was significantly higher than controls (8.4 ± 3.9 , $p = 0.003$). Using $20 \mu\text{mol/L}$ as the clinical decision threshold for CB, 16% ($n = 12$) of neonates with AMH had an elevated CB compared to 2.5% ($n = 11$) in the control group (Table 1). This translated to a relative risk of 6.7 (95% CI, 3.1 - 14.5; $p < 0.0001$) for elevated CB in AMH.

Conclusion: Antibody-mediated hemolysis is a common cause for elevated conjugated bilirubin in the early neonatal period and inclusion of AMH status may improve the sensitivity of conjugated bilirubin in identifying patients with biliary atresia.

Conjugated Bilirubin umol/L		<5	5-9	10-14	15-19	20+
DAT-ve	Number	32	298	76	25	11
	Mean total bili	180.5	223.5	253.5	256	228
	Mean conj bili	4	7	11	16	24
	Mean conj/total bili	0.020	0.031	0.043	0.060	0.112
DAT+ve	Number	6	36	15	5	12
	Mean total bili	143	193.5	257	269	253.5
	Mean conj bili	3.5	8	10	16	25.5
	Mean conj/total bili	0.022	0.035	0.039	0.067	0.105

Table 1: Conjugated/total bilirubin levels stratified by DAT status and level of conjugated bilirubin

1006 *A 20-YEAR PERSPECTIVE OF PEDIATRIC GALLSTONE DISEASE IN A CHILDREN'S HOSPITAL IN JAPAN*

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Objectives: Gallstone is a rare condition in children compared to adults. A specific, underlying condition is likely to be found in pediatric gallstone patients. Though obesity has increasingly accounted for many cases of pediatric gallstone in the world, in Japan, few case reports can be found. Extensive data about the epidemiology and the etiology of pediatric gallstone are still unclear. We therefore examined the underlying condition, clinical features, laboratory data, complications, treatment and prognosis of pediatric gallstone patients in Japan.

Methods: Data were obtained through a review of the medical records of children under 18 years of age, whose cholelithiasis was diagnosed by ultrasonography from December 1996 to December 2015 at a tertiary children's hospital.

Results: Fifty patients (mean age: 6.4 years, range: 0 - 17 years) had gallstones. Twenty-four were males. Out of 50 patients, 9 cases (18%) also had choledocholithiasis. Twelve patients (24%) were infants. Common underlying diseases or conditions were hemolytic disorder (14%), followed by intestinal resection (10%), post-cardiac surgery (10%), receiving TPN (6%), cholestasis (6%) and congenital biliary dilatation and/or anomalous arrangement of the pancreaticobiliary ducts (6%). Thirteen patients (26%) had no apparent underlying disease. In these 13 patients, only one male patient's Rohrer index was over 160 (BMI was normal), but he did not have hyperlipidemia or any other obesity-related disorders. The initial symptoms of all patients were abdominal pain (44%), visible jaundice (20%) and vomiting (4%). 21 patients (42%) were asymptomatic. Acute cholecystitis was found in 4 patients (8%). Cholecystectomy was performed in 20 individuals (40%), whereas endoscopic sphincterotomy was performed in 5 patients (10%). Percutaneous transhepatic gallbladder drainage was performed in 3 individuals (6%) and ursodeoxycholic acid was administered in 31 patients (62%). Five cases (10%) were resolved without operation (mean observation period: 7.3 months, range: 0.5 - 32 months), but 24 (49%) had remaining gallstones and were followed-up conservatively (mean observation period: 43 months, range: 3 - 145 months).

Conclusion: The underlying conditions of gallstone in Japanese children were almost the same as the disease previously reported. Our patients had weaker linkage to obesity, because obese children in Japan were less common than in Western countries. Surgical and endoscopic therapy were both effective, but twenty-nine pediatric gallstone patients (58%) were observed conservatively. Unlike adults, surgical indication should be considered on the basis of the underlying cause in children.

1007 *HEMOLYTIC ANEMIA WITH ACUTE LIVER FAILURE IN WILSON'S DISEASE IN CHILDREN*

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Background: Wilson's disease is an autosomal, recessive, inherited disorder of copper metabolism with different clinical forms in children: liver, neurological, and rarely, non-immune hemolytic anemia with acute liver failure, but with more severe prognosis.

Objective: The aim of our study was to analyze the clinical, laboratory and evolution in children with hemolytic anemia and acute liver failure as presented in the form of Wilson's disease.

Material and Methods: We retrospectively analyzed data from 47 children with Wilson's disease diagnosed or followed-up in our unit during the last 10 years. The diagnosis was done using clinical features, copper metabolism tests and genetic testing, following the up-to-date Wilson's disease guidelines. Data were analyzed comparing the patients with acute liver failure and non-immune hemolytic anemia to the patients with other clinical manifestations (acute or chronic liver disease, neurologic disease) for the hepatic parameters, copper metabolism, genetic mutations, treatment and disease evolution.

Results: Wilson's disease was diagnosed in 47 children (26 males, with age between 5 years and 18 years 1 month). Hemolytic anemia with acute liver failure was present at onset in 7 patients (16.27%) and four years after the diagnosis in one non-compliant patient. The other clinical manifestations at presentation were liver disease in 37 patients (78.72%, three of them with autoimmune features and one as acute hepatitis), neurologic in two patients (4.25%) and by screening as a relative of an index case in one patient (2.13%). Molecular analysis of the ATP7B gene revealed the presence of a Wilson's disease characteristic mutation in 43 patients in homozygous or compound heterozygous status (91.49%). All patients with hemolytic anemia and acute liver failure were girls, with a mean age of 14.95 years (compared with 11.86 years for the rest of the patients), with lower serum ceruloplasmin level (7.98 mg/dL compared with 11.15 mg/dL), higher 24h-urinary copper excretion (2136.4 mcg/24 h compared to 419.46 mcg/24 h). Two of those 8 patients with hemolytic anemia and acute liver failure had fatal evolution (compared with one in the rest of the patients), two received emergency liver transplantation and four received medical treatment with good evolution.

Conclusions: The majority of children with Wilson's disease in our population presented with hepatic manifestations. Hemolytic anemia with acute liver failure was a relatively rare form of onset in our Wilson's disease patients, frequent in girls, during adolescence, with lower ceruloplasmin level and higher urinary copper excretion and with a severe prognosis in severe cases if emergency liver transplantation was not possible.

1008 SERUM TOTAL BILIRUBIN LEVELS AT 3 MONTHS PREDICTS LONG-TERM SURVIVAL WITH NATIVE LIVER AFTER KASAI PORTO-ENTEROSTOMY FOR BILIARY ATRESIA

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Background: Biliary atresia (BA), a progressive sclerosing inflammation of the bile ducts, is managed by early Kasai porto-enterostomy (PE) and subsequent liver transplantation (LT) when indicated. The long-term course following PE is characterized by an increasing discrepancy between those surviving with native livers and those who deteriorate, thereby requiring LT. Recently, there have been data that suggest early jaundice clearance predicts short-term outcomes at 2 years.

Aim: We aimed to evaluate the outcomes of children with BA following PE and to determine if there are predictors for the need for early LT as well as long-term survival with native liver.

Methods: Retrospective medical record review of all BA patients who underwent PE at our institution from 1989 until 2015. We investigated patient demographics, pre- and post-operative laboratory data, time taken to become jaundice-free, incidence of cholangitis and outcomes. Outcomes were defined as one of the 2 categories: Group 1: alive at latest follow-up with native liver and Group 2: listed for LT or received LT. Results: The cohort consists of 64 patients (40 females) with 45 in group 1 and 19 in group 2. None underwent primary LT. The median (range) follow-up is 130 (4 - 300) months. There were 5 deaths; all from group 2 (2 while awaiting LT and 3 after LT). The overall survival of BA patients with/without the need for LT (93.7%) is significantly better than the survival without the option of LT after PE (71.8%), $p < 0.05$. The median (range) survival with native liver following PE for groups 1 and 2 was 146.5 (4 - 300) and 22 (6 - 226) months, respectively. Of the 45 children in Group 1, 17 are well and complication-free. The remaining 28 are clinically well, but with evidence of portal hypertension and/or borderline biochemical jaundice. Of these 45 children, 23 have survived for more than 10 years following PE (17 completely well, 6 with evidence of portal hypertension and/or borderline biochemical jaundice).

The post-PE serum total bilirubin levels at 3 months were significantly lower in children who survived >10 years with their native livers compared to those who required LT within 2 years of PE (15 $\mu\text{mol/L}$ versus 131 $\mu\text{mol/L}$, respectively), $p = 0.0001$. This difference was potentially seen as early as 1 month post-PE (60 $\mu\text{mol/L}$ versus 123 $\mu\text{mol/L}$, respectively), $p = 0.06$. PE at ≥ 60 days or the occurrence of cholangitis did not seem to adversely affect the long-term survival of BA children with their native liver ($p = \text{NS}$).

Conclusions: Overall survival of BA in the era of liver transplantation is excellent at 93.7%. The post-PE, 3-month serum total bilirubin levels appear to predict not only for the need for early LT, but also long-term survival with the native liver.

1009 STUDY OF PREVALENCE OF FATTY ACID OXIDATION DEFECTS IN CHILDREN AND ADULTS WITH ACUTE LIVER FAILURE: SIGNIFICANCE OF CARNITINE/ACYLCARNITINE AND AMINO ACID PROFILE

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Objectives: Limited pediatric data suggest that fatty acid oxidation defects (FAODs) may underlie or modify the course of acute liver failure (ALF) in a patient, but there are no adult data on this aspect. Significance of carnitine/acylcarnitine and amino acid profile in patients with ALF is similarly undetermined. Thus, this study was undertaken to determine the prevalence of FAODs and to study the significance of abnormalities in carnitine/acylcarnitine and amino acid profile in patients with ALF.

Methods: A prospective study was performed, including all cases of acute liver failure (ALF) defined as per standard criteria. Detailed evaluation of subjects was done including metabolic testing (Tandem Mass Spectrometry/TMS for Carnitine/Acylcarnitine Profile/amino-acid analysis and Gas Chromatography Mass Spectrometry/GCMS).

Results: A total of 55 patients (33 pediatric and 22 adult cases) were included in the study. In both pediatric and adult groups, predominant etiology was acute viral hepatitis constituting 42% and 64% of total cases, respectively. Three cases (a 1-year, 6-month-old child, a 13-year-old pediatric patient and a 21-year-old adult male patient). 5.5% of all ALF cases were confirmed to be of metabolic etiology (Carnitine Palmitoyl Transferase-1 or CPT-1 deficiency) based on biochemical testing based on classical carnitine/acylcarnitine profile (Table 1). Almost three-fourths of patients (43 out of total 55 patients, 78%) had evidence of serum hyperaminoacidemia (defined as elevation of any aminoacid levels in blood as per age-wise, cut-off levels) with methionine, phenylalanine, tyrosine, arginine, citrulline and alanine in varying combinations. Thirty-one patients (out of a total of 55) had evidence of abnormal carnitine/acylcarnitine profile with predominant abnormality (23 out of 55 patients) being low C0 levels (as per age wise cut-off). Higher levels of serum tyrosine and lower levels of serum C0 in the pediatric population and higher levels of serum phenylalanine in the adult population were predictive of poor outcome (death/LT). In the overall group, high serum methionine levels, high serum phenylalanine levels and high serum tyrosine levels were significantly associated with poor outcome. Presence of high tyrosine levels in children with ALF (20-fold higher risk) could independently predict poor outcome. But none of the factors were found to be independently predictive of poor outcome in adult population.

Conclusions: Metabolic liver diseases (FAODs) may not be an uncommon entity in cases of ALF with a prevalence of around 5%. CPT1 deficiency, can cause ALF or modify the natural course of ALF caused by other etiologies. Hyperaminoacidemia, as a marker of severity of hepatic damage, may predict poor outcome in ALF cases.

Disclosure of interest: None declared (for all authors)

Table 1: Clinical and Laboratory Parameters of the 3 Patients with CPT1 deficiency

Parameter	Patient 1	Patient 2	Patient 3
Age/Sex	1 year 6 months/Male	13 Year/Male	21 years/Male
Baseline Data			
INR	2.96	2.4	5.48 → 5.3
Ammonia (μmol/L)	174	270	492 → 877
Bilirubin(T/D) (mg/dl)	1.2/0.8 → 4.4/2.8	8.6/7.1 → 42.6/22.1	12.9/8.3 → 11.9/8.9
AST/ALT (IU/L)	163/223 → 143/281	335/438 → 209/131	231/1110 → 425/950
Protein/Albumin (gms/dl)	5.1/3.2 → 5.5/2.9	7.4/4.1 → 7.8/3.6	4.7/2.6 → 4.9/2.6
Metabolic Testing			
Fasting Blood Sugar (mg/dl)	38 → 76	98	72
Arterial pH/Lactate	7.37/1.7	7.4/1.3	7.22/4.9
Urine Ketones (twice)	Negative	Negative	Negative
Urine NGRS (twice)	Negative	Negative	Negative
AFP (ng/ml)	10.5	8.2	127.63
Total CPK (IU/L)	12	24	28734
Serum Cholesterol (mg/dl)	131	354	NA
Serum Triglycerides (mg/dl)	234	813	NA
Serum HDL (mg/dl)	30.4	42.7	NA
Serum LDL/VLDL (mg/dl)	46.5/54.10	145.5/165.80	NA
C-0 levels (μmol/L)	195.27 (Range 24 – 63)	208.69 (Range 22 – 65)	80.06 (Range 25–54)
C0/C16+18 ratio (Normal < 100)	849.3	994	1269.8
Liver Biopsy (Supplementary Digital Content, S3 and S4)	<ul style="list-style-type: none"> Hepatocytes with diffuse severe macrovesicular and moderate microvesicular steatosis 	<ul style="list-style-type: none"> Hepatocytes with moderate macrovesicular steatosis, ballooning degeneration, Mallory Denk bodies Prominent pericellular, periportal fibrosis 	NA
Last Follow up Data			
INR	0.8	1.20	NA
Ammonia (μmol/L)	98	221	NA
Bilirubin(T/D) (mg/dl)	0.8/0/3	28.7/19.9	NA

Abbreviations- CPT1- carnitine palmitoyltransferase IA, INR – International normalised ratio, T/D- Total/Direct, AST- Aspartate aminotransferase, ALT- Alanine aminotransferase, NGRS- Non glucose reducing substances, AFP- Alpha Fetoprotein, CPK Creatinine Phosphokinase, HDL- High Density Lipoprotein, LDL- Low Density Lipoprotein, VLDL- Very Low Density Lipoprotein, NA- Not available

1010 MOTHER-TO-CHILD TRANSMISSION OF HEPATITIS B VIRUS: A FAMILY-BASED STUDY

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Background and Aims: Immunoprophylaxis reduces, but does not completely eradicate, diseases related to hepatitis B virus (HBV) infection. Mother-to-child transmission (MTCT) is the major route of infection in the era of universal hepatitis B vaccination. This study investigated MTCT of HBV by a family-based study design.

Methods: We retrospectively included 176 hepatitis B e-antigen (HBeAg)-positive mothers. Each mother had two children who had received immunoprophylaxis against HBV. Children's hepatitis B surface antigen (HBsAg) seropositivity for more than 6 months was defined as chronic infection. Children's median age at initial HBsAg testing was 6.4 years (range, 0.5 - 18.2 years). Sixty-two mothers and infected children had viral load and HBV genotype results determined by real-time polymerase chain reaction with subsequent melting curve analysis. A *p*-value <0.05 was considered significant, and a *p*-value between 0.05 and 0.1 was considered as showing a trend.

Results: Of the 176 HBeAg-positive mothers, 8 had both children chronically infected with HBV, 20 had an infected first child and an uninfected second child, 8 had an uninfected first child and an infected second child and 140 had both children not infected. The sex-distribution, rates of Caesarean section and timeliness of passive-active immunoprophylaxis were similar between the first child group and the second child group. The first child had a trend to be infected despite immunoprophylaxis than the second child (15.9% vs. 9.1%, *p*=0.053). Mothers having an infected first child were more likely to have an infected second child than mothers having an uninfected first child (28.6% vs. 5.4%, *p*<0.001). Among the 62 mothers with HBV genotype results, 71% (44/62) had genotype B, 12.9% (8/62) had genotype C and 16.1% (10/62) had undetermined genotype. Compared with genotype B infected mothers, genotype C-infected mothers were more likely to have a second child infected (20.5% vs. 62.5%, *p*=0.025) and had a trend to have both children infected (11.4% vs. 37.5%, *p*=0.094) and had higher viral load (6.3 ±

2.0 versus $8.0 \pm 0.6 \log_{10}$ copies/mL; $p=0.0232$), although the viral load was not tested prior to, or at, delivery. The ages at the first child's delivery, at the second child's delivery and at viral load testing were comparable between genotype B and genotype C mothers. In the 33 mother-children pairs with HBV genotyping results, the mothers' and childrens' HBV genotypes were 100% concordant. Conclusions: Despite immunoprophylaxis, the first child of a HBeAg-positive mother has a trend to be infected versus the second child. High maternal viral load and maternal HBV genotype C infection may be associated with MTCT at an older maternal age and familial clustering of hepatitis B immunoprophylactic failure.

1011 NETWORK SIGNATURES OF IGG IMMUNE REPERTOIRES IN HEPATITIS B-ASSOCIATED CHRONIC INFECTION AND VACCINATION RESPONSES

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The repertoire of IgG antibody responses to infection and vaccination varies depending on the characteristics of the immunogen and the ability of the host to mount a protective immune response. Chronic hepatitis B virus (HBV) infections are marked by persistent infection and immune tolerance to vaccination. This disease offers a unique opportunity to discover key repertoire signatures during infection and in response to vaccination. Complementarity determining region 3 of an antibody heavy chain (CDR-H3) has a major impact on the antigenic specificity of an antibody. We used next-generation sequencing to characterize the CDR-H3 sequences in paired siblings of 4 families in which only one member of each pair had chronic HBV infection. Blood samples were obtained before, and 2 weeks after, HBV vaccination. The analysis revealed a huge network of sequence-related CDR-H3 clones found almost exclusively among carriers. In contrast, vaccination induced significant increases of CDR-H3 cluster diversities among siblings without hepatitis B. Several vaccination-associated clone clusters were identified. Similar findings of vaccination-associated clone networks were observed in healthy adults receiving HBV boosters. These strategies can be used to identify signatures of other infectious diseases and accelerate discoveries of antibody sequences with important biomedical implications.

*1012 DEFECTS IN MYO5B CAN CAUSE A SPECTRUM OF PREVIOUSLY UNDIAGNOSED LOW Γ -GLUTAMYLTRANSFERASE CHOLESTASIS IN CHILDREN

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Cholestasis in childhood and infancy with low or normal serum gamma-glutamyltransferase (GGT) is usually linked to heterogeneous genetic defects. While most of these defects are known, many remain undiagnosed. Defects in MYO5B cause microvillus inclusion disease (MVID, MIM251850) with recurrent watery diarrhea. Cholestasis has been reported as one of the atypical presentations, or a side effect of parenteral nutrition, in MVID. In the current study, biallelic mutations in MYO5B were observed in 5 out of 24 undiagnosed normal-GGT cholestatic patients, without recurrent diarrhea, who presented with conditions ranging from transient to progressive cholestasis. Significantly higher frequencies of MYO5B homozygotes or compound heterozygotes were found in the normal-GGT cholestatic group than in groups with other presentations ($p 4.84 \times 10^{-6}$). Liver biopsies of these patients revealed giant-cell cholestasis with abnormal expression of BSEP (also known as ABCB11) in the canaliculi, as well as coarse granular dislocation of MYO5B. Mass spectrometry of plasma bile acids demonstrated significantly increased total bile acids, primary bile acids, secondary bile acids and conjugated bile acids, and decreased free bile acids in the plasma compared to the healthy controls, which is strikingly similar to changes in BSEP/ABCB11-deficient patients. No significant differences were found in the presentation or locations of the mutations in MYO5B-impaired patients with or without cholestasis, indicating that the genotype-phenotype correlation is complex.

Conclusion: MYO5B deficiency can cause a spectrum of cholestasis, with normal GGT and without diarrhea, which represents a form of familial intrahepatic cholestasis with hampered bile-acid excretion mediated by impaired targeting of BSEP and failed canalicular formation.

1013 ANTI-HBs SEROPOSITIVITY CONTINUITY AFTER NEONATAL HEPATITIS B VACCINATION: SINGLE-CENTER STUDY

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Background: It is known that anti-HBs seropositivity rate after three doses of hepatitis B virus (HBV) vaccination since birth is higher than 90%. However, a considerable number have no formation of protective anti-HBs or chronologic decrease of anti-HBs. We performed this study to investigate seropositivity continuity of anti-HBs after neonatal HBV vaccination and the immunogenicity by booster vaccination in one institute of Korea.

Methods: We retrospectively collected data of HBV serologic test results in 20,738 individuals from 2000 to 2015. These subjects were born after 1988 when HBV vaccination was already actively executed in Korea. After exclusion criteria were carried out to secure the subjects, 19,072 individuals were investigated. We analyzed anti-HBs seropositivity rate, anti-HBs disappearance rate, anti-HBs positive seroconversion rate after receiving booster vaccine, and difference of anti-HBs positivity between the subjects born while both recombinant vaccines and plasma-derived vaccines were used (born before 2005) and in those born after 2005 when only recombinant vaccine was used by national regulation.

Results: Anti-HBs seropositivity rate is 55.8%. Age-specific positivity rate of anti-HBs was highest in infants (90.0%), and lowest at the age 15 (43.5%). Disappearance rate of anti-HBs after previous seropositivity was 19.6%. Among those in whom booster vaccinations were given, anti-HBs positively seroconverted in 87.4%. Overall anti-HBs seropositivity rate between the two birth cohorts before 2005 was 62.6% and after

2005 was 78.1%, separately. The anti-HBs seroconversion rate was higher in the individuals who were vaccinated only with recombinant vaccines.

Conclusion: We suggest that physicians need to be more concerned about the lifelong immunogenicity of HBV vaccine after neonatal period and the necessity of booster vaccination.

INFLAMMATORY BOWEL DISEASE

1037 RESOLUTION OF CHRONIC DIARRHEA IN PEDIATRIC PATIENTS FOLLOWING ADMINISTRATION OF A BIOACTIVE POLYPHENOL SUPPLEMENT

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Background: Chronic diarrhea (>3 weeks), a major cause of morbidity in children, is caused by multiple infectious agents, food proteins and inflammatory bowel disease (IBD). Treatment with antibiotics is not recommended for the majority of bacterial gastrointestinal infections and can exacerbate the condition, which is why alternative treatments are needed. Polyphenols have been shown to down-regulate cytokines and inhibit transcription factors necessary for both inflammation and infection processes. The objective of this study was to assess the capability of a bioactive polyphenol supplement to attenuate chronic diarrhea in children caused by multiple intestinal infections and other conditions.

Methods: With parental consent, a prospective, open-label study was conducted in a pediatric gastroenterology outpatient setting on patients with chronic diarrhea who had not responded to standard treatment. These patients were given a polyphenol-based supplement (LiveLeaf Bioscience, San Carlos, CA) daily for three weeks, in serving sizes based on their weight. Positive clinical response was measured as resolution of diarrhea and/or negative bacterial cultures and stool inflammatory markers after 3 weeks' use of the supplement. Adverse events were recorded as to type and treatment given, if needed.

Results: A total of 40 patients, ranging in age from 1 month to 18 years, were followed for up to four weeks. The primary symptom for all patients was chronic diarrhea, with etiologies of *Clostridium difficile* (40%), *Salmonella* (12%), *Shigella* (5%), *Campylobacter* (3%) and intolerance to cow's milk and other proteins causing enterocolitis (22%). IBD was the sole diagnosis or comorbidity in 30% of the patients. Diarrhea resolved completely in 65% of all patients in the study, in 67% of those with cow's milk protein enterocolitis and in 90% of all non-IBD patients following consumption of the supplement. Of those with a response, 85% of the diarrheal episodes resolved within 14 days after starting use of the supplement; 42% resolved within the first week. After administration of the supplement, 13 out of 16 *C. difficile*, 3 out of 5 *Salmonella*, and 2 out of 2 *Shigella* cultures were negative in subsequent testing. Those whose diarrhea did not resolve had comorbidities of ulcerative colitis (10%) and Crohn's disease (10%). No adverse events were reported in any child.

Conclusion: Polyphenols have both anti-inflammatory and anti-infective properties. We evaluated a bioactive polyphenol supplement in a pediatric population with chronic diarrhea and demonstrated that its consumption was an effective treatment alternative, with no side effects. This supplement warrants further investigation in a randomized, controlled, clinical study.

1038 CAN TISSUE AND PERIPHERAL EOSINOPHILIA BE USED AS PREDICTORS FOR DISEASE OUTCOME IN CHILDREN WITH ULCERATIVE COLITIS?

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Background: Eosinophils are implicated in the pathogenesis of ulcerative colitis (UC).

Aims: To evaluate the magnitude of mucosal and blood eosinophils in newly-diagnosed, pediatric UC patients and investigate its clinical significance in predicting short- and long-term disease outcome.

Study: We retrospectively evaluated colorectal biopsies of 96 patients. Samples were taken from diseased areas of the colon and examined by a gastrointestinal pathologist. The most inflamed site was used for assessment of mucosal eosinophils. Demographic data, disease characteristics and long-term outcomes were extracted from medical charts. Associations between histologic features and clinical outcomes were analyzed.

Results: Samples from 96 diagnostic colonoscopies as well as 70 follow-up colonoscopies (49 patients) were evaluated. Median age was 13.3 years (IQR 10.1 - 15.3). Median duration of follow-up was 12.8 years (IQR 7.2 - 17.1). Median number of tissue eosinophils at diagnosis was 45 (IQR 22 - 73) compared to 10 eosinophils (IQR 8 - 25) during histologic remission ($p < 0.0001$). Peripheral absolute eosinophil counts correlated significantly with tissue inflammation ($p = 0.001$) and with tissue eosinophilia ($p = 0.001$). Severity of both mucosal eosinophilic infiltration ($p = 0.02$) and peripheral eosinophilia ($p = 0.04$) was associated with clinical severity of UC at diagnosis. Multiple logistic regression analysis showed that severe eosinophilic infiltration is associated with corticosteroid therapy following diagnosis ($p = 0.04$), but not with a long-term risk for step-up therapy or colectomy.

Conclusion: Tissue and peripheral eosinophilia in pediatric UC patients correlate with disease severity at diagnosis and with short-term corticosteroid requirement. However, for our cohort, these did not serve as predictors for poor long-term outcome including colectomy.

*1039 FACTORS ASSOCIATED WITH RELAPSE AFTER INFLIXIMAB CESSATION IN PEDIATRIC CROHN'S DISEASE PATIENTS TREATED WITH COMBINED IMMUNOSUPPRESSION

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Background and Aims: There are no data regarding the clinical course of Crohn's disease after discontinuing infliximab treatment in the pediatric population. We aimed to investigate the outcome of pediatric Crohn's disease patients who had discontinued infliximab after maintaining clinical remission after combined immunosuppression with infliximab and thiopurines for at least 1 year and to reveal risk factors associated with clinical relapse in these patients.

Methods: We performed a single-center, observational study of 56 patients who had discontinued scheduled infliximab after maintaining clinical remission under combination treatment with azathioprine for at least 1 year. Demographic, clinical, biological and endoscopic factors at

influximab cessation were evaluated for their association to time to relapse using Cox proportional regression analysis. Influximab trough levels and antidrug antibodies were also measured in serum samples collected at the time of influximab cessation.

Results: After a median follow-up period of 4.3 years, 64% (36/56) of patients had experienced a clinical relapse. The cumulative relapse rate at 1, 2 and 4 years was 19%, 36% and 62%, respectively and the median relapse time was 3.3 years from influximab cessation. According to multivariable analysis, complete mucosal healing status and serum influximab trough levels less than 2.2 µg/mL were negatively associated with clinical relapse (hazard ratio 0.223, 95% CI, 0.094 - 0.53, $p < 0.001$, and hazard ratio 0.6812, 95% CI, 0.515 - 0.851, $p < 0.001$, respectively). Retreatment with influximab was effective in 92% of patients.

Conclusions: Approximately 50% of patients with pediatric Crohn's disease, who received combined immunosuppression with influximab and thiopurines for at least 1 year, experienced a clinical relapse within 3.3 years from influximab cessation. A subgroup of patients with complete mucosal healing status and subtherapeutic serum influximab trough levels at influximab cessation may better sustain clinical remission without a clinical relapse after influximab discontinuation.

1040 AMELIORATION OF 5-FLUOROURACIL-INDUCED INTESTINAL MUCOSITIS BY ORALLY-ADMINISTERED PROBIOTICS IN A SCID MICE MODEL

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Background: Intestinal mucositis is a frequently encountered side effect in oncology patients undergoing chemotherapy. The anti-metabolite 5-fluorouracil (5-FU) is one of the most commonly used chemotherapeutic agents in clinical oncology, due to its ability to exert its cytotoxic effects through incorporation into RNA and DNA and finally inhibit DNA synthesis and to improve tumor-free status and survival rates. However, studies estimate 50% - 80% of patients undergoing 5-FU chemotherapy develop clinical intestinal mucositis. Destruction of the intestinal mucosa results in reduced food and fluid intake, altered gut motility and pH value, colonic crypt damage and changed composition of the gut microbiota. Mucositis has a huge clinical and economic impact, because it may require chemotherapy interruption and discontinuation of therapy. Recently, probiotics have been investigated as a therapeutic approach in a range of disorders, such as inflammatory bowel disease, colitis, pouchitis, enteric infection, irritable bowel syndrome, colon cancer, radiation-induced enteropathy and chemotherapy-induced mucositis. Thus, we test whether *Lactobacillus* and *Bifidobacterium* have the potential to attenuate chemotherapy-induced mucositis.

Aim: To study a novel way to alleviate mucositis, we investigate the effects of probiotic supplementation in ameliorating 5-FU-induced intestinal mucositis in an experimental SCID mouse model.

Methods: Male NOD/SCID BALB/c mice (6 weeks of age, $n=6$ per group) received 5-FU (30 mg/kg/day) administration via intraperitoneal injection for 5 days. Mice were fed with or without a mixed suspension (Infloran®) (IF) of *Bifidobacterium* (1×10^7 cfu/mg) and *Lactobacillus acidophilus* (1×10^7 cfu/mg). Assessment of clinical conditions was measured by body weight (BW) loss results and diarrhoea scores. Barrier dysfunction is determined by duodenum, jejunum and colon histology. Villus height and crypt depth were assessed.

Results: Experiments showed that probiotics could not suppress the body weight loss and diarrhoea. We found that BW began to decrease from Day 0 to Day 5 (91.57 ± 1.77 to 91.3 ± 3.3 %) in 5-FU group when compared to 5-FU+IF group ($P=0.834$). Diarrhoea scores began to increase from Day 0 to Day 5 (1.75 ± 0.27 to 1.5 ± 0.0 in 5-FU group when compared to 5-FU+IF group ($P=0.08$). Increased Villus height was showed in 5-FU group when compared to 5-FU+IF group (257 ± 73 to 85 ± 92 , $P=0.01$). In addition, villi and mucosa integrity were maintained well in probiotics group.

Conclusion: Systemic 5-FU administration caused mucositis. Probiotics treatment does not improve clinical performance, but appeared to attenuate the severity of 5-FU-induced intestinal mucositis. We conclude that oral probiotics administration can ameliorate chemotherapy-induced intestinal mucositis in a SCID-mouse model. This suggests probiotics may serve as an alternative therapeutic strategy for the prevention or management of chemotherapy-induced mucositis in the future.

1041 VEN120, A PLANT-DERIVED HUMAN LACTOFERRIN, ATTENUATES MURINE INTESTINAL INFLAMMATION VIA MODULATION OF THE MUCOSAL IMMUNE RESPONSE

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Background: Current hypotheses suggest that inflammatory bowel disease (IBD) may develop through a dysregulated mucosal immune response toward the commensal enteric flora in genetically susceptible individuals. Multiple animal studies indicate that regulatory T cells (Treg) regulate the immune response in normal intestinal mucosa and thereby prevent colitis development. A breakdown of this tolerance to luminal antigens via activation of the Th17 cells plays a pivotal role in IBD development. We hypothesize that plant-produced human lactoferrin, Ven120, can safely modulate the adaptive immune system in IBD to ameliorate inflammation.

Methods: Ven120 grown in rice and purified was provided by oral gavage or by subcutaneous Alzet pump to 10 - 12-week-old TNFΔ;ARE mice with ileitis or 8 - 12 week old C57BL/6 mice treated with the dextran sodium sulfate (DSS). After 2 weeks (TNFΔARE) or 1 week (DSS), these mice were evaluated for intestinal permeability by FITC dextran flux, inflammation by histology, cell isolation and flow cytometry as well as Treg function. Finally, IL-10 and IL-17 output was measured both by ELISA and by intracellular cytokine staining. In addition, *in vitro* studies were completed to assess the affect of Ven120 on T cell activation, differentiation and signaling.

Results: Despite an increase in IL-2 secretion by naïve CD4+CD25- T cells treated with Ven120 we noted decreased proliferation of these cells. However, these cells produced increased quantities of IL-10 suggesting a possible mechanism. In the TNFΔARE mouse model of IBD after 2 weeks of treatment with Ven120 vs. vehicle there was a significant drop in influx of naïve CD44^{low}CD62L^{hi} T cells into the lamina propria of the intestine with a concurrent increase in IL-10-producing Treg cells and a decrease in IL-17 producing Th17 cells. Histology of the intestines from these mice demonstrated that all indices of inflammation were improved. Similar studies were carried out in the DSS model of colitis with comparable results. *In vitro* differentiation of naïve CD4 T cells in the presence of Ven120 identified a significant increase in Treg and decrease in Th17 cell development. Suggesting a potent shift of balance toward an immunosuppressive phenotype which can be beneficial in IBD.

Conclusions: Our studies have effectively demonstrated the therapeutic potential of Ven120 in murine models of inflammatory bowel disease. Specifically, Ven120 decreased naïve T cell infiltration and proliferation in the intestinal lamina propria in 2 murine models of IBD. An increase

in IL-10-producing CD4+Foxp3+ regulatory T cells and a decrease in IL-17-producing Th17 cells was noted in the Ven120-treated mice. Finally, the Ven120-treated mice exhibited improved histological indices and had improved intestinal barrier function, indicating efficacy for oral and subcutaneous Ven120 in decreasing inflammation in a preclinical models of IBD.

1042 RISK FACTORS ASSOCIATED WITH PERIANAL CROHN'S DISEASE IN CHILDREN

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Background: According to the increasing incidence of pediatric Crohn's disease (PCD) in Korea, several reports about focusing on the incidences and treatment are published. But one of the relatively rare complications, perianal lesions is not well known. Therefore we investigated the incidence and the risk factors of perianal Crohn's disease in Korean children.

Objective: The aim of our study was to find out the risk factors in children with perianal Crohn's disease.

Methods: We retrospectively reviewed medical records in children (age \pm 18 years) who confirmed with Crohn's disease in Gachon university Gil hospital between 2000 and 2014. After dividing into two groups according to the perianal lesions, we identified the risk factors of the PCD with logistic regression analysis.

Results: Of 69 children, mean age was 15.4 ± 2.2 years, 51 (73.9%) children were male, and 54 (78.3%) children had perianal PCD. Gender, BMI, age at initial diagnosis, chief complaints, other associated symptoms and signs were not significantly different between two groups, but mean duration of symptoms was more longer in perianal PCD (p 0.007). Of laboratory findings, Hb was lower and Hct was higher in perianal PCD (OR 0.05; 95% CI, 0.00-0.82; p =0.04, OR 2.98; 95% CI, 1.06-8.35; p =0.04). Penetrating lesions were more predominant in perianal PCD (p 0.049). Paris classification was not different between two groups.

Conclusions: The relatively higher incidence and longer symptom duration in Korean children with PCD suggest the delayed diagnosis. Therefore, clinical suspicion about Crohn's disease is needed in children with perianal lesions.

1043 SAFETY OF HOME INFLIXIMAB INFUSIONS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Background: Infliximab has been shown to be both safe and efficacious in treating pediatric patients with Crohn's disease (CD) and ulcerative colitis (UC). Traditionally, maintenance infliximab therapy requires patients to return to the hospital every 8 weeks for an intravenous (IV) infusion. In the pediatric population, this results in absences from school and loss of work for the accompanying parent. In our practice, compliant patients are permitted to receive home infusions after their first maintenance infusion. Therefore, the goal of this study was to formally evaluate the safety of maintenance home infliximab infusions by analyzing and comparing our practice's home and hospital infusions to date.

Methods: A systematic chart review was conducted at a tertiary referral center for pediatric patients with CD or UC treated with infliximab. Baseline characteristics including age, gender and diagnosis were collected. The use of pre-medications and the rate of the infusion were the same in both groups; infliximab dose ranged from 5 to 15 mg/kg. For all hospital infusions, nursing notes were evaluated and all reactions were recorded. Likewise, documentation of each home infusion was analyzed with a nurse from the infusion company. For every reaction, the type and subsequent treatment was recorded. A repeated measures logistic regression was used to compare the number of reactions in the home and hospital infusion groups.

Results: 136 patients who received a total of 1410 maintenance infliximab infusions were identified of which 56 (41%) patients received home infusions and 80 (59%) patients received infusions in the hospital infusion center. In the hospital group 40 (50%) were female, the average age was 14.9 years, and 60 (75%) had CD. In the home group, 28 (50%) were female, the average age was 16.5 years, and 48 (86%) had CD. Of the 681 hospital infliximab infusions, 7 reactions were documented; all resulted in the drug being stopped temporarily and IV fluids were administered. Two patients received diphenhydramine, none required epinephrine and 1 was sent to the emergency department (ED). Of the 729 home infliximab infusions, 5 reactions were documented; 3 patients were given IV fluids, none required additional medications and 2 were sent to the ED. There was no significant difference between the number of reactions that occurred in the home vs. hospital infusion groups (p =0.48).

Conclusions: The number of reactions to infliximab in our pediatric UC and CD patients did not differ based on the location of infusion and no significant adverse outcomes occurred. Home infliximab infusions should be considered given the similar safety profile, increased flexibility and reduced number of missed days of school and work.

1044 SIX-MONTH 6-THIOGUANINE LEVELS PREDICTS FUTURE THIOPURINE FAILURE IN PEDIATRIC IBD

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Background: The efficacy of thiopurines as a maintenance strategy has been challenged by recent clinical trials. However, none of these trials employed metabolite monitoring to dose optimize proactively, raising the question as to whether thiopurines would perform better both in the short- and long-term if metabolite levels were therapeutic. We aimed to compare 6-month outcomes between standard and optimized dosing strategies and define long-term predictors of thiopurine durability.

Methods: Pediatric IBD patients (< 21 years) at Cedars Sinai Medical Center were identified who had received thiopurines between 2001 and 2013 and had 1) at least one metabolite level (Prometheus Labs, San Diego, CA) measured within 8 weeks of therapy 2) a baseline CBC, and 3) a follow-up visit and repeat metabolites at 6 months. The 216 eligible patients were grouped according to starting dose: \geq 2.5 mg/kg/day azathioprine (AZA) or 6-MP equivalent (Group 1) or <2.5 mg/kg/day start dose (Group 2). The primary outcome, thiopurine durability, was measured using Kaplan Maier survival analysis. Spearman rank correlation and univariate analysis were performed to test associations between metabolite levels, laboratory data, and clinical efficacy, which was measured by steroid free remission (SFR) (defined as HBI < 4 for CD patients and partial Mayo Score (pMS) < 2 for UC patients and off corticosteroids) at 6 months and last follow-up. Group 1 and Group 2 were further analyzed depending upon whether they were dose optimized based on initial metabolite measurement.

Results: Only 46% of Group 1 patients (n=155) were dose escalated after initial metabolite levels compared to 70% in Group 2 (n=61) (p 0.0014), with median [range] initial 6-TGN levels of 195 [131-270] vs. 161 [124-229], respectively (p 0.1). Only 32% of Group 1 patients had

an initial 6-TGN level $>/ 235$, which was no different than those in Group 2 (26%). In non-optimized Group 1 patients (n=83), 6 month 6-TGN levels, SFR rate, and percentage of patients with 6-TGN $>/ 235$ were no different than the optimized Group 2 patients (n=43) (Table 1). 6-TGN level <235 at 6 months was the only variable that predicted thiopurine failure (2.5 [0.83-5] years vs. 3 [1.7-7.7] years; log-rank $p<0.001$). Initial dosing strategy, first 6-TGN level, 6-month SFR, 6MMP:6TGN ratio, and delta-MCV all did not predict thiopurine failure. Conclusions: 6-TGN levels at 6 months were no different between a standardized, "SONIC-like" thiopurine dosing strategy and a metabolite-driven, optimized dosing strategy. 6-TGN level <235 at 6 months was the only significant predictor of thiopurine failure, suggesting that either dosing strategy may confer durability as long as the 6-month 6-TGN level is therapeutic.

	Group 1 (≥ 2.5 mg/kg/day)	Group 2 (<2.5 mg/kg/day)	Optimized Group 1	Non-optimized Group 1	Optimized Group 2	Non-Optimized Group 2
N	155	61	72	83	43	18
Median Initial 6-TGN (Range)	195 (131-270)	161 (124-229)	140 (122-205)	238 (169-322)	152 (124-191)	207 (151-312)
Initial 6-TGN >235 (%)	32%	26%	8%	52%	16%	44%
Median Initial 6MMP/6TGN Ratio (Range)	16 (9-35)	10 (5-23)	20 (11-37)	14 (7-35)	9 (5-22)	13 (5-30)
Median 6 mo 6-TGN (Range)	209 (155-272)	196 (139-274)	204 (105-262)	213 (163-294)	191 (117-271)	231 (175-275)
6 mo 6-TGN >235 (%)	25%	29%	33%	33%	28%	44%
Median 6 mo 6MMP/6TGN Ratio (Range)	22 (9-39)	11 (5-18)	24 (13-43)	18 (8-28)	13 (6-19)	6 (4-17)
% SFR at 6 mo	74%	74%	68%	78%	30%	16%

1045 THE HIGH AFFINITY RECEPTOR FOR PACAP (PAC1) IS PROTECTIVE IN INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory bowel disease is a chronic inflammatory process involving intestinal mucosa. Despite extensive research, the pathogenesis remains unclear. There is increasing evidence, however, that neuropeptides and the enteric nervous system regulate intestinal inflammation. Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide that is released by the autonomic nervous system, myenteric neurons, and T-cells in the gut. *In vitro* and *in vivo* studies have shown that PACAP regulates immune responses by inhibiting the release of pro-inflammatory cytokines and stimulating anti-inflammatory cytokines. PACAP exerts its effects through three receptors: PAC1, VPAC1 and VPAC2, which are present throughout the GI tract and lymphoid organs. PACAP has high affinity for PAC1, VPAC1 and VPAC2, whereas vasoactive intestinal peptide (VIP) binds only to VPAC1 and VPAC2. Published data show that VIP^{-/-} mice are resistant to the effects of DSS, in contrast to PACAP^{-/-} mice, which demonstrate an increase in the severity of DSS-induced colitis with an associated increase in pro-inflammatory cytokines within colonic mucosa. **Rationale:** Based on these results we hypothesized that the anti-inflammatory effects of PACAP are attributed to the expression of its specific receptor, PAC1, in a DSS model of colitis.

Aim: We examined mice deficient in the PAC1 receptor to establish the role of the PACAP-PAC1 receptor axis in regulating the inflammatory response in DSS induced colitis.

Methods: A total of 14 PAC1^{-/-} mice and 16 wild-type (WT) C57BL/129SV mice were given 2.5% DSS-treated water for 5 days. The mice were allowed 6 days of recovery with normal drinking water and sacrificed on day 11. Daily weights, water and food intake, as well as physical activity were measured throughout the study. Stool appearance was also observed. Upon euthanasia, intact colons from both groups of mice were extracted. To verify the extent of colitis, the colonic weight to length ratio was determined. Colonic tissue was examined histologically by H and E staining and scored in a blinded fashion.

Results: PAC1^{-/-} mice treated with DSS demonstrated a higher colonic weight to length ratio (4.23 ± 0.15), $p=0.004$, indicating worsened colitis, compared to WT mice (3.57 ± 0.15). The mortality rate of the PAC1^{-/-} mice was 50% versus 12.5% in the WT group. H&E staining of colonic tissue indicated that inflammation was augmented in the PAC1^{-/-} mice compared to WT mice.

Conclusions: PAC1 receptor-deficient mice exposed to DSS showed a significantly higher mortality rate and developed more severe colitis with higher levels of colonic inflammation than wild type mice. This is in agreement with prior studies on PACAP^{-/-} mice and suggests that the anti-inflammatory role of PACAP is mediated through activation of its specific receptor, PAC1.

1046 PROVIDING TIMELY AND RELIABLE CARE: A QUALITY IMPROVEMENT INITIATIVE TO IMPROVE FOLLOW-UP VISIT RATES IN IBD PATIENTS

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Background: Inflammatory bowel disease (IBD) is a chronic condition that requires lifelong therapy. Non-adherence to medications and office visits can result in poor outcome. Timely care is one of the six dimensions of quality the Institute of Medicine established as a priority for improvement in the health care system. ImproveCareNow (ICN) is a national quality improvement network focusing on improving care and outcomes of pediatric IBD patients. Preventative care leads to better outcomes in patients with chronic illness; hence ensuring timely and reliable care is one of several ICN measures.

Aim: As an ICN Center, we sought to improve the care of our IBD patients by increasing the percentage of patients with a documented visit within 200 days over a 6-month period.

Methods: The division of Pediatric Gastroenterology and Nutrition at Children's Hospital at Montefiore (CHAM) joined ICN in 2012. ICN provides monthly QI measure reports for each center. Percent of patients with documented visit within 200 days is one of 14 ICN clinical measures, so we used 200 days as our metric for determining timely follow-up. We assembled a multidisciplinary quality improvement (QI) team, reviewed our monthly QI measure reports from May 2015 to September 2015, identified reasons for poor follow-up (fishbone diagram), determined key drivers and intervention steps, and implemented changes to improve follow-up visit rates in IBD patients. Interventions were implanted as Plan-Do-Study-Act (PDSA) cycles and included maintaining an accurate active IBD patient list by inactivating patients that have

moved or transferred care, calling patients that needed to be seen monthly and offering them appointments, and conducting “office visits” during the time of Remicade infusion for Remicade patients. Outcomes were presented using a run chart with pre-intervention and post-intervention data.

Results: A total of 133 IBD patients have been enrolled in ICN at CHAM, in the past three years. Patients who relocated or transferred care to adult providers were inactivated, and there are currently 86 active IBD patients in our ICN registry. During the five months preceding the interventions, 63% of ICN enrolled IBD patients had a documented visit within 200 days. After multiple PDSA cycles, the median percentage of patients with a documented visit within 200 days has increased to 72%, and this increase has been sustained for seven months.

Conclusions: A multidisciplinary QI team and focused QI interventions increased the percentage of patients with a documented visit within 200 days. Efforts will continue to increase visit rates and to maintain timely reliable care.

1047 HEALTH SERVICES UTILIZATION IN ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE TRANSITIONING FROM PEDIATRIC TO ADULT CARE: A POPULATION-BASED, COHORT STUDY

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Background: Inflammatory bowel disease (IBD) is a chronic condition with increasing pediatric incidence. The transition from pediatric to adult care may be associated with disruption in the life of a child with a chronic disease, and a change in patterns of specialist health care. The aim of this study was to determine whether the transition from pediatric to adult care was associated with changes in health service utilization for patients with childhood-onset IBD.

Methods: We used the Ontario Crohn's and Colitis Cohort,¹ a population-based cohort comprising all children <18 yrs diagnosed with IBD from 1994-2008 identified from health administrative data using validated algorithms. Included patients were treated by a pediatric gastroenterologist for at least 2 years prior to transfer to the care of an adult gastroenterologist. Self-controlled case series analyses (using a patient as their own control) compared health services utilization in the 2 years before transfer (control period) and 2 years after transfer (risk period), with an interceding 6 month wash-out period at the time of transfer. Outcomes evaluated included IBD-specific or IBD-related outpatient visits, hospitalizations, emergency department (ED) utilization, and laboratory utilization. Relative incidence (RI) in the post-transfer was compared to pre-transfer periods using a conditional Poisson regression analysis. Analyses were stratified by IBD type: Crohn's disease (CD) and ulcerative colitis (UC), which were defined based on validated algorithms of the diagnosis assigned to the most recent outpatient physician visits.¹

Results: 557 patients were included in the study (388 CD, 148 UC, 21 IBD type unclassifiable). Outpatient visit rates were higher after transfer (CD: RI 1.56, 95% CI, 1.42-1.72; UC: RI 1.48, 95% CI, 1.24-1.76), as was ED utilization rate (CD: RI 2.12, 95% CI, 1.53-2.93; UC: RI 2.34, 95% CI, 1.09-5.03) combined ED/hospitalization rates for (CD: RI 1.54, 95% CI, 1.18-2.01; UC RI 2.56, 95% CI, 1.32-4.96), and laboratory utilization (CD: RI 1.43, 95% CI, 1.26-1.63; UC: 1.38, 95% CI, 1.13-1.68). Hospitalization rates were not statistically different post-transfer (CD: RI 0.70, 95% CI, 0.42-1.18; UC: RI 2.41, 95% CI, 0.62-9.40). Sensitivity analysis revealed similar results when only the first year after transfer to adult care was assessed.

Conclusions: In the largest study to date examining the transfer from pediatric to adult IBD care, health services utilization increased significantly in the two years after transfer. In particular, increased ED utilization represents an undesirable and expensive outcome associated with transfer to adult care. Identifying the underlying causes of the increase in health services utilization to inform the development of effective transition programs may decrease the cost of caring for patients with IBD.

Reference: 1. Benchimol *et al. Gut.* 2009;58(11):1490-7.

1048 ANALYSIS OF HEPATITIS B IMMUNE STATUS AMONG UNC PEDIATRIC IBD PATIENTS ON BIOLOGIC THERAPY: ARE OUR PATIENTS PROTECTED?

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Background: Pediatric inflammatory bowel disease (IBD) patients on biologic therapy are at higher risk of hepatitis B reactivation than the general pediatric population due to the immunosuppressive nature of these agents. Moreover, the efficacy of hepatitis B vaccination is impaired in these patients. Even among vaccinated individuals, IBD patients may have hepatitis B surface antibody titers below the accepted threshold of protection. Therefore, NASPGHAN and other leading GI organizations recommend assessing hepatitis B immune status prior to initiating biologic therapy. The goal of this quality improvement (QI) initiative was to investigate hepatitis B immunity among pediatric IBD patients at the University of North Carolina (UNC).

Methods: We assessed hepatitis B immune status of pediatric IBD patients on biologic agents at UNC. At the time of initial review, no standardized protocol existed for determining hepatitis B immune status within this population. We subsequently implemented a screening protocol for checking hepatitis B antibody titers and antigen in this population and then determined if this improved screening rates within this patient cohort.

Results: On initial review, 17% of patients on biologic therapy (16/92) had been screened for hepatitis B immunity. Among this minority of individuals, only two patients had reactive surface antibody titers, one had an equivocal titer, and the remainder were non-reactive. After initiation of the screening protocol over a two-month period (3/8/2016-5/8/2016), 55/92 patients were screened for hepatitis B with antibody titers. Among those screened, 29% (16/55) had reactive titers, 62% (34/55) had non-reactive titers, and 9% (5/55) had equivocal titers. All 48 patients screened for hepatitis B antigen were found to be negative, including 11 patients screened prior to protocol initiation.

Conclusion: These data suggest that, prior to initiation of a formal screening protocol, the majority of pediatric IBD patients receiving biologic therapy at our institution were not screened for hepatitis B. After implementation of a screening protocol, rates of hepatitis B assessment improved; however, a substantial percentage of these patients had nonreactive hepatitis B surface antibody titers despite previous vaccination. These results emphasize the importance of assessing hepatitis B immune status prior to or as soon as possible after initiating treatment with biologic agents. Ongoing QI efforts include developing a protocol for vaccinating patients found to have insufficient hepatitis B immunity and investigating the impact of IBD and immunosuppressive agents on the ability to mount an immune response against hepatitis B.

1049 *INFANT MICROBIAL INTESTINAL DYSBIOSIS RESULTS IN ALTERED T CELL RECEPTOR SIGNALING AND COMPROMISES ANTI-VIRAL IMMUNITY*

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Introduction: We recently reported that maternal antibiotic treatment (MAT) during pregnancy and lactation dramatically reduces the density and composition of the intestinal microbiota of infant mice, with *Enterococcus faecalis* as the dominant species. MAT infants exhibit enhanced susceptibility to systemic viral infection and altered innate and adaptive immune cell populations. Particularly, CD8+ effector T cells from MAT infants are unable to sustain IFN-gamma production *in vivo* following vaccinia virus infection and *in vitro* upon T cell receptor (TCR) stimulation compared with control (CTRL) infants. Several studies have shown that Toll like receptor (TLR) signals can provide costimulation to T cells and enhance proliferation, cytokine production and survival and modulate the expression of inhibitory receptors. We hypothesize that T cells that develop in infant mice with microbial intestinal dysbiosis display intrinsic defects that compromise their effector function. Our goals in this study are to determine if MAT infant T cells have altered expression or activation of critical TCR signaling proteins and if such defects can be reverted by stimulation with TLR ligands or microbial metabolites that are missing or limited in the MAT environment.

Methods: To assess TCR signaling, splenic T cells from day of life (DOL) 15 MAT and CTRL mice were stimulated *in vitro* with anti-CD3 and anti-CD28 antibodies with or without TLR2 (Pam3CSK4), TLR4 (LPS), TLR5 (Flagellin) and TLR9 (CpG) ligands or with short chain fatty acids (SCFA) for 72 hours and then evaluated for the expression of ZAP-70, pZAP-70, pErk1/2, c-Rel, total phosphotyrosine and IFN-gamma by flow cytometry. To determine if TLR signals are able to enhance T cell function and protect MAT infants to succumb from systemic viral infection, DOL 15 MAT and CTRL mice were infected with vaccinia virus and treated with LPS and 11 days post-infection we evaluated the viral titers and the phenotype and cytokine production capacity of T cells.

Results: *In vitro* TCR/CD28 stimulated MAT infant T cells failed to sustain total tyrosine phosphorylation and Erk1/2 phosphorylation and such defects were partially reverted by TLR agonists and SCFA. LPS-treated MAT infected mice had reduced viral titers and increased frequency of IFN-gamma and TNF-alpha producing CD4+ and CD8+ effector T cells than their untreated counterparts and similar to CTRL infants.

Conclusions: T cells from infant mice with a restricted microbial intestinal flora display intrinsic TCR signaling defects that can be partially reverted by stimulation with TLR ligands and bacterial metabolites. Our results show the importance of a diverse microbial intestinal flora to shape optimal T cell responses during infancy and suggest that TLR ligand stimulation could represent an effective intervention to restore T cell function.

1050 *COMPARISON OF TRANSPERIANAL ULTRASONOGRAPHY WITH COLONOSCOPIC GROSS EXAMINATION AND PERIANAL MAGNETIC RESONANCE IMAGING IN PEDIATRIC CROHN'S DISEASE*

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Objectives Perianal fistula and/or abscess are important complication of Crohn's disease, especially in children. Magnetic resonance imaging (MRI) and examination under anesthesia are known as accurate diagnostic modality to evaluate perianal lesions. However, both methods are expensive and require experienced investigators. We assessed the accuracy of transperianal ultrasound (TPUS) and gross examination under colonoscopy, in comparison with MRI as gold standard.

Methods: A total of 31 consecutive patients with perianal Crohn's disease who underwent MRI, TPUS, and colonoscopic gross examination under sedation were included. Fistulae were classified according to Parks' and St. James' classification. Abscesses were also identified by their presence and direction.

Results: Forty one fistulae (22 superficial, 15 intersphincteric, 4 transsphincteric) and 14 abscesses were detected by MRI. Thirty-eight fistulae and 10 abscesses were detected by TPUS. Twenty-nine fistulae (sensitivity 70.7%, positive predictive value (PPV) 83.4%, kappa value 0.307) and 9 abscesses (sensitivity 64.3%, PPV 89.8%, kappa value 0.678) on TPUS corresponded to MRI findings. Thirty-six fistulae and 12 abscesses were detected by colonoscopic gross examination under sedation. Thirty-one fistulae (sensitivity 75.6%, PPV 89.3%, kappa value 0.476) and 7 abscesses (sensitivity 50.0%, PPV 59.7%, kappa value 0.397) on colonoscopic gross examination corresponded to MRI findings.

Conclusions: Our results reveal that TPUS is simple and real-time method to detect perianal fistula and/or abscess, with relatively good diagnostic accuracy, in children with perianal Crohn's disease. Because perianal MRI has some limitations despite its excellent accuracy and colonoscopic gross examination has the lowest accuracy, TPUS may be suitable for the preliminary assessment and follow-up of perianal lesions in pediatric Crohn's disease.

1051 *TREATMENT OF IRON DEFICIENCY AND IRON DEFICIENCY ANEMIA IN 100 PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE*

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Introduction: Iron deficiency (ID) is the most common cause of anemia in inflammatory bowel disease (IBD). In children, anemia and iron deficiency should be treated with intravenous iron (IV) as first line. Oral iron can have a negative impact on disease activity.

Objectives and Methods: The objective of this study was to calculate the prevalence of iron deficiency anemia in children with IBD followed in a Pediatric Gastroenterology Unit and evaluate the experience of this unit in the treatment with IV iron in these patients. A retrospective cohort study was designed involving the pediatric population with IBD followed in that unit between January 2001 and April 2016. Anemia was defined according to OMS criteria: children under 5 years with hemoglobin (Hb) levels <11 g/dL, from 5 to 11 years Hb <11.5g/dL, women between 12 to 13 years Hb <12 g/dL, and men Hb <13 g/dL. ID was defined as serum ferritin <30 µg/L when CRP <10 mg/L and <100 µg/L when there was evidence of inflammation. Disease activity was defined according PCDAI index and PCR values in Crohn's disease (CD) and PUCAI index and clinical features were used in ulcerative colitis (UC) to divide patients in mild, moderate and severe disease.

Results: IBD was diagnosed in 100 patients: 67% with CD and 33% with UC, a total of 50% male. At diagnosis 56% of patients had IDA and 28% ID. After a year follow-up, ID decreased to 25% (p 0.024) and IDA was manifested in 15% of patients (p 0.035). Ferritin and CRP values

are superior at diagnosis (p 0.01 and $p=0.04$) and Hb is higher after 1 year of follow-up (p 0.010). CD presented with higher CRP (p 0.035) and ferritin (p 0.012) values. IV iron was administered to 69.7% of patients and 13 patients tried treatment with oral iron. During this period 459 administrations of IV iron were conducted in a total of 542 ampoules. An average of $2.18 \text{ g/kg} \pm 1.29$ of IV iron in DC and $2.76 \text{ g/kg} \pm 1.9$ in UC ($p<0.05$) was consumed. No adverse reactions were reported. The average time until the first dose of IV iron was 4.5 (0-72) and 13.5 (0-64) months for DC and UC, respectively. Analyzing all the administrations we found significant higher values of hematocrit (p 0.017), CRP (p 0.004) and ferritin (p 0.001) at CD; Hb (p 0.06), mean corpuscular volume (p 0.338) and RDW (p 0.118) were similar in both pathologies. Severe disease appears to show a tendency to lower Hb values at diagnosis and a higher consumption of IV iron (r -0.372 and r 0.290, significant correlation for significance level 0.01). The sample also showed a tendency for a higher IV iron consumption when the diagnosis is at an earlier age (r -0.210, significant correlation for significance level 0.01). Conclusion: IV iron is the first-line treatment of IDA in IBD and has proven quite safe and effective. The need of use of IV iron is significantly higher in UC.

1052 SOLAR RADIATION IS INVERSELY ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE ADMISSIONS IN CHILE

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Background: A latitude gradient for inflammatory bowel disease (IBD) has been suggested in the northern hemisphere, which may be explained by vitamin D (VD) deficiency at higher latitudes that have lower solar radiation (SR). VD has multiple biological effects on the immune and gastrointestinal systems and VD deficiency could have a causal role in IBD flares. Chile is a long and slender country spanning latitudes 17° and 56° South, with a wide range of SR, providing an excellent opportunity to evaluate the association between regional SR, as a proxy for VD status, and hospital admissions due to IBD.

Methods: Using the national hospital discharge database from the Chilean Ministry of Health, we analyzed admissions due to Crohn's disease (CD) and ulcerative colitis (UC) between 2001 and 2012. Children were considered those younger than 18 years. Admission rates were calculated per 100,000 inhabitants. Average annual SR intensity data for the different regions was obtained from the Chilean Solarimetric Registry. This study was approved by the Ethics Committee of the Pontificia Universidad Católica de Chile Medical School.

Results: Between 2001 and 2012, there were 12,869 admissions due to IBD, (31% CD, 69% UC); 57% of all patients were female. Pediatric hospitalizations accounted for 11% of all IBD admissions (42% CD, 58% UC). Median age for IBD admissions was 36 years (IQR 25-51) and for pediatric admissions was 12 years (IQR 7-15). The national admission rates for CD in children was 1.0 (95% CI, 0.9-1.1) vs. 2.5 (95% CI, 2.4-2.6) in adults, $p<0.001$. The national admission rate for UC in children was 1.4 (95% CI, 1.3-1.5), and 5.7 (95% CI, 5.6-5.8) in adults, $p<0.001$. Although an increasing trend for CD over the 12-year period was not significant in children (β 0.015, 95% CI, -0.040-0.069), it was for adults (β 0.153, 95% CI, 0.096-0.210). A significantly increasing trend in UC admission rates throughout the 12-year period was observed (β 0.143, 95% CI, 0.099-0.187 in children; β 0.143, 95% CI, 0.108-0.178 in adults). In terms of latitude, the highest admission rates for pediatric CD and UC as well as adult UC were observed in the southernmost region of Magallanes (latitude 48-56°S), which also is the region with lowest annual SR. Univariate linear regression analysis showed regional SR was inversely associated with IBD admissions in Chile (β -0.43, $p=0.03$). Regional poverty, rurality and indigenous population rates were not significantly associated with IBD admissions in univariate linear regressions. A multilinear regression model that included regional SR and rurality rate predicted CD admissions in adults (R^2 0.45), and UC admissions in both children (R^2 0.62) and adults (R^2 0.53).

Conclusions: Regional SR is inversely associated with IBD admission rates in Chile, which are highest at the southernmost region with the lowest SR. Our results support the potential role of VD deficiency on IBD flares.

1053 SLEEP PATTERNS IN PEDIATRIC CROHN'S DISEASE: AN INTERIM ANALYSIS

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Objectives: Recently, sleep is suggested as an environmental factor that may be associated with disease activity in patients with inflammatory bowel disease (IBD). Self-reported sleep disturbances are common in adults and teenagers with IBD and adversely affect quality of life, however, no objective sleep data exists in adult or pediatric IBD populations. Objective sleep data is limited by the feasibility of performing reference standard, polysomnography, especially in a diseased population. The purpose of this ongoing study is to demonstrate feasibility of the use of actigraphy as an objective measure of sleep in pediatric Crohn's disease (CD), as well as characterize sleep patterns in adolescents with CD. We hypothesize that both subjective and objective measures of sleep in adolescents with CD will negatively correlate with pediatric CD Activity (PCDAI) score.

Methods: Children with CD age 12-18 years were invited to participate. Exclusion criteria included history of known sleep disorders. Subjective sleep assessment was done using the validated Adolescent Sleep-Wake Scale. Sleep patterns were objectively assessed using a triaxial accelerometer (GT3X; Actigraph, Pensacola, US) worn on the non-dominant wrist for 7 consecutive days (24 h/day). Total sleep time (TST) and sleep efficiency (SE; total sleep time/time in bed x100) were calculated. Demographic, anthropometric, and clinical data were used to calculate PCDAI scores. Descriptive statistics and Pearson correlation coefficients comparing subjective and objective markers of sleep and disease activity were calculated. P -values of <0.05 were considered significant.

Results: At interim analysis, 23 out of 28 subjects (82%) approached were consented, 18 (78%) participants had completed clinical questionnaires, and 11 (48%) had completed actigraphy (remaining subjects are currently undergoing actigraphy). 11 (100%) had valid actigraphy data. The median PCDAI was 12.5 (2.5-20). The mean TST in those completing actigraphy was 466 ± 62 minutes per night, similar to reported ranges of TST for healthy adolescents (476 ± 56). No significant correlations between subjective sleep quality or objective measures of sleep and disease activity were identified (Table 1). All subjects reported no issues with compliance with the actigraph.

Conclusions: Actigraphy is a feasible tool for examining sleep patterns in pediatric IBD. Interim analysis has not identified a correlation between disease activity and either subjective or actigraphic measures of sleep, possibly due to small sample size and homogeneity in population

(only mild-moderately active patients). These findings are being further explored in a larger number of subjects, including subjects with moderate-severe disease activity (recruitment ongoing).

Table 1 (Pearson Correlation Coefficient)

Variables	Correlation Coefficient	P-Value
ASWS-TST	-0.34	0.30
ASWS-SE	-0.06	0.87
ASWS-PCDAI	0.05	0.88
TST-PCDAI	0.24	0.47
TST-ESR	-0.31	0.36
TST-CRP	-0.16	0.64
SE-PCDAI	-0.29	0.39
SE-ESR	-0.33	0.33
SE-CRP	-0.26	0.43

ASWS- Adolescent Sleep Wake Scale, TST- total sleep time, SE- sleep efficiency, PCDAI- Pediatric Crohn's Disease Activity Index, ESR- Erythrocyte Sedimentation Rate, CRP- C-reactive protein.

1054 GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR BIOACTIVITY AND TIME TO SURGICAL RECURRENCE IN PATIENTS WITH ILEAL CROHN'S DISEASE

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Background: Surgical recurrence for patients with ileal Crohn's disease (CD) is reported to be as high as 50% within 10 years after initial ileocolic resection. We have previously reported that elevated levels of neutralizing Granulocyte-Macrophage Colony-Stimulating Factor auto-antibodies (GM-CSF Ab) are associated with stricturing behavior and surgery in CD. Whether GM-CSF bioactivity would also be associated with surgical recurrence (T2) was not known. The Aim of this study was to examine the association of GM-CSF bioactivity with recurrence of surgery after initial ileocolic resection for ileal CD. We also included additional clinical, serologic and genetic factors in the analysis.

Methods: Patient characteristics were recorded and blood samples were obtained from 411 subjects from the Digestive Diseases Research Core Center (DDRCC) at Washington University Medical Center in St. Louis, MO. All patients had ileal CD and history of surgery for management of disease. Serum and DNA were isolated and samples were analyzed for GM-CSF Ab, GM-CSF cytokine, ASCA IgA, and ASCA IgG assays and genetic risk markers, respectively. Genetic risk markers tested included IBD risk alleles for NOD2, ATG16L1, IRGM, CARD9, XBP1 and ORMDL. In order to detect risk factors associated with early surgical recurrence, a cox proportional hazard model was fitted with main effects and first-order interactions of clinical, serologic, and genotype variables.

Results: The serum GM-CSF Ab level was elevated at a median (IQRs) of 3.81 (0.93-11.01) mcg/mL consistent with our previous studies. Factors associated with early surgical recurrence (T2) included elevated serum GM-CSF Ab level, exposure to anti-TNF therapy, and a smoking history. Patients with elevated GM-CSF Ab level and simultaneously elevated ASCA IgG had longer survival to T2 but this interaction had a small effect. Patients with low GM-CSF cytokine level had significantly more C difficile infections ($p=0.02$) and concomitantly a shorter time to surgical recurrence. Conversely, patients with elevated GM-CSF cytokine level and prior exposure to anti-TNF agents had significantly longer survival to T2. None of the genetic risk markers analyzed were associated with shorter survival to T2.

Conclusions: Elevated GM-CSF Ab likely results in reduced bioactivity of GM-CSF cytokine which plays an important role in the regulation of mucosal innate immunity. We report the complex interaction of these two markers with serologic and extrinsic risk factors and their impact upon surgical recurrence.

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1055 STUDY ON ASSOCIATION OF HLA-I GENE POLYMORPHISMS WITH PEDIATRIC INFLAMMATORY BOWEL DISEASE

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Objective: The purpose of this research is to study human leukocyte antigen-I (HLA-I) gene polymorphisms and analyze the association between HLA-I predisposing genes and clinical characteristics of pediatric inflammatory bowel disease with Han nationality.

Methods: Forty-five cases of pediatric inflammatory bowel disease with Han nationality were investigated for HLA-I alleles by PCR-SSO.

Controls include 283 healthy Han Chinese people, their HLA-I alleles were based on NCBI dbMHC database. The two groups' allele frequencies were compared using the Chi-squared test or Fisher's exact test, when appropriate. Association between HLA-I predisposing genes and disease were analyzed by calculating the odds ratio (OR) and 95% confidence interval (95% CI).

Result: The correlation between HLA-I gene polymorphisms and inflammatory bowel disease. Frequencies of HLA-A*02:01, A*30:01, A*68:01, HLA-B*13:02, B*15:11, B*39:01, B*40:06 and HLA-C*06:02 in inflammatory bowel disease patients were 24.44%, 11.11%, 4.44%, 11.11%, 8.89%, 6.67%, 11.11%, 15.56%, respectively, which were significantly higher than those (9.89%, 3.18%, 0.00%, 3.53%, 0.35%, 0.35%, 2.47%, 5.30%) in controls, and the ORs (95% CI) were 2.946 (1.345-6.453), 3.806 (1.214-11.928), 32.586 (1.538-690.199), 3.413 (1.109-10.497), 27.512 (3.001-252.216), 20.143 (2.047-198.169), 4.929 (1.493-16.275), 3.291 (1.261-8.590), respectively, the p -values were 0.005, 0.030, 0.018, 0.040, 0.001, 0.009, 0.015, 0.020, respectively. Frequency of HLA-A*02:03 in inflammatory bowel disease patients was lower than the control group (6.67% vs. 19.79%), and the OR was 0.290, 95% CI, 0.087-0.968, the p -value was 0.033. There was statistically significant difference in allele frequencies between the two groups. The association between HLA-I predisposing genes and clinical characteristics of inflammatory bowel disease. There was no significant difference between HLA-I predisposing genes and patients' age and gender ($p>0.05$). Compared to controls, the frequency of HLA-B*40:06 increased significantly in colonic Crohn's disease patients (33.3% vs. 2.5%, OR=19.714, 95% CI, 3.082-126.102, $p=0.012$), and the frequencies of HLA-A*30:01, HLA-B*15:11, HLA-C*06:02 increased significantly in Crohn's disease patients with upper gastrointestinal disease (25.0% vs. 3.2%, OR=10.148, 95% CI, 1.794-57.390, $p=0.032$; 25.0% vs. 0.4%,

OR=94.000, 95% CI, 7.466-1183.567, $p=0.002$; 37.5% vs. 5.3%, OR=10.720, 95% CI, 2.338-49.156, $p=0.009$, respectively). The difference of allele frequencies between the two groups was statistically significant.

Conclusion: HLA-A*02:01, A*30:01, A*68:01, HLA-B*13:02, B*15:11, B*39:01, B*40:06 and HLA-C*06:02 may be the predisposing genes in pediatric patients with inflammatory bowel disease with Chinese Han nationality, and HLA-A*02:03 may be a protective factor for inflammatory bowel disease. Among them, HLA-A*30:01, HLA-B*15:11, B*40:06 and HLA-C*06:02 are associated with the extent of Crohn's disease.

Key words: Inflammatory bowel disease, HLA-I gene, Genetic susceptibility

1056 SAFETY AND EFFICACY OF ORAL, DELAYED-RELEASE MESALAMINE IN CHILDREN AND ADOLESCENTS FOR THE MAINTENANCE OF REMISSION OF ULCERATIVE COLITIS

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Introduction: Approximately 15-20% of patients with ulcerative colitis (UC) are children. Oral, delayed-release mesalamine is approved by the FDA for the treatment of mildly to moderately active UC in both adults and children (>5 years), and for the maintenance of remission of UC in adults. This study investigated the safety and efficacy of oral, delayed-release mesalamine for the maintenance of remission in children and adolescents with UC.

Methods: This was a randomized, double-blind, parallel-group, multicenter, multinational study. Patients aged 5-17 years with a history of UC who had been in complete remission for >/ 1 month, with a baseline Pediatric Ulcerative Colitis Activity Index (PUCAI) score <10, a history of >/ 1 active episode in the past 12 months, and who had taken a stable dose of oral mesalamine for >/ 1 month prior to study entry, were eligible. Patients were randomized to receive low- (27-71 mg/kg/day) or high-dose (53-118 mg/kg/day) oral, delayed-release mesalamine for 26 weeks; dose was stratified by body weight (>/ 17 to <33 kg; >/ 33 to <54 kg; >/ 54 to </ 90 kg). Patients were clinically assessed at Weeks 12 and 26; the primary endpoint was the proportion of patients who maintained complete remission through Week 26 as determined by a PUCAI score <10 during the entire study period. Secondary endpoints included the proportion of patients who maintained complete remission through Week 26 using an amended PUCAI score in which the 3-level abdominal pain question was replaced by a 5-level abdominal pain question. Adverse events (AEs) were monitored throughout the study.

Results: 39 patients were randomized and 21 completed the study (11 in the low- and 10 in the high-dose group); 54% of patients were female and the mean (range) age was 13 (8-17) years. The main reason for discontinuation was termination of the study due to recruitment difficulties (n=9). In the ITT population (n=39), 45% (9/20) and 42% (8/19) of patients maintained complete remission through Week 26 based on the primary endpoint, and 45% (9/20) and 47% (9/19) based on the secondary endpoint, in the low- and high-dose groups, respectively. AEs were reported for 55% (11/20) and 68% (13/19) of patients in the low- and high-dose groups, respectively, and most AEs were classified as mild (70%) or moderate (26%). The most common AEs were diarrhea and headache, both occurring in 10% of patients overall (Table). One patient in each dose group had a serious AE: exacerbation of UC and anemia, respectively.

Conclusion: Both low- and high-dose oral, delayed-release mesalamine appeared to be a viable treatment option for the maintenance of remission for children and adolescents with UC. Based on these limited data, there does not appear to be an advantage to prescribing high-dose mesalamine during stable remission. Both the low and high doses of oral mesalamine were well tolerated and the nature and severity of AEs were consistent with previous studies in children and adults.

Table. Adverse events occurring in ≥5% of mesalamine-treated patients overall

n (%)	Low dose (n=20)	High dose (n=19)	Overall (N=39)
Any AE	11 (55.0)	13 (68.4)	24 (61.5)
Serious AEs	1 (5.0)	1 (5.3)	2 (5.1)
Discontinuation due to AEs	1 (5.0)	1 (5.3)	2 (5.1)
Deaths	0	0	0
AEs in ≥5% of patients overall			
Diarrhea	3 (15.0)	1 (5.3)	4 (10.3)
Headache	1 (5.0)	3 (15.8)	4 (10.3)
Abdominal pain	2 (10.0)	1 (5.3)	3 (7.7)
Sinusitis	1 (5.0)	2 (10.5)	3 (7.7)
Vomiting	2 (10.0)	1 (5.3)	3 (7.7)
Colitis ulcerative	1 (5.0)	1 (5.3)	2 (5.1)
Lipase increased	1 (5.0)	1 (5.3)	2 (5.1)
Nausea	1 (5.0)	1 (5.3)	2 (5.1)
Oropharyngeal pain	1 (5.0)	1 (5.3)	2 (5.1)
Pain in extremity	1 (5.0)	1 (5.3)	2 (5.1)
Upper respiratory tract infection	1 (5.0)	1 (5.3)	2 (5.1)

1057 ASSOCIATION OF SERUM AND MUCOSAL INFlixIMAB IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Influximab (IFX) is a monoclonal antibody targeting tumor necrosis factor alpha commonly used to treat inflammatory bowel disease (IBD). While serum IFX levels correlate with efficacy, there are limited data regarding how tissue IFX levels correlate with serum IFX

levels and with mucosal inflammation. The aim of this study was to determine whether there is a correlation between serum and tissue IFX levels and their relationship with endoscopic, histologic and clinical markers of disease activity.

Methods: Patients with IBD receiving IFX who had a concurrent serum sample and 2 colonic mucosal biopsies obtained at the time of colonoscopy were enrolled. Demographic and clinical features, disease activity scores, endoscopic and histologic findings, IFX dose, and IFX and Anti-IFX Ab levels were recorded.

Results: Thirty-two patients (21 Crohn's disease (65.6%), 9 ulcerative colitis (28.1%) and 2 indeterminate colitis (6.3%) were included. The mean age was 15.9 ± 4.9 years old. The median number of days between endoscopy and last IFX dose was 24. Serum IFX levels positively correlated with tissue IFX ($p < 0.001$, $r = 0.510$). There was a strong correlation in inflamed tissue ($p < 0.001$, $r = 0.625$) and moderate correlation in uninfamed tissue ($p = 0.016$, $r = 0.406$). In subjects with UC ($p = 0.001$, $r = 0.642$), serum and tissue IFX levels were strongly correlated. The mean tissue IFX levels in severely, moderately, mildly inflamed and non-inflamed mucosa (based on histology) were 0.077, 0.042, 0.047 and 0.043 $\mu\text{g/mL}$, respectively. Although tissue IFX levels in severely inflamed mucosa were higher, there was no significant correlation between histologic or endoscopic grading and tissue IFX levels. As expected, the time interval between last IFX dose and endoscopic sampling was inversely correlated with tissue IFX ($p < 0.001$, $r = -0.472$). Restricting the study group to subjects with samples collected within 24 days of last IFX infusion, tissue IFX was positively correlated with the degree of inflammation ($p = 0.013$, $r = 0.421$). All the antibody levels for tissue IFX were < 12 arbitrary units/mL. Only one patient had a measurable serum anti-IFX antibody level of 13.6 arbitrary units/mL (Tissue IFX: 0.015 $\mu\text{g/mL}$, serum IFX: 2.44 $\mu\text{g/mL}$ and no antibody in tissue).

Conclusion: Tissue IFX levels correlate with serum IFX in inflamed and non-inflamed colonic tissue. Within 24 days following IFX infusion, there was a correlation between tissue level of IFX and severity of histologic inflammation. These data suggest that tissue penetration of IFX occurs in both inflamed and non-inflamed tissue, and that persistent mucosal inflammation in patients on IFX may not be due to a lack of drug in the mucosal compartment, but rather to a different mechanism(s).

1058 ASSESSMENT OF NORTH AMERICAN PEDIATRIC GASTROENTEROLOGISTS ON UTILIZATION OF BOWEL ULTRASOUND IN DIAGNOSIS AND MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

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Objective: Inflammatory bowel disease (IBD) is a chronic relapsing disease that requires evaluation with multiple objective tools including endoscopy and imaging modalities. The use of radiologic techniques varies worldwide. Our goal was to identify the current practice patterns of North American pediatric gastroenterology practitioners in utilizing bowel US in IBD patients.

Methods: A 14-question survey was emailed to the NASPGHAN PEDGI Internet Bulletin Board composed of 2903 subscribers from 52 countries. The data collected included demographics of the practitioners, indications for using bowel ultrasound (US) in IBD patients and obstacles to performing bowel US, based on availability. The data were collected and stored on a secure network using RedCap.

Results: 143 participants completed the survey; 72.7% ($n = 104$) were from academic institutions, 15.4% ($n = 22$) from non-academic hospitals and 11.9% ($n = 17$) were in private practice. In North American practices, where pediatric gastroenterology practitioners had access to bowel US the main indications were 90.0% for evaluating strictures or abscesses in Crohn's disease, 70.0% for monitoring therapeutic response in Crohn's disease, 35.0% for initial diagnosis and surveillance of Crohn's disease and 5.0% for initial diagnosis and surveillance in ulcerative colitis. Bowel US was utilized more frequently in patients with Crohn's disease than those with ulcerative colitis. 86.6% of practitioners would consider prescribing bowel US if it were available at their institution. The main limitations or obstacles to using bowel US were unfamiliarity with bowel US indications and techniques, concern for inter-observer variability and operator dependent factors in addition to perceived lack of radiologist interest and specialized US technologist training. The most common modalities currently utilized in evaluating IBD include 94.0% MRI, 53.0% CT and 41.0% fluoroscopy.

Conclusion: Our data shows that there is a significant interest among North American pediatric gastroenterology practitioners (86.6%) in utilizing bowel US. However, lack of education, availability, training, perceived low inter-observer variability and reproducibility of US are concerning limitations. Further research needs to be completed to overcome these limitations and decrease overall health care costs and ionizing radiation risks for our ever increasing younger population with IBD.

1059 USE OF INFLIXIMAB LEVEL IMMEDIATELY PRIOR TO THIRD DOSE IN DETERMINING MAINTENANCE DOSE AND FREQUENCY

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Trough level above 5 prior to 14 weeks in Infliximab (IFX) induction is associated with higher remission rate. By measuring Infliximab level early in induction may result in more optimal trough level prior to first maintenance dose.

Methods: We searched our IBD registry of all IBD children and adolescents who were treated with IFX over the last 2 years and had trough level performed at week 6 prior to third dose infusion. We aimed to determine how the 3rd level alters the dose and frequency of IFX infusion in children and adolescents

Results: We have 19 patients with trough level measured prior to 3rd dose. Twelve were male. Ten patients had Crohn's, 5 with ulcerative colitis and 1 IBD-undifferentiated. Mean age of 11.5 yrs. Mean duration to start of IFX is 142 days. Doses were 5 mg/kg round up to multiple of 100. No patient had undetectable levels. Two patients with levels less than 5 but had detectable level required dose increase and shorten duration. All 4 patients with levels between 5- 10 required shorten infusion to every 4 weeks. Those with level > 10 were infused at every 6 to 8 weeks. Prior to the 4th dose, all patients had detectable level prior to 4th dose. Only 2 patients had level 2.5 and 1.8 respectively. One patient had a level at 3.8 and the remaining patients had level above 4.

Conclusion: Using week 6th trough level, to determine frequency and dose of first maintenance, we were able to achieve adequate trough level in most of our patients post-induction.

1060 FREQUENCY OF INFLUENZA VACCINATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS AT AN URBAN TERTIARY CARE CENTER

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Background: Patients with inflammatory bowel disease (IBD) are at increased risk of vaccine-preventable illness because of underlying disease, malnutrition, and immunosuppressive therapies. Compared to their immunocompetent peers, these children are at greater risk of complication from illness as well. Barriers to vaccination in this population include concerns from the patient and physician about safety and efficacy of the vaccine, lack of knowledge about vaccination guidelines, and belief that it is the primary pediatrician's responsibility to administer vaccines. Clinical guidelines, both internationally and from the Center for Disease Control (CDC), recommend annual influenza immunization for patients with IBD, noting that caution should be used with administration of live vaccine. Though the influenza vaccine is safe and recommended for children with IBD, influenza vaccination rates in this population continue to be suboptimal, with published rates ranging from 7.8% to 50% internationally.

Methods: Chart review was performed of all encounters of patients with IBD, defined as Crohn's disease, ulcerative colitis, or indeterminate etiology, seen in the gastroenterology clinic at St. Christopher's Hospital for Children, an urban tertiary care facility, from September 2015-March 2016. Progress notes and immunization data in the EMR were reviewed. Phone calls were made to primary pediatricians in the case that influenza vaccination status was not documented in the EMR. We noted whether patients received the influenza vaccine in the 2015-2016 season and if the recommendation for vaccination had been documented in the gastroenterology note.

Results: A total of 95 pediatric patients with IBD met our criteria including 71% with Crohn's disease, 24% with ulcerative colitis, and 5% of indeterminate etiology. 81% were on immunosuppressive medications, which included biologics, immunomodulators, and/or systemic corticosteroids. 40% of patients received the influenza vaccine during the 2015-2016 season. Gastroenterologist documentation of the patient's vaccine status or documentation of recommendation to vaccinate was made in 39% of cases. There was a general trend, although not statistically significant, showing documentation being associated with improved vaccination rates ($p=0.12$).

Conclusions: Influenza vaccination rates in children with IBD continue to be suboptimal. The CDC reports that for the 2014-2015 flu season, 59.3% of all children between 6 months and 17 years in the US received the influenza vaccine, compared to only 40% of those with IBD at our institution. Our patient population in an urban center may be less adherent in following through with recommended vaccination, as our rates were suboptimal. Verbal recommendations may not be sufficient and further interventions may be needed. Documentation of vaccination recommendation may cause the provider to further stress this advice as well as recruit primary care support.

1061 RISK FACTORS FOR COLECTOMY IN PEDIATRIC PATIENTS WITH ULCERATIVE COLITIS: A SINGLE-CENTER EXPERIENCE

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Aim: Despite improvement of medical treatment in ulcerative colitis (UC), many patients undergo colectomy. The aim of this study was to evaluate the frequency of colectomy and to determine predictive factors of colectomy in pediatric UC patients.

Methods: We retrospectively analyzed 220 UC patients who visited Asan Medical Center between January 1991 and September 2014. Clinical, demographic and therapeutic parameters were compared between patients who did and did not undergo colectomy.

Results: A total of 18 (8%) patients underwent colectomy. The cumulative probabilities of colectomy at 5, 10, 20 years after diagnosis were 6.9%, 8.7%, 15.3%, respectively. Indications for colectomy included refractory symptoms on maximal medical therapy in 3 patients (1.4%), corticosteroid dependency/intolerance in 10 patients (4.5%), colorectal dysplasia or cancer in 2 patients (0.9%), perforation in 3 patients (1.4%). Multivariate Cox analysis revealed that extensive colitis at diagnosis (risk ratio, 5.058; 95% confidence interval, 1.13-22.644; $p=0.034$).

Conclusion: Extensive colitis was associated with increased risk of colectomy. Risk stratification will help to guide therapy that may improve the natural history of disease.

1062 CAN INFLIXIMAB MONOTHERAPY BE AS EQUALLY EFFECTIVE AS COMBINED THERAPY? – A STUDY IN 100 PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Crohn's disease (CD), ulcerative colitis (UC) and indeterminate colitis (IC), commonly known as inflammatory bowel disease (IBD), represent a heterogeneous group of diseases with unknown aetiology and variable evolution, diagnosed in a pediatric age at 25 to 30% of cases. Infliximab (antitumor necrosis factor) is used in IBD moderate to serious, without response to corticosteroid treatment, immunosuppression or intolerance to conventional therapy. The therapeutic scheme with infliximab is usually combined, but the increased risks have trigger debate and concern.

Aims and Methods: Characterization of the pediatric population diagnosed with IBD and treated with infliximab, followed in a Pediatric Gastroenterology Unit of a tertiary hospital center. Retrospective and descriptive study was designed between January 2001 and April 2016. Porto Criteria - ESPGHAN were used to define IBD at presentation. We considered disease control when CRP was negative (<2.9 mg/L) without symptoms. Patients with infliximab in monotherapy or combined therapy were analyzed.

Results: IBD was diagnosed in 100 patients, 67.0% with CD ($n=67$), 31.3% with UC ($n=33$), a total of 50% male. The age at diagnosis varied between 11 months and 17 years old, with median age of 14 years. Average time between the beginning of symptoms and diagnoses was 0.6 years \pm 0.8 years (7 months); median follow-up was 4 years (minimum 1 month, maximum 15 years). Rise in incidence of IBD over the last 8 years (2009-2016), $p=0.03$ (total 75: average 9.3 cases/year), comparatively to the period of 2001-2008 (total 26: average 3.25 cases/year). A third of the patients (33.0%) are being treated with infliximab (29 with CD, 4 with UC) for present active and refractory disease to the conventional treatment (enteric nutrition, immunosuppression and corticotherapy). Three patients began infliximab in top-down regimen for fistulising, stenotic and/or severe perianal CD. During the treatment with infliximab 3 allergic/anaphylactic reactions were documented and switch to adalimumab. Among the patients who began the clinical protocol with infliximab, 23 (69.7%) are treated with monotherapy, from which 16 (69.6%) are controlled. Fourteen patients are not strictly controlled. There was no significant difference between infliximab monotherapy group and the one treated with combined therapy (infliximab and azathioprine), $p=0.165$.

Conclusions: The results show an increasing incidence of IBD, particularly in CD. Similar to the literature, infliximab was reserved for the most severe cases and proved to be safe and effective in the control of IBD. The use of combine therapeutic did not reveal to be more effective when

compared to the infliximab in monotherapy. Due to the increase of infections and neoplasia, especially in pediatric population, we should embrace the challenge of infliximab as monotherapy. However, there's a need for further studies, randomized and clinically controlled.

1063 *EVOLUTION OF GROWTH IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE FOLLOWING ANTI-TNF ALPHA THERAPY*
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Introduction : Growth delay is common in pediatric inflammatory bowel diseases (IBD). Improvement of growth is one of the goals of treatment. The efficacy of anti-TNF α on clinical remission has been proved. But the effects on growth are still unclear. The aim of this study was to analyze the growth development of children with IBD treated by anti-TNF α . Then we studied the factors capable of changing growth development.

Subjects and Methods: Sixty-five prepubescent patients (54 Crohn's disease, 7 ulcerative colitis and 4 unclassified colitis) treated with infliximab (n=49) or adalimumab (n=16) were retrospectively included in the University hospitals of Toulouse and Strasbourg between 2003 and 2015. Weight and height, pubertal stage, nutritional state, clinical and biological remission were noted at diagnosis, initiation of the treatment (T0), 1 year before (T-1), 1 year after (T+1), 2 years after (T+2) and at maximal time under anti-TNF α . Z-scores of height, growth velocity and difference between height and genetic target height or between height and height before the disease were compared at T-1, T+1, T+2 with regard to T0. Evolution of the Z-scores of height and growth velocity were compared for 2 modalities of the following factors: clinical and biological remission, puberty stage, initial growth delay, malnutrition, type of pathology, type of anti-TNF α , duration of corticotherapy. Results : Growth velocity improved from 4.4 standard deviations (SD) at T+1 and 4.2 SD at T+2 in univariate and multivariate analyses ($p < 1.10 \cdot 10^{-5}$), reaching 1.3 SD at T+2. Median height was -0.07 SD at T0 and improved by 0.2 SD at T+1 ($p = 0.02$) and 0.3 SD at T+2 ($p = 0.002$). Difference with genetic target height went from -0.7 SD at T0 to -0.5 SD at T+1 ($p = 0.004$) and -0.4 SD at T+2 ($p < 0.001$). Difference with height before the disease (-0.9 SD at T0) decreased by 0.2 SD at T+2 ($p = 0.04$). Modifications of these 3 indicators were not significant in the multivariate analysis. A growth delay persisted in 17% of patients at maximal time. Initial growth delay was associated with a greater improvement in growth velocity between T0 and T+1 (+5 SD versus +1.5 SD, $p = 0.01$). Children with pubertal progress during the follow-up presented increased growth velocity compared with prepubertal children (+1.7SD vs. -1.9 SD, $p = 0.01$). Corticotherapy associated with anti-TNF α for less than 3 months resulted in a more significant improvement in height compared with a longer period of corticotherapy (+0.3SD vs. -0.1SD, $p = 0.003$).

Conclusion : Instauration of anti-TNF α treatment is followed by a clear increase in growth velocity. But the effects on height and on difference with genetic target height seem to be less significant. Optimization of anti-TNF α therapy, with a better follow-up of inflammation and earlier initiation of treatment, may help to improve these benefits.

1064 *EFFECT OF ANEMIA ON HEALTH RELATED QUALITY OF LIFE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE*
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Background: Health-related quality of life (HRQL) is an important outcome measure in pediatric inflammatory bowel disease (IBD) research. The adverse effects of gastrointestinal symptoms on HRQL are well documented, but little is known about the impact of anemia, the most common extra-intestinal manifestation of IBD.

Objective: Evaluation of the impact of anemia on HRQL in children with IBD in remission.

Methods: Patient inclusion criteria: Age 0-18 years, diagnosis of IBD and treatment with infliximab to avoid possible confounding effects of various medications. Disease activity for Crohn's disease (CD) and ulcerative colitis (UC) was assessed with PCDAI and PUCAI respectively. For both indices scores <10 are consistent with remission. HRQL was assessed with the PedsQL 4.0 survey. HRQL scores include six domains, child-reported psychosocial, physical, total scores and parent-reported values for the same. Scores below 1 standard deviation from population means are consistent with at-risk status for impaired HRQL according to published data. Laboratory studies included hemoglobin (Hb), transferrin saturation (TSAT), ferritin and C-reactive protein (CRP). Anemia was defined according to general WHO criteria. Iron deficiency was defined as either low ferritin or TSAT, according to IBD consensus criteria. Mean HRQL scores and hematology indices were compared using a two-sample t-test. Comparisons of the proportions of subjects with at-risk HRQL scores between subgroups were conducted using Fisher's exact test. All p -values are two-sided and $p < 0.05$ was used for defining statistical significance.

Results: 27 patients (11 females), 24 with CD (10 females), 3 with UC (1 female) participated in the study. Mean age was 11 (range 5-16) years at diagnosis and 13.7 (7-18) years at the time of the study. 14/27 patients had anemia (3/3 with UC and 11/24 with CD) and all were iron deficient. 3/3 UC patients and 16/24 CD patients were in remission. Of these 19 patients, 8 were anemic with a mean (\pm SE) Hb of 10.9 (± 0.6) g/dL and 11 were not anemic with a mean (\pm SE) Hb of 13.3 (± 0.2) g/dL. Mean (\pm SE) HRQL scores for the 8 patients with anemia vs. the 11 without anemia were: 71.8 (± 7), 73.0 (± 6.8), 72.3 (± 6.4), 66.1 (± 6.5), 75.0 (± 6.7), 68.6 (± 6.6) vs. 83.9 (± 3.7 , $p = \text{NS}$), 91.1 (± 2.7 , $p = 0.01$), 86.3 (± 3 , $p = 0.04$), 84.8 (± 2.4 , $p = 0.008$), 91.9 (± 2 , $p = 0.01$), 87.1 (± 1.7 , $p = 0.006$). The proportion of patients with at-risk scores in at least one HRQL domain among those with vs. without anemia was 62.5% vs. 9.1% ($p = 0.04$).

Summary and Conclusions: Our findings show that anemia has significant impact on HRQL in children with IBD regardless of disease activity. Given the high prevalence, a proactive approach to the diagnosis and treatment of anemia could significantly improve HRQL for a substantial number of these children.

1065 *LIVER RECEPTOR HOMOLOG-1 MEDIATES LIGAND-DEPENDENT PROTECTION OF INTESTINAL EPITHELIUM FROM CELL DEATH*

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Background: Epithelial-based therapeutics have the potential to enhance wound healing and reconstitution of the epithelial barrier that is compromised in IBD. We have previously shown the nuclear receptor Liver Receptor Homolog-1 (LRH-1, also known as NR5A2) is involved in maintaining intestinal epithelial viability and barrier integrity. Our goal is to define the mechanism behind these findings and to develop a biologically relevant platform for drug discovery.

Methods: To evaluate the contributions of LRH-1 to intestinal pathophysiology, we pursued a combination of mouse and intestinal organoid studies utilizing conditional intestinal epithelial LRH-1 knockout (termed Lrh1IEC-KO). Because of critical species differences in the LRH-1 ligand binding pocket between mouse and human isoforms that result in greater ligand dependence for human LRH-1 (hLRH-1) activity, we created methodologies to humanize LRH-1 expression in both intestinal organoids and in intestinal epithelium of mice. Following Lrh1 knockout, the intestinal epithelium was examined for morphology, viability, and cell death using a combination of biochemical assays and immunofluorescence microscopy. To probe the genetic regulatory mechanisms underlying our findings we performed RNA-Seq mRNA profiling. Using an hLRH-1 mutant defective in ligand uptake (hLRH-Mut), we evaluate the role of ligand binding in viability.

Results: Cell death marked by Caspase-3 activation following LRH-1 loss is detected by Western blot analysis and immunofluorescence. Marked Caspase-3 accumulation is found in the intestinal crypts of both organoid and animal knockouts. This finding is reversed by hLRH-1. Surprisingly, villus morphology of Lrh1IEC-KO animals is altered, showing goblet cell expansion throughout the crypt-villus axis. Transcriptomic analysis of Lrh1IEC-KO and hLRH-1 organoids demonstrates significant alterations in cell death and cell signaling pathways and identifies potential new anti-inflammatory targets for hLRH-1. Finally, we show the mutant receptor hLRH-Mut is unable to rescue epithelial viability following TNF α challenge.

Conclusions: Loss of LRH-1 results in induction apoptosis in intestinal crypts and activation of cell death pathways. Small intestinal goblet cell expansion, together with transcriptomic analysis showing altered epithelial differentiation factor expression, suggest LRH-1 plays a role in epithelial differentiation and Notch signaling. Failure of hLRH-Mut to rescue intestinal viability demonstrates the importance ligand binding and suggests hLRH-1 is a viable target for novel, epithelium-targeted IBD therapy. We are now using humanized organoids to screen LRH-1 small molecule agonists we predict will suppress TNF α -mediated inflammatory damage.

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**1066 IMMUNOGENICITY AFTER SWITCHING FROM REFERENCE INFlixIMAB TO BIOSIMILAR IN CHILDREN WITH CROHN'S DISEASE*

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Background: Immunogenicity of biosimilar were tested in clinical trials in rheumatoid disease. Based on good comparison with reference infliximab, biosimilars have been approved to the same indications as originator. Lower price of biosimilar involved their common use, unavailability of reference infliximab lead to switching patients to biosimilar infliximab.

Aim of the study was to compare immunogenicity before and after switching.

Methods: All patients with Crohn's disease who had changed drug from reference infliximab to biosimilar in the same course of therapy were enrolled. All patients were asked for permission to take blood sample for assessment of drug level and presence of anti-TNF antibodies performed by ELISA method. Plasma were frozen till time of laboratory analysis. Retrospective assessment of IFX level and ATI presence were performed before drug change, around 2nd and 5th infusion of biosimilar. PCDAI (Pediatric Crohn's Disease Activity Index), patients characteristics, laboratory value as albumin, Hb, PLT, ESR, CRP were recorded. Statistical analysis were performed.

Results: 16 CD patients (11 M, 5 F) were enrolled to the study. Mean age at switching was At time of switching 14/16 patients had therapeutic level of IFX (>1.5 $\mu\text{g/mL}$) and 7 of them presented positive ATI level (>2 ng/mL). 1 patient had subtherapeutic level of IFX with presence of ATI and 1 patient presented with negative level of IFX (<0,035 $\mu\text{g/mL}$) with negative ATI level (<2 ng/mL). There were not recorded any correlation to disease activity or laboratory value. Assessment of immunogenicity around 5th dose of biosimilar which was made in 15 patients showed decrease of ATI level versus assessment before switching. All 15 patients had therapeutic IFX level and among them only 4/15 had ATI >2 ng/mL. We observed dependence that higher antibody level correspond to inferior drugs value. Statistical significance was marked on level antibody and PLT value - the higher antibodies level corresponded with higher PLT value.

Conclusion: Our study shows first assessment of immunogenicity in pediatric Crohn's disease patients who needed switching to biosimilar. After drugs change we have not detected higher immunogenicity. Lack of correlation before switching can be due to small group. Further analyses are needed.

1067 NETWORK MODELLING OF CROHN'S DISEASE INCIDENCE

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Background: Numerous genetic and environmental risk factors play a role in human complex genetic disorders (CGD). However, their complex interplay remains to be modelled and explained in terms of disease mechanisms.

Methods and findings: Crohn's disease (CD) was modelled as a modular network of patho-physiological functions, each summarizing multiple gene-gene and gene-environment interactions. The disease resulted from one or few specific combinations of module functional states. Network aging dynamics was able to reproduce age-specific CD incidence curves as well as their variations over the past century in Western countries.

Within the model, we translated the odds ratios (OR) associated to at-risk alleles in terms of disease propensities of the functional modules. Finally, the model was successfully applied to other CGD including ulcerative colitis, ankylosing spondylitis, multiple sclerosis and schizophrenia.

Conclusion: Modelling disease incidence may help to understand disease causative chains, to delineate the potential of personalized medicine, and to monitor epidemiological changes in CGD.

1068 HEALTH-RELATED QUALITY OF LIFE IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS RECEIVING INFlixIMAB: A PILOT STUDY USING THE IMPACT-III QUESTIONNAIRE

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Background: Anti-TNF α agents are effective in the induction and maintenance of remission in pediatric inflammatory bowel disease (IBD). While health-related quality of life (HR-QoL) has been shown to improve with anti-TNF α therapy, little is known about the risk factors in those patients who persist with poor HR-QoL. The IMPACT-III HR-QoL assessment tool has been validated in IBD patients age 9 through 17.

Through this cross-sectional pilot study, we aim to further characterize the HR-QoL in patients receiving infliximab (IFX) in our institution, hypothesizing that many patients have a low HR-QoL despite being in clinical remission.

Methods: The IMPACT-III HR-QoL assessment tool was used by permission (Dr. Anthony Otley, Dalhousie University, Halifax, NS, Canada) and scored according to guidelines in six domains: bowel symptoms, emotional functioning, social functioning, systemic symptoms, body image, and treatments/interventions. We administered the IMPACT-III to 71 patients during their scheduled IFX infusion. Results were retrospectively recorded and compared with demographic and disease characteristics. Standard two-tailed T-tests and ANOVA were used to evaluate significance between disease characteristics and HR-QoL.

Results: 58 (82%) patients had CD, 13 (18%) patients had UC/IC. The mean patient age was 15.4 years (range 9.3-17.9). Mean length of treatment on IFX was 2.1 years. The mean IMPACT-III score of patients on IFX was 74.5 ± 12.7 (74.8 ± 13.5 for CD, 72.8 ± 8.4 for UC/IC, NS). The total HR-QoL score was significantly lower among female patients ($P=0.008$), patients with active disease ($p=0.021$), and patients not in sustained remission ($p=0.017$). Factors affecting individual HR-QoL IMPACT-III domain scores are listed in Table 1.

Discussion: We were able to demonstrate feasibility of HR-QoL assessment in a cohort of IBD patients on IFX therapy. Overall, the mean IMPACT-III score in patients receiving IFX was 74.5, a score that generally correlates with patients who describe themselves as feeling only "fair", raising concerns about underlying disease activity and/or poor psychosocial functioning. With preliminary implementation of IMPACT-III screening in our patient population, we were able to identify at-risk individuals to whom we could consider directing psychosocial resources. Limitations of this study include small sample size, the lack of a comparison group and the retrospective, cross-sectional study design. Future studies should include longitudinal assessments of HR-QoL. Our results underscore the importance of HR-QoL assessment as part of a multidisciplinary care model in pediatric IBD.

Table 1: Factors significantly decreasing HR-QoL IMPACT-III domain scores.

	Female Gender	Active Disease (PGA)	Not in Sustained Remission	Perianal Crohn's Phenotype	Time on IFX (<1 year or >3 years)	Elevated CRP	ED Visit or Hospitalization
Bowel Symptoms	NS	NS	$p=0.008$	NS	NS	$p=0.005$	NS
Emotional Functioning	$p=0.002$	$p=0.045$	$p=0.020$	NS	$p=0.017$	NS	$p=0.037$
Social Functioning	NS	$p=0.024$	NS	NS	NS	NS	$p=0.034$
Systemic Symptoms	NS	$p=0.010$	NS	NS	NS	NS	NS
Body Image	NS	NS	NS	NS	NS	NS	NS
Treatment/Interventions	$p=0.014$	NS	NS	$p=0.014$	NS	NS	NS
Total Score	$p=0.008$	$p=0.021$	$p=0.017$	NS	NS	NS	NS

1069 SPECIFIC CARBOHYDRATE DIET: RELATIONSHIP OF CLINICAL RESPONSE, MICROBIOTA, AND CYTOKINE PROFILES IN PEDIATRIC CROHN'S DISEASE

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Background and Objective: Emerging evidence suggests therapeutic potential of Specific Carbohydrate Diet (SCD) in Crohn's disease (CD). However, longitudinal biochemical and microbiota data are lacking to substantiate SCD as conventional therapy. We aimed to: 1) determine pilot clinical responsiveness in pediatric CD patients on SCD, and 2) evaluate changes to patient-level microbiota and cytokine profiles.

Methods: We conducted a prospective cohort study in 8 children with CD with longitudinal follow-up from pre-SCD to 1-6 months after SCD initiation. Stool microbial alpha- and beta-diversity were compared from similarly-aged healthy non-CD controls with the SCD CD cohort.

Results: SCD was started at a mean age of 13.2 ± 3 years. While on SCD, 6 of 8 patients completed the full 6 months of follow-up; 4 of 8 patients achieved clinical response or remission as measured by PCDAI, symptomatology, and lab values (Table 1). Multiplexed serum cytokine analysis revealed distinct subsets of patients distinguished by polarized trends in pro-inflammatory cytokine levels. Temporal cytokine profiles did not correlate with clinical responses in all patients. For all six patients on SCD for 6 months, there was an overall decline in IL1B, IL6, MIP1a, and MIP1B levels, although 2 patients had initial variability. Baseline alpha diversity indices (Chao I, observed species) in healthy controls had greater microbial diversity than the SCD CD cohort. Persistence on SCD increased microbiota diversity, trending towards the microbiota profiles of healthy controls. No association was observed using beta diversity indices in PCoA between SCD responders vs. non-responders.

Conclusion: Clinical response or remission is feasible and potentially sustainable on SCD in pediatric CD patients. In a small pilot cohort, no correlation between pro-inflammatory cytokines and microbiota OTU clustering was noted. However, increased microbiota diversity on SCD may explain a potential therapeutic mechanism of SCD.

Table 1. Clinical response of pediatric Crohn's disease patients on SCD

Gender	Age (yrs)	PCDAI Start	PCDAI FU	ESR (mm/hr) Start	ESR (mm/hr) FU	Alb (g/dl) Start	Alb (g/dl) FU	Calprotectin (ug/g) FU	Clinical Response
F	8.2	12.5	2.5	25	26	3.9	4	286	Yes
M*	12.1	15	30	3	11	4.1	3.7	***	No
M	11.5	12.5	0	25	8	2.9	3.8	<15.6	Yes
F	12.5	5	0	15	8	3.2	3.7	<15.6	Yes
M	18.7	40	10	29	17	3.8	3.8	283	Yes
M†	13.7	35	42.5	39	48	2.9	2.7	***	No

M	13.2	0	0	8	2	4	4.2	48	Yes
M	15.4	42.5	15	72	53	2.6	3.7	80	No

*Completed 3 months of follow-up

†Completed 1 month of follow-up

1070 VITAMIN D STATUS AND BONE MINERAL DENSITY IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE COMPARED TO THOSE WITH FUNCTIONAL ABDOMINAL PAIN

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Introduction: All patients with inflammatory bowel disease (IBD) are at risk of developing reduced bone mineral density (BMD) although the pathophysiology is not completely understood. In children with IBD, vitamin D deficiency is common and considered as one of the contributors to low BMD. Our study evaluated differences in serum 25-hydroxyvitamin D [25(OH)D] and BMD Z-scores in children with Crohn's disease (CD), ulcerative colitis (UC), and abdominal pain-related functional gastrointestinal disorder (AP-FGID) as the control group. We also examined the correlation between serum 25(OH)D and BMD Z-score, and the factors that affect each of these parameters.

Methods: A total of 105 children (68 boys and 37 girls, aged 5-20 years) were included in this retrospective study and divided into 3 groups: AP-FGID (n=45), CD (n=43), and UC (n=17). Anthropometric data and laboratory test results, including serum 25(OH)D measured by liquid chromatography-tandem mass spectrometry, were reviewed. Total body less head (TBLH) BMD was expressed as Z-scores adjusted for age and sex.

Results: Although serum 25(OH)D levels were not significantly different among the 3 groups, TBLH BMD Z-scores were found to be significantly different (0.5 ± 0.8 in CD vs. 0.1 ± 0.8 in UC vs. -0.1 ± 1.1 in FGID, $p = 0.037$). Correlation between 25(OH)D and TBLH BMD Z-score was not observed within each study group. Factors found to affect the TBLH BMD Z-score were sex ($p = 0.018$), age ($p = 0.005$) and serum haemoglobin ($p = 0.041$). Factors found to affect 25(OH)D were sex ($p = 0.018$), CD with reference to AP-FGID ($p = 0.020$), and serum phosphorus ($p = 0.018$).

Conclusion: While vitamin D status was not found to significantly influence the TBLH BMD Z-score in children with IBD, factors such as gender, age and haemoglobin may affect BMD in these children. Given the complex pathophysiology of low BMD in pediatric IBD, more studies need to be conducted to better evaluate IBD children at risk of developing low BMD and poor bone health later in life.

1071 PREVENTION OF PERIANAL DISEASE AMONG PEDIATRIC PATIENTS WITH CROHN'S DISEASE IN A PEDIATRIC INFLAMMATORY BOWEL DISEASE QUALITY IMPROVEMENT COLLABORATIVE

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Background: Although perianal complications of Crohn's disease (CD) are commonly encountered in clinical practice, evidence for effective preventive strategies are lacking. We sought to determine if early effective therapy was associated with reduction or delay in development of perianal disease in a large population of pediatric CD patients.

Methods: We used the ImproveCareNow (ICN) Network registry to identify CD patients (May 2006-October 2014); inclusion in this study required consent. ICN is a multicenter pediatric inflammatory bowel disease (IBD) quality improvement collaborative. Clinicians prospectively record physical examination, Paris phenotype classification and medication usage at each outpatient IBD visit. Perianal exam findings and concomitant change in perianal phenotype were used to corroborate time of new-onset perianal disease. We included only patients who had no perianal fistula within 4 mo after diagnosis. Early medication usage (started in first 3 months after diagnosis) was evaluated regardless of later medication changes. "Effective therapy" was defined as immunomodulator (thiopurine or methotrexate) or anti-tumor necrosis factor alpha therapy (anti-TNF α). Bivariate analyses used Chi-square. Time to perianal fistula development was analyzed by robust Cox proportional hazard models clustered by practice site.

Results: The ICN registry included 10,969 patients (44% female) from 65 sites; 7,076 (65%) were classified as having CD and 397 (6%) were excluded for missing/conflicting entries. Complete data were available for calculating cumulative incidence of perianal disease in 6,679 patients, among whom 2,034 (30%) met inclusion criteria. Overall 38% were treated early with immunomodulators, 11% with anti-TNF α and 44% with steroids. Patients ≥ 10 yrs at diagnosis were more likely receive early anti-TNF α (12% vs. 5%; $p < 0.001$). There were no racial differences in early medication treatment. Regionally, early anti-TNF α was most commonly prescribed in the western US (23%) and least in England (8%; $p = 0.02$).

In total, 98 (5%) patients developed perianal disease after 4 months. Patients receiving early effective therapy were less likely to develop perianal disease (2% vs. 7%; $p < 0.001$). Early immunomodulator or steroid use was associated with decreased perianal disease although this was not significant in multivariate analyses (see Table). Multivariate analysis revealed early effective therapy without steroids was associated with greater time free from perianal disease (HR 0.06, $p = 0.003$). There were no interactions between medications and race.

Conclusions: In this large multicenter study of pediatric CD, early use of immune suppressive therapy was associated with delay or prevention of perianal disease development. This is the first known evidence that perianal disease may be preventable. Prospective studies should be developed to determine if these findings are replicable so effective preventive strategies could be developed.

	Bivariate HR (95% CI)	Multivariate HR (95% CI)
Female	0.74 (0.48 – 1.13)	0.64 (0.40 – 1.00)
Age at diagnosis		
<6 yr	1.26 (0.32 – 5.07)	1.59 (0.38 – 6.60)
≥6 to <10 yr	0.51 (0.18 – 1.45)	0.65 (0.20 – 2.13)
≥10 to <14 yr	0.69 (0.29 – 1.63)	0.81 (0.33 – 2.02)
≥14 to <17 yr	1.18 (0.50 – 2.80)	1.55 (0.68 – 3.56)
≥17 yr†	--	--
Race		
Asian	5.64 (2.03 – 15.67)**	4.44 (1.14 – 17.4)*
Black	1.35 (0.75 – 2.45)	0.89 (0.40 – 1.97)
White†	--	--
Multiracial / other	2.02 (0.87 – 4.69)	1.97 (0.42 – 9.13)
Region		
London, UK	--	--
Midwest US	0.85 (0.52 – 1.41)	1.30 (0.44 – 3.87)
Northeast US	1.31 (0.79 – 2.16)	1.40 (0.61 – 3.22)
Southern US†	--	--
Western US	1.82 (0.85 – 3.90)**	1.88 (0.99 – 3.58)
Immunomodulator [^]	0.32 (0.18 – 0.58)**	0.43 (0.03 – 5.28)
Anti-TNF [^]	1.41 (0.68 – 2.93)	1.89 (0.17 – 20.8)
Steroids [^]	0.32 (0.19 – 0.55)**	0.12 (0.03 – 0.59)**
Effective therapy [^]	0.86 (0.12 – 6.20)	5.98 (0.25 – 142.6)
Effective therapy but no steroids [^]	0.68 (0.30 – 1.56)	0.06 (0.01 – 0.39)**

*p<0.05; **p<0.01

†Reference group

[^]Medication use in first 3 months after diagnosis

HR, Hazard Ratio; CI, Confidence interval; TNF, tumor necrosis factor

1072 MAGNETIC RESONANCE ENTEROGRAPHY (MRE) SURVEILLANCE OF ASYMPTOMATIC PEDIATRIC CROHN'S DISEASE PATIENTS

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Background: Magnetic resonance enterography (MRE) has become the primary imaging modality for evaluating small bowel disease activity in pediatric Crohn's disease (CD) patients. Standard practice includes imaging patients at the time of diagnosis and at symptomatic periods during their disease course. The role for MRE in surveillance of asymptomatic CD patients is not known. The purpose of this study is to analyze MRE studies performed on asymptomatic CD patients and to identify imaging features associated with future clinical recurrence.

Method and Materials: A retrospective search was performed to identify CD patients at MassGeneral Hospital for Children who were 18 years of age or younger and had MRE performed while asymptomatic. An asymptomatic state was defined by a physician's global assessment of clinical remission (quiescent) at the time of the MRE and was confirmed by health record review. MRE studies were reviewed by an experienced pediatric radiologist blinded to clinical data for presence or absence of four imaging features of activity: wall thickening, T2 hyperintensity, mural hyperenhancement, and vasa recta engorgement (Comb sign), as well as for overall assessment for active CD. Two pediatric gastroenterologists blinded to the radiographic findings reviewed the health records of all patients for the 6 months following MRE to evaluate for clinical recurrence, defined as CD-related hospital admission, surgery, or treatment escalation.

Results: 37 MRE studies performed in 36 asymptomatic CD patients were identified. 78% of patients were on anti-TNF α therapy at the time of the MRE. 10 patients (27%) demonstrated clinical recurrence within 6 months of MRE. Overall assessment of disease activity by MRE was observed in a higher proportion of patients with clinical recurrence within 6 months (80%) compared to patients without recurrence (29.6%), a statistically significant association ($p=0.01$). Among individual MRE features, mural hyperenhancement demonstrated the highest accuracy (76%) for clinical recurrence and was observed in 80% of patients with clinical recurrence vs. 26% without ($p<0.01$).

Conclusions: MRE evidence of active inflammation in asymptomatic CD patients is predictive of future clinical recurrence. Mural hyperenhancement is the imaging feature most strongly associated with clinical recurrence within 6 months. These results suggest a role for MRE in asymptomatic pediatric CD patients on treatment as such imaging may provide a window for therapy modification to prevent clinical recurrence.

1073 COMPARATIVE EFFECTIVENESS OF INFLIXIMAB AND EXCLUSIVE ENTERAL NUTRITION THERAPY IN PEDIATRIC CROHN'S DISEASE

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Background: Although exclusive enteral nutrition (EEN) and infliximab therapy have multiple advantages in treating pediatric Crohn's disease (CD), rare studies showed comparative effectiveness of those approaches in growth, symptoms improvement.

Methods: In a prospective study of children initiating EEN or infliximab therapy for CD, we compared clinical outcomes using the pediatric Crohn's disease activity index (PCDAI), growth improvement as evaluated by height for age (HFA) Z-score and body mass index for age (BMIFA) Z-score, and adverse effects. PCDAI, HFA Z-score, BMIFA z score were measured at baseline and after 8 weeks of therapy. **Results:** We enrolled 26 children with CD-PCDAI, 28.4 ± 9.5 ; HFA Z-score, -0.6 ± 1.5 ; and BMIFA Z-score, $-1.56 \pm 1.2\%$, of whom 13 were treated with infliximab, 13 with EEN. Clinical response (PCDAI reduction ≥ 15 or final PCDAI ≤ 10 was achieved by 76.9% on infliximab and 92.3% on EEN. BMIFA Z- scores were significantly increased in both groups (p -value was 0.008 in infliximab group and 0.04 in EEN group). No differences were observed in PCDAI, HFA or BMI recovery between two groups. Adverse effects were detected in 30.1% on infliximab and 0% on EEN. **Conclusion:** EEN provided similar improvement in clinical symptoms and growth. EEN therapy has less adverse effects when compared with infliximab.

***1074 GD3-GANGLIOSIDE EXERTS A PROTECTIVE EFFECT ON COLONIC MUCOSA BY MODULATING EXPRESSION OF LIPOPOLYSACCHARIDE INDUCED TNF- α FACTOR (LITAF) IN MURINE DEXTRAN SODIUM SULFATE (DSS) COLITIS**
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Background: GD3-ganglioside (GD3), a glycosphingolipid rich in membrane microdomains, protects enterocytes by binding to pathogenic bacteria and modulating Th1/Th2 responses. We recently reported that dietary GD3 mitigates ileal injury in a rat model of necrotizing enterocolitis (NEC), by enhancing mucosal Foxp3+ Treg cell responses, including suppression of TNF- α expression. TNF- α dysregulation is also a key feature of inflammatory bowel disease (IBD). A recently described transcription factor, LITAF, has been shown to modulate TNF- α gene transcription by binding to the promoter CTCCC sequence. Colonic LITAF mRNA and protein levels are increased both in human IBD and in experimental murine colitis. To date, a potential protective role for GD3 in IBD has not been reported. Employing a murine DSS colitis model, the aims of this study were to investigate effects of GD3 on the clinicopathologic expression of disease, on colonic Foxp3+ Treg cell responses and on LITAF expression.

Methods: 24 8-wk-old male BALB/c mice were randomized into 3 groups: Group 1 control; Group 2 DSS alone; Group 3 DSS + GD3 (GD3 added in drinking water at a concentration of 15 μ g/mL). DSS colitis was induced in groups 2 and 3, as previously described. At day 7, animals were killed, and colons removed for histologic and biochemical analyses. Histologic colitis scores were determined by established methods, and expression of Foxp3 and LITAF was measured by immunoblot assay. All data are expressed as mean \pm SD. Statistical significance of the 3 different groups of mice was assessed by one-way ANOVA and post-hoc Tukey test. Significance was defined as $p < 0.05$.

Results: In the DSS acute colitis model, colons from DSS + GD3-treated animals, compared with DSS alone, exhibited a significant reduction in histologic colitis score. GD3 treatment significantly suppressed colonic LITAF levels in association with markedly increased Foxp3 expression, compared both to DSS alone and to control mice.

Conclusions: Similar to its effects in experimental NEC, GD3 treatment ameliorates colonic inflammation in a murine DSS colitis model. GD3's cytoprotective effects in experimental colitis are manifested, in part, by modulating LITAF and Foxp3 Treg cell responses.

Speculation: These data support the need for further studies evaluating the role of a naturally occurring ganglioside, GD3, as a novel therapeutic approach targeting TNF- α expression in IBD.

***1075 EXCLUSIVE ENTERAL NUTRITION (EEN) INDUCES SIGNIFICANT CHANGES IN THE METABOLIC CAPACITY OF GUT MICROBIOMES IN PEDIATRIC CROHN'S DISEASE (CD) PATIENTS**

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Background: EEN, a first-line therapy in pediatric CD, is thought to induce remission through gut microbiome changes. With microbiome assessment focused on microbial taxonomy and diversity, it remains unclear to what extent EEN induces functional changes. We used metagenomics to investigate the impact of EEN on functional capacity. Pathway abundance was compared in three settings: i) between CD patients at baseline (BL) and controls, ii) before and after EEN, and iii) between patients that sustained remission (SR) and those that did not. **Methods:** Fecal samples were obtained from 15 pediatric CD patients and 5 healthy sibling controls. BL samples were collected prior to EEN therapy, with additional samples taken from most patients at 12 weeks (end of EEN). Further sampling on a subset of patients occurred at 24, 36 and 48 weeks. Metagenomes were sequenced, human reads removed, and the remaining reads were mapped to KEGG pathways, where possible. Differences in pathway abundance were tested using a Kruskal-Wallis H-test in the three settings described above.

Results: We identified 131 pathways. Interestingly, certain bacterial genes were homologous to genes for human pathways. We retained those pathways because some play a role in IBD-related signalling and metabolism. Seven pathways differed significantly between BL CD patients and controls (e.g., NOD-like receptor signalling $p=0.0016$, nitrotoluene degradation $p=0.00034$ and butanoate metabolism $p=0.026$). Three pathways changed significantly after EEN (inositol phosphate metabolism, ER protein processing and pyruvate metabolism). Eleven pathways differed significantly between the SR and non-SR patients ($p < 0.003$ to 0.04). Interestingly, in all 11 cases, pathway abundance in the SR patients was closer to the healthy controls.

Conclusions: Significant differences before and after EEN, and also between SR and non-SR to EEN, is consistent with the notion that it induces a functional change that contributes to its therapeutic effect. Moreover, our finding that SR patients were more similar to healthy controls suggests that community microbial function, as inferred from fecal microbiomes, could serve as a valuable diagnostic tool. Bacterial genes that map to homologs critical to human pathways may represent an important link between IBD and the gut microbiome. An example is the bacterial chaperone HtpG. This gene is a homologue of HSP90, which contributes to the NOD-like receptor pathway. The NOD pathway is involved in regulating the innate immune response, and mutations in the human genes of this pathway are associated with IBD. We found that HtpG was prevalent in both healthy controls and SR patients, and increased over the course of EEN treatment. Based on these results, we speculate that the therapeutic effect of EEN is mediated through functional changes in the microbial community, including activities that also impact human metabolism and signalling.

1076 BARRIERS AND PREDICTORS OF MEDICATION ADHERENCE IN DIVERSE INNER CITY PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: THE PEDIATRIC BRONX COHORT

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Background: Inflammatory bowel diseases (IBD) are chronic gastrointestinal diseases requiring medical therapy to maintain clinical remission. Non-adherence to medications is associated with poor outcome. Our center participates in ImproveCareNow, a national quality improvement network with a goal to improve the care and outcome of children with IBD. Identifying non-adherence, medication barriers, and depression in our patients can lead to interventions that will improve clinical remission.

Aim: The aims of this study were: 1) to identify barriers to medication in pediatric IBD patients and in their parents, 2) to identify depression in our pediatric IBD patients, and 3) to identify predictors of medication adherence in pediatric IBD patients.

Methods: From April 2014 to January 2016, as part of a quality improvement project, 64 IBD patients ages 11 to 21 years were asked to fill out the Adolescent Medication Barrier Scale (AMBS), 8-item Morisky Medication Adherence Scale (MMAS-8), a self-reported adherence tool, and a 9-item depression scale (PHQ-9) at their visit. Forty-five parents who accompanied their children to the visit were asked to fill a demographic questionnaire and Parent Medication Barrier Scale (PMBS). Physician global assessment was collected from patient charts.

Results: Sixty-four IBD patients were studied: 41 with Crohn's disease and 23 with ulcerative colitis. The mean age was 16.7; 46.8% were female. Hispanics comprised 51.4% of our patients and African Americans comprised 25% of our patients. Eighteen percent of participants met criteria for high adherence, with 33% and 48% falling in the medium and low categories, respectively. Fifteen subjects (25%) were identified to have mild depression, two (3%) moderate and one (2%) moderate to severe depression. Depression and disease duration correlated with lower adherence scores (P 0.03). Gender, age, race, physician global assessment, and disease type were not associated with adherence. The most common patient-reported barriers for adherence were: feeling tired of having a medical condition (48%), tired of taking medications (38%), did not feel like taking medication (29%) and forgot to take their medication (29%). Parents perceived children feeling tired of having a medical condition (47%) and being forgetful (38%) as major barriers for adherence.

Conclusions: This study reveals that adherence to medications is challenging for diverse pediatric IBD patients. Routine medical clinic screening for depression and medication barriers is feasible and important in identifying patients at risk of non-adherence who might benefit from interventions that will improve patient care and outcome.

1077 CURCUMIN LOADED POLYETHYLENE GLYCOL: POLYCAPROLACTONE MICROPARTICLES FOR TREATMENT OF INFLAMMATORY BOWEL DISEASE

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Topical agents have the most favorable side effect profile of drugs used to treat inflammatory bowel disease (IBD). However, these drugs are inadequate as monotherapy for most patients. Polymeric microparticles have great potential to overcome the challenges inherent to drug delivery to the gut. Particles can be customized to load and deliver high concentrations of drugs in a targeted and sustained fashion that exceeds traditional extended-release mechanisms. Curcumin is a naturally occurring compound that has gained attention for its anti-inflammatory effect and was selected as a model drug for this application. Particles were synthesized using an oil-in-water (organic/aqueous phase) single emulsion method, and particle size and morphology were assessed using scanning electron microscopy. An amphiphilic block co-polymer made of polyethylene glycol (PEG) and polycaprolactone (PCL) was used to create particles with a PEG coat. The PCL core efficiently loads and slowly releases hydrophobic drugs while PEG acts to enhance particle migration through mucus of the gastrointestinal tract. Curcumin encapsulation efficiencies into the particles have been determined, and the rate of drug release from the particles in simulated gastric, small intestinal, and colonic fluids has been analyzed. The particles have been assessed for cytotoxicity to J774A mouse macrophage cells using flow cytometry, and the impact of particles on macrophage cytokine release has been assessed. Particles of a consistent size (1-15 microns) and spherical morphology were achieved. Drug encapsulation efficiency was found to vary between 48 and 69% depending on specific batch parameters in the synthesis process. Drug release from the particle core was found to be slow with approximately 30% of drug retained at 3H. A dose of 0.1mg particles/mL media was found to be well tolerated by mouse macrophages with only minimal cytotoxicity. Finally, curcumin microparticles significantly reduced expression of TNF- α from macrophages stimulated by the pro-inflammatory compound lipopolysaccharide (LPS) relative to cells that did not receive particle treatment. This work has developed of a novel polymeric vector which may hereafter be used to load and transport a host of additional drugs to the intestines and enhance treatment of IBD. Microparticles may offer advantages over traditional drug delivery systems and they warrant ongoing study for their potential role in the treatment of IBD.

1078 RATES OF MUCOSAL HEALING AND CORRELATION TO CLINICAL ASSESSMENT IN PEDIATRIC CROHN'S DISEASE

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Background: Therapeutic endpoints for inflammatory bowel disease (IBD) have evolved over time with the addition of mucosal healing as a viable clinical endpoint. Recent adult data suggest that patients who achieve this endpoint have fewer hospitalizations, lower surgery rates, and remain in remission longer than those who do not achieve mucosal healing. There are few pediatric studies reporting the rate of mucosal healing and whether this matches the clinical assessment of the patient.

Aim: Our aim was to examine the rate of mucosal healing with standard therapies for pediatric Crohn's disease and, secondarily, to correlate mucosal healing with clinical remission rates.

Methods: A retrospective chart review was performed on patients seen by the Division of Pediatric Gastroenterology, Hepatology & Nutrition at Rainbow Babies & Children's Hospital in Cleveland, OH from 2011 to 2015, specifically patients diagnosed with CD between 5-18 years of age and who had two or more endoscopies within two-year intervals. Data collected included patient demographics, medical therapy [immunomodulators, anti-tumor necrosis factor (anti-TNF) alone and with immunomodulators] and laboratory findings. Clinical activity was

assessed using the Physician Global Assessment (PGA). Endoscopic images were independently reviewed by two staff physicians and mucosal healing was defined as the absence of mucosal ulceration. Analysis was performed using Fisher's exact test and Chi-square analyses.

Results: 37 patients and 91 endoscopies were reviewed. Ages ranged from 6.6 to 17.5 years (mean age of 12.5). 20 males and 17 females were reviewed, (73% were Caucasian and 21.6% African American). The majority of patients had 1-2 repeat endoscopies, approximately 1 year apart. The overall mucosal healing rate was 40.7%; however, the association between mucosal healing and clinical remission as defined by PGA was not clinically significant ($p = 0.137$). Moreover, anti-TNF combination therapy (anti-TNF with immunomodulator) was the only therapy significantly associated with mucosal healing ($p = 0.037$).

Conclusion: The overall mucosal healing rate for our cohort was 40.7%, with anti-TNF plus immunomodulator as the most effective therapy. In addition, our results indicate that clinical assessment with the PGA is not a reliable means of identifying mucosal healing. Our findings are in line with the adult IBD literature. Prospective data is required to confirm our observations and to further compare rates of mucosal healing between anti-TNF therapy alone and in combination with immunomodulators. Examining the clinical outcomes for patients who achieve mucosal healing would be of great benefit in the management of pediatric Crohn's disease.

1079 THE NATURAL HISTORY OF ULCERATIVE COLITIS IN A PEDIATRIC POPULATION: A SINGLE-CENTER EXPERIENCE BETWEEN 1988 AND 2013

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Background: Limited data are available on the natural history of pediatric ulcerative colitis(UC) in Eastern Asia. Our aim was to report the presentation and progression of patients diagnosed with UC during childhood in Korea.

Method: We reviewed medical records for all 211 patients diagnosed in the period 1988-2013 with childhood onset UC in Asan Medical Center, Seoul, South Korea.

Result: Mean age at diagnosis is 13.1 ± 3.3 years. The male:female ratio was 120:91 and median follow-up time was 6.5 years (0.3-29.3).

Extraintestinal symptoms were experienced by 16.1% (34/211) of the children. Family history was present in 10.9% (23/211). At diagnosis, 27.5% (n=58) of patients had proctitis, 25.1% (n=53) left-sided colitis, and 39.3% (n=83) extensive colitis. At diagnosis, 95.2% of patients received 5-aminosalicylic acid, and 41.2% received steroids. During follow-up, 34.6% received an immunomodulator, and 9.9% received anti-tumor necrosis factor agents. The cumulative risk of proximal extension in patients with proctitis or left-sided colitis was 34.2% after 5 years and 41.8% after 10 years. Among patients with an E1 localizations, eleven (11/58, 19.0%) progressed to E2 and fifteen (14/58, 24.1%) to E3; among patients with an E2 localizations, nineteen (35.8%) progressed to E3. The cumulative relapse rate after 1, 5, 10, and 15 years was 32.1%, 54.1%, 62.3%, and 72.9%, respectively. The cumulative rate of colectomy was 1.4% after 2 years, 2.4% after 5 years, 8.8% after 10 years and 15.3% after 20 years. The cumulative risk of colon cancer was 0% after 10 years, 2% after 15 years, and 12.0% after 20 years.

Conclusion: The disease extent of Korean children with UC at diagnosis is similar to those of Western children. However, UC in Korean children may have a milder course than in Westerners, as indicated by the lower rate of colectomy and disease extension.

1080 VEDOLIZUMAB RESPONSE AT 14 WEEKS PREDICTS 52 WEEK OUTCOME IN PEDIATRIC CROHN'S DISEASE

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Background: Vedolizumab is a monoclonal antibody which binds integrin $\alpha4\beta7$ and is approved for adult patients with Crohn's disease (CD). Little data is available on pediatric experience with vedolizumab. We describe our experience using vedolizumab for CD in a pediatric tertiary IBD center.

Methods: A retrospective review identified pediatric CD patients (age <21 years) receiving vedolizumab for at least 52 weeks. Data on disease activity, demographics, and previous treatments was obtained. Disease activity was evaluated with the weighted pediatric Crohn's disease activity index (wPCDAI).

Results: 15 patients with CD were identified who completed at least one year of therapy on vedolizumab. Their dosing plan was 6 mg/kg up to 300mg per dose infused at 0, 2, 6 and then every 8 weeks, however 6 (40%) required interval shortening to optimize therapy. There were no adverse reactions that required discontinuation of therapy. Mean age at diagnosis was 11.0 years (range 2-17 years) and mean age at vedolizumab initiation was 15.8 years (range 7-21 years). Five patients (33%) had prior bowel surgery. All 15 patients failed at least one anti-TNF and 14 patients (93%) failed 2 or more anti-TNF. Mean CRP at initiation of therapy was 2.9mg/dL. 8 patients (53%) used concurrent immunomodulators. Mean wPCDAI at weeks 0, 6, 14, and 52 were 70, 56, 36, and 24 respectively. At 6 weeks, 3 patients showed moderate response defined as XXXX to therapy, none were in remission. At 14 weeks, 8 patients showed moderate response or were in clinical remission and 7 patients showed no significant response. Of the 8 patients who showed response, 7 maintained response or remission at 52 weeks. 4 patients (27%) in remission and 3 patients (20%) with maintained response. Of the 7 patients with no response at 14 weeks, all either transitioned to another therapy or failed to respond to vedolizumab by 52 weeks. Week 6 response did not predict response at week 52 as evaluated by Chi-squared analysis ($p=0.15$). However, week 14 response did predict week 52 response ($p=0.001$).

Conclusion: In our experience, vedolizumab is safe for pediatric patients. The response/remission rates are similar to those published in adult studies. Week 14 response but not week 6 response predicted long-term 52-week response to vedolizumab. Vedolizumab is an effective therapy for anti-TNF refractory CD patients.

1081 THE ROLE OF THE HYPERINFLAMMATORY PATHWAY IN VERY EARLY-ONSET INFLAMMATORY BOWEL DISEASE

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Background: Defects in genes involved in the perforin cytolytic pathway, a key component of cytotoxic cells and can lead to hyperinflammatory disorders, have been detected in patients with very early onset inflammatory bowel disease (VEO-IBD). These variants can result in impaired immunological responses, cytokine storm and progression to hemophagocytic lymphohistiocytosis (HLH). Our primary aim is to identify an enrichment of rare or novel variants that result in perforin defects in our cohort of patients with VEO-IBD as compared to healthy controls.

Methods: We analyzed 101 trios composed of IBD patients 5 years and younger and their parents by WES using the Agilent SureSelect V4 capture kit and the Illumina HiSeq platform. Novel and rare (MAF <0.01) likely deleterious (CADD score ≥ 10) missense and loss of function mutations within 17 HLH-related genes were selected for further analysis. We compared the number of variants found in this gene list in the VEO-IBD cohort and an independent healthy control cohort. We also compared 10,000 randomly chosen gene lists of equal number between the two cohorts to evaluate the significance of our results. Data was analyzed as a whole and segregated based on type of variant, including missense, nonsense or indel, and mode of inheritance.

Results: We detected an enrichment of variants in 17 genes involved in perforin deficiency in VEO-IBD patients compared to the healthy controls. Examples include a female with severe pancolitis and heterozygous mutations in STX4, UNC13D and CCDC88B. These genes are involved in degranulation and cytotoxic killing. A heterozygous mutation in STX8 was detected in a female who presented at 6 months with severe panenteric VEO-IBD. The mutation was inherited from the mother who has ileocolonic Crohn's disease with perianal involvement and was diagnosed with T cell Leukemia. STX8 is expressed in lytic granules and is required for sorting and trafficking of cytotoxic molecules to functional lytic granules in cytotoxic T cells. Compound heterozygous mutations in UNC13D were detected in a male who presented at 4 months of age with diarrhea and severe failure to thrive and diagnosed with ileal Crohn's disease. Overall, VEO-IBD patients were more likely to harbor 2 or more variants in these genes than the controls ($p < 0.01$). Similar tests performed in 10,000 randomly chosen gene lists of equal number showed a comparable number of variants between the two cohorts, supporting the specificity of the enrichment to the HLH gene list.

Conclusions: The hyperinflammatory pathway has been implicated in the pathogenesis of VEO-IBD. Defective cytotoxic killing mediated by perforin defects can result in HLH, an uncontrolled ineffective immune response that can have catastrophic results. As such, identification of these variants may have drastic implications on the potentially life-saving therapeutic approach.

***1082 ADALIMUMAB TREATMENT IMPROVES LINEAR GROWTH IN CHILDREN WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM THE IMAGINE 1 TRIAL**

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Objective: Approximately 1/3 of children with Crohn's disease (CD) experience growth impairment. We evaluated the effect of adalimumab (ADA) on height velocity in pediatric patients (pts) with moderately to severely active CD and baseline (BL) linear growth impairment in the IMAGINE 1 trial.

Methods: Pediatric pts with BL Pediatric CD Activity Index (PCDAI) > 30 and concomitant use of or intolerance to corticosteroids or immunosuppressants received open-label (OL) induction ADA at wks 0/2 dosed by body weight (> 40 kg, 160/80 mg; < 40 kg, 80/40 mg). At week 4, pts were randomized to double-blind high-dose (> 40 kg, 40 mg; < 40 kg, 20 mg) or low-dose (> 40 kg, 20 mg; < 40 kg, 10 mg) ADA every other wk (EOW) until wk 52. At wk 12, pts with flare or non-response could escalate to weekly ADA dosing, continuing with the same dose. After another 8 wks pts could receive OL weekly high-dose for continued flare or nonresponse. Female and male pts with growth potential (BL bone age < 13 and < 14 yrs, respectively) were categorized as having BL growth impairment (height velocity Z-score < -1.0) or normal growth (height velocity Z-score > -1.0). Height velocity Z-scores based on bone age were compared between these groups at wks 26 and 52. Subgroup analysis by BL disease severity (BL median PCDAI < 40 , > 40), BL corticosteroid use, and wk 4 response was also performed. Change in height velocity Z-score from BL was assessed at wks 26 and 52 by current remission status and by durable remission (PCDAI < 10 at $> 80\%$ of visits after wk 4). Data reported as-observed.

Results: 73/100 pts with growth potential (mean age, 12.0 y) had BL growth impairment (median BL height velocity Z-score: - 3.25). Linear growth normalized with ADA treatment at wks 26 and 52 in pts with BL growth impairment (median Z-score: wk 26, - 0.34; wk 52, 0.21; both $p < 0.001$ vs. BL); normalization of linear growth was achieved in these pts regardless of BL disease severity (PCDAI < 40 or > 40) or corticosteroid use. Linear growth remained stable over time in pts without BL growth impairment. Pts who remained on EOW ADA had greater height velocity Z-scores compared with those who escalated to weekly ADA (median Z-score: wk 26, 0.03 vs. - 1.25; wk 52, 1.71 vs. - 1.36 [$p = 0.007$] for EOW and weekly ADA). Significantly greater growth improvement was observed at wk 26 in wk 4 responders compared with non-responders (median Z-score, 0.09 vs. - 2.92, respectively; $p = 0.023$); a numerical difference persisted at week 52. Significantly higher median height velocity Z-score and greater change from BL in Z-score at wks 26 and 52 were observed in pts with remission and with durable remission (Table). Previously reported safety data identified no new signals.

Conclusions: ADA significantly improved and normalized growth as early as wk 26 in children with moderately to severely active CD and growth impairment at BL. Restoration of normal growth with ADA treatment was significantly associated with clinical remission.

Table. Growth rate in adalimumab-treated patients, based on remission status (PCDAI ≤10; durable if achieved at ≥80% of visits after week 4; group median z-scores)

	Week 26 (N=52)	Week 52 (N=44)
Height velocity z-score		
With durable remission	2 (n=12)	3 (n=9)
Without durable remission	-0.39 (n=40)	-0.33 (n=35)
P value	0.040	0.006
Change from baseline in height velocity z-score		
With durable remission	4.86 (n=12)	5.78 (n=9)
Without durable remission	2.3 (n=40)	3.04 (n=35)
P value	0.241	0.043
Height velocity z-score		
Remitters	1.33 (n=23)	2.17 (n=27)
Non-remitters	-0.78 (n=29)	-1.57 (n=17)
P value	0.01	0.001
Change from baseline in height velocity z-score		
Remitters	4.35 (n=23)	5.15 (n=27)
Non-remitters	1.96 (n=29)	2 (n=17)
P value	0.026	0.018
PCDAI, Pediatric CD Activity Index		

1083 PRE-MEDICATION USE PRIOR TO INFLIXIMAB ADMINISTRATION: A CROSS-SECTIONAL ANALYSIS FROM THE CLINICAL CARE AND QUALITY AND INFLAMMATORY BOWEL DISEASE COMMITTEES OF NASPGHAN

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Background and Objective: Premedications are commonly given to IBD patients prior to infliximab infusions. Review of the literature suggests insufficient strength of evidence for all-case premedication use. We hypothesize that there exists a non-standardized approach to premedicating IBD patients receiving infliximab. The objectives of this study were to 1) describe the variability of premedication use, and 2) determine clinical rationale for premedication use among clinicians treating IBD patients.

Methods: The NASPGHAN Clinical Care and Quality and Inflammatory Bowel Disease committees conducted a cross-sectional electronic survey distributed through members-only NASPGHAN and CCFCA listservs and AGA and ACG discussion boards. To ensure that only 1 survey was captured per respondent, the Qualtrics web-based software screened computer IP addresses matched with provided e-mails. Survey content was developed after a comprehensive review of the literature and was designed to take 3 minutes to complete. An optional 4-question post-survey quiz was developed to assess practitioners' understanding of evidence-based practice.

Results: 297 unique respondents with an 89% survey completion rate were collected from 271 (91%) and 24 (8%) board-eligible or certified pediatric and adult gastroenterologists. The majority of practitioners ordered infliximab from a standardized order set (67%) and infused over 2 or 3 hours (74%). Among the numerous options for premedications, acetaminophen (68%) and diphenhydramine (66%) were most often given prior to each infliximab infusion; only 19% of the respondents did not use premedications. There was reported heterogeneity of premedication use between gastroenterologists within the same clinical practice (35% "individual preference only"; 33% "sometimes" or "often"; 32% "always"). 245 (88%) respondents opted to take the four-question quiz to test knowledge about evidence-based premedication use. Per-question correct percentage was 54% (risk of a reaction), 68% (non-immunologic basis of a reaction), 18% (association of diphenhydramine use with increased reaction), and 71% (association of anti-TNF antibodies with increased reaction).

Conclusion: There is high variability of premedication use prior to infliximab infusions among gastroenterologists. A substantial proportion of premedication use, particularly in diphenhydramine, may represent unnecessary standard of care. Improved knowledge of the evidence may be assist in updating observed clinician practices.

1084 EFFECT OF EXCLUSIVE ENTERAL NUTRITION AND CORTICOSTEROID INDUCTION THERAPY ON THE INTESTINAL MICROBIOME OF PEDIATRIC PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS

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Introduction: Exclusive enteral nutrition (EEN) and corticosteroids (CS) are effective induction therapies for pediatric inflammatory bowel disease (IBD). EEN results in higher rates of mucosal healing in patients with Crohn's disease (CD). CS is first-line therapy for induction of remission in moderate to severe ulcerative colitis (UC), while EEN has not been shown to be effective for UC. The reason is unclear, but host-microbial interactions may be implicated. Patients with active IBD have decreased microbial diversity compared to healthy controls, and mucosal inflammation is associated with decreased *Bifidobacterium* and *Firmicutes*. Patients with CD and UC may have unique microbial signatures; CD is characterized by increased *Prevotella* (decreased in UC) and increased *Proteobacter* (variable in UC). Studies have suggested that CS treatment leads to increased microbial diversity in UC, while EEN reduces diversity in CD. This is the first, and largest prospective

cohort study to longitudinally characterize changes in the bacterial community structure of pediatric UC and CD patients, receiving EEN or CS induction therapy.

Methods: Prospective, observational cohort study of patients with CD/UC followed at McMaster Children's Hospital (Hamilton, Canada). Fecal samples were collected from patients, ages 5-18 years old, undergoing 8 weeks of continuous induction therapy with EEN or CS. 7 samples were collected per patient during therapy, and an eighth was collected 4 weeks after. Choice of treatment was decided by the primary clinical team. Fecal samples were submitted for 16s rRNA sequencing. Simpson's index of α -diversity, and relative abundance of specific bacterial taxa were compared using a linear mixed model.

Results: 22 pediatric patients with active CD or UC requiring therapy for induction of remission were recruited. 12 received EEN (12 CD, 0 UC) and 10 received CS (3 CD, 7 UC) as induction therapy. The study included children with preexisting (4 CD, 4 UC) and new diagnoses (11 CD, 3 UC). Simpson's α -diversity increased over treatment in all groups. Changes did not reach statistical significance ($p>0.05$). Patients with UC receiving CS had increased abundance of *Bifidobacteria*, and *Clostridium*, and decreased abundance of *Faecalibacteria*. Patients with CD had decreased abundance of *Prevotella*, *Bifidobacteria* and *Enterobacteriaceae*, with both EEN and CS therapies. Changes in taxonomic abundance did not reach statistical significance ($p>0.05$).

Conclusion: This is the first prospective, observational cohort study to assess microbial changes in pediatric patients with IBD receiving EEN or CS. Variable changes in bacterial community structure and diversity occur across all treatment groups and time-points. Study recruitment and sample collection is ongoing. Additional results will help further characterize changes between bacterial taxonomy, disease, and therapeutic response to exclusive enteral nutrition or corticosteroids.

1085 ACCELERATED STEP-UP APPROACH AND LONG-TERM DISEASE OUTCOMES IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE

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Introduction: The use of accelerated step-up or anti-TNF before first remission in combination with immunomodulators (IM) remains controversial in pediatric Crohn's disease (CD).

Methods: Five-year follow-up data from BELCRO (Belgian observational prospective cohort of pediatric CD) were analyzed. Disease severity was scored as inactive, mild or moderate-to-severe on a 3-point scale based on PCDAI and/or PGA scores at diagnosis and monitored yearly. Univariate analyses were performed between patients treated with anti-TNF before or after first remission and correlations were assessed between treatment variables and the outcomes average disease severity and sustained remission, defined as inactive disease for ≥ 2 yrs follow-up.

Results: Of 66 anti-TNF exposed patients (median (IQR) age 13.1 (11.5 – 15.2) yrs, 50% male), 5% never reached remission and 47% had accelerated step-up. Accelerated step-up was associated with older age (13.3 (12.1 – 15.9) vs. 12.5 (10.2 – 14.1) yrs; $p= .02$), higher average disease severity (1.8 (1.6 – 1.9) vs. 1.6 (1.3 – 1.8); $p< .01$) but similar disease location and severity at diagnosis compared to anti-TNF after first remission. Delay to steroids and IM and duration of steroids was similar in both groups, but delay to anti-TNF or combination and duration of IM was shorter with anti-TNF before first remission, resulting in longer duration of anti-TNF but similar duration of combination therapy. Time to first remission was longer in accelerated step-up group but delay to and duration of sustained remission was similar in both groups (Table). Rates of surgery and hospitalizations for CD were similar and at 5 yrs, inactive disease (68% vs. 69%, $p= .93$) was similar and IM use (24% vs. 59%; $p< .01$) lower in the group treated with anti-TNF before first remission. Accelerated step-up correlated with average disease severity (AUC= .70; $p< .01$) but not sustained remission (no correction for multiple testing). No other correlations were found between treatment and outcomes.

Conclusion: Accelerated step-up was prescribed for more severe disease and in older children not remitting on IM. IM exposure was limited compared to anti-TNF upon relapse despite IM. Only patient age was associated with initial response to IM. Sustained remission was similar for all children needing anti-TNF.

Treatment or outcome variable, median (IQR) in yrs	Anti-TNF before first remission (n= 31)	Anti-TNF after first remission (n= 32)	P value
Delay to first steroids	0 (0 – 0.05)	0 (0 – 0.01)	.60
Duration of steroids	0.4 (0.3 – 0.6)	0.4 (0.3 – 1.0)	.96
Delay to first immunomodulator	0.08 (0.01 – 0.16)	0.09 (0.01 – 0.46)	.55
Duration of immunomodulator	2.0 (1.2 – 2.7)	3.9 (2.0 – 4.8)	.02
Delay to first biological	0.6 (0.4 – 0.9)	2.1 (1.4 – 3.3)	< .0001
Duration of biological	4.6 (4.0 – 4.9)	2.7 (1.6 – 3.6)	< .0001
Delay to combination	0.6 (0.2 – 1.0)	2.4 (1.5 – 3.5)	< .0001
Duration of combination	1.0 (0.5 – 2.0)	1.3 (0.6 – 2.1)	.57
Time to first remission	1.5 (1.1 – 3.0)	0.5 (0.3 – 0.8)	< .0001
Time to sustained remission	3.1 (2.6 – 4.0)	2.7 (2.0 – 3.6)	.14
Duration of sustained remission	2.1 (1.4 – 4.0)	2.7 (1.3 – 4.6)	.45

1086 THE MONTREAL EXPERIENCE USING USTEKINUMAB IN PEDIATRIC REFRACTORY CROHN'S DISEASE

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Background: Crohn's disease (CD) is a chronic inflammatory bowel disease with a relapsing course, which can lead to debilitating symptoms. New therapies are emerging for managing CD. Ustekinumab is a monoclonal antibody against the p40 subunit of interleukin-12/23. It was shown to be superior to placebo in inducing clinical response and maintaining remission in adult patients with moderate to severe CD. There are scarce data on the use of this therapy in pediatrics.

Aims: To describe the experience in two academic centers in Quebec using ustekinumab in pediatric patients with refractory CD, pertaining to safety and efficacy of the medication.

Methods: We report the cases of 12 patients who received open-label ustekinumab between July 2013 to May 2016 for CD refractory to anti-TNFs. Data were retrieved retrospectively from medical charts.

Results: There were 9 boys and 5 girls, of which 2 boys did not finish induction and therefore were excluded. Median age at initiation of therapy was 16 years (10–18) and median duration of disease was 3.54 years (1–9). Location of disease according to Paris classification was L1 in 1 patient, L2 in 5 patients and L3 in 6 patients. Seven patients were found to have upper involvement: 6 patients had a Paris classification of L4a, one was L4b and 1 was L4ab. Behavior was non penetrating non stricturing in all patients except one. All patients had failed or were intolerant to immunomodulators (9 patients to thiopurines and 8 to methotrexate). Infliximab was discontinued in 11 patients with a median duration of treatment of 10 mo (3–32): 3 for primary non-response, 5 for secondary loss of response and 3 for allergies/adverse events. Eight patients failed adalimumab. Doses of subcutaneous ustekinumab administered during induction therapy were 45 mg (if weight \leq 45 kg) per week or 90 mg (if weight > 45 kg) per week, at 0, 1 and 2 weeks. Following induction, clinical response was noted in 7 and clinical remission in 1. There was no response in 4 patients. Ten patients continued onto maintenance therapy with 45 mg every 8 weeks or 90 mg every 8 weeks depending on doses received during induction. Dose escalation was necessary in 8 cases. Median follow-up on ustekinumab for those who continued to maintenance therapy is so far 6 mo (2–18 mo), however, 3 additional patients discontinued therapy for non-response or loss of response. At their last appointment, 3 patients were in clinical remission at 18 mo, 3 had clinical response (at median 2mo (1–6)) and 1 patient relapsed. One adverse event noted was post-injection migraines in 2 patients.

Conclusion: Ustekinumab is well tolerated in pediatric patients. The long-term clinical remission after induction was 30%. Randomized controlled studies are required to assess efficacy in this patient group. Guidelines on optimization of therapy and the role of antibody levels could also help direct therapy.

1087 INFLIXIMAB LEVELS AND CLINICAL DECISIONS

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Introduction: Low trough concentration of infliximab (IFX) and the presence of anti-IFX antibodies (AIFX) are associated with loss of therapeutic response in patients with inflammatory bowel disease (IBD). The therapeutic approach at our hospital has been based on clinical (PCDAI and PUCAI) and biochemical markers of disease activity (C-reactive protein and fecal calprotectin). Since 2014 it has been possible to obtain serum levels of IFX and AIFX in a research protocol at each infusion, but the time lag of the results has prevented immediate clinical decision.

Objectives: To compare the therapeutic decisions based on clinical outcomes with the decisions that would have been made if IFX and AIFX levels were immediately available.

Methods: We analyzed the therapeutic decisions in pediatric patients with Crohn's disease (CD) and ulcerative colitis (UC) under IFX and compared them with those that would be taken according to the algorithm from TAXIT study (Vande Casteele N, 2015). Adequate therapeutic IFX concentration was 3–7 μ g/mL and antibody concentration positive if >1.7 μ g/mL.

Results: 44 cases were analyzed (38 CD, 6 UC) and 214 clinical decisions reviewed. Mean age was 16.2 years. Subtherapeutic and supratherapeutic IFX levels occurred in 30.5% and 30%, respectively. AIFX concentrations above 8 μ g/mL were found in 2 patients. There was a weak correlation between decisions based on clinical features and those that would be taken based only on IFX and AIFX trough concentrations (kappa 0.087, $p=0.002$) according to the published protocol. Therapeutic regimen was maintained in 186 cases (43.5% discordant), shortened interval in 10 (50% discordant), increased dose in 7 (100% discordant), decreased dose in 1 (100% discordant) and spacing the interval in 10 (30% discordant). Treatment with IFX was not suspended in any case (2 discordant). Analyzing the conflicting decisions, it was found that: when decision was to maintain therapeutic regimen and decrease IFX dose, patients were clinical and analytically well; decisions to increase the interval corresponded to induction phase, for which there are no standard cut-off levels; cases where interval between infusions was decreased and those to whom the dose was increased, corresponded to worsening of clinical and analytical parameters. Treatment with IFX was suspended in one of the discordant cases and in the other discordant case therapeutic switch to adalimumab is being considered after endoscopic review.

Discussion: Treatment decisions are taken on an individual basis and specific context, but the adoption of algorithms helps to standardize, audit and review them when appropriate. Despite treatment based on IFX and AIFX trough concentrations does not appear better than based on clinical outcome, it may help to guide biological treatment. In particular, the identification of subtherapeutic levels and high titers of antibodies may lead to rapid switch treatment rather than scale up useless dose and cost.

*1088 UTILIZING NAILFOLD CAPILLAROSCOPY TO MONITOR DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE

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Background: Inflammatory bowel disease (IBD) is a chronic condition affecting up to 80,000 children in the United States with a rising disease incidence. Methods for monitoring disease activity including serum markers, imaging studies, and endoscopy can be invasive and traumatic. Implementation of a non-invasive technique for disease monitoring would be ideal to improve the experience of patients with IBD. Nailfold capillaroscopy (NFC) is a validated technique utilized for surveillance of disease activity in patients with juvenile dermatomyositis (JDM). This involves magnified photography of nailfolds highlighting capillaries in the nail bed called end row capillary loops (ERL). Previous studies show

that patients with IBD have unique end row capillary patterns. The aim of this study is to identify variations in nailfold patterns in active and quiescent IBD patients and to correlate findings with disease activity.

Methods: Patients ages 2-22 with Crohn's disease (CD) or ulcerative colitis (UC) and healthy controls were recruited. Patients with indeterminate colitis or other co-morbidities were excluded. NFC was performed on 3 groups of patients: 1) newly diagnosed, active IBD patients prior to initiating therapy; 2) patients with an established diagnosis in disease remission; and 3) healthy controls. ERLs were quantified, and the area above the capillary end row, called the subpapillary venous plexus (SVP), was analyzed for the presence or absence of branching or poor vessel density (SVP dropout). Information was collected regarding disease history, including disease location, extraintestinal manifestations, duration of disease, surgical treatments, medication regimens, disease activity score, and demographic information. Statistics were performed using Mann-Whitney t-testing or Kruskal-Wallis test by ranks.

Results: A total of 28 patients (64% male) were recruited for this pilot investigation. This included 13 patients with newly diagnosed, active disease (9 CD/4 UC), 6 patients in disease remission (5 CD/1 UC), and nine controls. ERL density was significantly decreased in patients with active disease compared to controls (15.4 ERL/3 mm vs. 18.4 ERL/3 mm, $p<0.0001$) and when compared to patients in clinical remission (15.4 ERL/3 mm vs. 17.3 ERL/3 mm, $p=0.04$). ERL density was similar between patients in remission compared to controls (17.3 ERL/3 mm vs. 18.4 ERL/3 mm, $p=0.21$). Significant SVP dropout was seen in active IBD patients (6/13 patients) when compared to remission patients (0/6) and controls (0/9), $p=0.0008$. There was no statistically significant variation in SVP branching among the three groups.

Conclusions: Our data demonstrate that patients with active IBD have abnormal NFC patterns. ERLs are reduced, and SVP dropout is more prominent in patients with active IBD when compared to patients in remission and controls. This suggests NFC may be a biomarker of disease activity and utilized in the future for disease monitoring.

1089 CROHN'S DISEASE ACTIVITY AND NUTRITIONAL STATUS IN BLACK CHILDREN AND ADOLESCENTS: A SINGLE-CENTER EXPERIENCE

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Objectives: Growth failure represents a major clinical feature of pediatric Crohn's disease; however, limited information is available with respect to racial differences in nutritional status among affected children. This single-center study examines nutritional variables and disease activity in urban, inner-city, black pediatric Crohn's disease patients at diagnosis, at 1-yr and at 3-yr follow-up.

Methods: We reviewed the records of 37 black patients (16M, 21F; age 5-19 yr; median age 16.8 yr) with a diagnosis of Crohn's disease, cared for at the Children's Hospital at Downstate, SUNY-Downstate Medical Center from 2007-16. Data were analyzed at diagnosis (baseline), after 1-yr (mean 14.3 mo) and after 3-yr (39.5 mo). Calculations of Ht, Wt, and BMI Z-scores, as well as PCDAIs, were determined at each time. Changes from baseline nutritional variables were analyzed by Student's t-test for paired values. Time-related differences in mean PCDAIs were assessed by one-way ANOVA and Tukey HSD tests (*post hoc* analysis).

Results: At baseline, Ht, Wt and BMI Z-scores >2 SD below the National Center for Health Statistics published means were found in 8.1% (3/37), 10.8% (4/37) and 16.0% (8/37) of patients, respectively. At 3-yr after diagnosis, 8.1% (3/37; $p=NS$), 2.7% (1/37; $p=NS$) and 7.0% (1/37; $p=NS$) of Ht, Wt and BMI Z-scores, respectively, measured >2 SD below the mean. The baseline PCDAI ($m \pm SD$ 50.1 \pm 12.8) decreased significantly, both 1-yr (25.1 \pm 18.5; $p<0.01$) and 3-yr after diagnosis (10.7 \pm 11.3; $p<0.01$ vs. baseline, $p<0.01$ vs. 1-yr).

Conclusions: In a single-center experience, Crohn's disease-associated growth failure and overt malnutrition among black children was less prevalent at diagnosis than previously reported in predominantly white populations. Despite marked improvement in the mean PCDAI, nutritional variables did not change significantly over a 3-yr follow-up (although the mean BMI trended higher; $p=0.06$).

Speculation: These data suggest growth failure in black children is a relatively uncommon presenting sign of Crohn's disease. In this population, reliance on nutritional status alone may not represent a valid measure of disease activity. Future studies, examining specific Crohn's disease characteristics, are required to further elucidate these and other possible racial/ethnic differences.

1090 FINAL ADULT HEIGHT OF PEDIATRIC ONSET INFLAMMATORY BOWEL DISEASE PATIENTS IN JAPAN: ANALYSIS AND COMPARISON OF NATIONWIDE REGISTRY BETWEEN 2005 AND 2011.

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Background: Growth failure is recognized as a significant complication of Crohn's disease (CD) and ulcerative colitis (UC) in pediatric patients. Interruption of IGF1-GH axis and malnutrition, and use of corticosteroids are considered as its etiology. Recently, biologics are reported as effective for improving the patients' growth, and its use is increasing in those years. Therefore, we compared the final adult height of pediatric onset CD and UC patients, between 2005 (before biologics were approved in Japan) and 2011 (the newest available data in 2015) by analyzing Japanese national registry data.

Methods: Using available Japanese national registry data, final adult height was analyzed using data of patients who were 20-39 years old at the time of registration and had an onset of CD or UC at 18 years of age or younger.

Results: The number of patients eligible were 1324 (CD) and 2206 (UC) in 2005, and 1719 (CD) and 2897 UC in 2011. Average height of male CD and UC patients, and female CD patients were lowered when compared with healthy individuals in Japan. In 2011, the percentage of patients whose were lower than -2 height SD was 5.1% and 3.3% in male and female CD, and 2.9% and 3.2% in male and female UC patients, respectively. It was significantly increased in male and female CD, and male UC patients when compared with healthy adults. The percentages was significantly decreased among age 13-15 in CD males when compared 2011 patients with those in 2005. Biologics were used in 40.0% of CD and 2.0% of UC patients registered in 2011. There were no correlation between current use of biologics and final adult height.

Conclusion: Some pediatric-onset IBD patients, especially those with CD, still show reduced final adult height. However, new therapeutics may improve their growth prognosis.

1091 LINEAR GROWTH IMPAIRMENT IN CANADIAN CHILDREN PRESENTING WITH NEW ONSET IBD: A MULTICENTER INCEPTION COHORT STUDY

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Background: An important target in the management of pediatric inflammatory bowel disease (IBD) is normal linear growth and pubertal development. Greater awareness of IBD and more effective therapies are anticipated to reduce the prevalence of linear growth impairment as a complication of chronic intestinal inflammation.

Aim: To evaluate the current magnitude of linear growth impairment at diagnosis in pediatric Crohn's disease (CD) and ulcerative colitis (UC). **Patients/Methods:** Since April 2014, the Canadian Children IBD Network (CIDsCANN) inception cohort study prospectively enrolled children and adolescents aged < 17 years, presenting to 12 participating academic centers across Canada where IBD care is provided. Recommended assessment of linear growth at presentation includes height measurement, pubertal staging, ascertainment of pre-illness heights and mid-parental height (MPH) calculation. All growth parameters are standardized utilizing the Centers for Disease Control (CDC) 2000 reference tables. **Results:** Among the initial 640 participants (58% male; CD: 59%, UC: 30%, IBD-unclassified: 11%), median age at presentation was similar for the three disease sub-categories (12.9 yrs; IQR 10.8-15.0), but duration of symptoms prior to diagnosis was significantly longer in CD (5 months, IQR 3-12 months) vs. UC (3 months, IQR 1-6 months) ($p < 0.001$). Macroscopic disease location based on Paris classification for UC was: 70% E4; 12% E3; 16% E2 and for CD was: 58% L3; 23% L2; 18% L1. Linear growth impairment, based on historical growth parameters, occurred in 21% of CD patients (8% as the main presenting feature), and 3% of UC patients (but none as the main presenting feature). Predicted height Z-scores (based on MPH) were normally distributed (mean 0.07, SD 0.8). As shown in Table, the UC cohort had normal height at diagnosis, but mean height Z-score in the CD cohort was reduced compared to healthy population, especially among younger vs. older CD patients ($p = 0.05$), despite similar symptom duration (median 5 months) prior to diagnosis (Table). Neither gender nor CD location were significantly associated with greater alteration in height Z-scores.

Conclusions: Linear growth impairment still occurs prior to recognition of Crohn's disease in young patients, but its magnitude is less than in previous eras.

	All pts	UC	CD	CD: Pre-pubertal (Age < 11yrs)	CD: Post-Pubertal (Age > 15yrs)
Mean Ht z-score	-0.24	0.07	-0.44	-0.52	-0.29
(SD)	1.2	1.1	1.2	0.9	1.3
95% CI			-0.58 to -0.30	-0.74 to -0.31	-0.58 to +0.01

1092 IMMUNE RESPONSE TO PRIMARY HEPATITIS B VACCINATION SERIES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

Uma Padhye Phatak, Danilo Rojas-Velasquez, Anthony Porto, Dinesh S. Pashankar, Yale University, School of Medicine, New Haven, CT, USA **Background:** Patients with inflammatory bowel disease (IBD) are often placed on immunosuppressive medications which put them at a potential risk for reactivation of hepatitis B (hep B). Immune response following hep B vaccination is reported to be around 90% in children from the general population. The aim of this study was to assess the rate of adequate immune response to primary hep B vaccination series in children with IBD.

Methods: We performed a retrospective chart review of children with IBD who had serologic samples tested for hepatitis B surface antigen (HbsAg) and hepatitis B surface antibody (HbsAb) from February 2012 to July 2015. The study was conducted at Yale New Haven Children's hospital. Patients up to 22 years of age were included. Adequate immune response to hep B was considered to be present when the HbsAb level was above ≥ 8 mIU/mL by our laboratory standard. Age, gender, BMI (presence of obesity), type of IBD, and medications were noted to assess association of these factors with inadequate response to hep B vaccination.

Results: HbsAg and HbsAb levels were tested in 121 children with IBD. Mean age of the patients was 15.5 (± 3) years; 47 females and 74 males. Forty-seven children had ulcerative colitis and seventy four had Crohn's disease (CD). None of the patients had a positive HbsAg. Seventy-seven (64%) patients were found to be non-immune to hep B with HbsAb level less than 8 mIU/mL despite history of primary hep B vaccination. In 44 children with an adequate immune response, the mean level of HbsAb was 97 mIU/mL (range 9 to 682 mIU/mL). Sixty-two percent of children receiving anti-TNF therapy had an inadequate immune response to Hep B. Use of infliximab (44% in non-immune group vs. 47% in immune group) or immunomodulators (27% in non-immune group vs. 25% in immune group) was not significantly different between the two groups. Factors such as gender, type of IBD, presence of obesity, use of infliximab or immunomodulators were also not significantly different in the non-immune and immune group. 39 out of the 77 patients with an inadequate HbsAb level received a booster dose of hep B vaccine. Only 21 (53%) patients developed an adequate level of HbsAb after receiving booster dose.

Conclusion: Immunity to hepatitis B after primary vaccination series is lower in children with IBD as compared to the known immune response in the general population (64% vs. 90% respectively). Use of immunomodulator or anti-TNF therapy is not associated with lack of immune response to hepatitis B vaccine. Only about half of the children who received a booster dose of hep B vaccine were able to mount an adequate immune response.

1093 QUALITY OF LIFE IN PEDIATRIC CROHN'S DISEASE: DATA FROM THE IMAGEKIDS STUDY

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Background: The evaluation of health-related quality of life (HRQOL), using the validated disease-specific IMPACT-III questionnaire, has a key role in ascertaining the effect of disease on patients with Crohn's disease (CD). We sought to describe HRQOL variations across a large prospective cohort of pediatric CD patients with varying disease experience.

Methods: We used the prospectively collected data from the ImageKids study (a multicenter, multinational study designed to develop the pMEDIC and PICMI scores for magnetic resonance enterography) on children diagnosed with CD. IMPACT-III (35-item self-administered scale) was used to assess HRQOL in this cohort.

Results: Data from 180 patients were analyzed, 94 males (52.2%) with a mean age of 14.2 ± 2.2 y and a median of 27 month (IQR 0.05-4.2) of follow-up. According to wPCDAI, 29.0% of patients were in clinical remission, whereas 39%, 13%, and 19% had mild, moderate, and severe disease, respectively. IMPACT-III total score had a poor but significant correlation with degree of mucosal inflammation judged by the SES-CD ($r = -0.285$, $p < 0.0001$). Correlation was strong with clinical activity judged by wPCDAI ($r = -0.550$, $p < 0.0001$). Patients with higher disease activity had lower total IMPACT-III score, as did the 4 domains (wellbeing, emotional functioning, social functioning, and body image, Table I). Differences across wPCDAI groups were higher for wellbeing and lower for body-image domains. Patients with perianal disease had lower wellbeing ($p = 0.026$) and body image ($p = 0.004$) domain scores. Steroid treatment was associated more with lower emotional functioning score than enteral nutrition was ($p = 0.028$).

Conclusions: In this ImageKids cohort, HRQOL was lower in patients with higher disease activity and in those with perianal disease. An awareness of which domains within IMPACT may be differentially affected by various therapies or disease characteristics could help the clinician by focusing interventions (ie, psychological) to address these areas of concern.

1094 THE CLINICAL CHARACTERISTICS OF INFLAMMATORY BOWEL DISEASE IN CHINESE CHILDREN

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Background: There is a steadily increasing trend of pediatric IBD in China. It has been speculated that Chinese pediatric IBD is a distinct disease entity, with probably different disease subtypes. We aimed to describe various clinical manifestations, and endoscopic findings by using the pediatric modification of the Montreal classification, the Paris classification.

Methods: 171 cases of newly-diagnosed IBD in patients less than 18 years of age were documented from 2000 to 2014. Relevant data were extracted from their corresponding medical records.

Results: A total of 171 IBD cases were included in the study. Among them, 114 were males and 57 were females (male/female ratio, 2:1). 115 had Crohn's disease (CD) and 57 had ulcerative colitis (UC). The most common symptoms of CD were diarrhea (55.7%), abdominal pain (44.3%) and bloody stool (37.4%); The most common symptoms of UC were bloody stool (67.9%), diarrhea (44.6%) and abdominal pain (21.4%). More CD than UC patients had anemia and extraintestinal manifestations (eyes, skin, liver, joints). 53.9% of the CD patients had ileocolonic involvement, and 28.7% had involvement of the upper gastrointestinal tract. 48.2% of the patients with UC had left-side colitis. The average value of PCDAI is 35.3 ± 14.2 , and the average value of PUCAI is 33.1 ± 16 .

Conclusions: The Paris classification is a useful tool to capture the variety of phenotypic characteristics of pediatric IBD in China. Chinese CD children are similar to Western children, but Chinese UC children are similar to adults.

1095 LABORATORY VALUES IN JAPANESE CHILDREN WITH NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE: A SINGLE-CENTER EXPERIENCE

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Background and Aim: Laboratory values in children with newly diagnosed inflammatory bowel disease (IBD) have been reported from Europe and North America but not Asia. We therefore characterized laboratory values in Japanese children with newly diagnosed IBD.

Methods: We retrospectively reviewed patients under 16 years old who were newly diagnosed with ulcerative colitis (UC) or Crohn's disease (CD) at Kurume University Hospital between January 2008 and December 2015. Clinical and demographic characteristics, including type, extent, and activity of IBD at time of diagnosis were recorded. We also reviewed children diagnosed with irritable bowel disease who had normal lower endoscopic findings as controls. Diagnosis was based on generally accepted clinical, endoscopic, and histologic criteria. IBD location was determined using the Montreal classification, and disease activity was determined using the Pediatric Ulcerative Colitis Activity Index (PUCAI) or Pediatric Crohn's Disease Activity Index (PCDAI). We evaluated hemoglobin (Hb), platelet count (Plt), albumin (Alb), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), comparing values in our IBD patients with those in controls and in Western reports.

Results: Subjects with UC and CD numbered 31 and 15, respectively. Percentages of normal values of Hb, Plt, Alb, CRP, and ESR in UC/CD were 45/47, 68/53, 84/40, 81/7, and 35/0 %, respectively. Plt and CRP in UC did not differ significantly from values in controls. Alb and ESR were significantly different between UC and CD in both mild and moderate-severe groups. In patients with onset before age 10 years, values in UC did not differ significantly from CD. In UC, ESR correlated positively, while Hb and Alb correlated negatively, with PUCAI. In CD, CRP and ESR correlated positively with PCDAI.

Conclusions: Percentages of Japanese children with IBD showing normal laboratory values at time of diagnosis resemble those reported from Western countries. With early onset, UC may be difficult to distinguish from CD using laboratory values. ESR is a useful marker for disease activity at time of diagnosis in both UC and CD.

1096 THE MUTATION OF INTERLEUKIN-10/INTERLEUKIN-10 RECEPTORS AND CLINICAL CHARACTERIZATION OF CHINESE CHILDREN WITH VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE: A SURVEY OF CHINESE VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE STUDY GROUP

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Background: Interleukin-10 (IL-10) signaling genes play an important role in the pathogenesis of very early onset inflammatory bowel diseases (VEO-IBD) children that occurs in the first year of life. However, little information is available about the defect of IL-10/IL-10R in the VEO-IBD children of China.

Materials and Methods: A Chinese VEO-IBD study group was set up from 6 hospitals to collect the VEO-IBD children with IL-10R deficiency from 2015.3-2016.4. The parents and their siblings of the patients were also enrolled. The whole exome sequencing or Sanger sequencing were performed to detect the IL-10 and IL-10 receptor mutations. Moreover, the clinical presentation, laboratory, treatment information and prognosis were followed up.

Results: 51 VEO-IBD patients were enrolled in this study. 28 patients from 28 families, included 12 siblings, were identified with IL-10RA. There were 23 compound heterozygous mutations and 5 homozygous mutations of IL10RA in these patients. Among them, 6 point mutations had been described and 7 novel mutations were not reported. c.301C>CT (p.R101RW) and c.537G>GA (p.T179T) were the hotspots mutation in these patients account for 46.4%, 30.3% separately.

In the first symptoms of those patients, the diarrhea accounts for 82.2% (23 cases) with the time of onset 11.1 ± 8.0 days, mouth ulcer accounts for 14.3% (4 cases) with the time of onset 10.0 ± 3.5 days, 3.5% with both diarrhea and mouth ulcer (1 case) with the time of onset 12 days. 10/28 patients had the family history with their siblings dead with similar symptom. Extraintestinal manifestation in these patients included recurrent eczema (10/28), oral ulcer (14/28), perianal skin tag (5/28), perianal abscess (10/28), perianal fistulae (10/28) and rectovaginal fistulae (8/28). Colonoscopies were carried out in 24 children. The colon ulcerations were seen in all the patients.

Included were 18 mesalazine treated patients and 16 thalidomide-treated patients and 8 steroid-treated patients and 2 immunosuppressive agents treated patients, and 5 biological agents treated patients, and 3 patients with hematopoietic stem cell transplantation, and 2 patients with fecal microbiota transplantation, and 10 patients suffered enterostomy. After follow-up, 5 patients died because of sepsis.

Conclusions: This study revealed the character of genotype and phenotype of IL-10R mutation in the Chinese infants with VEO-IBD. The study expands the phenotype of IL10R in the VEO-IBD patients.

Keywords IL-10R, very early onset inflammatory bowel diseases, Chinese children.

NEUROGASTROENTEROLOGY & MOTILITY

1106 GUT MICROBIOME BIOMARKERS ARE ASSOCIATED WITH INCREASED PSYCHOSOCIAL DISTRESS IN CHILDREN WITH FUNCTIONAL

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Background: Childhood abdominal pain-related functional gastrointestinal disorders (AP-FGIDs) are heterogeneous with several factors (including the gut microbiome and psychosocial distress) potentially playing a role. Recent studies suggest that adults with anxiety and/or depression have a distinct gut microbiome composition. Whether children with AP-FGIDs have a different gut microbiome based on the presence or absence of psychosocial distress is unknown.

Objective: Characterize both gut microbiome composition and functional metabolic capacity in children with AP-FGIDs with psychosocial distress vs. those with AP-FGIDs who do not have psychosocial distress.

Methods: Children with Rome III AP-FGIDs enrolled in observational studies completed the Behavioral Assessment System for Children, 2nd Edition. Anxiety and depression T-scores were calculated for each individual; a T-score ≥ 60 indicated an at-risk and ≥ 70 a clinically significant scale elevation. Subjects provided a baseline stool sample for 16S rRNA gene sequencing. Sequences were quality controlled including chimera removal and closed reference operational taxonomic unit (OTU) picking with QIIME 1.9.1 using Greengenes 13.8 as a reference database. Functional (metabolic) predictions were inferred using the PIRCRUST 1.0 package. Linear Discriminant Analysis Effect Size (LEfSe) biomarker detection was completed on the OTU and functional (KEGG ortholog) predictions.

Results: 89 children were included of whom 68 (76.4%) had irritable bowel syndrome and the remainder functional abdominal pain. The overall group (mean \pm SD age 9.6 ± 1.5 years) was composed of 55 (61.8%) girls. Eighteen (20%) were at risk for anxiety whereas eight (9%) were at-risk for depression. Four (4.5%) children had elevated T scores for both anxiety and depression. LEfSe analysis identified 11 OTUs (majority from the family *Lachnospiraceae* (n=4), and order (n=3) *Clostridiales*) that were enriched (more commonly found) in those with elevated anxiety. Three OTUs (from the families *Porphyromonadaceae*, *Ruminococcaceae*, *Coriobacteriaceae*) were enriched in those without elevated anxiety. LEfSe analysis identified 36 OTUs (majority from the families *Lachnospiraceae* (n=24), *Ruminococcaceae* (n=8), and *Christensenellaceae* (n=2) enriched in those with elevated depression; one OTU (from the family *Porphyromonadaceae*) was enriched in those without elevated depression. *Lachnospiraceae* were most commonly from the genera *Blautia*. While no KEGG orthologs were associated with elevated anxiety, 7 KEGG orthologs (majority representing genes associated with sugar transport) were associated with elevated depression.

Conclusions: Though further studies are needed these preliminary findings suggest that microbiome biomarkers of both composition (particularly *Lachnospiraceae*) and metabolic pathways are associated with psychosocial distress (anxiety and/or depression) in children with AP-FGIDs.

1107 PREVALENCE AND POSSIBLE RISK FACTORS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS ACCORDING TO THE ROME III CRITERIA IN SPANISH, IN SCHOOL CHILDREN AND ADOLESCENTS FROM CUERNAVACA, MEXICO

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Introduction: Prevalence of functional gastrointestinal disorders (FGIDs) in Monterrey, Mexico was 41.7%.

Objective: To determine the prevalence of FGIDs according to the Rome III pediatric gastrointestinal symptoms survey in Spanish in children from Cuernavaca, Mexico.

Methods: Prevalence study in 238 school children (n=140) and adolescents (n=98) of a public school (n=103) and private school (n=135) in Cuernavaca, Mexico. Family, sociodemographic and clinical variables were obtained. Statistical analysis included estimation of the prevalence of FGIDs and its corresponding 95% CI, estimation of other descriptive measures of interest, association analysis and multiple logistic regression.

Results: In these children with mean age of 12.1 ± 2.0 years (between 8 - 18 years), 53.4% females, 28.0% singletons, 52.0% firstborn, 55.0% with parents separated/divorced and 2.0% with family history of FGIDs; we found a FGIDs prevalence of 31.1%, the most frequent FGIDs were functional constipation (EF) 15.5% and irritable bowel syndrome (IBS) 9.2%. The presence of nausea was predominant (OR 4.47; 95% CI, 1.85-11.09; $p = 0.0001$), with the presence of nausea as a possible risk factor (OR 5.70; 95% CI 1.13-28.81; $p = 0.035$). Overlap of FGIDs was present in 40.5%, mixed IBS (diarrhea and constipation) was more frequent.

Conclusion: A third part of the children in Cuernavaca, Mexico have some FGIDs type, the most frequent were EF and mixed IBS, the presence of nausea was identified as a possible risk factor

*1108 ESTRADIOL MEDIATES RELAXATION OF PORCINE LOWER ESOPHAGEAL SPHINCTER

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Background: Most pregnant women have symptoms of gastroesophageal reflux disease (GERD) during pregnancy. In addition to the effect of growing uterus pushing on the stomach, the effect of estradiol on the lower esophageal sphincter (LES) motility and GERD during pregnancy is not known. The purpose of this study is to investigate effects of estradiol on the LES motility.

Methods: Relaxations of clasp and sling strips of porcine lower esophageal sphincter caused by estradiol were measured using isometric transducers. We investigated the mechanism of estradiol-induced relaxation on the porcine LES using tetraethylammonium (TEA) (a non-selective potassium channel blocker), apamine (a selective inhibitor of the small conductance calcium-activated potassium channel), IbTX (an inhibitor of large conductance calcium-activated potassium channels), glibenclamide (an ATP-sensitive potassium channel blocker), KT 5720 (a cAMP-dependent protein kinase A inhibitor), KT 5823 (a cGMP-dependent protein kinase G inhibitor), NG-nitro-L-arginine (a competitive inhibitor of nitric oxide synthase), tetrodotoxin (a selective neuronal Na⁺ channel blocker), ω -conotoxin GVIA (a selective neuronal Ca²⁺ channel blocker) and G-15 (an estrogen receptor antagonist). Reverse transcription polymerase chain reaction (RT-PCR) analysis and immunohistochemistry (IHC) were performed to determine the existence of G-protein coupled estrogen receptor (GPER) in the porcine lower esophageal sphincter.

Results: In endothelin 1-precontracted porcine LES strips, the estradiol caused marked relaxations in a concentration-dependent manner. The mechanism of estradiol-induced relaxation on the porcine LES was associated with the potassium channel. RT-PCR analysis and IHC revealed that GPER was expressed in the clasp and sling fibers of porcine LES. This suggests that GPER mediates relaxation of the porcine LES.

Conclusions: GPER mediates relaxation of the porcine LES. Estradiol may play a role in the LES motility and, possibly, GERD during pregnancy.

1109 ASSESSMENT OF ANATOMICAL POSITION OF THE ANUS AND ITS RELATIONSHIP WITH BOWEL HABITS IN HEALTHY CHILDREN 1 TO 12 MONTHS

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Introduction: The importance of calculating the Ano Genital Index (AGI) is to detect Anterior Ectopic Anus (AEA) is diagnosed when the anal orifice is located proximate to the vulva or scrotum, being this a controversial entity.

Aim: To determine the normal anatomical position of the anus by measuring the AGI in healthy children aged 1 to 12 months, knowing the impact of the AEA and the relationship with bowel habits.

Material and Methods: A descriptive, transversal and analytical study where AGI was performed in 140 children. Study period: July 1, 2015 to December 31, 2015. The AGI was obtained by dividing the distances (cm): vulvar-ano fork/fork-coccyx (girls) and scrotum-year/scrotum-coccyx (children). The bowel habits survey was conducted according to Rome III criteria. Quantitative variables were described as mean \pm standard deviation (SD). Comparing groups and the level of variables was performed using Student's t-test. To determine relationships between AGI/bowel habits a model of bivariate logistic regression (logit) and their respective odds ratio was used.

Results: Of 140 patients analyzed, 51.4% were female. Statistical significant differences between mean female AGI (0.38 ± 0.04 mm) and male AGI ($0.04\text{mm} \pm 0.44$) ($p < 0.0001$) were observed. The incidence of AEA determined by mean value -2 SD was 1.38% for males (0.35 mm) and 0% for women (0.29 mm). Regarding the relationship between AGI/bowel frequency bi-variated relation the variable AGI/boys found to be significant ($p = 0.04$) for explaining the lower the value of AGI the more likely lower stool frequency (OR 9.85). Among AGI / stool consistency by sex the variable AGI/girls resulted to be significant ($p = 0.05$) to explain the lower the value of AGI the more likely to have very hard / hard stools consistency (OR 5.90). Analyzing AGI / history of painful bowel movements was observed in the girls group there is a higher probability of painful bowel movements ($p = 0.01$), this explains the lower the value of AGI, the more likely to have a history of painful bowel movements (OR 5.65).

Conclusions: Our study evidenced the value of the measurement of AGI, which is useful for screening AEA or early detection of bowel habits disorders.

***1110 STUDY OF ERYTHROMYCIN (EES) FOR THE TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) IN PREMATURE NEONATES**

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Background: GERD in premature neonates may include symptoms such as apnea, bradycardia, poor growth, aspiration or feeding intolerance in part due to gastrointestinal hypomotility. EES, a motilin receptor agonist, inducing smooth muscle contractions in the stomach and small intestine, is often used as a pro-kinetic in the management of GERD, despite lack of evidence from randomized controlled trials to support its efficacy.

Objective: To study the efficacy of EES in decreasing the frequency of GER events as determined by multichannel intraluminal impedance-pH monitoring in a randomized double-blind, placebo-controlled trial.

Methods: Eligible subjects included infants <37 weeks gestational age (GA) and >14 days old who were non-intubated and receiving full enteral feeds with clinical signs of GERD defined as feeding intolerance, frequent emesis, or unexplained apnea, bradycardia or desaturations. Subjects who met criteria underwent 24 h multichannel intraluminal impedance-pH (MII-pH) monitoring. If >5 reflux events were found on MII, then subjects were stratified by GA and randomized to receive either placebo or EES (50 mg/kg/day divided every 6 h x 7 days). All study personnel, participants and caregivers were blinded to the intervention. Repeat 24h MII-pH was performed on day 7 of study treatment and compared to initial MII-pH.

Results: 43 patients were enrolled in the study and 31 met criteria for randomization (84% <30 week GA). 15 patients received EES and 16 received placebo with average total reflux events of 33 and 32 events in pre-treatment 24-hour MII-pH, respectively. There was no significant difference between EES and placebo groups in pre- and post-treatment total reflux events (EES increased 5 vs. placebo decreased 12 events/24 h, *p* 0.09). There was no difference in acidic reflux (*p* 0.14), non-acidic reflux (*p* 0.46) or proximal reflux (*p* 0.54) events in the EES and placebo groups. There was also no significant difference in total reflux time (*p* 0.502), percent reflux time (*p* 0.86), bolus clearance time (*p* 0.49) or longest bolus clearance time (*p* 0.92) in the pre- and post-MII studies of both treatment groups. Gestational age subgroups were similar and there were no cases of pyloric stenosis.

Conclusions: EES at the dose of 50 mg/kg/day did not decrease reflux events on 24-hour MII-pH monitoring. EES did not improve additional measures of reflux including proximal reflux events, total reflux time or bolus clearance time. This study supports the NASPGHAN guidelines that discourage the use of prokinetic agents for infants with GERD.

1111 THE CLINICAL FEEDING EVALUATION IS INADEQUATE TO ASSESS PEDIATRIC SWALLOW FUNCTION

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Background: The evaluation of pediatric swallow function has historically been a two-step process, with radiologic studies only being obtained after a clinical feeding evaluation raises sufficient concern. Prior studies have suggested inconsistent agreement between clinical feeding evaluation and videofluoroscopic swallow studies (VFSS) but there is continued reluctance on the part of providers to expose pediatric patients to radiation with a fluoroscopic study. The aim of this study was to determine the sensitivity of a clinical feeding evaluation in making the diagnosis of aspiration compared to VFSS in an infant population.

Methods: We retrospectively reviewed the records of infants who had evaluation for oropharyngeal dysphagia using both clinical feeding evaluation and videofluoroscopic swallow studies at Boston Children's Hospital and compared the correlation between these assessments. All clinical feeding evaluations were performed by speech language pathologists and all videofluoroscopic swallow studies were read by attending radiologists.

Results: We evaluated 31 total subjects with a mean age of 51 ± 6.1 days who had both clinical feeding evaluations and VFSS performed. Presenting symptoms for evaluation included choking (35.5%), coughing (19.4%), cyanosis (51.6%), respiratory distress (25.8%), and reflux (22.6%). We found poor agreement between the two assessments of swallow function, as shown in the table. The clinical feeding evaluation incorrectly identified 38.7% of patients as having no oropharyngeal dysphagia when in fact aspiration or penetration was present on VFSS. The two approaches were found to be poorly concordant by McNemar's test (*p* 0.02) with a tetrachoric correlation score of 0.28, indicating low correlation.

Conclusions: There is poor agreement between clinical feeding evaluation and VFSS in making a diagnosis of aspiration. The algorithm for oropharyngeal dysphagia evaluation should be revised to always include an assessment of VFSS as clinical feeding evaluations are inadequate to assess for aspiration.

Table: Clinical Feeding Evaluation vs. VFSS

Results

Test	Aspiration	Penetration	Normal
Clinical Feeding Evaluation	35.5% (11)	0% (0)	64.5% (20)
VFSS	22.6% (7)	41.9% (13)	35.5% (11)

Data are expressed as % (n)

1112 ILLNESS PERCEPTIONS IN PATIENTS UNDERGOING MOTILITY TESTING AND THEIR PARENTS: EXAMINATION OF PRE-POST CHANGE

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The concept of illness perception involves several aspects regarding one's beliefs about their illness. This may include how long they anticipate being impacted by their illness, the perceived controllability of their illness, and if they believe treatment will be beneficial. One's perception of their illness has been shown to impact health outcomes, including adherence, coping, somatic symptoms, and anxiety about medical symptoms. The role of illness perceptions have been examined for several pediatric populations, including cerebral palsy, cancer, asthma, and Type 1 diabetes. In our motility center, parents and patients arrive for diagnostic testing often feeling that they have little understanding of their illness. As such, we felt it of interest to investigate parents' and patients' illness perceptions at admission, and then after our multidisciplinary collaborative assessment experience.

The team approach consisted of interaction and consultation with physicians, nurses, psychologists, social workers, and child life specialists. Following testing, families participated in a collaborative feedback session with a physician and psychologist (as needed) to discuss test results and recommendations. Parents and patients (ages 8 and older) completed the Brief Illness Perception Questionnaire (BIPQ) at admission and then following collaborative feedback. Parents reported statistically significant changes in personal control ($p.003$), treatment control ($p.01$), concern ($p.01$), and coherence ($p.002$). Patients reported statistically significant changes in personal control ($p.02$) and treatment control ($p.02$). All changes were in the anticipated direction.

The outcomes of our study demonstrated that following a multidisciplinary collaborative assessment, parents reported greater personal control, greater belief in treatment effectiveness, decreased concern and greater understanding of their child's illness. Children reported greater personal control and greater belief in treatment effectiveness. While the exact mechanism for this change cannot be identified, we postulate that a multidisciplinary team evaluation and collaborative feedback approach may influence changes in illness perceptions. Future research should examine longer-term changes in illness representation post-motility evaluation, as well as any resultant outcomes that would be related to this cognitive change.

1113 ROLE OF T-TYPE $\alpha 1H$ Ca^{2+} CHANNELS (CAV3.2) IN SPONTANEOUS MECHANICAL ACTIVITY OF COLONIC MUSCLE OF RATS WITH EXPERIMENTAL HIRSCHSPRUNG'S DISEASE

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Background: Hirschsprung's disease (HSCR) has been shown to be associated with abnormal distribution and function of interstitial cells of Cajal (ICC). It has been shown that T-type $\alpha 1H$ Ca^{2+} Channels (Cav3.2) are required for entrainment of pacemaker activity within ICC and for active propagation of slow waves in ICC networks.

Aim: To study the role of Cav3.2 in spontaneous mechanical activity of the rat model of HSCR.

Methods: HSCR rat model was established by microinjection of 0.2% benzalkonium chloride (BAC) solution into the rectum of neonatal SD rats of 6-8 days old. At post-operative week 4, 6 and 8, ten rats were sacrificed randomly and colonic tissues were assessed by histopathological examination and immunofluorescent staining. The role of Cav3.2 in abnormal colon of HSCR rat model was determined by tensile force *in vitro*.

Results: After 8 weeks of BAC treatment, HSCR rat model was successfully established, with decrease or lack of ganglion cells in distal colon. In *in vitro* studies, circular colonic muscle strips of control rats showed a regular pattern of spontaneous mechanical activity, which were vanished in that of HSCR rats. When $ZnCl_2$ (selective inhibitor of Cav3.2) was added into muscle incubation bath, colonic muscle strips of control rats exhibit the pattern of muscle contractions similar to that of HSCR rats, not the regular pattern of spontaneous activity. In contrast, when Na_2S (activator of Cav3.2) was added into incubation bath, colonic muscle of HSCR rats exhibited no change in the mechanical activity. Interestingly, in control animals, tensile forces of colonic muscle in $ZnCl_2$ -added bath significantly increased after subsequent addition of Na_2S , which were similar to that of acetylcholine.

Conclusion: Cav3.2 is important in spontaneous mechanical activity of colonic muscle and mediates functional change of ICCs, resulting in intestinal dysfunction in a rat model of HSCR.

1114 PREVALENCE OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN THE EUROPEAN-MEDITERRANEAN AREA: PRELIMINARY DATA.

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Background: Functional gastrointestinal (GI) disorders (FGIDs) are frequent disorders often misdiagnosed and associated with significant morbidity and high health-care costs. Data on the prevalence of FGIDs in children are scarce. This multicenter study aimed at assessing the prevalence of FGIDs in children and adolescents in a community sample of the European-Mediterranean Area.

Methods: The prevalence of FGIDs has been assessed using translated versions of the questionnaires on pediatric GI symptoms based on Rome III Criteria (QPGS-RIII). The parent-report form has been used for subjects aged between 4-10 years (Group A), while the self-report form has been used for subjects aged between 11-18 years (Group B). Children and adolescents have been enrolled in schools distributed throughout the national territory of the involved countries.

Results: We enrolled 3419 subjects aged between 4-10 years (mean age, 7.37 ± 4.24 years; females 53.9%), and 4143 subjects aged between 11-18 years (mean age, 14 ± 4.9 years; females, 54.9%) from 6 countries: Croatia (Group A, 546, and Group B, 594); Jordan (Group A, 773, and Group B, 815); Israel (Group A, 323, and Group B, 772); Italy (Group A, 482, and Group B, 593); Macedonia (Group A, 692, and Group B, 863); and Serbia (Group A, 603, and Group B, 506). Among subjects from group A, 7.65% met criteria for functional constipation, 3.27% for irritable bowel syndrome, 3.04% for aerophagia, 2.56% for abdominal migraine, 1.01% for cyclic vomiting syndrome, 0.61% for functional abdominal pain (lower abdominal location), 0.61% for functional abdominal pain (upper abdominal location), 0.55% for functional dyspepsia; 0.44% for nonretentive fecal incontinence; 0.06% for functional abdominal pain syndrome (lower abdominal location), 0.03% for functional

abdominal pain syndrome (upper abdominal location), and 0.01% for adolescent ruminant syndrome. Prevalence of FGIDs in children from group B was: 13.9% for functional constipation; 8.87% for abdominal migraine; 6.26% for aerophagia, 5.76% for irritable bowel syndrome, 4.43% for functional dyspepsia, 1.27% for functional abdominal pain (lower abdominal location), 1.26% for cyclic vomiting syndrome, 0.91% for functional abdominal pain (upper abdominal location), 0.57% for functional abdominal pain syndrome (lower abdominal location), 0.55% for nonretentive fecal incontinence, 0.39% for adolescent ruminant syndrome, and 0.29% for functional abdominal pain syndrome (upper abdominal location). There were no significant prevalence differences among the participating countries.

Conclusions: FGIDs are commonly found in children and adolescents from the European-Mediterranean area, especially in subjects older than 10 years of age. Functional constipation and abdominal migraine are the most common disorders. There are no significant differences in FGIDs prevalence among the involved countries.

1115 OUTCOME OF BIOFEEDBACK TREATMENT IN CHILDREN WITH FECAL INCONTINENCE AND ESTABLISHMENT OF AN "ENVY SCORE".

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Background: Fecal incontinence (FI) or encopresis secondary to chronic constipation (CC) is a frequent indication for pediatric gastroenterology consultation. Polyethylene glycol (PEG) is the first-line treatment for CC. Children above 6 year-old and suffering from FI may benefit from biofeedback. CC induces a remodeling of the rectum, increases the maximum volume to trigger defecation (i.e. "need volume" when inflating the balloon) and increases the sensation expressed by the child to defecate (i.e. "envy score"). Need volume and envy score are respectively an objective and a subjective evaluation of the child's need to defecate. The envy score is a novel score developed in our department and used in the last 3 years for children treated with biofeedback for encopresis.

Objectives: To analyze the outcome of biofeedback with a special emphasis on the evolution of need volumes and envy scores.

Methods: Retrospective study including 25 children (20 boys) with a median age of 10 years (range 7-17) and suffering from FI (according to Rome III criteria). The initial management included enemas, PEG treatment and weekly biofeedback sessions after ano-rectal manometry to rule out Hirschsprung disease. Two children needed Peristeen® enemas for severe fecal impactions resistant to regular enemas. Children were asked during each session for their envy score to defecate on a scale of 0 to 100 corresponding to the need volume. The outcome was considered a success when soiling completely disappeared, partial success when soiling frequency was reduced by more than 50% and failure when reduced by less than 50%. Data were analyzed using the R statistical software version 3.0.2.

Results: All children had suffered from FI for more than 3 years. Five children out of 25 had not received any previous treatment for their CC. The mean dosage of PEG used was 0.43g/kg/d (range 0.15-1.14). Children had a mean of 2.6 sessions of biofeedback (range 1-5). At the end of biofeedback sessions, 13 children had no soiling (52%, after median of 3sessions), 6 children had less than 50% of soiling (24%) and 6 had more than 50% (24%). The need volumes decreased during the biofeedback sessions (-9ml/session, $p=0.05$) without statistical difference between the 3 categories of children. The envy scores also decreased with time (-1.25/session, $p<0.01$). The scale was well accepted by all children.

Conclusion: Biofeedback is an efficient tool for treating children with FI. Improvements were observed in the decrease of need volumes and envy score respectively. An envy score during biofeedback sessions enhances the communication with children. This score needs to be validated on a larger scale.

1116 BLASTOCYSTIC HOMINIS AND CHRONIC ABDOMINAL PAIN: IS THERE A RELATIONSHIP?

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Abstract: Chronic abdominal pain is one of the most frequent causes of pediatric consult and is divided into functional and organic. The etiology of chronic abdominal pain is diverse, although it has been described with parasites such as *Giardia lamblia*, *Ascaris lumbricoides* and *Blastocystis hominis* (Bh). This last parasite in particular is extremely controversial, since it is unclear whether it is a commensal or a pathogen of the gastrointestinal tract, because it is often found in asymptomatic individuals. Some recent publications propose Bh as an etiologic agent of functional abdominal pain, predominantly irritable bowel syndrome, the proposed pathogenic mechanism being production of proteases, proteolytic enzymes and cytokines, such as I-6 proinflammatory TNF- α and degradation of secretory IgA. Azizian *et al* have shown that the severity and the presence of disease is different according to the parasite load and *Blastocystis* subtype, with variability in the plasma concentration of cytokines and enzymes; all involved in the development of irritable bowel syndrome. Therefore the aim of this study was to find an association between chronic abdominal pain and the presence of *Blastocystis hominis*.

Materials and Methods: Retrospective, comparative and analytical study. We reviewed the electronic data base of our hospital, searching all coproparasitoscopic studies from January 2003 to October 2015 positive for Bh. We chose the clinical records of patients with Bh and chronic abdominal pain according to the Rome III criteria, and then we compared the patients who improved with treatment against Bh and those who didn't improve. Gender, age, treatment, response, and results of control coproparasitoscopic were collected. Those cases that didn't meet the criteria for chronic abdominal pain and who didn't have complete information in the clinical record were excluded. Chi-square test was used for statistical analysis.

Results: Of the 101 patients treated, 69 improved, while 32 continued with symptoms; conversely, of the 37 patients who didn't receive treatment 13 improved, while 24 continued with symptoms. By comparing the improvement of symptoms of patients who received treatment versus those who didn't receive antimicrobial treatment we found a statistically significant difference ($p<0.001$) (Figure 1). The drugs that had better effect in improving symptoms were tinidazole/mebendazole and secnidazole ($p<0.001$), followed by nitazoxanide ($p<0.04$). Metronidazole and trimethoprim/sulfamethoxazole didn't show any statistical difference.

Conclusion: The etiology of chronic abdominal pain is wide in variety, and many patients are classified with a functional gastrointestinal disorder, like irritable bowel syndrome and functional abdominal pain; however, we found that in patients who have Bh and present symptoms of chronic abdominal pain it is appropriate to give treatment.

1117 GASTROSTOMY FEEDING TUBE IN RETT SYNDROME: WHO, WHEN AND WHY?

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Introduction: Rett Syndrome is a neurodevelopmental disorder caused by mutations on the X chromosome on the MECP2 gene (>200 mutations). It almost always affects girls (1:10,000 births) during infancy. It can impact sensory, motor, emotional and autonomic functions of the brain that can affect oral motor function resulting in feeding problems. Depending on the severity of involvement many need a gastrostomy tube for feeding. There is dearth of information on the clinical profile of individuals with Rett Syndrome who need a G tube for supplemental feeding.

Aim: To describe the clinical characteristics of a cohort of individuals with Rett Syndrome who have a gastrostomy tube for feeding.

Methods: An IRB approved, retrospective study was conducted on children, identified from the institutional database, who were diagnosed with Rett Syndrome and had a G Tube. Demographic, anthropometric, genetic and clinical data were gathered and tabulated. Statistical analysis was performed on the results.

RESULTS: A total of 32 subjects were identified (30 females). Mean age of the girls at the time of study was 19 years and the boys were 11 years; none were deceased. Seventeen had a G tube before 10 years of age and 13 had the G tube placed after age 10. Mutational analysis on the MECP2 gene done on 31 subjects revealed that most had a deletion. The timing (before or after 10 years age) for a G tube was not affected by the type of mutation. Even though dysphagia was the most common indication for a G tube placement in both age groups, aspiration and medication administration were the 2 indications in the over 10 years group that were significantly more common when compared to the younger group ($p=0.032$ and $p=0.033$). Most received a standard cow's milk based formula. 62% received bolus feeds, 19% received continuous and 19% got a combination of daytime boluses and night-time continuous. Complete anthropometric data was available in 18 and the mean z-score for weight before G tube placement for the entire cohort was -1.86 and after 3 months -1.47 (Delta= -0.4; range= -0.02 to 1.76). Most had a low profile (button) G tube but one subject was switched to a GJ tube due to vomiting and aspiration risk. Only 7 subjects had a fundoplication surgery with the G tube. Oral intake did not change significantly after G tube placement in 75% ($p=0.007$ vs. a null hypothesis of 50%). In 21 subjects with seizures, the seizure frequency did not change in 76% after G tube feeds (improved in 3 and worsened in 2). The most common complication after G tube placement was local cellulitis (in 23%) but 66% had no reported complications.

Summary: We provide preliminary guiding evidence for determining the criteria for gastrostomy tube placement and timing of insertion in patients with Rett Syndrome. We also share the outcome of this intervention in our cohort of patients.

1118 FUNCTIONAL GASTROINTESTINAL DISORDERS IN JORDANIAN CHILDREN: CROSS-SECTIONAL STUDY

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Aim: Functional gastrointestinal disorders (FGIDs) are common in children. Data from our part of the world are scarce. Our aim is to perform a population-based study using Rome III criteria to estimate the prevalence of FGIDs in Jordanian children.

Methods: We performed a cross-sectional study of school children in the four major cities in Jordan. Children between 4 and 10 years recruited. Parents were asked to complete the Arabic version of the Questionnaire on Pediatric Gastrointestinal Symptoms–Rome III (QPGS-III). Sociodemographic data of the child and the family were obtained.

Results: A total of 773 subjects (49 % male, median age 7.9 years, range 4-10 years) completed our study. A total of 192 subjects (24.8%) met criteria for a FGID. Defecation disorders were the most common group of FGIDs. Functional constipation was diagnosed in 12.2 %. Abdominal pain predominant FGIDs were seen in 7%. Abdominal migraine and irritable bowel syndrome were the most common 3.6 and 3.2 respectively.

Conclusion: FGIDs are common in school-aged children in Jordan. Functional constipation is the most common disorder.

1119 CAN PERISTEEN TRANSANAL IRRIGATIONS PREVENT SURGICAL INTERVENTION IN PEDIATRIC PATIENTS WITH ORGANIC DEFECATORY DISORDERS?

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Background: In children with organic constipation and fecal incontinence the Malone antegrade colonic enema (MACE) is the gold standard when traditional therapy has failed. However, the MACE requires surgery which has a potential for associated complications, and is not successful in all patients. Additionally, there is a reluctance to create MACE stomas in younger patients. Transanal irrigations (TAI) provide a non-surgical option for treatment. The Peristeen system (coloplast) enables patients to perform TAI independently.

The primary aim of this study was to assess the effectiveness of Peristeen in treating patients with organic constipation and/or incontinence who had been referred for surgical intervention for a MACE or had failed to demonstrate improvement after the MACE procedure.

Methods: The study included 13 patients that were either referred for MACE surgery (9) or had failed MACE irrigations (4). All participants completed the Fecal Incontinence Quality of Life and the Neurogenic Bowel Dysfunction Scales (0-very minimal dysfunction, ≥ 14 - severe dysfunction), and an overall satisfaction with their bowel management on a 0-10 Likert-like scale. All study participants received a private two hour standardized training session from the same nurse practitioner (FP). During the session the appropriate balloon and fluid volumes were decided, and patients and caregivers were instructed on its use. Participants were evaluated after using Peristeen for a minimum of two months using the same instruments listed above. Statistical analysis was performed using t-paired test and Chi-square.

Results: Thirteen subjects were included, age ranged from 7-24 years (mean 18.8 ± 5.6). The main diagnoses were anorectal malformations, spina bifida, and Hirschsprung's disease. Percentage of patients reporting fecal incontinence went from 77% to 54% ($p= .03$) post-Peristeen. Four patients reported anxiety related to their bowel symptoms, this number decreased to 2 patients post-Peristeen ($p= 0.09$). As seen in *Table 1*

post-Peristeen there was a statistically significant improvement in bowel control and care, neurogenic bowel dysfunction scores, and bowel satisfaction scores. From the 4 patients that failed MACE, all stopped antegrade colonic enemas, and 3 became fully continent with Peristeen. Conclusion: Transanal irrigations are effective for the treatment of organic constipation and fecal incontinence, and may be an alternative to MACE surgery. These results support the use of Peristeen prior to surgical intervention and in cases where surgical intervention has failed to demonstrate improvement of bowel symptoms.

1120 *PROLONGED CHEMICAL CLEARANCE IN CHILDREN WITH CYSTIC FIBROSIS COMPARED TO SYMPTOMATIC AGE-MATCHED NON-CYSTIC FIBROSIS CHILDREN IS NOT pH-DEPENDENT*

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Background: The post-reflux swallow-induced peristaltic wave (PSPW) index is a new impedance-pH parameter that has been used to assess chemical clearance (CC) efficiency in gastroesophageal reflux disease (GERD). Calculation involves the counting of gastroesophageal reflux (GER) episodes that are followed within 30s by a PSPW, and then multiplying by 100; the higher the PSPW Index, the greater the CC efficiency. The PSPW Index is typically calculated using both acid (pH <4) (AGER) and nonacidic (pH ≥4) GER (NAGER) episodes.

Aims: To calculate two separate PSPW Indices, one for AGER and one for NAGER, and then use these to compare children with and without CF.

Methods: EPM-MII tracings from 16 CF children (3-18 years) and 16 age-matched non-CF children were blindly analyzed. For each child, a PSPW-AGER and a PSPW-NAGER Index was calculated. Median PSPW-AGER and PSPW-NAGER Indices were calculated and compared between CF and non-CF cohorts. Results are expressed as median (IQR). An additional aim for this study was to compare the PSPW-GER (across all 32 patients) to the PSPW-AGER (across all 32 patients) to see if the potential difference was significant. We also compared PSPW-AGER to the PSPW-NAGER (across all subjects) to see if CC was more efficient for either the PSPW-AGER or the PSPW-NAGER.

Results: PSPW Index for total GER episodes was 41.1% (29.8-63.5) for CF children and 56.7% (49.5-70.1) for non-CF children ($p = .021$).

Similarly, PSPW Index for CF and non-CF children was: 1) 42.6% (30.6-53.3) vs. 58.1% (47.5-67.2), $p = .029$, respectively, for AGER episodes, and 2) 31.6% (0-50) vs. 88.8% (52.5-100), $p = .003$, respectively, for NAGER episodes. Comparisons between PSPW-GER and PSPW-AGER ($p = 0.73$) or PSPW-NAGER ($p = .65$) revealed no significant differences. Similarly, PSPW-AGER and PSPW-NAGER were not different ($p = .60$).

Discussion: The purpose of this investigation was to derive PSPW indices that were calculated using both 1) AGER + NAGER, 2) only AGER, and 3) only NAGER and to use them to compare CC between children with CF and without CF. The data show that CC efficiency, as determined using the new impedance-pH parameter (PSPW Index), is less efficient in our CF cohort. These results confirm our previous study in which we showed, using durations of acid neutralization during CC of AGER episodes, that CC is prolonged in CF. Remarkably, this study shows that delays in CC do not appear to be pH-dependent, as evidenced by the fact that PSPW-AGER and PSPW-NAGER Indices were both significantly greater for the non-CF cohort. Additional studies involving larger samples sizes are needed to further study the importance of these findings and to elucidate the mechanisms that underlie CC delays in children with CF. Also, additional studies assessing the importance of CC during NAGER are also needed.

*1121 *ABNORMAL MITOCHONDRIAL BIOENERGETICS IN FUNCTIONAL DISORDERS CORRELATES WITH DISABILITY SCORE*

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Background: Limited information links mitochondrial abnormalities to migraine and cyclic vomiting syndrome, but no data address other functional disorders. Mitochondrial supplements may benefit some patients clinically, but standard evaluation (muscle biopsy, genetic analysis) is usually unrevealing. We hypothesized that patients with functional disorders (FD e.g., chronic migraine, functional gastrointestinal disorders, chronic fatigue syndrome, etc.) show impaired mitochondrial bioenergetics.

Methods: We compared blood from youth with an FD from the pediatric autonomic and neuro-gastroenterology clinics at Children's Hospital of Wisconsin with carefully screened healthy controls (HC) with no functional disorder or chronic medical condition. The Oxygen Consumption Rate and Extracellular Acidification Rate (ECAR) measurements utilized the Seahorse XF96 Extracellular Flux Analyzer (North Billerica, MA), in unbuffered/serum free RPMI assay media supplemented with 1mM pyruvate. Peripheral Blood Mononuclear Cells (PBMCs) were seeded in a PS V7 cell culture plate at a density of 3.25×10^5 cells per well, then placed in a non-CO2 incubator for one hour. Oligomycin (1 μ g/mL), Carbonyl cyanide-4-phenylhydrazone (FCCP) (1 μ M) and Antimycin A (10 μ M) were used to determine the mitochondrial stress test parameters. A Mann-Whitney test compared skewed variables, and Fisher's exact test dichotomous variables. A regression tree examined predictors (among age, gender, basal, ECAR and SRC) of functional outcome (Functional Disability Inventory, FDI) optimized by least absolute deviation and 10% leave out samples for cross validation.

Results: 45 subjects (36 female) with a median (range) age of 16 years (10, 20), did not differ by age or gender between 15 FD and 30 HC FD subjects. FD subjects demonstrated lower resting mitochondrial function (basal respiration BR: FD 33.7 [13.3, 96.8] pmol/min units for all values, HC 56.0 [27.1, 171.1] $p = 0.002$), and lower reserve energy (spare respiratory capacity - SRC: FD 68.4 [5.2, 264.7]; HC 118.0 [32.6, 377.3] $p = 0.016$). BR correlated with SRC ($p < 0.0001$). Interestingly, of all factors, SRC best predicted clinical functional disability (SRC ≤80, median FDI of 30; SRC > 80, median FDI of 14; $p = 0.06$) in the FD group. Non-mitochondrial energy generation did not differ between groups (ECAR: FD 17.0 [5.6, 55.8]; HC 21.0 [12.0, 37.9] $p = 0.092$).

Conclusion: Both mitochondrial resting function and reserve energy are impaired in functional disorders, but non-mitochondrial bioenergetics appear unaffected. Of great interest, the reserve energy (SRC) predicts clinical functional disability in FD, and could explain their profound fatigue. The mechanism of the bioenergetics impairment could involve predisposing genetic factors or acquired changes that reverse as disease improves. Prospective longitudinal studies will distinguish these possibilities.

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1122 *UTILITY OF HIGH-RESOLUTION ANORECTAL MANOMETRY IN YOUNG CHILDREN WITH CHRONIC CONSTIPATION*

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Background: Childhood constipation is a common problem accounting for 30% of visits to pediatric gastroenterologist. Only 5-10% have organic cause, with Hirschsprung disease (HD) as the major one. Anorectal manometry (ARM) is a non-invasive tool to demonstrate recto-anal inhibitory reflex, which is absent in children with HD. There is scant literature on utility of ARM in management of chronic constipation in young children.

Aim: The aim of the present study was to evaluate the role of high resolution ARM in young children ≤ 5 yr of age with constipation at a tertiary care referral centre.

Patients and Methods: Consecutive patients ≤ 5 years of age who underwent anorectal manometry for chronic constipation from August 2012 to January 2015 were identified. All patients underwent anorectal high resolution manometry (16 channel water perfusion) at our motility lab. Demographic data, manometry findings and subsequent outcome were recorded.

Results: A total of one hundred and thirty-seven cases [mean age 3 ± 1.2 yrs, 80 (58.3%) boys] were evaluated. On anorectal manometry the mean basal resting pressure was measured 55 ± 20 mm Hg with no difference observed with respect to gender or final diagnosis. The mean length of the high pressure zone in children varied from 2.6 to 3.2 cm. The mean rectal balloon volume to elicit rectoanal inhibitory reflex was 30 cm^3 . Barium enema done elsewhere was reported as suspicious for HD in 40/137 (29%) cases. Of these 137 cases, 12 (8.7%) had absent rectal anal inhibitory reflex suggestive of Hirschsprung disease. Of them, 10/12 cases had absent ganglion cells on rectal biopsy confirming diagnosis of HD and subsequently underwent surgery. All ARM procedures were done under midazolam sedation with no intra- or post-procedure adverse events.

Conclusion: High definition ARM is a reliable and safe tool in the management of chronic constipation in young children.

1123 APPROPRIATE EVALUATION OF CONSTIPATION IN THE PEDIATRIC EMERGENCY DEPARTMENT

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Background: Due to increased utilization of emergency departments (ED) for primary care services, it is one of the first sites to which children present with abdominal pain and constipation. This study investigated whether children are appropriately evaluated and managed for constipation in the ED.

Methods: Medical charts of patients seen at the University of Maryland Medical Center's pediatric ED for abdominal pain or constipation from September 2013 – December 2013 were retrospectively reviewed. The presence or absence of 13 constipation-related screening questions and physical examination elements was assessed. Encounters were classified as insufficient, moderate, and complete based on the number of components present. The presence of 0 to 3 components was considered insufficient, 4-8 components was moderate, and 9 or more was complete. Patients' abdominal radiographs (KUBs) were interpreted by three blinded pediatric gastroenterology (GI) physicians who then selected their recommended management for each patient. The GI physicians' interpretations were compared to that of radiologists and their proposed management was compared to that which the patient received in the ED. Inter-observer agreeability was assessed by utilizing kappa values (k).

Results: 64.9% of 131 encounters were insufficient evaluations of constipation. 35.1% were moderate and 0% were complete. Encounters most consistently assessed nausea/vomiting (96.1%) and current medications (94.7%). Stool frequency and caliber were assessed 22.9% and 26.7% of the time, respectively. Fecal soiling/encopresis and a diet history were each assessed in 1.5% of encounters. Of the physical examination components, palpation for an abdominal mass/palpable stool, perianal examination, and digital rectal examination were performed in 16.8%, 3.1%, and 1.5% of encounters, respectively. Assessment of toilet training was never assessed. Of the KUBs ordered, radiologists commented on stool burden 63.6% of the time. There was poor agreement between GI and radiology physicians on interpretations of the degrees of stool burden and poor agreement between GI and ED physicians on constipation management. Among GI physicians there was fair-to-moderate agreement on KUB interpretations and management of constipation.

Conclusion: Children are being insufficiently screened for constipation in the pediatric ED. The lack of agreeability between pediatric GI physicians and the ED and radiology physicians in evaluating and managing patients with abdominal pain or constipation in the ED, suggests that an algorithm outlining screening by history, physical examination, subsequent management, and standardized guidelines for radiological evaluation may be beneficial. A prospective study on the efficacy of such an algorithm may be a future direction for this study.

1124 AVAILABILITY OF LOW-DOSE CT IN THE DIAGNOSIS OF APPENDICITIS IN CHILDHOOD AND COMPARISON OF ABDOMINAL USG AND STANDARD DOSE CT

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Objective: Acute appendicitis is the most common abdominal disease in pediatrics that requires a surgical procedure. Diagnostic accuracy of acute appendicitis gets higher while negative appendectomy rate gets lower as imaging techniques have developed. Ultrasonography (USG) is considered as safe diagnostic method, however, its diagnostic accuracy is variable due to operator factors and it is difficult to apply in obese patients. Computed tomography (CT) scan should be carefully used due to radiation hazard, which is why interest in low-dose CT has increased recently. Most studies in the past were performed in young adults or adolescents; moreover, there has been no clinical study for childhood, especially early age. Therefore, we evaluated usefulness and accuracy of low-dose CT in diagnosis of acute appendicitis in childhood and compared it to abdominal USG and standard-dose abdominal CT.

Methods: 484 childhood patients younger than 10 years old who were presented to Chung-Ang University Hospital between March 2005 and December 2014 and examined and/or treated for acute appendicitis were recruited for this study. The subjects were divided into 4 groups according to performed radiologic methods; low-dose CT group, abdominal USG group, standard-dose CT group and USG + standard-dose CT group. The subjects were categorized according to age classification and BMI.

Results: Of patients evaluated with radiologic methods, surgical procedure was performed in 312 patients after diagnosis of acute appendicitis. (low-dose CT; 90, USG; 40, standard-dose CT; 167, and USG + standard dose CT; 15). The low-dose CT was a contributive tool in appendicitis, and there was no significant difference by comparison with USG or standard-dose CT in sensitivity (94.4% vs. 95.0% and 95.2%, $p = 0.879$), specificity (96.4% vs. 80.0% and 97.5%, $p = 0.025$), positive predictive value (96.6% vs. 92.7% and 98.8%, $p = 0.031$) and negative

predictive value (94.1% vs. 85.7% and 90.7%, $p = 0.944$). In perforated patients, the low-dose CT was diagnosed in all patients. Both early childhood and middle childhood were effectively diagnosed using low-dose CT. In comparison, according to obesity, low-dose CT was useful and represented similar results to USG and standard-dose CT in all BMI groups.

Conclusion: Low-dose CT is effective and relatively accurate in diagnosis of acute appendicitis in childhood, as well as in early age or obese patients. Also, there was not insufficient irrespective of early age or obesity. Therefore, the low-dose CT could be an effective diagnostic method for acute appendicitis in childhood as well as in adolescence.

Conflict of interest: The authors have indicated they have no potential conflicts of interest to disclose.

1125 COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE (MII) – pH-METRY: CLINICAL EXPERIENCE IN PEDIATRIC POPULATION OF BOGOTA, COLOMBIA

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Objectives: 1) To analyze the importance of practicing combined Multichannel intraluminal impedance (MII)-pH-metry in the pediatric population, 2) to assess the prevalence of acid reflux, acid and hypersensitive esophagus in the pediatric population, 3) to discuss the importance of symptomatic index in patients with gastroesophageal reflux through the realization of MII - pH monitoring.

Background: Currently there are few studies to determine the clear utility of MII - pH monitoring patients with gastroesophageal reflux disease (GERD) and mainly atypical symptoms of the disease. So with this study we aim to evaluate the usefulness of this test and above all achieve precise therapeutic approach to patients who actually if required.

Methods: We carried out a retrospective study to evaluate the results of MII –pH monitoring in order to evaluate the prevalence of acid and non acid reflux, characterizing the significance of the symptomatic index in children and the incidence of esophageal hypersensitivity. The study was carried out in a cohort of 149 patients aged between 1 – 18 years who underwent MII –pH monitoring between April 2012 and February 2016 in a gastroenterology center in Bogota - Colombia.

Results: One hundred forty-nine studies were analyzed, the 46.73% of them were women, with an average age of this population of 9.09 years (SD 0.50 years). Among the main findings the most common type of reflux was acid reflux with a prevalence of 20.80% (31 subjects), followed by non-acid reflux with 18 cases (12.08% prevalence) and 12.75% reflux was acid and non-acid (19 subjects). As for evaluating symptomatic this index was negative in 51.00%, 20.8% were positive for acid reflux index and 18.8% (28 subjects) reported hypersensitive esophagus.

Conclusions: The MII - pH monitoring is considered a useful test to determine the specific characteristics of the type of reflux in a patient with GERD, its association with atypical symptoms and functional processes that can be likened to a disease.

1126 ARE PROXIMAL EXTENT OR BOLUS CLEARANCE TIME RELEVANT DATA IN EVALUATION OF GASTROESOPHAGEAL REFLUX IN INFANTS WITH APPARENT LIFE THREATENING EVENTS?

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Background: Apparent life-threatening events (ALTE) are a frequent cause of hospitalization in infants. These can be idiopathic in half the cases; however, gastroesophageal reflux is one of the potential diagnoses to be ruled out.

Aim: To evaluate characteristics of gastroesophageal reflux (GER) (acid and non-acid), bolus clearance time (BCT) and proximal extent with multichannel intraluminal impedance-pH 24hs (MII-pH24 hs) in infants admitted to the hospital because of an ALTE event

Materials and Methods: From May 2005 to October 2015, a retrospective study was conducted in infants under 6 months of age who were hospitalized for a choking episode assumed to be an ALTE. Exclusion criteria: ventilatory support, treatment with caffeine, permanent nasogastric tube and genetic disorders.

Evaluation of GER was performed by a MII-pH24 hs. Patients were divided according to: GI had choking episodes during hospitalization and GII had not. T-test and mann- whitney was used for statistical analysis.

Results: A total of 125 infants (68 girls), median 53.6 days of age (r 6-110 days) were evaluated. GI: 41 infants had choking and GII: 84 had not. The variables analyzed showed: Total episodes of GER 50.05±SD17.77 vs 41.67±SD15.89 $p0.012$; Acid GER 25.37±SD14.58 vs

19.74±SD12.72 $p0.060$; NonAcid GER 25.95±SD15.96 vs 21.95±SD12.29 $p0.305$; BCT 15.63±SD3.83 vs 9.82±SD6.28 $p0.0001$; Proximal Extent 29.59± SD14.66 vs 21.57± SD13.78 $p0.005$. Table 1. According to proximal extent, GI had >50% reached channel 1-2 vs. GII <50%.

Conclusions: An overall mean increase in the number of episodes which reach proximal channels, in total episodes of GER and in acid reflux, with longer bolus clearance time are all the features observed in infants with ALTE and choking. The MII/pH 24hs study can shed some light on the dynamic disorders implicated .

Table 1.

	GI (X±SD)	GII (X±SD)	t	Z sub t	p
Total Episodes GER	50.05 ± 17.77	41.67 ± 15.89	3064.5	2,505	0.012
Acid GER	25.37 ± 14.58	19.74 ± 12.72	2945.0	1,878	0.060
Non Acid GER	25.95 ± 15.96	21.95 ± 12.29	2782.0	1,026	0.305
BCT	15.63 ± 17.77	9.82 ± 6.28	3542.0	4,608	0.0001
Proximal Extent	29.59 ± 14.66	21.57 ± 13.78	3125.0	2,813	0.005

1127 APPLICATION OF 24-HOUR MULTICHANNEL INTRALUMINAL IMPEDANCE AND pH MONITORING FOR EVALUATION OF GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH NEUROMUSCULAR DISEASES

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Background: Twenty-four hour esophageal multichannel intraluminal impedance and pH monitoring (MII-pH) is a novel method for diagnosis of both acid- and non-acid gastroesophageal reflux disease (GERD). However, its application on the patients with neuromuscular diseases (NMD) has not been well investigated.

Methods: Patients with documented NMD who received 24-hour MII-pH monitoring during the past 3 years were retrospectively recruited for the study. A total of 17 subjects were recruited, aged from 2 to 44 years old, including spinal muscular atrophy in 9, Duchenne muscular dystrophy in 4, and other diagnosis in 4. The GERD symptoms, diagnostic evaluations such as MII-pH monitoring, videofluoroscopic swallowing study/ upper gastrointestinal series (VFSS/UGI), radionuclide scan of gastric emptying time, and treatment effects were analyzed. Esophagogastroduodenoscopy (EGD) was not regularly arranged in this study.

Results: The most common presenting symptoms were acid regurgitation and heart burn (9/17), followed by easily choking (4), postprandial fullness (3), vomiting (2), dysphagia (2), upper gastrointestinal bleeding (1) and recurrent pneumonia (1). MII-pH monitoring was performed successfully on 12 subjects but failed on 5 subjects due to intolerance of the procedure. Significant acid regurgitation, defined by Reflux Index $\geq 5\%$, was discovered on 8 patients by pH monitoring. Two patients with normal pH study were found to have weakly acid or non-acid reflux by MII monitoring. Only 3 out of 13 subjects who received VFSS/UGI were found to have gastroesophageal reflux. Furthermore, 2 out of 5 subjects who received gastric emptying study were found to have gastroesophageal reflux. Patients with abnormal pH study were treated with proton-pump inhibitor (6/8), Histamine-2 receptor antagonist (1/8), or prokinetic therapy (1/8). Other 2 patients with only weakly acid or non-acid reflux were treated with prokinetic agents alone. Improvement of symptoms was reported by all of the patients. Noteworthy, one patient presented by chronic cough got complete symptom free under treatment of prokinetics.

Conclusions: Compared with VFSS/UGI and radionuclide gastric emptying scan, 24-hour MII-pH study shows better sensitivity in detecting acid and non-acid GERD among patients with NMD and is more tolerable than EGD. It may provide superior guidance on GERD management for patients with NMD. However, normal values for the number of retrograde bolus movements among NMD patients need to be further investigated.

1128 DISIMPACTION IN CHILDREN WITH FECALOMAS AND ENLARGED RECTUM USING POLYETHYLENE-GLYCOL AND SODIUM PICOSULPHATE

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Background: Polyethylene glycol (PEG) is the gold standard for oral faecal disimpaction. A regimen of PEG with the stimulant sodium picosulphate (SPS) produced disimpaction in children with chronic constipation in a suburban clinic. We wished to know if it worked in more difficult cases.

Aim: Determine stool output and effect on faecaloma of combined PEG and SPS children with long established constipation with very hard impacted stools and enlarged rectums.

Methods: Inclusion criteria: 2 yrs chronic constipation, ongoing laxatives, palpable fecaloma confirmed by enlarged stool-filled rectum on x-ray and rectal:pelvic ratio >0.6 . Daily diary recorded for week before and 1 week treatment. X-rays were taken on day 1 and day 8. Laxative doses were based on child's age and stool volume on day 1. Movicol (PEG + electrolytes 13.7 g/sachet) dose was 4-8 sachets (day 1-2), 2-4 sachets (day 3), 1 sachet for 4 days. Each sachet was dissolved in 125 ml water plus equal volume of juice/milk. Children drank 125-250 mL per half hour in the morning and 10-20 drops of SPS (Dulcolax SP) at night.

Results: 94 children (4-15 yrs) with palpable faecaloma and enlarged rectum were recruited from tertiary teaching hospital. Patients produced a large volume of soft stool over 4 days, 0.5- 4.0 L of stool over day1-4 and 4.2 ± 0.6 L (mean \pm SEM) over 7 days. Stool volume (median) increased from 1.0 L/wk pre- to 2.3 L/wk during the disimpaction week. Stool consistency increased from (mean \pm SD) BSS 4 ± 2 to 5 ± 1 . Stool volume in the x-ray, extent and number of patients with fecalomas reduced. Gastrointestinal symptom scores (PEDsQL) improved significantly. Parents but not children perceived that the child's QOL improved. Using the MOTIVATE method, children were easily able to drink the large volume of PEG solution and compliance was high. Half of the patients required a second high dose to achieve disimpaction. Conclusion: In children with very hard stools and rectal enlargement, combined PEG and SPS given at high dose on day 1 and 2 are effective in producing large volumes of stool. The method was well tolerated but further refinement of dose is required as only half of the patients had complete emptying.

1129 URINARY AMINO ACID METABOLOMIC PROFILING IN PEDIATRIC PATIENTS WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

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Objectives and Study: Chronic intestinal pseudo-obstruction (CIPO) is a rare disorder with significant morbidity and mortality. Unlike short bowel syndrome (SBS) mainly caused by anatomical bowel resection, CIPO is a functional defect in intestinal motility. These patients may display altered metabolomic profiling, and therefore, this study aimed to 1) investigate the differences in amino acids profiling between SBS and CIPO, 2) assess the alterations in amino acid profiles that may potentially help improve the management of CIPO.

Methods: A prospective study was performed in pediatric patients with SBS or CIPO who were admitted to our hospital between 2015 and 2016. Nutritional intake was daily monitored. Patient history, biochemistry tests and clinical outcomes (length of hospital stay, length of ICU stay and death) were collected from medical record. Spot urine samples were collected every 3 days during hospitalization. Amino acid metabolomic profiling was performed by LC-MS.

Results: A total of 182 urine samples collected from 26 pediatric patients were determined, including 16 SBS patients (5 males; age range 0.2-10.0 years and median age 0.7 years) and 10 CIPO patients (6 males; age range 0.3-9.1 years and median age 0.6 years). Compared to control

group (n 20, age-matched patients with nongastrointestinal symptoms), concentrations of 5 metabolites (putrescine, methionine, ornithine, lysine and spermidine) were increased in both SBS patients and CIPO patients. Six metabolites from CIPO group exhibited statistically significant differences ($p<0.01$) compared with SBS group, including putrescine (increased, 1.5-fold), serotonin (increased, 2.8-fold), glutamic acid (increased, 1.7-fold), aspartic acid (increased, 1.9-fold), glutamine (decreased, 0.6 -fold) and asparagine (decreased, 0.4 -fold). Enteral calories (%) in CIPO patients and SBS patients were 26% and 67%, respectively. Urinary excretion of serotonin might be a potential marker of enteral autonomy in CIPO patients. It negatively correlated with enteral calories (%) in CIPO patients ($R = -0.758, p<0.001$), but did not correlate with that in SBS patients. It also appears that those with low-excretion of serotonin (<0.01 uM/uM creatinine) had better clinical outcomes than those with high-excretion of serotonin (>0.01 uM/uM creatinine). Glutamine/glutamic acid ratio was significantly decreased in CIPO group (median 6.14) in comparison with SBS group (median 12.96, $p<0.0001$). This ratio might have clinical significance in help identify complicated cases with bowel resection accompanied by potential dysmotility \pm from those patients with simple SBS. The area under ROC curve was 0.83, at cut-off value 7.04 with sensitivity of 65% and specificity of 92%.

Conclusion: Pediatric patients with CIPO have distinct amino acids profiles in comparison to patients with SBS.

Urinary serotonin and glutamine/glutamic acid ratio may potentially help improve the management of CIPO.

1130 ILEAL MOTILITY IS ABNORMAL IN CHILDREN WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION BUT NOT IN CHILDREN WITH INTRACTABLE CONSTIPATION

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Background: Ileal motility has been poorly valued in children with refractory constipation, little is known about normal patterns and no information is available in terms of its utility in identifying abnormal patterns in chronic intestinal pseudo-obstruction (CIPO). We present our experience with children undergoing ileal manometry.

Methods: Children undergoing ileal manometry for 2 indications: evaluation of intractable constipation and CIPO. Ileal motility catheter was placed via colonoscopy through the ileocecal valve or via ileoscopy through an ileostomy. Normal manometry was defined when phase III of the migrating motor complex (MMC) was observed during fasting and/or with octreotide challenge.

Results: A total of 26 children were included, 13 were female and median age was 6.8 years (range 0.5-22.5 years). A total of 21 patients had an ileostomy and underwent the study via the ileoscopy and 5 patients underwent the study by placing the catheter through the anus via colonoscopy and advancing it through the colon and the ileocecal valve. The indication of the procedure was intractable constipation in 15 and CIPO in 11. Medians were compared using nonparametric tests, proportions using Chi-square and logistic regression to evaluate the joint effect of different factors on the presence of a normal ileal manometry. We found no association between age, gender and response to erythromycin with normal ileal motility. We did find a significantly higher rate of normal ileal manometry among patients with intractable constipation compared to CIPO (14/15 or 93% vs. 3/11 or 27%, respectively, $p<0.001$). If we exclude those patients in whom the ileal manometry was performed via the colon the results do not change, in fact, the only subject with constipation and an abnormal ileal manometry was performed that way, he had significant abdominal distention. We then evaluated the joint effect of age, gender and study indication and we found only study indication for constipation was significantly associated with the observation of a normal study ($p = 0.019$).

Conclusion: Ileal motility can be performed in children via an ileostomy as well as via the colon through the ileocecal valve. Ileal manometry is abnormal in patients with CIPO and normal in children with constipation, it may be not needed in patients with intractable constipation being evaluated for the first time or in those evaluated for consideration of ostomy closure.

*1131 METABOLOMICS ANALYSIS IDENTIFIES NOVEL BIOMARKERS OF EXTRAESOPHAGEAL REFLUX

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Introduction: Diagnosing extraesophageal reflux disease (EERD) is difficult; current testing methods are not very sensitive and largely rely on measuring esophageal reflux burden, which may not reflect the amount of reflux reaching the lung. To overcome these limitations, new diagnostic tests are needed. Metabolomic profiling may offer a promising approach to EERD diagnosis. While metabolomic analyses have identified biomarkers of airway inflammation, there are no studies in patients with EERD. The aim of this study was to characterize the metabolome in bronchoalveolar lavage (BAL) fluid in children with and without pathologic reflux.

Methods: In this cross-sectional study, BAL fluid was collected from children 1 – 18 years of age who underwent bronchoscopy and multichannel intraluminal impedance (pH-MII) testing for evaluation of chronic respiratory symptoms. The pH-MII study was considered abnormal if there was abnormal esophageal acid exposure (pH <4 for $\geq 6\%$ of the study) or an abnormal number (>73) of reflux events during the study. To identify potential biomarkers of EERD, we performed global metabolomic profiling on all samples using ultrahigh performance liquid chromatography-tandem mass spectroscopy (UPLC-MS/MS). ANOVA contrasts were used to identify biochemicals that differed significantly between groups.

Results: Metabolomic analysis was performed on BAL fluid collected from 43 children (mean age 9.0 ± 4.3 years, 54% male). 23 children had abnormal pH-MII testing and were classified as having pathologic reflux. 17 patients were on proton pump inhibitor (PPI) therapy during the study. A total of 255 metabolites were identified. Children with pathologic reflux who were not on PPI treatment had significant elevations in a variety of phospholipid classes (including derivatives of glycerophosphoethanolamine, glycerophosphorylcholine, glycerophosphoserine, glycerophosphoglycerol and glycerophosphoinositol) ($p<0.05$). Interestingly, these phospholipid disturbances were not seen in patients without pathologic reflux or in patients with reflux treated with proton pump inhibitors, suggesting that these metabolites may be true biomarkers of EERD. In addition to the phospholipids, several non-lipid metabolites involved in pathways of nucleotide and carnitine metabolism were also elevated in BAL samples from children with untreated reflux, though differences between groups were of lesser magnitude.

Conclusions: Metabolomic analysis of BAL fluid can identify biomarkers of EERD in children with chronic respiratory symptoms. The most significant metabolic alterations were seen in glycerophospholipids.

1132 QUALITY IMPROVEMENT ANALYSIS OF BARIUM ENEMA UTILIZATION IN SCREENING FOR HIRSCHSPRUNG DISEASE FOLLOWING THE INTRODUCTION OF A NEW SCREENING TOOL, ANORECTAL MANOMETRY

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Background: Infants and children with refractory constipation and/or delayed passage of meconium are suspected of having Hirschsprung Disease (HD). The diagnostic evaluation is invasive and includes a rectal suction biopsy and if unequivocal then a full thickness biopsy. Biopsies may involve risk (bleeding, perforation, and anesthesia); therefore, other less invasive techniques may be used to screen for HD such as Barium Enema (BE) and Anorectal Manometry (ARM). BE has significant radiation exposure and lower sensitivity/specificity compared to ARM and biopsies. ARM is less invasive, does not include anesthesia or radiation exposure, and is performed in children ≥ 3 months of age. Aims: To observe the effects of a new screening tool ARM on a) frequency of BEs to rule out HD, b) subspecialty utilization of BE, c) surgical interventions (full/rectal biopsies) based on BE findings.

Methods: ARM was introduced to Seattle Children's Hospital on August 1, 2013 in conjunction with education of hospital and community providers regarding the use of ARM in screening children ≥ 3 months with suspected HD. We retrospectively analyzed data from 127 children of ≥ 3 months who had BE to rule out HD spanning 28 months pre- and post-introduction of ARM. The number of BEs, characteristics of the ordering subspecialty, the number of rectal biopsies based on BE findings, and the number of ARMs were compared between the two time periods to assess for change in practice and quality improvement measures.

Results: There was a significant difference between the number of BE ordered pre- and post-introduction of ARM (pre-ARM n 104 vs. post-ARM n 23; $p < 0.001$). The number of BE ordered by the different subspecialty groups declined following intervention; the greatest changes were seen within outpatient Gastroenterology [pre-ARM n=60 (57.7%) to post-ARM n=8 (34.8%) of which BE ordered at 1st clinic visit declined from 26% to 8.7%] and Primary Care [pre-ARM n=21 (20.2%) to post-ARM n=4 (17.4%)] settings. The number of surgical biopsies declined (pre-ARM n=14 to post-ARM n=4).

Conclusion: The introduction of ARM as a new screening tool for HD, and the educational intervention in the utility of ARM to screen for HD in children ≥ 3 months at Seattle Children's Hospital, resulted in a significant decline in the overall number of BE. This decline was seen across all subspecialty services, markedly within the Gastroenterology and the Primary Care outpatient services. Most notably there was a decline in the unnecessary radiation exposure and unwarranted surgical rectal suction and full thickness biopsies following the introduction of ARM.

1133 A QUALITY IMPROVEMENT INITIATIVE: DEVELOPMENT OF AN EVIDENCE-BASED GUIDELINE FOR DECREASING GASTROSTOMY TUBE PLACEMENT IN PEDIATRIC PATIENTS WITH ASPIRATION

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Introduction: Gastrostomy (g-tubes) tubes are a commonly used method for achieving enteral access in pediatric patients with aspiration. Unfortunately, g-tubes are often associated with significant morbidity and potential increased rates of hospitalization. With the creation of an Aerodigestive Center at Boston Children's Hospital in 2012, orally thickened feeds as a first-line treatment option have been promoted as a safer feeding alternative in aspirating patients, especially given the dynamic natural history of aspiration in young infants and children.

Unfortunately, little data exists about the rates of g-tube placement in these patients since the initiation of Aerodigestive Centers; in addition, wide practice provider variation often still exists in the evaluation and treatment of these patients.

Methods: A quality improvement retrospective review was conducted of all new patients < 2 years with aspiration, as confirmed by videofluoroscopic swallow study (VFSS), at Boston Children's Hospital between January 2014 and September 2015. Frequency of patients undergoing subsequent primary g-tube placement within one year of the initial VFSS were reviewed, as well as frequency of VFSS prior to g-tube placement.

Results: 754 patients underwent an initial VFSS during the study period with 476 patients (63.3%) noted to have aspiration or penetration; aspirating patients had a median age (SD) of 8 (6.3) months and 60% were male. During this time period, 54 (11.5%) aspirating patients underwent g-tube placement within a year of the initial VFSS. Of the patients who did not undergo G tube placement, 137 (44%) had repeat VFSS within one year of their initial VFSS, suggesting that clinicians were tracking swallow function over time for resolution of aspiration. Discussion: Despite the low rates of gastrostomy tube placement in aspirating patients, less than half of patients were found to undergo a repeat VFSS to reassess swallowing function. Therefore, development of a hospital wide quality improvement algorithm for standardizing the approach to aspirating patients is warranted in order to decrease the potential for patients undergoing unnecessary g-tube procedures and help standardized pre-operative swallow study evaluation prior to tube placement. Further longitudinal monitoring will be needed in order to assess the guideline's clinical impact on aspirating patients' rates of g-tube placement, repeat VFSS, use of hospitalization and other emergency services over time.

1134 THE EFFECTIVENESS OF COMREST (CONSTIPATION MANAGEMENT, RELIEF AND SUPPORT THERAPY) REGIMEN FOR THE TREATMENT OF FECAL IMPACTION AMONG PEDIATRIC PATIENTS IN A TERTIARY HOSPITAL

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Introduction: Fecal impaction can be defined as either having a hard mass in the lower abdomen identified during physical examination, a dilated rectum filled with a large amount of stool found during rectal examination, or excessive stool in the colon identified through abdominal radiography. Evidence-based guidelines recommend polyethylene glycol (PEG) for three days (up to six days) or Fleet enema if PEG is not available for the treatment of fecal impaction. The COMREST regimen offers a one-day novel combination of oral and rectal laxatives for the treatment of fecal impaction that consists of Fleet enema, bisacodyl suppository, and castor oil.

Objectives: The primary objective of this study was to validate COMREST, a structured management scheme for the treatment of fecal impaction

Methods: Pediatric patients aged 2-18 years old admitted for fecal impaction were randomized to receive either Fleet enema (3-day regimen, n=30) or COMREST (1-day regimen, n=28). Assessor-blinded evaluation of symptom improvement was obtained during treatment and the Blethyn radiographic scoring system for fecal impaction was acquired after treatment. The primary outcome was the proportion of successful disimpaction between the two treatment groups defined as relief of symptoms present prior to the disimpaction regimen and/or a Blethyn Score of 0 or 1.

Results: Fifty-eight patients were included in the study. The demographic and clinical profiles of the treatment group (n=28) and control group (n 30) were comparable. At the end of treatment, only one (3.57%) patient from the experimental group and two patients (6.67%) from the

control group remained symptomatic. We also assessed the symptoms after treatment completion and noted fewer complaints of abdominal pain (p -value 0.019) and faster symptom relief (p -value 0.013, 1.6 versus 2.2 days) in the experimental group compared to the control group. At the end of treatment for disimpaction, only 10.71% ($n=3$) in the experimental group remained to have fecal impaction compared to 53% ($n=16$) in the control group. The difference in the radiologic findings between the two groups was statistically significant (p -value 0.001). Overall, more patients experienced struggle with the administration of the experimental treatment compared to the control regimen (57.14% versus 36.67%). Administration of treatment through the rectum contributed to the majority of the adverse events for both the experimental (46.43%) and control group (36.67%). Also, vomiting was noted in four (14.29%) patients in the experimental group. We assessed the acceptability of the two regimens and found no sufficient evidence to determine a difference between the two groups.

Conclusion: COMREST regimen may be used as an alternative therapeutic option to once-daily three-day Fleet enema regimen for obtaining faster symptom relief and resolution of fecal impaction assessed through abdominal radiograph taken after treatment.

1135 DOES THE DENGUE VIRUS PREDISPOSE CHILDREN TO POSTINFECTIOUS-IRRITABLE BOWEL SYNDROME?

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Functional gastrointestinal disorders (FGIDs) are common. The prevalence of FGIDs is fairly homogeneous worldwide. Acute gastroenteritis commonly predisposes children and adults to the development of FGIDs. We hypothesize that the local epidemiology influences the prevalence of FGIDs. Dengue is a mosquito-borne viral infection that is common in some countries but is not present in others. We conducted a study in 12 schools (10 cities) throughout Colombia, a country with endemic and epidemic dengue to assess whether dengue predisposed children to develop FGIDs.

Methods: School children were given an age-appropriate validated questionnaire to diagnose FIGDs according to the Rome III criteria (QPGS-III). Additionally, children were asked questions about their health including whether they had dengue in the previous year.

Results: 4023 children completed the questionnaires. 301 children reported having dengue in the past year (7.5%). 13% of school children who had dengue during the previous year vs. 0.66% without dengue were diagnosed with FGIDs (OR 1.98; 95% CI, 1.53-2.56; $p=0.0000$) at the time of the interview. A history of dengue was significantly associated with the presence of IBS (OR 2.36; 95% CI, 1.53-3.56; $p=0.0000$) and functional constipation (OR 1.69; 95% CI, 1.21-2.33; $p=0.0008$). There was no significant difference in the prevalence of any other FGID between children with and without a history of dengue.

Conclusion: Children with a history of dengue are at higher risk of developing FGIDs in the following year. The health problems of dengue seem to exceed the acute period. The study suggests that post-infectious-IBS is not only associated with the previously described bacterial and viral gastrointestinal agents but also with the virus of dengue. Despite the fairly similar prevalence of FGIDs across countries the etiological agents preceding the development of FGIDs may vary by region. Future prospective studies should clarify this association.

1136 CASE REPORT: DISTAL INTESTINAL OBSTRUCTION SYNDROME COMPLICATED BY INTUSSUSCEPTION

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Introduction: Distal intestinal obstruction syndrome (DIOS) is characterized by acute partial or complete ileocecum obstruction by inspissated intestinal content, exclusively in cystic fibrosis (CF) patients.

Case Description: A 17-year-old female patient, with CF (Homozygous F508 deletion), and associated pancreatic insufficiency, diabetes, pulmonary hypertension, and malnutrition, was evaluated after four weeks of outpatient treatment of CF pulmonary exacerbation. She complained of diffuse colicky abdominal pain and vomiting for the last 2 weeks. In the first 5 days she had diarrhea, but then returned to her regular bowel habit - soft stools three times daily. She had sought medical care twice, and was discharged home. Physical exam revealed a weight loss of 2.3 kg in the past month, and a painful palpable mass in the right lower quadrant, with no signs of peritonitis. Abdominal x-ray did not show a classic pattern of complete obstruction. For the initial management of DIOS, Polyethylene Glycol was administered orally, as she refused a nasogastric tube. She responded with elimination of large amounts of feces and inspissated secretions, relief of the abdominal pain and resolution of vomiting, but the palpable abdominal mass, although smaller, persisted. CT revealed ileocecal intussusception associated with inspissated bowel contents. Colonoscopic approach was chosen, and during bowel preparation the abdominal mass disappeared. Colonoscopy was performed and showed an enlarged colon and no intussusception at the time of the procedure.

Discussion: Incidence reported of DIOS can reach up to 10-47% of patients with CF. It can affect any age group, but most cases are reported in adolescents and young adults. Risk factors include: severe genotype, pancreatic insufficiency, poor control of malabsorption of fat, dehydration, and prior history of DIOS. The most common site of obstruction is the ileocecal junction. Typical manifestations include crampy abdominal pain in the right lower quadrant, abdominal distension, palpable mass, flatulence, vomiting, weight loss. Bowel habit may remain unchanged or patients may present either diarrhea or constipation. Plain abdominal radiographs and abdominal ultrasound can help the diagnosis, but computerized tomography shows proximal small-bowel dilation and inspissated fecal material in the distal ileum, as well as is useful to identify other causes of the symptoms, such as appendicitis and intussusceptions.

Intussusception is a more rare complication in CF, with an incidence of 1%. The lead point is usually the mucofaeculant bolus associated with DIOS, distending the appendix. Signs and symptoms overlap with those of DIOS and the differential diagnosis may be difficult.

Conclusion: A high index of suspicion for early recognition of DIOS in cystic fibrosis patients is essential. The case presented illustrates first a delay in its diagnosis, and second an associated complication of intussusception.

1137 PRENATAL NICOTINE EXPOSURE IMPAIRS GASTRIC EMPTYING, GLUCOSE METABOLISM AND GROWTH IN NEWBORN RAT PUPS USING AN INTRAUTERINE GROWTH RESTRICTION MODEL

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Background: Nicotine exposure delays gastric emptying and results in metabolic derangement in adults. The effects of prenatal nicotine exposure (PNE) on neonates have not been explored.

Aims: To evaluate the effects of PNE on 1) gastrointestinal motility, 2) glucose metabolism and 3) growth, in newborn rat pups using an intrauterine growth restriction model.

Methods: the Animal Review Committee at the University of Mississippi Medical Center approved the protocol. Starting two weeks before mating, nulliparous female rats (200-250 g) were randomly assigned to receive daily subcutaneous injections of nicotine bitartrate (1 mg/kg/day) or vehicle (saline). Maternal injections were continued until weaning (postnatal 21 days). Weight and caloric intake were compared between groups. Glucose metabolism was evaluated using the Insulin Tolerance Test (ITT). Gastric emptying (GE) was evaluated using the Evan's Blue method.

Results: PNE rats (n=4) weighed less than controls (n=4) at 3 months post-natal age (PNE 358 ± 16 g vs. control 402 ± 9 g, $p < 0.05$). PNE rats consumed less feed (PNE 16.24 ± 0.13 g/d vs. control 18.14 ± 0.21 g/d, $p < 0.05$) and fewer calories than controls (PNE 48.53 ± 0.37 kcal/d vs. 54.43 ± 0.63 kcal/d, $p < 0.05$). Glucose metabolism was impaired in PNE rats (n=4) compared to controls (n=4) by ITT (baseline glucose g/dL: 104 ± 2 vs. 105 ± 3 , $p = \text{NS}$; 30 min: 104 ± 8 vs. 76 ± 2 , $p < 0.05$; 60 min: 103 ± 13 vs. 53 ± 1 , $p < 0.05$; 120 min: 102 ± 9 vs. 56 ± 2 , $p < 0.05$). GE was slower in PNE rats (n=5) compared to controls (n=5) (PNE GE 11% vs. control GE 28%, $p < 0.05$).

Discussion: The model used in this study mimics fetal and neonatal exposure from a smoking mother on breast-fed offspring. These findings suggest PNE plays a role in growth, metabolism and motility in rat pups. The effects were observed several weeks after weaning; therefore, PNE continues to affect offspring in an indirect fashion.

1138 GASTRIC ELECTRIC STIMULATION IN TEENAGE CHILDREN: A 2-YEAR FOLLOW-UP STUDY

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Introduction: Gastric electric stimulator is a surgically inserted device in the distal stomach, which emits electrical impulses to aid peristaltic activity and improve nausea and vomiting. Gastric electrical stimulators are commonly used in adult population for patients with gastroparesis often secondary to diabetes. The incidence of teenagers with chronic nausea and vomiting with unknown aetiology is increasing. Children with Idiopathic gastroparesis refractory to treatment with prokinetic agents and proton pump inhibitors are challenging.

Methods: Prospective review of patients who underwent insertion of gastric stimulators for intractable nausea and vomiting unresponsive to drugs.

Results: 7 teenagers underwent surgical insertion of gastric stimulators for intractable nausea and vomiting. 6 were females and one was male. The median age was 15 years (range 13-18 years). Symptoms at presentation included nausea and vomiting in 7 children, associated abdominal pain in 3 patients and 1 had early satiety along with nausea and vomiting. 6 of them had gastric emptying studies which showed delayed gastric emptying and the other was unable to tolerate the study. Electrogastrography showed gastric dysrhythmias in all 6 children, with increased episodes of tachygastria in 4 and mixed dysrhythmias in 2. Of the 7 patients, 2 had cyclical vomiting syndrome unresponsive to medication, 2 had post-surgical fundoplication, 2 had Ehlers-Danlos syndrome and 1 had Addison's disease. Median duration of symptoms prior to gastric stimulator insertion was 2.25 years (range 1.25-11 years). Stimulator was inserted using laparotomy (2 patients) and laparoscopic approaches (4 of 5 robotic assisted). None had any peri or post-operative complications. Median duration of hospital stay was 3.5 days (range 1-6 days). Patients were followed up at 3, 6, 12, 18 and 24 months. At 2-year follow-up, one patient had the pacemaker removed at 16 months, as she had not improved. Five of seven patients (71%) with nausea and vomiting improved, and were able to tolerate oral feeds. One of three patients with abdominal pain preoperatively recovered completely and 1 patient with early satiety made complete recovery post-operatively. 7 patients were on artificial feeding (6 Jejunal feeds and 1 on TPN) before the procedure. Five of seven patients (71%) are feeding orally now and gaining weight. One patient lost weight and is on TPN.

Discussion: Gastric electrical stimulation (GES) has been shown to be effective in selected adult population with gastroparesis but has been done infrequently in children. Our results demonstrate that GES can be both safe and effective in children with intractable nausea and vomiting. However the results are limited by small sample size and relatively short follow-up.

NUTRITION & INTESTINAL REHABILITATION

1146 LIPID CHARACTERIZATION IN BREAST MILK

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Breast milk (BM) is considered the optimal form of nourishment for infants during the first six months of life (WHO) and among its macronutrients, the lipid fraction is crucial, representing almost 50% of the calories supplied to the newborn infant. Lipids occur in milk in the form of fat globules mainly composed of triacylglycerols (~98% of total lipids) surrounded by a structural membrane composed of phospholipids (PL), cholesterol, enzymes, proteins, glycosphingolipids and glycoproteins, (Bitman, 1984). Progress in analytical technologies together with quantitative sampling of BM allows for a better identification and quantification of BM nutrients and thereby providing a deeper understanding of the composition of BM. To improve our knowledge on lipid BM composition, analytical methods to quantify fatty acid (FA) regioisomeric distribution in triacylglycerol (TAG), phospholipid (PL) species, cholesterol and gangliosides (GD) have been developed and validated. These technologies were applied to quantify lipid classes in BM samples collected at 30, 60, 90 and 120 days postpartum. FA regioisomeric distribution in TAG from human milk did not change along the lactation period. PL class distribution slightly changes over lactation stage and a decrease in intensity due to the lower concentration of PL at later lactation stages was observed. Major GD class distribution changes during the lactation period, with GD3 decreasing and GM3 increasing over the time. In conclusion, our developed methodologies are sensitive and robust for application to large cohorts to gain insights into not only the nutritional intake of breastfed infants but also the impact of maternal nutrition on lipid output in BM.

1147 THE INFLUENCE OF THE TYPE OF FEEDING ON WEIGHT GAIN AND METABOLIC BALANCE OF HIGH-RISK NEWBORNS

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Background and Aim: High-risk newborns are often much smaller than healthy infants when are discharged from hospital. Different types of feeding: breast milk, formula or mixed can influence growth rates and improve development. The aims of the study were to evaluate the growth rates; catch-up rate and some biological parameters of the nutritional status such as: hemoglobine, iron, calcium, phosphor, magnesium, the level of plasmatic protein, nitrogen balance at differents ages: 1-2-4-6 months in three different types of nutrition: breast milk, special formula for premature , breast milk with premature formula or started formula .

Material and Methods: A retrospective study was performed in a tertiary neonatal care unit between 2011–2013 in the County Hospital of Cluj, Romania on 383 infants presented to periodical examination in the follow-up program: 465 records. We divided into 3 categories : group I-VG ≤ 32 weeks, group II-VG between 32-36 weeks and group III-VG ≥ 36 weeks of gestation. The evaluation consultations were performed at 1-2-3-4-5-6 months. Each evaluation consisted of determining: weight, CBC, calcium, iron, magnesium, protein, blood urea nitrogen (BUN) levels. Informed consent was obtained. Statistical analysis was made with Microsoft Excel 2016 and IBM SPSS v.23.

Results: Growth rate up to 6 months wasn't significantly influenced by the type of feeding ($p = 0.319$). Hemoglobin at 2 months highlighted statistically higher values in the formula-fed group: 11.77 ± 2.07 g compare with premature formula-fed group: $10.848 \pm 1,7556$ g ($p = 0.008$). The values of iron at 2 months hasn't presented any significant differences according to the types of feeding ($p = 0.475$). There is a significant decrease of iron levels that occurs gradually with age in the breastfed ones, $r -0.89$. Different calcium levels were registered according to types of feeding ($p = 0.003$) until 6 months. Magnesemia were not influenced by feeding type at any groups. BUN in group I was significantly smaller in breastfed compared with premature formula fed infants ($p = 0.000$) at 2 months. Up to 6 months the value is significantly lowered in cases of breastfed, $p = 0.001$. The values of the protein in ≤ 32 weeks is directly influenced by the type of feeding, $p = 0.024$. Protein levels are significantly influenced in group II ($p = 0.026$). Phosphatemia is significantly influenced by the type of feeding in group II ($p = 0.043$).

Conclusions: Increase in body weight of newborns under 32 SS isn't influenced significantly by the type of feeding up to 6 months. Calcium registered significantly different values under the different types of feeding in the prematures ≤ 32 weeks of gestation in the first 6 months of life. Phosphoremia is significantly influenced by the type of feeding in the second group. Iron drops significantly with age in breastfedgroup. The level of protein in group I is directly influenced by the type of feeding. At 2 months of age BUN is significantly influenced by the type of feeding

1148 FACTORS AFFECTING COPPER LEVELS IN CHOLESTATIC INFANTS ON PARENTERAL NUTRITION

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Objective: To determine the proportion of cholestatic infants who develop low serum copper while receiving parenteral nutrition with restricted copper and to evaluate potential clinical factors that affect serum copper in cholestatic infants to guide protocols of assessing and supplementing copper in this population.

Background: Copper levels are primarily regulated by biliary excretion. In cholestatic patients, there is a concern that the standard dose of copper in parenteral nutrition (PN) will result in excessive copper levels. Based on such recommendations, conventional practice is to reduce or eliminate copper supplementation in the parenteral nutrition of infants with cholestasis due to the increased risk of hepatotoxicity. However, copper deficiency has been documented in several pediatric patients with cholestasis when parenteral copper was reduced or removed. Little is known regarding the rate at which deficiency occurs, the factors that can contribute to the deficiency, as well as the management of copper deficiency in the pediatric population.

Method: Data were collected retrospectively on a cohort of 37 infants who developed cholestasis while receiving PN and who had serum copper measured at Golisano Children's Hospital, from September 2007 until September 2014. Infants with metabolic or structural liver anomalies were excluded from the review. Age-adjusted references were used to determine normality of serum copper levels. Descriptive statistics was used to report baseline characteristics of the cohort; statistical significance of baseline differences between the 2 groups was assessed via Fisher's exact test.

Results: Copper deficiency was identified in 26 (70%) of the 37 infants, who required copper supplementation despite cholestasis. In the cohort of 37 patient, 34(81%) had primary gastrointestinal disorders. On average, the infants received 80% of their energy intake from PN, 26 (70%) of the infants were receiving soybean lipid emulsions and 11(30 %) were receiving omega-3 fatty acid emulsion. Copper deficiency was commonly present in infants with necrotizing enterocolitis (42%, $p = 0.000035$). The subset of patients who underwent intestinal resection and developed copper deficiency typically had resection of the ileum (31%, $p = 0.0122$). Anemia developed in 15% ($p = 0.0066$), neutropenia developed in 15% ($p = 0.0201$) and thrombocytopenia developed in 34% ($p = 0.0696$) of the infants with copper deficiency compared to infants with cholestasis who did not develop copper deficiency. Serum alanine aminotransferase did not correlated with serum copper levels.

Conclusion: Elimination of copper from PN in setting of cholestasis appears to result in a high number of infants with copper deficiency. In fact, infants with primary gastrointestinal disorders may require copper supplementation despite being cholestatic. Monitoring copper levels appears to be necessary to appropriately regulate copper dosing for cholestatic infants receiving PN.

1149 INFLUENCE OF GESTATIONAL AGE ON SERUM INCRETIN LEVELS IN PRE-TERM INFANTS

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Aim: Glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) are the incretin hormones secreted from the intestine in response to enteral feeding to stimulate insulin secretion. We investigated the relationship serum GIP and GLP-1 levels with gestational age and insulin secretion in pre-term infants.

Methods: Serum GIP and GLP-1 levels were measured at birth and at 1, 2, and 4 weeks after birth in 30 infants, including 12 born prior to 30th week of gestation (early group) and 18 born after 30th week of gestation (late group). Blood glucose and serum insulin levels were measured, and the quantitative insulin sensitivity check index (QUICKI) was also calculated.

Results: The levels of GLP-1 at 2 and 4 weeks were significantly higher in the early group than those in the late group. The levels of GIP were not significantly different between two groups. At 4 weeks, serum insulin level was significantly higher and QUICKI was significantly lower in the early group. Furthermore, GLP-1 levels were significantly correlated with QUICKI and the serum insulin levels in all infants at 4 weeks.

Conclusion: In pre-term infants, enteral feeding to premature intestine may be associated with GLP-1 secretion. GLP-1 is also related to stimulated insulin secretion in early postnatal period.

1150 MATERNAL FISH OIL DIET RESCUES THE INFERTILITY AND REDUCES THE NEONATAL MORTALITY ASSOCIATED WITH MATERNAL HIGH-FAT DIET IN MICE

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Purpose: Nutrition in pregnancy has a fundamental influence on overall development of offspring. In utero exposure to a high-fat diet is known to cause infertility and developmental problems in offspring in several animal models. Some human studies revealed that omega-3 polyunsaturated fatty acids prevent premature birth and improve neonatal development. Fish oil is rich in omega-3 fatty acids. The aim of this study was to investigate whether fish oil can rescue high-fat diet induced perinatal problems.

Methods: Following ethical approval (#32238), we bred C57BL/6 mice and then separated pregnant dams into two different diet groups: i) Group 1 (n=6): high-fat diet (HF) (36% kcal from fat, 0.29% w/w omega-3); ii) Group 2 (n=4): fish oil enriched high-fat diet (FO) (36% kcal from fat, 0.92% w/w omega-3). The number of pups delivered, and the survival until postnatal day 5 (P5) were analyzed. Data were analyzed using Mann-Whitney test or Fisher's exact test.

Results: The first week after breeding, mean body weight gain was 13.2 ± 8.0 g in HF and 5.2 ± 2.4 g in FO, respectively ($p=0.067$). Mean length of time from breeding to delivery was 33.2 ± 9.8 days in HF and 22.0 ± 1.6 days in FO, respectively ($p=0.024$). Mean number of pups delivered from HF dams and FO dams was 3 ± 1.3 and 7.5 ± 1.9 respectively ($p=0.0095$). Of these pups, survival rate until P5 was 16.7% in HF and 93.3% in FO, respectively ($p<0.0001$). The mean number of pups that survived until P5 per mother was 0.5 ± 1.2 in HF and 7 ± 2.6 in FO, respectively ($p<0.0001$).

Conclusions: Although the percentage of calorie intake from fat was similar in both diets, FO mothers delivered significantly more pups and mortality of the pups was significantly lower. Our results indicate that consumption of an omega-3 enriched diet during the neonatal period can rescue the infertility and mortality related to high-fat diet in mice.

1151 KLOTHO AT BIRTH: CORD BLOOD KLOTHO, ANTHROPOMETRICS, AND METABOLIC HORMONES

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Background: Klotho serum levels reflect nutritional state in adults including obesity and anorexia. The relationship between cord blood klotho levels at birth and parameters of growth including anthropometrics markers of nutritional health are not known.

Methods: We evaluated the relationship between cord blood klotho, leptin and adipocyte hormones and infant and maternal anthropometrics in a cohort of 73 children. Student's t-tests were used to assess differences between dichotomous predictors and klotho levels and we linear regression models to assess the relationship between klotho levels and continuous predictors.

Results: Mean klotho levels were 2864.9 ± 1409.7 pg/mL in cord blood and we found no relationship with infant sex, delivery specifics or anthropometrics at birth although there was trend towards lower klotho levels with higher infant gestational age ($p=0.07$) and a statistical significance with higher head circumference ($p=0.03$). Leptin levels at birth were inversely correlated with klotho levels (B -0.20; $p=0.035$) and trended towards an inverse correlation with insulin levels (B -0.21; $p=0.09$).

Conclusions: We found no associations between klotho at birth with anthropometrics. However, there was a pattern found for higher klotho with larger head size and better metabolic health (lower insulin). Klotho levels in newborns should be further investigated to better understand the possible role of this hormone in regulating infant nutritional status and weight gain in relation with leptin and other hormones.

1152 OUTCOME OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN CHILDREN: A 15-YEAR REVIEW

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Introduction: Percutaneous endoscopic gastrostomy (PEG) is the preferred method to provide long-term nutritional support for children with a variety of diseases. Relevant data on the long-term outcomes of children receiving PEG is limited.

The aims of this study were to evaluate the long-term nutritional outcomes of children receiving PEG, to determine the incidence of procedure-related complications and of post-PEG reflux.

Methods: Single-center retrospective study including all patients who underwent PEG placement in our tertiary center between January 1999 and December 2015. All PEGs were placed by the same team of pediatric gastroenterologists using the same procedure (standard pull technique), and prophylactic perioperative antibiotics. PEG-related complications, reflux (clinical, radiological, or pH probe evidence) and nutritional rehabilitation (weight gain and change in weight Z-score after PEG placement) were analyzed.

Results: PEG placement was attempted in 293 patients. In 34 (13.1%) patients, PEG could not be performed because of inability to find adequate gastric access. In the 259 patients who underwent successful PEG placement, diagnoses were as follows: neuromuscular disease (n=134, 52%), cystic fibrosis (n=29, 11%), metabolic disease (n=15, 6%), congenital heart disease (n=7, 3%), neoplasia (n=6, 2%) and others (n=68, 26%). One hundred sixty-four patients (63%) were neurologically impaired (NI). Median age at the time of PEG placement was 3.9 years (0.4-19.9 years) and median follow-up duration was 3.2 years (0-16 years). In children weaned from gastrostomy feeding (n=68, 26%), median duration of enteral feeding was 2.6 years (0.2-8.2 years). A total of 41 complications were recorded in the first 3 months: 27 cellulitis requiring intravenous antibiotics, 9 dislodgements before button placement, and 3 perforations with 2 requiring surgery. No PEG related death was recorded. New onset reflux occurred in 25 (10%) patients and 28% (n=28) of patients with known reflux prior to PEG placement had worsening of their symptoms and/or escalation of treatment. Among patients with new or worsening reflux, 43 (81%) were NI. Anti-reflux procedure was required in 23 patients, all were NI. Weight was available at the time of PEG placement and at the time of last follow-up in all patients. At the time of PEG, mean weight-for-age Z-score was -2.09 SD with undernutrition (weight z score < -2 SD) found in almost half of patients (n=126, 49%). At the time of last follow-up, mean weight z score was -1.7 and undernutrition was still present in 98 patients.

Conclusions: PEG placement in pediatric patients: 1) carries an overall low risk of major procedure-related complication and a 10% risk of local infection, 2) may lead to new onset reflux or worsening of pre-existing reflux in 10% and 28% of patients respectively, particularly in those neurologically impaired 3) is associated with improved weight Z-score.

1153 THE STUDY OF EXTRAUTERINE GROWTH RETARDATION OF PRE-TERM INFANTS IN SHANGHAI

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Objective We discussed the different stages of extrauterine growth retardation (EUGR) in pre-term infants in order to provide a more reasonable reference basis for improving nutritional management .

Method: We retrospectively reviewed the clinical records of premature babies whose gestational age <37 weeks and stayed in the hospital more than 3 days from October 2012 to September 2015 in the NICU in Xinhua hospital affiliated to Shanghai Jiao Tong University. We collected the data in the perinatal period of each cases, weight increase or decrease during hospitalization, the actual intake from both enteral and parenteral nutrition, related complications, etc. In this study, we used the standard (2013 Fenton curve) to evaluate the weight of every pre-term infants at day 14, day 28 and the day of discharge. We defined EUGR while the pre-term infants whose weight ≤10% 2013 Fenton curve standard of the same age and the same gender at those three stages And we called the EUGR at day 14 as EUGR-14, the EUGR at day 28 as EUGR-28, the EUGR at the discharge as EUGR-D.

Results: This study included 773 premature infants, there were normal birth weight 16.8%(n=130), low birth weight 70% (n=541) ,very low birth weight 11.8% (n=91) ,and extremely low birth weight 1.4% (n=11) .There were almost98.3% preterm babies used parenteral nutrition, and their birth weight were around2500 g and their gestational age were around 33 weeks. The rate of EUGR-14, EUGR-28 and EUGR-D were 43%, 58.2% and 47.5%, respectively. The lower birth weight infants had higher the incidence of EUGR in each of the three stages. Please see the table for more details.

Conclusion: The incidence of EUGR remains high in pre-term neonates. Some pre-term infants who didn't have fetal growth restriction (FGR) became EUGR during hospitalization. The incidence of EUGR at day 28 was the highest , so we should prevent EUGR as early as possible in the neonatal period.

Keywords: Premature infants; extrauterine growth retardation

Table. Incidence of EUGR in different birth weight premature infants at different day(%)

	NBW (n=130)	LBW (n=541)	VLBW (n=91)	ELBW (n=11)	Average
Day0	0	14.4	23	30	13.2*
Day14	0	42.8	51.1	77.8	43
Day28	0	51.5	62.7	75	58.2
Discharge	10.7	50.4	78	90	47.5

NBW: normal birth weight; LBW: low birth weight; VLBW: very low birth weight; ELBW: extremely low birth weight; n=the number in this case

Incidence of fetal growth restriction (FGR)

1154 EFFECTS OF ZINC SUPPLEMENTATION ON CATCH-UP GROWTH IN CHILDREN WITH NON-ORGANIC FAILURE TO THRIVE AS PRE-TERM INFANTS

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Aims: This study aimed to analyze the effect of zinc supplementation on serum insulin like growth factor-1 (IGF-1) and catch-up growth on children with non-organic failure to thrive (NOFTT) born as pre-term infants compared to those born as term infants.

Method: A total of 156 children less than 6 years of age with NOFTT were included in this study. Oral zinc sulfate was supplied to 84 of 110 children born as term infants and 28 of 46 those born as pre-term infants. Serum zinc, IGF-1, weight and height measured at baseline and at 6 months were retrospectively reviewed.

Results: There were no differences in baseline serum zinc levels between NOFTT children born pre-term and those born at term. In NOFTT children born pre-term, zinc levels increased significantly after 6 months only in the supplemented group ($p = 0.017$). Although there were no significant changes in IGF-1 or weight for age Z-scores after 6 months of supplementation, significant increases were found in height for age Z-score ($p = 0.021$), but without any differences between zinc-supplemented group and non-supplementation group. In NOFTT children born at term who received zinc supplements, zinc levels significantly increased after 6 months ($p < 0.001$), but there were no significant increases in IGF-1. In the supplementation group, weight for age Z-score and height for age Z-score had increased at 6 months ($p = 0.005$ and $p = 0.004$ respectively), but these gains were not significantly different from the non-supplementation group.

Conclusion: Zinc supplementation in children with NOFTT born pre-term improves serum zinc status, but without any significant effects on serum IGF-1 level or weight gains, and increases their height for age Z-score, but not significantly more so than those without supplementation. Overall nutritional support rather than single nutrient supplementation may be more effective for catch-up growth of pre-term born NOFTT children.

1155 ASSESSMENT OF THE IMPACT OF FEEDING METHOD (BOLUS VS. CONTINUOUS INFUSION) ON CARBOHYDRATE METABOLISM IN ENTERALLY FED CHILDREN WITH NEUROLOGICAL IMPAIRMENT

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Background: Continuous enteral nutrition (EN) is often the only possible way to obtain adequate body mass and length increases in malnourished children with neurological impairment not tolerating EN provided in boluses. That manner of feeding may induce carbohydrate metabolism disorders and potentially entail risk of vascular complications. Literature offers studies that only assess carbohydrate metabolism in

enterally fed patients with diabetes mellitus; there are no data concerning other groups of patients, especially children with neurological impairment receiving long-term EN.

Objective: Assessment of the impact of feeding method (bolus vs. continuous infusion) on carbohydrate metabolism in enterally-fed children with neurological impairment.

Material and methods: Study enrolled 39 patients with neurological impairment (level IV and V, Gross Motor Function Classification System) who were enterally fed for at least 6 months (24 girls, 15 boys, mean age of 8 years and 7 months, SD 5.38 years). All the patients received Home Enteral Nutrition service provided by professional team. 25/39 of those were nourished by boluses (group Bf), 14/39 received continuous infusion lasting 18-20 hrs. (group Cf). Blood glucose level was measured as short- and HbA1c as a long-term mean glucose level. 70-99 mg/dL was considered normal glucose concentration and 4.8 to 6.0 % was the normal range of HbA1c.

Results: Mean HbA1c level in the whole study group was $5.04 \pm 0.43\%$. No statistically significant differences in HbA1C depending on the feeding method were found (mean HbA1c in group Bf was $5.00 \pm 0.36\%$ vs. $5.11 \pm 0.53\%$ in group Cf, $p=0.45$). Mean glucose level in both the groups was 83.69 ± 8.5 mg/dL (Bf: 81.56 ± 4.25 mg/dL; Cf: 87.48 ± 6.5 mg/dL; $p>0.05$). There were no statistically significant differences in hyperglycemic episodes between the study groups (3/25 in group Bf vs. 2/14 in group Cf, Chi-2 test 0.6). On the other hand hypoglycemia was statistically significant more common in children in Bf group compared to Cf group (6/25 vs. 1/14; $p=0.046$). Mean diet energy value for children fed by boluses was lower compared to that for children fed by continuous infusion (62.3 kcal/kg in group Bf vs. 73.36 kcal/kg in group Cf).

Conclusions: Continuous enteral feeding did not affect short- and long-term hyperglycemia risk in children with neurological impairment. Bolus feeding impacted on hypoglycemia risk the above group of patients.

1156 THE EXPERIENCE OF CAREGIVERS OF CHILDREN WITH MEDICAL COMPLEXITY RECEIVING; BLENDERIZED TUBE FEEDING: A QUALITATIVE STUDY

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Background: Children with medical complexity (CMC) are defined by complex chronic conditions, functional impairment, technology dependence and high resource utilization. CMC often rely on enteral feeding tubes. Blenderized tube feeding (BTF) is an alternative to formula that may improve feeding tolerance and oral intake. The opportunity to feed and nourish ones child with BTF as opposed to formula has been hypothesized to improve parental experience with feeding and enhance the caregiver-child relationship, however, there is no research to date to explore this.

Objective: Our primary objective was to understand the caregiver experience with BTF and its affect on the caregiving relationship.

Design/Methods: We conducted a qualitative, grounded theory study of 10 mothers of CMC. Eligible families include those whose child received at least 50% of their diet through BTF for a minimum of three months. A research assistant trained in qualitative methodology conducted the interviews. The interview guide was developed by expert consultation, pilot-tested and refined as appropriate. Interviews were transcribed verbatim. Methodological rigor was established through member checking. Analysis included coding interviews and memoing ideas throughout data collection to allow creation of concepts and themes that are grounded in the experience of BTF. A grounded theory approach includes the following: 1) generate questions, 2) gather data and identify theoretical concepts, 3) identify linkages between the core concepts and data, 4) verify, summarize and develop theory. Research Ethics Board approval was obtained.

Results: All participants expressed a high level of satisfaction with BTF. Outcomes from BTF were categorized into three main themes: 1) well-being of the child (improved health; more enjoyable feeding experience; more time to engage in other activities; and an increased interest in food), 2) normalization (more normal feeding experience for child and caregiver, less stigmatization and improved social interactions), 3) empowerment (increased sense of control and choices over decisions related to their child's feeding).

Conclusion: This study demonstrates that BTF can improve a child's well-being and provide a sense of normalcy and choice to a plan of care that is otherwise unpredictable and medically driven. Caregivers are interested in offering BTF to their children and it is a feasible option for CMC. Further research is needed on the efficacy and outcomes associated with the use of BTF as well as an expansion of training and capacity within the health care setting to allow for more broad use and dissemination.

1157 INTERNATIONAL SURVEY ON NUTRITIONAL HABITS AND DIETARY PATTERNS IN A PEDIATRIC CYSTIC FIBROSIS COHORT: DIFFERENCES AMONG EUROPEAN COUNTRIES

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Objective: To achieve an optimal nutritional status is one of the main goals of the treatment in Cystic Fibrosis (CF), especially in pediatric patients. The MyCyFAPP project (www.mycyfapp.eu) aims to empower the patients' self-management of nutrition as well as pancreatic enzyme replacement therapy (PERT) by means of a co-developed mobile APP. Throughout the project, tailored and evidence-based tools and resources will be developed. In a first stage, we aimed to identify the nutritional habits of European pediatric CF patients in order to develop patients' oriented nutritional recommendations/guidelines and educational resources.

Methodology: 210 pediatric patients with CF (1-17 years old), recruited from 6 European CF-units from Hospital La Fe (Spain), Hospital Ramón y Cajal (Spain), Hospital Santa Maria (Portugal), Erasmus Medisch Centrum (The Netherlands), UZ Leuven (Belgium) and Ospedale Maggiore Policlinico (Italy) were asked to complete a specific and detailed 4-day food record. A specific database was developed in the first stage of the project to perform the nutritional analyses and calculations. Afterwards, food products were classified into food groups (e.g., milk and dairy) and subgroups (e.g., yoghurt, cheese, milk, etc.) and the information about energy and nutrient composition was extracted.

Results: Common patterns among all the included centres were found, these being, the highest daily lipid intake was registered at dinner, and the dietary sources of lipids were in decreasing order: milk and dairy products, meats, refined products and fats and oils. Additionally, all the centres

had a low fish and legume consumption and a high sweets and savoury snacks intake in common. In contrast, main differences were found between the southern and northern centres. In the Northern centres, dinner is the main meal and lunches are composed of one bread-based course with different protein-based sources; conversely in the Southern centres lunch turns out to be the main meal and is composed of 2-3 dishes, including pasta or rice-based dishes and a dessert.

Conclusion: The nutritional habits of children with CF in Europe vary a lot, especially between Northern and Southern centres. When developing nutritional and educational resources for the APP under construction, these differences and the identification of main nutritional imbalances, have to be taken into account. In this way a focused and more efficient nutritional therapy and higher adherence to nutritional recommendations can be achieved.

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1158 EARLY-ONSET METABOLIC SYNDROME AND RISK FACTORS OF DEVELOPING NON-ALCOHOLIC FATTY LIVER DISEASE IN OBESE PREPUBERTAL CHILDREN

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Introduction: Although the prevalence of metabolic syndrome (MS) and non-alcoholic fatty liver disease (NAFLD) is increasing in obese children, their prevalence and risk factors in the prepubertal period have not been clearly reported yet. NAFLD is a serious complication of obesity, but there are some limitations in performing abdominal ultrasonography on all obese prepubertal children. The aim of this study was to evaluate the prevalence of early onset MS and NAFLD, and risk factors of early onset NAFLD in obese pre-pubertal children.

Methods: A total of 356 obese children and adolescents (233 boys, 123 girls) were included, with 172 aged less than 10 years and 184 aged 10 years or more. Anthropometric data, blood pressure, laboratory tests, and abdominal ultrasonography were evaluated in all subjects. MS was diagnosed according to the NCEP-ATP III criteria, while NAFLD was diagnosed by abnormal liver enzyme levels and ultrasonographic findings to produce 2 groups: children without NAFLD (n=110) and children with NAFLD (n=62).

Results: In obese children under 10 years of age, prevalence of MS and NAFLD was 40 out of 172 (23.3%) and 62 out of 172 (36.0%), respectively ($p = 0.020$), whereas in those aged 10 years or more the prevalence was 65 out of 184 (35.3%) for MS and 130 out of 184 (70.7%) for NAFLD ($p = 0.001$). In prepubertal children, there were significant differences in rGT ($p < 0.001$), triglyceride ($p = 0.042$), and HOMA-IR ($p < 0.001$) between the non-NAFLD and the NAFLD group. Logistic regression analysis revealed statistical significance for raised serum rGT (odds ratio 1.168, 95% CI, 1.1-1.3; $p < 0.001$) and serum uric acid levels (odds ratio 7.7, 95% CI, 1.1-53.6; $p = 0.039$) as risk factors for developing NAFLD in obese prepubertal children.

Conclusion: Although MS and NAFLD were more prevalent in puberty, obese prepubertal children also had a portion of MS and NAFLD as obesity-related complications. Our results suggest that increased serum rGT and uric acid levels in obese prepubertal children might be useful biomarkers for the presence of NAFLD before investigation with abdominal ultrasonography.

1159 INCREASED INTESTINAL INFLAMMATION IN CHILEAN INFANTS FED WITH BOVINE FORMULA VERSUS BREAST MILK

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Introduction: Breast milk (BM), has unique properties that confer the neonate-infant the ideal setting to face the challenge of coming to the external world. Other than nutrients, compared to bovine formula milk (BF), BM contains: hormones, growth factors, immunoglobulins, cytokines and bacteria which confers protection against diarrhea, infections, necrotizing enterocolitis, allergy, celiac disease and diabetes. In the newborn intestine there is a homeostatic balance between the counterparts of the immune system which allows a physiologic inflammation. Few studies have attempted to understand the effect of BF versus BM, at the level of the intestinal epithelia. Regarding the scarce evidence, we think is important to assess the effect of BM and BF in the homeostasis of the intestine. Using a non-invasive technique, based on stool analysis, we assessed whether there are changes in the first three months of life regarding intestinal inflammation in infants fed with BM or BF.

Aim: To associate BM or BF feeding in infants, with stool markers of intestinal inflammation.

Patients and methods: This is a cohort study of newborn infants during their three first months of life. Inclusion criteria included vaginally-delivered term-infants, who were on exclusive BM or receiving BF supplements $\geq 20\%$ of the milk volume ingested per day. In order to analyze the association with markers of inflammation over this three months period, clinical assessments and collection of 2 stool samples were taken; at 1 and 3 months of life (T1 and T3), within a range of ± 5 days for those specific dates. From the stool samples, we quantified mRNA of Interleukin (IL)-8 and calprotectin (S100A8) coding genes by RT-qPCR, and protein concentrations of IL-8 and calprotectin by ELISA.

Results: 15 BM and 8 BF infants were included in this study. Demographic data showed no difference between groups, regarding gender, birth weight/length or number of stools a day. IL-8 gene expression analysis at T1, showed a 2.3 ± 0.46 folds of increased expression in BF group, compared to BM. No difference was found at T3. S100A8 expression analysis showed no differences between groups at T1, but at T3 there was a 1.9 ± 1.17 folds of increased expression in BF group, compared to BM. For protein analysis, 8 patients per group were considered. Protein concentrations of IL-8 were undetectable in both groups at T1 and T3. Calprotectin levels in BF were significantly higher compared to BM at T1 (471 ± 45 mg/kg vs. 234 ± 51.9 mg/kg; $p = 0.0034$). No difference was found at T3.

Conclusions: Using two non-invasive methods on stools we found a basal state of inflammation in the infant intestine based on IL-8 and calprotectin markers. Infants receiving BF exhibited higher levels of inflammation compared to BM. These results might confer BM a protective role in ameliorating inflammation, probably modulating the intestinal homeostasis in the infant during their first months of life.

*1160 HIGH-SENSITIVITY C-REACTIVE PROTEIN IN CHILDHOOD OVERWEIGHT AND OBESITY: CHARACTERIZATION OF A PEDIATRIC POPULATION

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Introduction: The high-sensitivity C-reactive protein (hsCRP) is an independent and predictive marker of cardiovascular risk. Group risks can be defined according to hsCRP values, in which values less than 1 mg/mL are associated with a low risk profile and values above 3 mg/mL are associated with a high risk profile.

Objective: To study the association between hsCRP and the anthropometric and metabolic profile of the overweight and obese children of a Pediatric Gastroenterology, Hepatology and Nutrition Unit in a tertiary hospital.

Methods: The sample includes 243 children attending their first visit to the obesity outpatient consultation in which an analytic study was made, including hsCRP. The visit took place between 2 February 2011 and 29 February 2016. The hsCRP values above 10mg/mL were excluded.

Results: Children were aged between 3 and 17 years old, median age of 10 years, 50.7% were female and 86.3% were obese. Total cholesterol, triglycerides and high density lipoprotein levels were abnormal in 15%, 11.2% and 10.1% of children, respectively; 20% of children had hepatic steatosis; 6.4% were in prediabetes state taking into account glycated hemoglobin levels. The hsCRP values were in the high risk profile range in 25.5%. There was a statistically significant positive correlation between hsCRP and the age of obesity onset (p 0.029); body mass index (p 0.038); the presence of acanthosis nigricans (p 0.041), cellulitis (p 0.041) and vasculitis (p 0.027); glycosylated hemoglobin (p 0.045), total cholesterol (p 0.035), fasting glucosis (p 0.003), alanine aminotransferase (p 0.021). It was also found an inverse correlation between hsCRP and the frequency of physical activity (p -0.43). There wasn't a statistically significant correlation between hsCRP and the levels of high density lipoprotein, triglycerides and the presence of hepatic steatosis.

Conclusion: The high levels of hsCRP in overweight/obese children demonstrate that this population has already an increased cardiovascular risk. The increased frequency of physical activity was found to be a protective factor.

1161 OUTCOMES OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN CHILDREN WITH SEVERE NEUROLOGICAL DISABILITIES *Ka ming Cheung, Yiu kay Chan, Chun hung Ko, Caritas Medical Centre, Hong Kong SAR, China*

Development Disabilities Unit (DDU) in the Caritas Medical Centre is the largest hospital-based clinical unit in Hong Kong providing residential and rehabilitation services to children with severe neurological disabilities (GMFCS level 5). PEG has been shown to be safe in the short-term and effective in improving nutrition in children with neurological disabilities,¹ but Hong Kong data were sparse. One study reported the mortality rate of 11%, 21%, 27% and 39% after 1, 2, 3 and 13 years after PEG placement.² Mortality was regarded as due to comorbidities and underlying etiologies of disabilities rather than the procedure.²

Objective: To study the long-term outcome of PEG in a cohort of severe neurologically disabled children.

Method: From 1998, PEG was placed in DDU children who required long-term tube feeding. 24-hours esophageal pH studies were performed before PEG and within one year after PEG, and when patient had clinical deterioration or new occurrence of gastroesophageal (GE) reflux symptoms. Abnormal GE reflux index was defined as greater than 4%. The children were followed every three to six months. Data were censored at the end of June, 2012 or the last recorded date (discharge or death). Body weight, episodes of vomiting, chest infection, gastrointestinal bleeding and date of discharge or death were extracted from patient records. The body weight at baseline and each follow-up years were recorded. The pre-operation and the post-operation GE reflux index of the patients were compared by paired T-test.

Results: Eighteen patients (13 boys) had PEG performed from 1998 to 2009. The median age was 15.7 (range: 5.0-18.8) years. Mean body weight before PEG was 19.7 ± 4.0 kg. Mean weight gain was 2.41 kg (0-10.5 kg) one year after PEG (Table 1). Median follow-up patient-days was 2801 days (234 to 3939 days). Pre- PEG reflux index was $2.2 \pm 2.3\%$, mean long reflux >5 minutes was 2.1 ± 2.2 ; mean longest reflux was 12.3 ± 12.2 minutes. For post-PEG pH study, the mean reflux index was $3.8 \pm 3.8\%$ ($p < 0.005$), number of long reflux >5 minutes was 1.8 ± 2.4 ($p = ns$), longest reflux times was 12.6 ± 22.64 minutes ($p = ns$). Four deaths occurred. Two children died of respiratory failure due to degenerative brain disease (0.6 years and 2.6 years after PEG, respectively). Two children developed worsening dystonia and recurrent aspiration pneumonia. They died of respiratory causes 2.0 and 9.9 years after PEG. Mean survival was 9.31 ± 0.92 (95% CI, 7.50, 11.12) post-operative years.

Conclusion: After PEG feeding, weight gain was achieved. Reflux index increased. No death occurred within 6 months after PEG.

References: 1. Fortunato JE *et al.* Outcome after percutaneous endoscopic gastrostomy in children and young adults. *J Pediatr Gastroenterol Nutr.* 2010; 50:390-393 2. Catto-Smith AG, Jimenez S. Morbidity and mortality after percutaneous endoscopic gastrostomy in children with neurological disabilities. *J Gastro Hepatol.* 2005;21:734-738.

Patient	Gender	age (year)	Body weight (kg)							Average yearly increase	Remarks
			pre- PEG	1 year	2 year	3 year	4 year	5 year	9 year		
1	M	18.83	19.8	24.6	NA				24.24%	discharged	
2	M	12.18	20.9	23.2	25.8	25.6	26	26.8	NA	5.61%	
3	M	11.97	28.2	29.7	30.3	28.9	37.5	40.8	NA	8.93%	
4	F	4.98	10.9	14.8	17.7	17.9	21.5	21.5	NA	16.51%	
5	F	7.59	11.4	12	14.3	16.8	18	18.3	NA	12.11%	death at 9th year
6	F	6.87	17.8	18.1	17.1	18.9	24.1	23.9	34.3	10.30%	
7	M	19.64	16.4	16.4	NA				0%	discharged	
8	M	14.57	33.3	NA				NA		NA	death unrelated to PEG
9	M	5.47	15.5	17	17.2	21.1	21	22.2	NA	8.65%	
10	M	5.91	14.1	15.7	21.6	21.6	24.8	27	28.8	11.35%	
11	F	5.04	14.3	17.7	21.6	26.2	24.8	29	NA	20.56%	
12	M	5.39	17	19.8	19.4	19.4	21	18.2	NA	1.41%	
13	M	6.99	11.6	12.3	13.1	17.4	17.7	19.2	NA	13.10%	
14	F	11.99	27.1	26.7	34.7	33.2	33.3	37.1	NA	7.38%	discharged
15	M	14.44	28	28.8	28.8	30.6	31.6	35.5	NA	5.36%	discharged
16	M	15.52	29	34.1	29.2	NA			0.34%		death at 3rd year
17	M	8.66	13.5	14.2	16.2	18.3	21	20	NA	9.63%	
18	M	12.63	25.4	35.9	39.1	NA			27.00%		death at 3rd year
									Median = 9.63%		

Table 1 Demographic data and body weight of patients after percutaneous endoscopic gastrostomy (NA: not available)

1162 QUANTIFICATION OF 18 B-VITAMERS FROM RELATIVELY LOW VOLUME OF HUMAN BREAST MILK

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WHO recommends exclusive breastfeeding up to 6 months of age and as complementary to other food beyond 6 months, for as long as mutually agreeable by the mother-infant dyad, with introduction of complimentary foods. Presumably human milk provides all the key nutrients relevant for infant survival, health and growth. Among them are B-vitamins that are essential for the physical growth and cellular metabolism of the infants. In order to understand the infant vitamin intake, it is essential to study the evolution of these B-vitamins in human breast milk employing a reliable analytical techniques to identify and quantify these vitamers. To this date many B-vitamins in human milk have been reported in the literature, but using separate methods to quantify each B-vitamin and thus requiring a relatively large volume of human breast milk. Therefore, we designed an analytical methodology to simultaneously quantify 18 B-vitamins using relatively low volume of human breast milk (200 µL) to evaluate the profile of 5 different B-vitamins.

In short, a protein precipitation was applied to extract all vitamers. Their separation was achieved by reversed-phase chromatography and detection by tandem mass spectrometry in positive ionization mode. The performance of the analytical approach was validated following European Medicines Agency guidelines. Breast milk from a subset of 8 different mothers delivering term-infant (clinicaltrials.gov handler NCT #02052245) was collected at CHUV, Lausanne, Switzerland. The B-vitamin profile of breast milk at W1 (week 1 after delivery) and at W6 (week 6 after delivery) was evaluated applying the above mentioned methodology. Each of the studied vitamer had a lower concentration at W1 compared to W6. Flavin adenine dinucleotide (predominant B2 vitamer) concentration evolved from 42.4 to 81.5 µg/100 mL and 5 methyl tetrahydrofolate (predominant B9 vitamer) concentration from 0.4 to 1.7 µg/100 mL. This analytical approach presented here is the first attempt to simultaneously quantify 18 B-vitamins in breast milk in a single analytical run and using relatively low volumes of precious milk samples.

1163 ORIGIN OF MATERNAL MILK MICROBIAL COMMUNITIES AND SEEDING OF THE INFANT GUT

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Background: Breast milk contains bacterial populations that significantly influence microbiota composition in infant gut. However, not much is known about the sources of bacteria in breast milk and milk microbe-mediated seeding of infant gut.

Methods: Bacteria were characterized by 16S rRNA sequencing using Illumina MiSeq to identify core breast milk microbiota from 15 mother-breastfed infant pairs followed prospectively. Site contribution to breast milk and infant stool were determined using QIIME and SourceTracker on maternal (milk, rectum, areola, vagina, oral) and infant (stool, oral) samples. Shotgun metagenomic sequencing was performed on a subset (n 6) for in-depth multi-site analysis.

Results: The median infant age was 22.5 days (3-111 days old), 53% were vaginally delivered, and 67% were Hispanic. About 40% of infants exclusively breastfed, while 60% received breast milk and formula. Except for mothers who underwent caesarian section and received antibiotics at delivery (n=7), there was no antibiotic use during pregnancy or lactation. Twenty-seven operational taxonomic units (OTUs) were common in 85% of all breast milk samples, and are considered core breast milk bacteria. Core bacteria include *Bifidobacteria*, *Enterobacteria*, *Corynebacterium*, *Lactobacillus*, *Neisseria*, *Haemophilus*, *Staphylococcus*, and *Streptococcus*. In the first month of life, 26 ± 10% microbes could be sourced from breast milk. All genera present in the core breast milk microbiome were found in infant stool, and mainly overlapped with infant oral cavity and areolar skin microbes. Delivery mode did not influence microbial clustering on principal coordinate analysis. Strikingly, metagenomic sequencing identified one distinct strain of *Bifidobacteria breve* that is identical in maternal breast milk and her infant stool, suggesting direct transmission. Follow-up source tracking of 16S data revealed *Bifidobacteria* in breast milk is shared with maternal

rectum. Comprehensive shotgun analysis reveal breast milk has the lowest overall biomass and feces the largest. There was largely low detection of fungal and viral sequences compared to bacterial dominance in breast milk.

Conclusion: Although breast milk has low overall biomass, breast milk microbes play an important role in seeding the infant's gut. Interestingly, our data indicating a connection between *Bifidobacteria* in maternal gut and breast milk are consistent with the murine studies suggesting that intestinally-derived bacteria translocate to the mammary gland. Recent evidence by Perez *et al* (2007) proposes migration of these bacteria through the entero-mammary cellular pathways utilized by IgA cells. More investigation is needed to further elucidate seeding of the infant gut by breast milk microbiota.

1164 FEEDING DIFFICULTIES IN CHILDREN WITH DEVELOPMENTAL DISABILITIES

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Background: Approximately 80% of children with developmental disabilities are at increased risk for developing feeding problems.

Objectives: 1) To determine the prevalence of feeding difficulties in children with developmental disabilities; and 2) to determine the association between feeding difficulties and the developmental diagnosis, demographics (child, parent, household), parent concerns on feeding, adequacy of the diet and malnutrition.

Methods: This is a cross-sectional study done from January to November 2015 on 255 pediatric patients 0-19 years old, previously diagnosed with a developmental disability at the outpatient clinics of a tertiary hospital. Data on sociodemographic factors, feeding difficulties, diet and growth parameters (weight, length/height, BMI) were collected. The Identification and Management of Feeding Difficulties (IMFeD) questionnaire was used to identify feeding difficulties and the child's current diet. Anthropometric measurements were plotted on the WHO growth charts and the CDC growth charts for children with special needs. Continuous variables were expressed as mean and standard deviation. Categorical variables were expressed as frequency and percentage. A Chi-square test for independence was used to determine the significant difference between variables. The significance was set at 0.05 level. *Post hoc* test was done using Bonferroni correction to control for familywise error rate.

Results: Feeding difficulties were identified in 236 (92.5%) children. The most common type of feeding difficulty was highly selective intake (65.4%), followed by poor appetite suggestive of organic disease (25.7%), poor appetite in a child who is fundamentally vigorous (5.8%), fear of feeding (1.5%) and poor appetite in a child who is apathetic and withdrawn (1.5%). Majority of feeding difficulties were seen in children with Autism spectrum disorder (29%), followed by global developmental delay (24%), attention deficit hyperactivity disorder (14%), intellectual disability (14%), language and communication disorders (13%), and learning disability (16%). Majority of parents had concerns about their child's feeding (52.9%). All subjects whose parents had concerns were identified with feeding difficulties, while those without concerns, 84% had feeding difficulties. An adequate diet was seen in 55.2% and an inadequate diet in 44.7%. Majority had normal weight (58.6%), length/height (80.3%) and BMI (55.1%). Five variables were found to be significantly associated with feeding difficulties in our study: 1) parental concerns on feeding ($p < 0.0001$); 2) adequacy of the diet ($p = 0.0003$); 3) parent educational status ($p = 0.0002$); 4) parent income ($p = 0.0006$); and 5) person responsible for decision making on how much is spent on food ($p < 0.0001$).

Conclusion: Feeding difficulties are seen in a huge percentage of children with developmental disabilities. Child, parent and environmental factors play a role.

1165 THE STUDY FOR ASSOCIATIONS AMONG DEGREE OF NON-ALCOHOLIC FATTY LIVER, METABOLIC SYNDROME, DEGREE OF OBESITY IN CHILDREN AND PARENTAL OBESITY

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Objective: There is no report about the factors affecting the degree of non-alcoholic fatty liver and degree of obesity associated with metabolic syndrome and parental obesity in children.

Methods: From March 2010 to February 2015, the study was prospectively done in 198 children with obesity who visited the pediatric obesity clinic in Jeju National University Hospital. The degree of non-alcoholic fatty liver was classified into negative, mild, moderate and severe. The degree of obesity was classified into mild, moderate and severe. For the statistical analysis, we used χ^2 test and likelihood ratio test for trend of the SPSS 18 version.

Results: Mean age of 198 children with obesity was 9.6 ± 3.1 years-old (mean \pm SD). Of 132 patients evaluated for the degree of non-alcoholic fatty liver and metabolic syndrome, the p -value of correlation between two factors showed 0.009. Metabolic syndrome might affect much of the progress of the degree of non-alcoholic fatty liver. Of 158 patients evaluated for the degree of non-alcoholic fatty liver and degree of obesity, the p -value was 0.122. Of 154 patients evaluated for degree of obesity and father's obesity, the p -value was 0.075. Of 159 patients evaluated for the degree of obesity and mother's obesity, the p -value was 0.000. Mother's obesity might affect much to the progress of degree of obesity in child. Of 142 patients evaluated for the degree of obesity and metabolic syndrome, the p -value was 0.286.

Conclusion: Metabolic syndrome may affect the progress of the degree of non-alcoholic fatty liver. Mother's obesity may be a inducing factor in the progress of the degree of obesity in children.

Table 1. The crosstabs between the degree of non-alcoholic fatty liver and metabolic syndrome in 132 children with obesity

Degree of Fatty liver	Metabolic Syndrome	
	Negative	Positive
Negative (n=69)	55 (79.7%)	14 (20.3%)
Mild (n=30)	18 (60.0%)	12 (40.0%)
Moderate (n=23)	10 (43.5%)	13 (56.5%)
Severe (n=10)	5 (50.0%)	5 (50.0%)

($p=0.009$, χ^2 test, Likelihood ratio test for trend)

1166 EFFECTS OF MORINGA OLEIFERA LEAF POWDER IN IMPROVING THE ANTHROPOMETRIC STATUS, HEMOGLOBIN LEVELS AND DIETARY INTAKE OF CHILDREN AGED 6-8 YEARS OLD WITH MODERATE TO SEVERE MALNUTRITION IN A PUBLIC ELEMENTARY SCHOOL IN MANILA

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Objective: To determine the effects of Moringa oleifera leaf powder on the anthropometric measurements, hemoglobin levels and dietary intake of children with moderate to severe malnutrition aged 6-8 years old.

Study Design: Double-blind, randomized, placebo-controlled trial.

Setting: Public elementary school in Manila.

Study Population: Grade 1 pupils with moderate-to-severe malnutrition aged 6-8 years old.

Methodology: Sixty-eight children were randomly assigned into two groups, intervention group (n=34) and placebo group (n=34). Baseline weight and height were taken and were monitored weekly. Hemoglobin and hematocrit levels were taken pre- and post-treatment and 24-hour total caloric intake were monitored daily. Both groups were given rice porridge everyday. 1.5 g Moringa oleifera leaf powder was added to the food prepared for the intervention group while the other group was given 1.5 g placebo for 56 days. Toffee mixed with either 1.5 g M.oleifera leaf powder or placebo were given during weekends. Independent comparisons using T test and repeated ANOVA at 0.05 level of significance were performed.

Results: A total of 56 pupils were able to complete the study. The intervention group (n=27) had 1.75 kg weight gain as compared to placebo (n=29) which is 1.16 kg which is statistically higher with *p*-value 0.010 but no significant height increment was noted. Comparing the nutritional status of both group post-supplementation, intervention group showed significant improvement based on weight for age, weight for height, Z-scores of pupils (*p*-values 0.000 and 0.001, respectively). No significant improvement was seen in the height for age Z-score and in the hemoglobin and hematocrit levels after supplementation. Intervention group had higher 24 hour total caloric intake, with mean change of 315.56 calories with 19.72% difference from baseline (*p*-value= 0.000).

Conclusion: Moringa oleifera leaf powder showed a statistically significant improvement on the mean weight gain, underweight status, wasting status and total caloric intake of malnourished pupils. Hemoglobin levels did not improve and height was not significantly increased.

Keywords: Moringa oleifera, Malungay, Malnutrition, Pupils, Children, Philippines, Underweight, Stunted, Wasted

1167 EARLY ADMINISTRATION OF PARENTERAL CHROMIUM ALLOWS FOR INCREASED GIR IN NEONATES

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Objective: Chromium is one of the trace minerals recommended in parenteral nutrition (PN) therapy. However, due to concerns for elevated serum chromium levels and potential renal toxicity with long-term TPN use, there has been a move in recent years to omit or decrease chromium in TPN based mainly on adult and chronic TPN data. Premature infants present a unique population at high risk for post-natal growth failure who depend on nutritional support for accrual of nutrients, growth, and development; however, hyperglycemia in the first week of life is common and often limits the caloric support that can be provided. Since chromium has been shown to potentiate the action of insulin, we hypothesized that early introduction of chromium into PN in neonates would induce tolerance of higher glucose infusion rates (GIR) thereby permitting increased parenteral calorie administration compared to those infants who received chromium supplementation later on.

Methods: We prospectively collected TPN utilization, growth, and serum glucose data in neonates admitted to our NICU during two eras that involved a change in practice of when supplementation with parenteral trace minerals (TM) at the recommended dose of 0.2 µg/kg/d was initiated. The first group (A) had the TM mixture administered daily starting on the 5–7th day of PN therapy while the second group (B) had TM mixture administered daily from initiation of PN therapy. The two groups were compared on the basis of the average birth weight, proportion of very low birth weight infants (VLBW, <1500 g), GIR required to maintain euglycemia during the first week of life, total calories delivered during the first week of life, and rates of growth during the first two weeks.

Results: Three hundred forty-eight infants were enrolled in group A and 358 in group B. The proportion of VLBW infants in groups A and B was 42% vs. 37%, *p*=0.114. For similar mean serum glucose concentrations in groups A and B: 107 ± 48 vs. 111 ± 52 mg/dL, *p*=0.3, infants in group B tolerated higher GIR and received more PN calories during the first week of life: 7.9 ± 1.6 vs. 8.4 ± 1.5 mg/kg/min, *p*<0.001; 72 ± 12 vs. 75 ± 23 kcal/kg/d, *p*=0.017. The difference in calories delivered was more pronounced among the VLBW infants compared to higher birth weight (>1500 g): 72 vs. 77 kcal/kg/d, *p*=0.009; 70 vs. 74 kcal/kg/d, *p*=0.079. The rate of weight gain during the first two weeks in groups A and B was similar, median (IQR): 9.6 (4.9, 19.6) vs. 9.9 (6.1, 17.3) g/kg/d, *p*=0.74.

Conclusions: PN therapy supplemented with chromium resulted in better glucose tolerance and greater calorie delivery during the first week of life. This effect was most pronounced in VLBW infants who are at higher risk for glucose intolerance, post-natal growth failure and worse neurodevelopmental outcomes. These findings support the essential role of chromium in enhancing glucose tolerance in newborns and VLBW infants during the first week of life.

1168 CLINICAL PROBLEMS IN INFANTS WITH TEMPORARY SHORT BOWEL SYNDROME: A RETROSPECTIVE, SINGLE-CENTER STUDY

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Background and Aims: Enterostomies are commonly performed on neonates with surgical acute abdomen. These infants are at high risk of malnutrition and growth retardation due to temporary short bowel syndrome, caused by an enterostomy. They are vulnerable to develop severe complications which may be lethal to them. We mainly focused on high risk factors for their morbidity and mortality in this study.

Methods: A retrospective study of children, who were admitted to our hospital with temporary short bowel syndrome (tSBS) secondary to an enterostomy done in neonatal period, was performed. Patients were divided into two groups: the death group and the survival group. The data

included birth weight, admission age, weight-for-age on admission, first surgery age, the length of residual small bowel, the presence of the ileocaecal valve (ICV), the duration of PN and complications (PNALD and sepsis).

Results: A total of 23 children (14 males and 9 females) who had been diagnosed with tSBS between January 2000 and June 2016 were followed up. The median follow-up was 27 months (range 3-140 months) and six patients died. No statistical significance was found in the birth weight (p 0.39), weight-for-age on admission (p 0.38), the presence of the ICV (p 0.64) and the first surgery age (p 0.889) between two groups. The mean length of residual small bowel (p 0.016) and the presence of complications (p 0.019) of the two groups had statistically significant differences. The duration of parenteral nutrition-dependency varied widely with each individual on the basis of conditions.

Conclusions: In this small series, mortality of tSBS infants was related to the length of residual small bowel and complications. The timing of ostomy closure should be individual.

1169 EFFECTS OF PRE-TERM FORMULAS ON THE GROWTH AND FEEDING TOLERANCE IN PRE-TERM INFANTS: A PROSPECTIVE MULTICENTER STUDY

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Objective: Poor growth is a common problem for premature neonates in developing countries. The purpose of this prospective multicenter study was to evaluate effects of pre-term formulas on the growth and feeding tolerance in a population of premature infants.

Methods: Pre-term infants with a birth weight between 1000 g and 1800 g, gestational age less than 34 weeks from ten tertiary referral hospitals in China were enrolled between May 2014 and September 2015. The study was divided into two stages. Stage 1: In hospital, pre-term infants who met the enrollment criteria were fed with liquid pre-term formulas with or without parenteral nutrition until discharge. Stage 2: At discharge, all pre-term infants with birth weight \leq 1500 g were fed with a post-discharge formula (PDF) until the body weight is \geq 25th percentile of growth expectation based on corrected age (P25) or until reached 9 months corrected age. Growth (weight, length and head circumference), feeding tolerance, parenteral and enteral intakes, and complications were collected and evaluated.

Results: A total of 128 pre-term infants were enrolled. During hospital stay, the velocity of gaining weight, head circumference, and length was 15.23 ± 3.80 g/kg/d, 0.98 ± 0.51 cm/wk, 0.71 ± 0.37 cm/wk, respectively. Incidence of EUGR for weight, length and head circumference at discharge was 35.8%, 31.1% and 16.0% respectively. Time to full enteral feeding was 18.00 (17.00, 20.00) days. Univariate analysis showed that gestational age ($X^2=18.317, p=0.001$), Apgar scores ($X^2=6.470, p=0.011$) and SGA ($X^2=0.009, p=0.010$) were the important factors affecting EUGR incidence. Incidence of vomiting (\geq 3 times in 24h, or with bile/blood contamination), abdominal distension (abdominal circumference increased by \geq 2 cm in 24 hrs, or with visible intestinal pattern) and gastric retention (gastric residual volume exceeded 50% of the last feeding amount) was 3.9%, 2.3%, and 5.5%, respectively. 46 infants (35.9%) were monitored for any withheld feedings due to abdominal distention, gastric residuals, vomiting or others causes. 12 infants (9.4%) developed any periods of NPO. Incidence of defecation or stool abnormalities (diarrhea, bloody stool or fecal occult blood positive) and necrotizing enterocolitis (NEC) was 8.6% and 2.5%. After discharge, 14 pre-term infants were enrolled. The velocity of gaining weight, head circumference, and length was 41.32 ± 10.05 g/d, 1.27 ± 0.32 cm/wk, 0.61 ± 0.18 cm/wk, respectively.

Conclusion: Pre-term formulas (liquid pre-term formulas and PDF) are effective and safe alternative for the growth of pre-term infants.

Key words Pre-term formula; Growth; Feeding tolerance; EUGR; Pre-term infant

1170 METABOLOMIC APPROACHES TO EXPLORE CHEMICAL DIVERSITY OF HUMAN BREAST MILK, FORMULA MILK AND BOVINE MILK

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Human breast milk (HM) is the essential and primary source of nutrition for infant healthy growth; therefore, comprehensive understanding both the composition and function of breast milk components is vital to the improvement of infant formula recipes. Although many studies have been conducted on the components present in HM, research on the differences between HM, bovine milk (BM), and formula milk (FM) is limited, especially in regards to chemical metabolites. The objective of this study was to explore the chemical diversity of HM, BM, and FM by metabolomic approaches. Gas chromatography-time-of-flight mass spectrometry (GC-TOFMS) and ultra-performance liquid chromatography-quadrupole-time-of-flight mass spectrometry (UPLC-QTOFMS) were applied to investigate the metabolic compositions of HM, FM, and BM. A total of 280 metabolites (carbohydrates, amino acids, organic acids, amines, fatty acids, bile acids, etc.) were annotated from the GC-TOFMS and UPLC-QTOFMS spectrum. Partial least squares-discriminant analysis showed a unique metabolite profile of HM compared to FM and BM. HM contained a large variety of fatty acids, including polyunsaturated fatty acids (C18:2, C18:3, C20:2, C20:3, C20:4, C20:5, C22:5, and C22:6), which were quite scarce in FM. The levels of tricarboxylic acid (TCA) intermediates (2-ketoglutaric acid, citric acid, fumaric acid, malic acid, and nicotinamide) in FM were found to be 8- to 54-fold higher than those in HM. Additionally, the levels of fructose and urea in FM were found to be much higher than those in HM and BM. The global comparison of small molecule metabolites among HM, FM, and BM may help to maximally improve the nutritional quality and the biological impact of artificial milk.

1171 THE CONTRIBUTION OF DESSERTS AND SWEETS TO THE DIETS OF INFANTS, TODDLERS AND PRESCHOOLERS IN THE US

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Background: Dietary patterns emerge in young childhood, and food choices between 12-24 months of age model dietary choices later in life. We have previously shown that as infants reach toddlerhood they eat fewer fruits and vegetables and larger amounts of grains, meats and sweets, a pattern that can contribute to excessive energy, fat, and added sugar intakes as well as certain micronutrient and fiber gaps. The purpose of this

study is to examine the intake of desserts and sweets to gain a better understanding of their age of introduction and their contribution to young childrens' diets.

Methods: Data from the Feeding Infants and Toddlers Study (FITS) 2008, a cross-sectional national survey of young children in the U.S., were analyzed to understand the contribution of desserts and sweets to the dietary intake of infants (6-11.9 months; n=505), toddlers (12-23.9 months; n=925), and preschoolers (24-47.9 months; n=1461). Twenty-four-hour dietary recalls were conducted by telephone with parents or primary caregivers of 3273 children age 0-4 years.

Results: The sample is 50.5% male, 54.7% non-Hispanic white, 22.6% Hispanic, and 13.8% non-Hispanic black, with 36.7% participating in WIC and 43.3% attending daycare. Forty-three percent of infants consumed desserts and sweets before the age of one year, and these were increasingly prevalent foods in toddlerhood and preschool age. By the age of one year, desserts and sweets contributed 5% of total daily energy intake (46 kcal/day), and reached 17% of daily energy (221 kcal/day) by preschool age. Desserts and sweets contributed 1.3% of daily total fat (0.5 g/day) by the end of infancy and increased to 11.3% of total fat (5.3 g/day) by preschool age. Desserts and sweets contributed 8.6% (3.0 g/day) of daily added sugar at one year of age, and became the leading source of added sugar by preschool age at 61.2% (24.8 g/day). The contribution of desserts and sweets to sodium intakes was 3.3% and 6.5% for infants and preschoolers, respectively. Cakes/pies/cookies/pastries were the major source of fat and sodium from the desserts and sweets categories, and sweetened beverages were the leading contributor of added sugar. The contributions to iron and fiber intakes were small, with 0.8% and 2.7% for older infants and 8.7% and 8.0% for preschoolers, respectively. Overall, the contribution from desserts and sweets to protein, calcium, and potassium intakes was low ($\leq 5\%$).

Conclusion: Infants and toddlers begin consuming desserts and sweets at an early age, with increasing proportional contributions to daily energy, fat, and added sugar intakes in the toddler and preschool years. These foods make much smaller contributions to the intake of essential nutrients that many children fall short on, including iron, calcium, fiber, and potassium. Educational efforts are needed to help parents limit sweets and choose nutrient-dense foods such as fruits and vegetables to help improve diet quality for their children.

1172 MINERAL STATUS OF INFANTS REQUIRING DIETARY MANAGEMENT OF COW'S MILK ALLERGY BY USING AN AMINO ACID-BASED FORMULA

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Cow's milk allergy (CMA) is the most common food allergy in infancy. CMA symptoms are gastrointestinal, cutaneous and respiratory related and many allergic patients present with multiple symptoms. Fundamental to the management of food allergy is complete elimination of the offending proteins. However, as a result of dietary elimination CMA patients are at risk for inadequate nutritional intake and micronutrient deficiencies. Management approaches in infants and young children include the use of hypoallergenic formulas that need to be fully tolerated, support normal growth and also assure an adequate nutritional status in these patients. Dietary management of CMA with an amino acid-based formula (AAF) has been proven to be effective and safe while providing adequate infant growth and hypoallergenicity and tolerance of AAF have widely been reported. Data on mineral status after dietary management by AAF are however scarce.

In a prospective, randomized, double-blind controlled study, full term infants with diagnosed CMA received an AAF (n 110) with or without synbiotics (neutral and acidic oligosaccharides, *Bifidobacterium breve* M-16V) for 16 weeks. Primary outcomes were growth and formula tolerance and have been reported previously.^{1,2} Mineral status was assessed by further analyses of blood samples obtained at baseline and 16 weeks, which included calcium, phosphorus, chloride, sodium, potassium, magnesium and total iron. Furthermore, total protein, albumin, prealbumin, hemoglobin and ferritin were also determined. To assess average daily formula intake and ensure whether daily energy requirements were significantly met, formula intake was recorded through diaries at weeks 0, 4, 8 and 16 during the study.

Average age of infants at inclusion was 4.5 ± 2.4 months (mean \pm SD). Median study product intake ranged from 704 ml/day (23.8 oz/day) in the first week to 789 ml/day (26.7 oz/day) at week 16. At baseline, averages (mean; median) of blood levels of calcium, phosphorus, chloride, sodium, potassium, magnesium and iron were within reference ranges. After 16 weeks on AAF, averages (mean; median) of blood levels of all these minerals were again within the specified reference ranges set for the corresponding ages of the infants. Also such averages of total protein, albumin, prealbumin, hemoglobin and ferritin were within reference ranges. Among some minerals, there were a number of individual values at baseline that were below the reference ranges, i.e., calcium (n=1), phosphorus (n=1), chloride (n=1), and sodium (n=1), whereas at week 16 none of these minerals had individual values that were below reference ranges.

This study shows that an AAF with or without synbiotics, which have been reported previously to be equally tolerated and to support normal growth^{1,2}, are effective in managing an adequate mineral status in CMA infants.

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1173 BIOAVAILABILITY OF IRON-FORTIFIED DAIRY COMPLEMENTARY FOOD WITH IRON PICOLINATE

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Iron food fortification is generally regarded as the most cost-effective and sustainable long-term approach for reducing the incidence of Fe deficiency which is especially prevalent in infants, young children and women of child bearing age. A technological gap for the Fe fortification of difficult-to fortify products, like wet and acid food products containing polyphenols, with stable and bioavailable Fe exists. Fe picolinate, a novel food ingredient, was found to be stable over time in this type of matrix. The main purpose of the work was to establish the first of kind bioavailability data in humans. A double blind, randomized clinical trial with a cross-over design was conducted in 20 young adult women (25.1 \pm 4.6 yrs). The fractional Fe absorption was measured from iron picolinate (2.5 mg 57Fe per serving) and from ferrous sulfate (FeSO₄) (2.5 mg 54Fe per serving) fortified dairy complementary food (i.e. yogurt containing fruits). Fe absorption was determined based on erythrocyte incorporation of isotopic labels 14 days after consumption of the last test meal. Fractional iron absorption from Fe-picolinate and FeSO₄ were 5.2 % (3.8%-7.2%) and 5.3% (3.8%-7.3%), respectively. Geometric means and 95% CIs are presented. Relative bioavailability of Fe picolinate vs. FeSO₄ was 0.99 (90%CI, 0.85-1.15) which is within the boundaries for bio-equivalence according to FDA: (90%CI, 0.80, and 0.125).

Therefore, Fe picolinate could be a promising compound for the fortification of difficult-to fortify foods, to help in meeting Fe requirements of infants, young children and women of child bearing age.

1174 CHILDHOOD FEEDING DIFFICULTIES FACED IN CHILDREN BY MOTHERS FROM 6 MONTHS TO 2 YEARS IN A TERTIARY HEALTHCARE FACILITY

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Background: Infant feeding and nutrition provision is one of the major obstacles faced by the caregivers of the children. About 25% of the normal developing, healthy children experience this difficulty, but very little data is available in this region if any, regarding feeding difficulties. Guidelines regarding feeding of children are not available locally and those present internationally cannot be related to our local scenario. Objective: To determine the childhood feeding difficulties faced by mothers in their healthy infants, from 6 months to 2 years in a Tertiary Health Care Facility of Pakistan.

Methods: An ongoing cross-sectional study with a total sample size of 288, of which a preliminary data of 98 infants from 6 months to 2 years in a tertiary health care facility from January 2016 to May 2016, is presented based on the childhood feeding difficulties faced by mothers. Permission from parents and principal of the respective institution was obtained. IRB was taken from Karachi Medical and Dental College. The infants were broadly categorized into four groups (6-12 months of age, 13-18 months, 18-24 months and 25-30 months). A convenience sampling technique was used by means of collecting data from middle socio-economic mothers accompanied by their healthy children of the ages mentioned, who visited the hospital for various reasons. The data were collected from the mothers via the Behavioral Pediatrics Feeding Assessment Scale (BPFAS) questionnaire and was statistically analyzed using SPSS.

Results: Ninety-eight mothers and their children from Abbasi Shaheed Hospital participated in the study. Out of 98 participants, 54 were male while 44 were female and from the total, 80.6% of the children were between the ages of 6 months to 18 months respectively. According to the data collected up till now, the score on BPFAS questionnaire to assess feeding difficulties, 22 children had a score <85, whereas 76 children had a score of 85 and above. Therefore, more than 22 out of 98, i.e., 22%, had feeding difficulties while remaining 76 did not have feeding difficulties. The children plotted between 25th to 50th centile for both height and weight on the CDC chart. Parents mentioned that they faced difficulties in feeding their children however their children's diet though it included junk food was sufficient to prevent malnutrition.

Conclusion: Based on the current results of the ongoing study regarding frequency of feeding difficulties in children aged 6 months to 30 months, faced by parents, around 22% of healthy children in this region had feeding difficulties. Keywords: feeding difficulties, childhood, nourishment, healthy.

1175 ASSESSMENT OF GROWTH AND NUTRITIONAL STATUS IN SHWACHMAN-DIAMOND SYNDROME PATIENTS

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Background: Shwachman-Diamond syndrome (SDS) is a rare autosomal recessive disorder characterized by exocrine pancreatic dysfunction with malabsorption, short stature and bone abnormalities. Different nutritional conditions have been noted in SDS during growth. The aim of this study was to assess nutritional status, body and diet composition in different age groups of SDS subjects.

Methods: A total of 31 subjects (age 1 to 39 years) with SDS were examined. Anthropometric parameters (height, weight, four skinfold thicknesses, arm and waist circumferences) and clinical parameters (pancreatic and vitamin status) were assessed. Muscular strength, nutritional intake and physical activity level were measured in order to evaluate their relationship to body composition. Subjects were classified into three groups according to their age: 1 to 8, 8 to 18 and above 18 years old.

Results: Nutritional status changed with age. The 1-8 year age group presented a mean BMI Z-score of -0.64 ± 1.09 , the 8-18 year age group had a mean BMI Z-score of 0.05 ± 1.27 and the adult group had a BMI of 24.9 ± 4.2 . The percentage of body fat increased from $23.6 \pm 12.2\%$ in the 8-18 year group to $27.5 \pm 5.4\%$ in the adult group. The mean percent of predicted arm and waist circumferences, triceps skinfold thickness and arm fat area increased significantly with age. Diet composition was similar between the groups, calcium intake was around 650 mg/day, protein, fat and carbohydrate intakes were the 16%, 37% and 47% of total calories, respectively. Vitamin A deficiency occurred in the 82% of the young subjects, in the 37.5% of the 8-18 year age subjects and in the 28.5% of the adults despite vitamin supplementation. The 25% (0-8 years old), 22% (8-18 years old) and 28.5% (>18 years old) of the patients had pancreatic sufficiency. Fat mass was inversely associated with muscular strength while no association were found with physical activity level or energy intake.

Conclusions: Different nutritional approaches according to patient's age should be adopted. Nutritional intervention should be focused on diet composition, fat and calcium intake. Fat soluble vitamin level should be routinely monitored. A large incidence of vitamin A deficiency is present in toddler and children. Future research assessing energy expenditure and obesity-related hormones in SDS subjects is necessary.

*1176 EARLY DISCHARGE OF INTESTINAL FAILURE PATIENTS FROM THE NICU: A PILOT QUALITY IMPROVEMENT INITIATIVE

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Introduction: Historically at our institution, intestinal failure patients were managed primarily by the neonatal intensive care unit (NICU). There were no standard discharge criteria and patients were often held for serial attempts to advance to full enteral feedings or to arbitrary goals of enteral and parenteral nutrition rates. Gastroenterology consultation was inconsistently requested of rotating attendings not committed to post-discharge long-term outpatient management. We hypothesized that these patients could be discharged earlier, and would succeed with enteral feeding advancement and complementary parenteral nutrition as outpatients.

Methods: A pilot quality improvement project was undertaken for nine months. A single gastroenterologist responsible for and committed to the outpatient management of parenteral nutrition and intestinal failure patients began conducting weekly rounds on all surgically-related, short bowel syndrome intestinal failure patients in the NICU. Simple early discharge criteria were instituted including: 1) tolerating continuous enteral feeding at 5 mL/hr or more, 2) parenteral nutrition cycled to 20 hours per day or less, 3) an indwelling central venous line, and 4) no other medical conditions requiring NICU care. We compared the length of stay, readmission rate, and Central Line Associated Blood Stream Infection (CLABSI) rate of the pilot QI group with a historical cohort of intestinal failure patients, matched 4:1 on gestational age.

Results: Six patients met early discharge criteria with gestational ages ranging 30-41 weeks. The underlying diagnoses were: necrotizing enterocolitis, cystic fibrosis with meconium perforation, gastroschisis, duodenal atresia with imperforate anus, ileal atresia and small bowel volvulus. Patients managed in this pilot project had a shorter length of stay (59 vs. 11 days, $p=0.05$), fewer readmissions (0.2 vs. 2.5 readmissions per outpatient day, $p<0.01$) and fewer CLABSIs (0 vs. 11.6 per 1000 catheter days, $p<0.01$).

Discussion: Regular inpatient involvement of a single gastroenterologist in charge of long-term outpatient management of intestinal failure patients and elimination of arbitrary feeding advancement goals resulted in a dramatic reduction in NICU length of stay. Patients cared for in this new system had fewer readmissions and CLABSIs. This pilot study was limited by a small sample size. While we controlled for gestational age in a historical cohort, there was no control of intestinal anatomy, medical comorbidities or psychosocial situations that all affect length of stay. At an estimated minimum cost of \$3,000 per NICU day, this pilot project saved \$936,000 in direct care costs and resulted in fewer adverse events.

1177 DIETARY MANAGEMENT OF NON-IGE MEDIATED COW'S MILK ALLERGIC INFANTS WITH A SYNBIOTICS-SUPPLEMENTED AMINO ACID-BASED FORMULA: EFFECTS ON FAECAL MICROBIOTA AND CLINICAL SYMPTOMS

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Infants and children with cow's milk allergy (CMA) have been shown to have an aberrant fecal microbiota associated with their allergic pathology. Pre- and probiotics (synbiotics) have been suggested to improve early life microbiota development of CMA infants and may subsequently reduce allergy burden. This study describes the effects of an amino acid-based formula (AAF) with synbiotics on fecal microbiota composition, stool characteristics and clinical symptoms in infants with non-IgE mediated CMA. In a prospective, randomized, double-blind controlled study (registered as NTR3979), full-term infants with suspected non-IgE mediated CMA received an AAF (control; n=36) or an AAF with synbiotics specifically designed for dietary management of CMA (oligofructose, inulin, *Bifidobacterium breve* M-16V) (test; n=35) for 8 weeks. The primary outcome measures were *bifidobacteria* and the *Eubacterium rectale/Clostridium coccoides* (ER/CC) cluster as percentage of total fecal bacteria determined by fluorescent in situ hybridization. Other outcomes were Scoring Atopic Dermatitis (SCORAD) and via parent diaries collected data on (allergic) symptoms and stool characteristics. In addition, secretory IgA and short chain fatty acids (SCFA) were analyzed in stool samples at baseline and 8 weeks. The same analyses were performed in stool samples from a reference group of non-randomized healthy breastfed infants, which were age-matched with age of CMA infants at week 8 of intervention. Average age (\pm SD) of CMA infants (n 71) was 6.00 ± 2.98 months at inclusion of the study and 7.84 ± 3.25 months in the reference group (n 51). Ninety percent of the CMA subjects presented predominantly GI symptoms and 10% dermatological symptoms; stratification was based on these manifestations. Sixty CMA infants completed the 8 weeks intervention (control n=32; test n=28). Using the intention-to-treat data set and ANCOVA technique, levels of bifidobacteria at 8 weeks were significantly higher in the test (35.6%) vs. control group (14.7%) ($p<0.001$) and ER/CC cluster was significantly lower in the test (12.1%) vs. control group (26.6%) ($p<0.001$). Clinical outcomes and stool characteristics are currently being analyzed and will be presented.

*1178 DOES GUT MICROBIOTA-INDUCED METABOLIC IMPROVEMENT AFTER GASTRIC BYPASS REQUIRE TOLL-LIKE-RECEPTOR SIGNALING?

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Background: Obesity is a leading cause of morbidity and mortality in adults and children. It is linked to a state of chronic inflammation where pediatric and adult obese subjects have elevated levels of serum cytokines. Toll Like Receptor (TLR)-4 is involved in innate immunity response and is required for high-fat diet (HFD) induced insulin resistance and obesity-associated diabetes. TLR4 deficient mice, are resistant to obesity, have decrease inflammatory markers, and improved insulin sensitivity and animals fed HFD change their gut microbiota composition to express signs of chronic inflammation in a TLR4 dependent pathway. Roux en-Y gastric bypass (RYGB) is one of the most effective bariatric procedures to treat obesity though not with negligible risks. The new developed gut microbiota after RYGB promotes weight loss when transferred into germ-free mice. Understanding the mechanism by which RYGB exerts its metabolic effects will help facilitate treatment of obesity in children in a less invasive way.

Hypothesis: RYGB requires TLR-4 signaling to induce its metabolic effects in manner that is dependent on gut microbiota.

Methods: Diet induced obesity was induced by feeding 6 weeks old C57Blk/6 males with HFD for 13-14 weeks before undergoing RYGB or a sham surgery. Food intake and body weight were measured daily and feces from all animals were collected, in sterile containers and stored in -80 °C. Tissues (intestines, liver, adipose) and serum were collected at time of sacrifice (1, 3 and 10 weeks after surgery). Serum Cytokines were analyzed by Meso-Scale Discovery immunoassays and gene expression of TLR3, TLR4 and TLR5 was examined in intestines using qPCR. Feces from RYGB vs. sham-operated animals were homogenized in liquid solution and transferred by daily gavage into lean C57Blk/6 males for 2 weeks. Food intake, body weight, and serum cytokines were also measured in mice recipients of RYGB vs. sham-fecal material.

Results: RYGB-operated mice lost more weight and body fat over time and had minimal changes in daily caloric intake compared to their sham counterparts. RYGB induced a significant decrease in feeding efficiency (gain in body weight per Kilo-joule consumed) and an increase in calculated energy expenditure. Serum cytokines (IFN- α , IL-1 α , IL-2, IL-4, IL-5, IL-6, KC/GRO, IL-10, IL-12p70, and TNF- α) were not different between the two groups nor was gene expression of intestinal TLRs. Moreover, recipients of RYGB fecal material gained less body weight than sham-recipients with no significant change in either food intake or serum cytokine profile.

Conclusion: Contrary to our hypothesis we found no changes in TLR4 expression or level of circulating cytokines after RYGB. Transferring microbiota from RYGB into lean mice induced a similar phenotype of weight balance and cytokine profile to the donors. Therefore, RYGB might not require TLR4 signaling for its metabolic effects.

Future Studies: Examine the effects of RYGB in TLR4 deficient mice.

1179 A DESCRIPTIVE STUDY ON THE PREVALENCE OF FEEDING DISORDERS IN FILIPINO CHILDREN AGED 1 TO 5 YEARS OLD IN A TERTIARY HOSPITAL IN THE YEAR 2014

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Background: Feeding problems in children are an increasing concern of parents worldwide and have been studied using different classifications. This study aims to determine the prevalence of and the factors associated with feeding disorders in Filipino children aged 1 to 5 years old in a tertiary hospital in the year 2014.

Methods: This is a cross-sectional study conducted in private clinics of pediatricians. Using random cluster sampling, a total of 215 Filipino children aged 1 to 5 years old with an accompanied parent or guardian, who gave consent and has denied limitation of food availability, were given a questionnaire based on the Diagnostic Classification of Mental Health Disorders in Infancy and Early Childhood, Revised edition (DC: 0-3R) classification of feeding disorders. Anthropometric measurements were also taken using standardized tools.

Results: Prevalence of Feeding disorders as classified in DC:0-3R is 1.7%. If only descriptive features were considered, prevalence of feeding disorders is at 22.7%, decreased to 10.7% if duration and age limits are also considered. These may indicate prevalence of possible feeding disorders since only the lack of faltering weight, manifested by a weight-for-age Z-score of below -2, is the criterion that most children failed to meet. The most common type of feeding disorder are Feeding Disorder Associated with Concurrent Medical Condition and Feeding Disorder Associated with Insults to the Gastrointestinal Tract, followed by Sensory Food Aversions and Infantile Anorexia. Parents' or respondent's educational attainment, a history of feeding difficulty in the family and a parent having growth delay are the factors which showed significant difference between groups with and without features of feeding disorders. The most common strategies to cope with feeding disorders are: 1) to give vitamins and appetite stimulants, 2) change the texture and presentation of food, and 3) feed children in between meals to compensate small amount of food taken. The least used methods to cope are 1) raise voice to the child, 2) threaten the child, and 3) let the caregivers feed the child instead of the parents. These strategies may have prevented the children to have faltering weight which disqualified them to be classified under feeding disorder, despite showing feeding concerns and difficulties.

Conclusion: Prevalence of feeding disorder in Filipino children aged 1 to 5 years old in a tertiary hospital in the year 2014 as classified in DC: 0-3R is 1.7%. Prevalence of children with descriptive features of a feeding disorder is 22.7%, which shows a possibility of feeding disorder.

***1180 COMPARISON OF WEIGHT-FOR-HEIGHT Z-SCORE AND MID UPPER ARM CIRCUMFERENCE FOR ASSESSING ACUTE MALNUTRITION IN 6 TO 59 MONTHS OLD BANGLADESHI CHILDREN: AN ANALYTICAL STUDY**

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Background: Wasting in childhood is primarily assessed using weight-for-height Z-score (WHZ), particularly in clinical settings. The use of WHZ can be problematic and may be difficult to measure reliably, especially with inexperienced staff, in the field situation. Mid-upper-arm-circumference (MUAC) as a cheap and simple measure that closely relates to mortality-risk, has been recommended in the community with a cut-off of <115 mm for severe-wasting (WHZ <-3) and <125 mm for moderate-wasting (WHZ <-2 to -3). However, our recent experience indicates that many wasted children were not identified when these cut-off values were used.

Objective: To find an appropriate cut-off value of MUAC to detect 6-59 months old wasted children.

Design/Method: A secondary analysis was carried out on data from 27,767 children aged 6 to 59 months. This comprised: i) 9131 children (from 113 sub-districts across Bangladesh) who participated in the 2004 baseline survey for the National Nutrition Programme, and ii) 18,636 children enrolled in a surveillance study in the Dhaka Hospital of icddr,b during 1996 to 2014. Sensitivity, specificity, positive- and negative- predictive values of MUAC were generated for WHZ at -3 and -2 cut-offs. Receiver operative characteristics (ROC) curves were generated for MUAC and WHZ.

Results: Of the total children 45% were female. The mean \pm SD age for the entire group was 21 ± 14 months, WHZ -1.18 ± 1.23 , HAZ -1.63 ± 1.39 , and MUAC was 136 ± 14 mm. MUAC correlated with WHZ (Pearson correlation: 0.618, $p < 0.001$). The area under the receiver operating curve (AUC) (to aid identification of cut-off values for MUAC in relation to WHZ) was 0.855 ± 0.005 at -3 WHZ and 0.825 ± 0.003 at -2 WHZ ($p < 0.001$). Cut-off values for MUAC (selected at the point of highest cumulative values of sensitivity and specificity) were 125 mm for WHZ <-3 and 132 mm for WHZ <-2 with a sensitivity of 73% and 76%, and specificity of 82% and 72% respectively. In contrast, currently recommended MUAC cut-off values resulted in sensitivities of 44% and 54% respectively.

Conclusions: MUAC-cut-off values of <125 mm to detect severe-wasting and <132 mm to detect moderate-wasting should be considered for use in our context for children aged 6-59 months in settings where weight and heights is difficult to measure. The findings from this analysis would provide a more secure basis for policy formulation and advice for practice.

1181 WITHDRAWN

1182 EVOLUTION OF PROTEIN COMPOSITION IN BREAST MILK OF CHINESE URBAN MOTHERS AND IMPACT OF CAESAREAN SECTION DELIVERY

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Human breast milk (BM) protein composition may be impacted by lactation stage or factors related to geographical location. The present study aimed at assessing the evolution of BM major proteins over lactation stages with focus on the impact of mode of delivery on immune factors, in a large cohort of urban mothers in China, a country presenting one of the highest rate of Caesarean-section birth in the world.

BM was collected from mothers from three Chinese cities, who delivered apparently healthy, term infants. 450 BM samples covering 8 months of lactation were analyzed for alpha-lactalbumin, lactoferrin, serum albumin, total caseins, immunoglobulins (IgA, IgM and IgG) and transforming growth factors (TGF) beta-1 and beta-2 contents by microfluidic chip- or ELISA-based quantitative methods. Concentrations and changes over lactation were aligned with previous reports. alpha-lactalbumin, lactoferrin, IgA, IgM and TGF-beta-1 contents followed similar evolution profiles characterized by highest concentrations in early lactation that rapidly decreased before remaining stable up to end of lactation. TGF-beta-2 content displayed same early dynamics before increasing again. Total caseins followed a different evolution pattern, showing initial increase before decreasing back to starting values. Serum albumin and IgG levels appeared stable throughout lactation. No consistent impact of C-section delivery was observed on immune factors. In conclusion, this unique multi-centric cross-sectional study covering 8 months of lactation for 450 Chinese mothers demonstrated that their BM content in major proteins did not differ from previously published worldwide references and that Caesarean-section delivery had only very limited impact on BM immune factors.

1183 INFLUENCE OF DIETICIANS IN PREVENTING PARENTERAL NUTRITION PRESCRIPTION ERRORS IN A PEDIATRIC SETTING
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Background: Dieticians play an important role in the overall nutritional care of pediatric patients by conducting nutritional assessments and providing recommendations regarding parenteral nutrition (PN) infusion rates. Errors in PN prescriptions may compromise patient safety and result in significant preventable costs. However, there is limited data on whether dietician involvement in prescribing PN results in reduced prescription errors.

Methods: A prospective audit of PN prescriptions was undertaken at a single pediatric hospital over 50 weeks. Prescriptions for PN, which had dietician involvement (dietician group) were compared with prescriptions in which dieticians were not directly involved (non-dietician group). The number of total prescriptions, number of prescriptions with errors and types of errors from both groups was recorded. Errors were classified into "dietician preventable errors" and "non-dietician preventable errors". "Dietician preventable errors" included errors of incorrect solution, incorrect electrolytes, weight not recorded, PN rate missing or incorrect, vitamins/ trace minerals missing or incorrect, Vitalipid N[®] (Fresenius Kabi) incorrect, lipid rate missing or incorrect on the prescription, or PN unnecessarily ordered. If the intravenous access was not specified, prescription not signed, date was missing or incorrect, or name was missing then these were considered "non-dietician preventable errors". Chi-square analysis was used to compare prescriptions with and without errors and compare dietician preventable and non-dietician preventable errors.

Results: The total number of PN prescriptions was 725 (from 45 patients) and 471 (from 66 patients) for the dietician and non-dietician groups respectively. The dietician group was less likely to prescribe PN incorrectly than the non-dietician group (12.4% (90/725) vs. 18.0% (85/471); $p=0.0071$), with the non-dietician group having 1.5 times more prescriptions with errors (RR 1.5, 95% CI, 1.1-1.9). The total number of prescription errors was 126 and 146 for the dietician and non-dietician group respectively. The dietician group was less likely to be associated with dietician preventable errors than the non-dietician group (65.9% (83/126) vs. 87.0% (127/146); RR 1.3, 95% CI, 1.1-1.5; $p<0.0001$).

Conclusion: Increased dietician input into prescription of PN significantly reduced number of prescriptions with errors.

1184 HYPOPHOSPHATEMIA ASSOCIATED WITH NEOCATE JUNIOR ELEMENTAL FORMULA IN CHILDREN: A CASE SERIES
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Introduction: Children with feeding difficulties secondary to intestinal failure or gut dysfunction are at high risk for poor growth and development due to inadequate digestion and absorption of various nutrients. Neocate Junior is an elemental formula that is commonly prescribed by gastroenterologists for this patient population. Recently, it has been discovered that children who are exclusively fed Neocate Junior can develop hypophosphatemia. Patients with mild hypophosphatemia are generally asymptomatic but can experience weakness and bone pain. However, patients with severe hypophosphatemia can develop osteopenia, rickets and pathologic fractures. We report a series of 5 patients exclusively fed Neocate Junior who developed severe hypophosphatemia that resolved in 4 of the patients when they were switched to Elecare Junior, suggesting that the hypophosphatemia was due to a problem related to the formula. Cases: We present 5 patients (ages 3-13 years) followed in the pediatric gastroenterology clinic at Columbia University Medical Center who developed hypophosphatemia while exclusively on Neocate Junior. Two patients had gut dysmotility, 1 patient had short bowel syndrome and 1 patient had severe gastroesophageal reflux. Due to feeding difficulties, all of the patients were exclusively fed Neocate Junior and subsequently developed metabolic bone disease, including pathologic fractures, osteopenia and rickets secondary to hypophosphatemia. Evaluation by pediatric endocrinologists for other potential causes of hypophosphatemia was unremarkable. Hypophosphatemia resolved in 4 patients by changing formula from Neocate to Elecare Junior and in 1 patient with phosphorus supplementation (change in formula was not tolerated). Patient 3 was switched back to Neocate because he did not tolerate Elecare, and he required phosphorus supplementation. Patients' demographics, biochemistry, bone disease and treatment responses are summarized in the table.

Discussion: Neocate Junior can be associated with severe hypophosphatemia and metabolic bone disease in some children and resolved in 4 of our patients by changing their formula to Elecare Junior, despite the fact that phosphorus concentration in both formulas is almost comparable. The underlying mechanism of hypophosphatemia is unclear. It could relate to a difference in the bioavailability of phosphorus in Neocate Junior, to formula-induced impaired phosphorus absorption in certain children or to an underlying genetic predisposition that impairs phosphorus absorption, as not all the children on Neocate Junior develop hypophosphatemia. More studies need to be done to elucidate the mechanism of hypophosphatemia.

Conclusion: These cases emphasize the importance of monitoring for nutritional deficiencies and monitoring bone health in patients who are exclusively on elemental formulas. Specifically, we recommend monitoring serum phosphorus levels in children who are exclusively fed Neocate Junior formula.

Table: Characteristics of Patients with Hypophosphatemia on Neocate Junior

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	13	3	6	3	3
Sex	Female	Male	Male	Male	Female
Primary GI Diagnoses	Severe gastroesophageal reflux, TPN dependence	Short bowel syndrome	Severe gastroesophageal reflux, esophageal stricture, chronic diarrhea	Gut dysmotility	Gut dysmotility, TPN dependence
Secondary Diagnoses	MRCP, Seizure disorder, failure to thrive	Prematurity (25 weeks), chronic lung disease, seizure disorder	Epidermolysis bullosa, bone marrow transplant	Hypoxic ischemic encephalopathy, developmental delay, seizure disorder	Failure to thrive
Phosphorus level (mg/dL)	0.5	2.5	0.5	2.3	1.8
Alk Phos (IU/L)	672	225	477	600	855
Bone Disease	Osteopenia	Fractures, Rickets, Osteopenia	Fractures, Osteopenia	Osteopenia	Fractures, Rickets, Osteopenia,
Age at Start of Neocate	5 months	15 months	Birth	4 months	4 weeks
Treatment	Elecare Junior	Phosphorus supplementation	Elecare Junior	Elecare Junior	Elecare Junior
Phosphorus level after treatment (mg/dL)	4.1	4.6	3.5	4.5	4.1
Feeding method	G Tube	G Tube	G-J tube	G Tube	G-J tube

The normal range of phosphorus levels is 3.0 – 6.0 mg/dL.

1185 PERSISTENT COW'S MILK PROTEIN ALLERGY

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Background: Cow's milk protein allergy (CMPA) is the fourth food allergy in children and the first in infants. Currently a decrease in the recovery rate and a rise in the rate of children with persistent CMPA is noted. The aim of our study was to describe the epidemiological, clinical and evolutionary features in patients with persistent CMPA and to identify predictive factors of persistence.

Methods: This was a retrospective study over a period going from January 2005 until March 2014 and concerning patients with CMPA followed in pediatric department of Mongi Slim Hospital La Marsa. Two groups were identified: group 1 (persistent CMPA) and group 2 (non-persistent CMPA).

Results: We included 44 children with CMPA. 28 (63.6%) had persistent CMPA. In group 1 sex ratio was 2.1. A family atopy was found in 15 cases (53.5%). The median age of first taking cow milk proteins (CMP) was 89.5 days. Clinical manifestations at presentation were dominated by cutaneous signs (92%), followed by gastrointestinal (60.7%) and respiratory (14%) symptoms. A severe form was found in 13 patients. The median rate of the first control CMP-IgE was 5.9 KU/l. Univariate analysis showed that predictive factors of persistence were: the father atopy ($p = 0.037$), the instantaneous reactions ($p = 0.012$), cutaneous signs ($p = 0.019$), urticaria ($p = 0.03$), gastrointestinal symptoms ($p = 0.022$), other associated food allergies ($p = 0.036$), the rate of the first F2 ($p = 0.02$) and the median diameter of the first Prick Test ($p = 0.026$). The median diameter of the first Prick Test ($p = 0.008$), the presence of urticaria during evolution ($p = 0.021$) were independent factors of persistence, gastrointestinal symptoms ($p = 0.013$) were an independent predictor of tolerance.

Conclusion: Persistent CMPA is difficult to manage and determining markers of persistence is very useful to improve its monitoring and management.

*1186 ASSOCIATING NUTRITIONAL RISK WITH CLINICAL OUTCOMES IN PEDIATRICS PATIENTS: AN APPRAISAL OF DIFFERNET SCREENING TOOLS AND MEASUREMENTS

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The high prevalence of malnutrition in hospitalized children has resulted in a widespread interest for routine screening on admission. However, validation of malnutrition screening tools (MSTs) in children is still scarce. The study aimed to determine the associations between 3 pediatric MSTs and clinical outcomes (length of stay-LOS; complications: infection, delayed wound healing, transfer to another hospital or unplanned use artificial nutrition; nutrition status on discharge-NS) in children admitted to a tertiary referral hospital, in comparison to baseline weight and body composition (BC) scores.

A total of 152 children (mean age 10.7 yrs; 50% male; 51.3% surgical) admitted under any specialty with an expected stay >3d were enrolled in the study. 3 MSTs (Paediatric Yorkhill Malnutrition Score-PYMS; Screening Tool for the Assessment of Malnutrition in Paediatrics-STAMP; Screening Tool for Risk of Impaired Nutritional Status and Growth-STRONG) were implemented on admission. Weight (WT), height and BC

measurements (lean (LM) and fat mass (FM) using dual Energy X-ray Absorptiometry) were obtained within 48 hours of admission and SD scores (SDS) calculated using UK BC reference data (Wells *et al*, 2012). Discharge WT, LOS and complications during stay were also recorded. Most patients were classified as moderate risk (MR) by STAMP and STRONG, and low risk (LR) by PYMS. As expected, a decreased appetite significantly increased the risk of being classified high risk (HR) by all MSTs (risk ratio (RR) 1.9, 1.7, 2.2 PYMS, STAMP and STRONG respectively), while dietary restrictions and artificial nutrition support were also predictors of HR using STRONG (RR 3.5, 2.7). Patients with mobility issues also had an increased risk using STAMP (RR 1.8). All MSTs showed a significant association with LOS, with a high proportion of HR patients staying longer than predicted and having an increased risk compared to MR and LR patients. Although HR patients had a tendency for higher complication rates, this was not significantly different for any of the MSTs. A decreased weight during hospitalization as marker for worsening NS was found in 43% of HR patients by PYMS, but was not significant for the other tools. In comparison, low WT or BC scores (<-2 SDS) on admission indicated a significantly increased risk for longer than predicted stays and, particularly in the case of low LM, increased complications and worsening NS.

In summary, children had a high risk of malnutrition on admission, with proportions varying according to the MST used. All MSTs had significant associations with LOS and, in the case of PYMS, for worsening NS during hospitalization. Baseline BC, particularly low LM, was better able to predict complications and worsening NS in addition to increased LOS. The different MSTs seem to show strengths and limitations, as compared to BC/WT measurements, that suggest further validation in different settings with specific clinical outcomes might be necessary.

1187 NUTRITIONAL REGULATION OF FIBROBLAST GROWTH FACTOR 19 SECRETION IN NEONATES

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Background: The fibroblast growth factor 19 (FGF19) hormone is secreted mainly by the terminal ileum and its primary function is to control the hepatic biosynthesis of bile acids and regulation of glucose and lipid metabolism. Animal and adult human studies have shown that circulating FGF19 concentrations are low in the fasting state and increase in response to enteral feedings. Nutritional regulation of FGF19 secretion has not been evaluated in pre-term and term infants.

Objective: The objective of this study was to compare serum FGF19 concentrations in pre-term, late pre-term, and term infants at birth and after full enteral feedings have been established (≥ 80 ml/kg/d). We hypothesized that serum FGF19 concentrations are low at birth and increase after enteral feedings have been achieved.

Methods: Using enzyme-linked immunosorbent assay, plasma FGF19 concentrations were quantified in prospectively enrolled term (n=6), late pre-term (n=4), and pre-term (n=9) AGA infants. FGF19 concentrations were measured at birth while infants were NPO, and on a weekly basis until full enteral feeds had been achieved. Serum FGF19 levels were also measured in a cohort of 5 healthy fasting adult volunteers. Data were analyzed using one-way ANOVA, Newman Keuls post-test on GraphPad Prism (V5). Statistical significance was set at $p < 0.05$.

Results: Compared to adults (132.5 ± 15.2 pg ml⁻¹), FGF19 concentrations (mean \pm SE) were significantly lower in term and late pre-term infants at birth (47.9 ± 7.5 pg ml⁻¹ and 53.1 ± 20.7 pg ml⁻¹, respectively). FGF19 concentrations were comparable between adults and pre-term infants at birth (98.1 ± 18.1 pg ml⁻¹). FGF19 concentrations remained low in term (45.3 ± 20.9 pg ml⁻¹) and late pre-term (22.3 ± 5.4 pg ml⁻¹) infants receiving full enteral feeds on day of life (DOL) 7. FGF19 concentrations significantly decreased over time in pre-term infants (22.9 ± 17.7 pg ml⁻¹ on DOL 14 and 16.9 ± 2.2 pg ml⁻¹ on DOL 28).

Conclusions: In this study, we have shown that in term and late pre-term infants, FGF19 concentrations are low at birth and remain low after establishment of full enteral feeds, suggesting that the neonatal gut requires postnatal development beyond the first few weeks of life to achieve a mature function. In contrast, pre-term infants have adult-like FGF19 concentrations at birth that significantly decrease with increasing postnatal age and volume of enteral feeds. These results suggest that newborns may have increased susceptibility to liver disease as FGF19 prevents and protects against cholestasis.

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*1188 IMPROVED PULMONARY FUNCTION AND WEIGHT GAIN, REDUCED RESTING ENERGY EXPENDITURE, AND IMPROVED GUT INFLAMMATION AFTER 3-MONTH IVACAFTOR TREATMENT IN CYSTIC FIBROSIS

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Background: Ivacaftor potentiates the cystic fibrosis transmembrane conductance regulator (CFTR) channel in patients with cystic fibrosis (CF) with gating mutations. It has been shown to improve weight and pulmonary function and decrease sweat chloride concentration in subjects with CF. The mechanism of weight gain is not clear.

Objectives: To determine the outcomes associated with weight gain and improved pulmonary function in subjects with CF with gating mutations following 3 months of treatment with Ivacaftor.

Methods: Subjects with at least one CFTR gating mutation who were 5 years or older were recruited from the United States, Canada, and Italy. Study visits were conducted at baseline and after 3 months of Ivacaftor treatment. Height, weight, and BMI were measured and Z-scores were calculated for subjects <20 years of age. Forced expiratory volume at 1 second percent predicted value (FEV₁) was assessed with spirometry. Fat mass (FM), fat free mass (FFM), and percent body fat (% fat) were determined by dual x-ray absorptiometry (DXA). Resting energy expenditure (REE) was determined by indirect calorimetry after an overnight fast and expressed as a percent predicted (Schofield equation, REE%). Total energy expenditure (TEE) was determined by the doubly labeled water method using isotopes of deuterium and oxygen-18. Fecal elastase (μ g/g stool) and calprotectin (μ g/g stool) were assessed from a spot sample to evaluate pancreatic exocrine function and gut inflammation, respectively.

Results: 23 subjects completed the study (17 ± 13 y, 61% female, 74% pancreatic insufficient). Study subjects had 19 different genotypes. Following 3-months treatment with Ivacaftor, subjects had significant increases in FEV₁, weight, height, BMI, FM, FFM, and % fat (Table 1). In subjects < 20 years (n=18), weight Z-score and BMI Z-score both increased significantly (+0.20 and +0.29, respectively, $p < 0.01$). Calprotectin and REE significantly decreased (Table 1). There was no significant change in TEE. The change in weight after 3 months of

Ivacaftor treatment was positively correlated with a change in FEV1 (r 0.46, $p=.028$) and negatively correlated with a change in REE% (r 0.50, $p=0.017$). The change in FEV1% was positively correlated the change in weight and BMI (r 0.41, $p=.05$) and negatively correlated with a change in calprotectin (r -0.49, $p=0.02$) and REE (r -0.64, $p=.001$).

Conclusions: 3 months of Ivacaftor treatment resulted in improved pulmonary function, weight, BMI, muscle mass, percent body fat, and reduced REE and gut inflammation in subjects with CF and gating mutations. Increases in both FM and FFM played a role in weight gain. An improvement in pulmonary function correlated with a reduction in REE, improved gut inflammation, and improved weight.

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	FEV ₁ , % predicted	Weight, kg	Height, cm	BMI, kg/m ²	FM, kg	FFM, kg	% Fat	REE %	Calprotectin, µg/g stool
Baseline	85.5	44.1	149.5	18.9	13.9	30.4	30.8	95.6	77.6
3 Months	95	46.6	150.9	19.6	15.5	31.3	32.5	90.1	47.3
Change	9.5***	2.5***	1.4***	0.7***	1.6**	0.9*	1.7***	-5.5*	-30.3**

Table 1. Change in Outcomes after 3 months of Ivacaftor Treatment, (* Change significant $p<0.05$, ** $p<0.01$, *** $p<0.001$)

1189 CLINICAL PREDICTORS OF ACTIONABLE HISTOLOGIC ABNORMALITY ON UPPER ENDOSCOPY FOR AN INDICATION OF FAILURE TO THRIVE

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Objectives: Failure to thrive (FTT) is a common indication for upper endoscopy (EGD) in young children. We characterized a cohort of children who underwent EGD for an indication of FTT and examined clinical predictors of abnormal EGD biopsy histology.

Methods: We performed a retrospective cross-sectional study among all children ages 0 to 36 months who underwent EGD for a provider-determined indication of FTT from January 1, 2009 through December 31, 2014. The outcome of interest was presence of actionable histologic abnormality (AHA), defined as findings that could change management. Logistic regression was used to identify independent predictors of AHA.

Results: A total of 667 EGDs were performed and 111 (16.6%) identified AHA. The most common actionable findings were esophageal eosinophilia and non-specific esophagitis. Predictor variables retained in the final model were the symptoms of vomiting (adjusted odds ratio [aOR] 2.00, 95% CI, 1.18-3.39) and diarrhea (aOR 2.66, 1.41-5.00), serum absolute eosinophil count > 500 (aOR 4.47, 2.52-7.92), and proton pump inhibitor (PPI) use at the time of EGD (aOR 0.54, 0.31-0.93). The c-statistic was 0.71. Growth parameters were not found to be independent predictors of AHA. Patients on PPI with none of the other predictors had a 6.7% probability of AHA; 75.5% of patients not taking PPI therapy with all three predictors (vomiting, diarrhea, eosinophilia) had AHA.

Conclusions: Symptoms, medication history, and laboratory findings, but not growth parameters, can be used to predict the probability of clinically important findings on EGD in children with FTT.

1190 STOOL MICROBIOTA IN TERM INFANTS FED FORMULA SUPPLEMENTED WITH SYNTHETIC HUMAN MILK OLIGOSACCHARIDES IS ASSOCIATED WITH REDUCED LIKELIHOOD OF MEDICATION

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Background and Aims: HMOs may provide health benefits to infants partly by shaping the development of the intestinal microbiota. We explored stool microbiota in relation to reported morbidity and medication use in infants fed formula supplemented with 2 HMOs.

Methods: Healthy term infants <14 days old were randomly assigned to infant formula (Control) or the same formula with 1.0 g/L 2'-Fucosyllactose and 0.5 g/L Lacto-N-neotetraose (Test) from enrolment to 6 months; all infants received the same follow-up formula without HMOs from 6-12 months. Breastfed infants (BF) served as a reference group. Stool microbiota was analyzed by 16S rDNA sequencing.

Microbiota community types were established by Dirichlet multinomial mixture model. Their associations with formula supplementation and with reported morbidities identified a priori and medication use through 12 months were analyzed using X²-tests.

Results: At 3 months, microbiota composition in the Test group (n=58) appeared closer to BF (n=35) than control (n=62) by microbiota alpha (within group) and beta (between groups) diversity analyses, and distribution of microbiota community types (A, B, or C). HMOs supplementation decreased number of infants with formula specific C-community and increased those with BF specific B-community. Likelihood of cumulative reported antibiotic use through 12 months was increased in infants harboring the C-community and decreased in babies with the B-community.

Conclusions: Infant formula with HMOs shifted microbiota towards that of breastfed infants. Previously reported reduced likelihood of medication use with HMOs may thus be linked to gut microbiota community types.

PANCREATOLOGY

1198 THE ROLE OF THE GENETIC FACTORS AND PANCREATICOBILIARY MALJUNCTION IN THE RECURRENT ACUTE PANCREATITIS

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Recurrent acute pancreatitis (RAP) is defined as at least two distinct episodes of acute pancreatitis. Some causes of RAP appear to be associated with alterations in the SPINK1, PRSS1 and CFTR genes or with pancreaticobiliary maljunction (PBM). PBM is a congenital anomaly defined as a junction of the pancreatic-biliary ducts located outside the duodenal wall and reflux of bile into the pancreatic duct occurs. A common

pancreaticobiliary channel (CPBC) more than 15 mm in length is considered abnormal in adults and CPBC more than 5 mm in length was defined high confluence pancreaticobiliary maljunction (HCPBM). However, there are no data on the normal length of the CPBC in children. A length of 5 mm was used as the upper limit of "normal" for the CPBC in pediatric studies by Fitoz *et al.* The CPBC more than 10 mm in length is considered as long common channel (LCC) in children. HCPBM was defined as CPBC at ≥ 5 mm in children by Guo *et al.*

Methods: Between 2012-2015, 14 patients followed with ARP were enrolled in the study. PRSS1, SPINK1 and CFTR genes were analyzed by DNA sequencing. The length of the CPBC was assessed by an experienced radiologist via MRCP. LCC and HCPBM were defined as the length of CPBC at ≥ 10 mm and ≥ 5 mm respectively. Genetic analysis were compared with the imaging findings. The other causes of RAP (infection, medication, metabolic disorders) were ruled out.

Results: We detected PRSS1 compound heterozygous mutation in 5 patients and CFTR compound heterozygous mutation in 3 of 14 patients. One of the patients had both CFTR heterozygous mutation and PRSS1 heterozygous mutation. Two patients had CFTR heterozygous mutation. There was any mutation in 3 patients. There was family history in 5 patients. The measurement of CPBC was done in 12 patients via MRCP and we found CPBC ≥ 10 mm in 3 patients. In 8 of 12 patients CPBC were between the range of 5-10 mm. But, MRCP examination was unsuccessful in 2 patients, because of technical problems. The 2 of 5 patients who we have identified PRSS1 compound heterozygous mutation had LCC and 3 patients had HCPBM. Additionally, we detected HCPBM in 3 patients with CFTR compound heterozygous mutation. In brief, we identified compound heterozygous mutation in 8 of 14 patients with ARP and all of these 8 patient had PBM.

Conclusions: PBM and genetic factors are a well-known cause of acute recurrent pancreatitis. But, it is unusual to observe both genetic alteration and structural anomaly. Bertin *et al* have found pancreas divisum in almost half of patients with genetic mutations (CFTR) and pancreatitis. They have expressed that pancreas divisum synergizes with genetic mutations to cause ARP (7). Rho *et al* have reported 2 cases with PBM and SPINK1 mutation. We detected PBM in all patients with compound heterozygous mutation in the PRSS1/CFTR genes. To the best of our knowledge an anomalous junction of the pancreatic and biliary ducts may be a contributing factor to recurrence of pancreatitis in hereditary pancreatitis.

1199 ETIOLOGY OF CHRONIC PANCREATITIS IN CHILDREN: A SINGLE-CENTER EXPERIENCE

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Introduction: Chronic pancreatitis (CP) is of a rare occurrence in childhood. The etiology of CP in children is varied and includes anatomic anomalies, gene mutations, metabolic disorders and others. The aim of this study was to investigate the etiological aspects of CP in children from well-defined homogeneous single-center cohort.

Methods: 313 children with CP (aged: 0.6-18 years; mean 8.8; F-171, M-140) hospitalized between 1988 and 2016 were enrolled into the study. Clinical and epidemiological data were recorded and analyzed. All patients were screened for gene mutations predisposing to CP. All children had preceding imaging studies, including US, CT, MRCP and/or ERCP.

Results: Gene mutations were found in 194 children (61%) (PRSS1 mutation in 42 children, CFTR in 46 patients, SPINK1 in 76 children, CTSC in 78 patients, CPA1 in 2 children). Anatomic anomalies of pancreatic duct were diagnosed in 51 patients (16%) (31-pancreas divisum, 10-ansa pancreatica, 4-ABPU, 2-two main pancreatic ducts, 4-other). Toxic-metabolic risk factors were found in 41 patients (13%), with dominance of lipid disturbances (21 children). CP was associated with biliary tract diseases in 26 patients (8.3%). Autoimmune pancreatitis was diagnosed in 6 children (1.9%). History of trauma was present in 20 cases (6.4%). Idiopathic CP was diagnosed in 50 children (16%).

Conclusions: Gene mutations and anatomic anomalies of pancreatic duct are the most common etiologic factors of CP in children. Our data demonstrate the need for genetic testing in children with CP.

1200 CONTINUOUS GLUCOSE MONITORING FOLLOWING PANCREATECTOMY WITH ISLET AUTOTRANSPLANTATION

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Background: Total pancreatectomy (TP) with islet autotransplantation (IAT) is offered to patients with chronic pancreatitis and incapacitating pain or debilitating acute recurrent pancreatitis that is not amenable to medical or endoscopic therapies. IAT is performed with the goal of preventing the development of brittle diabetes following TP. In the early post-operative period, hyperglycemia is detrimental to the autotransplanted islets and can reduce the chance of achieving insulin independence. Therefore, strict glycemic control is critical, especially early in the post-operative course.

Objective: To determine if a continuous glucose monitoring (CGM) device can monitor blood glucose (BG) trends in an accurate fashion during the initial post-operative period following pancreatectomy and IAT in pediatric patients.

Methods: Between April 2015 and March 2016, 5 patients underwent TPIAT and one patient underwent subtotal pancreatectomy with IAT at our institution. Post-operatively, as part of an intense glucose monitoring protocol, patients used a CGM device (Dexcom G4 Platinum, Dexcom, Inc., San Diego, CA) to monitor BG trends. The CGM device was used as a comparative tool between serum glucose and point of care (POC) glucose results, but was not used for clinical decision-making. After IRB approval, a retrospective chart review of serum glucose, POC glucose and CGM data from the duration of their Intensive Care Unit (ICU) stay was performed. Mean absolute difference (MAD) and mean absolute relative difference (MARD) were calculated between CGM data and serum glucoses, and between POC glucoses and serum glucoses.

Results: A total of 61 time-matched measures by all 3 monitoring methods were found. From these measures, 66% of the CGM readings were within 15 mg/dL and 54% were within 10 mg/dL when compared to serum glucose values (12.7% false positive readings). The MAD and MARD comparing CGM readings and serum glucose were 15.4 mg/dL and 13.4%, respectively. For POC glucose values, 93% were within 15 mg/dL and 90% were within 10 mg/dL of serum glucose values (0% false positive readings). The MAD and MARD comparing POC glucose and serum glucose were 5.9 mg/dL and 5.0%, respectively. Serum glucose did not differ significantly from CGM readings (p 0.15) or from POC glucose values (p 0.39).

Conclusion: The CGM device was found to be a reliable tool in monitoring trends in blood glucose values in the post-operative IAT patients in an ICU setting. Future studies are needed to validate the use of CGM in the care and outcomes of patients that undergo pancreatotomy with islet autotransplantation.

1201 NASOGASTRIC OR NASOJEJUNAL TUBE FEEDING IN PEDIATRIC ACUTE PANCREATITIS: A CLINICAL RANDOMIZED STUDY

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Objectives and study: Recent clinical studies have shown that nasogastric tube feeding is safe in the majority of adult patients with acute pancreatitis. But the safety and efficiency of nasogastric tube feeding in pediatric acute pancreatitis has not been investigated. This study aims to compare the safety and efficiency between nasogastric feeding and nasojejunal feeding in children with acute pancreatitis.

Methods: The study design was a randomized controlled trial. Children with acute pancreatitis were fed via NG (candidate) or NJ (comparative) route within 72 hours after admission. The primary outcome was tolerance of enteral nutrition support. Secondary endpoints were duration of hospital stay, duration of tube feeding, occurrence of any complication (tube-associated, infections, feeding-associated).

Results: A total of 33 children with acute pancreatitis were recruited into this study and were randomized to NG group (16) or NJ group (17).

Age, gender, pediatric acute pancreatitis scores, CTSI scores and gastrointestinal symptoms or abdominal pain did not significantly differ between the two groups. 81% (13/16) of NG group and 94% (16/17) of NJ group can tolerate with tube feeding ($p>0.05$). The duration of hospital stay was 18.9 ± 4.7 d for NG group and 18.3 ± 6.3 d for NJ group. For duration of tube feeding were 16.8 ± 7.4 d and 15.8 ± 4.4 d separately. One child of NJ group has tube-associated complication. 5 patients of NJ group and 2 of NG group have feeding-associated complications such as diarrhea, vomit and abdominal pain. None of all patients has complication of any infection.

Conclusion: NG tube feeding appears effective and safe for acute pediatric pancreatitis comparing with NJ tube feeding. Before recommendation to clinical practice, further high qualified, large scale, randomized controlled trials are needed.

1202 RISK FACTORS FOR ASPARAGINASE-ASSOCIATED PANCREATITIS: A SYSTEMATIC REVIEW

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Background: Acute pancreatitis is a life-threatening disease that causes the hospitalization of more than 275,000 Americans each year. Drug-induced pancreatitis contributes to a sizeable portion of the disease burden, particularly in children; however, the mechanism of action is poorly understood. Among the most frequent offenders of drug-induced pancreatitis is the chemotherapeutic agent called asparaginase. Since the 1960s, asparaginase has been a mainstay of treatment in cancer protocols for acute lymphoblastic leukemia (ALL) and some types of non-hodgkin's lymphoma. The purpose of this systematic review is to identify potential risk factors for developing asparaginase-associated pancreatitis.

Significance: The significance of this study is to identify risk factors for patients at high risk for developing pancreatitis while using asparaginase. As ALL is the most common childhood cancer, this work could lead to further clinical studies that address these risk factors and potentially prevent the large burden of disease due to drug-induced pancreatitis, specifically asparaginase-associated pancreatitis.

Methods: We conducted a systematic review of published articles written or translated in English from 1926 to June 2015 on risk factors for asparaginase-associated pancreatitis. The searched databases included PubMed, EMBASE, CDSR, gray literature and the US FDA database. Data extraction was based on pre-defined outcome measures. A meta-analysis was not performed due to the small number of articles that fit our inclusion/exclusion criteria.

Results: Across the 10 articles reviewed, only age, ALL risk stratification, and asparaginase formulation could predict some level of risk, albeit modest, of developing pancreatitis with asparaginase. Patients older than 10 years had about a 2.4 fold increased risk in two studies but there were no significant differences identified in three other studies that examined age. High risk ALL patients had a higher frequency of pancreatitis identified in only two studies, but this was independent of asparaginase cumulative dose or frequency of administration. One study identified a statistically significant increase in the incidence of asparaginase-associated pancreatitis when using PEG-asparaginase.

Conclusion: The literature fails to clearly identify from demographic, as well as treatment regimens, any major distinguishing risk factors for developing asparaginase-associated pancreatitis. Both the quantity and quality of available studies are low; thus more rigorous basic science and clinical research is warranted.

Keywords: asparaginase, pancreatitis, acute lymphoblastic leukemia

1203 BURDEN OF PEDIATRIC ACUTE PANCREATITIS ON THE HEALTHCARE SYSTEM

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Objective: The incidence of acute pancreatitis (AP) in children has increased over the past two decades and is estimated to be between 3-13/100,000 annually. The impact of rising AP incidence on the healthcare costs is unknown. The aim of this study was to examine the burden of AP on the healthcare system relative to all other pediatric admissions and trends over the past decade.

Design/Methods: Admission and cost data of patients with the diagnosis of AP for Cincinnati Children's Hospital Medical Center (CCHMC) was extracted from the Pediatric Health Information System (PHIS) from 2004-2014. PHIS is a comprehensive database that contains clinical and financial data from 45 pediatric hospitals across the United States allowing the opportunity to study the impact of AP on the healthcare system. We determined the percentage of all admissions each year for AP. The cost for AP admissions was compared to the overall cost of all admissions to CCHMC to calculate the cost percentage of AP. We also examined the median length of stay (LOS) and daily cost for AP annually from 2004-2014 and the effect of Intensive Care Unit (ICU) admissions on these estimates.

Results: Between 2004-2014 there were 1,210 admissions to CCHMC with a diagnosis of AP of which 623 had a primary diagnosis of AP. The number of new cases with a primary diagnosis of AP significantly increased ($p=0.001$) during this time, from 24 cases in 2004 to 42 cases in 2014. Primary AP admissions ranged from 30 to 89 per year and constituted 0.07-0.17% of all hospital admissions. The percentage of admissions for AP significantly increased over this time period ($p<0.0001$). The percentage of costs for AP relative to all admissions ranged from 0.16-0.41%. The AP cost percentage was between 1.5 to 3.7 times higher than the AP admission percentage. Overall, the median LOS for

AP admissions was 4.0 days and cost per day was \$3149, however these differed if there was an ICU admission. ICU was part of the admission for AP 2-15% of the cases each year. The median LOS for those with an ICU admission was significantly higher compared to those without (11.0 vs. 3.0 days, $p < 0.0001$). The median cost per day for those with an ICU admission also was significantly higher than those without (\$4011 vs. \$3007, $p < 0.0001$).

Conclusions: AP admissions constitute an expensive burden on the healthcare system relative to the percentage of admissions that they comprise each year. If AP admissions continue to increase, the cost of AP admissions may pose a substantial financial burden on the healthcare system.

1204 ACUTE PANCREATITIS IN CHILDREN: SPECTRUM OF DISEASE AND PREDICTORS OF SEVERITY

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Background: Acute pancreatitis (AP) has an estimated incidence of 3.6-13.2 cases/100000 children. Optimal predictors of severity at admission are lacking. Scores like DeBanto, Ranson, modified Glasgow and the Ministry of Health, Labour and Welfare of Japan scoring systems try to find correlations with severity.

Aim: To describe the clinical presentation, etiology, complications of pancreatitis in children and to determine predictors of severity.

Methods: Retrospective study of cases of acute pancreatitis in children between 2002 and 2015. Patients were identified by searching the hospital's electronic discharge records for the International Classification of Disease, Ninth Revision (ICD-9) code 577.0 (acute pancreatitis). Acute recurrent pancreatitis (ARP) was considered as two or more episodes of with intervening return to baseline. We analyzed: demographic information, clinical, laboratory and imaging test results, etiology of pancreatitis, medical and surgical management, length of hospitalization, and outcome. Analytical and imaging data were tested for predictors of severity according to the Atlanta criteria.

Results: We identified 53 episodes of pancreatitis in children, 42 patients, 35 with AP, 7 with ARP. One patient with 4 episodes. The predominance were males 62.2%, median age 14 years (minimum 2, maximum 17 years). Five of the patients had a family history of pancreatitis. The most common early symptom was abdominal pain (91.3%) referred to the epigastrium in 48.9% of cases, followed by nausea and vomiting (51.1%). The most common etiology was lithiasic (n=11, 21.1%), followed by idiopathic (n=10, 19.2%) and trauma (n=9, 17.3%). It conducted a genetic study in 5 patients and has been identified two cases of cystic fibrosis. One patient had pancreas divisum and one pancreatic tumor. All patients performed imaging, showing edematous pancreatitis in 25 cases (51%) and necrotizing in 3 cases (6.1%). Parenteral nutrition was instituted 22 patients (41.5%) median of 7.5 days (minimum 3, maximum 90 days).

According to the Atlanta criteria, occurred mild pancreatitis in 73.5% (n=36), moderate in 24.5% (n=12) and severe disease in one case. There were no deaths in either case. The total value of leukocytes at admission correlated with disease severity ($p = 0.047$) as well as C-reactive protein (CRP) ($p = 0.021$) and presence of systemic inflammatory response syndrome (SIRS) ($p = 0.003$). Traumatic etiology ($p = 0.006$) is related to the severity of the disease.

Conclusions: Pancreatitis presented a wide spectrum of etiology and remains idiopathic in 19% of the cases, less than expected, 33%. The amount of leukocytes, presence of SIRS and traumatic etiology also significantly predict the severity of the disease in these cohort. CRP as a marker of severity, although it is not a criteria in most of scoring systems, show to be a single, not expensive and quite interesting of predictor of severity.

1205 HOW DO IV FLUIDS AFFECT HOSPITAL COURSE IN CHILDREN WITH ACUTE IDIOPATHIC PANCREATITIS?

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Background: Acute Idiopathic Pancreatitis (AIP) is diagnosed when no identifiable etiology can be detected after thorough clinical evaluation, extensive diagnostic tests, and noninvasive imaging. Occurrence of AIP has been reported to be as high as 40% among adult patients with Acute Pancreatitis (AP). To our knowledge, pediatric literature appears to be lacking studies on AIP, including its management and outcome.

Objective: To study the role of Intravenous fluid (IVF) types and administration rates and hospital outcomes among children with AIP, as measured by hospital length of stay (LOS) and complications.

Methods: A cross-sectional observational study, of patients (n=138) between 0-18 years of age, admitted to Children's Hospital of Michigan (CHM), with a diagnosis of AIP, between January 2010 and December 2015 was undertaken. All patients with mild, moderate, and severe AIP were included. Excluded patients were those with diagnosis of recurrent or chronic pancreatitis, and patients discharged from Emergency Department or outpatient clinic. Data on demographics, presentation features, diagnostic imaging, types and rates of IV fluid administered, and etiology of AP were collected. 138 AIP patients were studied for impact of different IVF types and rates on hospital outcomes of LOS and complications. For comprehensive understanding of IVF management implications on hospital outcomes, these 138 AIP patients were also compared with 120 NIAP patients. Statistical analysis (SPSS 21.0) included Chi-square, t-tests, and Cross Tabulation to examine proportional differences between three categorically scaled variables.

Results: More patients admitted with AIP (58%) had received 1x maintenance rate compared to patients that received 1.5x maintenance rate (42%). More patients with AIP that received fluids at 1.5x maintenance rate had a shorter hospital LOS of ≤ 3 days (59%), compared to those who had received 1x maintenance rate (49%). In this study, AIP patients had decreased rates of complications (5%) during hospitalization compared to NIAP patients (20%). AIP patients that had received 1.5x maintenance rate had lower incidence of complications (22%) compared to those that had received 1x maintenance rate (78%). In regards to IV fluids, higher rate of complications (8%) was noted in AIP patients that had received D5 0.45 NS. However, higher rates of complications (44%) were noted in NIAP patients that had received NS.

Conclusions: Due to the lack of management guidelines of AIP in children, there is no standard rate of fluid resuscitation that is followed at our institution. Our data suggests that aggressive fluid resuscitation correlates with shorter LOS and decreased rate of complications during hospital stay. In this study, no statistically significant difference was found among varying types of IVF related to better outcomes.

1206 GENETIC ANALYSIS IN JAPANESE CHILDREN WITH ACUTE RECURRENT AND CHRONIC PANCREATITIS

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Background: In children with acute recurrent pancreatitis (ARP) and chronic pancreatitis (CP), the cause of the pancreatitis is sometimes difficult to determine. In such patients, genetic analysis may be helpful. Recent reports have demonstrated a high prevalence of genetic mutations among pediatric patients with pancreatitis, the relationship between these mutations and their clinical features are not clear. The aim of this study was to analyze mutations in the protease serine 1 (PRSS1), serine protease inhibitor Kazal type1 (SPINK1), chymotrypsin C (CTRC), and carboxypeptidase A1 (CPA1) genes in Japanese children with ARP or CP, and to clarify the clinical features of these children. Methods: We analyzed the patients who had a diagnosis of ARP and CP in INSPPIRE criteria. Participants comprised 128 patients (50 girls, 78 boys), all of whom were under 16 years old. DNA samples were extracted for analysis from their peripheral blood leukocytes. We performed polymerase chain reaction (PCR). Genetic analysis of mutations in 4 genes (PRSS1, SPINK1, CTRC and CPA1) was conducted. Clinical information (age at onset; concomitant pancreatic or biliary disorders; family history of pancreatitis; underlying disease; treatment and prognosis) were retrospectively reviewed from their medical records of the patients.

Results: Fifty of the 128 (39.1%) subjects had at least 1 mutation (median age at first onset, 7.6 years). One hundred twenty-three patients (96%) had abdominal pain at the first onset of pancreatitis. Fifteen of those 50 (30.0%) patients had a family history of pancreatitis. Seventy-eight (60.9%) patients had no mutations. Twenty-six patients had gene mutations in PRSS1, 23 in SPINK1, 3 in CTRC, and 5 in CPA 1, respectively. In the 31 patients with mutations in SPINK1, CTRC, and CPA1, 16 (51.6%) had homozygous or heterozygous mutations with the other mutations. Pancreatitis occurred in patients having PRSS1: R122R/H without underlying disease. In contrast, 4/7 patients with a SPINK1 heterogeneous mutation had underlying disease. Three patients underwent surgery and another 4 patients underwent endoscopy to manage their ARP or CP. None of those 7 patients had any episode of ARP after treatment.

Conclusions: The patients with the R122R/H mutation of the PRSS1 gene occur pancreatitis without a merger of another gene mutations nor anatomic abnormalities, therefore the R122R/H mutation induces pancreatitis. Other mutations might be risk factors for pancreatitis together with additional mutations or factors for the development of pancreatitis. In pediatric patients with ARP and CP, genetic analysis is useful for identifying the cause and possibly improves the prognosis in this population.

Saturday, October 8, 2016

CONCURRENT SESSION VII 4:00 PM

PANCREATIC INSUFFICIENCY / CYSTIC FIBROSIS / PANCREATITIS

1207 TARGETED INHIBITION OF PANCREATIC ACINAR CELL CALCINEURIN IS A NOVEL STRATEGY TO PREVENT POST-ERCP PANCREATITIS

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Acute pancreatitis is the most common and burdensome iatrogenic complication of endoscopic retrograde cholangiopancreatography (ERCP). There is a crucial need to develop effective prophylactic therapies for post-ERCP-pancreatitis (PEP). In recent work, we described for the first time, that early PEP events are regulated by the calcium-activated phosphatase calcineurin (Cn) and that global Cn deletion abolishes PEP in mice. However, it is unclear whether pancreatic acinar cell Cn controls the initiation of PEP *in vivo*. In this study, we used two complementary genetic approaches to selectively delete the critical regulatory subunit B1 (CnB1) in pancreatic acinar cells. Firstly, we crossed a mouse line containing floxed alleles for CnB1 with a tamoxifen-inducible Cre line driven by an acinar cell specific elastase promoter. PEP was induced by retrograde pancreatic ductal infusion of normal saline at 10 μ L/min for 5 min (ductal manipulated, DM) or radiocontrast infusion at 20 μ L/min for 5 min (PEP). We demonstrated that pancreatic injury was reduced by 75% in CnB1 deficient mice (CnB1 Δ/Δ) receiving PEP. Secondly, we used a novel approach of intraductal adeno-associated virus (AAV) gene transfer to delete acinar cell calcineurin. The AAV contained an elastase-driven iCre (AAV6-Ela-iCre) and was infused into a CnB1 floxed mouse (CnB1f/f) line. AAV6-Ela-iCre infusion resulted in acinar cell-specific CnB1 deletion, and upon recovery from the intraductal procedure, pancreatic injury induced by PEP was reduced by 90% down to control levels. Finally, to examine the translational relevance of these findings, a single, acute intra-ductal application of the Cn inhibitors FK506 or cyclosporine (1-10 μ M) was given along with the radiocontrast infusion. This novel formulation largely reduced the severity of PEP by 61% and 37%, respectively with no adverse effects observed. These data confirmed that pancreatic acinar cell Cn plays a pivotal role in PEP, and provides the impetus for launching clinical trials to test the efficacy of a novel ERCP infusion formulation containing Cn inhibitors to prevent PEP.

1208 ZINC MEDIATES PANCREATITIS RESPONSES IN IN VITRO AND IN VIVO MOUSE MODELS OF ACUTE PANCREATITIS

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Background: Zinc is an essential trace mineral that plays important roles in growth and development, neurologic function, wound healing, reproduction and immunity. The manifestations of severe zinc deficiency in humans include changes in immunity and wound healing; zinc deficiency in mice and rats is associated with increased inflammation. Zinc supplementation has been shown to be beneficial in several conditions including acute diarrheal illness and pneumonia in children. Zinc is also a regulator of autophagy, a key cellular response in acute pancreatitis. We hypothesized that zinc treatment would decrease zymogen activation, a process that is associated with autophagy, in a mouse acinar cell model of acute pancreatitis. We also hypothesized that zinc deficiency in mice would worsen pancreatitis *in vivo*. Methods: For our *in vitro* studies, we isolated mouse pancreatic acini and pre-treated cells with either 0, 10 or 50 μ M of zinc chloride for 1 hour. We then induced acute pancreatitis with a pathologic dose (100 nM) of the secretagogue cerulein, a cholecystokinin orthologue. Zymogen

activation and amylase secretion were then measured. For our *in vivo* studies, we induced zinc deficiency by feeding mice a zinc-deficient (<1ppm) diet for three weeks. Control mice were fed a zinc-adequate (50 ppm) diet for three weeks. We then induced experimental pancreatitis with six hourly intraperitoneal injections of cerulein (40 µg/kg) and euthanized the mice 1 hour after the last injection. Zymogen activation, serum amylase and other markers of pancreatitis were then measured.

Results: *In vitro*, we found that zymogen activation was significantly decreased in acini pretreated with either zinc chloride 10 µM ($p<0.005$) or zinc chloride 50 µM ($p<0.0001$). The effect appeared to be concentration-dependent, with 50 µM zinc chloride showing a more significant decrease in activation than 10 µM zinc chloride. *In vivo*, zinc-deficient mice had significantly increased cerulein-stimulated zymogen activation ($p<0.05$) and increased serum amylase ($p=0.06$) compared to zinc-adequate mice. Zinc deficiency had no significant effect on pancreatitis-related edema.

Conclusion: Zinc supplementation in a cellular mouse model of acute pancreatitis appears to reduce zymogen activation, thereby conferring a protective effect in acute pancreatitis. *In vivo*, mice with zinc deficiency exhibited more severe pancreatitis than control mice. These findings may have therapeutic implications. Zinc supplementation may have protective effects in humans with acute or chronic pancreatitis – conditions for which current treatment in both adult and pediatric populations remains largely supportive.

Saturday, October 8, 2016

CONCURRENT SESSION VII

4:00 PM

CELIAC AND OTHER LUMINAL DISORDERS

1209 OBETICHOIC ACID REGULATION OF INTESTINAL MICROBIOTA COMPOSITION PROTECTS AGAINST CLOSTRIDIUM DIFFICILE INFECTION

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Background: Obeticholic acid (OCA) is currently receiving much attention as FDA-expedited therapy for diverse liver and intestinal diseases, including insulin resistance. The numerous clinical benefits attributed to this synthetic bile acid are generally thought to be mediated via its agonist action on the farnesoid X receptor (FXR), a key nuclear hormone regulator of metabolic and immune function. Symbiotic gut microbial activity is also emerging as a potent modulator of host metabolic and immune function. Whether OCA also mediates its health outcomes via FXR-independent targeting of the gut microbiome is not known. Here we examined the effects OCA on the intestinal microbial community compositional shifts by using toxigenic *Clostridium difficile* as a prototypical example.

Methods: Obeticholic acid (10-50 mg kg⁻¹ day⁻¹) was tested in an established mouse model of *C. difficile* infection using wild type C57bl/6 and FXR (-/-) genetically deficient strains. Microbiome analysis and stool bile acid levels were measured in all groups. *In vitro*, we assessed OCA minimum inhibitory concentration as well as the effect of OCA on spore germination of *C. difficile* VPI1640, 630 and clinical BI/027/NAP1 strains.

Results and Conclusions: Microbiome analysis indicated that OCA preferentially targeted the peptostreptococcae family, which includes *C. difficile*, in a mouse model of *C. difficile*. Infective colitis mortality and morbidity, as measured by weight loss and clinical health scores, were significantly improved in both wild-type and FXR- deficient mice treated with OCA. *In vitro* studies demonstrated inhibition of the CspC bile acid germinant receptor on *C. difficile* spores by OCA forms the basis of preventative therapy in both strains of mice. In summary, microbial-OCA interactions induce significant changes in the regulation of gut microbiota composition. This previously unappreciated finding provides a new conceptual framework to explore off-target clinical responses to this first-in-class therapeutic being developed for diverse diseases with expected future applicability to pediatric intestinal and hepatic disorders.

1210 ANTIBIOTIC EXPOSURE IN THE FIRST YEAR OF LIFE AND RISK OF CELIAC DISEASE: A NATIONAL REGISTER-BASED STUDY

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Background: Early environmental exposures contributing to the risk of celiac disease (CD) are still to be identified. The gut microbiota in the first year of life influences development of the immune system and has been suggested to play an important role in this respect. Antibiotic exposure is common in this period and has a crucial impact on the gut microbiota. Studies have suggested an association between antibiotic exposure in the first years of life and risk of celiac disease.

Methods: We included all children born in Norway during January 1, 2004 and December 31, 2012. Diagnosed CD was defined as two or more registrations of CD in the Norwegian Patient Register. Antibiotic exposure was defined as a dispensed prescription for a systemic antibiotic (J01) registered in the Norwegian Prescription Database before the age of one year. Antibiotics administered in hospitals were not available for this study. Neonatal exposure to antibiotics may be of particular importance for gut colonisation and cannot be evaluated in this study. After the neonatal period antibiotics are mainly administered outside hospitals, and most inpatient treatments continued after discharge and were thus included in this study. We categorized antibiotic exposure as any exposure (yes/no), number of courses (0, 1, 2, 3+), type (penicillin, extended spectrum penicillins, macrolides, and other systemic antibiotics), and timing of first exposure (0-3, 3-6, 6-9, and 9-12 months of age). We analyzed data with logistic regression adjusting for birth year because of different follow-up time. Furthermore, we adjusted for the potential confounders: gestational age, weight for gestational age, mode of delivery, season of birth, parity, maternal age and educational level.

Results: We included 512,412 children after exclusions for missing data (n=28,624). CD was registered for 1890 children (0.37%). A dispensed prescription for a systemic antibiotic in the first year of life was registered for 80,749 children without CD (15.8%) and 346 children with CD

(18.3%). Antibiotic exposure was associated with CD (aOR 1.28, 95% CI, 1.14-1.44). Regarding type of antibiotics, the strongest association was for 'other systemic antibiotics' (aOR 1.44, 95% CI, 1.07-1.94), then penicillin (aOR 1.24, 95% CI, 1.05-1.45), extended spectrum penicillin (aOR 1.16, 95% CI, 0.95-1.42), and macrolides (aOR 1.14, 95% CI, 0.93-1.39). We found no trend for number of antibiotic courses (a *p*-trend 0.89) or age at first exposure (a *p*-trend 0.14).

Discussion: In this large, national, register-based study, antibiotic exposure in the first year of life was associated with an increased risk of diagnosed CD. This finding supports the hypothesis that gut microbiota is important for development of CD.

1211 MODE OF DELIVERY AND RISK OF CELIAC DISEASE IN AT-FAMILY-RISK INFANTS PROSPECTIVELY INVESTIGATED FROM BIRTH: THE CELIPREV STUDY

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Objectives and Study: The relationship between the risk of celiac disease (CD) and the mode of delivery is unclear. To determine whether the mode of delivery is associated with the risk of CD in genetically predisposed children within the Risk of CD and Age at Gluten Introduction (CELIPREV) trial.

Methods: We recorded information by telephone interview on the mode of delivery of children participating the CELIPREV, a multicenter, prospective intervention trial that compared early and delayed introduction of gluten in infants with a familial risk of CD. 832 newborns with a first-degree relative with CD were enrolled. The HLA genotype was determined at 15 months of age, and serologic screening for CD was evaluated at 15, 24, and 36 months and at 5, 8, and 10 years. Patients with positive serologic findings underwent intestinal biopsies. The final study group included 553 children who were positive for HLA-DQ2, HLA-DQ8, or both. The primary outcome of the current study was the prevalence of CD autoimmunity and overt CD among the children at 5 years of age according to the mode of delivery. Secondary outcome was the interplay between the mode of delivery and nutritional and genetic variables studied (breast-feeding, age at gluten introduction, genotype, gender, CD-affected first-degree relative, intestinal infections) in influencing the risk of CD.

Results: We obtained data on the mode of delivery from 431 children of the 553 with a standard-risk or high-risk-HLA genotype. At 5 years of age, there was no difference between children born by cesarean or vaginal delivery for autoimmunity (24% and 19%, *p*=0.2) or overt disease (19% and 14%, *p*=0.2). None of the variables studied was associated with the development of CD, with the exception of HLA genotype: the risk of CD autoimmunity was higher among children with high-risk HLA than among those with standard-risk HLA (42% vs. 19%, *p* <0.001), as was the risk of overt CD (29% vs. 15%, *p*=0.02).

Conclusion: The mode of delivery did not modify the risk of CD. The HLA genotype is the only known risk factor for CD development.

1212 RE-EXPLORING THE ICEBERG OF CELIAC DISEASE IN CHILDREN: PRELIMINARY RESULTS OF A MULTICENTER ITALIAN SCREENING PROJECT BASED ON A RAPID HLA DQ TYPING TEST

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Background: Celiac disease (CD) is increasing in several countries and no recent epidemiological data are available for the Italian general pediatric population. The real contribution of typing the human leukocyte antigen (HLA) DQ2 and DQ8 for screening of CD is still uncertain.

Aim: To assess the prevalence of celiac disease (CD) autoimmunity and overt CD in school age children by using HLA typing as the initial screening test.

Methods: Students aged 5-10 years living in 2 different cities in Italy (Ancona and Verona) were invited to participate. A rapid, single PCR reaction HLA test (Celiac Gene Screen, Biodiagene Italy) on a single blood drop was used to identify subjects susceptible to CD. Serum anti-transglutaminase antibodies (TTG) and IgA were performed in HLA positive patients. Anti-endomysium (EMA) and anti deamidated gliadin peptides (DGP) antibodies were subsequently searched in TTG positive and IgA deficient patients respectively. CD was diagnosed according to the ESPGHAN guidelines. Children with CD diagnosed before the screening were included.

Results: 3800 subjects have been enrolled and HLA screened so far. The screening has been completed in 1089 patients with HLA results available for 1060 subjects. Four-hundred and thirty five patients were HLA positive (41%, 95% CI, 38-43.9) and 427 (98.1% of the screened population) underwent the serological evaluation. CD autoimmunity was found in 20 patients with 10 receiving a diagnosis of CD (0.94%, 95% CI, 0.36-1.52). According to the ESPGHAN criteria 5 subjects required biopsy for further confirmation (2 for lack of symptoms and 3 for low titer antibodies). Previously diagnosed CD was found in 6 children (0.55%, 95% CI, 0.11-0.98) with a total prevalence of CD in the screened cohort of 1.46% (95% CI, 0.75-2.17) and a female to male ratio of 1.8 to 1.

Conclusions: CD prevalence of 1.46% is higher than the previously reported data in Italian age school children (0.54%). Based purely on a clinical indication or using a screening strategy evaluating only patients at risk, there are still 2/3 of CD cases remaining undiagnosed.

Considering its high sensitivity and feasibility, the rapid HLA test would be an appropriate test for screening CD in the general population.

Saturday, October 8, 2016

**CONCURRENT SESSION VII
4:00 PM**

ENDOSCOPY / IMAGING

1213 SMALLER PATIENT SIZE IS ASSOCIATED WITH TECHNICAL FAILURE IN PEDIATRIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY: A PROSPECTIVE MULTICENTER STUDY

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Introduction: There are no prospective or multicenter studies evaluating technical outcomes in pediatric ERCP.

Aim: To report technical outcomes in pediatric ERCPs utilizing a prospective multicenter approach.

Methods: Consecutive ERCPs on children <19 years from 13 IRB approved centers were entered into a REDCap database. Inclusion criteria for analysis included: ERCPs entered between 5/1/2014 to 4/27/2016, all data collection forms completed and the pre-procedural form completed prospectively. Technical success was defined by the endoscopist as meeting the diagnostic or therapeutic goal during the course of the procedure. Adverse events (AE) and procedural difficulty grade were defined using ASGE criteria. Fischer's exact test was utilized to identify factors associated with technical failure.

Results: 412 ERCPs met inclusion criteria and were analyzed. These were performed in 325 unique patients (79%), of whom 251 (61%) were female, 171 (42%) were Hispanic, and 289 (70%) had a native papilla. 386 (94%) were performed independently by a pediatric GI. 373 (91%) were performed for a therapeutic indication, 313 (76%) for a biliary indication, 108 (26%) for a pancreatic indication. Mean age was 12.1 yrs (IQR 9.1-15.6) and mean weight was 50.2 kg (IQR 28.8-66.3). ERCP was technically successful in 382 (93%) cases. When attempted, successful cannulation occurred as follows: bile duct 94% (327/347), pancreatic duct 91% (106/117), minor papilla 70% (16/23). Inadvertent pancreatic duct cannulation occurred in 58/295 (20%) cases and unintentional pancreatogram occurred in 26/285 (9%). On univariate analysis the following were associated with a failed procedure: ASGE difficulty grade>3 ($p<0.0001$), weight <15 kg ($p<0.0005$), age<3 yrs ($p<0.005$), presence of a native papilla ($p<0.05$), and prior failed cannulation ($p<0.05$). There was no association between technical failure and demographic factors, ASA class, pancreatitis at time of procedure, trainee involvement, or performing center. AEs occurred in 39 (9%) and included post-ERCP pancreatitis (PEP) in 19 (5%, 15 mild, 3 moderate, 1 severe); pain not related to PEP in 13 (3%, 9 mild, 3 moderate, 1 severe); bleeding in 3 (1%, 2 moderate, 1 severe); and other in 8 (2%, 5 mild, 2 moderate, 1 severe). All AEs occurred within 14 days of the procedure. There was no mortality.

Conclusion: This is the first prospective multicenter study evaluating technical outcomes in pediatric ERCP and demonstrates that pediatric ERCP is performed with a high rate of technical success with AE rates comparable to adult patients. This is the first study to associate small patient size with technical failure, highlighting the need for continued advocacy for creation of appropriate equipment for smaller pediatric patients. It is also the first time the ASGE difficulty grade classification system has been applied prospectively and been shown to be associated with technical failure, suggesting its utilization in pediatrics may be appropriate.

1214 QUALITY INDICATORS IN PEDIATRIC DIGESTIVE ENDOSCOPY: LESSONS LEARNED FROM A HIGH VOLUME ENDOSCOPY UNIT

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Importance: Pediatric gastrointestinal endoscopy must be performed by an experienced operator within an appropriate environment for the safety of patients. Studies evaluating the quality and safety of pediatric endoscopy are scarce and none has attempted to evaluate the whole process. Quality indicators in adult digestive endoscopy exist but may not be translated to children.

Objective: Our aim was to identify quality indicators in pediatric digestive endoscopy and to implement a quality and security program in a university hospital center. Design: The study consisted of two cohorts; the first from March to December 2013 and the second from June to July 2015.

Setting: The study took place in the Gastroenterology unit of St-Justine University Hospital in Montreal, Canada. Participants: All consecutive patients, aged 2 months to 18 years old, who were scheduled for an upper or lower endoscopy during the study period were included.

Main outcome(s) and Measure(s): After a literature review and multidisciplinary focus groups, 233 variables (such as demographic factors, indication of procedure, number of biopsies, waiting time, pain and comfort, results and outcomes) were identified and prospectively recorded for each patient in the operating room.

Results: A total of 1135 procedures were performed on 837 patients (422 males), with 978 procedures (87%) in cohort 1 and 157 procedures (14%) in cohort 2. The median (range) age of patients was 12 years (2 months-18 years). There were a total of 754 esophagogastroduodenoscopies and 355 colonoscopies and 26 rectoscopies. Two-thirds of the procedures were under general anesthesia whereas one-third were under sedation. The median (IQR) waiting time to procedure was 36 days (58). The median waiting time for children with a high index of suspicion of inflammatory bowel disease was 8 days (24) Despite the prescription of bowel preparation regimens, 95

(25.98%) patients had very poor bowel preparations for their colonoscopies. A higher proportion of sedated patients (59.1%) expressed pain during colonoscopies than during esophagogastroduodenoscopies (31.4%). Macroscopic and microscopic agreements were reached for the majority of procedures.

Conclusion and Relevance: Among the variables analyzed, those that seem relevant as quality indicators include: waiting times to procedure, cancellation rate, quality of sedation and of colic preparation, duration of procedure, indication of procedure, number of biopsies according to the indication, rate of complications, ileal intubation rate and completion of procedure. Some indicators identified in adult studies were less relevant for the pediatric perspective such as adenoma detection rate and retrieval time. A follow-up study is planned to confirm the usefulness of these indicators and their impact on the satisfaction both from the physician and the patients perspectives.

1215 ENDOSCOPIC ULTRASOUND GUIDED DRAINAGE OF PANCREATIC FLUID COLLECTIONS IN CHILDREN

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Background: Endoscopic ultrasound (EUS) guided drainage of pancreatic fluid collection (PFCs) is standard of care in adult patients. However, the experience of EUS guided drainage of PFCs is limited in pediatric population.

Aim: The aim of present study was to evaluate the feasibility, safety and efficacy of EUS guided drainage of PFCs in children.

Methods: We retrospectively evaluated a large cohort of children (≤ 18 years) over 3 years (January 2013 to December 15) who underwent EUS guided drainage of PFCs at our institution using either plastic or metal stents. PFCs were categorized into walled off necrosis (WON) or pseudocyst as per revised Atlanta classification. Linear EUS scope (Olympus 180, Japan ; outer diameter-14.5 mm, channel-3.7 mm) was used for the drainage of PFCs. We used one or more short (5 cm) 7Fr double pigtail plastic stents for drainage of pseudocysts and WON with minimal debris. Single dedicated biflanged metal stent (BFMS) was used for drainage of WON. All the children were followed up with imaging for resolution of PFCs. Technical feasibility, safety and efficacy were assessed.

Results: Fifty one children (44 boys and 7 girls; median age 14 years, range 5-18 years) underwent EUS guided drainage of PFCs. The etiology of acute pancreatitis was blunt abdominal trauma (6), gall stone related (2) and idiopathic (43). The median interval between onset of acute pancreatitis and EUS guided drainage was 58 days (range 30–288 days). The median size of PFCs was 92 mm (55-175 mm) with mean wall thickness of 4.39 ± 0.94 mm. The PFCs were classified as pseudocyst (24) and WON (27). Double pigtail plastic stents (7 Fr, 5 cm) were used in 30 children (26 had two stents and 4 had single stent). BFMS was used in 21 children. The route of drainage of PFCs was trans-gastric in 47 and trans-esophageal (all plastic) in 4 children. The technical success for placement of stents (both metal and plastic) was 100% . There were no major adverse events. Few minor adverse events included – self limited bleeding in four children, spontaneous external migration of the stent in one child with BFMS and internal migration in one child with plastic stent. Most of the stents were successfully removed within 8 weeks. Difficulty in removal of metal stent due to tissue overgrowth was noted in one child with metal stent with late follow-up (10 months). After a median follow-up of 360 days (range:30–1020 days), there was one symptomatic and one asymptomatic recurrence of PFC. The child with symptomatic recurrence of PFC underwent repeat EUS-drainage followed by resolution of the same.

Conclusions: EUS-guided drainage of PFCs is safe and efficacious in children. The utility of BFMS in children should be further explored and compared with plastic stents.

1216 POLYPOID GANGLIONEUROMAS: AN UNRECOGNIZED ASSOCIATION WITH SPORADIC JUVENILE POLYPS

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Background and Aims: Gastrointestinal ganglioneuromas (GNs) are benign hamartomatous tumors characterized by the presence of ganglion cells, nerve fibers, and supporting cells. The microscopic appearance is supported by positive S-100 immunohistochemical staining. Lesions may be subgrouped as solitary polypoid GN, ganglioneuromatous polyposis, and diffuse ganglioneuromatosis. The latter two forms are known to be associated with neurofibromatosis type 1 (NF1) and multiple endocrine neoplasia (MEN) type 2B. Polypoid GN has been associated with Cowden syndrome, a phenotypic form of the PTEN hamartoma tumor syndrome (PHTS). GNs are otherwise reported rarely as solitary polypoid mucosal lesions found incidentally in the gastrointestinal tract of children and adults, often involving the colon. We have occasionally identified solitary polypoid GNs in the colon of children presenting with one or more juvenile polyps in the absence of clinical features of NF1, MEN 2b, or PHTS. We sought to determine the frequency of GNs in patients with juvenile polyps and further characterize this subgroup.

Methods: We performed a retrospective review of the Boston Children's Hospital pathology database from 1992 to 2016 to identify all patients with mucosal GNs and juvenile polyps. Medical records were reviewed to determine basic demographics, relevant clinical findings e.g. macrocephaly, developmental delay, penile freckling, café-au-lait or other skin lesions, congenital malformations, endocrine tumors, available laboratory and genetic test results, and endoscopy and histology findings.

Results: One or more GNs were found in 21 of 424 (5%) patients with at least one juvenile polyp. No patients had clinical features suggesting NF1 or MEN 2b. A clinical diagnosis of PHTS or a pathogenic mutation in the PTEN gene was found in 7 of 21 patients. The remaining 14 of 424 (3.3%) patients with GNs lacked sufficient clinical or genetic criteria for a diagnosis of PHTS. No pathogenic mutations in the PTEN gene were found in 9 of 14 patients tested. Analysis for mutations in SMAD4 and BMPRIA was also negative in 8 of 14 patients. Among these 14 patients, the first GN was first detected at a median age of 11.5 years, 8 (57.1%) were male, and 11 (78.6%) were Caucasian. A single GN was found in 10/14 (71.4%) patients, two GNs in 3 patients, and three GNs in one patient. GNs were located in the left colon in 11/14 (78.6%) patients. Juvenile polyps were first detected at a median age of 6.9 years. Three patients had a solitary polyp, one patient had two polyps and the remaining 10 patients had multiple (range 4-18) polyps.

Conclusion: Polypoid mucosal ganglioneuromas may be a previously unrecognized feature that accompanies sporadic juvenile polyps in patients without a defined predisposing genetic disorder such as PHTS. Alternatively, this association may represent a subgroup of patients with a novel gene mutation awaiting further characterization.