North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Annual Meeting October 8 - 11, 2015 Washington, DC

Scientific Abstracts

POSTER SESSION I
***Poster of Distinction**

ENDOSCOPY/QI/EDUCATION

2 *THE CLINICAL CHARACTERISTICS AND MANAGEMENT OF PEDIATRIC ESOPHAGEAL STRICTURES IN SAUDI CHILDREN*

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Introduction: Esophageal strictures in children are not uncommon and the causes are variable ranging from structural defects, corrosive injury and different inflammatory/allergic conditions. Endoscopy is the most frequently used modality for diagnosis and management of esophageal strictures

Aim: To describe the clinical characteristics, causes and management outcomes of esophageal strictures among Saudi children

Patients and methods:

This is a retrospective analysis of children diagnosed with esophageal strictures over a period of seven years in a single tertiary care center. We included children younger than 18 years of age with diagnosis of esophageal strictures. We collected data about the clinical characteristics of the patients, details of the strictures, endoscopic findings, treatment and the outcomes. Esophageal atresia cases were not included.

Results: Twenty eight children were identified with esophageal strictures. Twenty were males (71.4%) with a median age of 9 years (range: 6 months-18 years). The most common presentation was dysphagia in 25 (89.3%) and vomiting in 17 (60.7%) followed by food impaction in 5 (17.9 %), epigastric pain in 3 (10.7%) and hematemesis in 1 (3.6%).

Gastro-esophageal reflux disease (GERD) 9 (32%) and eosinophilic esophagitis (EOE) 6 (21.4%) were the leading causes of esophageal strictures followed by different types of structural causes; Achalasia 4 (14.3%), Congenital esophageal stenosis 2 (7.1%), esophageal web 1 (3.6%), external compression from vascular ring and from neck mass were seen in 1 (3.6%) each. Caustic strictures were seen in 4 (14.3%).

Lower esophageal and short segment strictures were the main features in GERD, EOE and achalasia, long strictures were present mainly in caustic ingestions and few cases of EOE.

Endoscopic dilatation under general anesthesia was the primary modality of treatment in all of these cases. Median number of dilatation sessions per patient was 6.6 (range 1-12) with median duration of 12 weeks (range; 8-18 weeks). No morbidity (esophageal perforation, bleeding) or mortality were associated with the balloon dilation.

Conclusion: Esophageal strictures are not uncommon in children. GERD and EOE are the primary causes of esophageal strictures in our group, followed by structural causes. Endoscopic dilatation is a safe modality in managing different types of esophageal strictures.

3 *EFFECT OF AGE, WEIGHT AND PRE-PROCEDURE MEDICATIONS ON PROPOFOL DOSING FOR ESOPHAGOGASTRODUODENOSCOPY IN CHILDREN*

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Background: Propofol sedation has now become standard of care for children undergoing esophagogastroduodenoscopy (EGD). Anecdotal clinical experience suggests significant variability in the dose of propofol required to achieve adequate safe sedation based on factors like patient's age, weight and pre-medication. Sub-optimal propofol dosing during EGD can lead to patient discomfort, adverse respiratory events (AE) and/or interruption of endoscopy.Aim: To examine the relationship between patient characteristics and propofol dosing in children undergoing EGD in an ambulatory setting. Methods: Data were collected in a prospective observational study from October 2013 to May 2015 on patients (ages 1-18 yrs) who underwent EGD with biopsies in the endoscopy suite at Connecticut Children's Medical Center. Children with pre-existing airway issues, unstable medical/surgical disease, active bleeding, or foreign bodies were ineligible for the study. All EGDs were performed entirely by a board certified pediatric gastroenterologist and not a trainee. Propofol was given by a board certified pediatric anesthesiologist. Patient's age, weight, gender, and pre-procedure midazolam/fentanyl doses were recorded. Initial propofol dose to complete 30 seconds of the EGD (induction dose), total propofol dose, and any AE were recorded. Patients were grouped by age (1-5.9 yrs, 6-12.9 yrs, 13-18 yrs), and weight ($\leq$19.9 Kg, 20-49.9 Kg, $\geq$50 Kg). Induction and total propofol dosing differences were compared between age and weight groups using analysis of variance (ANOVA) and the effect of pre-medication using Student's t-tests. P-value < 0.05 was considered significant.Results: Complete data were available for 493 subjects (52% male). Mean age ± SD was 11.4 ± 4.4 years, mean weight 43.1 ± 21.9 kg, and mean EGD duration was 286 sec ± 79 sec. Induction and total propofol dosing related to age and weight are shown in the table. Younger age and lower body weight were both associated with a significantly greater dosage

(mg/kg) of propofol given both by 30 sec and to complete the procedure. The total time of EGD was significantly less in lower weight groups [≤19.9 Kg (263.81sec) vs. 20-49.9 Kg (297.49 sec) vs. ≥50 Kg (298.58 sec); p<0.0001] and in lower age groups [1-5.9 yrs (271.74 sec) vs. 6-12.9 yrs (278.71 sec) vs. 13-18 yrs (298.97 sec); p=0.0076]. Approximately 50% of the youngest children (<6 yrs) received pre-medication with midazolam or fentanyl. Compared to the similarly aged non-pre-medication group they required a significantly lower induction dose of propofol (5.75 vs. 6.72 mg/kg; p=0.04). Significant respiratory events requiring bag/mask ventilation or termination of the EGD were seen in 0.01% of cases. Conclusions: Propofol is a safe and effective agent for EGD in children. Both younger age and lighter weight are associated with increased propofol dosing (mg/kg) requirements in children undergoing EGD. In young children pre-medication with midazolam/fentanyl decreased propofol dosing requirements. Knowledge of the effect of these parameters on propofol dosing is required for safe and effective sedation in children undergoing EGD.

Categories		n	Mean induction propofol dose (mg/kg +/- SD)*	Mean total propofol dose (mg/kg +/- SD)*
Weight (Kg)	< or = 19.9	163	5.86 +/- 1.60	7.65 +/- 2.11
	20 - 49.9	150	4.47 +/- 1.17	6.30 +/- 1.62
	> or = 50	181	3.45 +/- 0.99	4.85 +/- 1.37
Age (years)	1 - 5.9	57	6.26 +/- 1.79	7.92 +/- 2.55
	6 - 12.9	218	4.93 +/- 1.49	6.78 +/- 1.86
	13 - 18	218	3.72 +/- 1.13	5.20 +/- 1.58

*p-value < 0.0001

4 *ENDOSCOPIC RISK FACTORS FOR GI BLEEDING IN BILIARY ATRESIA*

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Background: GI bleeding secondary to portal hypertension (PHT) in biliary atresia (BA) may cause significant morbidity and mortality. However, the natural history of PHT in BA is poorly characterized and the risk factors leading to GI bleeding in these patients are not fully understood. We aim to characterize risk factors of GI bleeding in children with BA who have portal hypertension at our institution.

Methods: We performed a retrospective chart review of data extracted from the electronic medical record (EMR) and related data sources of all patients with BA at our institution between 2004 and 2014 using diagnostic codes, procedure codes, and lab values to classify episodes of GI bleeding and the presence of portal hypertension. Portal hypertension was defined a priori as splenomegaly and thrombocytopenia or either diagnosis and a complication of portal hypertension. Patients were included in the analysis until liver transplant (LT). The IRB at Lurie Children's Hospital approved this study

Results: Thirty patients (50% Male) with BA and PHT had a total of 91 endoscopies during the time period of this study. On initial upper endoscopy (EGD), 24 (80%) patients had esophageal varices, including 10 patients less than 2 years of age. Seventeen (57%) patients presented with at least 1 GI bleed of which 3 patients had multiple GI bleeds. The average age at time of EGD evaluating for an initial GI bleed was 4.5 years (range 0.49 - 17.81 years). 9/17 (53%) patients who bled were less than 2 years of age. 17/30 patients with portal hypertension had 36 screening endoscopies. The average age at initial screening EGD was 9.36 years (range 0.29 - 17.90 years). We performed 21 endoscopies for on-going therapy of varices and 14 surveillance endoscopies to follow-up therapy. Of the patients who had a screening endoscopy, 4 patients later had a GI bleed; 3 had small varices, 2 patients had red markings on the esophageal varices, 2 had gastric varices, and all 4 had portal gastropathy. Three patients had an intervention during screening endoscopy. All 3 had large esophageal varices with red markings and portal gastropathy, and 2 had gastric varices. In EGDs performed for bleeding, 12/20 (60%) patients had large esophageal varices, 13/20 (65%) had red markings, and 11/20 (55%) had gastric varices. Only 11/36 (31%) screening endoscopies showed large esophageal varices, 3/36 (8%) had red markings, and 12/36 (33%) had gastric varices. The presence of both red markings on esophageal varices and gastric varices were noted in a significant number of patients with GI bleeds compared to patients who did not bleed (p=0.0485). The mean time to transplant in the 11/17 patients (65%) who bled was 1.26 years (range 0.04 - 7.47 years) from the first GI bleed.

Conclusions: The combination of red markings and gastric varices were noted in a significant number of patients with BA and PHT receiving an EGD for GI bleeding. Presence of these findings may denote a patient at risk for GI bleeding. While prospective natural history studies need to be done to characterize the risk of GI bleeding, primary prophylaxis should be considered in BA patients with PHT who have red markings and gastric varices on EGD.

5 *DEVELOPMENT OF A STANDARDIZED PROTOCOL TO ASSESS SUCCESSFUL INITIAL PEG REPLACEMENT: A QUALITY IMPROVEMENT INTERVENTION*

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Introduction: Although serious and even fatal outcomes can occur when percutaneous endoscopic gastrostomy (PEG) tubes are initially replaced, there is a paucity of data to indicate the optimal way to confirm successful replacement. Several methods of assessment are currently utilized, including fluoroscopic contrast imaging, direct visualization by endoscopy and the collection of gastric contents through the replacement tube. Our review of current guidelines and best practices at a variety of private and academic institutions found no standardized protocols or consensus on the optimal method to demonstrate successful replacement. We undertook this study after a serious safety event occurred at CNHS following an initial PEG replacement. The study was designed to evaluate the accuracy of three methods to confirm successful initial replacement of PEG tubes.

Methods: All children undergoing initial PEG replacement have been prospectively enrolled in this quality improvement study; patients enrolled from the inception on 4/1/2012 to 3/31/2015 are included in this analysis. Approval for the study was obtained from the CNHS IRB. PEG tubes were removed either by the traction pull or endoscopic snare technique. Choice of removal technique was made by the individual provider. Successful replacement of PEG tubes was assessed in all patients either by direct visualization by endoscopy or 2-view fluoroscopic contrast imaging. Collection of gastric contents was also attempted in the majority patients.

Results: 112 consecutive patients have been enrolled in the first 3 years of the study and all have had successful replacement of their initial PEG tubes without complication. Patients ranged in age at time of initial PEG change from 4.5 months to 21 years; 51% were female. The median time from PEG placement until initial replacement of the PEG was 6 months (range 2 months to 6.5 years). Endoscopic confirmation of successful replacement was obtained in 59 (53%) patients; radiographic confirmation was obtained in the other 53 patients. Collection of a gastric aspirate was attempted in 80 patients and an aspirate was successfully obtained in 65 (81%).

Conclusions: These data demonstrate uniformly successful outcomes for initial PEG replacement after the implementation of a standardized protocol. Fluoroscopic and direct endoscopic methods were equally effective in demonstrating successful replacement. These findings may have programmatic implications, given the lower direct costs and lack of anesthesia associated with traction removal and fluoroscopic evaluation. In addition, successful outcomes also occurred in each patient who had a gastric aspirate obtained. Additional data are required to determine the reproducibility of these gastric aspirate results in larger populations of children.

8 *CORRELATION OF SIGMOIDOSCOPIC FINDINGS IN INFANTS WITH MILK PROTEIN INTOLERANCE*

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Background: Milk protein intolerance is an immunologically mediated reaction to the cow's milk proteins. It can be IgE mediated or non-IgE mediated. It is becoming more common and can affect the skin, lungs and the gastro-intestinal tract. It can present with regurgitation, vomiting, diarrhea, fussiness, rectal bleed and failure to thrive. Sigmoidoscopy is done to evaluate infants with rectal bleed and can show redness, friability and lympho-nodular hyperplasia (LNH). Histology shows elevated eosinophils.

Objective: 1. to correlate the symptoms of milk protein intolerance with sigmoidoscopic findings of LNH. 2. To determine any association between LNH and number of eosinophil count/hpf.

Methods: Retrospective study of chart from September 2007 to September 2010 after IRB approval. Infants under one year of age with symptoms and signs suggestive of milk protein intolerance were included. Children with infections, anatomical abnormalities, malignancy, celiac disease, pancreatic malabsorption and metabolic disorders were excluded. The infants were divided into two groups: with rectal bleeding and or Guaiac positive stools and without rectal bleeding and guaiac negative stools.

Statistics: The results were analyzed using chi-square test.

Results: 95 charts reviewed and 4 were excluded. Out of 91 infants 48 (53%) were girls and 43 (47%) were boys. 83% were less than 6 months of age and 17% were 6 months to 1 year of age.

76% presented with regurgitation and or vomiting, 60% fussiness, 27% constipation, 19% poor weight gain, 17% eczema, 12% abdominal distension, and 11% with wheezing. 30% had gross blood in the stool and 50% had guaiac positive stools. 40% were guaiac negative or no gross blood in the stool.

62% were on protein hydrolysate formula,16% on cow's milk based formula, 9% on soy formula, 6% on breast milk, 4% on elemental formula and 3% on breast milk and formula.

40% of the infants with rectal bleeding had LNH compared to 24% with no LNH. In infants without rectal bleeding 13% had LNH and 26% had no LNH. There was no statistical difference between the two groups.

The number of eosinophils was not statistically significant between the infants with rectal bleeding and without rectal bleeding with a p value of 0.77 by chi-squared analysis.

Infants on protein hydrolysate and elemental formulas had less number of eosinophils compared to other formulas.

Conclusions: 1. 63% of the infants who were on protein hydrolysate and elemental formulas in both the rectal bleed and non-bleed had less eosinophils. 37% of the infants on other formulas had higher number of eosinophils, but were not statistically significant. 2. There were no correlation between LNH and number of eosinophils. 3. T-cells may useful in evaluating food intolerance and may off benefit in future study.
Sigmoidoscopy in infants with rectal bleed

Number of eosinophils	LNH	No LNH
0	16	9
1-10	8	1
11-20	9	9
21-30	0	2
31-40	1	0
41-50	1	1
51-60	1	0

9 *ERCP CAN BE PERFORMED EFFECTIVELY AND SAFELY BY AN INDEPENDENT PEDIATRIC GASTROENTEROLOGIST AT A FREESTANDING CHILDREN'S HOSPITAL*

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Objective: The aim of our study was to evaluate if an appropriately trained pediatric gastroenterologist can independently perform endoscopic retrograde cholangiopancreatography (ERCP) for both biliary and pancreatic indications safely and effectively.
Method: We performed a retrospective chart review of pediatric patients at a freestanding Children's hospital from May 2012 to November 2014. ERCP was performed by a single pediatric gastroenterologist trained in ERCP. Adverse events data was collected and defined based on America Society for Gastrointestinal Endoscopy (ASGE) lexicon.
Results: A total of 95 ERCP's were performed. Median age range was 12 yrs (2 months - 20 years). Median weight was 42kgs (3.4kg to 132kgs). Based on ASGE grading of ERCP degree of difficulty, 56% were grade 2, and 33% were grade 3. 63 (66%) procedures were for biliary indications and 32 (34%) were for pancreatic indication. 42 ERCPs were for choledocholithiasis or suspected choledocholithiasis, 10 for biliary strictures, 2 for suspected biliary atresia and 1 for bile leak. Successful cannulation was achieved in 90 (95%) ERCPs. For indication of choledocholithiasis cannulation rate was 41 out of 42 (98%) procedures. Of the 5 unsuccessful cannulations, two ERCPs were for chronic pancreatitis, 1 for biliary stricture at a choledochoduodenostomy site and 1 for an infant for suspected biliary atresia. There were a total of 9 complications (9%). These included 1 episode of bleeding (in a patient requiring continued anticoagulation due to congenital heart disease), 1 episode of perforation that was treated conservatively and successfully with biliary stent placement. 7 (7%) episodes of pancreatitis were recorded, out of which 4 were from ERCPs done for chronic or recurrent pancreatitis. One of the episodes of pancreatitis was severe.
Conclusion: A previous study demonstrated that an appropriately trained pediatric gastroenterologist can perform ERCPs effectively for choledocholithiasis. Our study demonstrates that a pediatric gastroenterologist can independently perform ERCP for a range of biliary and also pancreatic indications both safely and effectively at a freestanding children's hospital, with adverse events rates similar to those reported by the American Society for Gastrointestinal Endoscopy Quality Task Force.

11 *ERCP IS SAFE AND EFFECTIVE IN PATIENTS UNDER ONE YEAR OF AGE*

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Introduction:Use of ERCP for the treatment of pancreatic and biliary disorders has increased in the pediatric population, but little has been reported about indications, safety and success of ERCP in infants. The purpose of this project is to describe the patient population, safety and efficacy of ERCP in children less than one year of age.
Methods:Retrospective chart review of all ERCP's performed in patients less than 12 months of age at Children's Medical Center Dallas and Parkland Memorial Hospital between November of 2006 and March of 2015. All ERCP's were performed by a pediatric gastroenterologist, some with supervision by an adult trained gastroenterologist. Data collected included indications, comorbidities, diagnostic and therapeutic success rates, and complications from the procedure.
Results: A total of 13 ERCP's were performed on 10 patients less than 12 months of age over this time frame (less than 2 cases per year). Mean weight was 6.82 kg (3.6 kg to 9.8 kg). Mean age was 221 days (42 to 335 days). All cases were

performed under general anesthesia using the Olympus PJF160 pediatric duodenoscope. Indications were biliary obstruction (n=11), treatment of idiopathic pancreatic duct leak (n=1), and treatment of biliary cutaneous fistula following surgical, external biliary drain placement (n=1). Of the 11 with suspected biliary obstruction, stones were found and removed in 5 patients. Desired cholangiogram or pancreatogram was achieved on the initial ERCP in all 10 cases. However, deep cannulation of selective duct was successful in only 70% (7/10) cases. Of the 3 failures, cholangiogram dictated that therapy was indicated in only one, thus attempts at deep cannulation were limited and may have affected success rate. All of the failures of deep cannulation occurred early in the series, suggesting that lack of endoscopist experience may have played a role. The one failed cannulation where therapy was indicated was subsequently successful when attempted by adult trained GI 4 months later. Significant co-morbidities were present in 7/10 patients including prematurity (EGA 25-34 weeks) (n=5), short bowel syndrome (n=2), VACTERL association (n=1), hypoplastic left heart (n=1), neuroblastoma (n=1). Bleeding from the sphincterotomy site was noted in one of 8 sphincterotomies (TPN related liver disease with thrombocytopenia) requiring hemostasis with epinephrine.
Conclusions:ERCP is rarely indicated in children under one year of age, even at large volume centers. Biliary obstruction is the most common indication for ERCP in this age group and endoscopic stone removal is possible. Prematurity and significant co-morbidities which increase risk and complication rate are common, and endoscopist experience and location of procedure (pediatric versus adult facility) must be carefully considered. Significant expertise and training is needed in the field of pediatric ERCP, and with increased volume, pediatric providers can successfully perform therapeutic ERCP in medically complex infants at pediatric centers.

13 *SINGLE-CENTER EXPERIENCE OF 50 PEDIATRIC PATIENTS UNDERGOING TAG-LESS PATENCY CAPSULE EXAMINATION PRIOR TO CAPSULE ENDOSCOPY*

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Background: Patency capsules (PCs; length, 26 mm; diameter, 11 mm) are swallowable, dissolvable capsules used to non-invasively assess risk of capsule retention during capsule endoscopy (CE). The suitability of PCs for pediatric use is unclear. Internationally licensed PCs contain a radiofrequency identification tag, whereas those licensed in Japan do not.
Objective: To evaluate the suitability of using tag-less PCs to facilitate CE in pediatric patients in Japan.
Methods: Pediatric patients (6-18 years old) with suspected or confirmed small intestinal disease were examined for intestinal patency by using a tag-less PC prior to undergoing CE. Patient characteristics, PC swallowing success rate, ingestion time, and outcomes of PC and CE capsule ingestion were evaluated. Patients who took more than 30 min to ingest or who failed to swallow the PC were considered as having swallowing difficulty.
Results: Fifty patients (median age, 12.8 years; range, 7.4-17.3 years; 36 male) were enrolled. At the initial swallowing trial, time taken to ingest the PC was 30 min or less in 32 subjects (64%) and greater than 30 min in 6 subjects (12%); twelve patients (24%) failed to swallow the PC. Patients with difficulty swallowing the PC were significantly younger (11.5 ± 2.3 vs. 13.0 ± 1.9 years [mean ± SD]; $P = 0.036$), shorter (142 ± 15 vs. 154 ± 13 cm, $P = 0.007$), and lighter (36.2 ± 12.8 vs. 43.4 ± 12.6 kg, $P = 0.042$) than those without. Cut-off values for age, height, and weight for defining PC swallowing difficulty were 11.0 years (odds ratio, 5.6), 141 cm (odds ratio, 7.6), and 36.2 kg (odds ratio, 5.7), respectively. Ingestion time in the patients who successfully ingested the PC at the initial trial was 24 ± 62 min (mean ± SD); however, their CE capsule ingestion time was significantly shorter (10 ± 35 min). Five of the 12 patients who failed to swallow the PC retried and four succeeded. Abdominal X-ray was used to evaluate PC passage in 19 of the 42 patients who successfully swallowed the PC at the initial or repeat trial; the PC was confirmed to have reached the colon in 17 patients. The abdominal X-ray results were inconclusive in two patients; however, these two patients later spontaneously excreted the PC. None of the swallowed PCs dissolved. One patient with multiple areas of intestinal narrowing took 71 h to excrete the PC but was able to spontaneously excrete the CE capsule.
Conclusion: Age- and body size-dependent difficulties in swallowing PCs should be considered in pediatric patients. To ensure safe capsule passage during CE, PC location and passage require careful evaluation.

16 *PRIMARY PERCUTANTEOUS ENDOSCOPIC GASTROJEJUNOSTOMY TUBE FOR INFANTS WITH COMPLEX CONGENITAL HEART DISEASE: SAFETY, FEASIBILITY, AND RECOMMENDATIONS*

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INTRODUCTION: Infants with complex congenital heart disease commonly experience feeding intolerance and may require enteral access devices to ensure adequate nutrition. A recent multicenter review of over 400 Hypoplastic Left Heart Syndrome (HLHS) patients examined the relationship between feeding methods and outcome. Feeding methods including oral, nasogastric, and gastrostomy tube with or without Nissen fundoplication were discussed. There is little to no mention of the primary percutaneous endoscopic gastrojejunostomy tube (PEG-J) as a viable feeding method in this patient population.
AIMS: Our primary aims are to describe demographic and safety data of the primary PEG-J procedure performed in

complex congenital heart disease patients at our institution. Our secondary aim is to determine the ideal minimum weight of the patient for safe placement .
METHODS: A chart review of all complex congenital heart disease patients, including HLHS patients at interstage palliation, at as single tertiary care center between the years of 2010-2015 who underwent PEG-J (16 Fr Peg with 6 F jejunal tube) placement was conducted, and descriptive statistics were used.
RESULTS: 25 patients (12 F) underwent PEG-J at a mean age of 63 days (28-150 days). The most common congenital cardiac lesions were HLHS (11/25) and Tetralogy of Fallot (7/25). 16/25 patients had significant comorbidities including 7 with chromosomal abnormalities. All patients had inadequate PO, 22/24 had clinical GERD, and all patients had failed attempts at gastric feeding. Mean weight at time of procedure was 3.94 kg (2.9-5.95 kg). 6 patients were less than 3.5 kg There were 37 jejunostomy tube changes, 34 of which were conducted without anesthesia, with the most common indication being clogged jejunostomy tube. Three complications occurred, including E. coli skin infection, mucoal prolapse, and esophageal mucosal rent (in a 3.3 kg patient). One patient progressed to Nissen fundoplication. 14 patients were able to transition to gastric feedings, and 7 patients were weaned completely off of tube feeds during followup.
For the subgroup of patients with HLHS, 11 patients underwent PEG-J at a mean of 44 days (28-70 days). Mean weight at time of procedure was 3.56 kg (3.08-4.9 kg). There were 6 deaths, none attributable to the PEG-J procedure.
CONCLUSION: This is the largest review of the PEG-J for complex congenital heart disease patients to date. We found the PEG-J to be a safe, feasible option for small infants with complex congenital heart. Based upon our experience, we prefer to wait until 3.5 kg if possible to place the PEG-J. At weights lower than 3.5 kg, we have shown that the the PEG-J is safe and feasible, however we have successfully performed a 12 Fr PEG with 5 Fr jejunal tube in 2 noncardiac patients at weights less than 3.5 kg and are considering adapting this to congenital heart disease patients. The PEG-J can potentially avoid the need for Nissen fundiplication or long term TPN.

18 *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, histological findings, and region of origin reported in the existing literature.
Methods: All full-length articles published in English during 1966-2014 were included if: (i) participants had EGD for evaluation of hematemesis, coffee-ground emesis or melena, (ii) etiology of bleeding was unknown prior to EGD, (iii) EGD outcomes (e.g., gross findings, histopathology, interventions) were reported, (iv) age of participants was under 18 years.
Results: Thirteen studies including 2,136 EGDs in 2,126 children fulfilled the inclusion and exclusion criteria. Three studies were performed in the United States, 4 in Asia, 3 in Europe, 2 in the Middle-East, and 1 in Africa. The largest study examined 614 procedures and 3 studies examined less than 50 procedures. Specific endoscopic findings included: 185 (8.7%) cases of erosive gastritis, 182 (8.5%) varices, 149 (7.0%) duodenal ulcers, and 91 (4.3%) gastric ulcers were reported. In studies reporting histopathology, 232 (10.9%) cases of H pylori were reported and the prevalence of H pylori ranged from 6.4% and 55.5%. The most common endoscopic interventions included 67 cases of sclerotherapy, 21 band ligations, hemoclip application in 15 cases, and local drug injection in 15 cases. The primary non-endoscopic intervention was PPI use (266 cases). No articles attempted to describe the impact of EGD on quality of life or cost-effectiveness. None of the studies analyzed the association of specific symptoms or signs to diagnostic yield.
Conclusions: We reviewed 13 studies including 2136 EGDs in children with upper gastrointestinal bleeding and discovered that H. pylori and erosive gastritis are the most common findings.

20 *MOST EFFICIENT BOWEL CLEAN-OUT FOR CONSTIPATION? INPATIENT VERSUS OUTPATIENT*
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A bowel clean-out may be necessary for a constipated child's condition to improve. Home clean-outs can be unsuccessful requiring a more aggressive clean-out in the hospital setting. The purpose of this study was to determine which bowel clean-out is fastest and, therefore, the most cost effective. METHODS: A retrospective chart review of 103 children with constipation was done to determine the time it took from the start of the clinic clean-out until abdominal radiograph (KUB) verification of successful stool evacuation. The protocol was identical except intravenous fluid was given during GoLYTELY. The protocol included an initial KUB, Reglan (metoclopramide) for nausea and vomiting, food coloring added to the clean-out agent, and milk and molasses enemas. The second KUB was done after three colored liquid stools were passed. RESULTS: 46 of the children (45%) underwent the GoLYTELY clean-out and 57 (55%) drank magnesium citrate. Their age range was 1-18 years with an average age of 8, and 45 patients were female (45%) and 59 patients were male (58%). The children on GoLYTELY required an average of 2.5 enemas whereas the children on magnesium citrate required an average of 3 enemas. Both GoLYTELY and magnesium citrate initial KUBs ranged from rectal impaction to massive amount of stool throughout the colon with the most frequent being moderate colonic stool. The average time for a GoLYTELY clean-out took 5 hours 15 minutes (range: 3 hours 30 minutes -7 hours) and 5 hours 30 minutes for

magnesium citrate clean-out (range: 2 - 8 hours). Overall, 7 (15%) of the GoLYTELY and 6 (10%) of magnesium citrate clean-outs did not achieve interval clearance of stool at the time of the second KUB. Vomiting was an adverse effect of both types of clean-outs and 7 (12%) magnesium citrate children were unable to drink the entire dose. CONCLUSION: The study findings indicate that both methods of clean-out take almost the same amount of time. In our institution, nasogastric (ng) GoLYTELY clean-outs are done inpatient (2-3 day cost: up to $14,000) while ng GoLYTELY (cost: $550) or oral magnesium citrate (cost: $455) are done in the outpatient setting. Although magnesium citrate can be difficult for some children to drink, it can be done in an outpatient setting and, therefore, is less costly. Furthermore, it is less invasive, safer than ng GoLYTELY, and can even be done at home.

23 *EFFICACY OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE FEEDINGS IN PATIENTS WITH CYSTIC FIBROSIS*

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Background: Cystic fibrosis (CF) is the most common genetic disease in Caucasians. In a recent consensus statement, the Cystic Fibrosis Foundation emphasized that adequate nutrition is a vital element in preserving lung function and survival in patients with CF. Malnutrition is a common problem in patients with CF as a result of their inability to meet nutritional demands. Improving the nutritional status of patients with cystic fibrosis (CF) has been shown to have a positive effect on body composition, pulmonary function, respiratory status, and survival. Few studies have investigated the safety, outcomes and efficacy of nutritional supplementation via percutaneous endoscopic gastrostomy (PEG) tube feedings.
Methods: With IRB approval, we queried the electronic medical record at All Children's Hospital Johns Hopkins Medicine. For patients with CF aged 18 years and younger who received dietary supplementation via a PEG tube for nutritional failure between 2010 and 2014. This study builds on a quality improvement project at our institution initiated in 2006. This QI project was instilled following the 2005 CF foundation recommendation that children with CF maintain a BMI> 50th percentile.
Results: Initial query of our census revealed 22 malnourished patients with cystic fibrosis who received PEG tube placement for nutritional supplementation. Of these, 45.5% (10/22) were females. Mean age at PEG tube placement was 11.8 years old (SD 4.7 years). In addition, PEG tubes were placed from age 1.3 to 18.8 years. Of these subjects, 95.5% (21/22) were Caucasian with the remaining subject being multiracial. FEV1 showed a progressive improvement when compared prior to PEG tube placement and at one year follow up, although it did not reach statistical significance (p=0.37). However, data obtained prior to PEG tube placement and one year post-operatively showed a significant improvement in BMI percentiles (p=0.005). Mean BMI percentile prior to tube placement was 18% as compared to 39% at one year follow up.
Conclusion: Our data suggests that PEG tube placement for nutritional rehabilitation in CF patients significantly improved BMI at one year follow up (p = 0.005). FEV1 showed a progressive improvement at one year, although it did not reach statistical significance. Longer follow up may be needed to observe significant change in FEV1. In addition, FEV1 may have been affected by other confounding factors, including advanced lung disease. We believe that PEG tube placement in nutritionally at risk patients with cystic fibrosis improves clinical outcomes.

24 *ASSESSMENT OF A TRAINING VIDEO AS AN EDUCATIONAL TOOL FOR SET-UP OF THE ENDOSCOPY TRAVEL CART FOR EMERGENCY PROCEDURES*

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Pediatric gastroenterology fellows are often responsible for setting up the endoscopic travel cart for emergency procedures. Expeditious and appropriate set-up of the travel cart is critical for appropriate treatment. Training for an emergency set-up has not been standardized and, at our institution, consists of a once yearly hands-on session. Given the infrequency of emergency situations, fellows at our institution were often uncomfortable with setting up for an emergency endoscopy and indicated the need for a better training method. The goal of this project was to assess the educational efficacy of a 20-minute video created by the authors to teach gastroenterology fellows the essentials of setting up an Olympus travel cart for an emergency situation. All fellows agreed to participate in the study and signed informed consent. Participants were anonymously given the same survey before and after watching the video. The survey consisted of 11 questions in Likert format using a 1-5 scale and one comment section. Questions assessed a participant's comfort with finding equipment, starting documentation software, attaching the scope and accessories for CO2 insufflation and irrigation, utilizing the electrocautery unit, preparing the scope for cleaning after the procedure, as well as a global assessment of a fellow's comfort with setting up the travel cart in an emergency. For the post test survey an additional Likert question determined if the video was an improvement over current training methods and whether it should be utilized as a regular part of future training. A total of 8 fellows participated, 3 first-year fellows, 2 second-year fellows, 2 third-year fellows, and 1 fourth-year

fellow. The results were then analyzed using a two tailed paired t-test. Across all questions for all education levels, there was an improvement of 0.89 ($p<0.0005$). 9 out of 11 questions had a significant improvement after watching the video ($p<0.05$). When comparing different fellowship years, there was no difference between 1st and 2nd years compared to 3rd and 4th years or 1st years compared to 2nd, 3rd, and 4th years. All fellows either agreed or strongly agreed that the video should be incorporated into training. Overall, the 20-minute video significantly increased the fellow's self-assessed knowledge level for setting up the endoscopic travel cart. There was no significant difference seen between different class years, indicating that the video could be beneficial to trainees of all levels. Video training offers the advantages of improved standardization, can be paused or rewound to clarify important points as well as viewed whenever a trainee feels that a refresher is necessary. Further refinements of the video which incorporate comments made by the trainees would make this video viable for further validation testing at other institutions who use similar equipment and publication on the internet.

NASPGHAN CAPSULE ENDOSCOPY PRIZE

25 *CLINICAL UTILITY OF PATENCY CAPSULE IN PEDIATRIC VIDEO CAPSULE ENDOSCOPY*

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BACKGROUND: Capsule Endoscopy retention is a concern among pediatric patients who undergo video capsule endoscopy. Current imaging modalities such as CTE, MRE and small bowel follow through do not reliably establish small bowel patency. The agile patency capsule (PC) has been used to determine small bowel patency in both adult and pediatric patients. An abdominal x-ray is often used to determine if the PC has passed through the small bowel within 30 hrs.

AIM: We report our experience of the use of the agile patency capsule in pediatric capsule endoscopy.

METHODS: We retrospectively reviewed the use of the patency capsule (PC) in our cohort of 528 pediatric patients undergoing capsule endoscopy. There were 86 patency capsules performed. Patients ingested the patency capsule 30 hours prior to obtaining an abdominal x-ray. The abdominal x-ray was read by board certified radiologists and also evaluated by the gastroenterologist performing the capsule endoscopy study.

The indications for the patency capsule evaluation were known Crohn's disease 38 (44.2%), Ulcerative Colitis 5 (5.81%), blood in stool 14 (16.3%), vomiting 3 (3.5%), anemia 1 (1.2%), weight loss 1 (1.2%), abdominal pain and diarrhea 5 (5.8%), failure to thrive with diarrhea 1 (1.2%), family history of Crohn's disease 2 (2.3%), abdominal pain 6 (6.9%), abnormal radiologic exam 1 (1.2%) and known inflammatory bowel disease with abnormal studies 9 (10.5%).

RESULTS: Of the 528 patients who underwent video capsule endoscopy, 86 patients (16.3%) underwent patency capsule study prior to capsule endoscopy. In 40 (46.5%) abdominal x-rays, the PC was not seen at 30 hours post ingestion, confirming complete passage throgh the GI tract.

In 44 (51.2%) abdominal x-rays, the radiologist reported presence of radiopaque foreign body/PC in the abdomen. In 27(31.4%) of these 86 x-rays where the foreign body/PC was noted in the abdomen, the radiologist commented that the PC was in the colon. However, in 15 (17.4%) abdominal x-rays, the location of the PC was not specifically identified to be within the colon. Instead, it was reported to be in various locations such as; right lower quadrant, overlying left sacrum and lower abdomen just to the right of midline at the level of the sacrum. The gastroenterologist therefore was required to further interpret these x-ray studies to determine whether these 15 were in the colon .

In 2 (2.3%) abdominal x-rays, the patency capsule was retained in the stomach due to delayed gastric emptying. The capsule then passed throught the small bowel after giving a prokinetic agent. In 2 (2.3%) abdominal x-rays studies, the radiologist interpreted the capsule to be in the distal ileum or cecal region. These PC's were confirmed by colonoscopy to be retained in the distal ileum. Capsule endoscopy was therefore not performed on these two patients.

The patency capsule retention rate within the small bowel at 30 hours post injestion was found to be 2.3% of patency capsule studies. The remaining 84 patients sucessfully completed video capsule endoscopy.

CONCLUSION: The patency capsule is useful in preventing Capsule endoscope retention and often requires careful interpretation by both the radiologist and gastroenterologist.

EOE/GERD/AERODIGESTIVE

27 *SPLIT-DOSING OF PEG-3350 FOR COLONOSCOPY PREPARATION IN CHILDREN: EVALUATION OF EFFICACY AND TOLERABILITY*

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Background: In adults, split-dose bowel cleansing is overwhelmingly supported to show superior efficacy and increased patient willingness to repeat such a regimen in comparison to the traditional approach of administering the entire preparation the day before the colonoscopy. A meta-analysis of several randomized controlled trials showed that split-dose preparations are better tolerated by patients compared to evening-before preparations. While extensive research has been conducted to optimize bowel preparation for adults, there is currently no standardized regimen established for pediatric patients. There have been no studies evaluating split-dose bowel preparation in children, despite the notable success of this regimen in adults. We hereby present the results of efficacy and tolerability in utilizing split-dose bowel preparation in children.

Methods: Our prospective observational study included patients who were undergoing colonoscopy and using a split-dose

bowel prep regimen. One day prior to procedure, patients followed a clear liquid diet. After school that day, patients consumed 2-3 g/kg of PEG-3350. Parents were permitted to administer a Pediatric Fleet Enema or bisacodyl tablet or suppository if there was still no bowel movement after administration of a few doses of PEG-3350. On the day of the procedure, patients consumed the same dose of PEG-3350 and finished no less than 2 hours prior to procedure. Prior to the procedure, patients and guardian(s) completed a questionnaire assessing compliance, tolerability, acceptability, side effects, and willingness to repeat such a regimen. Two readers used the Boston Bowel Preparation Scale (BBPS) to rate the quality of bowel cleansing. Adequate quality bowel preparation was defined as a score of ≥ 2 per bowel segment.
Results: Our study includes 16 subjects to date. We plan to enroll 100 subjects total. 15/16 (94%) patients had adequate BBPS scores in all bowel segments. All patients were compliant with the split-dose scheduling. 11/16 (69%) patients rated the tolerability as easy or acceptable, while 5/16 (31%) found it to be somewhat difficult to very difficult. 13/16 (81%) patients rated the overall bowel prep experience as good to fair, while 3/16 (19%) rated their experience as poor to bad. Of these 3 patients, 100% attributed their side effects to their baseline health problems. The most common side effects overall were abdominal pain, gas, and sleep disturbances due to using the bathroom more frequently. Of the patients who noted having side effects, 9/14 (64%) attributed their side effects to their baseline health issues. Overall, 15/16 (94%) participants said they were mostly willing or somewhat willing to follow a split-dosing of PEG-3350 again if they needed a colonoscopy in the future.
Conclusion: Our study is the first to evaluate split-dosing of PEG-3350 for colonoscopy preparation in children. Split-dosing is effective at producing quality bowel cleansing that is adequate for visualization during colonoscopy. The large majority of patients found the preparation experience to be tolerable, acceptable, and would be willing to use the same preparation schedule in the future. These findings should be considered in establishing a standardized regimen for children undergoing colonoscopy.

28 *DILATION OUTCOMES IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS*

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Background: A wide variety of practice patterns exist regarding the management of complicated pediatric Eosinophilic Esophagitis (EoE). Whereas initial adult studies examining dilation raised concerns for high rates of perforation (up to 8%) and hospitalization for pain control, subsequent reports demonstrate perforation rates similar to that observed in non-EoE patients (0.3%).1 These studies identify a role for therapeutic dilation in the management of complicated EoE in adults but the practice of dilation in pediatric EoE has been limited. The aim of our study was to report our experiences with dilation in the management of severe dysphagia in pediatric EoE patients.
Methods: Using an Endoworks and EPIC search strategy, we identified patients seen at our institution between July 2010 and December 2014 who underwent upper endoscopy with esophageal dilation. From these patients, we identified those with history of esophageal eosinophilia. Medical records were further reviewed for demographic, clinical, endoscopic and radiologic information. Adverse events from dilation were captured and confirmed using a prospective procedure log. This study was approved by the local IRB.
Results: During the study period, 338 total dilations were performed with an adverse event rate of 7.4% for any level of adverse event. Forty-seven dilations were performed in 33 patients with esophageal eosinophilia or confirmed EoE; who were a mean age 13.5 years old (SD 3.9 years), 72.7% male and 97% Caucasian. Dilations were accomplished with non-wire-guided Maloney dilators (76.6%) and through-the-scope balloons (23.4%). Thirty-six (76.6%) had mucosal split in response to dilation. The majority of patients had a single dilation (n = 24, 72.7%). Nine patients required repeat dilation within the follow up period (mean 15.5 months, range 0 to 61 months) with an average of 2.6 dilations per patient (range 2 to 4). At time of initial dilation, patients were on a variety of other therapies for EoE including swallowed steroids (21.2%), diet restriction (6.1%) or combined therapy (18.2%). Eleven (33.3%) were on PPI alone. Seven (21.2%) were on no medical or diet therapy. All but 1 patient who was lost to follow up was put on targeted EoE therapy including swallowed steroids (60.6%), diet restriction (12.1%), and combined therapy (24.2%). The most common procedural complication was pain (n = 7, 14.9%). Of those with pain, 6 received reassurance without sequel. One patient (2.1%) was admitted for observation. There were no perforations or other urgent evaluations as a result of esophageal dilation in this population.
Conclusions: Dilation for management of dysphagia in EoE can be performed safely in children. Post procedural pain was common (19.4%) in the setting of resultant mucosal split from esophageal dilation.
1 M.E. Bohm, J.E. Richter. Review article: oesophageal dilation in adults with eosinophilic oesophagitis. Aliment Pharmacol Ther, 33 (2011), 748-757

29 *THE PREVELANCE OF LAMINA PROPRIA AND SUBEPITHELIAL FIBROSIS IN MUCOSAL BIOPSIES WITH ESOPHAGEAL EOSINOPHILIA*

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Introduction: Eosinophilic esophagitis (EoE) is often complicated by tissue remodeling. Subepithelial fibrosis, a feature of

remodeling, is detected on mucosal pinch biopsies. However, not all mucosal biopsies contain sufficient lamina propria (LP) to evaluate for fibrosis. We examined the frequency of LP procurement from pinch biopsies and the prevalence of subepithelial fibrosis in esophageal eosinophilia. Methods: We reviewed esophageal eosinophilia (≥15eos/hpf) cases from 1/1/13-5/30/13. For each biopsy fragment, any amount of lamina propria without crush artifact was considered sufficient and evaluated for fibrosis. Crush artifact was identified when fibroblast nuclei were elongated and distorted. Results: We identified 55 esophageal eosinophilia cases and 32 control cases with normal esophageal histology (Table1). Significantly more eosinophilia cases had sufficient LP than controls (89% vs 47%, p<0.001). However, endoscopists took more biopsies in esophageal eosinophilia (6.7±2.3 vs 2.6±1.2, p<0.001). In esophageal eosinophilia, 160 of 371 (43%) fragments had sufficient LP, while controls had 27 of 82 (33%) sufficient LP. While 37 cases had fibrosis, 14% of the biopsies in those cases had no fibrosis (Table2). Forty-eight cases exhibited endoscopic inflammatory phenotypes (furrows, exudates, edema, or normal esophagus); of which 39 had fibrosis. Endoscopic features of remodeling (rings or strictures) were present in 7 cases, of which 4 had fibrosis. Conclusions: Evaluation for fibrosis is important in EoE management. The majority of inflammatory phenotypes without rings or strictures already have evidence of microscopic fibrosis. Less than half the time, mucosal pinch biopsies have sufficient LP. Fibrosis is patchy rather than uniform along the esophagus. While increasing the number of biopsies might increase LP yield, biopsy techniques and instruments need to be considered.

Table1

	Esophageal Eosinophilia N=55	Normal Esophagus N=32	*P* value
Mean age, y, (range)	9.7 (1.6 - 17.8)	9.8 (0.6 - 17.6)	0.97
Male, n (%)	34 (62)	13 (41)	0.07
White, n (%)	28 (51)	17 (53)	1.00
History of atopy/allergy , n (%)	44 (80)	14 (44)	<0.01
Symptom duration, y (mean ± SD)	2.2 ± 2.4	2.1 ± 2.8	0.66
Dysphagia, n (%)	18 (33)	0 (0)	<0.0001
Food impaction, n (%)	3 (5)	0 (0)	0.29
Heartburn or chest pain, n (%)	13 (24)	0 (0)	<0.0001
Abdominal pain, n (%)	26 (47)	25 (78)	0.01
Vomiting, n (%)	29 (53)	6 (19)	<0.01
Pinch biopsies/case (mean ± SD)	6.7 ± 2.3	2.6 ± 1.2	<0.0001
Peak eosinophil count/hpf (mean ± SD)	56.9 ± 34.9	0	<0.0001
Cases with Sufficient LP, n (%)	49 (89)	15 (47)	<0.0001
Cases with Insufficient LP, n (%)	6 (11)	17 (53)	
Fibrosis, n (%)	37 (67)	0 (0)	<0.0001
No Fibrosis, n (%)	12 (22)	15 (47)	

Table 2

Esophageal eosinophila cases with:	Fibrosis N=37	No Fibrosis N=12	Insufficient LP N=6	*P* value
Mean age, y, (range)	9.4 (1.6 - 17.8)	9.4 (1.6 - 16.2)	12.2 (6.8 - 16.3)	0.49
Symptom duration, y (mean ± SD)	2.5 ± 2.3	0.9 ± 1.1	3.3 ± 4.0	0.03
Peak eosinophil count/hpf (mean ± SD)	68.9 ± 33.1	27.1 ± 19.6	42.8 ± 30.7	<0.001
Fragments with fibrosis, n (%)	101 (37)	0 (0)	0 (0)	
Fragments with no fibrosis, n (%)	39 (14)	20 (44)	0 (0)	
Fragments with insufficient LP, n (%)	136 (49)	36 (56)	39 (100)	

32 *ADRENAL INSUFFICIENCY AND SWALLOWED TOPICAL STEROID TREATMENT OF PEDIATRIC EOSINOPHILIC ESOPHAGITIS*

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Background- Inhaled topical steroids have been used safely for decades for the treatment of asthma. Swallowed topical steroids (STS) are the only anti-inflammatory medications used to treat eosinophilic esophagitis (EoE). Data documenting STS safety in EoE treatment is limited to short prospective or small retrospective studies. Adrenal insufficiency (AI) is one of the most concerning potential STS side effects.

Hypothesis and Aims- We hypothesized that EoE children treated with STS would not experience clinically significant AI. The aims of our study were to determine how often AI occurs with chronic STS use and document co-morbid features.

Methods- We instituted a quality improvement program in our multi-disciplinary EoE program to increase awareness of potential chronic STS side effects. Initially, we completed a retrospective analysis of all STS-treated EoE patients seen in the program from 2007 to 2013 and documented how many had an abnormal a.m. cortisol level. This group was labeled as our retrospective group (RG). Cortisol levels performed in a fasting state and drawn between 7 am and 9 am were accepted as valid. Cortisol levels were deemed normal if >10 mcg/dl, intermediate if 5 to 10 mcg/dl, and abnormal if <5 mcg/dl. As a part of standard of care, we then prospectively measured morning cortisol levels of children treated with STS for over four months. This group was labeled as our prospective group (PG).

Results- Our RG consisted of 273 children (age 10.5 ± 5.1 yrs; 75% male). Of these patients, 8 had a morning cortisol level drawn and 2 were abnormal. One child had an abnormal ACTH stimulation test and was diagnosed with AI. In our PG, morning cortisol levels were obtained from 106 children (age 8.5 ± 4.7 yrs; 75% male) in whom 33 had a cortisol >10 mcg/dl (14.4 ± 3.3 mcg/dl), 45 had a cortisol between 5 mcg/dl and 10 mcg/dl (7.5 ± 1.4 mcg/dl) and 28 had a cortisol <5 mcg/dl (3.6 ± 1.2 mcg/dl). Of this last group, 3 had AI (peak cortisol on ACTH stimulation testing 12.6 ± 4.4 mcg/dl). None of these 3 patients had clinical features of AI prior to, or after, the AI diagnosis (i.e. fatigue, hypoglycemia, hypotension or cushingoid appearance). BMI percentiles ranged from 14.0% to 59.6%, height percentiles ranged from 1.2% to 49.3%. All 3 AI patients had been treated with Fluticasone STS as well as with other steroid treatments for asthma and allergic rhinitis. When comparing the RG (n=273) to the PG (n=106) we found that patients were similar in age, sex, and the number of steroid modalities used (Table 1). Data reported as mean ± standard deviation.

Conclusion- A small fraction of children with EoE treated with STS developed biochemical evidence of AI.

Implication- Proper identification of AI patients and administration of standard stress dose steroid precautions is necessary to prevent life-threatening hypotension and hypoglycemia.

	Retrospective Group (n=273)	Prospective Group (n=106)
Age (years,SD)	10.5 ± 5.1	8.5 ± 4.7
Sex	75% Male	75% Male
STS Type	11% Ciclesonide 23% Budesonide 54% Fluticasone 12% Changed from one type of STS to another	18% Ciclesonide 32% Budesonide 50.0% Fluticasone
Number of All Steroid Modalities, SD	1.9 ± 1.0	2.0 ± 1.1

33 *NO WHEY! MINOR COMPONENT ALLERGENS OF MILK MAY PLAY A ROLE IN ALLERGIC EOSINOPHILIC ESOPHAGITIS*

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Purpose: Understanding food and aeroallergen sensitivity in Eosinophilic Esophagitis (EoE) is critical for tailoring treatment. Elimination diets have been shown to improve clinicopathologic symptoms and signs, however, these are often empiric as identification of inciting foods is challenging-- skin-prick testing is often negative and serum IgE titers are low level-positive. Since re-introduction of milk, has been shown to cause recurrence, we sought to investigate the IgE specificity to the whole and component allergens of milk. In addition, to examine its potential as a biomarker for assessment of disease progression, we measured periostin levels in these patients. Methods: Children and adults with

biopsy-diagnosed EoE were evaluated with serum IgE testing to a panel of food and inhalant allergens using the ImmunoCAP (CAP) assay. To further investigate allergen component IgE specificity, sera were evaluated with CAP assays on dilutions of sera and CAP assays for allergen components of milk. Periostin concentration was measured by Periostin/OSF-2 (human) ELISA in the children and adults in our cohort. Results: CAP assay analysis of sera from 46 children and 33 adults yielded positive IgE titers to various inhalant and food allergens including: milk (31/79), wheat (37/79), and peanut (29/79). Serial dilutions of sera analyzed by CAP gave calculated IgE titer values at up to 6 times the original (undiluted) value for foods in contrast to aeroallergens, for which the values remained relatively unchanged. Food allergen component testing revealed a high number of elevated IgE titers (>50%) to minor milk (whey) components. Ten children with elevated specific IgE to multiple minor milk component proteins including alpha-lactalbumin, beta-lactoglobulin, and bovine serum albumin were identified in whom targeted elimination of milk based on elevation of milk-specific IgE resulted in improvement of clinical symptoms and decreased number of eosinophils per high power field in esophageal biopsy tissue. Periostin concentrations in adults (n= 19) were significantly lower (geometric mean (GM) = 73.3 ng/ ml) than in children (n= 22, GM = 315.8 ng/ ml) ($p< 0.0001$). Conclusions: In light of frequently negative skin test results for food allergens and presence of positive IgE titers to food allergens, serum component IgE measurements to foods may be preferential in guiding dietary therapy in EoE. Major and minor component IgE analysis suggests that the components of foods that are currently recognized as important allergens in food-induced immediate anaphylaxis may not be the relevant components in EoE. The dilution data provide evidence for IgE to minor component(s) of these food allergens, which is further supported by predominance of positive titers to minor milk allergens (whey). Our preliminary results indicate that periostin is present in the sera of patients with EoE and there may be an effect of age on the concentration of periostin. Future eosinophil enumeration in the biopsy tissues of the subset of patients with elevated IgE to milk who are restricting milk from the diet and have eliminated use of topical steroid therapy will be followed to investigate the effect of targeted, serum IgE-based, dietary elimination alone.

35 *INVESTIGATING THE SUCCESS OF DIETARY MODIFICATION OR MEDICATION IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS AND MINIMAL ESOPHAGEAL EOSINOPHILIA*

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Background: Eosinophilic esophagitis (EoE) is a chronic, immune-allergic condition characterized by eosinophilic infiltration, which can lead to esophageal dysfunction. To diagnose EoE, expert guidelines require ≥15 eosinophils (eos) in the middle (mid) and distal esophagus in a patient treated with high dose acid suppression for ≥8 weeks prior to biopsy, or with a normal pH probe. Gold standard therapy is dietary restriction. Pharmacologic therapy includes swallowed steroids, or in more severe cases, systemic corticosteroids. Post-treatment biopsies are used to evaluate treatment effectiveness with the goal of zero esophageal eosinophils. However, to date, no data exist to inform physicians about therapeutic management for EoE patients with minimal esophageal eosinophilia (MEE) after treatment.

Objective: To determine the effect of therapeutic modification on clinical and histological response in EoE patients with minimal esophageal eosinophilia (defined as 1-5 eos/HPF on biopsy following prior treatment for EoE).

Methods: A retrospective analysis was performed on patients with EoE treated at Children's National from 2000-2014. Fifteen patients who had established EoE with ≤5 eos/HPF after initial therapy, and who had follow up endoscopy status post subsequent treatment were included. The follow up treatments were addition of 1 food; addition of 2 foods; addition of >2 foods; decrease in medication; or decrease in medication plus addition of food. The following information was gathered for all cases: age, sex, date of birth, treatment (dietary modification or steroid therapy) pre- and post-treatment symptoms, and pre- and post-treatment biopsy results (eos/HPF). Change in esophageal eosinophilia following treatment was described and displayed stratified by biopsy location and treatment type. Physician-documented patient-reported symptomatology was recorded pre- and post-treatment including pain, nausea, vomiting, reflux, gassiness, dysphagia, and poor weight gain. Patient response to treatment was classified as improved, worse, no change or unknown.

Results: Patients with EoE and MEE have been treated with various therapies at Children's National. The distribution of patients per treatment intervention was as follows: addition of 1 food, 33%(n=5); addition of 2 foods, 33% (n=5); addition of >2 foods, 13% (n=2); decrease in medication, 7% (n=1); decrease in medication plus addition of food, 13% (n=2). We observed an overall trend of unchanged or increased esophageal eosinophilia post-treatment though this was not statistically tested for significance. The majority of patients (9/15 or 60%) experienced symptomatic improvement after treatment. There was no correlation between mid- or distal esophageal eosinophilia and post-treatment symptomatology, consistent with other studies.

Conclusions: Our results are the first to analyze the therapeutic response in EoE with MEE at our institution. The majority of patients with EoE and MEE experienced symptomatic improvement regardless of treatment type. Larger randomized, prospective studies are needed to determine the long-term effects of MEE and indications for therapy.

36 *COMPARISON OF ORAL TOPICAL CORTICOSTEROIDS IN PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS*

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Background: Eosinophilic esophagitis (EoE) is an allergic disease characterized by clinical symptoms of esophageal dysfunction and histopathological changes to the esophagus including eosinophil counts ≥15 eosinophils per high-powered field (eos/HPF). Treatment of EoE comprises dietary modification and/or pharmacologic management with swallowed oral topical corticosteroids. Swallowed fluticasone propionate (FP) and oral viscous budesonide (OVB) have proven to be effective in resolving symptoms and reversing histologic changes. However, no study has yet compared the two treatment options in children with EoE. Aim: compare histologic outcomes following FP versus OVB therapy in children with EoE. Methods: We performed a retrospective chart review of subjects diagnosed with EoE and treated with a minimum 8-week course of FP or OVB who had pre-treatment and post-treatment endoscopic evaluation at Connecticut Children's Medical Center (CCMC) between 2010-2014. A total of 68 patients (81% male), mean age 10.6 ± 5.2 years, range 1-20 years) were included in the study (20 FP and 48 OVB). Data including gender, age at steroid initiation, race, weight, BMI, past medical history including atopic, gastrointestinal and allergic history, endoscopic evaluation, and histologic outcomes were recorded. Histologic response was defined as <15 eos/HPF and remission as <5 eos/HFP. Results: A significantly greater number of patients responded to OVB (33/48, 68.8%) compared with FP (8/20, 40%) (P=0.033). There was a higher tendency to achieving remission in the OVB group (22/48, 46%) vs, the FP group (7/20, 35%), but this was not statistically significant (P=0.4). There was also a significantly greater difference in the change of absolute eos/HPF change from pre- to post- therapy in the OVB group (-32.9) vs. FP (-17.9), (P=0.047) and in the post-treatment peak eos/HFP in the OVB group (11.9) vs. FP (29.65), (P=0.016). In those treated with OVB, there were significantly greater number of patients without asthma who had a histologic response compared to those with asthma (P=0.031). In patients receiving OVB, the delivery vehicle (sucralose or Duocal™) did not have a statistically significant impact on histologic response. Among all patients, those who self-reported poor compliance were less likely to achieve histologic response following treatment (P <0.001). Patients who failed initial therapy and required a treatment course of different steroids where more likely to have received FP as the initial treatment (P=0.005). Conclusion: Treatment with OVB leads to better histologic outcomes than FP. Using Duocal™ as the OVB delivery vehicle is just as effective as sucralose. Compliance is a major determining factor in response to either treatment.

37 *EOSINOPHILIC ESOPHAGITIS IN A RACIALLY DIVERSE COHORT OF CHILDREN*

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Background: Eosinophilic esophagitis (EoE) is a chronic allergic inflammatory disease characterized by clinical esophageal dysfunction and pathologic evidence of dense eosinophilia in the esophagus. Current literature indicates that up to 90% of patients with EoE are Caucasian, whereas the pediatric EoE population treated at Children's National Health System is approximately 50% African American. Our group has previously reported that African American children present more severely and may be less likely to respond to standard EoE treatment.

Objective: This study evaluated the variability in presentation of patients who developed remission with treatment with those who did not in a racially diverse cohort with EoE.

Methods: A retrospective chart review was performed on patients diagnosed with EoE during a 3-year period. Remission was defined as complete symptom resolution and less than 15 eosinophils per high-power field in response to a specific therapy. Presenting symptoms, insurance status, age at diagnosis, race, sex, coexisting atopic disease, and treatment type were compared between remission and non-remission groups.

Results: The total study population included 30 patients and showed a male to female ratio of 2:1. Unlike prior studies, African American patients (43%) made up a larger proportion of the study population. Mean age of symptom onset differed based on race: African American (0.55 years) versus Caucasian (6 years). Common presenting symptoms included vomiting (70%), abdominal/chest pain (40%), poor growth (40%), and dysphagia (17%). Comorbid atopic conditions were seen in the study population including food allergy (63%), allergic rhinitis (63%), asthma (46%), and atopic dermatitis (43%). Initial endoscopy revealed a mean eosinophil count of 40 eosinophils per high-power field (distal) and 42 eosinophils per high-power field (mid). Of the 30 patients, only 8 (26%) went into complete clinical and pathologic remission. No differences between remission and non-remission groups were noted in each of these baseline characteristics: race (p 0.54), sex (p 0.71), insurance (p 0.312). However, there was an increased prevalence of baseline atopic dermatitis among patients with remission (p 0.035).

Conclusions: Baseline atopic dermatitis may predict likelihood of treatment response in children with EoE. Additional treatment modalities are needed for this difficult to treat pediatric disease.

39 *COST ANALYSIS OF DIET VS. STEROID THERAPY FOR THE TREATMENT OF PEDIATRIC EOSINOPHILIC ESOPHAGITIS*

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Background: The standard of care for the treatment of eosinophilic esophagitis (EoE) include either pharmacologic with steroids or elimination diet therapy. Effectiveness of different treatments have been studied but there is no data on cost comparison of different treatments in children.

Methods: Medical records relating to hospital charges and physician fees associated with the diagnosis and treatment of several pediatric patients with EoE treated with steroids, elemental diet and empiric four food elimination diet were analyzed. Also reviewed were pre- and post-diet therapy food diaries of patients to determine the costs of the different treatments to the patients. Costs were averaged from several patients to obtain this data. Parents were also contacted about their perceptions on the cost of their child's EoE treatment. Several assumptions were made to determine the average cost of each treatment including costs related to clinic follow up, the number of endoscopies, cost of the formula for those on elemental diet therapy including costs related to administration and generic medications.

Results: The initial diagnosis related costs for all patients was $18,808. The first year costs from steroid therapy were $35,732, for elimination diet was $78,325 and elemental diet incurred a cost of $45,762. During the second year of treatment patients treated with steroids incurred charges of $23,229, those on elimination diet, $15,546 and on elemental diet $44,880. The items making up the costs are 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 difficulties finding the right foods at the start of the treatment and the need to visit multiple grocery stores to find the right foods, and the increased cost of the groceries was also an impediment. The parents' perceived benefit of completing elimination diet therapy was identification of the specific food(s) triggering their child's EoE.

Conclusion:

In the first year of treatment, the cost of steroid therapy is lowest among the three treatment options. In the second year the costs with steroid treatment, though lower than in the first year, are higher than the costs of elimination diet.

Cost Comparison of Different Treatments for EoE

	Diagnosis	Steroid Therapy			Elimination Diet			Elemental Diet		
		Year 1	Year 2	Subsequent Years	Year 1	Year 2	Subsequent Years	Year 1	Year 2	Subsequent Years
Physician Consult	X	X	X	X	X	X	X	X	X	X
Allergy Consult	X									
Dietitian Consult					X	X	X	X	X	X
PPI Therapy	X									
EGD	X	X	X	X	X	X	X	X	X	X
Food					X	X	X			
Formula + Minimal Food								X	X	X
Steroid Medication		X	X	X						
Allergy Testing	X									
Labs	X	X	X	X	X	X	X	X	X	X
DEXA		X	X	X	X	X	X			
TOTAL COST	\$18,808	\$35,732	\$23,229	\$23,229	\$78,325	\$15,546	\$15,546	\$45,762	\$44,880	\$41,714

*40 *AUTOPHAGY-RELATED GENE 7 (ATG7) MAY SERVE AS A BIOMARKER OF EOE DISEASE STATUS*

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Introduction: The hallmark of Eosinophilic esophagitis (EoE) is eosinophil infiltration into the esophageal epithelium; however, additional pathologic features and markers of disease activity may aid in distinguishing EoE from other disorders such as Gastroesophageal Reflux Disease (GERD) and Proton Pump Inhibitor- Responsive Esophageal Eosinophilia (PPI-REE). Autophagy is a lysosomal degradation pathway through which cells break down unnecessary or dysfunctional components in response to a variety of physiologic and stressors. Alterations of autophagy-related gene (ATG) expression have been implicated in a variety of inflammatory diseases, however, have not yet been studied in EoE. Methods: Pediatric human esophageal biopsies from subjects with active EoE (≥15 eosinophils (Eo) per high-power field (hpf)), inactive EoE (<15 Eo per hpf), GERD and non-EoE control patients without esophageal inflammation were evaluated for markers of autophagy. qRT-PCR was utilized to study mRNA expression of a panel of ATGs. Transmission electron microscopy (TEM) and immunohistochemistry (IHC) were performed to confirm findings of upregulated autophagy, evaluating for epithelial autophagic vesicle (AV) content and expression of cleaved LC3, respectively. The students T test was used to analyze all data. Results: mRNA expression of ATG7 was elevated in subjects with active EoE (n=27) compared to subjects with EoE Remission (n=24)($p = p < 0.01$) and normal subjects (n=28) ($p < 0.01$). ATG-7 was also elevated in subjects with active EoE (n=27) compared to subjects with GERD (n=6) ($p < 0.01$), suggesting this finding may be specific to EoE-associated inflammation. Furthermore, logistic regression analysis of ATG-7 in this population revealed an odds ratio of 12.36 (p=0.002), suggesting that ATG7 may serve as a tissue biomarker for active EoE. TEM revealed significantly increased autophagic vesicle content in esophageal epithelial cells from subjects with active EoE (n=11) when compared to EoE Remission (n=7; $p < 0.01$) and normal subjects (n=7; $p = 0.05$). IHC revealed significantly upregulated active, cleaved LC3 expression in subjects with active EoE (n=15) compared to EoE Remission (n=9; $p < 0.05$) and normal subjects (n=9; $p < 0.05$). Conclusions: Indices of activated autophagy are elevated in the esophageal epithelium of human pediatric subjects with active EoE compared to those with inactive EoE and non-EoE controls. Specifically, ATG-7 expression in pediatric human esophageal epithelial biopsies is upregulated in subjects with active EoE and may potentially serve as a tissue biomarker for EoE disease status. This may be of particular value in patients who undergo endoscopy prior to adequate reflux therapy. Further studies are needed to evaluate autophagy markers as non-invasive biomarkers and to explore the mechanistic role of autophagy in the pathogenesis of EoE.

42 *EFFECTIVENESS OF TEST DIRECTED AND EMPIRIC ELIMINATION DIET IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS*

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The major dietary interventions used for eosinophilic esophagitis (EoE) include elemental diet, test-directed elimination diet and empiric removal of the major food allergens (4, 6 or 8-food elimination diet). The reliability of allergy testing in guiding elimination diet is still debated. We previously found that atopy patch testing (APT) allowed identification of foods contributing to eosinophilic esophagitis in 38% of cases. We subsequently used skin prick testing (SPT) in addition to APT in an attempt to increase the yield of allergy testing for the identification of foods responsible for EoE. Between February 2011 and June 2014, with few exceptions, all new patients diagnosed with EoE (biopsies with > 15 eosinophils/hpf and either a normal impedance study or absence of histological response to 2 months of PPI therapy) underwent SPT and APT. Elimination diet based on results of APT and SPT was recommended as first line therapy. For patients with a large number of positive tests (generally > 10), 6-food elimination diet (dairy, soy, wheat, eggs, nuts/peanuts, fish/shellfish) was recommended. A follow-up endoscopy was performed after at least 2 months of elimination diet and 3 biopsies were obtained from the middle and distal esophagus. Histological response was defined as a peak eosinophil count of 5 or less. We analyzed the effectiveness of combined SPT and APT and of 6-food elimination diet.

A total of 103 new patients with EoE were evaluated during that period. 58 patients were excluded from this analysis for the following reasons: 13 patients did not have both APT and SPT or had a technical problems with APT; 3 patients received two simultaneous treatments; 1 patient received inhaled steroids, which appeared to affect esophageal eosinophilia; 26 patients were treated with topical steroids; 15 were lost to follow-up. 35 patients (25 male) restricted their diet based on results of allergy testing; 10 patients (7 male) went on an empiric elimination diet (6-foods for 9 patients, 4 foods for one patient).

Esophageal eosinophilia resolved in 12 of 35 patients (34 %) who went on a test-directed diet and in 6 of 10 (60%) who went on an empiric elimination diet. In the group of patients on test-directed diets, age at diagnosis (mean; SD) did not differ between responders (8.78;4.85) and non-responders (9.62;5.84; P=0.53). The same was true for empiric elimination

diet: 7.85 +/-5.25 yrs for responders, 9.69+/- 2.98 yrs for non-responders. The number of foods detected by allergy testing did not differ between the 2 groups either: 6.42+/-2.91 for responders; 7+/- 3.57 for non-responders (P=0.38).
In our group of patients, the addition of SPT to APT did not increase our ability to identify the foods causing eosinophilic esophagitis. Empiric elimination of the major allergens yielded better results.

44 *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 the diagnosis of EoE, or as a biomarker of disease activity has not been established. The aim of this study is to: 1) determine the diagnostic utility of endoscopic features, and 2) assess if endoscopic changes after treatment correspond to histologic findings.
Methods: EoE was diagnosed based on the 2011 consensus guidelines. Children undergoing diagnostic upper endoscopy and those diagnosed with EoE undergoing follow-up endoscopy were included. Endoscopic findings were evaluated using a previously-described EoE Endoscopic Reference Score, that incorporates 5 major endoscopically identified esophageal features of EoE: edema, rings, exudates, furrows and strictures (EREFS). Findings were correlated with esophageal eosinophil counts, and the prevalence, sensitivity, specificity, positive (PPV) and negative (NPV) predictive values for each finding was determined for diagnostic and follow-up endoscopy. Remission was considered as a peak eosinophil count of <15 eosinophils/hpf (eos/hpf).
Results: Data from 188 diagnostic endoscopies and 431 follow-up endoscopies was evaluated in 315 children (mean age 9.7 years, 58% male, 78% white at diagnosis and mean age 9.5 years, 77% male, 82% white at follow-up). At diagnostic endoscopy, 79 children met criteria for a diagnosis of EoE. Endoscopic abnormalities were present in 86% of patients with EoE and included furrows (84%), edema (66%), exudates (52%) and rings (16%); 77% had multiple findings. At follow-up, active disease (≥15 eos/hpf) was present in 206 endoscopies and 81% of these had endoscopic abnormalities that included furrows (69%), edema (65%), exudates (42%) and rings (22%); 64% had multiple findings. Inflammatory endoscopic findings, which include edema, furrows and exudates, correlated with significantly increased eosinophil counts at diagnostic and follow-up endoscopy ($p<0.001$). There were no patients with stricture at diagnostic or follow-up endoscopy. For each additional endoscopic finding, eosinophil counts increased by 17 (diagnostic) and 15 (follow-up) eos/hpf. The presence of multiple inflammatory endoscopic findings at diagnostic endoscopy had a sensitivity of 75%, specificity 96%, PPV 94%, and NPV 84%. At follow-up, the presence of similar findings had a sensitivity of 63%, specificity 87%, PPV 82%, and NPV 72%. Pre- and post-treatment longitudinal data, available for 44 patients in remission, indicated 80% had complete or partial resolution of endoscopic abnormalities.
Conclusions: In children with EoE, the prevalence of abnormal endoscopic findings at diagnosis is 86%. The presence of multiple inflammatory endoscopic findings appears to be a reliable biomarker for active EoE. Most patients in remission have complete or partial resolution of endoscopic abnormalities.

45 *INCONSISTENT REMISSION CRITERIA IS A CONSISTENT ISSUE IN THERAPEUTIC TRIALS FOR EOSINOPHILIC ESOPHAGITIS*

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Background: Elemental diets, dietary elimination, and steroid therapies are the most common therapies in clinical trials for eosinophilic esophagitis (EoE). While endoscopic findings and symptom resolution are commonly reported in therapeutic trials, histologic findings (usually reported as eosinophils per microscopic high powered field (hpf)) remain the most common endpoint used to define response. Yet, the threshold for defining "response" and "remission" are ill-defined among consensus guidelines and may vary from study to study.
Method; We conducted a systematic literature review of articles on eosinophilic esophagitis, published between January 2005 and April 2015, in which histologic remission was the primary endpoint of treatment. We abstracted treatment information and definitions of histologic remission or response. Comparison of definitions of histologic remission across and within institutions was performed.
Results: A total of 29 studies were examined. Forty-one percent were conducted among children and 24% were randomized control trials. The treatments included elemental diet (17%), dietary elimination (35%), steroid (35%) and others (13%). Histologic definitions of remission of EoE ranged from ≤15 eosinophils/hpf to ≤1 eosinophils/hpf. The most common definition of remission was ≤ 5 eosinophils/hpf. A more stringent definition of remission (≤ 5 eosinophils/hpf) was used

more frequently among medication trials and trials of elemental diet. Remission was more inconsistently defined among food elimination trials. Definition of remission varied from trial to trial, even within the same center and among the same authors.
Conclusion: Clinical and histologic improvements are important measures of treatment effect. Histologic findings should be the most objective of the findings, and optimally should provide a method for comparing effectiveness of various treatments. Yet, our findings suggest a lack of consistent remission criteria in published trials. This inconsistency is highlighted at times by varying definitions among the same authors within the same institution. Among published reports, trials of medications and elemental diets tend to use a more stringent definition of remission than trials of dietary elimination. In light of these inconsistencies, it is difficult to compare effectiveness of various treatments. There is a need for definitive definition of histologic remission.
Definition used for histologic remission, all studies (N=29)

Eosinophils/HPF	N (%)
≤5	16 (55)
≤10	6 (21)
≤15	7 (24)

HPF--high powered field
Definition of histologic remission, by treatment type

	Eosinophils per high powered field		
	≤5	≤10	≤15
Treatment	N (%)	N (%)	N (%)
Elimination diet	4 (44)	2 (22)	5 (45)
Steroid	6 (60)	4 (40)	0
Elemental diet	3 (60)	2 (40)	0
Other	5 (63)	1 (12)	2 (25)

Other includes monoclonal antibodies, proton pump inhibitors

46 *COMPARISON OF THE GASTRIC FLUID MICROBIOME OF CHILDREN WITH AND WITHOUT EOSINOPHILIC ESOPHAGITIS*

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory disease of the esophagus characterized by tissue eosinophilia in the presence of a variety of upper GI symptoms. In adults, changes have been described due to PPI exposure with alterations in the gastric pH and in inflammatory conditions of the esophagus. Microbiota of the upper GI tract may have effects on barrier function and immune tolerance in patients with EoE. Therefore, we sought to investigate whether the gastric microbiomes differ in children with and without EoE, and if so, do these changes correlate with disease activity. We also assessed whether PPIs alters patient microbiota.
Methods: Gastric fluid samples were obtained from children ages 4-18 years who underwent endoscopy for dysphagia, reflux-like symptoms or disease surveillance between December-2011 and August-2014. DNA was extracted using the GeneJET Genomic kit and PCR was used to amplify the V4 region of the 16S ribosomal RNA gene. 16S amplicons were pooled and sequenced using an Ilumina MiSeq sequencer. The Ribosomal Database Project software was used to make taxonomic assignments. Significant differences at the taxa level were assessed by ANOVA. Medication data and dietary history at the time of endoscopy were recorded.
Results: 101 patients were recruited in the study but only 70 had detectable DNA in their samples. Based on the results of the esophageal biopsies (n=70), the samples were divided into 5 groups; controls (n=22), EoE-New (n=5), EoE-Active (n=16), EoE-Remission (n=19) and reflux esophagitis (n=8). EoE-Active (10.81%) and EoE-New (10.72%) had a higher proportion of order *Pasteurellales* vs. controls (6.63%); (p=0.04 and 0.07, respectively). There was relative abundance of order *Enterobacteriales* in EoE-Active (1.78%) and EoE-Remission (1.10%) compared to the other groups (<0.3%, p=NS). There were no significant differences in the microbiota of the EoE-Remission, reflux and control groups. 49% of patients were receiving proton pump inhibitors (PPIs). Order *Bacteroidales* was significantly more abundant in the PPI (+) controls (41.77% vs. 26.74%; p=0.02) whereas the relative proportion of *Lactobacillales* was higher in the PPI (-) controls (26.73%

vs. 16.59%; p=0.14). The results showed similar trends when the microbiomes of the entire cohort and were compared based on PPI use but did not reach the predetermined levels of significance.
Conclusions: Patients with active EoE have subtle changes in their gastric microbiome compared to healthy controls. Gastric dysbiosis may be most prominent during periods of active inflammation. PPI use is associated with expansion of order *Bacteroidales* and relative scarcity of order *Lactobacillales*, especially in healthy subjects. Further studies with larger cohorts are needed to determine specific microbiome differences and their significance, which may provide further insights into the pathogenesis of EoE.
Relative abundance of orders Lactobacillales and Bacteroidales based on proton pump inhibitor use.

	Lactobacillales (% abundance)			Bacteroidales (% abundance)		
	PPI+	PPI-	p-value	PPI+	PPI-	p-value
Controls (n=22)	16.59%	26.73%	0.14	41.77%	26.74%	0.02
Controls + Reflux (n=30)	22.39%	26.60%	0.43	35.40%	26.13%	0.06
Total cohort* (n=66)	25.44%	27.20%	0.51	27.69%	25.10%	0.27

47 *STRESS ASSOCIATED WITH PEDIATRIC EOSINOPHILIC ESOPHAGITIS*

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Background: Eosinophilic Esophagitis (EoE) is an increasingly common, chronic disease that can manifest in children by non-specific symptoms. While previous studies identified the impact of EoE on health-related quality of life (HRQoL) and psychosocial aspects of development, little attention has been paid to the stress that can be experienced by patients and care givers (CGs) of affected children.
Hypothesis and Aims: We hypothesized children with EoE and their CGs experience high levels of stress. The aims of this study were to characterize and measure parent/child psychosocial stressors and explore the impact of EoE on parent-perceived sibling behavior.
Methods: We performed a prospective study to measure stress experienced by parents and patients attending the American Partnership for Eosinophilic Diseases (APFED) patient education conference. Parents of children with EoE were asked to complete a series of questionnaires that measured CG stress (EoE stress Questionnaire-EoESQ); CG anxiety (State-Trait Anxiety Inventory-STAI); CG burden of food allergy (FA) (FAQoL Parental Burden questionnaire); HRQoL (HRQOL Peds QL Eosinophilic Esophagitis Module, V.3 - Parent Report/Child Report); child anxiety (Screen for Child Anxiety Related Disorders-SCARED); and child depression (Revised Children's Anxiety and Depression Scale: RCADS).
Results: Thirty-eight CGs (84% mothers, 92% Caucasian, mean age 39.4 yrs+/-4.9, SD) having a child (mean age 7.8 yrs +/-3.9 SD) diagnosed with EoE and 17 children (mean age 11.5, +/- 2.5 SD) provided self-report information. CGs indicated the most stressful element was related to delay in obtaining a diagnosis. (Table 1). CG stress and anxiety were highly correlated with financial strain, food preparation and family mealtimes (Table 1). CG state anxiety was significantly correlated with HRQoL overall score r (38) = -0.52, p = .02 and FAQoL-PB overall score, r (38) = 0.41, p = .03. PedsQL (mean cut off score <=37) demonstrated that 50% of children endorsed high frequency (Often, Almost Always) worry, anger and sadness related to food allergies and specialized diet. Children also indicated clinical levels of generalized anxiety as measured by the SCARED (mean score >25) while CG's perceived their children to be at risk for major depression (RCAD: mean T score >60). The EoESQ identified that 73% of children with EoE had one or more siblings and CGs identified acting out (21%) and jealousy (18%) as observed sibling behaviors.
Conclusions: CGs of and children with EoE experience stress and psychological distress (anxiety, depression) that is related to disease and treatments, especially treatments that involve dietary restrictions. Results suggest that psychological interventions aimed at coping with dietary restrictions and treatment could be benficial to CGs and children diagnosed with EoE.

Table 1: CG Stress/Anxiety: EoESQ - STAI: N=38

Factor	Not at all = 1	Somewhat = 2	Moderate = 3	Significant = 4	Severe=5
How stressful was it for your child to experience symptoms with no EoE diagnosis?	n=4 11%	n=3 8%	n=5 12%	n=14 37%	n=12 32%
Financial stress associated with cost of specialized foods. *r(38) = .54, p=.0005	n=4 11%	n=8 21%	n=7 18%	n=9 24%	n=10 26%
Stress associated with food preparation *r(38) = .38, p = .02	n=1 2%	n=8 21%	n=8 21%	n=12 32%	n=9 24%
Stress associated with family mealtimes *r(38) = .42, p = .01	n=5 15%	n=8 21%	n=6 16%	n=12 32%	n=6 16%
Financial stress associated with medical appointments.	n=10 26%	n=6 16%	n=8 21%	n=8 21%	n=6 16%

*Correlation CG stress and State Anxiety Mean Score

48 *DISORDER SPECIFIC PAIN AND ITS RELATIONSHIP WITH SLEEP IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS*

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Objective: This study aims to examine pain and sleep in children with Eosinophilic Esophagitis (EoE). EoE is a chronic inflammatory gastrointestinal disorder marked clinically by symptoms of upper gastrointestinal distress and by histologic findings of increased eosinophils in the esophagus. Initial studies have found that children with EoE have poorer health and well-being compared to children without EoE. Pain and sleep are important health factors related to well-being that have yet to be adequately addressed in children with EoE.

Methods: 22 children with EoE and 20 healthy children ages 4-12 years have been recruited along with their caregivers. Parents completed measures addressing their child's recent experiences of symptoms, including pain. Each child then wore an actigraphic sleep monitor for 12 days to evaluate sleep patterns.

Results: Children with EoE experiencing pain (N = 13) had 33.32 minutes less of total sleep each night than children with EoE not experiencing pain (N = 9), and 52.92 minutes less sleep than healthy children ($p<.05$). Children with EoE spent 12.35 minutes more awake after sleep onset than healthy children ($p<.01$). Children with EoE and pain experienced 80.71% efficient sleep as compared to the 82.17% efficiency of children with EoE and no pain and the 87.13% efficiency of healthy children ($p<.05$). Cohen's d effect sizes in the difference between healthy controls and children with EoE and pain ranged from medium to large.

Conclusions: Children with EoE who experience pain related to this disorder sleep less and have poorer sleep quality compared to children with EoE who do not experience pain and healthy children. It is possible that the experience of pain as well as disturbed sleep may be related, at least in part, to the health and well-being difficulties often experienced by children with EoE. Additional research addressing this possibility seems warranted.

49 *THE SEASONALITY OF EOSINOPHILIC ESOPHAGITIS FLARES IN CHILDREN AND ADOLESCENTS IN ARIZONA*

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Background: Eosinophilic esophagitis (EoE) is characterized by immune-mediated clinico-pathologic chronic esophageal inflammation with an incompletey described pathogenesis. Prior studies have shown a clear relationship between food allergens and EoE. While previously implicated, less is known regarding the role of aeroallergens in the disease pathogenesis. No studies to date have examined the role of aeroallergens and seasonality in relapse, or "flares," of patients in remission. Furthermore, the relationship between EoE and Arizona's unique desert allergen profile has not been described.

Methods: A retrospective study was performed by analyzing data from patients aged 5 to 18 years with diagnosis of EoE seen by the Phoenix Children's Hospital Pediatric Gastroenterology Department between June 2010 and June 2011.

Outpatient gastroenterology visits coded with ICD-9 Code 530.13 for eosinophilic esophagitis and associated endogastroduodenoscopies were identified. Following application of exclusion criteria, the data included 326 clinical visits and 148 patients. All patients were in remission at the beginning of the study. Demographic information, allergy status, and other disease co-morbidities were identified. Flares were defined as recurrence of symptoms of dysphagia, odynophagia, food impaction, abdominal pain, feeding refusal or severe food selectivity expressed by the patients or observed by the parents *and/or* histologic evidence of 15 or greater eosinophils per high power field on esophageal biopsy. A control group was identified as patients that did not experience flare as evidenced by defined EoE symptoms and/or histological evidence of eosinophilia within 8 weeks prior to the study. Arizona seasons were defined as: spring from February 15 to June 15, and fall from September 1 to November 30, according to the typical pattern of peak aeroallergen seasons. To analyze incidence and season of EoE flares, statistical methods used included Chi-square tests and logistic regressions.
Results: Our patient population was aged 5 to 18 years (mean age 10.8 years, SD 3.9 years) and included 101 males (68.2%) and 47 females (31.7%). Ninety-four of 148 patients (63.5%) flared during the study period. An increased incidence of flares in the fall compared with other seasons was statistically significant ($p = 0.041$). Flares in the spring also had an increased incidence. The flare rate was especially high in October. Of the 94 patients that flared, 70 patients (74.5%) had environmental allergy, 83 (88.3%) had food allergy, and 66 (70.2%) had both environmental and food allergy. Patients without GERD and without autism had a greater percentage of flares than those without GERD or autism.
Conclusions: We found a seasonal variation in the incidence of EoE flares in Arizona. A statistically significant increase in the incidence of flares in fall, a peak allergen in Arizona, may suggest a role for aeroallergens in the relapse of EoE disease.

*51 *PROPOFOL USE IN PEDIATRIC PATIENTS WITH SUSPECTED FOOD ALLERGY AND EOSINOPHILIC ESOPHAGITIS*

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Background: Propofol (2-6 diisopropylphenol) is a commonly used sedative agent in children undergoing endoscopy. Its use in children with soy and/or egg protein allergy is controversial due to concern that propofol may contain these allergens. A number of case reports and two smaller retrospective studies support the use of propofol in patients with egg and soy allergy but no studies have examined this issue in children with eosinophilic esophagitis (EoE), a population that undergoes frequent sedation.
Hypothesis and Aims: We aimed to 1) determine the rate of propofol use in pediatric patients with egg and/or soy allergy undergoing upper endoscopy; 2) compare the frequency of propofol use in patients with and without EoE and 3) describe complications in patients with egg and/or soy allergy who received propofol. We hypothesized that propofol is commonly used in patients with food allergy and its use is without significant adverse effects in patients with EoE or food allergy.
Methods: A retrospective observational study of all EGDs performed on pediatric patients 0 to 18 years of age between January 1, 2013 and June 30, 2014 was conducted using EPIC screening. Allergy history, comorbidities and procedural events were determined using chart review. Patients were considered allergic if it was documented in the chart irrespective of allergy testing results. Data was analyzed using multivariable logistic regression and Fisher's exact test.
Results: Of the 1,366 total EGDs performed, 1,285 unique patients were included in this study. Forty- eight anesthesiologists performed sedations. Two hundred one EGDs were performed on egg or soy allergic patients. Two hundred fifty six EGDs were performed on patients with EoE. Propofol was used in 68% of all procedures performed. Among patients without egg or soy allergy, it was used in 72% of procedures. Among patients with egg or soy allergy, propofol was used in 40% of all procedures. After controlling for patient age, history of anesthetic complications, as well as presence of egg and/or soy allergy, patients without EoE were significantly more likely to receive propofol than those with EoE ($p = 0.04$). Patients without EoE were 40% more likely to receive propofol than those with EoE (95% CI for OR 1.018, 1.926). The two possible complications observed in allergic patients receiving propofol included 1) easily-controlled nausea and vomiting and 2) coughing and rhonchi at discharge in a patient who had a recent URI and cough at the time of procedure. No anaphylactic reactions occurred. Amongst patients with soy and/or egg allergy, there was no significant difference in possible anesthesia complications in those who received propofol versus those who did not ($p = 0.70$).
Conclusions: Propofol is commonly used in patients with EoE and those with suspected food allergy.

INFLAMMATORY BOWEL DISEASE

53 *MISCLASSIFICATION OF REMISSION: ARE WE MISSING THE BOAT RELYING ON PATIENT REPORTED OUTCOMES (PROS) IN CLINICAL TRIALS?*

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Background/Aims: The PCDAI has been utilized to assess outcomes in clinical trials. The FDA is encouraging the use of patient reported outcomes (PROs) in addition to an objective measure of disease (e.g., endoscopy) to serve as co-primary

endpoints in pediatric Crohn's Disease (CD) clinical trials. As there is no validated pediatric CD PRO at this time it is inviting to use the PRO domains in the PCDAI as a surrogate. We sought to explore functioning of the PRO elements of the PCDAI. Methods: Data from the Pediatric IBD Collaborative Research Group Registry were limited to children with moderate to severe CD (PCDAI>30) at diagnosis to increase generalizability to patients targeted for pediatric CD clinical trials. Remission was defined by a total PCDAI score of ≤10. Assessments took place at baseline (prior to therapy), 12 weeks, and 1 year. The three subjective items on the PCDAI, abdominal pain (AP), stooling (ST), and general well-being (WB), were examined together as AP+ST (PRO A) and AP+ST+WB (PRO B). 0 scores were inferred to indicate that patients had "inactive" disease if based on PRO A (0 scores on both components) or B (0 scores on all three components) scores alone, where scores >0 indicated "active" disease. New scores on PRO A and PRO B were compared to disease activity classification based on full PCDAI scores. Relationships between PRO A, PRO B, and lab markers were examined using Pearson correlations. Results: 203 patients with complete PCDAI data at baseline and 12-weeks were included (mean±SD age 11.7±2.7 years, 55% male). At baseline, if disease activity was based on PRO A, 4 patients would have inactive disease (2 patients based on PRO B), and thus would be excluded from a clinical trial for patients with moderate-severe disease (Table). At the 12 week follow-up, 38 patients (29%) who were in remission (based on full PCDAI) would be classified as having active disease if based on PRO A, where 41 (32%) of patients would be said to have active disease if based on PRO B. For nonremitters at 12 weeks, 16 (22%) of patients would now meet criteria for remission if disease activity was based on PRO A criteria alone, and 14 (19%) of patients previously nonremitters would become classified as remitters if based on PRO B scores. Similar results were found when examining the misclassification of remitters/nonremitters at 1 year. The correlations between baseline PRO A and PRO B with baseline hemoglobin, ESR, and albumin were small and nonsignificant (p>.10). Conclusions: Reliance on subjective patient reported items alone, as currently measured on the PCDAI, could result in erroneous reporting of treatment effect though misclassification of remission. This misclassification would seriously impact feasibility of pediatric clinical trials, requiring larger sample sizes to be able to demonstrate a significant difference for an effective intervention.

	PCDAI component scores, n (%)			
	All 0	All 5	All 10	Mix of 0,5,10
Baseline, n = 203 PRO A	4 (2.0)	44 (21.7)	22 (10.8)	133 (65.5)
PRO B	2 (1.0)	30 (14.8)	13 (6.4)	158 (77.8)
Remitters at 12 weeks, n = 130 PRO A	92 (70.8)	4 (3.1)	0	34 (26.2)
PRO B	89 (68.5)	0	0	41 (31.5)
Non-remitters at 12 weeks, n = 73 PRO A	16 (21.9)	17 (23.3)	1 (1.4)	39 (53.4)
PRO B	14 (19.2)	9 (12.3)	0	50 (68.5)

AP+ST=PRO A; AP+ST+WB=PRO B

54 *CLINICAL CHARACTERISTICS OF VERY EARLY-ONSET INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED COHORT*

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BACKGROUND: Very early-onset (VEO) inflammatory bowel disease (IBD) is estimated to be 3-5% of pediatric-onset patients. VEO IBD patients tend to have more isolated colonic disease at presentation, but often progress to Crohn disease later in life. VEO IBD is increasing in incidence, suggesting that environmental factors may be involved in pathogenesis. We sought to describe the phenotype of VEO IBD in a population-based cohort, and to examine effect of birth-related factors such as cesarean birth rates, in a case-control study.

METHODS: We performed a retrospective review of all patients ages 0 to 18 years old diagnosed with IBD in the Intermountain western United States from 2005 to 2011. We extracted patient demographics, birth certificate data, including mode of delivery (vaginal or cesarean) and maternal characteristics for each patient. Liver biopsy and cholangiography data was extracted, if available. We compared demographics and analyzed certain clinical characteristics of VEO IBD against pediatric IBD patients.

KEY RESULTS: Within our cohort of 608 IBD patients, 5% (31/608) were VEO IBD patients. When compared to IBD, VEO IBD patients were more likely to have subtype of ulcerative colitis (68% vs. 55%, p = 0.01) and be non-Caucasian ethnicity (20% vs. 8.6%, p = 0.024). Primary sclerosing cholangitis (PSC) was diagnosed in a larger proportion of VEO IBD (14.3% vs. 4.9%, p=0.018). There was no clinical significance in VEO IBD prenatal characteristics, birth delivery method, birthweights, nor sex, when compared to IBD patients.

CONCLUSION: Our findings confirm that VEO IBD is more likely to have a colonic phenotype and disproportionately affects patients with non-Caucasian ethnicity. We found no evidence that deliver method was associated with early onset of IBD. The higher proportion of VEO IBD patients with PSC may be another unique aspect of this phenotype, and should be studied further.

55 *CORRELATION OF THE POINT-OF-CARE AND SEND-OUT CALPROTECTIN ASSAYS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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Background: Fecal calprotectin, a neutrophil- derived protein, has emerged as one of the most promising non-invasive biomarkers for the detection of active and subclinical disease activity in inflammatory bowel disease (IBD) monitoring. However, one of the major limitations in the use of fecal calprotectin is the length of time required for results, which is currently 10 to 14 days. A point-of-care (POC) assay can result in a quantitative calprotectin level in 15 minutes.

Aim: To estimate the correlation between the POC and the send-out assay for quantitative calprotectin levels in a pediatric IBD cohort.

Methods: Patients with known IBD were eligible for enrollment. Stool was collected in consented patients and divided equally into two samples. One sample was sent for standard ELISA calprotectin testing. The other sample was tested immediately after collection using the rapid Quantum Blue® calprotectin immunoassay which involved extracting the stool and diluting it with buffer then placing it on a test cartridge that is read by a specialized reader. Calprotectin results were reported within 15 minutes after collection.

Results: 48 patients with IBD were enrolled in the study. Results were analyzed in groups based on the standard ELISA test result for each sample. The mean calprotectin level for each group was as follows: calprotectin < 50 (ELISA 24.6, rapid 52.78; p=0.0296), 50-200 (ELISA 94.4, rapid 204.5; p=0.1589), 200-500 (ELISA 279.3, rapid 607.6; p=0.0241), >500 (ELISA 1278.0, rapid 879.6; p=0.998).

Conclusion: There was no statistically significant difference in the fecal calprotectin levels between our current standard ELISA testing and the novel rapid immunoassay method. This new immunoassay testing may provide a more rapid indication of disease activity in patients with IBD and allow for tighter disease control.

57 *INCREASING THE USE OF ENTERAL THERAPY IN PEDIATRIC CROHN DISEASE USING A SYSTEMATIC QUALITY IMPROVEMENT APPROACH: RESULTS AND CLINICAL OUTCOMES*

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Introduction: Enteral nutrition therapy (EN) is a safe and effective treatment modality for induction of remission in patients with Crohn's disease (CD). Despite its widespread use as first line therapy in many parts of the world, EN has been largely underutilized in the United States due to multiple perceived barriers. We implemented a standardized protocol which help providers, discuss, initiate, and overcome barriers related to EN. We hypothesized that implementing this protocol using a quality improvement-based approach would increase utilization of EN and successfully induce remission of CD.

Methods: Following a literature review, consultation with other medical centers, and feedback from our providers, an algorithm for administration of EN was developed and implemented in July 2013. Tools were developed for providers to more effectively discuss EN with patients and families, initiate the correct amount of formula, record use within the electronic medical record, and document medical necessity. Dietitians provided patient follow - up and providers assessed response to therapy. For induction of remission, children were given polymeric formula meeting 90-100% of their caloric requirements, most commonly by mouth, over a 12-week period.

To assess improvement in utilization, we compared the average number of patients per month who were prescribed EN before and after implementation of the protocol. Clinical outcomes were assessed for children ≤21 years with active CD and no history of intestinal resection that completed a minimum of 8 of the 12 weeks of EN between July 2013 and December 2014. The short pediatric Crohn's disease activity index (sPCDAI), body mass index (BMI), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin, and hemoglobin were compared before and after induction with EN.

Results: The average number of patients starting EN increased from 0.6 patients per month before to 3.5 after implementation of the protocol (580% increase in use). Between July 2013 and December 2014, a total of 62 patients started EN, of those patients, 22 (35%) completed 12 weeks of induction. 21 children met criteria for evaluation of medical outcomes, 12 (57%) were male and 18 (86%) were White. Average age at diagnosis was 13 ± 2.6 years. The majority (81%) had ileocolonic disease, and 4 had perianal phenotype. EN was started within 4 weeks of diagnosis for 17 (80%) patients. EN provided an average of 1885 ± 320 calories daily, which accounted for 89% ± 2.6 of total caloric requirement. After an average of 11.2 ± 2 weeks following initiation of EN, fifteen patients (71%) were in remission. There was a significant reduction in sPCDAI from 31.5 ±19 to 10.7 ±13 (p <.0001). ESR also decreased significantly from 26 ± 14 to 16 ± 9 (p < 0.001). Changes in BMI, CRP, albumin, and hemoglobin were not statistically significant. Seven (33%) children reported adverse effects, including nausea, bloating, and dislike of caloric restriction.

Conclusion: Systematic implementation of tools designed to increase utilization of EN is effective in overcoming perceived

barriers and therefore increasing the acceptance of primary enteral therapy. Remission was successfully achieved in children who completed induction therapy with EN.

59 *INFECTIONS IN CHILDREN RECEIVING ANTI-TNF ALPHA THERAPIES FOR INFLAMMATORY BOWEL DISEASE*

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Background: TNF alpha inhibitors (anti-TNFa) are commonly used for the treatment of inflammatory bowel disease (IBD). Adult data suggest an increased risk of infections; the etiology of pediatric infections has not been well characterized.

Methods: Retrospective review of children with IBD treated with anti-TNFa and laboratory-confirmed infections who received medical care at Nationwide Children's Hospital from 1/08 -12/13. Demographic, clinical, laboratory, and outcome data were reviewed. Infectious events were classified as mild or serious. Serious events were defined as hospitalization, IV antimicrobials, or deemed life-threatening. One event may include concomitant infections. Descriptive and non-parametric statistics were applied (significance $p<0.05$).

Results: 143 events were diagnosed in 90/267 (34%) children receiving anti-TNFa; 30 (33%) patients had ≥ 2 events. First infection occurred a median of 207.5 days [range 6 d - 5.6 y] after starting anti-TNFa. Patients with infection began anti-TNFa therapy at a younger age than those without infection (median 14.7 vs 15.8 y, p=0.007). There were no significant differences in number or severity of infectious events among patients receiving anti-TNFa monotherapy vs combination immunosuppressants. 53 (37%) of all events (Table 1) were classified as serious: 41 in children with CD, 12 with UC; patients were treated with infliximab (n=46; 5-10mg/kg once-q8wks), adalimumab (n=5; 40mg q2wks), or both (n=1), or golimumab (n=1; 50mg once). Patients with serious events had a higher PCDAI score than patients with mild events (median 25 vs 10, p=0.0085), but no differences in PUCAI. The median duration of hospitalization was 4 days [range 1-43]. Anti-TNFa was held in 7 serious and 2 mild events. 96 mild infections occurred in 65 patients. Patients with mild events were more likely to have underlying CD or IBDU (p=0.049), have a PGA score of remission or mild (p=0.014), be on anti-TNFa for a longer time (p=0.005), and be started on anti-TNFa at a younger age (median 13.9 vs 15.4 y, p=0.013) when compared with patients with severe events.

Conclusions: Our cohort of IBD patients had a higher frequency of serious infections than reported in the literature, occurring in the first year of anti-TNFa therapy. Continued detailed microbiological data of infections and prospective evaluations are warranted in children with IBD receiving anti-TNFa to determine whether anti-TNFa therapy independently increases risk of infection and to help guide management.

Table 1

	Serious Infections (n=53)				Mild infections (n=96) *Infections that occurred concomitantly with a serious infection and coded as a serious event		
Gastrointestinal							
		Intra-abdominal abscess Peritonitis Perirectal abscess	1 5 11		Esophagitis	Candida*	4
	Colitis	C difficile Campylobacter CMV Giardia Plesiomonas Rotavirus	10 1 5 1 1 1		Acute gastroenteritis	C difficile associated diarrhea Aeromonas Salmonella Plesiomonas Edwardsiella Crytosporidium	27 4 1 2 1 1
Respiratory							
	Pneumonia	Mycoplasma Influenza Human Metapneumovirus	2 1 1				
					Pharyngitis Rhinopharyngitis	Group A Streptococcus Adenovirus Rhinovirus Adenovirus	15 1 2 1
Systemic							
		Histoplasmosis Varicella Bartonella LTBI	5 2 1 1				
				Genitourinary		UTI STI*	10 10
Other							
		Oral HSV Skin/soft tissue abscess Pyelonephritis	1 2 1			Oral HSV* Skin/soft tissue Mononucleosis EBV viremia* Varicella Toxocara	1 8 2 4 1 1

60 *MEASURING ADHERENCE IN ADOLESCENTS AND YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASES*

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Background: Adherence patterns in adolescents and young adults (AYA) with inflammatory bowel diseases (IBD) are often problematic and understudied. For example, a recent study found that only 15-25% of older adolescents were 80% adherent to their oral medication regimens. We sought to: 1) describe patterns of adherence in AYA with IBD; 2) examine associations among different adherence behaviors; and 3) explore demographic and cognitive correlates of specific adherence behaviors.

Methods: 16-20 year olds with Crohn's disease and ulcerative colitis were recruited during outpatient GI clinic appointments at three Midwestern children's hospitals. AYA self-reported adherence via the 4-item Morisky Medication Adherence Measure (MMAM); scores of 0 indicate high adherence, 1-2 indicate medium adherence, and 3-4 indicate low adherence. AYA rated their cognitive functioning via the Metacognition Index of the Behavior Rating Inventory of Executive Function (BRIEF) with greater scores indicating greater impairment. Physicians rated disease severity via the Physician Global Assessment (PGA) Scale.
Results: Of the 43 participants, 30% reported high adherence, 58% reported medium adherence, and 12% reported low adherence. Item analysis indicated 65% of participants reported "sometimes forgetting medication" while 26% reported missing medication "within the last two weeks." Fourteen percent reported stopping their medication without telling their physician because it made them "feel worse" and 7% reported sometimes stopping medication when they perceived their IBD was under control. Only 2 of these 4 adherence items were significantly correlated with one another. Specifically, AYA who reported "sometimes forgetting medication" were more likely to report "missing medication within the last two weeks" (p=.04). Females were more likely to stop medication without telling their physician because it made them "feel worse" (p=.02). Those diagnosed more recently were more likely to stop their medication when they perceived their IBD was under control (p=.02). Age, disease severity, and cognitive functioning were not significantly associated with adherence.
Conclusions: AYA self-report variable adherence patterns on the MMAM, a simple tool that may be clinically useful in identifying adherence patterns in AYA. While some adherence behaviors may be interrelated, not all are. Thus, it is important for providers to consider each behavior independently when using the MMAM. Providers should target female AYA assessment and intervention around managing unwanted medication side effects. Future research is warranted to understand barriers to females communicating with their physicians, and what specific physical complaints result from certain medication regiments. Additionally, providers should emphasize education around consistent adherence even during symptom remission among those more recently diagnosed. Future research should also focus on further exploring adherence patterns in AYA and validate these findings in a larger population beyond those with IBD.

61 *ASSESSING DISEASE ACTIVITY IN PEDIATRIC CROHN'S DISEASE (CD): CAN WE RELY ON SUBJECTIVE OR OBJECTIVE PARAMETERS ALONE?*

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Background & Aims: Accurate, reproducible, and feasible assessment of disease activity in CD is critical in evaluating response to therapy. The PCDAI combines patient report, laboratory parameters, growth, physical exam, and extraintestinal manifestations (EIM). The Food and Drug Administration (FDA) began an initiative to critically appraise items of the PCDAI to identify those that drive change from moderate/severely active disease scores to remission. Knowing the importance of selected items in reflecting change in disease state will be helpful in designing improved measures of activity. Methods: Data from children with moderate to severe CD (PCDAI>30), with complete PCDAI at diagnosis and 12 weeks, from the Pediatric IBD Collaborative Research Group Registry were analyzed. Percentage contribution of PCDAI components to baseline and post-treatment scores were determined. Logistic regression used changes in individual PCDAI components to predict remission status at follow-up assessment. Remission was defined by a PCDAI score of ≤10. Results: 203 Registry patients (mean±SD age 11.7±2.7 years, 55% male) were treated across centres, with 64% in remission at 12 weeks. At baseline, the 3 symptom domains (abdominal pain, stooling, well-being) accounted for 42% of total score, growth 19%, and labs 27% (Table). Abdominal exam, perirectal exam and EIM contributed little to the total PCDAI score (≤5% each). Percentage contribution of changes in PCDAI subscores (at 12 weeks) to total PCDAI change were 42% for the symptom domains, 19% for growth, 6% for abdominal exam, and 27% for labs. Minimal contributions to change in PCDAI score were made by changes in perirectal (2%), or EIM (4%) scores. The collective contribution of PCDAI change scores from baseline to 12 weeks correctly predicted remission status of 86% of patients (Table). When the model was limited to individually significant predictors, abdominal pain, stooling, ESR, albumin, weight and height velocity remained, correctly classifying 87.7% of patients. Similar analyses were carried out examining "objective" (lab values, weight, height, abdominal exam, perirectal disease, EIM) vs. "subjective" (abdominal pain, stools, general well-being) parameters of disease activity. Objective or subjective measures resulted in a lower classification of remission status (76 and 79% respectively) at 12 weeks. Conclusions: Although classification of remission status using subjective or objective PCDAI questions was better than chance accuracy, these items correctly classified fewer patients than the full PCDAI scale or a representative composite of six questions.

	Baseline PCDAI	12 week PCDAI	BL to 12w Δ score
Total PCDAI, mean±SD	44.1±10.3	10.7±10.0	-33.4±13.8
	% contribution to total score		%
Abd pain	16.6	19.8	15.6
Stools	11.3	12.7	10.8
Well-being	14.0	9.5	15.5
HCT	4.6	6.7	3.9
ESR	7.3	12.1	5.8
Albumin	15.4	8.8	17.5
Weight	13.7	4.4	16.7
Height velocity	5.2	15.0	2.1
Abd exam	5.6	5.1	5.8
Perirectal	2.7	3.9	2.4
Extraintestinal	3.5	2.1	3.9

63 *ROUTINE PREMEDICATION WITH INTRAVENOUS METHYLPREDNISONE CAN PREVENT THE NEED FOR DOSE INTENSIFICATION OF INFLIXIMAB IN CHILDREN WITH CROHN DISEASE*

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Background: Significant subsets of patients with IBD receiving infliximab (IFX) develop antibodies to IFX (ATI) and loss of response. We hypothesized that administration of corticosteroids prior to IFX infusions prevents loss of response to IFX. Aims: To evaluate if intravenous methylprednisolone (IVMP) given prior to IFX in children with IBD (CD and UC) is associated with a reduction in dose escalation and/or preserving dosing interval and to analyze if premedication with IVMP delays formation of ATI and prevents infusion related adverse reactions (AE). Methods: A chart review was performed of patients with IBD who received IFX from 2009 to 2012 and who had ≥6 months follow up following standard IFX induction. Routine IVMP premedication was administered based on the preference of the ordering physician. Patients with IBD who received routine IVMP prior to IFX infusions were compared to patients who did not receive IVMP. The duration, dose and frequency of IFX infusions, IFX and ATI levels, and frequency of AE and disease flares were recorded. Dose escalation was defined as ≥ 20% increase in absolute IFX dose and increase in dose frequency as ≥ 1 week reduction in dosing interval. Any escalation was defined as either dose escalation or increase in frequency. No patients had prior infusion reactions to IFX. Differences between groups were assessed using student's t-tests and chi-square/exact tests. Results: Complete data were available in 147 patients (61% male; 72% CD). Mean age ± SD at diagnosis of IBD was 12.7 ± 3.6 years and at IFX start was 14.7 ± 3.6 years. IVMP premedication was given to 73 (50%) patients. For patients with CD (n = 107; 52 Premedication, 55 no-premedication), dose was increased in 11 (21%) vs. 18 (33%), frequency increased in 11 (21%) vs. 20 (37%) and any escalation in 14 (27%) vs. 25 (48%); $p<0.05$. For patients with UC (n = 40; 21 premedication, 19 no=-premedication), dose was increased in 7 (33%) vs. 3 (16%), frequency increased in 8 (38%) vs. 4 (21%), and any escalation in 11 (52%) vs. 6 (32%), (NS). Overall, IFX infusions were stopped in 21 (29%) premedication vs. 17 (23%) no-premedication patients. Among them, severe infusion reactions occurred in 8 (38%) vs. 7 (41%) patients. In the premedication group, 13 (18%) patients were switched to a different biologic vs. 11 (15%) in the no-premedication group. In all, concomitant immunomodulator therapy was used in 9 (12%) patients in the premedication group vs. 15 (20%). Of the 147 patients, 91 (49 receiving premedication) had at least 1 IFX/ATI levels checked (mean ± SD from IFX start to first ATI level = 8.8 ± 6.4 months). ATI were present in 12/49 (24%) vs. 5/42 (12%) patients. Conclusion: In children with CD, routine premedication with methylprednisolone decreased the need for dose adjustments/decreasing dosing interval of IFX. Limitations of this retrospective study include small patient numbers, possible confounders differentiating the pre-med and no pre-med groups, and lack of IFX/ATI levels in all patients. A prospective placebo controlled study could help to further delineate the effect of methylprednisolone premedication on efficacy of IFX infusions.

65 *GROWTH RETARDATION AND PSYCHOSOCIAL FUNCTIONING IN THE CONTEXT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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BACKGROUND: Inflammatory bowel disease (IBD) impacts development in children. Symptoms and therapies often effect a child's daily functioning, growth and maturation, consequently impacting their psychosocial adjustment. Awareness of the diverse psychobiologic effects of IBD on development is essential in providing holistic care for pediatric patients. The current study examines growth parameters, age at diagnosis, and timing of psychosocial evaluation as predictors of psychosocial outcomes.

METHODS: Psychosocial and growth parameters were collected retrospectively from 76 children (mean age= 14.2 years; 55.3% female) with IBD seen for psychosocial evaluation at a single institution. The majority of children were diagnosed with Crohn's disease (CD; 73.7%), 25.0% with ulcerative colitis (UC) and 1.3[DL1] % with indeterminate colitis. 32.3% of children [DL2] were newly diagnosed (psychosocial evaluation conducted within 3 months of diagnosis). Growth was assessed using age and gender specific Z-scores for height and weight. Psychosocial adjustment was measured using child self-report and parent-report questionnaires. Children completed the Child Depression Inventory (CDI), the Screen for Anxiety Related Disorders—Child Version (SCARED-C), and the Multidimensional Anxiety Scale for Children (MASC). Parents completed the Child Behavior Checklist (CBCL) and the Screen for Anxiety Related Disorders—Parent Version (SCARED-P). Hypotheses were tested using bivariate correlations and linear regression.

RESULTS: Newly diagnosed children reported higher rates of total anxiety on the MASC ($t = -2.06$, $p = .04$) and greater panic/somatic symptoms ($t = -2.18$, $p = .04$) and total anxiety ($t = -2.69$, $p = .02$) on the SCARED-C. Similarly, parent-reported social anxiety on the SCARED-P was significantly higher for these children, $t = -2.77$, $p = .01$. Children with CD had significantly lower z-scores for weight than children with UC. Across all children, weight was negatively correlated with harm avoidance on the MASC, $r = -.38$, $p < .01$. For children with CD, weight was negatively correlated with harm avoidance ($r = -.42$, $p < .05$), social anxiety ($r = -.36$, $p < .05$), and total anxiety ($r = -.43$, $p < .01$) on the MASC. In contrast, height was positively correlated with social anxiety, $r = .58$, $p < .01$. Further, the relation between weight and parent-reported social anxiety was significantly moderated by age at IBD diagnosis: weight was negatively correlated with social anxiety for [JK3] older youth (mean age= 15.69 years), and there was no relation between weight and social anxiety for younger children (mean age= 8.23 years), $r = -.30$, $p = .05$.

CONCLUSION: Children newly diagnosed with IBD are at higher risk for anxiety than children who have been treated for greater than 3 months. Furthermore, low weight is a risk factor for anxiety, particularly for children with CD, and this risk may be greater for children who are diagnosed in adolescence. Integrated medical and psychosocial support is important in the care of children and adolescent with IBD.

68 *PLASMA-INDUCED TRANSCRIPTIONAL SIGNATURE REVEALS INDUCTION OF IMMUNOREGULATORY MOLECULES IN TREATMENT-NAÏVE PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD)*

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In IBD, cytokines and other mediators are released at high concentrations in the inflamed GI mucosa. These are then released in to the peripheral circulation where they serve as important mediators of the systemic inflammatory process. However, peripheral cytokine levels are difficult to measure, and studies of peripheral cytokine profiles have yielded inconsistent results. Furthermore, measurement of a single or few cytokines may be uninformative as combinatorial effects are likely important. Alternatively, we have used a sensitive and comprehensive genomics-based assay whereby plasma-borne mediators are used to drive transcription in a well-controlled healthy peripheral blood mononuclear cell (PBMC) population.

Methods: Plasma-induced transcriptional analyses were conducted on plasma samples of 29 Crohn's disease (CD) patients, 15 ulcerative colitis (UC) patients, and 10 unrelated healthy controls (HC) with no family history of autoimmune disease. The transcriptional responses were measured using the Affymetrix GeneChip® human genome U133 plus 2.0. Differentially expressed transcripts were defined as FDR <1%, Fold change >1.4, ANOVA $p < 0.05$. Ontological analysis was performed using the DAVID annotation tool (http://david.abcc.ncifcrf.gov/) and Ingenuity Pathway Analysis (IPA) package. Receptor blocking studies were used to validate candidate mediators underlying the plasma induced signatures.

Results: In unsupervised analyses, the transcripts induced by IBD (CD and UC) plasma clustered distinctly from uHC plasma. We identified 1,224 differentially expressed probe sets between IBD and HC groups. There were 985 differentially induced transcripts in the CD group and 895 transcripts in the UC group compared to HC. About 54% (656) of 1224 regulated transcripts were common to both CD and UC. More than 3/4th of the transcripts were significantly downregulated by IBD plasma compared to HC. Unexpectedly, relative to HC plasma, IBD plasma suppressed the transcription of

numerous immune signaling molecules and receptors including IL-1, TNF family members, IL-6 and various chemokines. Ontological analysis of upregulated genes by CD plasma identified enrichment of molecules involved in response to viruses, and immune responses; upregulated probe sets by UC plasma identified enrichment of transcripts related to apoptosis and immune responses. The downregulated probe sets showed enrichment of molecules involved in cytokine response, inflammatory response and TLR signaling. Upstream regulatory analysis revealed activation of IL-10 and Smad7 and inhibition of TNF, IL-1, IL-17A and IL-6. Receptor blocking studies utilizing receptor neutralizing antibodies towards IL-10R and TGFβR directionally reversed induction of ~75% of the CD: HC signature confirming the presence of TGFβ and IL-10 as components of the overall cytokine milieu.
Conclusions: IBD plasma induces a distinct gene expression signature compared to uHC plasma. IBD plasma contains factors that predominantly suppress pro-inflammatory pathways in reporter PBMC. TGFβ and IL-10 contribute to this immunosuppressive signature in CD. The activation of Smad7 is likely the reason for unresponsiveness to TGFβ and the paradoxical immunosuppressive signature in the face of the overall inflammatory phenotype.

*70 *FACTORS ASSOCIATED WITH A DURABLE RESPONSE TO INFLIXIMAB IN PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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BACKGROUND: Infliximab is often used to treat children with inflammatory bowel disease (IBD). Although highly effective initially, a significant proportion of patients ultimately lose their response to treatment. The aim of this study was to identify factors associated with a durable response to infliximab.
METHODS: Patients under the age of 21 years with IBD who completed induction therapy with infliximab were identified. Age, gender, C-reactive protein level at induction and Week 14, Paris classification data, prior and concomitant use of immunomodulators were recorded. Patients with 1 year of follow-up were included. Patients with a primary non-response to IFX were excluded from the analysis. Primary response was defined as improvement in clinical symptoms as judged by treating clinician and proceeding to IFX maintenance therapy without corticosteroid dose escalation during IFX induction therapy. A CRP value <8mg/L was considered normal. Patients who were lost to follow-up were censored at the time of loss to follow-up. Data were compared using Fisher's exact test.
RESULTS: A total of 227 patients with pediatric IBD were included (179 with Crohn's disease (CD), 46 with ulcerative colitis (UC) , 2 with IBD-U) who received an average of 17.3 IFX infusions. The average age of IBD onset was 13.1 years and the group included 20.8% with A1a disease and 61.6% with A1b disease. IFX was started within 1 year of IBD diagnosis in 50.2%. A primary response was noted in 89% of patients. The durability of infliximab at 1 year was 77.9%. Durable response at 1 year was similar between CD and UC (79.5% vs. 71.1%, p=0.28). Baseline CRP elevation, concomitant use of immunomodulators, and the time between diagnosis and beginning IFX induction therapy were not associated with a durable response. A normal CRP level at Week 14(p=0.003), normalization of previously elevated CRP at Week 14 (p<0.001), and the prior use of immunomodulators (p=0.039) were associated with a durable response of IFX at 12 months.
CONCLUSION: Pediatric IBD patients demonstrate a durable response to IFX at 12 months. Normalization of CRP during IFX induction therapy is a strong predictor for durable response at 12 months.

73 *RELATIONSHIP OF THE PEDIATRIC CROHN'S DISEASE ACTIVITY INDEX (PCDAI) AND CROHN'S DISEASE ACTIVITY INDEX (CDAI) IN IMAGINE 1*

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Introduction: The Pediatric Crohn's Disease Activity Index (PCDAI) assesses disease activity in children and adolescents with Crohn's disease (CD), and was developed to take into account more objective measures than the Crohn's Disease Activity Index (CDAI). Although both indices have similar components, the PCDAI includes additional laboratory measures and disease features specific to children and adolescents with CD. In IMAgINE 1, a 52-week (wk), phase 3, multicenter, randomized open-label induction/double-blind maintenance trial of adalimumab (ADA) in 192 patients aged 6-17 yrs with CD, both PCDAI and CDAI were calculated for patients aged 13-17 yrs.[1] This post-hoc analysis evaluated concordance of remission status based on PCDAI and CDAI.
Methods: Patients in IMAgINE 1 had CD with a baseline PCDAI score >30 and were intolerant or resistant to conventional therapy. Patients received open-label ADA induction at weeks 0/2 based on body weight (≥40 kg, 160/80mg; <40 kg, 80/40 mg). At wk 4, patients were randomized to higher (≥40 kg, 40 mg every other wk [eow]; <40 kg, 20 mg eow) or lower dose (≥40 kg, 20 mg eow; <40 kg, 10 mg eow) ADA maintenance therapy. The agreement of PCDAI remission (PCDAI score ≤10) and CDAI remission (CDAI score <150) at wks 26 and 52 was evaluated in both dosing groups combined. Non-responder imputation was used for missing data.

Results: Of 188 patients who entered the double-blind maintenance period of IMAgINE 1, 122 were aged 13-17 yrs. PCDAI remission rates at weeks 26 and 52 were 37% (45/122) and 31% (38/122), respectively; CDAI remission rates at weeks 26 and 52 were 51% (62/122) and 36% (44/122) , respectively. At wk 26, 36% (44/122) patients achieved both PCDAI and CDAI remission, and 48% (59/122) had neither PCDAI nor CDAI remission (Table); thus, the agreement between measures was 84% (Kappa=0.6899; p<0.001) At wk 52, 30% (37/122) patients achieved both PCDAI and CDAI remission, and 63% (77/122) had neither PCDAI nor CDAI remission (Table); thus, the agreement between measures was 93% (Kappa=0.8535; p<0.001).
Conclusions: Agreement among PCDAI and CDAI was moderate to substantial at weeks 26 and 52. However, CDAI may over estimate remission in pediatric CD given the higher overall rates of remission by this metric. The agreement of PCDAI and CDAI with other outcome measures requires further exploration.
[1]Hyams JS, et al. *Gastroenterology* 2012;143:365-74.
Table. Concordance and discordance of PCDAI remission and CDAI remission in patients aged 13-17 yrs with CD treated with ADA in IMAgINE 1.

Week	PCDAI remission & CDAI remission n (%)	No PCDAI remission & no CDAI remission n (%)	Concordant n (%)	No PCDAI remission & CDAI remission n (%)	PCDAI remission & no CDAI remission n (%)	Discordant n (%)
26	44 (36.1)	59 (48.4)	103 (84.4)	18 (14.8)	1 (0.8)	19 (15.6)
52	37 (30.3)	77 (63.1)	114 (93.4)	7 (5.7)	1 (0.8)	8 (6.6)

74 *OUTCOME FOLLOWING AMINOSALICYLATE THERAPY IN CHILDREN NEWLY DIAGNOSED WITH CROHN'S DISEASE: A PROSPECTIVE MULTI-CENTER REGISTRY EXPERIENCE*

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Background/Aims: Despite a paucity of data supporting efficacy 5-aminosalicylate (5-ASA) use in pediatric Crohn's disease (CD) is common. We sought to describe the patterns/outcomes of 5-ASA use in a large multicenter inception cohort of children with CD. Methods: Data were obtained from the Pediatric IBD Collaborative Research Group Registry, a prospective observational study of newly diagnosed children with IBD. Patient data are recorded at diagnosis, 30 days, and quarterly. Patients are managed by physician dictate. Disease activity is classified by physician global assessment (PGA). The primary outcome was corticosteroid (CS)-free inactive CD at 1 yr following start of 5-ASA within 30 days of diagnosis (±CS) without the need for rescue therapy with IM, anti-TNFα agents, or surgery. Secondary outcome was PGA mild following similar constraints. Results: Of 1442 Registry patients with CD 440 received 5-ASA ± CS only within 30 days of diagnosis and had ≥1 yr of follow up (5-ASA n=177, 5-ASA+CS n=263) (study population). There were no differences in age, gender, disease distribution, baseline behavior, or Hb in the two groups. Baseline PGA was significantly different: mild, moderate, severe was 62%, 35%, 3% for the 5-ASA only group vs. 30%, 54%, 6% for the 5-ASA+CS group (p<0.001). Mean ESR (mm/hr) and albumin (g/dL) were significantly different between the 5-ASA only vs. 5-ASA+CS groups, respectively: 27±16 vs. 34±20 (p<.001), 3.62±0.57 vs 3.32 ±0.65 (p<.001). The table shows one year outcomes. For 5-ASA (±CS) treated patients 25% were PGA inactive, CS-free without rescue at one year with another 8% being PGA mild. For those treated initially with 5-ASA only the primary outcome was achieved in 39% of those with mild PGA vs 25% of those moderate/severe (p<.02). For those treated with 5-ASA+CS the primary outcome was achieved by 24% of those with mild PGA vs 16% of those with PGA moderate/severe (p<.04). Amongst patients with mild disease the primary outcome was achieved by 52% of those with small bowel disease, 34% of those with colon only disease, and 28% of those with both (p=0.07). In a multivariate model, achieving the primary outcome was significantly associated with both mild disease severity at diagnosis (p<.01), and absence of CS use within the first 30 days after diagnosis (p<.02). Baseline lab values were not independently associated with outcome. Conclusion: CS-free inactive disease without rescue was noted in 25% of 5-ASA (±CS) children overall though PGA moderate/severe and concomitant CS use early were associated with poorer outcomes, likely secondary to more significant disease. A small percentage of patients with newly diagnosed CD have good outcomes with early 5-ASA use. Questions that remain include dosing schedules and whether mucosal healing accompanies symptomatic improvement.

	CS-Free, PGA inactive, no rescue	CS-Free, PGA mild, no rescue	Other
5-ASA ± CS (study population N=440)	108/440 (25%)	37/440 (8%)	67%
5-ASA only N=177	60/177 (34%)	28/177 (16%)	50%
5-ASA only PGA mild N=110	43/110 (39%)*	21/110 (19%)	42%
5-ASA only PGA moderate/severe N=67	17/67 (25%)*	7/67 (11%)	64%
5-ASA+CS N=263	48/263 (18%)	9/263 (4%)	78%
5-ASA + CS PGA mild N=78	19/78 (24%)#	5/78 (7%)	69%
5-ASA +CS PGA moderate/severe N=185	29/185 (16%)#	4/185 (2%)	82%

*p<0.02; #p<0.04

75 *EVALUATION OF HEALTH-RELATED QUALITY OF LIFE IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE*

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Introduction: Pediatric patients with inflammatory bowel disease (IBD) report decreased quality of life, especially in various mental and social health domains. Various treatment regimens have also been shown to impact quality of life. The goal of this study was to determine whether having a lower quality of life score in one of the specific sub-domains of mental and social health (anger, anxiety, depression, and peer relationships) is associated with lower scores across other sub-domains. If such an association exists, clinicians may be able to employ quick screening of pediatric inflammatory bowel disease patients for decreased quality of life in one sub-domain of mental and social health in order to identify patients at risk for lower scores across the other sub-domains.

Methods: We recruited pediatric patients with inflammatory bowel disease and their parents to complete a survey on quality of life measures. The NIH validated PROMIS surveys were utilized to evaluate mental and social health sub-domains of quality of life, including anger, anxiety, depression, and peer relationships.

A retrospective chart review of these same patients was also conducted to determine whether any particular data points could be considered potential risk factors for patients with lower mental and social health quality of life scores. These data points included the following: age at diagnosis, gender, history of growth retardation, treatment history, presence of extra-intestinal manifestations, frequency of follow-up visits, PCDAI and PUCAI, vitamin and mineral deficiencies, vaccination history (for hepatitis B, hepatitis A, human papillomavirus, pneumococcal, and influenza), annual ophthalmology and dermatology visits, complications (such as stricture, fistula or surgery), and frequency of surveillance endoscopy and colonoscopy.

Results: Results are pending as data collection is ongoing. Data collection is expected to be completed by August 2015.

Key Words: inflammatory bowel disease, quality of life

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77 *A PROSPECTIVE STUDY OF CONCORDANCE AMONG PHYSICIANS FOR CLASSIFICATION OF NEW ONSET PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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BACKGROUND/AIMS Crohn's disease (CD) is differentiated from ulcerative colitis (UC) based on symptoms, endoscopic appearances, mucosal pathology, and small bowel imaging. Systematic literature review by a NASPGHAN working group (Bousvaros *et al.*, 2007) addressed controversial features that lead to inconsistency in labeling of type of IBD as CD/UC/IBD-Undefined (IBD-U). We aimed to determine the concordance among IBD specialists in diagnosing type of IBD in a national pediatric multicenter inception cohort study.

METHODS The Canadian Children IBD Network enrols children aged < 17 yrs newly diagnosed with IBD at pediatric IBD centres. Anonymized data including symptoms and reports of baseline endoscopy, pathology, magnetic resonance enterography, ultrasound, and serology are uploaded onto a central on-line database. Three central reviewers (JC, AG, HH) independently assign type of IBD (UC, CD, IBD-U favoring UC, IBD-U favoring CD, IBD-U). Concordance among central reviewers and with local site was assessed using kappa statistics. Features contributing to discordance and implications for therapy were determined.

RESULTS The 3 central reviewers independently assigned a concordant diagnostic label for 114 (84.4%) of 135 patients reviewed. Two of the 3 were concordant for an additional 20 (14.8%), making overall kappa=0.7375, $p<0.0001$. Site clinical diagnosis differed from the central consensus (2 or 3 out of 3 concordant) label for 16 (11.9%) (kappa=0.7133, $p<0.0001$). Each of these 16 have macroscopic left colonic disease, which was anticipated *a priori* to be more likely associated with discordant labeling. Variation in interpretation of upper tract and/or terminal ileal mucosal inflammation was associated with discordant labeling. Discordance of site diagnosis with panel consensus according to type of IBD is shown in Table 1. In 10 of 16 patients, discordance was between IBD-U and UC labeling with no therapeutic impact. Of 5 patients labeled by local sites as CD, but considered UC by the central panel, 2 received CD therapy that is non-evidenced-based for UC (exclusive enteral nutrition for 1, and methotrexate maintenance for another). Prednisone therapy followed by thiopurine maintenance, evidence-based for both CD and UC, was given to 2 of 5. 5-ASA maintenance given to 1, whilst not evidence-based for CD, is evidence-based for UC. One patient, considered CD by the panel, but labeled IBD-U locally, received prednisone followed by 5-ASA maintenance, which is not evidence-based for CD.

CONCLUSIONS Most IBD is consistently labeled as CD/UC/IBD-U. Discrepant diagnosis of CD and UC, whilst uncommon, has early therapeutic implications. Short-term treatment is not affected by variation in the use of IBD-U label, but more long-term implications for decision-making may exist. Feedback and discussion with local sites is planned with the goal of increasing concordance in diagnosis over time.

Table 1. Central panel consensus diagnosis vs. site diagnosis

Panel consensus diagnosis	Number (%) out of 135	Number discordant with site diagnosis (%)
CD	76 (56%)	1 (1.3%)
UC	42 (31%)	6 (14.3%)
IBD-U	16 (12%)	9 (56.3%)

80 *VITAMIN D INSUFFICIENCY IS ASSOCIATED WITH LACK OF RESPONSE TO INFLIXIMAB THERAPY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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Introduction: Low Vitamin D (VD) levels are common in inflammatory bowel disease (IBD) and have been associated with more severe IBD activity and increased risk for disease related complications. The role that VD plays in the response to treatment is poorly understood. We hypothesize that VD insufficiency is associated with a reduced response to infliximab (IFX).

Methods: Patients, whose VD levels were obtained within 3 months of initiation of IFX were included in this retrospective study. Demographic features and Paris classification were noted. Albumin, hemoglobin, hematocrit, erythrocyte sedimentation rate (ESR), C-reactive protein, 25 hydroxyvitamin D levels, and disease activity were evaluated at baseline and at week 14. A VD level below 30 ng/mL was considered to be "insufficient". The cessation of IFX before the 4th dose was defined as lack of response.

Results: Thirty seven (32 Crohn's disease, 5 ulcerative colitis) out of 107 patients evaluated had VD measurements available for analysis. The average age at the time of IFX initiation was 13.5±4 y (range 1.7-20.5y). VD insufficiency was identified in 22 of 37 (59.5%) patients. Prior to IFX, there were no differences in gender, race, IBD phenotype, season,

Paris classification or disease activity score between VD sufficient (VDS) and VD insufficient (VDI) groups. The mean decrease in the disease activity score after induction was similar in the two groups. However, in the VDI group the median ESR prior to IFX was 21 compared to 13, in the VDS group, p=0.045. During induction, the ESR in the VDI group decreased from 21 to 16; whereas, the ESR in the VDS group decreased from 13 to 2. Lack of response to IFX was observed in 36.4% of the VDI group, but in none of the VDS group, p=0.012.
Conclusion: These findings suggest that Vitamin D insufficiency may decrease the likelihood of response to anti TNF-α therapy.
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81 *HYPERLIPASEMIA IN PEDIATRIC INFLAMMATORY BOWEL DISEASES*
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Objectives: Acute pancreatitis is a rare complication of inflammatory bowel disease (IBD). This diagnosis can be difficult to make as many patients present with abdominal pain secondary to their underlying disease, but with simultaneous elevation in pancreatic enzymes. We sought to determine the frequency with which hyperlipasemia in pediatric IBD causes clinically relevant pancreatitis.
Methods: We conducted a retrospective chart review of 275 pediatric IBD patients presenting to a tertiary referral center between January 2010 and December 2012. The frequency of hyperlipasemia and the correlation with radiographic findings of pancreatitis were examined.
Results: Lipase was elevated in 19.3% of patients, but only 7.9% met clinical criteria for pancreatitis (including lipase ≥3 times the upper limit of normal). Thirty six percent (36%) of these episodes were attributed to drug-induced pancreatitis, 27.3% to acute infection, 27.3% to disease flare, and 9% to idiopathic pancreatitis. Altogether, only 22.7% of patients in our cohort with documented hyperlipasemia were diagnosed with pancreatitis. Notably, none of the patients with presumptive pancreatitis had radiographic findings to support this diagnosis.
Conclusions: Based on these observations, we conclude that hyperlipasemia may often be a nonspecific finding in pediatric IBD. Therefore, we recommend careful consideration when diagnosing pancreatitis in the setting of pediatric IBD.
Frequency of elevated serum lipase in the total study population and in different categories of IBD

	All Patients	CD	UC	IC
No. of Patients (%)	275 (100)	159 (57.8)	97 (35.2)	19 (6.9)
Lipase evaluated (%)	114 (41.5)	68 (42.8)	40 (41.2)	6 (31.6)
Elevated lipase (%)	22 (19.3)	12 (17.6)	10 (25)	0
Lipase ≥ 3x ULN (%)	9 (7.9)	5 (7.4)	4 (10)	0

CD = Crohn's Disease; UC = Ulcerative Colitis; IC = Indeterminate Colitis

82 *THE NATURAL HISTORY OF PEDIATRIC ULCERATIVE COLITIS IN THE ERA OF BIOLOGIC THERAPY*
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Background: The clinical outcomes of pediatric ulcerative colitis (UC) are not well known. Most of the population-based studies were conducted outside of the United States and prior to the introduction of biologic (anti-tumor necrosis factor α) agents in the standard treatment of pediatric UC. We aimed to describe the natural history of pediatric UC in the era biologic therapies.
Methods: We conducted a retrospective review of 152 pediatric patients at Texas Children's Hospital with a new diagnosis of UC between January 2003 and December 2009. The patient records were followed through July 2014. Localization of disease at diagnosis, use of steroids, immunomodulator therapy or biologic agents, presence of extraintestinal manifestations, and need for surgery at a minimum five year follow up were noted. A follow-up phone call was made to all patients who were lost to follow-up or transitioned to adult care within five years of diagnosis to assess these clinical outcomes. Only patients with a minimum of 5 years of follow up or need for surgery within the first 5 years of diagnosis were included in the final analysis.
Results: We identified 106 pediatric UC patients with a minimum of 5 years of follow up or colectomy within the first 5 years of diagnosis. Mean age at diagnosis was 10.7±4.1 years, with an average length of follow up of 6.5±1.9 years. Eight percent (8%) presented at diagnosis with ulcerative proctitis (E1), 12% had left sided disease (E2), 48% had extensive UC (E3), 18% had an incomplete scope at the time of diagnosis, and 13% did not have initial colonoscopic data available. Biologic medications were used in 36% of patients (97% infliximab, 10% adalimumab); 27% were treated with

immunomodulators (70% 6-mercaptopurine, 35% azathioprine, 13% methotrexate); 94% received 5-aminosalicylic acid therapy; and 90% were exposed to steroid therapy throughout the follow up period. Extra-intestinal manifestations occurred in 26 patients (25%). In respect to all patients, 4% had arthritis, 11% arthralgia, 10% had primary sclerosing cholangitis, 2% had autoimmune hepatitis, and 1% had aphthous stomatitis. Cumulative rate of colectomy was 20% at 5 years, with 8% progressing to colectomy within 1 year of diagnosis.
Conclusion: This is the largest pediatric cohort of UC patients with 5 year clinical outcomes. Compared to previous studies from the same geographic region in the pre-biologic era, pediatric UC patients in our cohort presented with more extensive disease and required a higher rate of colectomy; however, these rates are similar to other worldwide studies in the pre-biologic era. This work emphasizes the need for novel preventative and therapeutic measures to combat pediatric UC.

84 *BURDEN OF DISEASE IN PAEDIATRIC PATIENTS WITH MODERATE VERSUS SEVERE CROHN'S DISEASE IN THE IMAGINE 1 TRIAL*

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Introduction: Biologic therapy is generally reserved for children with moderate to severe Crohn's disease (CD), however, distinguishing moderate from severe disease by the Paediatric CD Activity Index (PCDAI) can be difficult.[1]
Aims & Methods: To compare disease burden in patients (pts) classified as moderate *vs* severe by PCDAI in IMAgINE 1,[2] a 52 week (wk) trial of adalimumab in which pts aged 6-17 years with CD and baseline (BL) PCDAI >30 were enrolled. All pts had failed concurrent or prior corticosteroids (CS) and/or immunomodulators (IMM) therapy. Infliximab (IFX)-exposed pts could enroll. BL characteristics, demographics, and the proportion of pts with a BL score of 10 (worst score) for at least one of the PCDAI components of abdominal pain (AP), stool frequency (SF), and general well-being (GW) were assessed in pts with moderate (PCDAI <40) and severe CD (PCDAI ≥40) as defined by the median PCDAI at BL.
Results: The intent-to-treat population included 188 of 192 pts enrolled. 43% (80) had moderate and 57% (108) had severe CD at BL. Demographics, CD activity, prior and concomitant CD-related IMM and CS use, prior IFX use, and IMPACT III scores at BL were similar for both groups (Table). Median CRP was numerically higher in pts with severe *vs* moderate CD (1.76 *vs* 0.65 mg/dL), but ranges largely overlapped. A similar proportion of pts with moderate and severe CD (83 *vs* 95%) had the most severe score of 10 at BL for at least one of the PCDAI components of AP, SF, or GW.
Conclusion: Clinical characteristics and treatments administered to pts with moderate or severe disease activity by PCDAI were similar. Overall, the disease burden in moderate pts was similar to severe pts in IMAgINE 1.
References: 1.Hyams et al JPGN 1991;12:439-47 2.Hyams et al Gastroenterol 2012;143:365-74
Table. Demographics and baseline characteristics by disease severity (intent-to-treat population)

	Moderate CD (PCDAI < 40) (N=80)	Severe CD (PCDAI ≥ 40) (N=108)
Age, years, mean (SD)	14.0 (2.4)	13.4 (2.5)
Male, n (%)	41 (51.3)	64 (59.3)
CRP, mg/dL, median (range)	0.65 (0, 16.8)[a]	1.76 (0, 14.4)
Prior CD-related immunomodulator use, n (%)	73 (91.3)	96 (88.9)
Prior CD-related corticosteroid use, n (%)	59 (73.8)	86 (79.6)
Prior infliximab use, n (%)	32 (40.0)	51 (47.2)
Concomitant CD-related immunomodulator use, n (%)	51 (63.8)	66 (61.1)
Concomitant CD-related corticosteroid use, n (%)	26 (32.5)	45 (41.7)
Disease duration , year, mean (SD)	3.1 (2.3)	2.9 (2.2)
PCDAI, mean (SD)	34.8 (2.4)	45.7 (5.5)
CD location, n (%)		
Anal/Perianal	20 (25.0)	34 (31.5)
Colon	67 (83.8)	87 (80.6)
Ileum	64 (80.0)	81 (75.0)
Draining fistulas, n (%)	12 (15.0)	24 (22.2)
IMPACT III score, mean (SD)	118.2 (16.1)[b]	112.0 (18.0)[c]
[a]N=78, [b]N=77, [c]N=104		

85 *PATIENT AND FAMILY PERCEPTION OF THE SPECIFIC CARBOHYDRATE DIET (SCD) IN INFLAMMATORY BOWEL DISEASE: AN ONLINE SURVEY*

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Background: Nutritional therapy for inflammatory bowel disease has been limited to exclusive enteral nutrition. However, more recent studies suggest possible efficacy of dietary management of inflammatory bowel disease, in particular the Specific Carbohydrate Diet (SCD). Given the limited data on its use, we created an anonymous online survey to better understand patient demographics, utilization and perception of the SCD.

Methods: The study was approved by SCH IRB (#15404). A survey was created using Redcap™, and the survey link was sent to known online websites and support groups.

Results: 501 individuals respond to the survey. 374 were adults 127 were children. Majority of individuals on the diet were female(71%). Age range was 0-10 years(13.1%), 10-17 years(18.9%), 17-40 (47%) and over 40(21.1%). Most individuals heard about the SCD from the internet (58.6%), friends/family(28.9%) or their healthcare provider(17.4%) Diagnoses were Crohn's (46%) and Ulcerative Colitis (43%) and indeterminate colitis (11%). 49.7% began SCD to avoid medication therapy, with 28.7% starting SCD because of only partial improvement with medical therapy, 30% reported no improvement with standard medical therapy and 19.6 % started secondary to having side effect from medication. The median amount of time on the SCD was 15 months, with the majority of respondents continuing for over 1 year. Almost half of the individuals on the SCD were on concurrent medications (n=223) with 57% on 5-ASAs, 21.5% on immunomodulators and 31.4% on biologics. When asked to rate overall severity of symptoms prior to starting the SCD, 80% rated their disease severity as either moderate or severe. Six months after starting SCD, only 12% of patients reported moderate or severe disease, and after 12 months of therapy only 5% reported moderate disease and less than 1% reported severe disease.

Conclusion: Though the SCD diet is unfamiliar to my medical practitioners, this diet is employed by many patients to treat their IBD as both adjunctive and primary therapy. Patients perceive a clinical benefit to use of the SCD despite the lack of rigorous scientific data. Further study is required to better understand dietary therapy for patients with IBD.

86 *A RETROSPECTIVE ANALYSIS OF FACTORS ASSOCIATED WITH HOSPITALIZATION IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE*

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BACKGROUND: Hospitalization rates for pediatric IBD patients have increased since the mid-1990s, and pediatric patients with IBD are at greater risk for readmission than older patients. Pediatric IBD patients have significantly greater inpatient healthcare utilization, complexity, and costs, with estimated annual inpatient pediatric burden of $152.4 million and 64,985 inpatient days. In the U.S. pediatric population, data pertaining to IBD hospitalizations is limited and few studies exist that describe the epidemiology associated with hospitalizations.

OBJECTIVE: Identify factors associated with frequency of hospitalization and long length of stay (LOS) (≥14 days) in pediatric IBD patients to strategize ways of reducing inpatient hospitalizations in this population.

METHODS: IRB-approved retrospective chart review of pediatric IBD patients hospitalized on the gastroenterology inpatient or consult services was performed at a single center between January 2008 and December 2013. Demographic data, date and type of diagnosis (Ulcerative colitis [UC], Crohn's [CD], indeterminate), and history of pain or surgical consultation, surgical procedure, parenteral nutrition, positive clostridium difficile PCR, penetrating disease (abscess, fistula, phlegmon, microperforation, perforation), and perianal disease were examined. Chi-square analysis and unpaired t-tests were performed.

RESULTS: Two hundred and six patients (56% male, mean age 12.48 ± 3.72 years at diagnosis) with IBD were hospitalized over the 5 year period, totaling 446 admissions.

No significant difference was observed between diagnosis type (CD or UC) and number of admissions or long LOS. Patients initially diagnosed in the hospital (vs. outpatient setting) had more frequent hospital admissions ($p<0.01$). Patients with long LOS were more likely to receive parenteral nutrition ($p<0.0001$), pain consultation ($p<0.0001$), scheduled opiates ($p<0.0001$), surgical consultation ($p<0.01$), surgical procedure ($p<0.01$), or have history of positive C. difficile PCR ($p<0.01$). CD patients with long LOS had more penetrating disease phenotype ($p<0.05$). No significant difference in number of admissions or LOS was observed between patients with Medicaid or private insurance ($p=0.995$, $p=0.886$). A relationship was noted between higher number of admissions and lower median income, though did not reach statistical significance ($p=0.077$). No association was observed between long LOS and average median family income ($p=0.807$).

CONCLUSIONS: No significant relationship was identified between patient socioeconomic status or insurance payer and LOS or number of hospitalizations in our IBD population. Multiple clinical care factors were identified as potential contributors to longer and more frequent hospitalizations. The identification of these factors in a specific subset of patients will now allow us to examine certain current institution-based practices and focus quality improvement efforts toward this patient population in an effort to decrease the length and number of hospitalizations in our pediatric IBD population, thereby improving patient care and reducing costs.

87 *INSURANCE COVERAGE OF CHILDREN AND YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE UNDER THE AFFORDABLE CARE ACT*

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BACKGROUND: 20-30% of patients with inflammatory bowel disease (IBD) present before age 18 yrs and will require transfer from pediatric to adult care. Vulnerability during transfer may be exacerbated by loss of insurance. An early provision of the Affordable Care Act (ACA) required eligibility for young adults to remain on parental private insurance until age 26 yrs. Nationally there has been a significant decrease in uninsured young adults since its implementation in September 2010. Little is known about insurance coverage for young adults with IBD and how it has been affected by this provision.

OBJECTIVE: To determine whether uninsurance and private insurance coverage in young adults with IBD has changed with extended dependent eligibility under the ACA.

DESIGN/METHODS: We conducted a cross-sectional analysis of hospitalized patients with IBD, identified in the Nationwide Inpatient Sample (NIS) using diagnostic codes, to estimate levels of insurance coverage. We analyzed the years 2006-2011 to include 4 years prior to and 1 year post-implementation. We compared coverage for 19-25 year olds (yo) with age groups not affected by the provision (2-18 and 26-35 yo) to account for underlying trends in coverage.

RESULTS: From 2006-2010 19-25 yo had the highest proportion uninsured with a peak of 14.5% 2010 (See Table). In 2011, the proportion of uninsured 19-25 yo abruptly decreased to 10.1%. This is acutally below the proportion of uninsured 26-35 yo in 2011, which is unprecedented in prior years. Private coverage was relatively stable from 2006-2008 for all age groups and then declined in 2009-2010 for 19-25 and 26-35 yo. In 2011, the proportion with private coverage increased for 19-25 yo to 57.8%, up from 51.6% in 2010. During the same period private coverage remained stable for 26-35 yo.

DISCUSSION: Previous research, using the NIS,years 2006-2009, cited an estimated overall proportion uninsured of 5% among patients of all ages with IBD who required hospitalization. This study indicates the proportion is higher for young adults with IBD. Lack of insurance is a potential barrier to successful transfer. Given the substantial decrease in the

proportion uninsured 19-25 yo since implementation of extended dependent eligibility, this study indicates that uninsurance is a barrier that may be modifiable through policy change. Further research should look at how uninsurance has changed since Medicaid expansion and health care exchanges went into effect in 2013.
Proportions Uninsured or with Private Coverage by Age Group and Year of NIS Data

Insurance Status	Year of NIS	Estimated Proportion (95% CI) by Age Group		
Uninsured		2 to 18 Year Olds	19 to 25 Year Olds	26 to 35 Year Olds
	2006	2.5 (1.5-4.1)	13.3 (11.7-15.0)	10.1 (9.0-11.4)
	2007	2.2 (1.5-3.4)	12.8 (11.2-14.6)	10.6 (9.4-11.9)
	2008	1.5 (1.1-2.1)	11.7 (10.1-13.6)	9.4 (8.2-10.7)
	2009	2.1 (1.4-3.0)	13.6 (12.1-15.3)	11.4 (10.1-13.0)
	2010	2.0 (1.3-2.9)	14.5 (12.5-16.8)	11.2 (9.8-12.7)
	2011	2.1 (1.3-3.5)	10.1 (8.8-11.6)	13.1 (11.8-14.4)
Private Coverage				
	2006	72.4 (68.0-76.4)	58.3 (55.3-61.2)	59.5 (57.0-62.0)
	2007	68.0 (63.5-72.3)	58.0 (54.8-61.1)	60.1 (57.2-62.8)
	2008	70.1 (65.5-74.3)	58.6 (55.1-62.0)	58.2 (55.4-61.0)
	2009	71.0 (66.4-75.2)	55.6 (52.7-58.5)	54.8 (52.0-57.7)
	2010	65.2 (60.5-69.7)	51.6 (48.4-54.8)	51.4 (48.7-54.2)
	2011	63.5 (58.7-68.0)	57.8 (55.1-60.4)	51.2 (48.7-53.8)

PANCREAS/CELIAC/MALABSORPTION

89 *ENDOSCOPIC PANCREATIC FUNCTION TESTING IN A PEDIATRIC PATIENT COHORT, A SINGLE CENTER EXPERIENCE*

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Introduction/Background: Exocrine pancreatic insufficiency (EPI) has consequential implications on a child's growth and nutrition. Proper diagnosis and treatment of EPI is key to help reverse malabsorption, and ensure optimal growth and development. Minimal data is available on the utility of direct endoscopic pancreatic function testing (ePFT) in pediatrics. Aim: We sought to determine the indications, interpretation, and clinical use of ePFT at a large pediatric tertiary care center. Methods: We performed a retrospective chart review of ePFT obtained from Dec 2007-Feb 2015. Testing was conducted either by administering cholecystokinin (CCK) followed by collecting a single duodenal pancreatic fluid (PF) aspirate at 10 minutes, or by administering CCK or secretin with subsequent collection of PF at 5, 10 and 15 minutes. The pH of each sample was recorded and enzymatic activities were determined for trypsin, chymotrypsin, amylase and lipase. A single reference lab performed all enzymatic testing and the reference ranges were consistent throughout the study period. Patients with normal enzyme activity were classified as exocrine pancreatic sufficient (EPS). Patients under two years of age with only a single enzyme activity abnormality were classified as EPS. Clinical data were obtained from the electronic medical record. Results: A total of 508 ePFTs were performed on 493 patients (481 were single sample testing; 27 were multiple sample testing). The most common indication for testing was failure to thrive or poor weight gain, followed by chronic diarrhea, less common indications were pain and chronic pancreatitis. Indication for testing was not different between EPI and EPS groups. A total of 42 samples were excluded due to suboptimal samples (pH<7 resulting in low enzyme activities; all were from single sample testing). From the remaining 466 samples, 373 (80%) had normal ePFTs and 93 (20%) had results of insufficiency with an abnormality in one (n=25), two (n=34), three (n=8) or all four (n=26) enzymes tested. For the 35% of patients that also had a fecal elastase obtained, results did not correlate with ePFT for EPS vs EPI. Based on available EMR data, 23% of EPI and 2% of EPS patients were prescribed pancreatic enzyme replacements. Using our cohort of EPS patients, we found a maturation of enzyme production where trypsin, chymotrypsin, lipase and amylase increase with age ($p<0.05$). In addition, curves plotted from the multi-sample testing protocol show enzyme activities peak at 5 minutes following pancreas stimulation and activity decreases at times 10 and 15 minutes. Conclusions: ePFT is a feasible test in children with suspected EPI and is a helpful tool to decide on the need for pancreatic enzyme replacement therapy. Single sample testing can result in an inadequate, uninterpretable sample where obtaining additional samples within minutes of pancreas stimulation can ameliorate this issue. Pancreatic enzyme activity levels increase with age. The EPS and EPI curves derived from this study can help clinicians interpret test results of ePFTs. Future studies are needed to validate the application of ePFTs in children as well as assess the effect of accurate and timely

diagnosis on growth outcomes.

96 *IDENTIFYING HISTONE DEACETYLASES AS A MOLECULAR SWITCH TO EXECUTE PANCREATIC REGENERATION FOLLOWING PANCREATITIS*

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Identifying the molecular switches that permit proper regeneration of the pancreas after major injury, such as during the disease pancreatitis, could yield vital insight for future therapies to mitigate the injury. We exploited a clinical clue that valproic acid (VPA), an anti-epileptic drug that is highly associated with pancreatitis, is known to inhibit the epigenetic regulators the histone deacetylases (HDACs). In recent work, HDACs were shown to mediate development of the pancreas. Because elements of development are recapitulated during regeneration of the pancreas after injury, we hypothesized that HDACs serve as a crucial switch to execute proper regeneration and recovery after pancreatic injury. In an experimental model of pancreatitis that leads to a predictable degree of pancreatic injury and subsequent recovery (CCK hyperstimulation), we found that VPA delayed recovery of the pancreas and reduced acinar cell proliferation. Importantly, pancreatic expression of class I HDACs (which are the primary VPA targets) rose in the mid-phase of pancreatic recovery. VPA administration led a delay in regeneration halfway through the process, with persistence of early regenerative structures, called acinar-to-ductal metaplastic complexes (ADMs), and the early development factors Sox9 and Pdx1. The mechanism for this delay in regeneration was through the inability of HDAC1 from silencing the TCF/b-catenin nuclear complex. These effects were not observed with an important negative control, valpromide, which is an analog of VPA that lacks HDAC inhibition. The results provide the first preliminary evidence that HDACs serve as molecular epigenetic switches that orchestrate proper pancreatic regeneration. The findings could provide a new paradigm for treating disorders that lead to pancreatic injury.

97 *VERY EARLY ONSET ACUTE RECURRENT AND CHRONIC PANCREATITIS ARE ASSOCIATED WITH PRSS1 OR CTRC MUTATIONS*

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Background & Aims: Genetic mutations and obstructive factors are common in pediatric acute recurrent pancreatitis (ARP) and chronic pancreatitis (CP). We investigated whether pancreatitis that starts at a very young age (<6 y/o) has unique risk factors and disease course.

Methods: Demographic and clinical information on children with ARP or CP, <20 years of age at the time of enrollment into INSPPIRE (INternational Study Group of Pediatric Pancreatitis: In Search for a CuRE) were collected at 15 centers. A cross-sectional study was performed comparing the differences between those first diagnosed at age <6 y/o and those diagnosed at age ≥6 y/o using Fisher's exact test for categorical variables, and Wilcoxon rank-sum test for ordinal/continuous variables.

Results: From September 2012 to February 2015, 263 children with ARP or CP were enrolled; 105 (40%) were younger than 6 years of age at the time of their first acute pancreatitis (AP) attack. The diagnosis of CP was not different between the age groups (46% for both <6 y/o and ≥6 y/o; p=0.98). The duration of disease was significantly longer in the younger age group with median duration of 3.81 (interquartile range (IQR) 1.44-6.59) years vs. 1.58 (IQR: 0.76-3.70) years in the older age group (p<0.0001). Younger children were more likely to have mutations in the cationic trypsinogen (*PRSS1*) or chymotrypsin C (*CTRC*) genes and a family history of AP or CP (all p<0.01). Although a rare risk factor (≤5%), choledochal cyst was more common in the younger age (p=0.04). Older children were more likely to be of Hispanic ethnicity (p<0.05), have medication history or autoimmune disease (p=0.036 and p=0.005 respectively). Pancreas divisum did not differ between the age groups, however, the data suggested a difference in the level of association of pancreas divisum with serine proteases inhibitor Kazal type 1 gene (*SPINK1)* mutations between the onset age groups (age**SPINK1* interaction p=0.08). This showed a significant association of pancreas divisum with *SPINK1* mutations in the older onset group (Odds ratio 7.33; 95% CI: 1.23, 50.89; p=0.013), but not in the younger onset group (Odds ratio 0.68; 95% CI: 0.01, 6.56; p=1.0). Disease burden, with significantly more constant pain, lifelong emergency room visits, hospitalizations and days of missed school days was higher in the older age group (all p<0.05).

Conclusions: Very early onset ARP or CP are more strongly associated with *PRSS1* and *CTRC* mutations compared to the older population, and older children with pancreas divisum are more likely to have *SPINK1* mutation. Disease burden is higher in older children. Future studies will investigate whether the disease course, response to therapy and/or outcomes are different in children diagnosed with pancreatitis at a very young age.

100 *SENSITIVITY AND SPECIFICITY OF SEROLOGICAL MARKERS IN CHILDREN WITH CELIAC DISEASE: A RETROSPECTIVE STUDY*

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Introduction: Screening for celiac disease (CD) is mainly based on measuring tissue transglutaminase (tTg) IgA. Although the sensitivity and specificity of tTg IgA has been reported to be >95%, it may perform at lower sensitivity and specificity in young children. Given the low and variable sensitivity of the tTg assays in children and no current consensus on the use of deamidated forms of gliadin peptides (DGP) antibodies for CD, we aimed to look into the specificity and sensitivity of the celiac serologic markers in children.
Objectives: To determine the sensitivity and specificity of the serological markers in CD in children
Methods: We included 2285 charts of patients from time period: 6/1/2002-12/31/2014, who had any of the celiac serological markers, tTg, DGP or gliadin antibodies ordered. Of the 2285 patients, 600 had histology reports from endoscopies. We collected demographic data including age, gender, family history of CD, laboratory test results, histology reports from upper gastrointestinal endoscopies, and reviewed physician notes. Positive histological result consistent with CD was defined as fulfilling Marsh criteria, 2-3c. Positive serological test results were determined by the upper limit of the reference values that were provided by the testing laboratory. The study was approved by the Institional review board.
Results: 1) tTg IgA had the best overall correlation with the histological results with sensitivity and specificity at 84 % and 92%, respectively and diagnostic accuracy at 88%. By combining the results of tTg IgA and DGP IgG, the sensitivity was increased from 84% to 92% but the specificity was decreased from 92% to 89%. 2) The sensitivity and specificity of DGP IgG was 100 % in children <2 years of age. The sensitivity of the DGP IgG in IgA deficient patients was only 67% with specificity of 83%. 3) The gliadin IgA and IgG did not correlate well with the histological findings and had a very low diagnostic accuracy 68% and 66%, respectively. 4) The average prevalence of CD was 52%. Eighty seven percent of the patients with a family history of CD were diagnosed with CD. 5) We compared the tTg and DGP antibody levels in patients who did not have celiac disease. In comparison with >4-10 yr and >10 yr age groups, children <4 yr of age had significantly lower levels of tTg IgA (4.2±5.8 versus 6.9±12.3 and 6.5±12.0 units/ml; $p<0.05$) and DGP IgA (4.4±4.4 versus 5.8±7.8 and 5.8±4.6; $p<0.05$), respectively. 6) Children with Diabetes Mellitus I (DM I) had higher levels of tTg IgA and DGP IgA in comparison with those without; 9.0±18.7 versus 5.3±7.5 and 9.3±7.8 versus 5.3±6.1 ($P<0.05$), respectively.
Conclusions: tTg IgA is a sensitive and specific marker for screening for CD in children. DGP IgG was also found to be very sensitive and specific especially in children younger than 2yr of age. Given that our sample size was small, further studies are needed in children less than 2yr of age to determine the best serological tests to be considered for screening for CD in this age group. The significant variation of celiac markers levels in different age groups and DMI suggests that the reference values should be based on the age and underlying medical conditions in order to provide accurate results.

106 *OCCURRENCE OF GASTROINTESTINAL SYMPTOMS AND DIABETES RELATED COMPLICATIONS ACROSS AGE GROUPS IN TYPE 1 DIABETES PATIENTS EVALUATED AS PART OF THE CD-DIET STUDY*

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Background: The reported frequencies and type of gastrointestinal (GI) symptoms in patients with type 1 diabetes (T1D) are variable across studies but appear to be related to age and complications of T1D.
Objectives: To describe GI symptoms and associated comorbidities in T1D children and adults.
Methods: Individuals aged 8-45 years with T1D duration ≥ 1 year completed a self-reported questionnaire - Gastrointestinal Symptom Scale (GISS) as part of the screening phase of the Celiac Disease & Diabetes - Dietary Intervention & Evaluation Trial (CD-DIET). GI symptoms were evaluated over the previous 7 days, with a 9-item symptom questionnaire and a Visual Analog Score (VAS, 0-100mm) for symptom severity; along with clinical characteristics such as glycemic control (HbA1c), diabetes duration, presence of complications and insulin therapy.
Results: 1595 patients completed the questionnaire; 384 (24.1%) children aged 8-12 years, 667 (41.8%) adolescents aged 13-18 years and 544 (34.1%) adults aged 19-45 years. Overall, 78.1% children, 82.0% adolescents and 73.3% adults reported no GI symptoms. Within the group that reported ≥1 GI symptoms (n=349), the most commonly reported symptoms in children were upper (44.0%) and lower (38.1%) abdominal pain, and nausea (26.2%); similar to adolescents who reported lower (38.3%) and upper (31.7%) abdominal pain as well as nausea (30.0%). In adults, loose stool (37.2%), lower (33.1%) and upper (26.9%) abdominal pain were most frequently reported. No statistically significant differences were seen within age groups in terms of frequency of symptoms. Between age groups, the only GI symptoms that were significantly different were loose ($p<0.001$) and hard stool ($p=0.018$), where adults reported these symptoms most often. Overall, subjects who reported ≥1 diabetes-associated complication (n=253) were 1.46 times more likely to report at least one GI symptom ($p=0.015$) with those reporting the presence of autoimmune thyroid disease or diabetes retinopathy being 1.58 and 2.97 times more likely to report a GI symptom ($p=0.027$ & $p=0.024$, respectively). Overall, those who reported a GI symptom had a significantly greater duration of T1D (10.9 years) compared to those who did not report any GI symptoms (9.5 years) ($p<0.01$). No significant associations were identified between GI symptoms and glycemic control (HbA1c), or between GI symptoms and the presence of Celiac Disease detected through serologic screening.
Conclusion: Although most subjects with T1D reported no GI symptoms, 21.9% of the entire cohort reported some symptom with upper and lower abdominal pain as well as nausea and loose stool as the main symptoms. The pattern of symptoms differed between age groups. Significant associations were seen between GI symptoms and T1D associated complications as well as T1D duration.

113 *CHRONIC PANCREATITIS IN CHILDREN AND ADOLESCENTS: HOSPITAL AND EMERGENCY DEPARTMENT UTILIZATION WITHIN THE UNITED STATES*

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Introduction: Clinical experience and limited epidemiologic data suggest chronic pancreatitis (CP) in children and adolescence is a debilitating disease with multiple associated medical concerns and leads to frequent use of health care resources. Our aim was to evaluate the hospital and emergency department (ED) single year utilization for pediatric CP within the United States.
Methods: We extracted data from the Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project Kids' Inpatient Database and Nationwide Emergency Department Sample for 2012. All data are presented as U.S. national level estimates. Comorbid burden was assessed using the Elixhauser comorbidity index, All Patient Diagnosis Related Groups (APR-DRG), and *a priori* knowledge of disease associations. Categorical data are reported as percentages and continuous data as medians with interquartile ranges (IQR). Chi-square test was used to compare differences between categorical and Kruskal-Wallis test for continuous variables. Patients with CP were matched by high-dimensional propensity score to patients who did not have CP, using a greedy matching algorithm, with a 1:5 matching ratio. Univariate and multiple variable logistic regression modeling were used to study the association of variables. Odds ratios (ORs), adjusted odds ratios (aORs), and 95% confidence intervals (CIs) are reported with a threshold for significance of $P<0.05$.
Results: In 2012, there were 1,777,238 estimated hospital discharges in children 1-18 years of age. 2,025 children (0.1%) at discharge had a principal (N=436) or secondary (N=1589) diagnosis of CP. In hospitalized children with CP, 59.1% were female. The median age was 14 years (IQR 6 years). Compared to other hospitalized children, those with CP were more likely to have ≥3 comorbidities (OR 2.9, 95% CI 2.5, 3.3), an APR-DRG for major or extreme risk of mortality (OR 2.8, 95% CI 2.3, 3.3), and an APR-DRG for major or extreme illness (OR 3.3, 95% CI 3.0, 3.7). Children with CP were more

likely to have been admitted from the ED (OR 1.3, 95% CI 1.2, 1.5). Of the hospitalized children with CP, 41.8% had a concurrent diagnosis of acute pancreatitis (AP) (OR 89.7, 95% CI 70.7, 113.6). Children with CP were more likely to have associated liver and biliary disease (OR 9.1, 95% CI 7.5, 11.1), cystic fibrosis (OR 9.0, 95% CI 6.6, 12.3), diabetes mellitus (OR 4.2; 95% CI 3.5, 4.9), and inflammatory bowel disease (OR 2.3, 95% CI 1.6, 3.1). Mortality was low in the two groups (0.3% vs 0.4%; P=0.22). Patients with CP had longer hospital stays (median 4 days, IQR 5 *vs* 2 days, IQR 2; P<0.001) and higher hospital charges (median $24,000, IQR $39,000 *vs* $16,000, IQR $22,000, P<0.001). In 2012, there were 26,365,637 ED visits for children 1-18 years of age. 1,656 (0.006%) had a diagnosis of CP (443 principal and 1,213 secondary diagnoses). 61.2% were admitted to the same hospital, 5.1% transferred, and 33.5% discharged to home. AP was the most common other diagnosis in those admitted (43.9% of CP patients). The presence of ≥3 comorbid conditions was an independent risk factor for admission (aOR 4.4, 95% CI 2.6, 7.6).
Conclusions: These data provide insight into the healthcare utilization and disease burden of children and adolescents with CP.

115 *ACTIVATION OF THE UNFOLDED PROTEIN RESPONSE IN A MUTANT EPCAM MODEL OF CONGENITAL TUFTING ENTEROPATHY*

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Background: Congenital tufting enteropathy (CTE) is an intractable diarrheal disease of infancy presenting with profuse watery diarrhea, electrolyte imbalances, and impaired growth. Intestinal pathology includes villous atrophy, crypt hyperplasia and epithelial tufts leading to intestinal failure. We have discovered mutations in *epithelial cell adhesion molecule (EpCAM)* as the cause of disease in CTE patients but we have yet to understand how these mutations are responsible for structural abnormalities of the villi in CTE. Recently, we made an observation that mutant forms of EpCAM are sequestered in the endoplasmic reticulum (ER) compared with the normal localization of WT EpCAM at the plasma membrane. We hypothesize mutated EpCAM causes increases in key molecular pathways involved in the Unfolded Protein Response (UPR), due to ER stress.
Methods: An *in vivo* mouse model, based on a mutation found in CTE patients, was developed allowing for inducible deletion of exon 4 in *Epcam* resulting in a mutant protein with decreased expression. Protein lysate and RNA from tamoxifen-induced $Epcam^{\Delta 4/\Delta 4}$ mice was used to evaluate UPR mediators, GRP-78 via western blot, and Blos1 and Scara3 via qPCR. The level of apoptosis was evaluated by immunofluorescence of caspase-3. Data presented are means + SEM and statistical significance was assessed by student's unpaired t-test.
Results GRP-78, an indicator of activation of UPR, was found to be significantly increased in ind.$Epcam^{\Delta 4/\Delta 4}$ mice (p=0.0227, n=5). Scara3 and Blos1 RNA was found to be significantly reduced by 51% and 46% respectively in mutant mice tissue (p<0.001, n=5). Apoptosis was not found to be elevated because no significant change in the levels of caspase-3 was seen between mutant and littermate control mice.
Conclusion: EpCAM causes elevated ER stress, indicated by an increase in GRP-78 and decreases in Scara3 Blos1 RNA transcripts. However, the level of ER stress is still below the apoptotic threshold, indicated by the lack of increase in caspase-3. These conditions indicate that the sequestration of EpCAM in the ER is causing activation of the UPR. UPR activation may be contributing to the structural and functional abnormalities of the villi in CTE patients.

117 *OUTCOMES OF THE FIRST 100 PEDIATRIC PATIENTS WITH SHORT BOWEL SYNDROME TREATED IN THE INTESTINAL REHABILITATION PROGRAM AT CHILDREN'S NATIONAL HEALTH SYSTEM (CNHS) - WASHINGTON DC.*

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Aim: To evaluate the outcomes of the first 100 children with Short Bowel Syndrome (SBS) treated in the Intestinal Rehabilitation Program (IRP) from 2007 to 2014.
Methods: Hundred SBS children (63 male) with 8.6 months mean time of parenteral nutrition (PN) dependency (1-156 months) were enrolled. Their median age at first evaluation was 4.5 months and their median small bowel length was 40 cm (mostly jejunum). Fifty three patients have no ICV, 10 have no colon and 16 have half a colon. Their median caloric requirement by PN at the time of enrollment was 100%. Sixty one patients have hyperbilirubinemia with a mean DB of 10.6 mg/dL, among them twenty seven had liver biopsy (12 had portal fibrosis, 9 had bridging fibrosis and 6 had cirrhosis). Height, weight Z score, platelet count, albumin, and bilirubin levels were measured at the beginning and end of the study.
Results: Sixty patients out of the 61 (98%) with hyperbilirubinemia, normalized their bilirubin with treatment over a mean time of 10 weeks, using ≤ 1 g/kg/day of soy bean oil base intravenous fat emulsion (SBIFE). Forty nine reversed their cholestasis while receiving PN (81.6%). Of the 100 SBS patients, four were listed for intestinal transplant; 2 out of the 4 patients were transplanted, (one with 4 cm of jejunum and the other with 10 cm of jejunum, enrolled at 6y of age). One listed patient with DB of 12mg/dL, 10 cm of bowel length and half colon was weaned off of PN, and the other one with

initial DB 19 mg/dL, 10 cm of jejunum join to his sigmoid colon (now s/p Bianchi and s/p STEP) is inactive with no signs of liver disease, his PN needs decreased from 100% to 20%. Two patients died; one with cardiac anomalies and one with Down syndrome left with 8 cm of small bowel, half of the colon, lack of esophagus and severe comorbidities. Of the remaining 96 patients, 24 patients had 37 lengthening procedures, 20 had the first lengthening at CNHS (9 Bianchi, 10 STEP, 1 Bianchi/Step). 13 had a second STEP and 4 had a third STEP, with no complications. Fifteen patients had ostomy in continuity due to severe bowel dysmotility. Eighty-two out of the 96 remaining patients were wean off PN over a median time of 4 months (1-60 months), 14 are in process of weaning PN. Five of the patients initially wean off PN needed to re-start PN due to intestinal complications and all but one were wean off again from PN. All laboratory parameters showed improvement ($p < 0.0001$). Overall survival was 98%
Conclusions: With careful medical/surgical approach, children with SBS can improve their liver functions and nutritional parameters with the ability to discontinue PN and avoid transplantation. Patients with SBS, treated by our IRP, reversed their cholestasis with medical management and the minimization of SBIFE, quickly and effectively in a shorter time than prior reports using fish oil base intravenous fat emulsion. The Intestinal Rehabilitation Program at CNHS has shown the best Survivability rates (98%) for patients with SBS with medical and non-transplant surgical treatment . The treatment of children with SBS PN dependent should be based on medical and non-transplant surgical options. Intestinal transplant should be considered when those measures fail.

120 *LOW UTILIZATION OF PANCREAS TRANSPLANTS IN CYSTIC FIBROSIS TRANSPLANT RECIPIENTS IN THE UNITED NETWORK ORGAN SHARING (UNOS) DATA 1987-2014*

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Background: Up to 90% of cystic fibrosis (CF) patients have pancreatic exocrine insufficiency which contributes to malnutrition and poor pulmonary outcomes. CF Related Diabetes (CFRD) is occurs in 5% of CF patients. There are no clear guidelines for use of pancreas transplants in CF.
Objective: To describe utilization and results of pancreas transplants among patients receiving other organ transplants for CF.
Methods: Patients with CF who had liver, lung and/or pancreas transplants 1987-2014 were identified in the UNOS database. Pre /post-transplant diabetes and post-transplant survival were analyzed using Kaplan Meier and log rank test.
Results: Among CF patients listed for liver transplant, 18% had CFRD. Of the 16 patients who had combined liver-pancreas transplant, 3 developed diabetes post-transplant (19%). (Table) In CF patients listed for combined liver-lung transplant 49% had CFRD, none received pancreas transplants, and 48% developed diabetes after transplant. Among CF patients listed for first lung transplant, 33% had diabetes prior to transplant, only 0.4% were listed for lung-pancreas transplant and 0.2% received a pancreas transplant. (Table) None of the patients receiving lung-pancreas transplants developed diabetes post-transplant. 9 of 20 combined solid organ and pancreas transplants were done in Region 10. Regions 3 and 8 performed 3 transplants each. The majority, 70%, of combined pancreas transplants were performed after 2000 (14/20). Among CF patients who had liver transplant, 2 year survival was 88% in both patients with and without CFRD. In CF patients who underwent liver-lung transplant, survival was slightly lower at 2 years (66%) in patients with CFRD than those without CFRD (76%), although not statistically significant (p=0.11).
Conclusions: CFRD is common in CF patients undergoing solid organ transplantation. Pancreas transplants are rare in this patient population despite a high prevalence of pancreatic exocrine and endocrine insufficiency. Further consideration of pancreas transplant in CF patients undergoing other solid-organ transplant is warranted, as this may be under-utilized.
Diabetes in Solid Organ Transplant CF Patients

Organ	First Time Transplants	DM at Listing	Listed for PT	PT	Post-Transplant New Onset DM	
					No PT	PT
Liver	250	45	31	17	79	3
Liver-Lung	49	24	1	1	20	0
Lung	4228	1410	6	3	1061	0

pancreas transplant (PT), diabetes mellitus (DM)

121 *EFFECTIVENESS AND SAFETY OF EARLY ORAL FEEDING COMPARED WITH NASOJEJUNAL FEEDING IN PEDIATRIC PATIENTS WITH MILD ACUTE PANCREATITIS*

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Introduction: Acute pancreatitis is a reversible process characterized by the presence of interstitial edema, infiltration by

acute inflammatory cells and variable degrees of necrosis, apoptosis, and hemorrhage. Its treatment is basically that of support, limiting exocrine secretion, maintaining an optimal hydrated state, and the timely detection of presenting complications.
Objective: To determine the efficacy and safety of early oral feeding compared with nasojejunal feeding in pediatric patients with mild acute pancreatitis.
Method: Randomized, non-blinded, controlled clinical assay carried out from March 2014 to May 2015 at the Pediatric Gastroenterology Service of a referral hospital. Early oral and nasojejunal feeding were compared. Patients aged <16 years with a diagnosis of mild acute pancreatitis with Balthazar tomography classification were included. Patients with severe, chronic, or recurring pancreatitis, or reactive pancreatitis associated with chronic diseases and pancreatitis after cardiac surgery were excluded. The presence was evaluated of ileum, vomiting, abdominal distension, exacerbation of pain, hospital stay, nutritional state, and frequency of hospital readmission at 1 month. Inferential statistics with chi-squared and Mann-Whitney *U* tests, intragroup comparison with Wilcoxon test. The association with Relative risk (RR) was determined. SPSS ver. 21.0 statistical package. Ethics Committee registration number 2014-1302-023.
Results: Eighteen patients were included: oral group, 11 (61%), and nasojejunal group, 7 (39%). Median age, 13 years (age range, 5–15 years) vs. 12 years (age range, 10–14 years) ($p = 0.93$), and masculine gender, 5 (45%) vs. 4 (57%) ($p = 0.236$). Clinical manifestations on admission: abdominal pain, 10 (91%) vs. 7 (100%) ($p = 0.412$), vs. vomiting, 4 (36%) vs. 3 (43%) ($p = 0.783$), and ileum, 3 (27%) vs. 4 (57%) ($p = 0.205$). Idiopathic etiology, 7 (64%) vs. 1 (14%) ($p = 0.387$). Presence of vomiting, 1 (9%) vs. 5 (71%) ($p = 0.006$), and hyperglycemia, 1 (9%) vs. 7 (100%) ($p = 0.000$). Hospital stay, oral group, median, 4 days (range, 3–5 days) vs. 9 days (range, 7–11 days) in enteral group ($p = 0.000$). Association of risk for vomiting, RR, 0.12 (range, 0.01–0.87), Relative risk of recurrence (RRR), 0.87 (range, 0.13–0.98), Absolute relative risk (RRA) 0.62 (range, 0.25–1.00), and Number to treat (NNT), 1.6 (range, 1.00–4.03). For hyperglycemia, RR, 0.09 (range, 0.01–0.59), RRR, 1.00 (range, 1.00–1.00), RRA, 0.91 (range, 0.74–1.08), and NNT, 1.10 (range, 0.93–1.35).
Conclusions: The result suggest that oral feeding is safe and effective for nutritional support in mild acute pancreatitis, diminishes the risk of vomiting and hyperglycemia, does not affect the nutritional state, and the hospital stay is shorter compared with enteral feeding.

122 *THE ROLE OF ENTERAL NUTRITION IN ACUTE PANCREATITIS MANAGEMENT IN PEDIATRICS*
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Background: Nutrition is an integral part of acute pancreatitis (AP) management and is not adequately studied in the pediatric population. Given the lack of pediatric guidelines, patients are managed by different diet regimens and the timing of introduction of nutrition varies between physicians. Aims: The goal from this study was to evaluate the effect of oral nutrition and fat content in the diet on the length of stay (LOS), pain severity and the clinical course of patients with AP. Methods: This is a retrospective chart review of our nutrition database that was prospectively collected on acute pancreatitis admissions between January, 1 2013 and December, 1 2014. Results: Pain levels were similar between patients who were allowed to feed and patients kept NPO. Higher fat intake g/kg/day was associated with significantly lower daily pain severity scores ($p<0.001$). LOS was not affected by the average fat intake during the hospitalization. LOS was shorter in patients allowed to eat on day 1, compared to NPO, but didn't reach statistical significance ($p=0.57$). Lipase levels were not affected by fat intake. Conclusions: Early feeds are feasible in pediatric patients with AP. Pain levels were similar between patient group that was NPO and patients that received feeds. Increased fat in the diet did not have a detrimental role on the pain severity. Studies are needed to further understand the role of nutrition and fat intake in the management of pediatric AP.

FUNCTIONAL/MOTILITY

124 *IMPORTANCE OF MAST CELL-DEPENDENT VISCERAL HYPERSENSITIVITY IN CHRONIC CHILDHOOD FUNCTIONAL GASTROINTESTINAL DISORDERS*
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Background: Functional gastrointestinal disorders (FGIDs) are characterized by chronic recurrent abdominal pain that is not due to an anatomic, infectious, inflammatory, or metabolic cause. FGIDs account for more than 50% of the consultations in pediatric GI practice and 2 to 4% of all general pediatric office visits. In children the pathogenesis of FGIDs is complex, with evidence that FGIDs represent a multi-factorial biopsychosocial disorder in which physiological, psychological, behavioral and environmental factors all contribute. Early life stress (ELS) such as parental neglect, sexual and physical abuse is more commonly reported in patients with FGIDs. Moreover, FGIDs are more frequently diagnosed in women, and ovarian hormones have been showed to modulate pain sensitivity. Studies have shown that the intestinal mucosa of irritable bowel syndrome patients contain an increased number of mast cells, therefore it is reasonable to speculate that blocking

mast cell function may improve symptoms of FGIDs in children. Hypotheses: Stress early in life increases pain sensitivity in adulthood through a mast cell-dependent mechanism. Methods: We employ a validated rodent model of ELS induced by neonatal classical conditioning via odor shock (OS) attachment learning. Neonatal rat pups receive a single series of OS conditioning per day on post-natal days (PND) 8-12. Each series consists of 11 separate, 30-sec odor presentations with a 4-min rest interval. Rat pups are assigned to 1 of 3 training groups: 1) predictable OS, 2) unpredictable OS, and 3) odor only. Predictable OS pups receive a shock at the base of the tail during the final sec of the odor presentation. Unpredictable OS pups receive a shock 2 mins after odor presentation. Odor only pups receive a 30-sec odor with no shock and serve as a control for ELS. At PND 90, visceral sensitivity is assessed via a visceromotor response to graded pressures (0, 20, 40, 60mmHg) of isobaric colonic distension. One week following the initial colonic sensitivity assessment, mast cell degranulation is prevented by administering a mast cell stabilizer, cromolyn sodium (Gastrocrom™) at 50mg/kg intraperitoneal 24-hrs and 1-hr prior to repeat colonic sensitivity assessment. Results: Compared to odor only controls (26.1 ± 1.2 abdominal contractions), rats exposed to unpredictable but not predictable ELS, exhibit visceral hypersensitivity ($p<0.001$) in response to colonic distension (60mmHg: unpredictable = 33.4 ± 0.7 abdominal contractions; predictable = 24.2 ± 1.4 abdominal contractions). Cromolyn sodium attenuated the visceral hypersensitivity seen in the rats exposed to unpredictable ELS (23.8 ±1.7 abdominal contractions, $p<0.001$). Cromolyn sodium had no effect in adult rats exposed to predictable ELS or odor only control rats. Conclusions: This study is the first to investigate the mast cell stabilizer cromolyn sodium for the treatment of visceral pain following adversity in early life induced by odor shock learning. Cromolyn sodium reversed the exaggerated pain response found in unpredictable ELS rats suggesting the involvement of mast cells in visceral pain. This provides a promising new treatment for children with chronic abdominal pain following early life stress.

*125 *ULTRASOUND GUIDED (USG) NERVE BLOCKS IN PEDIATRIC PATIENTS WITH FUNCTIONAL ABDOMINAL PAIN AND ABDOMINAL CUTANEOUS NERVE ENTRAPMENT SYNDROME (ACNES): IMPACT ON PAIN AND ASSOCIATED GASTROINTESTINAL SYMPTOMS.*

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Aims: To describe the outcomes of localized rectus abdominis injections of cortisone in pediatric patients with underlying functional abdominal pain (FAP) or irritable bowel syndrome (IBS) with an additional diagnosis of abdominal cutaneous nerve entrapment syndrome (ACNES) presenting as a highly localized abdominal pain.

Methods: Retrospective review of pediatric patients referred to a multidisciplinary abdominal pain program for evaluation that were found to have ACNES, and subsequently underwent USG nerve block procedures. Outcome measures include pain intensity scores (0-10 numeric rating scale; NRS), subjective reports of duration, extent of relief and improvement of associated gastrointestinal symptoms.

Clinical characteristics: All patients had a long standing history of abdominal pain (17 ± 3 months), and had seen multiple medical and GI providers. Eight patients had IBS, 13 patients had FAP and 3 had persistent abdominal pain in the setting of controlled IBD. All were intractable and sent for evaluation and treatment. 47% also had nausea and 41% had symptoms of anxiety or depression

Results: *ACNES treatment:* 59% had one block, 13% had two, 13% had three, 4% had four and 9% had five blocks. Eventually 4 patients underwent surgical intervention.

Abdominal Pain intensity: Average pain decreased from 4.3 ± 3 at baseline visit to 1.7 ± 2 at first follow-up visit post-block ($P<.002$) (1.7 ± 1.4 months after the first block).

Degree of relief: At first follow up 12.5% reported no relief; 25 % reported minimal relief (0-30% pain reduction), 12.5% excellent relief (>75% pain reduction) and 50 % complete relief.

Duration of relief: 77% percent reported immediate relief after the first block on the day of the procedure, 29% had relief for less than 1 month, 13% for 1- 3 months, 20% for more than 6 months and 6.7% more than a year.

Long term follow up: At the time of last follow up (7 ± 2 months), after all interventions for ACNES including multiple blocks and surgical interventions, 52% of patients had minimal abdominal pain relief, 8% a significant reduction, 8% good reduction, 4% had excellent pain relief, and 21% were asymptomatic.

Associated GI symptoms after ACNES treatment: Among those with additional GI symptoms 54% reported resolution of associated symptoms, 23% improved, 4% were worse, and 12.5% developed a new GI symptoms ($p<0.02$, compared with baseline).

Conclusions: ACNES is a frequently overlooked reason for abdominal pain in patients diagnosed with FAP and IBS. ACNES pain may exacerbate the pain vulnerability present in FAP and may be a treatable trigger. USG nerve block procedures are a viable treatment option for pediatric ACNES, with significant immediate pain relief reported by most patients. Relapses are common and can be treated with repeat blocks. A subset of patients experienced longer term relief of weeks to months. Resolution of the focal abdominal pain after treatment was also associated with improvement in other GI symptoms in a significant proportion of patients.

126 *EFFECT OF HIGH FAT DIET ON THE ENTERIC NERVOUS SYSTEM*

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Purpose: A high fat diet (HFD) has been shown to alter intestinal motility, and obesity is associated with GERD and enhanced gastric emptying. The aim of this study is to determine the effect of HFD on enteric neuronal proliferation and density.

Methods: Distal colon was isolated from mice fed a HFD for 9-18 months (n=3) and from control mice fed a standard diet (n=3). Whole-mount immunofluorescence was performed on longitudinal muscle-myenteric plexus (LMMP) preparations using anti-Hu antibody to detect enteric neurons. Neuronal density was compared statistically by Student's t-test. To test the role of gut epithelium in the HFD-mediated effect on neurons, intestinal epithelial organoids from HFD (n=3) or control (n=3) mice were co-cultured in a transwell system with enteric neuronal stem/progenitor cells (ENSCs) for 24 hours. The system physically separates the two cell types but allows diffusion of secreted factors. The thymidine analog, EdU, was added 6 hours prior to fixation to assess for neuronal proliferation, determined as cells expressing both EdU and the neuronal marker, PGP9.5. The proportion of proliferating neurons was compared statistically using a Chi Square analysis.

Results: More neurons are present in the distal colon of HFD-fed mice compared to controls (100.2±11.5 vs. 62.4±15.5 neurons/high-power field, p=0.031454367). Interestingly, the rate of ENSC proliferation was increased by 31% in cultures containing epithelial organoids from HFD-fed mice, although this did not achieve statistical significance (4.2±1.5% vs 3.2±1.2% proliferating enteric neurons, p=NS).

Conclusion: A HFD increases neuronal density in the distal colon. This may be mediated by a mitogenic effect derived from the gut epithelium, although additional experiments are needed to confirm this hypothesis. Understanding the mechanisms underlying this effect would help clarify the cause of intestinal dysmotility in the setting of a HFD and thereby offer potential new drug targets for ameliorating this phenomenon.

127 *POSTNATAL ENTERIC NEUROGENESIS OCCURS VIA GLIAL TRANSDIFFERENTIATION AND IS MEDIATED BY BOTH SEROTONIN AND LIPOPOLYSACCHARIDE*

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Background: Mechanisms mediating adult enteric neurogenesis are unknown. We previously demonstrated that experimental colitis was associated with neurogenesis in the adult colon. Colitis is known to increase gut serotonin as well as mucosal permeability which allows passage of luminal contents. The goal of this study was to test our hypothesis that serotonin (5-HT) and/or Lipopolysaccharide (LPS) are required for the neurogenic response in the setting of colonic inflammation.

Methods: HuC/D+ (Hu) neurons were quantified in 3 models of colitis: dextran sodium sulfate (DSS) (n=5), T cell transfer in RAG-/- (T-Rag) mice (n=7), and *Citrobacter rodentium* colitis (CC) (n=5). Sox2-CreER; ROSA26-lsl-EYFP (Sox2CreER::YFP) mice were used for glial cell-fate mapping. The effect of 5-HT and LPS were tested using soluble inhibitors of the 5-HT4 receptor and Toll-like receptor 4 (TLR4), respectively, both *in vitro* using immunoselected glia and *in vivo* with colitis models. Neuronal Sox2 expression in human colon from patients with infectious colitis or IBD was assessed as a marker of possible neurogenesis. Finally an avian hindgut transplantation model was used to explore glial-derived neurogenesis.

Results: DSS (38-72%) and CC mice had more colon neurons (27-42%), but T-Rag mice did not (+/-14%), and this increase was inhibited by 5-HT4 antagonism. Both in vitro and in vivo, 5-HT4 agonism increased glial cell proliferation (1.2 % baseline to 5.3% post-colitis), but not glial cell numbers, suggesting that glia may give rise to neurons. To test this, Sox2CreER::YFP mice were used to map the glial cell fate. As adults, these mice express YFP exclusively in glia. In contrast, after colitis YFP was expressed in 2.5-7% of neurons as well, consistent with glial transdifferentiation. The newly generated Sox2+Hu+ neurons did not incorporate EdU. Administration of LPS alone was able to cause a similar neurogenic effect (3.2-5.7% of neurons were Sox2+), and addition of a TLR4 antagonist blocked the neurogenic effect of colitis. Sox2+ neurons (4.2-7.3%) were seen in all cases of human colitis (infectious (n=15) and IBD (n=15)), but not in healthy controls. Finally, immunoselected glia gave rise to neurons in culture, and this was inhibited by 5-HT4 antagonism. Immunosorted glia also gave rise to neuronal networks following *in vivo* transplantation into avian aganglionic hindgut.

Conclusions: Colitis promotes enteric neurogenesis in adult mice via 5-HT4 and LPS-dependent mechanisms that drive glia

to transdifferentiate into neurons. In this way we prove how neural, mucosal and microbial systems are all involved in regulating postnatal enteric neurogenesis. Continuing to define the mechanisms underlying adult enteric neurogenesis will improve our understanding of inflammation-associated intestinal dysmotility and may identify targets for its prevention and treatment. It may also help to establish strategies for replenishing absent or injured neurons in neuroenteric disease.

128 *PERCEPTIONS AND KNOWLEDGE ABOUT CONSTIPATION IN ARGENTINE PEDIATRICIANS. RESULTS OF A PRELIMINARY SURVEY*

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Introduction: Constipation is a frequent cause of medical consultation in pediatric practice. However a lack of knowledge about good practice in the management and treatment of these patients is evidenced.
Aim: To evaluate the knowledge, attitudes and current practices of pediatricians with regard to constipation.
Methods: A closed-ended structured questionnaire was implemented in a cohort of pediatricians belonging to a continuous medical education program. Sample size: 123.
Results: 123 doctors were included. Females 70.8%. Age: 60.2% above 40 years. Professional practice: 56.6% more than 15 years with 43% working in both public and private practice. 95.6% ask about bowel habits in their patients, but only 40% know well Rome III criteria. 53.9% make the initial evaluation with abdominal palpation and inspection of the anal region but 76% never make a digital rectal examination on the first visit. The Bristol stool scale was known by 41.3% of doctors and they consider useful 98.1%. Only 19.4% ask additional studies, being the abdominal x-ray the most frequent (95%). Diet with fiber was the first line treatment for constipation (97%). Only 32% use laxatives to treat a constipated child, being lactulose the most used (64.4%). For disimpaction the use of Murphy enema (36.5%) and phosphate enemas (34.4%) were the most frequent. 63% of doctors consider that a diet with adequacy of soluble and insoluble fiber was the best (63%). Psychological assessment was "sometimes" considered in constipated children (64%).
Conclusions: Although argentine pediatricians ask about bowel habits in pediatric practice only a few know well Bristol stool scale and Rome III criteria. Dietary fiber is the first line treatment. Only one in every three pediatricians indicates laxatives in constipation showing the need to enhance medical education about this problem.

*129 *SUCCESSFUL BOOST IN INTESTINAL ADAPTATION WITH 12 WEEKS OF TEDUGLUTIDE IN PEDIATRIC PATIENTS WITH SHORT BOWEL SYNDROME AGED 1-17 YEARS*

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The absorptive capacity of remnant intestine is increased with teduglutide (TED); therefore, TED may promote intestinal rehabilitation in children with short bowel syndrome (SBS) aged ≥1 year who have failed to reach enteral autonomy by reducing parenteral support (PS) dependence and advancing enteral nutrition (EN). We sought to determine if TED ≤0.05 mg/kg/day over a 12-wk period would boost intestinal adaptation in children with SBS in whom PS reduction had reached a plateau and for whom no significant advance in EN could be achieved.
A 12-wk, open-label, multicenter, safety and pharmacokinetic/pharmacodynamic study was carried out in children aged 1–17 years with a history of SBS ≥12 months who had reached a plateau in intestinal adaptation (ie, PS could not be further reduced in a clinically significant way) and showed minimal or no advance in EN (ie, specialized nutrition provided via feeding tube or orally) for ≥3 months. Patients were enrolled sequentially into 3 TED dosing cohorts: 0.0125 mg/kg/day (n=8), 0.025 mg/kg/day (n=14), and 0.05 mg/kg/day (n=15); a fourth cohort received standard of care (SOC; n=5). Patients exposed to TED had a mean age of 4.7 years and required PS 7 days per wk. Mean weekly prescribed PS volume was reduced from baseline to Wk 12 in the TED cohorts (0.05 mg/kg/day, -39%; 0.025 mg/kg/day, -37%; 0.0125 mg/kg/day, -10%) and increased by 7% with SOC. Mean patient diary data revealed that EN volume increased by 58% and 51% in the 0.05- and 0.025-mg/kg/day cohorts, respectively, but by only 24% and 17% in the 0.0125-mg/kg/day and SOC cohorts. As a result, the 0.05- and 0.025-mg/kg/day cohorts gained 1.3 and 1.0 additional days off PS, respectively. 4 patients achieved PS independence with TED (0.05 mg/kg/day, n=3/15; 0.025 mg/kg/day, n=1/14). At follow-up 4 wks after study treatment was discontinued, PS requirements were resumed in 2 of these patients. However, after discontinuing TED, EN improvements were maintained or increased from baseline (0.05 mg/kg/day, 59%; 0.025 mg/kg/day, 44%; 0.0125 mg/kg/day, 60%; SOC, 52%).
Clinical nutrition status (ie, weight, albumin, calcium, magnesium, phosphate, and renal function) was maintained despite clinically relevant PS reductions with the highest TED doses. No deaths, discontinuations due to adverse events (AEs), or serious AEs related to TED were reported; 95% of patients completed the study. The overall safety profile was consistent with the SBS population. There were no reports of AEs related to fluid overload, intestinal obstruction, hepatobiliary complications, or colon polyps. Most AEs were mild or moderate and were related to gastrointestinal complaints and/or central line-related issues.

TED was well tolerated and reduced PS dependence while advancing EN in children with SBS intestinal failure whose intestinal rehabilitation had reached a plateau. TED dose of 0.05 mg/kg/day achieved the greatest PS reduction, including complete independence, and showed a boost in advancing EN even after discontinuation.

130 *EVALUATION OF THE BONTA CRITERIA IN CHILDREN UNDERGOING GASTRIC EMPTYING SCINTIGRAPHY*

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Background: Gastric emptying scintigraphy (GES) is considered to be the gold standard for detection of gastroparesis. Adult-based guidelines recommend imaging over a period of 4 hours, which can be inconvenient or difficult for patients, especially for young children. The Bonta criteria propose shortening GES time in the majority of patients using 2-hr gastric retention results with minimal loss of accuracy.

Objective: To determine the accuracy of applying the proposed 2-hr Bonta criteria in children.

Methods: Retrospective review of children, ages 4-18 yrs. who completed a 4-hr solid meal GES study at a tertiary care center. All included children ate the entire Tougas standard meal. Percent gastric retention was measured at 1, 2, 3, and 4 hrs. Abnormal gastric emptying was defined by 4-hour gastric retention > 10%. The Bonta criteria (at 2 hrs. retention >65% is abnormal; <45% is normal; if neither, continue to 4 hrs.) were applied to the 2-hr data. The accuracy of the Bonta criteria was calculated as compared to the gold standard 4-hr study results.

Results: Of the 188 subjects studied, 120 (61%) were female. Mean age of the subjects was 12.5 ± 3.6 (SD) years. A total of 48 (26%) 4-hr studies demonstrated gastroparesis. Using the Bonta criteria, 132 (70%) studies would have been terminated at 2 hrs. Comparisons between results using the Bonta criteria versus actual findings on 4-hr GES are shown in the Table. Fifty-six (30%) studies would have continued to 4-hrs. using the Bonta criteria, of which 20 (36%) had retention >10% at 4 hrs. The overall accuracy of the Bonta criteria in those studies which would have been terminated at 2 hrs. was 90.1%.

Conclusions: In a single center cohort of children completing 4-hr solid meal GES studies, use of the Bonta criteria would have shortened a large number of studies with an accuracy of approximately 90%. However, this accuracy is primarily driven by correctly identifying children who would go on to have normal studies and not in correctly identifying which children go on to have abnormal gastric retention.

Comparisons Between Results Using the Bonta Criteria Versus Actual Findings on 4-hr GES

Bonta Criteria	4-hr GES	4-hr GES	Bonta Criteria	4-hr GES	4-hr GES
> 65% retention at 2 hrs.	≥ 10%	< 10%	<45% Retention at 2 hrs.	≥10%	<10%
33/188 (18%)	24 (73%)	9 (27%)	99/188 (53%)	4 (4%)	95 (96%)
Abnormal	Abnormal	Normal	Normal	Abnormal	Normal

131 *A MULTI-CENTER STUDY OF THE PREVALENCE OF SUCRASE-ISOMALTASE GENETIC POLYMORPHISMS IN CHILDREN WITH FUNCTIONAL DIARRHEA OR FUNCTIONAL ABDOMINAL PAIN*

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Background: Sucrase-isomaltase (SI) deficiency is a potential etiology for chronic, idiopathic diarrhea and/or chronic abdominal pain. SI deficiency can be either genetic (primary) or acquired (secondary).

Hypothesis: SI genetic polymorphisms are more prevalent in children with functional diarrhea and/or functional abdominal pain compared to a control population.

Objective: To determine the prevalence of sucrase-isomaltase polymorphisms in a large population of children with functional diarrhea and/or functional abdominal pain and compare the prevalence to a control population.

Methods: In a prospective, cross-sectional, multi-institutional design, twenty one institutions obtained a buccal swab sample from subjects ≤ 18 years with functional diarrhea or functional abdominal pain. Genetic testing for 37 of the most commonly known polymorphisms was completed using the SNaPshot genetic platform. SI sequencing from two public exome sequencing databases, Exome Aggregation Consortium (ExAC) and the National Heart Lung Blood Institute's Exome Variant Server (EVS), were used as controls. Chi-square tests were used to compare the frequency of *SI* variants detected in case and control populations with a p-value < 0.5 considered to be statistically significant.

Results: This interim analysis included 750 subjects. Subjects were divided between a primary complaint of abdominal pain (n=375) or diarrhea (n=375). SI polymorphisms were identified in 24 (3.2%) of all subjects. *SI* polymorphisms were found in 15 (4%) of those with functional diarrhea with V577G, G1073D, R1124X, and F1745C being the most common variants. *SI* polymorphisms were found in 8 (2.1%) [CBP1] [h2] of those with functional abdominal pain with V577G, G1073D, F1745C, Q930R, and P348L being were the most common variants. *SI* polymorphism prevalence in the studied population

(notably, V577G and G1073D) was statistically significantly higher in the children with functional diarrhea compared to controls (Table 1). A statistically significant difference in *SI* polymorphism prevalence was not identified between subjects with functional abdominal pain and controls.
Conclusion: In this interim analysis, SI polymorphisms were identified more frequently in children with functional diarrhea but not in those with functional abdominal pain as compared to controls. Future evaluations to determine the potential clinical significance of this finding may be warranted.
Comparison of the Four Most Common Sucrase-isomaltase Variants in Diarrhea Predominant Pediatric Patients

	Cases	Controls- EVS	Controls- EXaC
SNP	N GSID Rate	N +SI Rate p-value	N GSID Rate p-value
V577G	375 5 1.3%	10 3,505 0.29% 0.0076	33,311 149 0.45% 0.032
G1073D	375 8 2.1%	13 3,504 0.37% 0.0044	33,315 111 0.33% 0.0002
R1124X	375 1 0.3%	1 3,510 0.03% 0.4623	33,317 8 0.02% 0.2039
F1745C	375 1 0.3%	13 3,502 0.37% 0.8950	31,402 110 0.35% 0.8671
All 4 SNPs	375 15 4%	37 3,505 1.06% 0.0002	32,836 378 1.15% 0.0001

132 *ASPIRATION RATHER THAN GASTROESOPHAGEAL REFLUX CAUSES APPARENT LIFE-THREATENING EVENTS*

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Background: Aspiration and gastroesophageal reflux present with identical symptoms in young children. As a result, symptoms such as gagging, choking, coughing, and blue spells are often treated with reflux medications, none of which effectively treat oropharyngeal dysphagia and subsequent aspiration. The most extreme presentation of these symptoms is the apparent life-threatening event (ALTE). No prior studies have evaluated the role of aspiration in the occurrence of ALTEs. The aim of this study was to investigate the frequency of evaluation for aspiration in patients admitted after ALTE, to determine the incidence of aspiration in these evaluations, and to determine if patients who are adequately treated for aspiration have reduced readmissions.
Methods: We reviewed the records of all patients admitted to Boston Children's Hospital from 2012 to 2015 with a diagnosis of ALTE to determine the frequency of evaluation for oropharyngeal dysphagia using videofluoroscopic swallow studies (VFSS) and clinical feeding evaluations along with the frequency of findings and interventions based on these results and the rate of readmission between patients who did and did not have an aspiration evaluation. Means were compared using t testing and proportions were compared using Chi square analyses.
Results: We found that of 188 total patients who presented with ALTE, 29% (n=55) had a videofluoroscopic swallow study and 72% (n=40) of those patients had evidence of aspiration or penetration on VFSS. Oropharyngeal dysfunction with resultant aspiration was the most commonly abnormal test in infants presenting with ALTE as shown in the table. Compared to patients without aspiration, patients with evidence of aspiration had higher rates of subsequent admissions (0.5±0.8 versus 0.4±0.6) and more admission days (2±4 versus 1±2) and both groups had higher rates of admissions and admission nights than patients who did not undergo VFSS studies (0.2±0.5 and 0.4±1.0 respectively, $p<0.003$). In patients that had both clinical feeding evaluations and VFSS, clinical feeding evaluation alone incorrectly identified 26% of patients as having no oropharyngeal dysphagia/aspiration when compared to VFSS. Each patient had a mean of 3.2±0.1 tests performed in their ALTE and the rate of abnormal testing other than VFSS was low (see table). Interestingly, 3% (n=5) of patients had reflux testing performed but 19% (n=35) of all patients studied were discharged with a diagnosis of reflux and 38% (n=71) were sent home on anti-reflux medications.
Conclusions: Aspiration is a common, underdiagnosed cause for ALTEs. The algorithm for ALTE should be revised to include an assessment of VFSS as clinical feeding evaluations are inadequate to assess for aspiration.
ALTE Testing Results

Test	EKG	CXR	EEG	VFSS
% (n) of patients tested	70% (131)	64% (120)	18% (33)	29% (55)
% (n) abnormal	3% (4)	5% (10)	12% (4)	72% (40)

133 *BETHANECHOL AND ITS PLACEBO EFFECT ON GASTROESOPHAGEAL REFLUX AND GASTRIC EMPTYING IN THE INFANT*

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Introduction: Gastroesophageal reflux (GER) is commonly treated with reassurance and lifestyle modifications which have not proven effective. Mucosal surface barriers and gastric antisecretory agents treat the symptom of passive regurgitation of stomach contents into the esophagus while prokinetic medications aid in gastric emptying. Inconclusive evidence exists for the prokinetic bethanechol and it's effect on lower esophageal sphincter pressure, improved pH probe testing results, and GER symptom scores. Thus, it has not been recommended as a standard treatment of GER in children.

Hypothesis: Bethanechol improves GER and increases gastric emptying. Specific Aim: Demonstrate a significant reduction in GER in infants aged 3-12 months after treatment with bethanechol using a validated reflux score, the Infant Gastroesophageal Reflux Questionnaire (I-GERQ-R). Secondary Aim: Demonstrate a correlation between reflux scores and ultrasound measurements of gastric emptying due to its muscarinic effect.

Methods: We conducted a prospective, double blinded, randomized case-control crossover study. Enrollees underwent a baseline I-GERQ-R questionnaire and an ultrasound to measure gastric emptying following a standardized milk feed. Patients were then randomized into 2 groups (Placebo-Bethanechol or Bethanechol-Placebo) and received 0.2 mg/kg/dose of bethanechol or flavored syrup, 4 times a day for 2 weeks. Follow up phone call obtained an I-GERQ-R score at week 1 and 3. Repeat scores and ultrasounds occurred at week 2 and 4. Data were then analyzed, comparing scores, change in percent gastric volume emptied, and their correlation.

Results: Five eligible infants were recruited into the study, with 4 completing the crossover trial. After one week, the scores for all four subjects decreased by 6-16 points, with the largest drop observed in a subject on placebo. The following week I-GERQ-R scores increased, trending towards baseline. Upon change of study medication from bethanechol to placebo or vice versa, 3 of the 4 subjects showed an improvement in score. The final scores from all 4 subjects were within 4 units of the baseline scores, or essentially unchanged. Statistically there was evidence of a period effect ($p=0.003$). There was no significant association between study drug and rate of gastric emptying. There was also no evidence of a correlation between the I-GERQ-R score and gastric emptying.

Conclusions: In normal infants with GER, initiation of either treatment resulted in a drop in I-GERQ-R score with a rebound the following week. The magnitude of the change was identical on drug or placebo. In fact, I-GERQ-R scores improved in 3/4 of patients while on placebo. Our data strongly suggest there is a significant placebo effect on infant GER. This study involved a very small sample size, and thus warrants further investigation.

134 *MEASURING THE EFFECTIVENESS OF SMALL-GROUP BEHAVIORAL HEALTH TREATMENT FOR PEDIATRIC ENCOPRESIS*

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Introduction

Encopresis in childhood is defined as the passage of feces into underwear or other unwanted place and is most commonly retentive. Encopresis treatment using a medical approach alone is 50-60% effective in reducing soiling and constipation. A combined medical/behavioral (individual and/or group) approach is preferred as it targets the medical symptoms and underlying behavioral concerns, although research is limited. Commonly used behavioral strategies include psychoeducation, skill building, scheduled toilet sits, contingency management, and tracking. Our institution began a group treatment (Soiling, Toileting, And Retraining Treatment, or START) that delivers standard intervention strategies augmented by separate child and caregiver groups. A unique aspect of START includes dedicated time for problem-solving and individualized goal setting with caregiver-child dyads.

Methods

START groups met weekly for five weeks; five cohorts (N=25 families) completed the program. Families were surveyed about their satisfaction using a Likert scale at the conclusion of the group. We obtained demographic and follow-up data from the hospital Electronic Medical Record. Caregiver interviews will explore perceptions of the effectiveness of START group, determine the most salient strategies, and assess encopresis symptoms since treatment completion.

Results

Child participants were 4-10 years old (M=6.96; SD=1.7), 72% male, and 84% White. Most families had private insurance (76%). The following comorbid behavioral health diagnoses were present among child participants: 24% ADHD, 16% disruptive behavior disorder, 8% anxiety, 8% adjustment disorder, 4% autism spectrum disorder, 4% Tourette's Syndrome, and 4% developmental delay. In 24% of families, multiple caregivers attended at least one group session; 84% of sessions were attended by mothers alone, 4% by fathers alone, and 8% by a grandparent alone. Ninety-two percent of families completed all five sessions and rated satisfaction at the conclusion of the group as ‘good' or ‘very good' (4 or 5 out of 5).

After START completion, 44% of families sought gastroenterology follow-up and 32% sought behavioral health follow-up. Ongoing collection of qualitative data will be organized into themes and compared to the current research on group treatments for children with pediatric encopresis.
Conclusions
Most families were able to complete all group sessions and had positive impressions of START across five cohorts within two years. Patients were mostly male, White, and had at least one comorbid behavioral health diagnosis; mothers were the primary participating caregiver. Less than half of families received follow-up treatment. Exploration of interview themes will aid in determining whether START is an effective and sustainable treatment modality for patients and families as research on group treatment for encopresis is limited. Individual interviews also allow for an in-depth understanding of the family's perception of the most salient features of treatment in order to improve the current START program as well as future group-based treatments for encopresis. Further, the current study purports to address a major gap in the research by providing information about long-term outcomes 3 to 24 months post treatment.

135 *CHARACTERIZATION OF ESOPHAGEAL MOTILITY DISORDERS IN CHILDREN USING HIGH RESOLUTION MANOMETRY*

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Introduction: Esophageal motility disorders in children present a diagnostic challenge because of the non-specificity of symptoms and their inability to describe them. The prevailing belief based on scant evidence is that the spectrum of esophageal motility disorders is similar to that in adults. There has been considerable progress made in characterization of esophageal motility disorders in adults based on high resolution manometry, but same cannot be said of motility disorders in children.
Aim: 1) Characterize esophageal motility disorders based on high resolution manometry in children with suspected esophageal motility disorders using the Chicago Classification. 2) Review demographic profiles and medical history to identify co morbid conditions and reveal underlying risk factors in children with esophageal motility disorders.
Methods: A retrospective review of the database of children evaluated for suspected esophageal motility using high resolution manometry with esophageal pressure topography over a four year period was conducted. All tracings were read and verified by neurogastroenterologists and data collected was analyzed using SPSS.
Results: A total of 137 cases were reviewed of which 131 cases met study criteria. Gender distribution was 71 (54%) males and 60 (46%) females. Majority (106, 81%) had two or more presenting symptoms. Symptoms included dysphagia in 87 (66.4%), nausea in 59 (45%), vomiting in 54 (41.2%), weight loss in 43 (32.8%), regurgitation in 42 (32.1%), abdominal pain in 31 (23.7%), feeding difficulty in 17 (13%) and cough in 3 (2.3%). The most commonly reported comorbid condition was allergic diathesis in 45 (34.6%). Other reported conditions included neurodevelopmental delay in 32 (24.4%), eosinophilic esophagitis in 15 (11.5%), and Nissen fundoplication in 14 (10.7%). Esophageal manometry was normal in 57 (43.5%), inconclusive in 3 (2.3%) and abnormal in 71 (54.2%). Of those that had an abnormal manometry and underwent an EGD (69), 41 were abnormal, including eosinophilic esophagitis in 15. UES was reported normal in 128 (97.7%), hypertensive in 2 (1.5%) and UES achalasia in 1 (0.8%). The LES was reported normal in 93 (71%), hypertensive in 23 (17.6%) and hypotensive in 12 (9.2%). EGJ outflow obstruction was reported in 7 (5.3%) of cases. Ineffective esophageal motility (IEM) was reported in 30 (22.9%), followed by absent peristalsis in 22 (16.8%), distal esophageal spasm (DES) in 10 (7.6%), hypercontracting in 6 (4.6%) and normal in 60 (45.8%). Achalasia was diagnosed in 15 (11.5%) cases, with type 2 being the most common (10) followed by type 1 (4) and type 3 achalasia (1).
Conclusion: The most frequent esophageal motility disorder in our study was that of esophageal body peristalsis, IEM being the most common. The profile and frequency of specific motor disorders as described in the Chicago Classification were similar to those reported in adults. Esophageal dysmotility was more prevalent in children with neurodevelopmental delay, eosinophilic esophagitis, and fundoplication.

136 *GUT TRANSIT IN DUCHENNE MUSCULAR DYSTROPHY IS NORMAL: RESULTS OF STUDY USING A WIRELESS MOTILITY CAPSULE*

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Introduction: DMD results from deficiency in dystrophin, a sarcolemma protein of skeletal, cardiac and smooth muscle. It is characterized by progressive striated muscle degeneration in mdx mice and humans. Its effect on enteric smooth muscle function has been studied in mdx mice and duodenal contractility, intestinal transit and fecal output have been shown to be significantly decreased. Despite a high prevalence of constipation, segmental gastrointestinal transit has not been studied in DMD patients.
Aim: The aim of this study was to evaluate gastrointestinal transit in patients with an established diagnosis of DMD.
Methods: DMD patients were screened for constipation using the Rome-III questionnaire and underwent an assessment of gastric, small bowel, colonic and whole gut transit using a wireless motility capsule.

Results: Six of the seven patients enrolled (age range 18-24 years) completed the study, none of which had concerns regarding constipation at the time of the study. Five of six patients were non-ambulatory. All patients were on long-term steroid treatment and 3/6 were on calcium supplements. Five of six patients were non-ambulatory and all were on long-term steroid treatment. Only one patient screened positive for constipation. One patient was unable to swallow the capsule. Five of six patients had normal whole gut transit times, including the one with constipation. Mean gastric emptying time was 3.45 hours (range 2.8-4.4 hours), mean small and large bowel transit time was 24 hours (range 4.6-49.3 hours) and mean whole-gut transit time was 27.5 hours (range 8.5-52.2 hours). One patient with a negative Rome-III screen had mildly increased gastric emptying time (4.5 hours, upper limit of normal 4 hours) and small bowel transit time (8.8 hours, normal<8 hours). This patient had normal colonic and whole gut transit times.
Conclusions: Gut transit in DMD patients is not impaired even in the presence of significant neuromuscular involvement. This is contrary to the reported findings in animal models of DMD.

137 *21 YEAR RETROSPECTIVE REVIEW OF FACTITIOUS ILLNESS BY PROXY (FIP OR MUNCHAUSEN SYNDROME BY PROXY) CONFIRMED BY VIDEO SURVEILLANCE*

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FIP is a form of child abuse that is difficult to diagnose and often unrecognized for years leading to extensive medical testing, treatment, and interventions. We conducted an IRB-approved retrospective chart review of all cases of FIP confirmed by covert video surveillance since installation of cameras in 1993. Patients were referred by their treating clinicians. In all cases a team including child advocacy, social services, risk management and security reviewed the cases prior to surveillance. We identified 36 cases over the study period. Age at diagnosis ranged from 2 months to 17 years of age, with a median of 2 years. 47% of the children were male, 91% Caucasian and 72% were on Medicaid. There were two sets of siblings.
Symptoms were reported very early with 24/36 (67%) initially hospitalized at 6 months of age or younger. We found that 14/36 (40%) had 5 or more documented admissions prior to diagnosis. The average length of time for each hospitalization was 7 days (range 2 to 30 days). The median time between first hospitalization and the diagnosis of FIP was 15 months. Only 5 were diagnosed on their first admission, all as infants, while another 8 were diagnosed before a year of age. Primary symptoms reported of those diagnosed at a year of age or less were reflux, feeding difficulty, apnea, and seizures. Common modes of producing symptoms included suffocation, forceful feeding, and induced vomiting. Older children were more likely to be victims of fabrication including false claims of a history of leukemia, muscular dystrophy, food allergy, and mitochondrial disorders.
There were a total of 24 surgeries in 9 children prior to diagnosis including multiple EGD's, 3 fundoplications, 1 pacemaker placement (and subsequent removal), 5 G-tube placements and 3 ENT surgeries. Multiple subspecialists were involved in evaluations. GI was consulted in 64% of cases, neurology 44%, and pulmonology in 42%. Other consultants included ENT, cardiology, genetics, orthopedics, rheumatology, palliative care and allergy. On average, nearly 3 specialty services were consulted per patient.
All of the abusers were women; 35 were biological mothers and one a foster mother. We found documentation in the health records that 7 of the mothers confessed shortly after confrontation. There was no documentation in the health record of legal outcomes. More recent approaches, including involvement of detectives trained in abuse, have led to higher rates of confessions shortly after arrest. All children were taken into protective custody, but surprisingly, over half of the children had no further encounters within our health system after diagnosis.
Covert surveillance has been critical in diagnosing FIP and ending the cycle of factitious and induced symptoms leading to unnecessary testing and treatments. Despite increased recognition of FIP and availability of surveillance, many children are not diagnosed until after multiple admissions, consultations and surgeries. Most children present with GI symptoms and were seen by GI prior to diagnosis, suggesting that gastroenterologists may be in a unique position to identify FIP. No data is available with regards to long-term outcomes and there appears to be little follow-up within our health system for many of the children.

138 *YIELD AND COST OF EVALUATING CHILDREN WITH CYCLIC VOMITING SYNDROME AS PER THE NASPGHAN CLINICAL PRACTICE GUIDELINES*

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Background: Cyclic vomiting syndrome (CVS) clinical guidelines recommend that the work- up for CVS include laboratory and imaging studies, but data to justify routine screening of children with suspected CVS is lacking.
Objectives: To determine if screening studies in CVS patients results in diagnostic change, and to estimate their healthcare cost.
Method: Charts of patients (1-18years) with suspected CVS (January 2008-December 2014) were reviewed. Results and

cost of laboratory and imaging studies were analyzed.
Results: A total of 541 patients were screened; 165 (30%) children (mean age 7.8±4.39; 90 females) had a diagnosis or chief complaint of CVS and were reviewed to determine if CVS criteria were met based on NASPGAN clinical guidelines. Of these, 141 (85%) children (mean age 7.8±4.2; 78 females) met CVS criteria. Of the 141 children who met criteria for CVS, 6 (4%) had a change in clinical diagnosis based on the CVS screening work up. Screening labs with basic metabolic panel, liver function panel, amylase, lipase, and gamma-glutamyl transpeptidase did not change management. Metabolic labs (urine ketones, lactate, urine organic acids, and carnitine) were beneficial in detecting an unspecified metabolic condition and carnitine deficiency in 2 patients (1.4%). Screening with an upper gastrointestinal series did not change management. Pelvic Ultrasound detected ureteropelvic junction (UPJ) obstruction in 1 patient (0.7%) and magnetic resonance imaging (MRI) of the brain detected increased intracranial pressure in 1 patient (0.7%). Upper endoscopy with biopsy changed management in 2 patients (1.4%) who had the diagnosis of lactose intolerance and Eosinophilic Esophagitis. Of the above conditions that were detected during CVS screening, UPJ obstruction and metabolic conditions had a higher prevalence in our patient cohort compared to the general population (0.06% and 0.7% respectively). The mean cost of screening per patient was United States Dollars (USD) $9,809.93 and total cost for all patients was USD $1,383,200.68.
Conclusion: The screening metabolic labs, pelvic ultrasound, MRI, and upper endoscopy resulted in a change of diagnosis in few patients screened for suspected CVS. Most children who met criteria for CVS did not benefit from screening labs or studies as results did not change clinical management. High health care costs were associated with the use of screening tests for suspected CVS.

141 *AVAILABILITY OF LOW DOSE CT IN THE DIAGNOSIS OF APPENDICITIS IN CHILDHOOD AND COMPARISON OF ABDOMINAL USG AND STANDARD CT*

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Objective: Acute appendicitis is the most common abdominal disease in pediatrics that requires surgical procedure. Diagnostic accuracy of acute appendicitis gets higher while negative appendectomy rate gets lower as imaging techniques has developed. Ultrasonography (USG) is considered as safe diagnostic method, however, its diagnostic accuracy is variable due to operator dependent and it is difficult to apply in obese patients. Computed tomography (CT) scan should be careful to prescribe 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 childhood with acute appendicitis and compared it to abdominal USG and standard dose abdominal CT.
Methods: 575 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.
Results: Of patients evaluated with radiologic methods, surgical procedure was performed in 365 patients after diagnosis of acute appendicitis. (low dose CT; 96, USG; 41, standard dose CT; 213, and USG + standard dose CT; 15). The low dose CT was contributive tool in perforated appendicitis as well as simple appendicitis, and there was no significant difference by comparison with USG or standard dose CT in sensitivity (96.8% vs 95.0% & 93.9%), specificity (91.2% vs 80.0% & 96.2%), positive predictive value (93.8% vs 92.7% & 97.5%) and negative predictive value (95.4% vs 85.7% & 90.7%) (P = 0.468). Both early childhood and middle childhood were effectively diagnosed using low dose CT (P = 0.817 & P = 0.704). In comparison according to obesity, low dose CT was useful and represented similar results to USG and standard dose CT (P = 0.408, P = 0.768 & P = 0.789).
Conclusion: Low dose CT is effective and relatively accurate in diagnosis of acute appendicitis in childhood, as well as early age or obese patients. Also, there was not insufficient irrespective of early age or obesity. Therefore, the low dose CT could be the effective diagnostic method for acute appendicitis in childhood as well as adolescents.

*143 *HIGH RESOLUTION ESOPHAGEAL MANOMETRY PATTERN IN CHILDREN WITH RUMINATION SYNDROME*

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Introduction : Diagnosis of rumination syndrome is mainly clinical and based on the ROME III criteria. The main clinical feature is a painless regurgitation appearing within seconds or minutes from food/liquid ingestion. Pathophysiology of rumination remains unknown, but involves a voluntary contraction of the abdominal wall muscles with a rise in intragastric pressure (R waves) and retrograde movement of gastric contents into the esophagus. High resolution esophageal manometry (HREM) allows identifying R-waves at the moment when episodes of rumination occur. The aim of this study was to determine the HREM pattern in children suffering from rumination.
Patients and Methods: Retrospective evaluation of pediatric patients with rumination syndrome according to Rome III

criteria who underwent an HREM between January 2011 and May 2015. Ten wet swallows followed by 100 mL of water or a test meal were administered during HREM. Rumination was defined as the presence of R-wave (elevation of gastric pressure > 30 mmHg) during an associated clinical rumination episode. Age and sex-matched children without rumination and for whom HREM was normal according to Chicago classification were considered as controls.
Results: Twelve patients (7 F; mean age 14.7 y, range 9-18) were identified. All fulfilled the Rome III criteria for rumination. Esophagogastroduodenoscopy was performed in 11 patients prior to manometry and was normal in all except one mild microscopic esophagitis and two mild microscopic gastritis. All had a normal manometry according to Chicago classification. Rumination was confirmed during HREM in 9 out of the 12 patients (75%) who displayed association of R waves with clinical episodes of rumination. Lower esophageal sphincter and upper esophageal sphincter relaxation were associated with all episodes.
In the control group (12 subjects, 6 F; mean age 14.5, range 12-16), no R-wave was seen, but a total of 41 episodes of elevated gastric pressure >30 in 3 out of 12 patients (25%) during episodes of vomiting, sneezing, belching or coughing could be seen. 35 of the 41 episodes occurred in the same patient because of tube intolerance and repetitive vomiting. The median (range) maximal gastric pressure during R-wave in patients was 69.3mmHg (35.2-126.7) in comparison to a median maximal gastric pressure of 95.9mmHg (43.9-168.4) in overall episodes of increased gastric pressure >30mmHg in patients. The median (range) maximal gastric pressure in controls was 89.2mmHg (40.4-127.4).
There was no significant difference in duration of HREM studies in the 2 groups: median (range) duration 17.7 min (10.3 - 36.1) in patients *vs* 13.3 min (9.5 - 24.2) in controls.
Conclusion: HREM is a simple tool that may help to confirm the diagnosis of rumination in children. Whether HREM may influence outcome of these patients remains to be determined.

*144 *HIGH RESOLUTION ESOPHAGEAL MANOMETRY IN PEDIATRIC ACHALASIA: CLASSIFICATION, PATHOPHYSIOLOGY AND CLINICAL OUTCOME*

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Background: In 2008, Pandolfino et al, using high-resolution manometry (HRM), described the Chicago classification of three classes of achalasia in adult patients. Achalasia subtypes corresponded with patient response to treatment. Other studies suggest that the result of administration of multiple liquid swallows (MLS) during HRM (which induces profound inhibition of esophageal smooth muscle tone) may indicate the level of remaining inhibitory interneurons in the lower esophageal sphincter (LES) of patients with achalasia.
Objective: Using the Chicago Classification, we sought to determine in a pediatric population of achalasia patients the distribution of HRM achalasia types and the esophageal motor pattern during MLS administration. We also aimed to study outcomes of patients in the different types.
Population: Retrospective review of achalasia patients evaluated with HRM in 3 North American Centres. 24 patients (9 females, median age 13 y, range 6-18) with achalasia were evaluated at diagnosis with HRM. MLS were administered at the end of the procedure.
Results: Nine patients (38%) were type I (classical) achalasia whereas 13 (54%) were type II and 2 (8%) were type III achalasia. MLS failed to induce LES relaxation in type I patients and tended to increase LES pressure in type II. Conversely MLS provided LES relaxation in patient with type III achalasia. Sixteen patients underwent Heller myotomy (8 with type I achalasia, 7 with type II). Data on follow up at 1 year were available in 10 children (7 type I, 3 type II). After surgery, 5 patients with type I achalasia had complete resolution of symptoms at one year follow-up. 4 patients (2 type I and 2 type II achalasia) remained with mild dysphagia to solids and/or slower weight-gain.1 patient type II had important dysphagia. Therefore, 5/7 type I achalasia patients responded to surgical treatment whereas 3/3 type II patients responded only partially.
Conclusion: Responses to MLS suggest a heterogeneous pathophysiology in pediatric achalasia. Considering our small population, a prospective and multicentre study is needed to confirm the clinical utility of such a classification system in the pediatric population.

145 *ADEQUACY OF RECTAL SUCTION BIOPSY IN TODDLERS AND CHILDREN*

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Hirschsprung disease (HD) affects 1 in 5000 live births and is diagnosed with full-thickness rectal biopsy. Rectal suction biopsy (RSB) is a viable screening test which avoids anesthesia risks, is widely available, and is sensitive and specific for HD. Data suggests that RSB may be used outside of infancy to age 3, but has not been evaluated in older children. To determine the yield of RSB in older children compared to infants and toddlers, we reviewed electronic health records of children undergoing RSB at a tertiary-care pediatric hospital from 2000-2014. Seventy-nine subjects were identified that

met inclusion criteria. Overall age ranged from 0.01-18.76 years (mean 5.1, IQR 0.2-8.7) and an average of 2.7 biopsies were obtained for each. Submucosa was present in 74.7%, and overall pathologist-determined adequacy for evaluation was 58.2%. Infants less than 6 months (n=27), infants and toddlers 6 months to 3 years (n=11), children age 3 to 8 years (n=17), and children age 8 to 18 years (n=24) were analyzed by cohort and compared across groups. There was no difference in number of biopsies obtained. Submucosa in at least 1 biopsy was present for 96.3% (26/27), 90.9% (10/11), 52.9% (9/17), and 58.3% (14/24) of subjects. Pathologist-determined adequacy for HD evaluation was 77.8% (21/27), 72.7% (8/11), 35.3% (6/17), and 45.8% (11/24). Analysis across groups (2-tailed Chi Square) revealed age-related differences in submucosa presence (P=0.001), and adequacy for HD evaluation (P=0.016). RSB yield of adequate tissue in infants and toddlers was higher than for older children. Adequate tissue was obtained in some older children, and RSB should be prospectively evaluated to determine whether modifiable factors (*e.g.* procedural technique) exist, or whether limited yield in older children is an intrinsic quality of the test itself.

146 *THE EFFECT OF A REGIMENTED COMBINED COGNITIVE BEHAVIORAL THERAPY AND HYPNOTHERAPY PROGRAM FOR THE TREATMENT OF PEDIATRIC FUNCTIONAL GASTROINTESTINAL DISORDERS*

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Introduction: Cognitive Behavioral Therapy (CBT) and Hypnotherapy (HT) are widely accepted therapeutic techniques employed in the treatment of pediatric Functional Gastrointestinal Disorders (FGID). The aim of this study was to review our experience a providing a regimented 7-session combined program of CBT and HT.
Methods:Our functional abdominal pain program utilizes previously published CBT techniques and a scripted HT protocol. The functional disability inventory (FDI) and PedsQL were administered as part of a quality improvement initiative as patients enter and exit the program. A retrospective review of patient charts was performed.
Results: 23 patients completed intake and discharge assessments (18 females). Mean age was 12 ± 3 years old. Primary diagnosis was irritable bowel syndrome (73%). 65% of patients had an endoscopy prior to referral to the program. Average number of clinical encounters prior to referral to the program was 4.6 ± 2. Average number of clinical encounters after completing the program was 0.4 ± 1. Children reported significantly improvement in health related quality of life after engagement in the program. Improved function was also reported although results did not achieve statstical significance. Comorbid conditions such as postural orthostatic tachycardia syndrome were predictors of failure in the program.
Conclusion: A combined cognitive behavioral therapy and hypnotherapy program is an effective therapeutic option in improving health related quality of life in pediatric functional gastrointestinal disorders.
Quality of Life after a combined CBT/HT Program

	Intake PedsQL	Completion PedsQL	p value
Child	61	72	0.03
Parent	63	71	0.09

higher scores are favorable
Function after a combined CBT/HT program

	Intake FDI	Completion FDI	p value
Child	18	13	0.1
Parent	14	9	0.06

lower scores are favorable

147 *ELECTROCARDIOGRAMS IN INFANTS AND TODDLERS ON LOW DOSE AMITRIPTYLINE*

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Amitriptyline is a tricyclic antidepressant used to reduce chronic pain and prevent cyclic vomiting in children and adolescents, but there are no safety data for amitriptyline in infants or toddlers. We hypothesized that one factor causing food refusal in medically fragile, tube-fed infants and toddlers is that eating is painful, and treating chronic pain with amitriptyline might facilitate advancing to oral feeding. In a prospective, double blind, randomized clinical trial we assessed the safety of amitriptyline in 19 tube fed patients (mean age 45 months, age range 18-93 months; 9 male, 17 white), 9 in the placebo group and 10 in the amitriptyline group. No patient had significant baseline ECG abnormalities. In a 15 week trial, we obtained ECGs at 9 intervals at scheduled visits. Amitriptyline 1 mg/kg/qhs was associated with no significant change

in heart rate, PR interval, QRS duration, or QTc interval compared to pre-study ECGs. Two patients developed mild ST-/T-wave changes, 1 patient a shortened QTc interval, 1 patient borderline sinus bradycardia. Amitriptyline was associated with no changes in complete blood counts or comprehensive metabolic panels. We conclude that it appears safe to use low dose amitriptyline in infants and toddlers with no pre-existing cardiac conduction abnormalities.

148 *CHILDHOOD DUODENOGASTRIC REFLUX AND USRODEOXYCHOLIC ACID THERAPY*

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Aim: Alkaline reflux gastritis arises as a result of reflux into the stomach of alkaline duodenal fluid. This leads to dyspeptic symptoms. The purpose of this study was to determine the clinical and histopathological features of children with duodenogastric reflux (DGR) and the effectiveness of ursodeoxycholic acid therapy.

Method: One hundred four patients with DGR under monitoring between January 2012 and May 2015 at two centers (Çukurova University Medical Faculty and Necmettin Erbakan University Medical Faculty, Pediatric Gastroenterology Departments) were assessed in terms of history, physical examination, endoscopy, histopathology and response to ursodeoxycholic acid therapy. Diagnosis of DGR was made on the basis of presence of widespread bile in the stomach during endoscopy and significant bile reflux from the pylorus. Most patients presented to other centers with dyspeptic symptoms and had used various antacids and proton pump inhibitors, but had observed no benefits. Patients were started on proton pump inhibitor+antacid and ursodeoxycholic acid therapy for DGR. Patients were evaluated and symptoms investigated at 3-monthy follow-ups over 1 year.

Results: Mean time from onset of symptoms to presentation to our hospital was 10.5 ± 10.6 months (0-60 months). Eighty-two (79%) had previously used various antacids and proton pump inhibitors for dyspeptic symptoms. Twenty-five had received eradication therapy for *H. pylori* in other centers. Twenty-six cases had chronic disease. Gastritis was detected at upper GIS endoscopy in all cases. Pangastritis was present in 17 (16%), esophagitis in 18 (17%) and duodenitis in 9 (8%). Histopathologically, 33 cases (32%) were *H. pylori* positive. Ulcer was detected in the antrum in one case and in the bulbus in two. *H pylori* was positive in all three cases with ulcers. Barrett's esophagus was observed in two cases. Symptoms decreased by more than half or resolved completely in 97 cases (93%) at 3-month follow-up. Symptoms resolved at 6th-month follow-up in 5 of the 7 patients who failed to respond at 3 months. Relapse occurred in 23 cases (22%) after discontinuation of ursodeoxycholic acid. Mean time to relapse was 5.7 ± 2.3 months. No drug side-effect was seen in any patient.

Conclusion: DGR should be considered in etiology in patients with dyspeptic symptoms who fail to respond to antacid and proton pump inhibitor therapy. The majority of patients with DGR respond well to 3-month ursodeoxycholic acid therapy. Relapse rates are relatively low.

149 *IS ENTERAL AUTONOMY POSSIBLE IN CHILDREN WITH SEVERE MOTILITY DISORDERS AND INTESTINAL FAILURE?*

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Introduction: Gastrointestinal motility is essential in terms of intestinal sufficiency. Severe motility disorders (SMD) can impair enteral autonomy and are currently one of the main indications of intestinal transplantation (IT). Pharmacological and surgical strategies have been described for the management of SMD, but results in patients with intestinal failure (IF) have been rarely reported.

Aim: To report our results in the management of children with IF due to SMD.

Methods: Retrospective and descriptive study based on a prospective database of patients managed by the IF multidisciplinary team from December 2007 to May 2015. Children with neuropathic or myopathic SMD and parenteral nutrition (PN) dependency for more than 3 months were included in the study. Extended Hirschsprung's disease (EHD) patients were managed with ostomies, avoiding bowel resection, and eventually IT. Children with visceral myopathy (VM) were treated with oral antibiotics and prokinetics, plus enteral nutrition, and in non-responding cases gastrostomy and or ileostomy were performed. Patients were listed for IT when PN complications arised.

Results: 89 children with IF were evaluated. 16/89 (18%) presented SMD: 2/16 EHD and 14 with confirmed VM, 5 of them with genitourinary involvement. Clinical symptoms appeared in the neonatal period in 13/16, with all cases presenting before age 5 years. 9/16 required a gastrostomy, and in 10/16 an ileostomy was performed. Both EHD needed jejunostomy and remained PN dependent. 6/14 (43%) children with VM achieved enteral autonomy and were off PN after a mean time of 6 months. BMI Z-score improved in a median value of +1.3, during a median follow up of 12.5 months. VM were all treated with oral prokinetics and antibiotics. 5/16 were evaluated for IT: 1 isolated small bowel transplantation, 1 discarded

for comorbidities, 3 currently waiting.
Conclusion: IT is unavoidable for extended neurogenic disorders. In cases of visceral myopathy, even though IT is a real option, intestinal rehabilitation is possible in a considerable amount of cases. Attempts for avoiding IT should be made in children with SMD, since medical and surgical management can improve symptoms, enteral tolerance and quality of life.

150 *PROSPECTIVE STUDY OF FUNCTIONAL GASTROINTESTINAL DISORDERS AFTER OF DENGUE VIRAL UNCOMPLICATED*

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Introduction: Previous studies have shown a high prevalence of FGDs in Colombia. There are increasing cases of viral infections in FGDs in child (post-infectious irritable bowel syndrome). Dengue virus infection is very common in Colombia and can affect the digestive system. Objective: To investigate the prevalence of post-infectious FGDs in children at 3, 6, 9 and 12 months after of dengue viral uncomplicated. Hypothesis: Dengue infection could explain the high prevalence of FGDs in Colombia. Methodology: A prospective study in children between 8 and 14 years old, who consulted the Hospital Universitario del Valle with dengue viral uncomplicated (n=73 cases) and healthy children from a Public Educational Institution (n=62 controls) in Cali, Colombia. A questionnaire validated (Pediatric gastrointestinal symptoms questionnaire Rome III in Spanish) at the time of dengue viral uncomplicated (baseline) and at 3, 6 and 12 month later, was made. Results: One hundred and thirty five children of 10.7±1.9 years, 51.2% male, were included. At 3, 6, 9 and 12 months; 7 vs 7 (p=0.5776), 6 vs 9 (p=0.8276), 6 vs 8 (p=0.6784), and 4 vs 3 (p=0.4495) of children with dengue and control, reported some FGDs. FGDs prevalence was 19.3%, being the most common functional constipation in 9.6% and irritable bowel syndrome in 3.7%. Conclusion: After of dengue viral uncomplicated the risk of FGDs in Colombian children after 3, 6, 9 and 12 months follow up does not increase.

151 *PREVALENCE OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN 349 NICARAGUAN SCHOOLCHILDREN AND ADOLESCENTS AND POSSIBLE ASSOCIATIONS*

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Introduction: The functional gastrointestinal disorders (FGDs) in Latin America are presented in the 20.3% -29.0%. Objective: To determine the prevalence of FGDs in Nicaraguan children through the Rome III criteria in Spanish and possible associations. Methodology: Study of prevalence in children in Managua, Nicaragua. Sociodemographic and clinical variables were considered. Statistical analysis included estimates of the prevalence of FGDs in school and their corresponding 95% confidence interval and estimate of other descriptive measures of interest and association analysis. Results: Observational descriptive study type prevalence in 349 Nicaraguan schoolchildren and adolescents of 12.2±2.6 years (range 8-18 years), 51.9% schoolchildren and 57.6% female. There was a prevalence of 14.3% for FGDs. The most common FGDs was the functional constipation (FC) in 10.9% (n=38), followed by irritable bowel syndrome in 1.4% (n=5) and aerofagia in 0.9% (n=3). 21 children (55.3%) with FC showed pain on defecation and 17 (44.7%), retentive position 1 to week. There was overlap in the diagnosis of FGDs in 16.0% (n=5), the most frequent, the IBS + FAP or FAPS. There were no significant differences in age, sex and the presence of nausea (p> 0.05). Conclusion: The prevalence of FGDs in Nicaraguan children was 14.3%. The most frequent FGDs in 10.9% was the FC and the most frequent symptom in 55.3% was the pain on defecation, with an overlap of FGDs in 16.0% and without associated risk factor.

152 *PREVALENCE AND POSSIBLE ASSOCIATIONS OF ABDOMINAL PAIN ASSOCIATED WITH FUNCTIONAL GASTROINTESTINAL DISORDERS IN SCHOOLCHILDREN AND ADOLESCENTS OF COLOMBIA, SOUTH AMERICA*

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Introduction: The prevalence of functional gastrointestinal disorders (FGDs) in Colombian schoolchildren is 29.0%. Objective: To determine the prevalence of abdominal pain (AP) associated with FGDs using the Pediatric Gastrointestinal Symptoms Questionnaire Rome III in Spanish and establish potential associations. Methodology: Study of prevalence in 4218 children between 8 and 18 years old, 7 private schools and 5 public schools, 10 Colombian cities. Family sociodemographic variables, and clinics were considered. Statistical analysis included estimates of the proportion of children with AP associated with FGDs and the corresponding confidence interval 95%, percentages, percentiles, averages, and other descriptive measures with their corresponding standard deviations and ranges. Various FGDs were defined according to the Rome III criteria. Results: 4218 children aged 11.9±2.3 years, 52.6% male and 80.5% of public schools were included. The prevalence of AP associated with FGDs was 9.5% (4.7% irritable bowel syndrome; 2.6% functional abdominal pain syndrome and functional abdominal pain; 1.4% abdominal migraine and 0.9% functional dyspepsia). FGDs were more common in children from public schools (OR=1.71 95%CI 1.33-2.18 p=0.0000), with separated or divorced parents (OR=1.40 95%CI 1.11-1.75 p=0.0025) and with nausea (OR=6.51 5.01 95%CI -8.43 p=0.0000); FGDs less common in girls (OR=0.69 95%CI 0.56 to 0.86 p=0.0006) and children with altered height for age (OR=0.59 95%CI from

0.39 to 0.87 p=0.0067). Conclusions: About 10% of Colombian children have AP associated FGDs with a predilection for public school children with separated or divorced parents and presence of nausea.

153 *FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS AND TODDLER NICARAGUAN*

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Introduction: The prevalence of functional gastrointestinal disorders (FGDs) in Latin American infants and toddler is unknown. Objective: To determine the prevalence of FGDs in infants and toddler Nicaraguans and possible associations through FINDERS Questionnaire in Spanish based on Rome III criteria. Methodology: Study of prevalence in 191 children. They were considered family sociodemographic variables, and clinics. Statistical analysis included estimates of the proportion of children with FGDs and its corresponding 95%, percentages, percentiles, mean, median and descriptive measures with their standard deviations and ranges. Results: There was a prevalence of 12.0% for FGDs (6.8% regurgitation; 1.6% rumination and functional constipation, respectively; 1.1% functional diarrhea, and 0.5% disquezia and cyclic vomiting syndrome, respectively); with an age of 13.9±8.7 months, 54.5% female, 50.3% singletons, 30.4% of divorced or separated parents, 17.3% with FGDs family, and 12% with diarrhea preview. There was no predominance of variables and associated factors. Conclusion: The prevalence of FGDs in infants and toddler in Nicaragua was 12.0%, the most common in infants, regurgitation and in toddler, functional constipation without associated factors

154 *REALIBILITY OF THE FINDERS QUESTIONNAIRE IN SPANISH BASED ON ROME III CRITERIA FOR FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS AND TODDLER FROM COLOMBIA, SOUTH AMERICA*

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Introduction: The identification of functional gastrointestinal disorders (FGDs) in infants and toddler (InfTod) Latin American can be performed by a Spanish questionnaire based on Rome III criteria (FINDERS Questionnaire in Spanish). Objective: To determine the reliability of the FINDERS Questionnaire in Spanish to identify FGDs in InfTod Colombians. Methodology: We included 436 InfTod between 1 and 60 months of age in 3 Colombian cities. Three experts assessed the questionnaire. Understanding the questionnaire it was applied in a pilot of 33 mothers, and administration of the final self-report questionnaire to 436 mothers of InfTod group. Internal consistency, stability and equivalence was assessed. A descriptive analysis was performed, and to establish the internal consistency, coefficient Cronbach's alpha (α-Cronbach) was calculated. The questionnaire consisted of 33 questions divided into 6 sections: A (regurgitation = 8); B (rumination = 7); C (vomiting = 2), D (colic = 5), E (bowel movements = 9) and F (irritability = 2). Results: We included 436 InfTod (age 25.8±16.7 months, 50.2% girls). The questionnaire was easily understood and used. The best result of the α-Cronbach was 0.71: 0.82, section A; 0.77, section B, 0.78, section C; 0.78, section D; 0.29, Section E, and 0.61, Section F. Conclusion: We found that FINDERS Questionnaire in Spanish based on the criteria of Rome III has high reliability, it is easy to understand and use for the identification of FGDs in InfTod Colombians and proposed to be used in other Spanish-speaking InfTod

155 *FUNCTIONAL CONSTIPATION IN COLOMBIAN SCHOOLCHILDREN AND ADOLESCENTS ACCORDING TO ROMA III CRITERIA IN SPANISH AND POSSIBLE ASSOCIATIONS*

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Introduction: The functional gastrointestinal disorders in Colombian schoolschildren and adolescents have a prevalence of 29.0%. Objective: To determine the prevalence of functional constipation (FC) in Colombian schoolchildren and adolescents (SchAdol) using the Pediatric Gastrointestinal Symptoms Questionnaire Rome III in Spanish and identify possible risk factors. Methodology: Study of prevalence in children between 8 and 18 years old, 5 public schools and 7 private schools, 10 Colombian cities. They were considered sociodemographic, family and clinics variables. Statistical analysis included estimates of the proportion of children with FC and its corresponding confidence interval 95%, percentages, percentiles, averages, and other descriptive measures with their corresponding standard deviations and ranges. FC defined by the Rome III criteria. Results: A total of 4218 children aged 11.9±2.3 years, 52.6% male, 80.5% of public school, 30.8% malnourished and 11.2% with altered height for age. FC occurred in 502 children (11.9%), compared with children without FC, there were significant differences in the frequency, consistency and size of stool, and the presence of painful bowel movements, fecal impaction, position retention and soiling (p=0.0000). There was more opportunity to present FC in school (OR=1.45 95%CI 1.18-1.78 p=0.0003), public school (OR=1.48 95% CI 1.17-1.86 p=0.0005) and nausea (OR=2.25 IC95 1.64-2.98 % p=0.0000). Conclusions: FC according to the Rome III criteria in Spanish, it is not uncommon in Colombian children, with preference at school age, be of public school and have nausea.

156 *PREVALENCE OF GASTROINTESTINAL, PSEUDONEUROLOGICAL AND PAIN SOMATIZATION IN COLOMBIAN SCHOOLCHILDREN AND ADOLESCENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS*

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Introduction: The pathogenesis of functional gastrointestinal disorders (FGDs) involving psychological characteristics, as gastrointestinal (GIS), pseudoneurological (NEUS) and pain somatization (PS). Objective: To determine the prevalence of somatization in Colombian schoolchildren and adolescents with FGDs from public schools and identify possible associations. Methodology: They were included schoolchildren (8-12 years) and adolescents (13-18 years) from public schools in three Colombian cities. Sociodemographic, family and clinics variables were analyzed. FGDs diagnosis was made according to the Rome III criteria and identification of somatization for Somatization Inventory for Children Kovacs in Spanish. Statistical analysis included estimates of the prevalence of other descriptive terms of interest and association analysis. Results: 198 children (116 adolescents and 82 schoolchildren) of 12.7±2.1 years, 50.0% female, 10.6% singletons, 49.5% of divorced or separated parents, 5.1% relatives FGDs and 21.7% malnourished were analyzed. The most common FGDs were functional constipation in 53.5% and irritable bowel syndrome in 18.7%. In 97% of cases it presented somatization: 95.0% PS, 90.9% NEUS and 86.4% GIS. There was no predominance of any of the sociodemographic, family and clinics variables, nor any possible associated factor. Conclusion: In schoolchildren and adolescents from Colombian public schools the somatization occurs primarily by pain, followed by gastrointestinal and pseudoneurologycal somatization, without the presence of possible associated factors.

157 *MULTICHANNEL INTRALUMINAL IMPEDANCE. SEARCHING FOR THE LIGHT*

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Objectives: Describe the parameters of a sample of one Spanish paediatric unit of reference for the multichannel intraluminal impedance (MII) technique. Methods: Single-center, retrospective, two year descriptive study. IMM pH (Greenfield™) catheter and (Ohmega) equipment was used in all patients. (SAS 9.3) application for statistical analysis has been used. Results: 324 records were analysed. The median time of test recording was 20.65 hours (Std Dev 1,572; Range 10-25). 59% male. The average age was 53.70 months (Std Typ 48,810; Range 0-196). 27.5% of the patients were younger than 12 months. The most frequent indications of the test were gastrointestinal symptoms (50%) and respiratory (28.4%). 132 tests (40.74%) were considered pathological according to the diagnostic criteria EURO-PIG ESPGHAN Working Group (61.4% by number and 38.6% for reflux symptoms index (SI)> 50%). The percentage of patients <12 months with pH IIM pathological was higher than the group of> 12 months ($p = 0.002$). Of the 56 patients diagnosed only with SI> 50%, 40 presented a symptom association probability (SAP)> 95%, not demonstrating correlation between both parameters in different types of reflux. In children < 12 months, weakly acidic reflux predominated ($p < 0.05$). In patients >12 months with respiratory symptoms, acid reflux content predominated and weakly acid in gastrointestinal symptoms ($p < 0.05$). Conclusion: Our series is one of the largest paediatric age single center study published. In children less than 12 months weakly acid reflux predominates, with a percentage of pathological impedance-ph-monitoring significantly higher. Is still being a diagnostic discrepancy with pH metria as single test. We observed no correlation between the symptom association probability and the symptom index. Therefore, with the current criteria that takes the symptom index as a referring, we might tend to overdiagnosis and overtreatment the gastroesophageal reflux disease.

158 *CLINICAL UTILITY OF EGD IN A PEDIATRIC POPULATION WITH CHRONIC ABDOMINAL PAIN: A RETROSPECTIVE STUDY*

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Esophagogastroduodenoscopy (EGD) utilization in children with abdominal pain has significantly increased in the last 20 years. There are few studies with a large sample size identifying the clinical effectiveness in this population. The aim of this study is to evaluate the usefulness of EGD in the workup and management of chronic abdominal pain. In a multi-site community-based pediatric gastroenterology practice, we conducted a retrospective chart review of all children diagnosed with chronic abdominal pain, ICD-9 code 789.0, who underwent EGD in 2011. The population included 60% females and 40% males ranging from ages 2 to 18. Charts were reviewed for visual endoscopic findings, histopathology, medication changes, and other diagnostic studies. A total of 224 endoscopic results were analyzed. Of these, 173 patients (77%) had normal visual endoscopic results and 148 patients (66%) had normal histopathology. Significant abnormal findings consisted of eosinophilic esophagitis (8%), lactose intolerance (6%), celiac disease (4%), gastroesophageal reflux disease (3%), and inflammatory bowel disease (1.7%). After upper endoscopy, 10% of patients had a significant change in management including initiation of steroids, antibiotics or a gluten-free diet. 48% of patients had a change in management, which included medication discontinuity, initiation of an antacid or probiotic, or diet change. The results of this study suggest that the vast majority of upper endoscopies done in children with abdominal pain are normal. In our study, only 10% of patients had a significant change in management. Based on these findings, the utility of EGD requires further consideration.

LIVER

*160 *HEPATITIS B INFECTION IN CHILDREN CAN PROGRESS TO END-STAGE LIVER DISEASE REQUIRING LIVER TRANSPLANTATION IN EARLY ADULTHOOD: ANALYSIS OF THE UNOS DATABASE.*

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Background: Chronic hepatitis B virus (HBV) infection has a mild course in most children which may delay initiation of treatment even when indicated. Unfortunately, a minority of children can progress rapidly to cirrhosis which may require liver transplantation (LT) in early adulthood. The aim of this study was to assess the characteristics of HBV-positive young adults who received LT, and to evaluate post-transplant outcomes including patient and graft survival and the need for re-transplantation.

Methods: United Network for Organ Sharing (UNOS) database was conducted from 1989 to 2012 and retrospective analysis was performed on all young adult patients (ages from 18 to 35 years) who underwent LT in the US with a primary diagnosis of HBV or were seropositive for HBV surface antigen at time of LT. Kaplan-Meier analysis was used to assess patient and graft survival.

Results: A total of 522 HBV infected subjects were included. Average age at time of transplant was 28.4 ± 5.2 years. 60.9% were male, 48.6% were Caucasian, the mean BMI was 25 ± 5.5 kg/m2, diabetes was present in 3.9%, hepatocellular carcinoma was presents in 4.4% and 10.4% were on dialysis prior to LT. Median follow-up after 1st LT was 48.2 months [12.5, 109]. During this time, 174 (33.3%) patients died with a mean age at the time of death of 31.6 ± 7.8 years including 144/ 522 (28%) after the first LT, 26/74 (35%) after the second Lt, and 4/12 (33%) after the third LT. The most common cause of death was graft failure (27.6%) followed by infection (16.6%). Overall, only 58% of patients were alive with their first LT at last follow up. Kaplan-Meier analysis revealed worse patient and graft survival after re-transplantation in comparison to initial LT.

Conclusion: LT in young adults for HBV acquired during childhood has poor outcomes and can be associated with premature death. These findings should prompt more aggressive evaluation and treatment for HBV in children.

163 *OVEREXPRESSION OF BILE ACID GENES IN PEDIATRIC NASH*

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Introduction: Bile acids (BA) are the major organic solutes in bile and the main excretory pathway for cholesterol. CYP7A1 is the rate-limiting enzyme in the biosynthesis of BA and CYP8B1 has a role in determining the hydrophobicity of the BA pool. Adult NASH livers exhibit increased expression of genes for BA synthesis with a preference toward the alternative pathway. We hypothesize that pediatric NASH patients have an increased gene expression for the BA synthesis pathway.

Methods: Biopsy proven pediatric patients with NASH were studied in comparison to matched healthy donor livers. Gene expression was evaluated by microarray and quantitative real-time PCR. Serum transaminases, fasting lipid panel, insulin and glucose were assessed in the NASH group. The University at Buffalo IRB approved study.

Results: Data from microarray and qRT-PCR revealed elevated expression of the BA synthesis enzymes, without a preference for classic or alternative pathways. The key rate-limiting enzyme CYP7A1 had a 24-fold increase expression compared to controls (PCR, $p<0.0001$). The alternative pathway CYP27A1 and CYP8B1 had a 9.85 and 11-fold increase in expression compared to controls ($p=0.001$, and $p=0.003$ respectively). Both Bile acid-CoA:amino acid N-acyltransferase (BAAT) and Bile Acid-CoA Sythetase (BACS) showed a 2.37 and 3.15 fold increase gene expression (PCR, $p=0.013$ and 0.003, respectively).

Hepatic Nuclear Factor 4 alpha (HNF4A) had 5.76-fold increased (PCR, $p=0.002$) expression compared to controls, and had positive correlation with its target genes CYP7A1 gene expression ($r=0.697$, $p=0.0002$), CYP27A1 ($r=0.863$, $p<0.0001$), CYP8B1 ($r=0.770$, $p<0.0001$), BACS ($r=0.660$, $p=0.0004$), and BAAT($r=0.547$, $p=0.0057$). FXR was up regulated (NASH/Control: 2.23; $p=0.008$) as well as its direct downstream target gene SHP (NASH/Control: 2.45; $p=0.06$) and indirect target gene FGFR4 (NASH/Control: 7.93; $p=0.003$).

All of the BA uptake proteins had increase gene expression; NTCP had a 2.12-fold increase ($p=0.027$), OATPB1 had a 2.10-fold increase ($p=0.07$), OATPB3 had a 2.28-fold increase ($p=0.03$). The main excretory protein, BSEP did not have a significant change in relative gene expression (NASH/Control: 0.97; $p=0.79$).

We found a correlation between the grade of steatosis and the relative gene expression of CYP27A1 ($r=0.758$, $p<0.0001$), CYP8B1 ($r=0.663$, $p=0.008$), HNF4A ($r=0.636$, $p=0.007$), SHP ($r=0.836$, $p<0.0001$) and FGFR4 ($r=0.749$, $p=0.001$). There was no correlation between fasting glucose, cholesterol or triglycerides with genes involved in BA synthesis or regulation.

Conclusion: There is an elevated expression of bile acid synthesis enzymes in obese pediatric NASH in which the classic pathway seems to predominate. The overexpression of CYP7A1 and CYP8B1 correlated with the high expression of HNF4A. Although both SHP-dependent and independent inhibitory pathways were overexpress they were ineffective to suppress BA production. There is an increase in BA uptake without significant increase in canalicular excretion, which

could be evidence of bile acid accumulation within the hepatocyte. Further studies are needed to identify a possible causal relationship between NASH pathogenesis and elevated BA synthesis.

*165 *PLASMA CYTOKERATIN-18 (CK18) LEVEL AS A NOVEL BIOMARKER FOR PREDICTING THE PRESENCE OF LIVER FIBROSIS IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)*

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Background: Nonalcoholic fatty liver disease (NAFLD) is the hepatic manifestation of the obesity epidemic and affects approximately 10% of children in the US. The presence of hepatic fibrosis may be the most important factor in determining the prognosis of NAFLD. Noninvasive methods to identify the presence of fibrosis in children with NAFLD are greatly needed. Hepatocyte apoptosis activates hepatic stellate cells and plays a central role in fibrosis progression in NAFLD. The aim of this study was to evaluate the use of plasma cytokeratin-18 (CK18) fragment levels, a marker of hepatocyte apoptosis, as a noninvasive biomarker in detecting liver fibrosis in pediatric NAFLD.

Methods: Consecutive children with biopsy-proven NAFLD were included and blood samples and anthropometric measurements were collected at the time of the biopsy. NAFLD activity score was calculated (0 - 8) and fibrosis stage was scored (0 - 4). We measured plasma CK18 levels using the M30-Apoptosense enzyme-linked immunosorbent assay kit.

Results: A total of 201 subjects were enrolled in the study. The mean age was 10.7 ± 2.5 years, and 37 % were male. 68% of the patients had any fibrosis, with 56% having F1, 6% having F2, and 6 % having F3. CK18 levels were found to be significantly higher in subjects with any fibrosis compared to those without fibrosis (304.6±124.8 vs. 210.4±70.9, $p<0.001$). CK18 level revealed good accuracy for prediction of any fibrosis (F1-F3) with AUROC of 0.75. Multivariate logistic regression was performed to assess whether CK18 in combination with another clinical factor could improve accuracy of prediction of fibrosis. Together, CK18 with waist circumference percentile generated an AUCROC of 0.842 for prediction of any fibrosis.

Conclusions: CK18 is a promising noninvasive biomarker for fibrosis in NAFLD in children. A fibrosis prediction model that includes CK18 and waist circumference percentile should be validated in other populations.

167 *STANDARDIZED DAILY COFFEE CONSUMPTION TO REVERSE NON-ALCOHOLIC FATTY LIVER DISEASE IN CHILDREN*

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Background & Aims: Non-alcoholic fatty liver disease (NAFLD) is increasing in global incidence and prevalence and has reached epidemic levels in both adult and pediatric subpopulations with high obesity rates. Although a leading cause of chronic liver failure, there is currently no effective treatment when conventional weight loss programs and health maintenance strategies fail. Lack of evidence-based therapies is especially problematic in children with NAFLD. We hypothesize that standardized daily coffee consumption may serve as a dietary supplement to reverse progressive liver inflammation and injury. We aimed to determine the effects of daily coffee consumption in known NAFLD patients age 8 to 21 years based on elevated liver function tests (ALT).

Methods: Our study is an IRB-approved prospective observational cohort study at Santa Clara Valley Medical Center (SCVMC) in Pediatric Gastroenterology. Patients meeting clinical criteria for NAFLD based on 2 consecutive elevated ALT (>37U/L) levels within 6 months of follow up and documented liver parenchymal fat deposition on ultrasound are being enrolled in the study. Study patients receive a monthly-distributed supply of ground coffee, single-cup filter, and measuring scoop at a centralized pick-up location at SCVMC. Ongoing standard of care and regular 3-month outpatient follow-up clinic visits with a designated gastroenterologist are required for continued study eligibility.

Results: 26 patients (age 14.4±3.19 years) are currently enrolled with more male predominance (n=19, 86%). Pre-coffee average cohort BMI was 25.9 +/- 4.1 kg/ m^2. Based on more than one post-coffee ALT measurements, 5 patients were available for preliminary analysis. All 5 patients improved their ALT after 2 follow up visits within 6 months. Pre-coffee ALT average of 113.2 ± 40.1 declined to a post-coffee ALT average of 88.1 ± 21.9 (paired Student's t-Test P=0.03). Post-coffee average cohort BMI is currently 26.1 +/- 5.5 kg/m^2.

Conclusions : Based on our preliminary data, standardized daily coffee consumption in children with fatty liver disease may be beneficial in NAFLD, regardless of BMI trends or absence of weight loss. Regular coffee intake in patients with NAFLD may represent a novel therapy to prevent progressive liver injury.

169 *FIC1 DISEASE MODELLING WITH HUMAN INTESINAL ORGANOIDS*

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Background: Biallelic mutations in *ATP8B1* causes FIC1-disease. It is a multisystem disorder, affecting liver, inner ear, pancreas and intestines. Majority have liver disease but extrahepatic manifestations are variable. The observation that mild

chronic diarrhea can progress to intestinal failure after liver transplantation points to a bile acid driven process. The mechanisms of FIC1 diarrhea is unknown. We hypothesize that stem cell derived human intestinal organoids (HIO)s can be employed to model Fic1 disease *in vitro*. Materials and Methods: Paraffin embedded samples from duodenum, terminal ileum (TI) and colon from a patient with compound heterozygous mutations in *ATP8B1* (R930X; IVS 15+1 G>A) who developed intestinal failure after liver transplantation and from heathy controls were obtained from the institutional BioBank, following IRB approval. Immunohistochemistry (IHC) for FIC1, the apical sodium-dependent bile acid transporter ASBT, and for CDX2, an intestinal differentiation marker, was performed. Embryonic stem cells were differentiated into HIOs by conditioning the media with activin A, WNT3A, FGF4, RSP01, EGF and NOG at the institutional Pluripotent Stem Cell Facility. Result: IHC with two different FIC1 antibodies, against the C and N-terminus, produced similar results in control samples: FIC1 was most abundantly expressed in colon, followed by TI, and localized to epithelial cytoplasm and cell membrane. A weak perinuclear and nuclear staining pattern was seen in the duodenum. ASBT was expressed on the apical membrane of enterocytes in TI, not in colon or duodenum. IHC for CDX2 stained the nuclei of enterocytes from all sections of the gastrointestinal tract. FIC1 staining was absent from patient's colon and TI whereas expression pattern for ASBT and CDX2 was similar to controls. IHC on HIO's revealed nuclear, cytoplasmic and membranous reactivity for FIC1 and ASBT in the epithelial layer. Nuclei of epithelial cells were positive for CDX-2 (see Table 1). Following culture of HIOs for 24 hours with 1mM of GW4064, a potent agonist of the bile acid receptor FXR, or 0.1% DMSO in controls, HIOs were collected for RNA and Taqman-based quantitative RT-PCR. mRNA expression of *FGF 19, FIC-1* and *ASBT* were upregulated by 51, 5.6 and 1.2 fold, respectively. Conclusion: Opposed to prior murine studies showing FIC-1 expression along the apical membrane of small intestinal enterocytes, we also found cytoplasmic expression in colonic epithelium which was absent in a FIC1 patient. Role of FIC1 in the colon is unknown. Studies on archived human tissue and ES-derived organoids revealed that HIOs express FIC1 and ASBT which are putatively linked to bile acid induced diarrhea and are typically expressed in the TI epithelium and respond to activation with bile acid agonists. We submit that studies on HIO's derived from induced pluripotent stem cells of patients with FIC1 disease may help to elucidate the mechanisms of FIC1 diarrhea and facilitate discovery of patient specific therapies.
Staining Pattern

Tissue	Antibody		
	ASBT	CDX-2	FIC-1
Colon	-	+	+
Duodenum	-	+	+
TI	+	+	+
ES-HIO	+	+	+

171 *LIPID PROFILE IN INFANTS AND TODDLERS WITH CHRONIC LIVER DISEASE (CLD) AND ITS CORRELATION WITH BODY COMPOSITION EVALUATED BY DUAL-ENERGY X-RAY ABSORPTIOMETRY (DXA)*
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Objective. To demonstrate that lipid profile correlate with body composition indicators evaluated by dual-energy X-ray absorptiometry (DXA).
Methods. *Design:* Cross-sectional. *Setting*: A pediatric referral hospital. Sample: 15 patients with CLD, age 3-36 months. *Variables*: a) Lipid profile: Total cholesterol (TC), triglycerides (TG), very low density lipoprotein (VLDL), low density lipoprotein (LDL), high density lipoprotein (HDL). b) DXA: Total mass (TM), Fat mass (FM), fat free mass (FFM) and bone mineral density (BMD). *Protocol*: Lipid profile was determinated by electrophoresis. DXA was performed with a whole-body scanner (Hologic Discovery W-series QDR) with pediatric software, Fomon's and Butte's reference patterns, BMD were handled as z-scores *Statistics*: Median, Intercuartilar range (ICR), and Pearson correlation.
Results. *Patients*: 10 females, median age 14 months. Lipid profile: TC 187 median (ICR 54), TG 131 median (ICR 93), VLDL 25 median (ICR 17), LDL 105 median (ICR 57), HDL 19 median (ICR 31). DXA. Fomon's reference pattern, 80% had low FFM and 66% FM. 80% had BMD z-score <-2SD. HDL correlated with TM (r=0.79, p=0.002); FFM (r=0.77, p=0.003); FM (r=0.73, p=0.007); BMD (r=0.82 p=0.001). No correlation was observed between CT, TG, VLDL, LDL with DXA indicators.
Conclusions. HDL correlated positively with all body composition indicators evaluated by DXA this finding reflect that HDL could be an indicator of nutritional state .

*173 *PAR 1 A/B REGULATES JAG 1 EXPRESSION AND BILE DUCT DEVELOPMENT IN MICE*

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Background: Partitioning defective (Par) 1a/b are members of a family of apico-basal polarity proteins. Par1a/b contribute to epithelial cell-cell adhesion and morphogenesis in vitro. They are functionally redundant serine-threonine kinases that compensate for each other in vivo. Complete loss of Par1 a/b leads to death early in embryogenesis, prior to liver development, while mice with only one out of four alleles, Par 1a -/-: Par 1b +/- (Par1a/b KH) and Par 1a +/-: Par 1b -/- (Par 1a/b HK) die postnatally. Par 1a/b HK and HK kidneys are hypoplastic with abnormal glomeruli and proximal tubules, similar to Notch mutant phenotypes. Alterations in signaling in the Jagged-1/Notch-2 pathways have been associated with several types of biliary tract abnormalities, including Alagille's Syndrome and biliary atresia.

Hypothesis: Par1a/b contributes to bile duct development and alters Jag-Notch signaling in fetal livers in vivo.

Results: Par 1a/b are expressed throughout liver development (E13-newborn period) and are expressed in adult bile ducts. Bile ducts were identified in newborn mice by light microscopy and immunofluorescent (IF) staining. While littermates had readily identifiable bile ducts around portal veins, newborn Par1a/b KH livers had decreased number of bile ducts and Par1a/b HK mice lacked bile duct development. To define effects on bile duct formation, IF biliary epithelial cells were identified by cytokeratin 19 and Sox9 expression in E16 and E18 livers. Par1a/b HK livers had decreased number of cells expressing bile duct markers surrounding portal veins. In addition, those biliary epithelial cells identified failed to form lumens. Loss of Par1a/b in kidneys was associated with decreased Jag1 expression, Notch2 activation, and Hes1 expression. Decreased Jag1 expression was identified in Par1a/b KH and HK livers.

Conclusions: Par 1a/b are expressed in the developing liver and are required for bile duct development in mice. Par1a/b deletion resulted in decreased biliary epithelial cells and impaired bililary epithelial lumen formation, likely via effects on Jag1 expression and Notch activation. Additional analysis of the Notch signaling pathway in Par1a/b HK livers is ongoing.

174 *FREQUENT OUTPATIENT CLINIC FOLLOW-UPS ARE NOT ASSOCIATED WITH IMPROVED OUTCOMES IN PEDIATRIC PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE*

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Background: In the setting of non-alcoholic fatty liver disease (NAFLD), weight loss is associated with reversal of steatosis, as well as attenuation of hepatic inflammation and fibrosis. Adult studies suggest that weight loss is linked to the frequency of ambulatory clinic visits; however, to date, this has not been studied in children. The aim of this study was to assess the impact of clinic visit frequency on the anthropometric and laboratory outcomes of pediatric patients with NAFLD.

Methods: This was a retrospective study performed in a single institution. Data were collected from two groups of patients who had been followed at two different clinics in the same institution. Patients followed in Clinic A were seen once a year and those followed in Clinic B were asked to return every 3 months. Similar management strategies, such as counseling around lifestyle changes, were followed in both clinics. This study addressed the change in anthropometrics and laboratory parameters over the year following the first clinic visit.

Results: Sixty patients (30 per clinic; 70% male), mean age 12 years, were included in this study. The mean time between first and 'yearly' visit was similar in both groups (A: 12.2±0.3 vs. B: 12±0.4 months) and the mean baseline BMI z-scores were identical (2.9±0.1). Clinic A patients had on average 0.3 visits between first and 'yearly' visit compared to 2.5 visits for those followed in Clinic B. Between the first and the 'yearly' visit, the change in BMI z-score (-0.19±0.07 vs. -0.25±0.05), ALT (-19±9 vs. -30±11 U/L), AST (-13±6 vs. -15±7 U/L), serum triglyceride (0.4±0.5 vs. 0.5±0.5 mmol/L) and total cholesterol levels (0.5±0.2 vs. 0.6±0.1 mmol/L) was not different between the groups ($p>0.05$).

Conclusion: Frequent monitoring of children and adolescents with NAFLD in outpatient clinics is not associated with improved anthropometric or laboratory outcomes.

175 *T CELLS OF OPERATIONAL TOLERANCE: SINGLE CELL MASS CYTOMETRIC ANALYSIS REVEALS A BIOMARKER OF TOLERANCE*

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Introduction: Liver allografts are well tolerated and indeed, some recipients of liver allografts have achieved operational tolerance (TOL). TOL is defined as graft acceptance without functional impairment in the absence of immunosuppression (IS) for at least one year. The major gap in the field is identifying patients who would retain healthy graft function without IS. Single-cell mass cytometry was performed using blood samples from pediatric liver transplant recipients to

comprehensively characterize the immune cell populations in the TOL state with the goal of identifying an immune signature or biomarker of TOL.
Methods: Peripheral blood mononuclear cells from TOL recipients [n=7, 15.8±5.1 years (y) post-transplant, mean age 16.5±5.2 y, mean time off IS = 8.6±4.7 y] in comparison to age-matched recipients on single agent IS (n=8; 12.8±4.1 years post-transplant, mean age 15.2±4.9 y), healthy controls (HC; n=5; mean age 18.8±1.8 y), and patients with acute rejection (AR; n=3; 3.8±5.9 years post-transplant, mean age 9.6±8.0 y) were analyzed by mass cytometry.
Results: Analyses of data was performed using Citrus with 1-fold cross validation using "glmnet" and "pamr" packages. When all groups were compared, one node was significantly increased in the TOL patients as compared to the IS, HC, and AR groups. As this $CD4^+CD5^+CD25^+CD38^{-/lo}CD45RA^-$ population discriminates TOL from all other groups, we have defined this subset as the T cells of Operational Tolerance, or TOT.
Conclusion: This technology, performed for the first time in a transplant population, identified a cellular biomarker to determine patients whom are tolerant and can be weaned successfully from immunosuppression.

176 *LIVER DISEASE IN CHILDREN WITH TYPE 1 DIABETES: ARE WE LOOKING HARD ENOUGH?*
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Introduction: Recent adult studies have demonstrated a previously unrecognized burden of chronic liver disease (CLD) in patients with type 1 diabetes including nonalcoholic fatty liver disease, hepatic glycogenosis and the presence of fibrosis/ cirrhosis. Limited data exist on the prevalence, etiology and impact of CLD in children with type 1 diabetes. Our aim was to evaluate the frequency of routine outpatient assessment of liver disease in diabetic children and the pattern of liver involvement.
Methods: A retrospective chart review was conducted on consecutive pediatric patients with type 1 diabetes followed by the pediatric endocrinology department of our tertiary care center. Data was collected for baseline characteristics, control of diabetes and assessment of liver disease including liver function tests (LFTs) and imaging done in an outpatient setting.
Results: A total of 197 children with type 1 diabetes were included in the study with a mean age at diagnosis of 7.7 ± 4.3 years, a mean age at last visit of 14 ± 5 years and mean follow up period of 6.3 years. The mean BMI percentile was 63.5% and the mean HbA1C was at 10.2%. Unfortunately, routine outpatient assessment of liver disease with LFTs was done in only 42 patients (21.3%). Nine out of the 42 patients (21.4%) who had LFTs checked had elevated ALT and this elevation did not correlate with BMI or HbA1c. Eight patients underwent an abdominal ultrasound, 4 for elevated ALT and 4 for abdominal pain. The ultrasound was normal in 7/8 and one patient had mild hepatomegaly suggestive of either fatty or glycogenic infiltration of the liver.
Conclusion: Children with type 1 diabetes are not routinely assessed for liver disease but the prevalence of elevated ALT in this group was 3-4 times that of the general population, pointing towards the presence of unrecognized liver disease.

177 *COMPONENTS OF METABOLIC SYNDROME ARE MORE COMMON IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS THAN MATCHED NHANES CONTROLS DESPITE SIMILAR PREVALENCE OF OBESITY*
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Introduction: Metabolic syndrome is a clustering of risk factors associated with long-term morbidity and mortality. Metabolic syndrome is highly prevalent after adult liver transplant. We studied whether pediatric liver transplant recipients (LTx) have a higher prevalence of metabolic syndrome than non-transplanted peers.
Methods: Cross-sectional, single-center study of pediatric LTx aged 8-30 years on stable immunosuppression. Patients matched by age, sex, and race/ethnicity with up to 4 controls from NHANES 2009-2012 cohorts. Abnormal values for body mass index (BMI), waist circumference (WC), blood pressure (BP), lipids, and glucose determined using age, gender, and height (for BP)-specific criteria from AAP, AHA, and ADA guidelines. Metabolic syndrome is defined as ≥3 of low HDL, or high triglycerides (TG), WC, BP, or fasting glucose.
Results:
In pediatric LTx (n=78), 28% were overweight or obese by BMI and 17% by WC criteria. NHANES controls did not have a significantly higher prevalence by BMI or WC (Table 1). 82% of all LTx were on tacrolimus, 10% on cyclosporine and 8% off all immunosuppression. Of the 6 LTx on steroids, 67% were overweight/obese, 50% had hypertension, 50% low HDL, and 33% elevated TG. Only 1 LTx with metabolic syndrome was on steroids. Of the 6 subjects off of immunosuppression, 2 were overweight/obese and 1 of those 2 had metabolic syndrome. After adjusting for overweight/obesity, LTx were more likely to have systolic hypertension and low HDL and less likely to have other dyslipidemias than matched controls (Table 1). Adjusting odds ratios (OR) for WC instead of BMI did not change results (data not shown). Subanalysis of LTx ≥5 years since transplant (n=64) and their matched controls (n=256) showed LTx had significantly higher prevalence of both systolic (11% vs. 2% controls, $p<0.001$) and diastolic (5% vs. 1% controls, $p=0.02$)

hypertension with persistently higher OR after adjustment for overweight/obesity. LTx ≥5 years since transplant were more likely than their matched controls to have metabolic syndrome (11% LTx vs. 4% controls, p=0.02). Among subjects with metabolic syndrome, 7/8 LTx and 14/14 controls were overweight/obese with elevated WC.
Conclusion: Pediatric LTx are at higher risk for metabolic syndrome than matched peers. Obesity is a strong risk factor. Further longitudinal study on risk factors, prognosis, and management is needed to prevent long-term morbidity.
Metabolic syndrome components in pediatric LTx and matched NHANES controls

	Liver transplant	NHANES controls	p	OR adjusted for overweight/obesity (95% CI)*	p
n	78	312			
Overweight/obese (BMI)	28%	39%	0.08		
Elevated waist circumference	17%	21%	0.43		
Systolic hypertension	9%	2%	<0.01	4.39 (1.16-16.66)	0.02
Diastolic hypertension	4%	1%	0.13	3.31 (0.51-21.42)	0.18
Low HDL	44%	31%	0.03	2.04 (1.18-3.54	0.01
High triglycerides**	18%	39%	0.01	0.39 (0.17-0.85)	0.01
High fasting glucose**	22%	19%	0.69	1.32 (0.59-2.91)	0.49
High LDL**	4%	18%	0.01	0.19 (0.04-0.92)	0.02
High total cholesterol	6%	33%	<0.01	0.13 (0.04-0.39)	<0.01
Metabolic syndrome	10%	5%	0.08	n/a	n/a

*LTx on glucocorticoid immunosuppression (n=6) excluded from analysis.
**N=55 liver transplant, 125 controls because TG, LDL, glucose only available on subset of controls ≥12 years.

179 *SHEAR WAVE ELASTOGRAPHY (SWE) OF THE NORMAL AND FIBROTIC PEDIATRIC LIVER*
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Purpose: SWE is a promising non-invasive technique to quantify liver elasticity and risk stratify patients with hepatic fibrosis. Accurate assessment may replace more expensive and invasive procedures including liver biopsy. The purpose of this study was:1.To establish normative data for shear wave velocities (SWV) in the normal pediatric liver over a range of ages and 2.To assess the accuracy of SWV quantification for predicting liver fibrosis staging in children with pathologically proven hepatic fibrosis.
Methods and Materials: A Siemens S-3000 ultrasound unit equipped with SWE was used to prospectively evaluate two groups. Group 1 consisted of children with no clinical evidence of hepatobiliary liver disease and group 2 consisted of patients with known liver disease undergoing liver biopsy. Data was collected on Couinaud segment VIII during free respiration with gentle pressure on the abdominal wall using C6 and 9L4 transducers. Two modes were utilized: VTQ, which is a quantification mode and VTIQ, which is a color and quantification mode. Using the C6 transducer in VTQ mode, 5 acquisitions at 4 cm depth were obtained. Using the L9-4 transducer, 5 acquisitions at 2 and 4 cm were obtained in VTQ and/or VTIQ. Average SWV was compiled for group 1 to establish normative values for children. Average SWV in group 2 were correlated with severity of histologic fibrosis using the Scheurer classification.
Results: Group 1 consisted of 48 children(2 months to 18 years). Of these patients, 42 had C6 VTQ, 17 had 9L VTQ, and 22 had 9L VTIQ. C6 mean SWV was 1.36 cm/s, 9L4 VTQ mean SWV was 1.27 cm/s . 9L4 VTIQ color mean SWV was 1.57 cm/s.
Group 2 consisted of 15 patients who underwent liver biopsy. 9 had pathologically proven hepatic fibrosis. Of these 9, 9 had C6 VTQ, 7 had 9L VTQ,and 4 had 9L VTIQ exams. Mean SWV was 1.82 cm/s and 1.78 cm/s for VTQ mode using the C6 and 9L transducers and 1.76 cm/s for the 9L in VTIQ mode.There was a statistical difference in velocity (Table 1) between the two groups using the L9 probe (p<0.0001) and the C6 probe (p<0.0001). No velocity difference was detected using the VTIQ modality (p=0.31). Of the hepatic fibrosis patients, 2 had pericellular fibrosis, 2 had stage II fibrosis, 1 had stage II with focal III, 2 had stage II-III, 1had stage III and 1 had stage III-IV. Velocities did not correlate with pathology grading.
Conclusions: Elevated SWV should raise suspicion for hepatic fibrosis. SWE in children may provide non invasive screening for hepatic fibrosis in children.

NASPGHAN ENDOSCOPY PRIZE

181 *SELF-ASSESSMENT ACCURACY OF PEDIATRIC ENDOSCOPISTS: A PROSPECTIVE CROSS SECTIONAL STUDY*

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Background: Self-assessment is considered to be an integral component of life-long learning and expertise development in medical education. However, studies across medical and surgical disciplines have consistently shown that clinician's self-assessment accuracy is poor for cognitive tasks and studies examining technical tasks have reported mixed results. The self-assessment accuracy of pediatric endoscopists remains unknown. This study aimed to establish if pediatric endoscopists of differing levels of expertise can reliably self-assess their ability to perform clinical colonoscopies using the Gastrointestinal Endoscopy Competency Assessment Tool for pediatric colonoscopy (GiECATkids).

Methods: Novice (performed <50 previous colonoscopies), intermediate (50-250), and advanced (>500) endoscopists from 3 North American academic teaching hospitals were enrolled. Endoscopists were assessed in real-time performing a colonoscopy by an experienced attending endoscopist using the GiECATkids. A second trained observer rated a subset of 22 procedures independently to determine expert inter-rater reliability of the GiECATkids. In addition, participants self-assessed their performance using the same instrument. Self-assessed GiECATkids scores were compared across experience level using Kruskal-Wallis test with post hoc Bonferroni-corrected Mann-Whitney U pairwise comparisons. Self-assessment accuracy and expert inter-rater reliability were determined using intra-class correlation (ICC). Bland-Altman plots were used to graphically represent the relationship between external and self-assessed scores.

Results: 56 endoscopists participated (25 novices, 21 intermediates and 10 advanced). Analysis of self-assessed total GiECATkids scores showed statistically significant increases with level of expertise (Kruskal-Wallis=34.18_2, $p<0.001$): advanced endoscopists scored significantly higher than intermediates ($p<0.001$), who scored higher than novices ($p<0.001$). Inter-rater reliability between the 2 expert raters for the GiECATkids was excellent (ICC=0.88). When external assessors' GiECATkids scores were compared with self-assessed scores for the entire cohort of 56 endoscopists the level agreement was moderate (ICC=0.68). Novice endoscopists' mean self-assessed GiECATkids score was 28.12+/-7.18 compared with the mean rater assigned score of 23.24+/-6.77. For intermediates the mean self-assessed GiECATkids score was 39.61+/-7.30 compared with the rater assigned score of 42.00+/-6.28. For advanced endoscopists, the mean self-assessed score was 50.2+/-0.66 versus a rater assigned score of 51.2+/-1.03. The Bland-Altman plot revealed that novices tend to overrate their performance as compared with external scores. Intermediate and advanced endoscopists showed no specific trend with regard to their self-assessed ratings.

Conclusions: Overall pediatric endoscopists' self-assessment accuracy using the GiECATkids was moderate. In particular, novices tended to overestimate their performance compared to external assessment, whereas intermediate and advanced endoscopists did not consistently under or overrate their performance. Nevertheless, the GiECATkids shows promise as a tool to help support pediatric endoscopists' self-assessment accuracy within the clinical setting.

182 *UTILITY OF ROUTINE COLONIC BIOPSIES DURING PEDIATRIC COLONOSCOPIC POLYPECTOMY FOR BENIGN JUVENILE INFLAMMATORY POLYPS*

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Introduction: Benign juvenile inflammatory polyps are commonly encountered in pediatric gastrointestinal practice. Most juvenile polyps are hamartomatous with little malignant potential however it can be difficult to differentiate these hyperplastic polyps from other types, i.e. adenomatous, on visual inspection alone thus requiring histologic examination. There is minimal data on the need for random biopsies from various parts of the colon during colonoscopic polypectomy for presumed juvenile hyperplastic polyps with an otherwise normal appearing colon. We hypothesize that in the absence of gross mucosal abnormalities the likelihood of finding a histologic abnormality from a routine random colonic biopsy would be low and therefore these biopsies may not be necessary.

Methods: We performed a retrospective chart review identifying all patients aged 1 to 18 years who underwent a complete colonoscopy and polypectomy for suspected colo-rectal polyps from January 1st, 2004 to July 1st, 2014 at Ann & Robert H. Lurie Children's Hospital of Chicago. Indication for procedure, age at procedure, number of polyps, gross and histologic findings, and any management changes that resulted from endoscopic findings were recorded. A colonoscopy was considered to be complete if it included examination of the cecum or terminal ileum. Exclusion criteria included known

history of polyposis syndrome, more than 5 polyps on colonoscopy, history or endoscopic findings suggestive of inflammatory bowel disease, and incomplete procedure documentation. The diagnosis of juvenile inflammatory polyps was established histologically. Practice variation related to this clinical setting was assessed using an online survey distributed via the National Pediatric Gastroenterology list serve.
Results: A total of 141 patients underwent colonoscopy with polypectomy of which 72 patients were included. 63% were male, the mean age was 6.5 years with a range from 1 to 17 years, and all had hematochezia at presentation. There were gross findings other than colorectal polyps in 7 patients (10%) and these included lymphonodular hyperplasia, a small ulcer in the sigmoid colon, and a small erythematous cecal patch. 68 patients (94%) had juvenile inflammatory polyps on histologic examination. Routine colonic biopsies were performed in 55 patients (76%). In 8 of these patients (15%), histologic abnormalities such as mild focal active colitis and mild chronic colitis were seen. In all of these cases, there was no change in management based on histologic findings.
A total of 72 providers responded to the online survey of which 90% were attending physicians. 56% of respondents reported they would not take any colonic biopsies during colonoscopic polypectomy in the absence of other mucosal abnormalities. 39% would routinely take biopsies from both the terminal ileum and the colon. 6% would biopsy the colon only and none reported they would biopsy the terminal ileum only.
Conclusion: In children undergoing colonoscopic polypectomy for benign juvenile polyps, routine colonic biopsies may not be performed in the absence of mucosal abnormalities. The overuse of pathology services and increased procedural time, risk and cost can be avoided.

Friday October 9, 2015

CONCURRENT SESSION 1 – MALABSORPTION

183 *IDENTIFICATION OF ION TRANSPORT DEFECTS RESPONSIBLE FOR SECRETORY DIARRHEA IN MICROVILLUS INCLUSION DISEASE (MVID)*

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Microvillus Inclusion Disease (MVID) is a rare inherited childhood disease that clusters in the Middle East and Navajo Indians and causes death in infants and children due to intractable secretory diarrhea. Diarrhea in MVID is often worse than cholera, with increased stool Cl^- and Na^+ concentrations. Secretory diarrhea is associated with brush border atrophy and microvillus-containing inclusions (MVIs) within mature enterocytes. Loss of function mutations in the apical recycling actin motor Myosin Vb (Myo5b) leads to MVID. But how loss of Myo5b leads to secretory diarrhea is not understood. We hypothesized that defects in CFTR (Cl), NHE3 (Na) and DRA (Cl/HCO3) transport are implicated in MVID diarrhea. We generated two independent polarized intestinal cellular (crypt and villus) models of MVID that lack Myo5b expression, and replicate all the key features of human MVID enterocytes. Results: CFTR localized to the BBM of human MVID enterocytes, similar to its normal distribution. Label for NHE3, and DRA confirmed internalization below the BBM, consistent with reduced Na and Cl- absorption. Electrophysiologic studies in crypt and villus cell models of MVID confirmed unopposed CFTR mediated chloride secretion, reduced NHE3 mediated Na absorption and reduced DRA mediated Cl absorption that is consistent with the secretory diarrhea profile in human MVID. These studies identify for the first time, the ion transport defects responsible for MVID
diarrhea.

184 *POOR SENSITIVITY OF TTG FOR PREDICTING MUCOSAL HEALING IN CHILDREN WITH CELIAC DISEASE ON A GLUTEN FREE DIET*

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Background: Approximately 33%of adult patients diagnosed with celiac disease (CD) have persistent intestinal damage despite following a gluten free diet (GFD) for more than one year. Given that serology tests, such as IgA tTG, are accurate at diagnosis but less accurate in predicting intestinal healing, the American College of Gastroenterology recommends consideration of a repeat endoscopy to ensure intestinal healing in adults with CD who have persistent or a relapse of symptoms while on a GFD. In pediatric patients, intestinal healing is thought to occur in the majority of cases within one to two years of diagnosis. This was recently confirmed in a prospective Australian study of 150 pediatric patients which found that only 5% of patients had persistent villous atrophy upon follow-up duodenal biopsy. Aim: To assess intestinal remission in pediatric patients with CD on a GFD and evaluate whether tTG correlates with intestinal disease activity at time of follow-up endoscopy. Methods: We performed a retrospective chart review of 71 patients ages 1-21 who were seen at MassGeneral Hospital *for* Children between January 2012 and Mach 2015.Patients were identified by ICD-9 code and procedure code or through the Celiac Center for Research and Treatment Research Registry. For inclusion patients must have had a diagnosis of CD, defined as Marsh 3 intestinal damage, and have undergone a second endoscopy with duodenal biopsy after embracing a GFD. Descriptive statistics using means and chi square analysis when appropriate were calculated using SAS. Logistic regression was performed to evaluate the odds ratios for several covariates. Results: The characteristics

of the cohort are described in Table 1. At follow-up endoscopy, despite 98% of patients describing strict adherence to a GFD and 100% of patients seeing a dietician, 27% of patients had villous blunting on a GFD. At follow-up endoscopy, 33%of symptomatic, 22% of asymptomatic patients and 15% of patients found via screening and thus never symptomatic had persistent villous blunting. IgA tTG as a marker of mucosal pathology at time of follow-up biopsy had a sensitivity of 39% and a specificity of 79%, a positive predictive value of 41% and negative predictive value of 78%. Age at diagnosis, gender, time on a GFD, and follow-up tTG were not associated with villous blunting at follow-up endoscopy, however this is likely due to our small sample size. Conclusion: In our cohort, 27% of patients diagnosed with CD who underwent a repeat biopsy had persistent mucosal damage meeting Marsh 3 criteria regardless of whether symptoms were present. The accuracy of IgA tTG in predicting intestinal remission is poor compared to initial diagnostic rates

Table 1. Characteristics Of Subjects

Age at Diagnosis (years) (SD)	10.8 (4.8)
Gender (%F)	58%
Comorbid Autoimmune Disease	26%
Initial tTG positive	96%
Months on a GFD (SD)(CI)	43 (33) (30-46)
Sympatomatic at 2nd Biopsy	51%
Active Disease	27%

Friday October 9, 2015

CONCURRENT SESSION 1 – NUTRITION

NASPGHAN NUTRITION PRIZE

185 *ETHANOL LOCK THERAPY IN CHILDREN WITH INTESTINAL FAILURE: INFECTION PREVENTION AND VASCULAR PRESERVATION*

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Background: Children with intestinal failure (IF) are dependent upon parenteral nutrition (PN) delivered via a central venous catheter. Presence of a central line introduces the risk of life-threatening central line associated blood stream infections (CLABSI), repeated line placements, disruption of nutritional rehabilitation and venous thrombosis. Recurrent sepsis or eventual loss of patent central vessels for catheter placement may necessitate small bowel transplantation. Previous studies suggest that ethanol lock therapy (ELT) may be an effective strategy to prevent CLABSI occurrence. However, these studies also raise concern that ELT may be associated with impaired catheter integrity and central venous thrombosis.

Objective: The primary objective of this study was to determine whether ELT was associated with a decreased rate of CLABSI in children with IF receiving home PN. The secondary objective was to evaluate the rates of central venous thrombosis and catheter rewires, repairs, and replacements while on and off ELT.

Design: A retrospective cohort study looked at all children in the Intestinal Rehabilitation Program at The Children's Hospital of Philadelphia (CHOP) who received ELT between July 1, 2011 and June 30, 2014. ELT was initiated according to CHOP Hospital policy in patients with silicone catheters after one or more CLABSI and consisted of daily instillations of 70% ethanol for $\geq$ 4 hours while the child was not receiving PN. Chart review was completed to determine the number of CLABSIs, central line replacements, rewires, repairs, and central line associated thrombosis on and off of ELT. Patients were evaluated from the time of their first central line while being followed at CHOP until the central line was discontinued and/or their care was transferred elsewhere.

Results: Twenty-six patients (age 6 months to 22 years at ELT initiation) were followed for an average of 537 days off of and 447 days on ELT. While off of ELT, there were 7.1 CLABSIs per 1000 catheter days, which decreased to 0.9 per 1000 catheter days on ELT (p=0.02). The rate of central line replacement decreased from 7.4 to 0.9 per 1000 catheter days (p=0.005) and the rate of rewiring of the central line decreased from 3.6 to 2.4 per 1000 catheter days (p=0.54), but the rate of central line repair increased from 0.3 to 1.5 per 1000 catheter days (p=0.04). The rate of central line associated thrombus decreased from 1.4 to 0.2 per 1000 catheter days (p=0.13).

Conclusions: In this largest study of ELT in the pediatric IF population to date, 70% ELT was associated with a significant reduction in the rates of CLABSI (89%) and central line replacement (93%). There was no increase in the rate of central line associated thrombus formation associated with ELT. These results demonstrate that ELT is an effective means of preventing CLABSI in children with IF, and that ELT may reduce the need for line replacement without an increased incidence of central line associated thrombosis.

Friday October 9, 2015

POSTER SESSION II

ENDOSCOPY/QI/EDUCATION

186 *USING A TRIAGE QUESTIONNAIRE TO PROCESS URGENT REFERRALS IN A PEDIATRIC GASTROENTEROLOGY CLINIC*

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Background: Subspecialty referrals are made by primary care physicians to obtain short-term consultation involving management advice or for long-term co-management, particularly for patients with chronic disease. The nationwide shortage of pediatric subspecialists can lead to longer wait times for appointments, which is associated with delays in diagnosis, greater costs, and worse outcomes. The adoption of a standardized referral system can mitigate the effects of the scarcity of subspecialists and improve both the referring and subspecialty physician's ability to make treatment decisions.
QI Objective: To devise an efficient and effective method to triage urgent general pediatric clinic referrals to a pediatric gastroenterology clinic.
Methods: A triage questionnaire was developed to identify clinical signs and symptoms that would warrant urgent evaluation in our pediatric gastroenterology clinic, such as bloody stools, weight loss, anemia, or dysphagia. Input from clinic staff (faculty, fellows, and nurses) was incorporated into questionnaire development. Variables analyzed included number of urgent referrals processed, percentage of referrals qualifying for an urgent appointment, number of calls pertaining to referrals, and referral processing times.
Results: The triage questionnaire was introduced in March 2014 at a main pediatric gastroenterology clinic in the Southwest with a catchment area of >1 million children. When a general pediatrician requested an urgent referral, the triage questionnaire was provided to the ordering physician. Ordering physicians were required to complete the questionnaire before the referral could be processed. Pediatric gastroenterologists processed an average of 67 (SD 16.5) urgent referrals per month, over the course of ten months, 19.9% (SD 9.3%) of which fulfilled criteria for urgent evaluation. Prior to initiation of the intervention, an average of 44 referrals were processed per month, with 20% fulfilling criteria for urgent evaluation. For all referrals with complete questionnaires, an average of 86% (SD 10%) were processed within 48 hours of receipt by a pediatric gastroenterologist for review, compared to less than 75% prior to the intervention.
Conclusion: The use of a triage questionnaire to process urgent general pediatric physician referrals to a pediatric gastroenterology clinic resulted in timelier processing of referrals. This enabled an increase in processed referrals per month. A future direction for investigation would be to examine whether this improved efficiency in referral processing results in improved patient outcomes and/or patient satisfaction scores.

187 *TRANSITIONS IN PEDIATRIC GASTROENTEROLOGY: A SNAPSHOT OF PROVIDER PERSPECTIVES*

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Introduction: Transition and transfer to adult-oriented health care is widely recognized as an important yet challenging task for the growing number of adolescents and young adults with chronic medical conditions. There is significant variability in transition practices and a paucity of data to inform best practice for improvement of transition or optimal timing of transition and transfer. In this study, we describe the preferences of pediatric gastroenterologists and their current transition practice patterns.
Methods: An on-line survey was distributed via email to members of the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). Survey was voluntary and confidential. Data was analyzed using descriptive statistics and associations between categorical variables were evaluated by the Pearson $\chi 2$-test.
Results: Responses were obtained from 175/1423 NASPGHAN members (12%). Respondents were half male (53%) and most (83%) practiced in an academic setting. 35% were in practice for >20 years, 15% for 11-20 years, 17% for 6-10 years, 26% for $\leq$ 5 years and 7% were fellows.
Almost three quarters reported providing transition or self-care management education, but only 22% used a structured tool or readiness assessment. Most respondents (88%) reported having age cut-offs above which they would no longer accept

new referrals, with the most common age being 18y (57%), followed by 21y (20%). Only one third reported the ability to provide age appropriate care to patients over age 21 years, with 27% indicating a preference that their institution *should* provide care to those >21y. This did not vary significantly by gender or years in practice. A majority (63%) of respondents indicated that their practice or institution has a policy regarding age of transfer, but for most (79%) the policy is flexible. There was wide variability about preferences for what ideally would trigger youth to transfer to adult care - age 18y (27%) vs. age 21y (27%) vs. milestones (22%) vs. psychology or readiness (15%).
The most common condition which providers had difficulty in transferring care was among adults with developmental delay/ neurologic impairment (81%), where identifying adult providers was the most frequently described challenge. Overall, common barriers to successful transition reported were parent (81%) and patient (74%) attachment to pediatric healthcare providers.
Conclusions: Preferences and practices surrounding transition preparation and transfer to adult care vary widely, without respect to gender or experience of provider. There is opportunity to integrate structured assessments for transition preparation, improve education, as well as create clearer transition policies for practices. Identification of problematic transition for subgroups of patients, such as those with neurodevelopmental disabilities, can help focus efforts to improve practices. As data emerges from all perspectives, ideal transition preparation and practice can be better described and implemented.

189 *EXPERIENCE WITH THE USE OF N-2-BUTYL-CYANOACRYLATE (HISTIOACRYL) FOR TREATMENT OF GASTRIC VARICES IN PEDIATRIC PATIENTS IN A TERTIARY HOSPITAL IN MEXICO*

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Background. Gastric varices (GV) are vascular dilations of the gastric venous system, produced by an increase in the pressure of the portal system. GV are presented in 5-33% of patients with portal hypertension with a bleeding- risk of 25% in the first two years and mortality of approximately 45%. The main complication is variceal bleeding.
Endoscopic obliteration with N-butyl-2-cyanocrylate (histioacryl) is considered the first-line treatment.
Aim. To describe the incidence of complications by treatment with sclerotherapy for gastric varices in the Paediatric Gastroenterology and Nutrition Department at the Instituto Nacional de Pediatría.
Methods. Patients 0 to 18 years-old with diagnostic of gastric varices who have received treatment with sclerotherapy since june 2010 to january 2014, were included. We reviewed the medical record, reporting all complications leaded by this procedure.
Results. Twelve medical records of patients treated with sclerotherapy were review. A total of sixteen procedures were performed, four of these sclerotherapies were done as a second procedure. The middle age of the patients was four years-old.
The whole gastric varices were reported as esophagus-gastric type (GOV) according with Sarin's classification, 13 (81.3%) GOV1 and 3 (18.7%) GOV2 type. Re- bleeding in the first 24 hours was reported in just one patient as a complication of sclerotherapy.
Conclusions
Endoscopic obliteration with N-butyl-2-cyanocrylate (histioacryl) is an efficient and secure treatment for gastric variceal bleeding.

195 *INCORPORATING ORAL HEALTH INTO A PEDIATRIC GASTROENTEROLOGY CLINIC DEDICATED TO CHILDREN WITH AUTISTIC SPECTRUM DISORDER*

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Background: Oral hygiene is known to be compromised in children with autism spectrum disorder (ASD), secondary to a combination of feeding difficulties and abnormal feeding practices (rigid food preferences, oral aversions, and sensory and behavioral issues). As a result, the American Academy of Pediatric Dentistry stresses the importance of early and thorough dental services in this population.
In our monthly Pediatric Gastrointestinal (GI) clinic specifically dedicated to patients with ASD, we introduced a multidisciplinary approach in which the gastrointestinal needs are addressed along with nutritional, feeding, and oral health issues. The clinic team includes a pediatric dental resident who performs a gentle evaluation, offers appropriate recommendations, provides fluoride treatment, and arranges further referrals when necessary.
Objectives: To assess overall oral health of children with ASD in a novel clinic setting combining nutritional and dental care and to determine the feasibility of delivering oral health care in this setting.
Methods: We developed a clinic intake form for patients attending the ASD GI clinic. This included a dental questionnaire

(teeth brushing, regular dental care), food consumption and preferences (texture, color, food groups/variety, sugary beverages), and feeding methods (bottle, nightly feeds). Along with the routine physical examination, the dental resident documented any oral findings (caries, malocclusion, bruxism, etc.)
Results: Thirty charts were reviewed in this pilot study (Table).
During the visit, 12 patients (38%) received a fluoride treatment and 5 patients (16%) were referred to the pediatric dental clinic. Parents were instructed in the two-person brushing technique when the child had severe tactile defensiveness and given a referral for mouth guards for severe bruxism. Feeding therapy and nutritional consultation were offered to all patients. Bottle use and juice consumption were discouraged.
Conclusion: Our preliminary results show that many parents of children with ASD struggle with oral care. They often do not present to the dentist until damage is done. In addition, we documented that many patients did not have healthy feeding and dental habits. A multidisciplinary approach, such as described here, offers a unique opportunity for improving oral health for this challenging group of patients. The clinic also offers the advantage of decreasing the number of clinic visits as both GI and oral health care can be delivered simultaneously.
Oral and Feeding Health Questionnaire

	Number of Patients (%)
Juice consumption 1-2 cups/day	18 (82%)
Juice consumption >2 cups/day	4 (18%)
Bottle usage >2 years of age	8 (27%)
Receiving feeding therapy	13 (43%)
Mashed/Liquefied Foods Only	18 (60%)
Limited Repertoire	22 (73%)
Dental visits: Never/once	11 (37%)
Dental visits: 1x-2x/year	19 (63%)
Brushing frequency: ≤1x/day	19 (63%)
Brushing frequency: ≥2x/day	11 (37%)
Caries	7 (23%)
Malocclusion/Snoring	10 (33%)
Bruxism	7 (23%)

196 *PERI OPERATIVE RISK REDUCTION IN FRAGILE PATIENTS WITH GASTROINTESTINAL DISEASES: PERFORMING MULTIPLE PROCEDURES DURING A SINGLE ANESTHESIA*

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Background: The morbidities associated with anesthesia have been well-documented, with patients under 2-3 years of age and those with recurrent exposure to anesthesia potentially at increased risk. Medically fragile children, such as those with autism, cerebral palsy, and multiple congenital anomalies often undergo a number of operative procedures, each of which may require separate preoperative, perioperative, and inpatient care. Many have gastrointestinal disorders. In our institution, we noted that quite a few of the children under the care of our Pediatric Gastrointestinal service whom required endoscopy also had additional operative procedures planned in the weeks around our procedure. As a service to such patients, we developed an initiative to coordinate these procedures during a single general anesthesia session. We hypothesized that with careful planning and an expeditious transition from one procedure to the other, anesthesia duration would be shortened while decreasing the number of visits to the hospital.
Objective: To estimate the potential time savings for children undergoing multiple procedures during one anesthesia session.
Methods: As a part of an ongoing QI project, we analyzed the charts of Pediatric Gastroenterology clinic patients who had

an endoscopy scheduled to be performed with other operative procedures during a single anesthesia or sedation. We noted the number of procedures, as well as the induction and recovery times.
Results: Of the 23 patients, 19 had two procedures and 4 had three procedures performed in the single session. In addition to the endoscopies, the other procedures included: laparoscopic cholecystectomy, laparotomy, gastrostomy with fundoplication, fluoroscopy examination of intestines, tonsillectomy and adenoidectomy, dental extraction and oral reconstruction, central line insertion, cystoscopy, circumcision, and arthroscopic repair of the knee. The median time of induction was 18 minutes (10,29) and the median time of recovery was 15 minutes (10,17).
Conclusions: By adding the induction and recovery periods, our data suggest that more than 30 minutes (two procedures) or 60 minutes (three procedures) of anesthesia/operating room time could potentially be saved by combining these procedures at the time of endoscopy. This analysis assumes that induction and recovery times would be the same when each procedure is done separately. Regardless, this single anesthesia approach offers the potential benefits of less total time under anesthesia as well as fewer pre-operative and post-operative visits to the hospital. Further prospective study is needed to better quantify the decrease in anesthesia exposure, as well as to assess other potential benefits, such as total cost and days of school/work missed.

198 *QUALITY OF LIFE IN CHILDREN WITH FUNCTIONAL CONSTIPATION*

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Background. Functional constipation (FC) is a chronic disease that translates the presence of fecal impaction, which often compromises the patient's quality of life, social functioning and ability to perform daily activities, predominantly in the area of psychological alterations over the physical ones.
Methods. In an analytical cross-sectional study, 70 patients were included 8 years to 15 years 11 months ROME III criteria for FC. The PedsQL scale generic Spanish version was applied to the child and the guardian, including the physical, emotional, social and school functioning areas. Statistical analysis: frequencies, percentages x^2, t student.
Results. The average age was 10.3 years, an average score of quality of life of 73.13 points (13.35± SD) and 68.11 points (17.20 ± SD) in the survey applied to the guardians, lower score with statistic difference p= 0.001 was observed. In the interview realized to patients the lowest score was in school performance with 67.92 points (14.28 ± SD), followed by emotional area with 68.78 points (20.17± SD), physics area with 75.40 points (14.11 ± SD) and finally the social area with 79.21 points (23.3±SD). In the guardians, the lower score was the emotional area with 54.92 points (21.6± SD), followed by school performance with 66.7 points (20.95± SD), physics with 69.43 points (18.44 ± SD), and the social with 73.4 points (23.73 ±SD). When comparing scores between children and parents, statistically significant difference was found in the physical, emotional and social areas. Defecation pain showed statistical difference in the scores of the child; and fecal incontinence and toilet obstruction, on averages reported by the tutors.
Conclusions. The deterioration of the quality of life of patients with FC was demonstrated, and had similar scores to those of other studies. The multidisciplinary management of patients with FC is necessary, the development of a specific instrument for measuring quality of life in children with FC is required

200 *PREVALENCE OF CELIAC DISEASE IN CHILDREN WITH DIABETES MELLITUS TYPE 1 AT HOSPITAL UNIVERSITARIO DEL VALLE "EVARISTO GARCÍA". CALI, COLOMBIA*

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Introduction: Celiac disease (CD) is more common in patients with type 1 diabetes mellitus (DM1) than in the general population; no data on this association in the Colombian population. Objective: To determine the prevalence of CD in children younger than 18 years diagnosed with DM1 from Hospital Universitario del Valle "Evaristo García" (HUV) in Cali, Colombia and establish potential associations. Methodology: Study of prevalence in children with DM1 of Pediatric Endocrinology at the HUV. They were taken from the medical record sociodemographic, personal, familial, physical examination and laboratory data; It was taken by IgA anti-transglutaminase for screening fingerstick. Being positive result, an upper digestive tract endoscopy was performed and takes 4 duodenal biopsy for histopathological analysis according to the Marsh classification and diagnostic confirmation. Results: 112 children were included with a mean age of 11±3.7 years, 58.4% female, born in Cali 63.39% and 56% white; 46.43% in family history of diabetes was found and 5.8% had thinness and overweight, respectively. They were seropositive for CD in 9.8% and was confirmed by histopathology in 2.7% of the population. The most common symptoms were irritability (46.3%) and abdominal pain (31.2%). Conclusion: In children with DM1 from HUV in Cali, Colombia, CD seroprevalence is 9.8% and 2.7% by histopathology, without finding possible associations.

201 *ESR AND CRP IN INFLAMMATORY BOWEL DISEASE: DO WE NEED BOTH?*

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Background: Measurement of serum inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) is common in patients with inflammatory bowel disease (IBD) These are often ordered to help assess for inflammation as routine screening and in the setting of increased symptoms. Though both tests are non-specific markers of inflammation, they are routinely obtained together. It is not known whether such patients could be routinely monitored with ESR or CRP alone, thus decreasing the number of laboratory studies and the costs associated with the care of these patients.
Aims: The primary aim of this quality improvement project was to determine the correlation and agreement of ESR and CRP in patients with inflammatory bowel disease. The secondary aim was to determine if correlation and agreement vary across different care settings.
Methods: All patients with IBD who were seen at least once in the gastroenterology office at The Children's Hospital of Philadelphia in 2014 were identified using ICD-9 codes. Results of every ESR and CRP obtained in tandem during 2014 were recorded. The patient care setting was also noted (outpatient, inpatient, ED, endoscopy suite). Qualitative (high/normal) results were examined for association using Chi-squared test and agreement by calculating the Kappa statistic. Absolute values were examined for correlation by calculating the correlation coefficient.
Results: 2420 paired ESR and CRP values were analyzed from 662 unique patients. There was a statistically significant association between qualitative ESR and CRP results (Chi-square $p<0.001$). There was only modest agreement between ESR and CRP (Kappa =0.463). There was positive correlation between absolute values of ESR and CRP (r=0.5098). The correlation was greater in patients seen in the endoscopy suite (r=0.5882). Otherwise care location did not impact association, agreement, or correlation.
Conclusions: There is a statistically significant association between the qualitative results of ESR and CRP. However, the agreement and correlation of the tests is only modest in this population. While identifying redundancy between ESR and CRP may represent an opportunity for reduction in lab testing and cost savings, this study does not demonstrate that such redundancy exists in this population as a whole. Further outcome-based research is needed to determine if either ESR or CRP could be eliminated from routine testing, perhaps based on certain clinical factors or scenarios.

202 *RETROSPECTIVE REVIEW OF THE EFFECT OF POSITIOINAL MODIFICATIONS ON GASTRIC TRANSIT TIME AFTER ORAL INGESTION OF WCE IN PEDIATRIC PATIENTS*

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Objective: To assess effect of positional modification, (upright, left lateral and right lateral) on gastric transit time of Wireless Capsule Endoscopy (WCE) after oral ingestion.
Background: WCE has several possible advantages compared with other means of visualizing the small bowel. It is noninvasive and permits examination of the majority of the small bowel mucosa, which is not possible with push enteroscopy or MRE. The main disadvantage of WCE is that it does not permit tissue sampling or therapeutic intervention. In addition, the capsule does not reach the cecum within recording time in approximately 16 % of cases. To the best of our knowledge there is no pediatric study evaluating the effect of positional modifications after WCE ingestion on gastric transit time.
Methods: Retrospective case-control of 23 pediatric patients who underwent WCE at URMC from 2013 to 2015. Demographic data, gastric transit time and medical diagnoses were collected. The primary outcome was to evaluate if the gastric transit time was altered by positional modification (upright, left lateral and right lateral). Patients remained in lateral positions for a half hour after ingestion of WCE. Summary statistics of the demographic variables were analyzed using frequency, mean, and standard deviations. Comparisons of these variables were performed using the fisher exact test and ANOVA analysis. A $P<0.05$ was considered statistically significant.
Results: The subjects had no significant difference in their demographic data and medical diagnoses among the 3 groups. The gastric transit time was significantly shorter (P=0.00756) in the right lateral group (27 minutes) compared to the left lateral group (42 minutes) and the upright group (62 minutes). There was no correlation between medical diagnoses and gastric transit time.
Conclusion: The gastric transit time is significantly shorter in patients who ingest the WCE and lay in the right lateral position, thus improving recording time, time to reach the cecum and mucosal evaluation.

205 *HEALTH DISPARITIES IN PEDIATRIC GASTROINTESTINAL PROCEDURES*

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Background: There is an insufficient amount of literature regarding the role of health disparities as related to pediatric

gastrointestinal (GI) procedures. We hypothesized that health disparity measures such as socio-economic factors, language and race play an important role in determining whether patients receive an emergent vs. non-emergent GI procedure. Identifying specific health disparities that predispose patients to emergent procedures may help improve timely care and possibly reduce health care costs.
Aims: The aims were to characterize the existing pediatric population undergoing GI procedures and assess whether specific health disparity factors are associated with emergent vs. non-emergent procedures.
Methods: We reviewed the medical records of 2,221 patients undergoing GI procedures at our institution from January 2012-December 2014. Emergent was defined as procedure performed in emergency manner as inpatient. Non-emergent was defined as procedure performed in elective manner usually as outpatient. Health disparity factors analyzed included: Age (0-5; 6-11; 12-17; or 18-25 years), Gender, Insurance type (Medicaid or commercial), Race (Caucasian, African American, Hispanic, or Other), and Language (English, Spanish, or Other). Logistic regression analysis was performed and odds of undergoing emergent procedures for each factor was identified.
Results: Most study patients were male (52.8%), Medicaid users (62.7%), Caucasian (43.6%), and spoke English (91.8%). 8.7% of all patients had an emergent procedure. Logistic regression analysis showed significant odds ratios [OR, p-value] for ages 0-5 years [1.55, 0.006], ages 6-11 years [0.63, 0.011], 18-25 years [1.70, 0.038], females [0.75, 0.008], commercial insurance users [0.62, 0.001], African Americans [1.83, 0.023] and other race [1.77, 0.018].
Conclusion: Health disparities in race, gender, insurance, and race were present in this population of pediatric patients undergoing emergent vs. non-emergent GI procedures. Patients were more likely to have an emergent procedure if they were ages 0-5 and 18-25 years, were African American or other race. Patients were less likely to have an emergent procedure if they were ages 6-11 years, female or had commercial insurance. More research is necessary to understand why these trends exist and how they influence the quality and cost of healthcare. Interventions designed to address these disparities should then be implemented to ensure appropriate and timely care for the population.

209 *NATURAL DISASTER PREPAREDNESS IN FAMILIES WITH TOTAL PARENTERAL NUTRITION DEPENDENT CHILDREN*

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Purpose: To assess disaster preparedness in families with total parenteral nutrition (TPN) dependent children
Background: Natural disasters can disrupt the community and the healthcare system. It can be more challenging for children dependent on technology for survival. A survey of families with children with special health care needs showed that their disaster preparedness level was lower than that of general population (Baker & Baker, 2010). At Childrens Hospital Los Angeles we care for many families with children requiring TPN to maintain their hydration and nutrition. Earthquakes are the disaster most likely to occur in California. Power outages or lack of transportation after an earthquake may have serious consequences for this vulnerable patient population.
Methods: CHLA organized its first intestinal rehabilitation day (IR day) on July 12th 2014. We took this opportunity to understand disaster preparedness in these families. Twenty six families attended IR day. Fourteen parents completed the anonymous survey. We used a mixed-methods research design for our survey and utilized a previously validated special health care needs survey developed by Dr.Baker. The survey was followed by focus group discussions to elicit more detailed information regarding their disaster preparations and specific concerns regarding disaster preparedness.
Results: No family had a written Emergency Communication Plan.69% did not have a 3-day emergency supply kit.Only one family had a Medical Emergency Plan.
Conclusion: Most families with TPN dependent children did not feel prepared for a natural disaster. Our long term goal is to provide each family with a individualized disaster plan and to increase their confidence in their ability to handle a natural disaster. Based on our initial learning we are progressing towards this goal with a pilot program for a specialized disaster tool kit for our patients.

Questions		No(%)	Yes (%)	N/A (%)	N/R
1	Does your family have a written Family Emergency Communication Plan in case you are separated during a disaster?	14(100)	0 (0)	0(0)	
2	Does your famaily have a designated meeting place outside of your home?	10(71)	4 (29)	0 (0)	
3	Does your family have a designated meeting place outside of your neighbourhood?	11(79)	3 (21)	0 (0)	
4	Does your family have an emergency supply kit that can last you for three days?	9 (69)	4 (31)	0 (0)	1
5	Does your family have a fire escape plan for your home?	9 (64)	5 (36)	0 (0)	
6	Does your family keep emergency supplies in each of your vehicles?	8 (57)	6 (43)	0 (0)	
7	Does your family have three gallons of water stored for each person in the household (3 days supply) ?	9 (64)	5 (36)	0 (0)	
8	Does your family have enough stored food that does not need refrigeration or preparation that can sustain your family for three days?	8 (57)	6 (43)	0 (0)	
9	Do you have a working flashlight with an extra set of batteries in your home ?	3 (21)	11(79)	0 (0)	
10	Do you have a packaged first aid kit at your home?	3 (23)	10 (77)	0 (0)	1
11	Do you have container that is both fireproof and waterproof for storing papers at your home?	11(79)	3 (21)	0 (0)	
12	All family members over 14 year old know how to turn off the gas, power and water in case of emergency	8(57)	5 (36)	1 (7)	
13	I have a copy of my childs Medical Emergency Plan (Emergency Information Form)completed by his/her doctor	13(93)	1 (7)	0 (0)	
14	All children over 5 years old in the house are able to spell their full name, address and phone number.	4 (29)	7 (50)	3 (21)	
15	Do you have medication on hand at all times for each family members with a chronic medical condition?	3 (25)	9 (75)	0 (0)	2
16	Do you a have back-up source of electricity for your child	4 (29)	10 (71)	0 (0)	
17	Do you additional supplies necessary for your child	4 (29)	10 (71)	0 (0)	
18	Do you have \"back-up\" nutrition for your child?	3 (21)	11 (79)	0 (0)	

Demographics		Frequency (%) N=14	No Response
Parent Gender	Female	7(54)	1
	Male	6(46)	
Parent Age	<30 Years	5(36)	
	30-<40 Years	6(43)	
	40 + Years	3(21)	
Marital status	Divorced	1(7)	
	Married	10(71)	
	Single	3(21)	
Child Gender	Female	5(42)	2
	Male	7(58)	
Child Age	<1 Year	3(23)	1
	1 to <4 Years	6(46)	
	4+ Years	4(31)	

210 *FOLLOWING ONE YEAR FOR CELIAC DISEASE IN COLOMBIAN CHILDREN WITH DIABETES MELLITUS TYPE 1*

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Introduction: Celiac disease (CD) is an autoimmune disorder caused by the ingestion of gluten in genetically predisposed children. You perform early screening and monitoring is justified in asymptomatic children and families as early intervention prevents complications. Objective: To determine the prevalence of CD in children with diabetes mellitus type 1 (DM1) and their family for following 1 year in the Pediatric Endocrinology from Hospital Universitario del Valle in Cali, Colombia. Methodology: Descriptive observational study of 112 children with DM1, who were followed up for one year. Children were initially took IgA anti-transglutaminase (IgA tTGA) and control one years later. When the result was positive, an endoscopy with four duodenal biopsies and serum HLA-DQ2/DQ8 were performed. In the relatives in first degree of consanguinity of the positive children were took tTGA. Results: Of the initial 112 patients, 11 (9.8%) were IgA tTGA positive. A year later, of thirty seven patients, 3 (8.1%) were IgA tTGA positive, 2 of them (5.4%) with initial IgA tTGA and HLA-DQ2/DQ8 positive. One of these children who underwent endoscopy, their duodenal biopsies were negative for CD. Relatives were IgA tTGA negative. Conclusion: The prevalence of CD in this population was 5.4% diagnosed by the presence of IgA tTGA positive and the presence of HLA-DQ2/DQ8. 1 case was found gluten intolerance but unconfirmed diagnosis of CD.

212 *PREVALENCE AND TREND OF HISTOPATHOLOGICAL ABNORMALITIES OF UPPER GASTROINTESTINAL TRACT IN CHILDREN*

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Background: Common histopathological findings in children undergoing an upper endoscopy include esophagitis,gastritis, and duodenitis. In this study we aimed to assess the prevalence and trend of these findings in a large cohort of children undergoing endoscopy over five years.

Methods: We studied all children who had an upper endoscopy and biopsies from 2008 to 2012 in our institution. We reviewed all histopathology reports for esophagitis, gastritis and duodenitis. We assessed the prevalence of each condition every year and noted annual trends. Coexistance of histopathological conditions were recorded and correlation between these were assessed by using Chi square test.

Results: Over 5 years, 2772 children had a total of 3064 upper endoscopies; 62% showed at least one histopathological abnormality in the gastrointestinal mucosa. The overall prevalence rates of esophagitis, gastritis, and duodenitis were 21 %, 48% and 12% respectively (Table). Esophagitis consisted of reflux esophagitis, eosinophillic esophagitis and other types. The prevalence of duodenitis and gastritis changed slightly over 5 years while the prevalence of esophagitis remained stable. The prevalence of reflux esophagitis decreased from 13% in 2008 to 7% in 2012 and of eosinophilic esophagitis increased from 5% in 2008 to 9% in 2012. There was a significant correlation between association of gastritis and duodenitis ($p < 0.001$). The correlation between other findings was not statistically significant; gastritis and esophagitis ($p=0.08$) and esophagitis and duodenitis ($p=0.45$).

Conclusion: Abnormal histopathological lesions were seen in 62% of endoscopies in our cohort. Gastritis was the commonest finding (48%), followed by esophagitis (21%) and duodenitis (12%). While overall prevalence of esophagitis remained stable over 5 years, the prevalence of reflux esophagitis halved while that of eosinophillic esophagitis almost doubled. Duodenitis is significantly associated with gastritis, probably due to a common underlying etiology.

Prevalence of upper gastrointestinal pathologies in 3064 upper endoscopies.

	2008	2009	2010	2011	2012	Mean
Esophagitis	21%	18%	21%	22%	22%	21%
Reflux esophagitis	13%	9%	9%	9%	7%	9%
Eosinophilic esophagitis	5%	7%	8%	12%	9%	8%
Gastritis	54%	46%	51%	39%	48%	48%
Duodenitis	9%	12%	12%	13%	14%	12%

214 *A COORDINATED MULTIDISCIPLINARY APPROACH TO COMPLEX PEDIATRIC AERODIGESTIVE PATIENTS REDUCES ANESTHESIA EXPOSURE: A SINGLE TERTIARY CENTER EXPERIENCE*

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Introduction: Children with concurrent respiratory, swallowing and digestive problems are often evaluated by multiple subspecialties, including pediatric gastroenterology, pulmonology and otolaryngology. The multidisciplinary Aerodigestive

Program at Texas Children's Hospital aims to improve the care of these complex patients through the coordination of evaluation and management. Synchronization of diagnostic endoscopic procedures is a key part of this approach, which not only improves efficiency but minimizes the number and duration of general anesthesia (GA) exposures and its associated risks. The aim of this study was to evaluate the impact of a coordinated approach to the endoscopic evaluation of children with aerodigestive disorders on anesthesia exposure and incidence of peri-operative complications.
Methods: Data were retrospectively collected on all patients aged 0-18 years who underwent coordinated diagnostic direct laryngoscopy and rigid tracheoscopy (DL), flexible bronchoscopy and bronchoalveolar lavage (BAL), and esophagogastroduodenoscopy (EGD) as part of the Aerodigestive Program at Texas Children's Hospital between December 2011 and December 2014. For comparison, patients who underwent elective DL, flexible bronchoscopy and BAL, or EGD individually under GA during the same time period were also analyzed and categorized as controls. Data collected included the patient's age, sex, ASA Physical Status (ASA-PS) classification, total anesthesia time, post anesthesia care unit (PACU) time, perioperative complications, and unexpected post-operative admission.
Results: There were 82 patients who underwent diagnostic triple endoscopy as part of the Aerodigestive Program. The median age of patients was 2.9 years, median ASA-PS classification was 3, average anesthesia time was 85 minutes and average PACU time was 157 minutes. Controls included 313 patients who underwent DL, 116 patients who underwent flexible bronchoscopy, and 1178 patients who underwent EGD. Aerodigestive program patients had 45 fewer minutes of anesthesia time and 60 fewer minutes of PACU time when compared to sum of average times for each procedure in the control group. There was no significant difference in rate of perioperative complications or unexpected admissions.
Conclusions: Given the potential risks of anesthesia, the decrease in cumulative anesthesia time provided by a multidisciplinary approach is a clear improvement in quality of care for the patient.

216 *THE ROLE OF INJECTION LARYNGOPLASTY IN TREATING DEEP INTERARYTENOID NOTCH ASSOCIATED DYSPHAGIA IN YOUNG CHILDREN*

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Deep Interarytenoid Notch (DIN) is the mildest form of laryngotracheoesophageal cleft defect and is frequently found in young children with dysphagia and aspiration. Treatment guidelines are not defined. IL is a surgical procedure injecting polymer gel into the tissue around the defect. Our objective was to evaluate the efficacy of IL in pediatric populations with severe dysphagia and aspiration. We conducted a pilot retrospective chart review of DIN patients under 36 months who underwent IL at PCH. Severity of dysphagia before and after IL was measured using modified barium swallows MBS (scale 0-10) and documented symptoms. Statistical analysis was done using paired two sample t-test with a p value of 5 percent. Twenty three patients under 36 months age, improved MBS scores an average of 1.2 points after IL ($p = 0.0085$). Thirteen patients with severe dysphagia (mean MBS of 8.15) had significant improvement of symptoms including choking and vomiting. IL treatment for DIN associated dysphagia results in improvement of MBS scores and symptoms in toddlers with severe aspiration. In general, patients with a MBS score of greater than seven are more likely to benefit from an intervention with IL than those with a score of less than seven, second, all patients treated with IL, independent of benefit, do not, on average, improve beyond a score of 5.5-6. Future prospective controlled studies are necessary to evaluate the role of IL and medical interventions in thickener wean and clinical improvement.

217 *SAFETY AND EFFECTIVENESS OF TREATMENT WITH ONCE DAILY DEXLANSOPRAZOLE MODIFIED-RELEASE IN ADOLESCENT PATIENTS WITH EROSIVE ESOPHAGITIS*

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PURPOSE: To assess the safety and effectiveness of oral, once daily (QD) dexlansoprazole modified-release (DEX MR) in adolescents (12 - 17 years) with erosive esophagitis (EE).
METHODS: The study comprised an 8-week open-label healing phase (OL-HP) where all subjects with endoscopically-proven EE received DEX MR 60 mg QD; a 16-week double-blind maintenance phase (DB-MP) where subjects from the OL-HP with endoscopically-confirmed healed EE were randomized to DEX MR 30 mg QD or placebo (PBO); and a 3-month drug-free follow-up phase (FP). Efficacy was assessed by endoscopy, eDiary entries, and investigator assessments of gastroesophageal reflux disease. Safety was monitored by adverse event (AE) assessments, physical exams, biopsies, and laboratory tests. All AEs during the OL-HP and DB-MP were recorded.
RESULTS: Subjects who entered the OL-HP and received at least one dose of DEX MR 60 mg (n = 62) were predominantly male (61%), white (98%), with a median age of 15 years. Baseline severity of EE based on the Los Angeles (LA) grade was primarily Grade A (55%) or Grade B (42%). All but one subject (status unknown) were negative for *Helicobacter pylori* infection. After 8-weeks' treatment with DEX MR 60 mg, 87.9% subjects had healed EE. For those with unhealed EE, the LA grade improved (n = 3), remained the same (n = 3), or worsened (n = 1; Grade B to C). Median percentage of days without any heartburn was 65.8% and without nighttime heartburn was 85.4%. Demographic characteristics of subjects with healed EE who were randomized in the DB-MP (n = 26 PBO; n = 25 DEX MR 30 mg) were similar between groups and to those in the OL-HP. After the 16-week DB-MP, 58.3% (PBO) and 81.8% (DEX MR 30 mg)

of subjects had maintained EE healing. Compared with PBO, subjects receiving DEX MR 30 mg had a higher median percentage of days without heartburn (any: 86.6% vs 68.1%; nighttime: 95.6% vs 90.3%). During the FP, no subjects were identified by investigators as having a recurrence of symptoms. During the OL-HP, 61.3% of subjects taking DEX 60 mg QD experienced AEs, most were mild in severity. The most common AEs were headache (12.9%), oropharyngeal pain (8.1%), diarrhea (6.5%) and nasopharyngitis (6.5%). During the DB-MP, the percentage of subjects experiencing AEs was similar between the DEX MR 30 mg (72.0%) and PBO (61.5%) groups. The most common AEs for DEX MR 30 mg were headache (24.0%) and for PBO were headache (15.4%) and nasopharyngitis (15.4%). No clinically significant changes or trends were observed for biopsy findings, laboratory results, physical examinations, or AEs.
CONCLUSIONS: DEX MR 60 mg QD was effective for healing EE and DEX MR 30 mg QD was more effective than PBO for maintaining healing of EE in adolescent patients. During the OL-HP and DB-MP, the doses of DEX MR provided improvement in symptoms. DEX was well tolerated with a safety profile similar to that observed in adults. NCT01642615; Sponsor: Takeda Pharmaceuticals.

*218 *FEEDING DISORDERS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS ARE ASSOCIATED WITH EOSINOPHILIC ESOPHAGITIS*

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Background: Autism spectrum disorders (ASD) are characterized by difficulties with reciprocal social interactions and restricted patterns of behavior and interest. One of these behaviors is food selectivity in type and texture which often leads to the diagnosis of a feeding disorder. Children with ASD often can't communicate symptoms such as dysphagia or odynophagia. Eosinophilic esophagitis (EoE) can present as food selectivity or feeding disorders in children. The rate of EoE in autistic children with feeding disorders is unknown.
Objective: We sought to determine and compare the rate of EoE between children with ASD with and without feeding disorders and controls with and without feeding disorders. We also sought to investigate additional risk for EoE in children with ASD to help risk stratify the need for endoscopic evaluation.
Methods: A retrospective matched case-cohort study was performed using the military health system database from Oct 2008 to Sept 2013. We performed a 1:5 case:control match by age, gender, and enrollment timeframe. Feeding disorders, EoE, and atopic disorders were defined utilizing diagnostic and procedure codes. Conditional logistic regression was used to evaluate and compare the risk of EoE by ASD and feeding disorder and evaluate predictors of EoE with stratified models by ASD.
Results: There were 45,286 children with ASD and 226,430 matched controls. 3,567 (7.9%) of the children with ASD and 2,392 (1.1%) of the controls had a diagnosis of feeding disorder. EoE was more common in children with ASD (0.4%) compared to controls (0.1),The rate and odds ratios of EoE by ASD and feeding disorder are presented in Table 1. Compared to control children with feeding disorder, children with ASD and feeding disorder had no statistically significant difference in the rate of the diagnosis of EoE (P=0.57). Feeding disorders also had higher odds ratios than other atopic conditions - 7.17 (95% CI 4.87-10.5) among children with ASD and 11.5 (95% CI 7.57-17.5) among controls.
Conclusion: Children with ASD are more likely to be diagnosed with EoE compared to controls; however there is no difference in the odds of EoE among those with feeding disorders between these groups. A diagnosis of feeding disorder was strongly associated with EoE. Feeding disorders in children with ASD should not be assumed to be solely behavioral and an esophagogastroduodenoscopy should be performed to evaluate for EoE.

Table 1: Incidence and Adjusted Odds Ratios for Diagnosis of Eosinophilic Esophagitis

	Total Number	Number with EoE	Multivariable Model Odds Ratios (95% Confidence Interval)	Multivariable Model including peripheral eosinophil count* Odds Ratios (95% Confidence Interval)
ASD & Feeding Disorder Status				
ASD with feeding disorder	2584	79	17.44 (10.15, 29.98)	24.19 (8.13, 71.96)
ASD without feeding disorder	42702	104	2.04 (1.60, 2.61)	2.69 (1.75, 4.14)
No ASD with feeding disorder	1335	40	17.49 (8.46, 36.14)	21.88 (5.45, 87.90)
No ASD without feeding disorder	225097	273	Reference	Reference
Atopic Disorders				
Allergic Rhinitis	14696	119	4.25 (3.02, 6.00)	3.24 (1.73, 6.07)
Eczema	56848	227	2.26 (1.77, 2.90)	1.72 (1.12, 2.64)
Asthma	5775	35	1.90 (1.12, 3.23)	2.76 (1.03, 7.39)
Food Allergy	8650	82	2.68 (1.79, 3.99)	1.90 (0.98, 3.71)
Elevated Eosinophil Count*	3879	51	-----	12.14 (5.11, 28.86)

*110,068 children with peripheral eosinophil counts available; absolute eosinophil count > 500 cells/mcL considered elevated

219 *THE ROLE OF PH IMPEDANCE IN PREDICTING THE RESPONSE TO THERAPY IN THE AERODIGESTIVE PATIENT WITH ESOPHAGEAL EOSINOPHILIA*

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Objective: The Pediatric Aerodigestive Clinic is a multi-specialty practice dedicated to evaluating and treating patients with complex airway, pulmonary, upper digestive tract, sleep and feeding disorders. Children seen in the aerodigestive clinic have a diagnostic triple scope with esophagogastroduodenoscopy (EGD), microlaryngobronchoscopy (MLB) and flexible bronchoscopy as well as a pH impedance study. Esophageal biopsies are done to assess for inflammation. The objective of this study was to determine 1) the prevalence of $\geq$ 15 eosinophils/high power field (Eos/HPF) on esophageal biopsy in the aerodigestive patient 2) if pH impedance findings could predict the clinical response to focused therapy of the esophageal eosinophilia.

Methods: We retrospectively reviewed the charts of 147 aerodigestive patients who received a triple scope and pH impedance study on the same day of their evaluation occurring between Sept 2012 and May 2015. pH impedance results were analyzed using Sandhill software for total impedance events, total acid and nonacid events, proximal impedance events, and Boix-Ochoa score. Symptom association was determined using the reflux index (% of total symptoms associated with a reflux event). Clinical response to treatment was assessed by providers in follow-up aerodigestive clinic.

Results: Six patients (4%) were identified with $\geq$ 15 Eos/HPF on esophageal biopsies. The predominant symptom was cough in 5 pts and noisy breathing and snoring in the sixth. Three patients had both an elevated Boix-Ochoa score of greater than16.6.and reflux index >10.0. These patients were on acid suppression at the time of the pH impedance study. Two of the 3 patients responded clinically to increases in acid suppression. The third patient did not respond to increasing acid suppression and was found to have an IgE antibody to pork; he subsequently responded to pork elimination and esophageal topical steroid therapy. Three patients had a Boix-Ochoa score less than 16.6 and a reflux index less than 4 and all 3 had clinically failed previous trials of acid blocking medication. One of these patients responded to food elimination and topical steroids despite comprehensive negative IgE antibody testing to foods. One pt did not respond to elemental formula via gastrostomy tube and had a fundoplication with clinical response. This pt had the highest number of nonacid impedance events at 66. The third patient was lost to follow-up after a poor response to hydrolyzed formula changes.

Conclusions: In the refractory aerodigestive patient, the Boix-Ochoa score, reflux index, total number of impedance events,

and percentage of proximal impedance events did not consistently associate with clinical responses to specific therapy for esophageal eosinophilia (PPI therapy, dietary changes or esophageal topical steroids) These findings suggest 1.) An abnormal pH impedance study does not rule out eosinophilic esophagitis as a cause of persistent aerodigestive symptoms 2.) Further analysis of the individual metabolism of PPI's in the refractory patient may be warranted 3.) Studies to elucidate the pathophysiology of esophageal eosinophilia may help in targeting specific therapies for the refractory aerodigestive patient.

220 *NORMAL VALUES OF OROPHARYNGEAL PH MONITORING FOR DETECTION OF LARYNGOPHARYNGEAL REFLUX IN CHILDREN*

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BACKGROUND: Gastroesophageal reflux disease (GERD) is a common condition affecting children, with symptoms of heartburn and chest pain. GERD is also implicated in extraesophageal symptoms like hoarseness and chronic cough, called laryngopharyngeal reflux (LPR). Testing for LPR has used combined pH/impedance or dual sensor pH probes, which can be confounded by artifact. The Restech Dx-pH system uses a minimally invasive probe placed through the nares to measure oropharyngeal pH and evaluate for LPR. Normal values have only been obtained for adults and it was found that mean pH differs in the upright and supine positions, so these are analyzed separately using different pH thresholds (5.5 for upright, 5 for supine). At these discriminatory thresholds, three components are integrated into a composite score called the RYAN score: percent time below that pH, number of reflux episodes, and longest episode. The aim of this study was to obtain pediatric normative values for oropharyngeal pH monitoring.

METHODS: Generally healthy children were recruited for participation. Participants were first administered a questionnaire to determine their reflux symptom index (RSI) score, which had to be 10 or below in order to continue participating (values above 10 suggest the presence of LPR). Other exclusion criteria were asthma, neurologic impairment, and use of acid suppressing medication. Weight and height was measured to calculate BMI. After informed consent and assent were obtained, the pH probe was placed and the oropharyngeal pH was recorded for 24 hours while subjects noted when they ate, drank or were in supine position. For each subject, mean upright and supine pH was recorded and the following components of reflux were measured at various pH thresholds (4, 4.5, 5, 5.5, 6, 6.5): percent time below the pH value, total number of refluxes, longest episode, and number of refluxes > 5 minutes. Mean, median, and 95th percentiles were then calculated.

RESULTS: Forty-one children were enrolled in the study. One child had uninterpretable data and was excluded, leaving forty completed studies. Mean age was 11.9 years. Mean BMI was 20.1 and mean BMI percentile was 57. Mean RSI score was 0.825. Mean study time was 23.1 hours. Mean pH in the upright position was 6.98 and 6.46 in the supine position. At the upright threshold currently used in adults (pH 5.5), the 95th percentile values of percent time below that pH, number of reflux episodes, longest episode, and number of refluxes > 5 minutes were 9.95, 39.7, 15.69, and 4, respectively. At the supine threshold currently used in adults (pH 5), the 95th percentile values of percent time below that pH, number of reflux episodes, longest episode, and number of refluxes > 5 minutes were 1.55, 8.9, 8.74, and 1.05, respectively.

CONCLUSIONS: We have established pediatric normal values for children over age one using an oropharyngeal pH probe to evaluate for LPR. Future analysis will compare this data to adult normative values to determine if discriminatory thresholds are the same for adults and children. Future analysis will also calculate a RYAN score for each child in this group and compare to adult normal values. Finally, we will direct future efforts towards collecting normal values for healthy infants.

222 *CORRELATION BETWEEN MULTICHANNEL INTRALUMINAL IMPEDANCE/PH MONITORING AND ESOPHAGEAL BIOPSY FOR ESOPHAGEAL SURVEILLANCE IN CHILDREN WITH ESOPHAGEAL ATRESIA*

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Introduction: Children with esophageal atresia and tracheoesophageal fistula (EA/TEF) have impaired esophageal motility and a high incidence of gastroesophageal reflux disease (GERD). Longstanding GERD causes esophageal injury, may lead to Barrett esophagus and development of esophageal cancer in EA/TEF patients. Subjective symptom description lacks reliability in infants and children and consequently many of GERD symptoms in infants and children are nonspecific making a clinical diagnosis more challenging. Furthermore, patients may lack symptoms despite significant esophagitis. For this reason, precocious diagnosis and treatment are essential. Although esophagogastroduodenoscopy (EGD) is commonly used as a surveillance technique, this is an invasive procedure and requires anesthesia. Multichannel Intraluminal Impedance and pH (MII-pH) monitoring offers a less invasive tool for esophageal surveillance and may provide sufficient information to guide treatment.

Aim: The aim of this study was to correlate the data obtained from MII-pH recordings with esophageal histology in children with esophageal atresia and tracheoesophageal fistula.

Methods: Infants and children with repaired EA/TEF who underwent simultaneous upper endoscopy and 24hr MII-pH

monitoring were identified through a retrospective chart review. Between September 2013 and February 2015, thirteen patients (5M/8F, median age 2.8 years (11 months to 7.5 years)) were included. A total of 14 studies were performed (one subject underwent EGD/MII-pH twice). All patients were on proton pump inhibitor (2mg/kg/day) at time of procedure. Biopsies of the distal esophagus were assessed for esophagitis. Reflux index (RI), symptom association probability (SAP), number of reflux episodes, and mean baseline values were calculated. MII-pH was considered positive in infants when RI was ≥ 10% and/or SAP was ≥ 95% and in children when RI was ≥ 3% and/or SAP was ≥ 95%.
Results: Correlation between esophageal histology and MII-pH results was found in 86% (12/14) of studies. In 7 of 12 studies, MII-pH was positive in the setting of histologic esophagitis. In the other 5, both MII-pH and histology were normal. In 2 of 14 studies, results were divergent; histologic esophagitis was seen with normal MII-pH result in one patient, and in the other, normal histology was observed despite positive MII-pH result.
Conclusion: Our data show that the results of MII-pH monitoring strongly correlate with esophageal histology in children with EA/TEF. MII-pH is an excellent tool that can be used to monitor GERD in children with EA/TEF with a potential to replace more invasive and frequent endoscopies. It is noteworthy that 7 of the 12 studies demonstrated esophagitis despite acid suppressive therapy. The high incidence of GERD and the increased risk of Barrett esophagus in patients with repaired EA/TEF further emphasize the lifelong need for esophageal surveillance. MII-pH monitoring can be an effective and reliable method to assess GERD, predict mucosal injury, and guide treatment in patients with EA/TEF.

223 *THE INCIDENCE OF GASTROINTESTINAL DISEASE IN AN ACADEMIC AERODIGESTIVE PROGRAM*

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BACKGROUD: The Aerodigestive Program at Children's of Alabama was established in 2013 to attend to the medical needs of children with gastrointestinal, airway, respiratory, and speech-language pathologies. With the knowledge and expertise of multiple pediatric subspecialties, our program provides optimized care to children with complex medical problems. Although specialized aerodigestive centers are continuing to become avenues for the effective management of children with complicated medical needs, literature describing these centers' design and patient populations is sparse. This project evaluated 80 pediatric patients referred to the Children's of Alabama's Aerodigestive Center with a primary focus on gastrointestinal (GI) specific disease incidence, evaluation, and intervention.
METHODS: We conducted a retrospective chart review characterizing 80 patients seen at the Children's of Alabama Aerodigestive Center.
RESULTS: Mean age of our patients at referral was 46 months with gastroesophageal reflux disease (GERD) functioning as the most common reason for referral with 76% of our patient population being referred for this reason. In addition, 60% of our patients suffered from dysphagia at referral, 40% from vomiting, and 26% from failure to thrive. 30% were fed through gastrostomy tube placement. Following referral, 78% of patients saw a pediatric gastroenterologist for treatment and management of their complex medical conditions. 50% underwent an esophagogastroduodenoscopy (EGD) for initial evaluation, 39% a pH/impedance study, and 64% a modified barium swallow. Surprisingly, eosinophilic esophagitis (EoE) was identified in 15% of EGD biopsies, and aspiration, laryngeal penetration, and oral aversion/discoordination were seen in 34%, 28% and 14% of our patients respectively.
CONCLUSIONS: Children referred to our Aerodigestive Center represent a broad spectrum of children who require multidisciplinary specialty care for effective management and treatment of their complicated medical needs. Many suffer from swallow dysfunction and other chronic digestive diseases such as EoE and GERD. The prevalence EoE in particular is increased in this population. Referral to an aerodigestive center facilitates coordinated diagnostic evaluation, treatment, and management of aerodigestive disorders resulting in both personalized care plans and optimized health outcomes. Future research initiatives will attempt to quantify such improvements in clinical outcomes.

225 *INCIDENCE OF ALLERGIC PROCTOCOLITIS IN A SINGLE PRIMARY CARE PRACTICE*

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Introduction: Allergic diseases have been dramatically rising in the United States and other developed nations over recent decades. Allergic proctocolitis (AP) is among the earliest and most common food allergic diseases of infancy, yet its incidence in the general population is not precisely known. We present the incidence of AP over 15 months in a single primary care pediatric office, with associated demographics of those infants who developed AP.
Methods: Pediatrics at Newton Wellesley is private primary pediatric office, located in Newton (suburb area of Boston), Massachusetts, serving about 10,000 pediatric patients from newborns to young adults, with a diverse ethnic background. We identified all newborn infants born into the practice and their families were approached to complete a questionnaire at

their initial well child visit after informed written IRB-approved consent. Those subjects' medical charts were then reviewed by a physician to confirm cases of allergic proctocolitis. Diagnosis required guaiac positive or grossly bloody stools excluding other explanation and a diagnosis code of allergic colitis, cow's milk protein allergy, or cow's milk protein intolerance.
Results: Of the 455 healthy newborns born into this practice over the past 15 months, 408 were enrolled in the study, and 355 completed a questionnaire. There were 38 physician-confirmed cases of allergic proctocolitis out of the 408 enrolled in the study, giving a cumulative incidence of 9.3% over 15 months. Of those 38 cases of clinically diagnosed AP, the mean age at diagnosis was 38 days (median 32 days, range 5-104 days). There was a slight male predominance of 20/38 cases (53%). 20/38 cases (53%) were the first-born child in their family. 16/38 cases (42%) had a positive family history of formula intolerance or bloody stools in infancy and 26/38 cases (68%) had a positive family history of atopy (asthma, allergies, eczema, or eosinophilic esophagitis).
Conclusions: To our knowledge this is the first birth cohort to report the precise incidence of AP in a healthy population, around 10% of healthy births. This rate is near our hypothesized rate and consistent with prior smaller reports in the literature. These data confirm that AP represents significant burden to primary care pediatricians and gastroenterologists alike. Current treatment strategies often require difficult dietary restrictions and/or formula changes that can be expensive. Therefore, further ongoing prospective research into its pathophysiology and treatment strategies has the potential to have significant impact on pediatric health care.

229 *OUTCOMES OF FUNDOPLICATION FOR PAEDIATRIC GASTRO-OESOPHAGEAL REFLUX DISEASE*

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Aims: The purpose of this study was to look at outcomes of fundoplication in a tertiary children's hospital. Variables looked at included patient selection and post fundoplication complications. As a secondary aim we also looked for any pre-operative predictive factors that could assist in patient selection and improved outcomes post fundoplication.
Method: In this single center retrospective cohort study, we reviewed the medical records of all children (< 18 years of age) who underwent fundoplication during a 7 year period (2006-2013). Data collected included patient demographics, comorbid conditions, use of anti-reflux medications (ARM) and gastrointestinal or respiratory symptomatology. Results of pre-operative investigations were noted. Outcomes were defined as the need for re-do fundoplication, and recommencement of ARM at 6 month follow up post-surgery. Data on post fundoplication complications (gagging/retching, dumping syndrome, gas bloat and dysphagia) was collated. Statistical analysis was completed using univariate binary logistic regression analysis in SPSS v17.0 for Windows.
Results: A total of 119 patients underwent fundoplication, with a mean age of 4.76 years and 55.5% male gender. Of these, 29 (24.4%) children had a comorbid condition (16.8% neurological impairment (NI), 5.9% oesophageal atresia (OA/TOF) and 1.7% Cystic Fibrosis (CF)), and 23 (19.3%) were under one year of age. 50 children (42.2%) had complications post fundoplication; 30% of those with complications had surgery at less than 1 year of age, and 36% also had an associated comorbid condition. Children with a comorbidity and/or <1yr did not have a significantly higher complication rate.
At 6 month follow up, 21 (17.6%) required re-do fundoplication and 64 (53.8%) were re-commenced on anti-reflux medication. In the subgroup of 23 infants <1 year of age who underwent fundoplication, 3 (13%) had redo fundoplication and 15 (65.2%) needed ARM within 6 months post-surgery. Being under the age of 1 was not significantly associated with either outcome. There was no statistically significant correlation between presence of comorbidity and either outcome. Nocturnal cough was the only symptom which was predictive of being back on anti-reflux medication at 6 months post-surgery ($p=0.04$), but not need for re-do fundoplication. There was no statistically significant correlation between presence of abnormal results in any of the pre-operative investigations and outcome post fundoplication.
Conclusion: Although fundoplication has a role in the treatment of severe GORD in children, at 6 month follow up, 17.6% required a redo and 53.8% were back on anti-reflux medications. Surprisingly neither young age at time of surgery nor associated co-morbidity was significantly associated with a poor outcome. Respiratory symptomatology (nocturnal cough) may be predictive of poor outcome, but this needs to be substantiated. As the majority of children in this study needed to restart their anti-reflux medications within 6 months of surgery, parents should be aware that fundoplication is unlikely to allow their child to remain off anti-reflux medications in the long term.

230 *THE USE OF PH-IMPEDANCE TO DETERMINE THE EFFECTIVENESS OF NISSEN FUNDOPLICATION OVER TIME.*

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Purpose: The purpose of this study was to determine the long-term clinical effectiveness of the Nissen fundoplication surgery to treat gastroesophageal reflux disease (GERD).

Methods: Patients from Cincinnati Children's Hospital with known date of Nissen fundoplication undergoing 24 hour esophageal pH-impedance (pH-MII) monitoring from May 2004 - July 2013 were retrospectively reviewed. All reflux counts were modeled as Poisson random variable as a function of time since fundoplication.

Results: A total of 239 patients had a clear date of fundoplication and participated in pH-MII monitoring. Seventy percent (n=169) of the patients fell into the category of 0-48 months since fundoplication. Range from surgery was 0-192 months. Median total reflux was 8 episodes (mean=20.9), acid reflux was 0 (mean=5.8), and proximal events were 2 (mean=7.3). There was no significant trend towards increasing reflux episodes over time.

Conclusions: Impedance tracings indicate that patients with Nissen fundoplication have few reflux episodes overall. This trend appears to be consistent over time. To our knowledge, this is the first large pediatric review showing the long-term clinical effectiveness of the Nissen fundoplication for reflux.

231 *IS SEROLOGICAL TESTING USEFUL IN PREDICTING CURRENT HELICOBACTER PYLORI INFECTION IN SYMPTOMATIC INNER CITY CHILDREN?*

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BACKGROUND: Helicobacter pylori (H. pylori) has infected more than 50% of the world's population and is associated with peptic ulcer disease and gastric carcinoma. Multiple non-invasive and invasive tests are used for detection of H. pylori infection and serological testing has been reported as an unreliable test for making the diagnosis. Our aim was to analyze the diagnostic accuracy of commonly used tests in an inner city pediatric population. Our hypothesis was that H. pylori serological testing can provide rapid reliable and cost effective diagnostic information in children referred for abdominal pain.

METHODS: The retrospective chart review was conducted for patients (1 to 18 years old) who underwent a first time esophagogastroduodenoscopy (EGD) between January 2009 and December 2013. Of those, patients who had prior fecal H. pylori antigen (Ag) and/or serum H. pylori IgG Ab testing, and subsequently had EGD were analyzed. Patients with previous known history of H. pylori infection or with a history of antibiotic use for other clinical indications between non-invasive testing and EGD were excluded. Results of serum H. pylori IgG Ab, fecal H. pylori Ag and gastric biopsy tissue rapid urease test were compared to gastric tissue histopathology as the gold standard to define H. pylori status.

RESULTS: A total of 395 patients had EGD and 52 patients (13.2% of total EGD cases) had biopsy proven H. pylori gastritis. The median age was 14 years (Inter quartile range IQR 9, 16). 240 patients (61%) were Hispanic and 150 (38%) were non-Hispanic. Indications for the endoscopy were persistent epigastric pain (51%), heartburn (44%), nausea or vomiting (43.5%) and non-epigastric abdominal pain (33%). Of the 52 patients who had positive H. pylori on histology, 45 patients had complaint of epigastric pain (87 %) with an OR of 7.71. Serum monoclonal IgG antibody testing had sensitivity (Se) of 88.4% and specificity (Sp) of 93.4%, positive likelihood ratio (LR) of 13.3, negative LR of 0.12 and on Receiver Operating Characteristic (ROC) analysis, the Area Under the Curve (AUC)=0.91. Fecal Ag testing had Se of 55.6% and Sp of 98.9, LR+ of 50.0, LR- of 0.45 with AUC of 0.77. Rapid urease test demonstrated Se of 89.3%, Sp of 89.9%, LR+ of 8.86, LR- of 0.12 and AUC of 0.89.

CONCLUSION: Our study demonstrated that Serum H. pylori serological testing has an excellent ability to discriminate between children with and without current H. pylori infection. It has higher specificity in our pediatric population compared to reported national data. Persistent epigastric pain and heartburn symptoms are strongly associated with current H. pylori infection. Patients with non-epigastric pain were less likely to have H. pylori infection. In conclusion, H. pylori IgG Ab testing should be re-considered as a diagnostic screening tool especially when routine blood work is indicated in symptomatic children belonging to inner city populations with a high prevalence of H. pylori.

232 *SALIVARY PEPSIN DOES NOT CORRELATE WITH GASTROINTESTINAL SYMPTOMS OR REFLUX TESTING*

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Background: Salivary pepsin has been proposed as a non-invasive marker of extraesophageal gastroesophageal reflux disease. There are no pediatric studies validating salivary pepsin against any gold standard measures of reflux. It is the goal of this study to compare salivary pepsin positivity to validated symptom and quality of life questionnaires and reflux testing using endoscopy and multichannel intraluminal impedance testing with pH (pH-MII).

Methods: We prospectively recruited children presenting to the gastroenterology program for the evaluation of GERD. Two groups of patients were recruited: those in the outpatient setting presenting for GERD consultation and those undergoing

reflux testing with endoscopy and pH-MII testing. Patients provided a salivary sample analyzed using the Peptest lateral flow device and these results were compared to: (1) three validated questionnaires completed in the outpatient setting (Pediatric Quality of Life Score (PedsQL), Pediatric Gastrointestinal Quality of Life Score (PedsGIQL), Pediatric Gastrointestinal Symptom Questionnaire (PGSQ)) or (2) pH-MII and endoscopy results. Means were compared using t testing and proportions were compared using chi square analyses.
Results: Ninety one patients (mean age: 106±61 months) were recruited to the questionnaire arm and 50 patients (mean age: 104±63) were recruited to the reflux testing arm. Questionnaire arm: 61% of Peptests were positive. There was no difference in any of the mean total or subgroup scores for PedsQL, PedsGIQL, or PGSQ between patients who were pepsin positive or negative ($p>0.1$). Patients who were pepsin negative were more likely to have ear infections ($p=0.009$) and pneumonia ($p=0.01$) in the two months prior to presentation. There were no differences in the rates of sinus infections, pharyngitis, or upper respiratory tract infections between the two groups ($p>0.2$). There were no differences in the rates of pepsin positivity in patients who had a recent history of H2 blocker ($p=0.3$) or PPI use ($p=0.2$). Reflux testing arm: 42% of Peptests were positive. There was no difference in any of the pH-MII reflux parameters (mean number of acid, non-acid, or total reflux, % time pH <4, and proximal reflux burden) and salivary pepsin positivity ($p>0.6$). There was no significant difference in the percentage of patients with reflux esophagitis and pepsin positivity ($p=0.2$).
Conclusion: Salivary pepsin did not correlate with gastrointestinal symptoms or standard reflux testing suggesting that standard esophageal reflux measures may be inadequate for the evaluation of extraesophageal biomarkers.

233 *STANDARD REFLUX TESTING FAILS TO PREDICT GASTRIC ASPIRATION: THE CASE FOR BILE ACIDS IN THE LUNGS*

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Background: Diagnosing reflux-related lung disease is very difficult and discovery of new biomarkers is critical. Measurement of bile in bronchoalveolar fluid (BAL) has been proposed, in the adult lung transplant population, as a marker of extraesophageal reflux disease. It is the goal of this study to determine (1) the incidence of bile in BAL fluid in children with respiratory symptoms; (2) the relationship between reflux detected by multichannel intraluminal impedance with pH (pH-MII), endoscopy, and BAL bile; and (3) the relationship between oropharyngeal dysphagia and BAL bile.
Methods: We prospectively recruited 67 patients undergoing combined endoscopy, bronchoscopy and pH-MII testing. 58 patients had complete sample sets and a minimum of 20 hours of pH-MII testing. We measured four types of bile acids in the BAL fluid using mass spectrometry and compared the results of the bile analysis to pH-MII, bronchoscopy findings including BAL pepsin, and reflux esophagitis by upper GI endoscopy. Means were compared using t tests and proportions were compared using Chi square analyses.
Results: 50/58 patients had bile detected in the BAL fluid. The mean concentration of bile was 0.00017±.00034 μM. The most common bile acids detected in BAL fluid were deoxycholic acid followed by cholic acid, lithocholic acid and finally taurocholic acid. There were no significant correlations between bile concentrations and: (1) the number of acid, non-acid, total or pH only reflux episodes ($p>0.5$); (2) the percentage of time reflux was in the distal or proximal esophagus ($p>0.4$); or (3) the percentage of neutrophils in the lung ($P=0.9$). There were no differences in the mean bile acid concentrations between patients with and without pathologic reflux by either pH criteria ($p=0.9$), impedance criteria ($p=0.7$) or endoscopy ($p=0.5$). Importantly, patients with bile in the lung were more likely to have pepsin in the lung as well ($p=0.07$). In a subset of patients with known swallow function based on videofluoroscopic swallow studies (VFSS, N=23), patients with aspiration on VFSS did not have higher bile concentrations than patients with normal swallow function ($p=0.7$)
Conclusions: Aspiration of bile is common in children with respiratory symptoms and current tests which measure esophageal reflux burden are inadequate to detect aspiration of gastric contents. Bile may therefore represent a new biomarker of reflux-related lung disease and its utility in predicting outcomes needs further study.

234 *GIVE SFED A CHANCE*

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Background: Eosinophilic esophagitis (EoE) is an emerging disease with evidence of food antigens playing a role in its pathogenesis. Therapeutic options include swallowed corticosteroids and food elimination diets. Our goal was to define the ideal length of time needed to be compliant with the six-food elimination diet (SFED) diet for marked improvement in histological and clinical signs of EoE. Additionally, we wanted to identify which of the six foods are most likely to be successfully reintroduced.
Methods: We performed an observational cross sectional study to examine which of our compliant patients with EoE responded to the SFED after strictly following the diet for a period of 8-12 weeks. 100 charts were retrospectively reviewed of which, 33 patients were treated with SFED. The diagnosis of EoE was defined as greater than 15 Eos/HPF and resolution/remission was defined as less than 5 Eos/HPF.

Results: 33/100 patients were treated with SFED and 23/33 were compliant with the treatment during the chart review period. 17/23 compliant patients (74%) had resolution of eosinophils at their first follow-up endoscopy compared to 1/8 (13%) of the non-complaint patients (p = 0.004). 100% of patients who were on the diet for a minimum of 12 weeks (n=7/7) had complete resolution of eosinophils compared to 67% for patients that were on the diet for 10-12 weeks (n=4/6), and 60% for patients on the diet for less than 10 weeks (n=6/10). Those who had <50 Eos/HPF prior to initiation of SFED therapy were more likely to respond compared to those with ≥50 Eos/HPF (p = 0.029). A total of 84 food challenges completed, of which 58 (69%) were successful with reintroduction of 1 or more of the 6 foods empirically eliminated. The least successful challenges in all 23 patients were milk and wheat (23% and 64% successful reintroduction rate respectively). Reintroduction success rates for Egg, soy, fish and nuts were 88%, 78%, 75% and 71% respectively.
Conclusion: The SFED is a very effective treatment option for children and adolescents with EoE. From this review, although our numbers are small, it appears that length of time on the diet (>12 weeks) and peak esophageal mucosal Eos/HPF (<50) prior to the first follow-up endoscopy play a crucial role in evaluating the response to diet therapy. Milk reintroduction was least likely to be successful.

235 *LAPAROSCOPIC FUNDOPLICATION IN CHILDREN WITH SPINAL MUSCULAR ATROPHY TYPE 1*

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Aim: Spinal Muscular Atrophy type-1 (SMA-1)patients are predisposed to lethal aspiration pneumonia due to combination of profound respiratory muscle weakness, the loss of swallowing function and an inability to protect their airway from gastroesophageal reflux (GER). Prior to the laparoscopic era, surgery to control GER was avoided due to the acute inhibition in respiratory effort caused by pain from large abdominal incisions and narcotic pain medications. Currently, SMA-1 patients at select institutions undergo early laparoscopic fundoplication (LF) and gastrostomy tube (g-tube) placement to control GER and reduce the risk of a lethal aspiration events. This approach, however, has not been adopted at all centers and reported outcomes are limited.

We hypothesized that due to the small size of the incisions (one 5mm incision, one 4 mm incision and three 3mm incisions) patients with SMA-1 undergoing LF would have minimal impairment in respiratory effort as measured by length of time to post-operative extubation. To test this we retrospectively compared outcomes in our SMA-1 population to pediatric patients with other neurological diseases (OND) group undergoing LF.

Methods and patients: Medical records of children with SMA type 1 and the OND group who underwent LF/g-tube placement between 2001 and 2014 were reviewed. Time to extubation, length of stay (LOS), time to initiation of gastric feeds and time to full feeds were determined. Long-term data was obtained on LF failure, the need for gastric prokinetic medications, and conversion to jejunal feeds when prokinetics failed.

Results 38 children with SMA-1 and 23 in the OND group underwent LF. Six of the SMA-1 patients had a pre-existing g-tube, in all others a g-tube was placed at surgery. All SMA-1 and OND patients were extubated the day of surgery. Follow-up was available in 36 SMA-1 and 23 OND patients (6 months to 12 years). There were 12 deaths in the SMA-1(32%) group and none in the OND group. There was one failed fundoplication in the SMA-1 group and none in the OND group . SMA-1 patients underwent surgery earlier (p<0.043), had a significantly longer LOS (P<0.023) and trended towards a higher rate of jejunal feeds (16% vs. 4%, P=0.238)) and prokinetic use (48% vs. 26%, p=.179) compared to the OND group.

Conclusion: These results support our hypothesis that LF surgery can be performed safely and has minimal untoward effect on post-operative respiratory effort in SMA-1 patients. SMA-1 patients underwent LF significantly earlier than the OND group, likely due to our approach that once a diagnosis of SMA-1 is made, surgery is undertaken prior to the loss of swallowing function. The greater use of prokinetics and jejunal feedings in SMA-1 patient suggest the presence of intestinal motor dysfunction in this population. Studies with a larger patient cohorts are needed to determine if these trends are significant.

	SMA (N38)	Controls N 23	P value
Median age at op months	7 (3-18)	10 (1-96)	0.043
Feeding started hours	20 (4-144)	10 (2-70)	0.814
Full feeds hours	40 (20-144)	33 (12-220)	0.497
Length of stay days	4 (3-8)	3 (2-70)	0.023
Jejunal feeds	6 (16%)	1 (4%)	0.238
Prokinetics	17 (48%)	6 (26%)	0.179

236 *HISTOLOGICAL, ENDOSCOPIC FEATURES AND PH TESTING IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE (GERD)*

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Background. Gastroesophageal reflux disease (GERD) is a common condition, defined by the passage of gastric contents into the esophagus, causing troublesome symptoms and/or complications, affecting up to 3% of the general population. The information on the agreement between histological, endoscopic and pH testing in patients with GERD is scarce and inconclusive.

Methods.In a retrospective study we included 30 patients, ages from 6 months to 15 years, diagnosed with GERD over a period of two years (2012-2014).

The histological description according to the classification of Esohisto which includes six histological parameters and determines the severity of the damage was performed. Numerically values were assigned, when classified as normal esophagus values were from 0 to 0.25, from 0.5 -0.75 were mild esophagitis and severe esophagitis is classified when was ≥ 1.

The endoscopic classification was made according to the scale of Hetzel-Dent. A normal esophageal mucosa was described with 0 to a degree IV when ulcers involved more than 50% of the circumference of the esophagus.

pH testing was considered normal when the reflux index was <3% and abnormal when the reflux index was >7%. From these findings frequencies and percentages were obtained.

Results.77% were male. Considering the histological classification of Esohisto, seven patients had a score ≥ 1 which were considered to have severe esophagitis; from these seven patients only 3 (43%) had esophageal damage grade IV according to the classification of endoscopic Hetzel-Dent, and only three had a reflux index greater than 7%.

Mild esophagitis was found in 19 patients, just one had esophageal erosions, corresponding to grade III endoscopic classification Hetzel-Dent and 16% of these patients had a pH testing with a reflux index greater than 7%.

In four patients (13%) no histological change was found.

Conclusions. Aware of the limitations of being a retrospective study, the present study suggests the frequency of patients with esophageal damage was greater when histologic findings were considered in comparison with the endoscopic findings and pH testing.

237 *CYTOKINE EXPRESSION IN DUODENUM AND RECTUM IN PATIENTS WITH NON IGE MEDIATED COWS MILK PROTEIN ALLERGY*

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INTRODUCTION

Cow's milk protein allergy (CMPA) it's a disorder of the gastrointestinal immune system, therefore probably an imbalance in Treg, TH1, TH2 and TH17 cells. The clinical picture could be multisystemic. In the case of non IgE-mediated CMPA there are a lack of understanding of the pathophysiology of the disease. There are few studies that have been evaluated all cytokines in tissue involved in the Treg, TH1 and Th17 response. Previous studies have not been evaluated cytokines at rectum, a place that certainly is affected. A previous study in our hospital have shown up to 27 % of infiltration of eosinophils in rectum in children with IgE and Non IgE CMPA. The aim of this study was to evaluate differential cytokine gene expression (IL-6, IL-9, IL-10, IL-17 and TNFα) in the mucosa of rectum and dodenum in patients with CMPA.

METHODS: In children with suspected CMPA open challenge were performed, if it were positive , specific IgE to milk proteins (Inmunocap), endoscopy and rectosigmoidoscopy with biopsies were performed. All biopsies were immediately placed in RNA later and stored at -70 °C until processing. Then total RNA was isolated using High Pure RNA Tissue. Two hundred nanograms of total RNA was reverse-transcribed into cDNA with random hexamer primers. The gene expression of IL-6, IL-9, IL-10, IL-13, IL-17 and TNFα were measured by real-time polymerase chain reaction (RT-PCR). Statistical analysis was performed using the SPSS 17 descriptive statistics and U-Man Whitney test were performed for comparasion of cytokines expressed. A p value ≤ 0.05 was considered as significant.

RESULTS. 30 patients were included in the study, the mean age were 4.03 months (±5.28), 13 boys and 17 girls. None positive specific IgE were found. The principal symptoms are resumed in table 1. The principal histopathological finding in rectum were nodular lymphoid hyperplasia and proctitis. The gene expression of inflammatory cytokines: IL-6, IL-13, IL-17 and TNFα were higher in rectal mucosa biopsies compared with duodenum (p=0.034, p=0.043, p=0.045, p= 0.037), respectively. Conversely, the gene expression of regulatory cytokines IL-10 was lower in rectal mucosa biopsies compared with duodenum (p=0.049). IL-9 was no detected in rectal and duodenum biopsies from patient with CMPA

CONCLUSIONS: In our knowledge this is the first depiction of the presence of IL-6, IL-9, IL-10, IL-13, IL-17 and TNFα

in the mucosa of rectum, in patients with CMPA, the rectum present the highest inflammation according with cytokine expression and histopathological finding. Much remains to be learned about the pathogenic mechanisms that lead to CMPA. This cytokine profiles imbalance (↑TH1 and TH17 and ↓Treg) may be implicated in the pathogenesis of CMPA

238 *GASTRIC LIPASE IS NOT LIKELY TO BE A VIABLE BIOMARKER FOR ASPIRATION IN PATIENTS WITH CYSTIC FIBROSIS.*

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Background: Patients with cystic fibrosis (CF) have increased gastroesophageal reflux (GER). CF patients also have a high risk of aspiration and data suggest that GER is associated with worsening lung function. Identifying children who are actively aspirating is important for preventing possible deleterious effects of both acid and non-acid GER. To date, gastric pepsin A and duodenal bile acids have been the only molecules used as biomarkers of aspiration. Aim: As part of an investigation aimed at identifying a biomarker that is more easily detected and, therefore, the best target for assessing potential aspiration, we analyzed bronchoalveolar lavage (BAL) samples for presence of both pepsin A and gastric lipase (GL). Methods: Twelve CF patients (median age 15.9 yrs, range 9.3-21.8 yrs) who were scheduled for a clinically indicated bronchoscopy were recruited into the study. BAL samples were collected and lyophilized 1 ml samples down to approximately 100 ml. Samples were then analyzed by ELISA for pepsin A (0.25 ng/ml sensitivity) and using an enzymatic assay for GL (3.4 pmol/ml/min sensitivity). For the pepsin ELISA, the primary antibody was directed against human pepsin A (Bio-Rad, Puchheim, Germany) and the secondary antibody was a biotin-conjugated goat polyclonal antibody directed against porcine pepsin A (Abcam, Cambridge, MA). Pepsin A levels are reported as the number of units of pepsin A, with one unit being equal to 0.1 ng/ml. The nonfluorescent EnzChek® lipase substrate in the presence of lipases produces a green-fluorescent product, BODIPY labeled free fatty acid (excitation/emission maxima ~507/515 nm). Results: Of the twelve CF patients recruited into the study, 8 (67%) tested positive for the presence of pepsin A in the BAL samples (median 6.7 pepsin units/ml, range 2.7-13.1). GL was not detected in any of the 12 samples, including those samples that tested positive for pepsin A. Discussion and Conclusions: Gastric lipase is less abundant by comparison to pepsin in the gastric juice. It is possible that the enzymatic assay used to detect the gastric lipase was not sensitive enough to detect the low levels gastric lipase that may have been present. As pepsin is a proteolytic enzyme, it is possible that the accompanying GL was hydrolyzed by the gastric pepsin A. While these data are preliminary, the absence of gastric lipase activity, particularly in the samples that contained pepsin, suggests that the gastric lipase assay (as measured by enzymatic activity) may not be sufficiently sensitive. Therefore, given the fact that enzymatic assays are incapable of detecting inactive or degraded lipase, an immunoassay (ELISA) is needed to substantiate these findings.

INFLAMMATORY BOWEL DISEASE

239 *DEVELOPMENT OF AN ALGORITHM TO ACCURATELY IDENTIFY FISTULIZING CROHN'S DISEASE IN ADMINISTRATIVE CLAIMS DATA*

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Background: Fistulas are common complications of Crohn's disease (CD). Little population-based data are available to describe the epidemiology of fistulizing CD, although prior reports indicate a prevalence range of 16-47%. Previous studies that have relied on claims data to identify fistulas have been limited by inconsistent use of diagnosis and procedure codes for fistula, resulting in poor specificity. We sought to develop and test an enhanced algorithm to improve the accuracy of identifying pediatric fistulizing CD using administrative claims data.

Methods: We identified a wide cohort of patients (age 5-21 years), with and without inflammatory bowel disease (IBD), seen at University of Michigan Health System between 2005-2012 via administrative claims. We included patients on any relevant IBD medication (5-aminosalycilates, thiopurines, methotrexate, anti-TNFα, steroids) or antibiotic (fluoroquinolones, metronidazole, rifaxamin); with any perianal lesion, abscess, or fistula; or any procedure on a perianal lesion or fistula. Electronic medical records were abstracted. Patients were categorized by CD vs. other IBD, presence of fistula, timing of fistula (before or after IBD diagnosis), type of perianal lesion and type of procedure. Preliminary candidate fistula algorithms were developed using sequences of identifiable events based on *a priori* evidence and expert opinion. Events included change in diagnosis, change in therapy, start of antibiotics, imaging studies (CT or MRI), seton placement, surgery, identification of perianal lesion, etc. Candidate algorithms were tested against chart data (gold standard) and refined through an iterative process. Test characteristics of algorithms and combinations of algorithms were assessed.

Results: Of the 3,264 charts identified, a random sample of 555 (17%) were abstracted, 141 (25%) with Crohn's disease, of

whom 55 (39%) had documented fistula or abscess, 131 had documented IBD medications, and 79 antibiotics. Candidate algorithms ranged in performance characteristics for both sensitivity (range: 0.28 to 0.78) and specificity (range: 0.79 to 0.99). The best performing single algorithm had a sensitivity of 0.75 (95% CI 0.63-0.85), specificity 0.79 (95% CI 0.72-0.85) with area under the receiver operator characteristic curve (AuROC) 0.77 (95% CI 0.71-0.83). Positive predictive value (PPV) 59% and negative predictive value (NPV) 89%. Combining the top 4 performing algorithms produced the most accurate predictions. Sensitivity 0.71 (95% CI 0.58-0.81), specificity 0.86 (95% CI 0.80-0.91), PPV 0.68 (95% CI 0.55-0.79), NPV 0.88 (95% CI 0.82-0.93), and AuROC 0.79 (95% CI 0.72-0.85). This combined algorithm identified a prevalence of 43% of CD patients with fistulizing disease. By comparison, use of only fistula billing codes performed more poorly (sensitivity 0.32, specificity 0.93, PPV 0.66, NPV 0.77, AuROC 0.63) and identified a prevalence of only 14%. Conclusions: This novel algorithm for identifying fistulizing Crohn's disease from administrative claims data outperforms methods based solely on the use of fistula billing codes. This pilot test establishes the use and accuracy of this novel method for conducting epidemiologic studies of fistulizing Crohn's disease using large administrative databases.

240 *EXTENT OF DISEASE IN ULCERATIVE COLITIS IN A PEDIATRIC INFLAMMATORY BOWEL DISEASE LEARNING HEALTH NETWORK*

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Background: The variation in presentation of ulcerative colitis (UC) during childhood has been incompletely characterized. It has been reported that patients with childhood onset UC more commonly present with extensive colitis than those with adult onset UC, and that young children more often present with pancolitis at diagnosis, though these generalizations are based on small studies. We sought to characterize the extent of disease at presentation of UC in a large cohort of pediatric patients.

Methods: The ImproveCareNow (ICN) Network is a multicenter pediatric inflammatory bowel disease (IBD) Learning Health Network in which pediatric gastroenterologists prospectively collect data about their IBD patients at each outpatient visit. We used the ICN registry to identify UC patients (7/1/2010 to 5/5/2015) at 61 sites. All consented patients with UC were included. Patients with indeterminate colitis or inconsistent initial diagnosis and enrollment diagnosis were excluded. We analyzed all patients as well as those who enrolled in ICN within 6 months of diagnosis. We used descriptive statistics and chi-square testing to analyze the association of extent of disease with gender and age group (age was calculated as age at enrollment). All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results: Of 3,016 patients 51% (n=1,537) were female. Overall, most (63%) had pancolitis (n=1885), while 11% had extensive disease (n=318), 19% had left-sided disease (n=566) and 8% had proctitis (n=245). Of the 1,167 patients enrolled within 6 months of diagnosis: 51% (n=599) were female, 5% (n=64) were <6 years old, 17% (n=204) were 6 to <10 years, 72% (n=841) were 10 to <18 years and 5% (n=58) were ≥18 years (Table 1). Most patients (61%) had pancolitis. The distribution of disease was not significantly different across age at diagnosis (p=0.37) or gender (p=0.38).

Conclusions: In the largest reported cohort of pediatric patients with ulcerative colitis, pancolitis predominated and the distribution of disease was remarkably uniform across the range of ages at diagnosis.

Number of patients by age and extent of disease

	Ulcerative Proctitis	Left-Sided	Extensive	Pancolitis	Total
<6 years	3 (5%)	8 (13%)	6 (9%)	47 (73%)	64 (5%)
6 to <11 years	17 (8%)	35 (17%)	25 (12%)	127 (62%)	204 (17%)
11 to <18 years	91 (11%)	151 (18%)	93 (11%)	506 (60%)	841 (72%)
≥18 years	3 (5%)	8 (14%)	10 (17%)	37 (64%)	58 (5%)
Total	114 (10%)	202 (17%)	134 (11%)	717 (61%)	1167

*241 *A SINGLE FECAL MICROBIOTA TRANSPLANT DOES NOT ALTER THE COURSE OF INFLAMMATORY BOWEL DISEASE WHEN TREATING A CONCOMITANT REFRACTORY CLOSTRIDIUM DIFFICILE INFECTION*

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Introduction: Clostridium Difficile Infection (CDI) is a relatively common condition in children causing Diarrhea and abdominal pain. CDI is found to flourish and colonize the colon especially in cases where the gut's normal flora has been altered. Fecal Microbiota Transplant (FMT) has been proven to be very effective in eradicating CDI refractory to

antibiotics. At Mayo Clinic we have over 90% success at eradicating recurrent CDI with FMT. Some recent reports including case series in children suggest that FMT may also be useful in altering the course of Inflammatory Bowel Disease. CDI in IBD patients is not uncommon, due to frequent use of antibiotics and immunosuppressants in this population. The objective of our study is to assess our IBD patients who received a single FMT for CDI and see if it altered the clinical course of their IBD.
Methods: We reviewed Mayo clinic records for IBD patients who underwent a FMT by colonoscopy for the purpose of treating refractory CDI. Patients under 3 years of age or over 18 were excluded. IBD medication, endoscopic findings, and Lab results before and after FMTs were compared. We contacted patients and used Global physician assessment to determine patients' status post FMTs.
Results: 10 patients with IBD were identified from within our group of patients who underwent FMT for recurrent CDI (7 males, 3 females with average age of 13). 6 patients had ulcerative colitis, 3 Crohn's, and 1 indeterminate colitis.
All patients showed clinical improvement post-FMT, this improvement was attributed to CD eradication.4 patients experienced exacerbation of symptoms within a month from FMT, 3 of whom were retested for stool CD toxin and were found negative. CRP was calculated pre-FMT in 8/10 patients, only 2 had elevated levels; these two also belonged to the group of patients who experienced early post-FMT exacerbation of IBD. All ten patients had inflammatory findings visualized by colonoscopy during the FMT procedure. Only 1 patient underwent a colonoscopy 5 months post-FMT which was unremarkable despite symptoms of relapse.
Discussion: While FMT is now established as a treatment for CDI, there are case reports that it has been used as a treatment or maintenance therapy for IBD. Several reports tout improvement of IBD symptoms or even remission following one or several FMTs. The results from our series show that FMT had no major impact on IBD activity. FMT does not appear to have altered the course of the underlying disease beyond the acute treatment of the CDI. No changes on IBD management resulted from the FMT and none of our patients stopped IBD maintenance therapy following FMT. Nine patients (90%) had exacerbation of IBD at some point following FMT and had a step up in their therapy. Only one patient (10%) reported no additional flare post- FMT and continued on maintenance therapy. While modest in number, this group of 10 patients is one of the largest cohorts of IBD patients with concomitant CDI treated with FMT. Further prospective studies are encouraged to establish the true effects of FMT on the underlying course of disease in IBD patients as our retrospective look suggests the benefits may be limited.

242 *MEASUREMENT OF ENDOSCOPIC SEVERITY IN A CROHN'S DISEASE MULTI-CENTRE PEDIATRIC INCEPTION COHORT: POOR CORRELATION OF SES-CD WITH PCDAI*

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Background: In the treatment of pediatric Crohn's disease (CD), intestinal healing is an increasingly important endpoint in clinical trials and in practice. It is well established in adults that activity assessed clinically via the Crohn's Disease Activity Index (CDAI) shows no correlation with endoscopic severity, but similar analyses comparing the Pediatric Crohn's Disease Activity Index (PCDAI) to endoscopic severity in children are lacking. The 'Simple Endoscopic Score for CD' (SES-CD) is a commonly used measure of endoscopic severity, but its evaluation in children has been limited.
Aims: We undertook to prospectively score SES-CD at time of diagnosis in a multi-centre pediatric cohort and to compare endoscopic severity with clinical measures of disease activity.
Methods: All children </= 17 years of age with new onset IBD at participating sites in the Canadian Children IBD Network, and consenting to enroll in its inception cohort study, undergo pre-treatment evaluation including ileocolonoscopy. Endoscopic severity of CD is assessed by SES-CD. Disease activity at presentation is evaluated by PCDAI, its weighted version (wPCDAI), physician global assessment (PGA), and conventional serologic markers of inflammation. The correlation between endoscopic and clinical disease severity in patients with CD was assessed using Pearson's test of correlation or Spearman's rank coefficient. The relative relationships between the indices, their subcomponents and the laboratory parameters were further explored using multi-variable linear regression models.
Results: 92 patients with CD from 8 pediatric IBD centers were included in the analysis. 82/92 patients (89%) had disease involving the colon (63% ileocolonic, 26% isolated colonic). 58 (63%) patients had moderate/severe disease assessed by PGA. Median PCDAI score was 30 (IQR 15 - 40) with 50% classified as 'moderate/severe' (PCDAI >30). Overall median SES-CD was 20 (IQR 11 - 29), with 61% classified as 'severely active' endoscopic disease (SES-CD >16). Distributions based on anatomic location are presented in the Table.
Both original PCDAI and wPCDAI scores correlated poorly with SES-CD ($r = 0.28$, $p=0.007$; $r= 0.22$, $p<0.001$ respectively). 'Stooling pattern' subscore of PCDAI correlated modestly with SES-CD in patients with colonic CD (L2 or

L3) (r=0.50, p<0.001). Multi-variate regression demonstrated that the three clinical symptom components of the Activity Indices accounted for the majority of the relationship with SES-CD (r^2=0.27, p<0.001) with biochemical and physical exam parameters being non-contributory.
Conclusions: New onset paediatric CD is frequently severe, both endoscopically and clinically. The poor correlation of PCDAI and wPCDAI with endoscopic severity precludes their use as a surrogate for mucosal inflammation. Ileocolonoscopic re-assessment should be performed to demonstrate mucosal healing. Accurate documentation of SES-CD score is vital to this process.
Distribution of SES-CD scores stratified by disease location and clinical activity

	L2/L3 All pts n=82	L1 All pts n=10	L2/L3 PCDAI 10-30 n=26	L2/L3 PCDAI >30 n=40	L1 PCDAI >30 n=5
Median SES-CD (IQR)	21 (15 - 30)	6 (5 - 8)	18 (12 - 26)	24 (18 - 33)	5 (4 - 8)

243 *VEDOLIZUMAB THERAPY IN SEVERE PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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BACKGROUND: Vedolizumab, a humanized IgG1 monoclonal antibody against α4β7integrin that inhibits T-lymphocyte migration into intestinal tissue, has recently been approved for adults with inflammatory bowel disease (IBD). There are limited published data on vedolizumab use in pediatrics, but it may prove to be a therapeutic option in children with disease refractory to current standard therapy.
AIMS: To evaluate the use of vedolizumab in pediatric patients with refractory IBD and determine clinical response measured by disease activity. Secondary aim was to describe adverse effects associated with vedolizumab use in this population.
METHODS: Children between the ages of 13-21 with severe IBD refractory to biologic therapy and initiating vedolizumab at The Children's Hospital of Philadelphia from June 2014 were included. Indications for initiation of vedolizumab therapy were determined by the primary gastroenterologist. Subjects were followed prospectively at each visit and clinical activity indices and outcomes were recorded. Dosing was the standard adult regimen of 300 mg at week 0, 2 and 6 followed by maintenance phase at 8 week intervals. Outcome measures included disease activity, measured by Pediatric Crohn Disease Activity Index (PCDAI), albumin, C-reactive protein (CRP) and steroid exposure. Wilcoxon sign ranked tests and exact logistic regression were used to evaluate paired continuous and binary variables, respectively.
RESULTS: Seventeen subjects, 15 with Crohn disease and 2 with indeterminate colitis, have completed the induction regimen. Fifteen patients have completed at least 14 weeks of therapy. The mean age (±SD) was 17.0 (±2.1) years. The mean PCDAI (±SD) at initiation of therapy was 30.1 (± 15.4). Clinical improvement based on change in PCDAI from baseline was seen at 6 weeks (p<0.05) and persisted to 14 and 22 weeks (p<0.01), with mean PCDAI (±SD) at 6 weeks of 16.0 (± 7.8). Remission based on PCDAI (score ≤10) was seen in 5/17 (29.4%) subjects at 6 weeks. There was a significant improvement in serum albumin from baseline to week 14 (p<0.05), but no improvement in CRP was seen. Prior to induction, 13/17 (76.5%) patients were treated with systemic corticosteroids, as compared to 8/15 (53.3%) subjects at 14 weeks. There were no infusion reactions. However, new extra-intestinal manifestations of bowel-associated dermatosis-arthritis syndrome occurred in one patient during induction, and 3 patients developed abscesses while on treatment. One patient discontinued vedolizumab due to severe symptoms and steroid-dependence requiring colectomy after 22 weeks.
CONCLUSION: This is one of the first experiences of vedolizumab therapy in pediatric IBD. Although this study is limited by the small number of patients, there appears to be significant improvement in disease activity measured by PCDAI from baseline to 6 weeks with sustained improvement through 22 weeks. Complications seen in this cohort may be unrelated to vedolizumab use. Further prospective follow-up of a larger cohort treated with vedolizumab at this center is underway to provide additional data regarding efficacy and safety in pediatric IBD.

246 *IRON SUCROSE TREATMENT FOLLOWING INFLIXIMAB INFUSIONS IMPROVES IRON DEFICIENCY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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Background : Anemia is the most common systemic complication of pediatric inflammatory bowel disease (IBD) with iron deficiency as a main contributor. Iron deficiency anemia has significant negative impacts on quality of life and cognition in children regardless of disease activity. Despite the high prevalence of iron deficiency and poor compliance with oral iron

supplementation, intravenous (IV) iron is used infrequently in pediatric IBD, perhaps due to concerns about hypersensitivity reactions, especially with iron dextran, and inconvenience for patients associated with IV drug administration. Iron sucrose (IS), the most widely used IV iron supplement in adults, has an excellent safety profile but has not been systematically studied in children with IBD. Utilization of IS for treatment of iron deficiency could circumvent non-compliance with oral iron supplements. For children receiving Infliximab (IFX), both IS and IFX can be administered on the same day, using the same IV access. This approach, if effective, can serve as a convenient alternative or adjunct to oral iron supplementation in this patient population.
Objective: Prospective study to evaluate the effectiveness of periodic IS treatment coordinated with IFX infusions in correction and prevention of iron deficiency anemia in pediatric IBD.
Methods: Inclusion criteria: Age 0-18 years (y), diagnosis of IBD, IFX treatment, normal serum B12 and folate. Study Protocol: Ferritin, Transferrin saturation (Sat), Hemoglobin (Hb), Mean corpuscular volume (MCV), and C-reactive protein (CRP) were measured prior to each IFX infusion. Iron deficient patients received 3 mg/kg (max. 200 mg) IS following IFX infusions. Iron deficiency was defined as Ferritin < 30 ng/ml or Sat< 20% with normal CRP (0-1), or Ferritin < 100 ng/ml and Sat< 20% with elevated CRP (>1). IS treatments continued until patients had two consecutive normal ferritin levels. At the interim review of data, we compared average laboratory values from the first IS treatment to the end of the calendar year 2014 ("post-treatment", 47 measurements) with historical data of participants' own from the entire previous calendar year ("pre-treatment", 54 measurements). Changes were evaluated using a paired t-test. All P-values are two-sided and $P<0.05$ was used for defining statistical significance.
Results: Demographics: 10 patients, 4 males, 6 females, 9 with CD, 1 with UC (female). Average age at diagnosis: 11 y (range 5-16); Average age at entering the study: 13.4 y (7-17). Average time in study: 5.7 months (1-9). IS infusions: Total number: 39. Time between infusions: 4 to 8 weeks, depending on frequency of IFX treatments. Adverse reactions: None. Pre- and post- treatment values (average ± SE), Ferritin: 20.12(±3.14) and 48.78 (± 7.79), p=0.03; Sat: 13.54(±2.20) and 22.18(±2.93), p=0.03; Hb: 11.63(±0.31) and 12.95 (±0.47) p=0.03; MCV 77.17(±1.72) and 81.82(±1.84), p=0.08.
Summary and Conclusions: Our findings indicate that administration of IS at the time of IFX treatments to iron deficient pediatric IBD patients can lead to significant improvement in ferritin, transferrin saturation and hemoglobin. Incorporation of IS into routine management of iron deficiency is worth considering for patients on IFX treatment.

249 *PHARMARCOKENETICS OF INFLIXIMAB IN CHILDREN WITH CROHN'S DISEASE TREATED IN A CLINICAL SETTING*

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Infliximab (IFX) is a murine chimeric IgG1 anti-TNFα monoclonal antibody shown in landmark clinical trials to be well-tolerated and effective for induction and maintenance of remission in pediatric and adult Crohn's disease (CD) and ulcerative colitis. A third to half of children with CD in Canada are treated with an anti-TNFα such as IFX. A low IFX trough level (< 2.2 µg/ml) at week 14, i.e. before the 4th infusion predicts IFX discontinuation in adults. A trough level of 5 µg /ml at week 14 is associated with higher remission rate. It is unclear if targeting a desired trough level after the 3rd dose will result in a better long term remission rate. Currently, there is no clear guideline on how to achieve the desired trough level after the 3rd dose; mainly because the pharmacokinetics of IFX in children is not well studied.
Aim: The aim of this pilot study is to assess the pharmacokinetics of IFX in children after the first three loading infusions in order to guide the interval and dose of IFX to achieve a trough between 5 and 10 µg /ml before the forth infusion and improve outcomes, i.e. using treat-to-level of IFX strategy.
Method: Children with CD deemed to require IFX by the treating physicians were prospectively recruited. Dose of IFX was 5mg/kg rounded up to multiple of 100 and given at week 0, 2, 6 and 14 weeks. IFX levels were measured at peak, after the third loading dose, week 12 and week 14, just before the 4th infusion.
Result: Ten children were recruited so far. Mean age was 12.3 years. Mean PCDAI score was 25. Mean dose of IFX at first infusion was 6.59 mg/kg (5.1 to 8.3). All received their first three infusions as per protocol. However the mean dose of IFX at third infusion dropped to 6.12mg/kg due to increase in patients' weight. Peak IFX level after the third dose was 28 ug/mL. One patient has level above max detection of 45. At week 12, the mean IFX level was 6.7 ug/mL with one patient has level less than 5 ug/mL (2.4). At week 14 the mean level was 4 ug/mL with only three patients with level $\geq$ 4.9 ug/mL. All ten patients went into remission. Two patients had the frequency of infusions shorten to Q6W over X time follow-up. One patient has dose increased and frequency shortened to Q6W. Two patients required dose increased by 100mg due to weight gain.
Conclusion: Children with Crohn's disease appear to have inadequate IFX trough level at week 14, prior to 4th infusion. A significant number requires dose adjustment to achieve adequate trough level and for weight gain. Our results could guide strategies on how best to treat to level using IFX.

251 *GENETIC POLYMORPHISMS IN INTERLEUKIN-23 RECEPTOR GENE IN KOREAN CHILDREN WITH CROHN'S DISEASE*

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Purpose: Genome-wide association studies have identified variants in the gene coding for its receptor (IL-23R) are strongly associated with Crohn's disease (CD). It is unknown whether the genetic variations in IL-23R determine susceptibility for CD in Asian pediatric population. The aim of this study was to evaluate the association between IL23-R gene polymorphisms and early onset CD in Korean children.

Methods: Five single nucleotide polymorphisms (SNP) of IL-23R gene (G149R, IVS4+17C>T, rs1004819, rs1495965, rs7517847), previously reported to be associated with western children and Korean adults of CD, were genotyped in 100 CD children and 100 controls. The promoter and exon regions of IL-23R are analyzed using DNA direct sequencing and risk allele, genotypes and haplotypes were compared in the patients with CD and controls.

Results: Two IL-23R gene variants, rs1495965 and rs7517847 were significant associations with Korean pediatric patients with CD; the odds ratio (OR) for rs1495965 was 1.563 (95% confidence interval [CI] =1.041-2.344, p=0.031) and OR for rs7517847 was 0.575 (95% CI= 0.381-0.868, p=0.008). The SNP rs1004819, which was reported to be responsible for CD in western children and Korean adults, showed no significant association with CD in Korean children. The SNP rs7517847, which had never been studied before among Asian population, showed a significant protective association in Korean CD patients.

Conclusion: We found significant association of IL-23R with pediatric CD in Korean patients. The study could reveal a distinct ethnic difference of genetic background of Asian population with CD, and also suggest genetic variants of early onset CD in Korean children.

252 *LONG-TERM MAINTENANCE OF CLINICAL REMISSION AND RESPONSE WITH REDUCED DOSING FREQUENCY OF ADALIMUMAB IN PEDIATRIC PATIENTS WITH MODERATE TO SEVERE CROHN'S DISEASE*

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Background & Aims: Adalimumab (ADA) was shown to induce and maintain remission and response in pediatric patients (pts) with Crohn's disease in IMAgINE 1.[1] In this sub-analysis, long-term maintenance of clinical remission and response were assessed in pts with reduction in dosing frequency from double-blind (DB) weekly (ew) therapy in IMAgINE 1 to every other week (eow) dosing in the open-label (OL) IMAgINE 2 trial.

Materials & Methods: Pediatric pts who successfully completed the 52-week (wk) IMAgINE 1 trial were eligible to enroll in the open-label extension IMAgINE 2 trial. 100 pts entered IMAgINE 2. Per protocol, pts who entered IMAgINE 2 received OL weight-based dosing of ADA (≥40 kg: 40 mg ADA eow; <40 kg, 20 mg ADA eow). At or after wk 8, pts experiencing flares (increase in Pediatric Crohn's Disease Activity Index [PCDAI] ≥15 points compared to PCDAI at previous visit) could move to ew dosing. Pts receiving ew DB 40/20 mg ADA at the end of IMAgINE 1 who enrolled in IMAgINE 2 were analyzed. Remission (PCDAI ≤10) and response (decrease in PCDAI ≥15 points from IMAgINE 1 baseline [BL]) were assessed over time in pts who dose de-escalated from ew DB to eow OL ADA, and in those that moved back to ew ADA during IMAgINE 2. Mean change in total PCDAI from IMAgINE 1 BL was evaluated over time. Endpoints are reported as observed. A data cut-off of Jun 30, 2013 was used for this analysis.

Results: 28 pts completed IMAgINE 1 on ew DB 40/20 mg ADA and entered into IMAgINE 2 on eow OL 40/20 mg ADA. Response was maintained in 18/21 (86%), 17/18 (94%), and 14/14 (100%) of pts at wks 36, 72, and 144, respectively. Remission was maintained in 13/21 (62%), 8/18 (44%), and 10/14 (71%) of pts at wks 36, 72, and 144 of IMAgINE 2, respectively. Mean reduction in total PCDAI from IMAgINE 1 BL was maintained over time to wk 144 (Table). During IMAgINE 2, 12/28 (43%) of pts receiving eow dosing re-escalated to ew ADA. In pts that re-escalated, response was achieved in 9/10 (90%), 8/9 (89%), and 7/7 (100%) at wks 36, 72, and 144, respectively; and remission was achieved in 6/10 (60%), 4/9 (44%), and 4/7 (57%) at wks 36, 72, and 144, respectively. During the IMAgINE trials, adverse event (AE) and serious AE rates were 502/100 patient-years (PY) and 30/100 PY, respectively, in the 28 pts who dose de-escalated.

Conclusion: Long-term clinical remission and response were maintained in a high proportion of pts after reduction of ADA dosing frequency from DB 40/20 mg ew in IMAgINE 1 to OL 40/20 mg eow during IMAgINE 2. Pts with disease flare after reduced dosing frequency were able to recapture response and remission after re-escalation. Safety rates were comparable to those observed in the overall trial.

References: 1. Hyams et al Gastroenterol 2012;143:365-74
Table. Mean change in total PCDAI from IMAgINE 1 BL through week 144 of IMAgINE 2 in ADA-treated patients who continued to receive de-escalated eow dosing (as observed)

Weeks during IMAgINE 2	N	Mean change
0	28	-27.7
36	21	-29.5
72	18	-29.0
108	16	-32.7
144	14	-34.3

253 *THIOPURINE DOSING IN PEDIATRIC INFLAMMATORY BOWEL DISEASE:COULD LESS BE MORE?*
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Background: 6-Mercaptopurine (6-MP) and Azathioprine (AZA) are often used as steroid-sparing agents and for the maintenance of remission for children with inflammatory bowel disease (IBD). Initial dosing guidelines are weight-based after stratification by TPMT enzyme status, but many patients receive thiopurine doses below those recommended and outcomes in these patients have not been well studied. We hypothesized that patients in clinical remission treated with thiopurine doses below the recommended range (BRR) would be more likely to have a flare of disease activity than those whose doses were within or above the recommended range (WRR).
Methods: Patients cared for in the pediatric IBD program at MassGeneral Hospital *for* Children who were treated with thiopurines without concomitant biologic therapy were identified. Weight-based thiopurine doses were compared to standard dosing recommendations (2-3 mg/kg for AZA and 1-1.5 mg/kg for 6-MP if TPMT activity were normal and 1-1.5 mg/kg for AZA and 0.5-0.75 mg/kg for 6-MP if TPMT activity were intermediate) to identify patients who were dosed BRR or WRR. TPMT evaluation was required for inclusion. Patients on allopurinol or who were on lower than recommended thiopurine doses because of leukopenia, elevated transaminases, pancreatitis, 6-TGN > 400 or 6-MMP > 5700 were excluded. Outcomes such as need for surgery, systemic corticosteroid use and disease flares, defined as any increase in physician's global assessment (PGA) from quiescent, were compared between the BRR and WRR groups.
Results: 47 IBD patients (34 with Crohn's disease, 12 with ulcerative colitis and 1 with IBD-U) treated with thiopurine monotherapy met all study criteria and were included. 29.8% had thiopurine doses BRR (n = 14) and 70.2% had doses WRR (n = 33). Median follow-up was 42 months (range 6-61 months). Patients who received thiopurine doses below the recommended range did not flare more often than those who received doses within the recommended range [BRR: 0.19 flares/year, WRR 0.24 flares/year, (p=0.64)]. Interestingly, significantly more patients in the WRR group required corticosteroids (48.4%) compared to those in the BRR group (7.1%) during follow up (p=0.004).
Conclusion: In our single center cohort, children/young adults with IBD who received below the recommended weight-based doses of thiopurines were <u>not</u> more likely to have an exacerbation of disease than children who received doses in the recommended range and were actually <u>less</u> likely to require systemic corticosteroids. Adjusting thiopurine dose based on 6-TGN and 6-MMPN levels instead of weight might provide better outcomes.

254 *CLINICAL CHARACTERISTICS AND LONG TERM OUTCOMES OF PEDIATRIC CROHN`S DISEASE : A SINGLE CENTER EXPERIENCE*
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Background: The incidence of Crohn`s disease (CD) is increasing in pediatric patients. However clinical features and course are poorly defined. The aim of this study is to investigate long term prognosis and clinical features of CD in the pediatric population.
Methods:
We retrospectively analyzed 610 pediatric patients with CD diagnosed at the Asan Medical Center Children`s hospital between March 1995 and December 2013.
Results: The male-to female ratio was 2.4:1 and the median age at diagnosis of CD was 14 years (range, 1-17 years). The median interval time from symptom onset to diagnosis was 12.7 months (range, 1-121 months). A family history of inflammatory bowel disease was present in 30 (4.9%). Seventy patients (11.4%) showed growth delay at the time of diagnosis. The Paris location at diagnosis was as follows; L1 in 67 (11%), L2 in 53 (8.7%), L3 in 472 (78.1%), and L4 in 159 (26%). The Paris behavior at diagnosis was as follows; B1 in 526 (88.8%), B2 in 56 (9.5%), and B3 in 10 (1.7%). In A1a Group, the proportion of growth delay (*P=0.000*) and isolated colonic disease (L2) at diagnosis (*P*=0.000) was

significantly higher than A1b group.
Three hundred and thirty three patients (54.5%) experienced perianal fistula before and/or after diagnosis of CD. The cumulative frequency of perianal fistula after 1, 5 and 10 years of diagnosis was 52%, 58%, 59% respectively. The cumulative probability of surgery after 1, 5 and 10 years was 5.4%, 20%, 38% respectively.
Conclusions: Unlikely to other western countries, CD show male-predominance, high frequency of perianal fistula and upper gastrointestinal involvement. However disease behavior and age distribution was similar with that.

256 *CLINICAL CHARACTERISTICS AND NATURAL HISTORY OF PEDIATRIC CROHN'S DISEASE PATIENTS WITH ENDOSCOPIC "SKIPPING" OF THE TERMINAL ILEUM*

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Introduction: The presence of active small bowel (SB) Crohn's disease (CD) despite a normal terminal ileum (TI) on ileocolonoscopy (IC) has been referred to as '*endoscopic TI skipping*', and refers to proximal inflammation (upper gut, jejunum, or proximal ileum), microscopic disease (visually normal TI with histologic inflammation), or intramural (IM) TI disease (radiologically active TI inflammation with visually and histologically normal TI). We sought to understand the natural history of pediatric CD patients with this finding.
Methods: We identified 170 CD pts less than 18 years of age who had a CT enterography (CTE) or MR enterography (MRE) and IC, performed within a 30-day period, between July 2004 to April 2014. Physician global assessment was used as the reference standard for SB CD activity. Medical records were reviewed to obtain clinical, radiologic, and endoscopic data before and after the index IC. We compared the need for subsequent steroids, hospitalization, and surgery between patients with endoscopic TI skipping and those with active endoscopic TI disease (n=97).
Results: Of 73 pts with normal or nonspecific (erythema, granularity, edema) IC findings, endoscopic TI skipping was present in 43 (59%) pts: 14 with IM disease, 9 with proximal disease, and 20 with microscopic disease. Evaluation data prior to the index episode (median: 21 months, range: 1.2-89.9) was available in 13/43 (30%) pts; 6 pts had prior IC, and 10 had MRE/CTE. Of pts with prior assessments, 2/6 (33%) had endoscopic TI disease and 8/10 (80%) had radiological TI involvement. Follow-up information was available in 28/43 (65%), median observation duration of 70 months (range: 4.9-105.9). Follow-up IC was performed in 22 pts, 9 (41%) had active endoscopic TI disease. Among 24 pts who had follow-up enterography, 19 (79%) had radiological involvement of TI. Of the pts with IM disease who underwent both prior and follow-up enterography, most had persistent IM inflammation (100 % and 89%) (Table 1). There was no significant difference detected in subsequent steroid use ($p = 0.8$), surgery ($p=0.2$) or hospitalization ($p=0.39$) in pts with and without endoscopic TI skipping. Improved radiologic parameters of active inflammation in response to medical therapy was more likely in pts with endoscopic TI involvement (30/61, 49%) compared to pts with endoscopic TI skipping (3/17, 18%) ($p=0.02$).
Conclusion: The endoscopic appearance of the TI can evolve in pediatric CD pts. IM inflammation may persist despite treatment. CT or MR enterography is complementary to endoscopy in the follow-up evaluation of SB CD. Pts with endoscopic TI skipping may be less responsive to medical therapy and represent a more severe disease phenotype.
Table 1: Follow-up Data on Pediatric CD patients with Endoscopic Skipping of the TI

Reason for TI skipping at the index IC (n=43)	Before index IC		After index IC	
	Radiologic TI disease	Endoscopic TI disease	Radiologic TI disease	Endoscopic TI disease
Microscopic Disease (n=20)	2/4 (50%)	1/5 (20%)	9/11(82%)	4/11 (36%)
Intramural Disease (n=14)	4/4 (100%)	0/0	8/9 (89%)	4/7 (57%)
Proximal Disease (n=9)	2/2 (100%)	1/1 (100%)	2/4 (50%)	1/4(25%)

257 *SPANISH AND ENGLISH LANGUAGE SYMPOSIA TO ENHANCE PATIENT ACTIVATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: A PILOT INTERVENTION*

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Background: Patient activation is necessary to optimize health in patients with inflammatory bowel disease (IBD). High activation levels are important for both pediatric IBD patients and their parents since patients and families co-manage the disease together. Lower activation and disengagement may be more prevalent in limited English-speaking families. The Patient Activation Measure (PAM) Score is a validated assessment of patient activation in adults but has not been formally

studied in a pediatric IBD cohort. Scores are continuous (0-100), and higher scores are associated with improved health outcomes. The parent PAM is a parallel tool for assessing parent activation for management of his/her child's health.
Aims: We aimed 1) to compare baseline PAM scores in both Spanish- (SP) and English- (ES) speaking cohorts of families affected by IBD; 2) to determine the feasibility of a pilot peer-group education symposium designed to enhance IBD self-management knowledge and skills.
Methods: We conducted a parallel IBD peer-group education symposium in Spanish and English designed to enhance patient activation. The bilingual lecturer and moderator were the same for both groups. A total of 10 primary SP and 21 ES families participated. PAM scores were obtained before and after the symposia in both groups for patients and parent(s). Descriptive statistics were used to assess effects of the intervention.
Results: Paired pre- and post-PAM scores were available from 24 patients (8 SP; 16 ES) and 41 parents (15 SP; 26 ES). Mean age for SP and ES patients was 11.6 and 12.0 years, and female gender in 80% and 62%, respectively. PAM scores uniformly increased for all four of the groups after the symposia (SP-patients 59.1 to 70.3, P=0.5; SP-parents 69.8 to 75.2, P=0.2; ES-patients 59.9 to 64.0, P=0.08; ES-parents 61.9 to 69.1, P=0.002). The incremental change from pre- to post-PAM scores in SP vs. ES groups was not statistically significant.
Conclusion: We report the first experience in assessing PAM scores in pediatric IBD patients and their parents. A family-centered, peer-group education symposium in either English or Spanish may be effective in enhancing patient and parent activation in families affected by pediatric IBD.
Table 1. Patient Characteristics and PAM Scores

	Mean (n)	P-Value	Mean (n)	
Spanish Patients				English Patients
Age	11.6 (10)	0.812	11.95 (21)	Age
Age at diagnosis	9.2 (10)	0.633	9.95 (21)	Age at diagnosis
%Female:%Male	80%(8):20%(2)	0.314	62%(13):38%(8)	%Female:%Male
%UC:%CD	80%(8):20%(2)	0.029	38%(8):62%(13)	%UC:%CD
% Government Subsidized Insurance	90% (9)	2.08x10-6	4% (1)	% Government Subsidized Insurance
Pre-Pam	59.1 (8)	0.888	59.9 (16)	Pre-Pam
Post-Pam	70.3 (8)	0.213	64.0 (16)	Post-Pam
Spanish Parents				English Parents
Pre-Pam	69.8 (15)	0.183	61.9 (26)	Pre-Pam
Post-Pam	75.2 (15)	0.207	69.1 (26)	Post-Pam

Table 2. Pre and Post PAM scores for English vs Spanish-speaking Patients and Parents

	Pre-Pam Score	Pre-PAM SD	Post-Pam Score	Post-Pam SD	P-values
S-Patients (n=8)	59.1	12.7422	70.3	10.975	0.05499582
S-Parents (n=15)	69.8	20.11	75.2	14.1797	0.2180803
E-Patients (n=16)	59.9	10.7273929	64.0	11.3981797	0.07817346
E-Parents (n=26)	61.9	12.4905139	69.1	15.1200081	0.00175724

258 *PILOT STUDY: RELATIONSHIP BETWEEN GROWTH MEDIATORS AND HEALTH RELATED QUALITY OF LIFE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE*
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Background: Fatigue is a common symptom in patients with Inflammatory Bowel Disease (IBD) which could diminish

overall health related quality of life (HRQoL). Lower levels of Insulin like Growth Factor (IGF)-1 have recently been linked to depression and cognitive deficits in animal models. The relationship between serum IGF-1 levels and functional outcomes have not been previously explored in pediatric IBD patients.
Methods: This study is a single center, prospective longitudinal study. English or Spanish speaking children with IBD, ages 10-16 years, without evidence of major co-morbidities were eligible. Recruitment and baseline testing occured at the time of a routine out-patient visit. Enrollment is ongoing. 76 eligible patients were approached and 40(53%) participated. This analysis includes baseline data obtained at enrollment. Patients and parents completed the PedsQL™ Multidimensional Fatigue Scale (PedsQL™ MF) and the PedsQL™4.0 Generic Core Scales (PedsQL™ 4.0). Patients completed the IMPACT III Quality of Life Questionnaire. Disease activity was scored by Pediatric Crohn's Disease Activity Index (PCDAI) or Pediatric Ulcerative Colitis Activity Index (PUCAI) and a Physician's Global Assessment (PGA). Serum for growth mediators (IGF-1) was obtained on the same day as survey. IGF-1 levels and age and gender specific z-scores were measured by Quest Diagnostics™. Comparisons between healthy controls and study sample were conducted using t-test and Wilcoxon-Mann-Whitney was used for comparing IGF-1 level groups (see table).
Results: 40 participants had a mean age of 13.8±1.8, and 21 (53%) were female. 30 (75%) had Crohn's disease, 8 (20%) had Ulcerative Colitis and 2 (5%) had Indeterminate Colitis. The median PCDAI was 0(0-10) and PUCAI was 0(0-10). 32 (80%) patients had inactive disease based on PGA. 18 (45%) patients were on biologics and 6 (15%) were on systemic steroids. The median IGF-1 z score was -0.6 (-1.7-0.2). Mean child self-report and parent proxy report for PedsQL™ 4.0 and PedsQL™ MF total scores were significantly lower than healthy controls (n= 157) ($p< 0.001$). Patients with IGF-1 z scores in the lowest quartile (< -1.7) had significantly lower scores on several measures.
Conclusions: Stable IBD patients in an ambulatory setting, report more fatigue and lower generic HRQoL than healthy children. Patients who have IGF-1 z scores in the lowest quartile have lower functional outcomes.
HRQoL by IGF-1 z Score Quartile

HRQoL Scores	Median IGF-1 z Score ≥-1.7 (n=30)	Median IGF-1 z Score <-1.7 (n=10)	p value
PedsQL 4.0 Parent Total	78.3(66.6-87.2)	65.9(56.3-73.9)	0.03
PedsQL 4.0 Parent Physical	81.3(68.8-93.8)	62.5(56.3-78.1)	0.04
PedsQL 4.0 Parent Psychosocial	76.7(65-88.3)	67.5(56.7-78.3)	0.04
PedsQL MF Child Total	76.4(66.7-86.1)	61.1(56.9-73.6)	0.01
PedsQL MF Child Sleep	75.0(62.5-87.5)	62.5(58.3-66.7)	0.01
PedsQL MF Parent Total	75.0(65.3-84.7)	57.6(51.3-77.8)	0.04
PedsQL MF Parent Sleep	75.0(62.5-87.5)	58.3(43.8-70.8)	0.04
IMPACT III	77.9(70-85)	68.9(63.6-77.1)	0.03

259 *IMPACT OF IMPROVE CARE NOW MODEL GUIDELINES IBD FORM ON CARE IN A PARTICIPATING PEDIATRIC IBD CENTER*

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Background: ImproveCareNow (ICN) is a collaborative chronic care network of 74 care centers enabling clinicians, researchers, patients and families work towards a collective goal to transform the health,care and cost of treatment for 17,000 children and adolescents with Crohn's disease and ulcerative colitis. As a participant, University of Texas Southwestern has made available an electronic IBD form based on the ImproveCareNow Model IBD Care guidelines to its providers during all visits with IBD patients. As part of a quality improvement initiative, we assessed whether compliance with this form demonstrated an improvement in the diagnosis, treatment and surveillance of patients with IBD.
Methods: A retrospective review was performed of all patient charts selected by a data extraction algorithm paired to our electronic medical record. Patient charts were selected based on ICD-9 codes and the presence of GI clinic encounters. Inclusion Criteria: all patients actively followed at UTSW pediatric gastroenterology clinic with at least one visit from 01/01/2014 to 4/29/2015 with a diagnosis of ulcerative colitis or Crohn's disease or IBD-unspecified. Exclusion criteria: patients not actively followed by UTSW treating physicians, patients with intestinal inflammation secondary to other processes besides IBD and those patients not seen in the GI clinic over the 16 month study period. Variables collected on each patient included age at last visit, diagnosis, completion of ICN IBD form, Paris classification of disease, completion of diagnostic bundle (defined as EGD, colonoscopy and MRE/UGI with small bowel follow through), PGA status or PUCAI, TB screen, remission at last visit, steroid free status at last visit, and nutritional status.
Results: 403 patient charts were reviewed, of which 334 met inclusion criteria. 193 of these patients have Crohn's disease and 141 have ulcerative colitis. The demographic distribution of our patient population was compared with that of ICN with

respect to age of diagnosis, sex, disease extent, and phenotype. Of the total 403 charts reviewed, 38% had a complete IBD form at the last vist. 33% of patients with ulcerative colitis and 41.5% of patients with Crohn's disease had a completed form. UC and Crohn's patients with a complete form had a complete disease classification versus those with an incomplete form. This difference was statistically significant. PGA status, both in Crohn's and UC, was found to be significantly different between patients whose providers employed the form versus those that did not. In addition, remission was also significantly higher in the patients whose providers used the form in comparison to those that did not. The remainder of IBD-focused care, as defined by the variables listed above, was not significantly different between the providers who completed the IBD form and those who did not.
Conclusions: This review suggests that overall, the IBD visit form based on the Model IBD Care guidelines does correlate with more accurate diagnosis and improved patient outcomes as evidenced by a quiescent PGA score and remission at last visit. Future studies will examine the difference between quiescent disease population and remission rates prior to the initiation of the IBD form at our center.

260 *INFLIXIMAB, ADALIMUMAB, AND VEDOLIZUMAB AS FIRST-LINE THERAPY FOR MODERATE-TO-SEVERE ULCERATIVE COLITIS: A COST-PER-REMISSION ANALYSIS*

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Introduction: Without head-to-head randomized, controlled trials (RCTs), it is difficult to assess the comparative effectiveness of biologic treatments for ulcerative colitis (UC). Determining the cost-effectiveness of infliximab (IFX), adalimumab (ADA), and vedolizumab (VDZ) as possible first-line treatment options will decrease clinical ambiguity and costs and improve health oucomes
Methods: We performed a head-to-head cost-per-remission analysis with mucosal healing (MH) as the end point for IFX, ADA, and VDZ, when used as first-line therapy in moderate-to-severe UC. Variables for our decision analytic model came from ACT, ULTRA, and GEMINI RCTs to compare the cost-effectiveness IFX, ADA, and VDZ for inducing clinical remission and MH in biologic-naïve patients with moderate-to-severe UC. Costs are direct costs as listed by HHS.gov and Red Book AWP.
Results: Using the base case of a 70 kg patient with UC, IFX at 5 mg/kg ($99,171.23/MH) was more cost effective than ADA ($316,378.13/MH at 160 mg dosing and $329,734.61 at 80 mg) and VDZ ($301,969.01/MH) at achieving mucosal healing after one year of fist-line treatment. IFX proved most cost-effective among the 3 biologic options due to its lower drug cost than VDZ and higher effectiveness than ADA. A probabilistic sensitivity analysis indicated that IFX was more cost-effective therapy in 95% of the 10,000 simulations. Considering drug costs, a sensitivity analysis showed that VDZ would have to be priced at $2537.08 or less for the VDZ to achieve superior cost-effectiveness. Similarly, ADA drug costs would have to be priced at $1235.56 or less for the 80 mg dosing and at $1155.85 or less for the 160 mg dosing to be cost-effective.
Discussion: Comparing health care costs required to induce deep remission in patients with moderate-to-severe UC, IFX as first-line therapy appears to be substantially more cost-effective than VDZ and ADA. High non-drug costs related to infliximab may decrease cost-effectiveness, since drug costs were used as the primary cost-driver in our analysis.

261 *PILOT TESTING OF TELEMEDICINE IN THE CARE OF PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE AS A QUALITY IMPROVEMENT INITIATIVE*

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Background. Standardization of Inflammatory Bowel Disease (IBD) care through participation in the Improve Care Now (ICN) Network has improved outcomes for pediatric patients with IBD, but under the current care model, our improvements have plateaued. Current ICN model care guidelines recommend health supervision visits every six months. We identified a gap in our practice's ability to ensure either a routine six month follow-up or a rapid follow-up after a disease flare, and a significant number of patients with active disease status during a six month period lacked timely reassessment after interventions or medication changes. Telemedicine provides an alternative method of care delivery to address these gaps, but has had limited use in patients with IBD.
Methods: A multi-step approach to offer alternative follow-up care options via telemedicine was developed with long-term goals of improving remission rates and quality of life. Short term goals of the pilot were to improve telemedicine access for patients with IBD by 1) increasing sign-up rates to the electronic medical record patient portal, 2) increasing communication using e-messaging via the medical record portal, and 3) establishing e-visits as an alternative visit model for patients with quiescent or mildly active disease. The expected outcomes of the e-visit model were to: maintain baseline care standards and health screening capabilities, improve access to care, and provide equivalent care delivery (no increase in the number of unplanned clinical encounters).

Results: Using the IHI model for improvement (Plan-Do-Study-Act) we have seen a progressive increase in the rate of patient signups for the electronic medical record patient portal, with a baseline median of 20% per clinic compared with a current median of approximately 70% after 6 months. We successfully implemented e-messaging in its pilot form among five providers and have seen steady uptake in patient use from 5 patient initiated messages during the first month to 76 messages/month over the past three months. E-visits have replaced a total of 32 visits to date. Medications, nutrition, and disease activity were appropriately screened and managed electronically without the need for a physical office visit by the treating gastroenterologist. Access to care was improved in that all patients completed their e-visits from their homes without missing school or work and did not require a physical office visit. One visit successfully identified worsening of the patient's clinical course and resulted in a scheduled office visit request, but no unplanned office visits or ED visits have occurred.
Discussion: This report represents the first description of telemedicine use in routine clinical care in children with IBD. We anticipate continuing use of this novel mode of health care delivery in pediatrics in an effort to increase the proportion of patients seen for interval follow-up, after IBD diagnosis, or mild flare in an effort to target early treatment changes that should result in improved remission and patient reported outcomes. E-visits are less expensive and time consuming than traditional visits and may serve as an additional method of cost savings by matching care to a patient's individual needs.

263 *INCIDENCE OF INFLAMMATORY BOWEL DISEASE IN RHODE ISLAND: REPORT FROM THE OCEAN STATE CROHN'S AND COLITIS AREA REGISTRY (OSCCAR)*

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Background: Epidemiologic studies of Crohn's disease (CD) and ulcerative colitis (UC), the two major forms of inflammatory bowel disease (IBD), are uncommon in the United States.
Methods: The Ocean State Crohn's and Colitis Area Registry (OSCCAR) is a state-based inception cohort of patients newly diagnosed with IBD in Rhode Island (RI).[1] OSCCAR was originally designed to study the epidemiology of IBD, determine the incidence of IBD in RI and extrapolate these rates to the general population of the United States. Utilizing population-based data, we sought to estimate the state-wise incidence of IBD in RI between 2008-2010.
Results: A total of 971 RI residents were diagnosed with IBD, including 444 with CD, 486 with UC and 41 with IBD-U in 2008-2010. The overall age- and sex-adjusted IBD incidence was 30.2 (95% CI, 28.3-32.1) per 100,000 in this time frame with 13.9, 15.1 and 1.3 per 100,000 persons diagnosed with CD, UC and IBD-U, respectively. Of the total incident cases, 30% (n=291) were enrolled in OSCCAR. The mean age at IBD diagnosis was 32.7 in OSCCAR versus 45.6 in the un-enrolled patients. The observed younger age of OSCCAR is attributed to there being a single, academic Pediatric Gastroenterology practice in the state, of which the division chief is a co-investigator. During the 3-year timeframe, a total of 110 children under 18 were diagnosed with IBD, 84 (76%) of which were enrolled in OSCCAR. When adjusting for age by removing children under the age of 18, the median age of those enrolled (40.76) versus unenrolled (46.9) was not appreciably different.
Conclusion: In this near complete enumeration of IBD incident cases among the total population of Rhode Island, we found an overall age and sex-adjusted incidence of 30.2 per 100,000 persons for IBD, 13.9 per 100,000 persons for CD and 15.1 per 100,000 persons for UC in 2008-2010. These incidences are within the highest quintile rank of published incidence rates worldwide[2] and higher than those reported recently for specific populations in North America.[3,4] Ongoing prospective follow up of individuals enrolled in the community-based OSCCAR cohort is providing a basis for predictive models of IBD prognosis.

COMPARISON OF OSCCAR vs. UNENROLLED PATIENTS NEWLY DIAGNOSED WITH IBD IN RHODE ISLAND, 2008-2010

	OSCCAR - PEDIATRIC N = 84	OSCCAR - ADULT N = 207	UNENROLLED - TOTAL N = 680
Mean Age, range	12.79, 4-17	40.76, 18-87	45.64, 2-99
Female n (%)	34 (40)	122 (59)	347 (51)
White n (%)	65 (77)	189 (91)	N/A
CROHN	63 (75)	111 (54)	269 (40)
L1 - Ileal	15 (24)	24 (22)	N/A
L2 - Colonic	13 (21)	33 (30)	N/A
L3 - Ileocolonic	34 (55)	53 (48)	N/A
L4 - Upper Tract*	25 (40)	11 (10)	N/A
B1 - Inflammatory	55 (87)	93 (84)	N/A
B2 - Stricturing	5 (8)	13 (12)	N/A
B3 - Penetrating	3 (5)	5 (5)	N/A
P - Perianal*	13 (21)	5 (10)	N/A
ULCERATIVE COLITIS	18 (21)	91 (44)	376 (55)
E1 - Proctitis	1 (6)	21 (23)	N/A
E2 - Left Sided	4 (22)	28 (31)	N/A
E3 - Pancolitis	13 (72)	42 (46)	N/A
IBD-U	3 (4)	5 (2)	35 (5)

*Concomitant upper tract (L4) or perianal (P) disease. N=2 had isolated upper tract (L4) disease.

264 *THE DYSBIOSIS INDEX DOES NOT DISTINGUISH CHILDREN WITH CROHN'S DISEASE FROM HEALTHY SIBLINGS*

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Introduction: Patients with Irritable Bowel Syndrome (IBS) are often used as controls in studies of the Crohn's disease (CD) microbiome. However, digestive symptoms among the IBS-controls could be associated with microbial dysbiosis. An alternative design is to use healthy siblings of CD patients as controls.

Aims & Methods: Our aims were to compare the microbial community composition of stool samples from healthy siblings and pediatric CD patients, to characterize their microbiomes at the functional level and to investigate the familial effect on measurements of community diversity and the potential relationship between dysbiosis and CD, using the Dysbiosis Index (DI), a recent measure of microbial dysbiosis, which was originally derived from a dataset dominated by biopsy samples taken from CD patients(1), and was shown to be associated with clinical disease severity. Metagenomic sequences from stool of 5 pediatric CD patients and their siblings were obtained (MiSeq): both whole-metagenome and16SrRNA. Microbial composition profiles based on 16SrRNA were derived from the greengenes-database. To obtain functional assignment, sequences were searched against 28 representative KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways, with putative functions assigned using HUMAnN. Microbial composition profiles were analyzed using QIIME and STAMP, and functional profiles were inferred using STAMP and BiomeNet. Microbial dysbiosis was determined for each sample as implemented in QIIME.

Results: Examination of phylotypes that contribute to the dysbiosis index revealed that considerable among-sample variability was shared between siblings. For example, some pairs of healthy and CD siblings exhibited highly similar frequencies of phylotypes that contribute to the dysbiosis index. Clearly, in these cases it is inappropriate to attribute the CD phenotype to the presence of those lineages. Furthermore, none of the samples scored as dysbiotic according to the ensemble index, and there was no consistent relationship between sibling pairs in terms of the magnitude of their scores. Similar results were obtained at the functional level. Bayesian modeling of metabolic structures via BiomeNet also revealed a close association between many healthy and CD siblings.

Conclusion: The DI of stool samples is not able to distinguish healthy siblings from pediatric patients with Crohn's disease. We hypothesize that this is because the DI is based on too few microbial lineages. We suggest that the dysbiosis index might be improved by inclusion of more indicator lineages and functional information. Comparison to sibling controls indicates that there is a strong familial effect on both microbiome composition and function that can vary considerably among sibling pairs. This effect must be accommodated if microbiome-derived information is going to make a practical contribution to clinical care in the future.
References: 1. Gevers et al. Cell Host Microbe. 2014;15(3):382-92.

265 *CLINICAL REMISSION INDUCED BY EXCLUSIVE ENTERAL NUTRITION (EEN) IN PEDIATRIC CROHN'S DISEASE IS ASSOCIATED WITH COMMUNITY LEVEL CHANGES IN METABOLIC FUNCTIONS*

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Introduction: EEN is a first-line induction therapy in pediatric Crohn's disease (CD). The mode of action of EEN is proposed to involve changes in gut microbiome structure and function.
Aims & Methods: Our aims were to compare microbial community structure and function in pediatric CD patients before and after induction of remission by EEN treatment. 16SrRNA and whole-metagenome sequences were obtained from stool samples of both pediatric CD patients (at week 0, 4, 8 and 12) and healthy controls. Each 16S sequence was inferred according to the green genes reference database. The whole-metagenome sequences were searched against 28 genomes that had been annotated according to KEGG functional pathways, and community pathways were inferred by using the HUMAnN analytical pipeline. Taxonomic composition was analyzed using QIIME and STAMP, and functional profiles were analyzed using STAMP and BiomeNet.
Results: Changes in CD patient microbial community structure before and during EEN were variable. However, functional profiling of CD patient microbiota before and during EEN treatment revealed a significant increase in metabolic functions related to biodegradation and metabolism of xenobiotics, such as benzoate ($p<0.05$). In addition, preliminary analyses using BiomeNet uncovered large-scale changes in community metabolic interactions during weeks 4 and 8 of EEN treatment relative to baseline samples. All patients exhibited clinical remission at week 12, but some required additional treatment within 6 months due to flare-ups. It is noteworthy that the microbiomes of patients experiencing a flare-up differed at week 12 from those that did not. The gut microbiomes returned to baseline levels in those patients that did not require additional treatment, whereas patients experiencing flare-ups were characterized by microbial interactions that had not rebounded to the baseline. A successful course of EEN treatment was also characterized by a decrease in microbial diversity followed by an increase.
Conclusions: The microbiome of CD patients is functionally altered during EEN treatment. Metabolic potential for xenobiotic biodegradation and metabolism increases during treatment, but then, after 12 weeks, it returns to a state similar to pretreatment and controls. Changes in functional diversity induced by EEN are related to changes in taxonomic diversity. This is presumably because the metabolic repertoire of the community is heavily influenced by the genes of the microbes that transiently dominate a community during EEN. Return to a state similar to baseline should not be interpreted as indicating that the communities are functionally, or taxonomically, equivalent. Finer-scale profiling will likely reveal cryptic functional diversity, as these states are taxonomically divergent. It is clear, however, that a dramatic cycle of community disturbance is initiated by EEN, after which the community experiences a "rebound-like" effect. Thus, the therapeutic effect and duration of EEN might be predicted by monitoring changes in community level metabolic structures over the course of treatment.

267 *AN AUDIT OF INFLUENZA VACCINATION STATUS IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE*

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BACKGROUND: Patients with inflammatory bowel disease (IBD) have an increased risk of infections due to immunosuppressive therapies. Current guidelines recommend that patients with IBD should receive routine immunizations, including annual influenza immunization. Empirical pediatric data suggests vaccines are underutilized in this population. Our study aimed to explore rates of influenza vaccinations in a pediatric population with IBD and factors affecting immunization status.
METHODS: The prospective study audited pediatric patients with IBD at the Pediatric Gastroenterology IBD Clinic at McMaster Children's Hospital between April 2014 - April 2015. Patients/parents were asked to complete a questionnaire regarding demographic and clinical parameters, influenza vaccination status, side effects and reasons for not vaccinating if

applicable. Bivariate analysis was performed to determine the effects of variables on the reception of influenza vaccinations.
RESULTS: The study population included 76 patients (64% male) with a median age of 13.2 years (range 4-17). Fifty-four patients (71%) were on immunosuppressant therapy. 93.4% of patients had a primary care physician (PCP), with 67.7% reporting their PCP discussed the need for annual influenza vaccination. Only 22 patients (28.9%) were immunized against influenza in the last 12 months. Of the group who received influenza immunizations in the last 12 months, 63.6% received their immunizations in physicians offices, 54.5% did not report any side effects of the immunization and none reported perceived worsening of their IBD. The main reasons for not vaccinating included concerns regarding vaccine safety and vaccine efficacy, as well as lack of awareness that it was needed. Variables including age, gender, diagnosis, disease severity, immunosuppressant medications and immunization status did not significantly affect influenza vaccination status. Patients who received an influenza vaccine in the last 12 months were more likely to have had a discussion about the need for immunization (most commonly with a PCP) compared to the group who did not receive a flu shot in the last 12 months ($p = 0.025$).
CONCLUSIONS: Influenza vaccination rates are low in the pediatric population with IBD. Quality initiatives need to be developed to improve immunization rates among pediatric patients with IBD. Strategies to enhance education of parents and health professionals may improve immunization uptake.

268 *GD3 GANGLIOSIDE (GD3) SUPPRESSES DEXTRAN SODIUM SULFATE (DSS)-INDUCED COLITIS IN MICE*
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Background: GD3, a sialic acid-containing glycosphingolipid rich in enterocyte microdomains, is cytoprotective, both by acting as a "decoy" receptor for pathogenic bacteria and by mitigating inflammatory mediators. We recently showed dietary GD3 protects newborn rats from a cold/hypoxia model of necrotizing enterocolitis (NEC), by augmenting mucosal Foxp3+Treg cell immune responses, down-regulating both TNF-α and other proinflammatory cytokines (JPGN 2013; 57:550). To date, GD3's potential protective role in IBD has not been investigated. This study seeks to determine effects of dietary GD3 on intestinal inflammation in a murine DSS colitis model.
Methods: Three groups of 8 week-old male BALB/c mice were studied as follows: Group 1 = control; Group 2 = DSS alone; Group 3 = DSS + GD3. Both groups 2 and 3 were treated with DSS for 7 days as previously described, to induce colitis. At day 7, all animals were killed, and colons removed, fixed in 4% paraformaldehyde, embedded in paraffin, sectioned and stained with hematoxylin-eosin. Histologic scores were compared by established methods.
Results: At day 7 of study, colons from DSS + GD3-treated animals, compared with DSS alone, exhibited a marked reduction in inflammation and in mucosal wall thickening. Observed mucosal differences in GD3 treated animals included preservation of goblet cells, maintenance of mucosal architecture, reduced inflammatory cell infiltration, and absence both of crypt abscesses and of mucosal ulceration.
Conclusions: 1. Similar to its cytoprotection in experimental NEC, GD3 treatment ameliorates the inflammatory effects of DSS in a murine IBD model; 2. When administered concurrently with DSS, GD3's effects on colonic mucosa include maintenance of architecture and abridgement of the local inflammatory response.
Speculation: These data strongly suggest GD3, a naturally occurring ganglioside, represents a novel, anti-inflmmatory nutritional approach to IBD management and possibly to treatment.

269 *MR ENTEROGRAPHY FINDINGS AND ENDOSCOPIC FACTORS FOR PREDICTION OF LOSS OF RESPONSE TO INFLIXIMAB TREATMENT IN PEDIATRIC CROHN DISEASE*
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BACKGROUND & AIMS : Crohn disease (CD), characterized by transmural involvement of the bowel wall, is one of the most important chronic intestinal diseases in children and young adolescents. Tumor Necrosis Factor (TNF) blocker therapies are established as the effective treatments for induction and maintenance in treating pediatric CD. However, TNF blocker therapies still have issues to solve such as loss of clinical responses and need of dose intensification (DI). So far, a few parameters which are related to predictive of response to TNF blockers have been identified. Magnetic resonance enterography (MRE) is an emerging imaging modality in CD for the assessment of small bowel involvement and various complications. Our aim was to determine MRE findings and endoscopic factors in pediatric CD to predict the responsiveness of TNF blocker therapy.
METHODS: Clinical, endoscopic and radiological database of 36 CD patients who underwent a complete MRE prior to TNF blocker (Infliximab, IFX) therapy were enrolled. All the patients were evaluated with full ileocolonoscopy and other laboratory exams. Twenty patients were changed to dose intensification up to 10mg/kg per dose (or maintenance interval every 6weeks) for loss of responsiveness during the follow-up period (DI subgroup), and 16 remained in standard regimen

(NDI subgroup). MRE examinations were independently reviewed by 3 pediatric radiologists. The findings of MRE, initial endoscopic disease location (the Paris classification), and laboratory were analysed according to the IFX responsiveness.
RESULTS: Overall, there were no significant differences in sex, age, follow-up duration, infliximab therapy duration and disease activity score (PCDAI) at initial therapy between two subgroups. But initial MRE findings were related significantly with DI. These were more severe lower small bowel wall thickness (jejunum and ileum), severe mesenteric fat proliferation, obvious comb sign (mesenteric vascular engorgement) and presence of ascites. Terminal ileum wall thickness and presence of perianal fistula abscess were not significantly related. Colonic disease (Paris classification L2) was significantly higher in DI subgroup. OR to DI was 53.6 when the endoscopic exam displayed colonic disease and 21.9 when MRE findings showed comb sign with multivariate analysis.
CONCLUSION: In this cohort of IFX-treated patients, specific MRE findings that indicate the presence of severe intestinal inflammation were related to the poor responses to TNF blocker therapy in pediatric CD. MRE may provide complementary information to endoscopic and laboratory evaluations in predicting loss of response to IFX therapy. The combination of Endoscopy and MRE may warrant further investigation for its value in predicting loss of response to IFX therapy in pediatric CD patients.

NUTRITION

271 *HIGHER INTAKE OF FRUCTOSE CONTAINING PROCESSED FOODS IN OBESE CHILDREN IN WEST MEXICO: CASE CONTROL STUDY*

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Background: Fructose consumption from industrialized foods has significant effects on most components of metabolic syndrome.
Objective: To compare the intake of containing fructose processed foods and beverages in obese and normal weight children.
Material and methods: A case-control study of a random sample of 99 obese and 104 normal weight 6-12 years-old children was conducted from February to September 2014. The independent variable was fructose ingestion and was evaluated by two 24-hour food recalls and an *ad hoc* food frequency questionnaire designed to measure fructose equivalents from processed foods and sweetened beverages. The nutritional status was assessed by BMI z-score (WHO criteria). Statistics: Mann-Whitney U, Chi square.
Results: No differences in age, gender and socio-demographic status were shown between the study groups. Energy, macronutrient and processed foods with fructose intake estimated by the 24-hour recall showed no differences between the study groups. The intake frequency of dairy products without fructose was higher in obese children (p=0.003). This survey showed a higher intake of fructose containing processed foods by 9-12 years old obese children. This difference was shown in three food groups: cereals with fat and sugar, p=0.021 (example: donnut), sugar-sweetened beverages, p=0.039 (example: soda), sauces (example: ketchup) and dressings (example: ranch dressing), p=0.040.
Conclusions: Despite the lack of difference in the energy and macronutrient intake between the study groups, an increased consumption of containing fructose processed products was observed in the obese children. The particular metabolic fructose path may play a role in fat storage in obese children.

272 *FEEDING GUIDELINE IMPLEMENTATION IN INFANTS AT RISK OF INTESTINAL FAILURE*

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Background: Feeding practices vary widely for surgical infants at risk for intestinal failure from bowel loss or dysfunction. Our objective was to implement feeding guidelines to reduce the incidence of intestinal failure-associated liver disease (IFALD), a common complication among infants needing parenteral nutrition (PN).
Methods: A multi-disciplinary team developed guidelines for intestinal surgical infants <6 months old requiring >7 days of PN. Infants with pre-existing liver disease or surgery at outside hospitals were excluded. Key modifications included higher initial enteral nutrition (EN) volumes of 20 cc/kg/day and daily advancement by the same rate if tolerated. Intestinal failure is rare, so pre-implementation data were collected for 2.5 years; post-implementation data have been collected for 15 months. The primary outcome was IFALD incidence (peak direct bilirubin >2mg/dl). Other measures included peak direct bilirubin, initial EN volume, time to reach EN goals, and incidence of necrotizing enterocolitis (NEC) after feeding. PN lipid reduction strategies did not change and were implemented once IFALD occured.
Results: There were 57 pre-implementation and 33 post-implementation infants. Adherence was very good after implementing weekly team rounds. The most common diagnosis changed from NEC pre-implementation to gastroschisis and intestinal atresia post-implementation. There was decreased IFALD incidence (70 vs 48%, *P*=0.041), and median peak direct bilirubin significantly decreased from 5.6 to 2.3 mg/dl (*P*=0.011). Table 1 displays patient characteristics and

outcomes. The initial EN volume improved from 10 to 20cc/kg/day (*P*=0.001). Time to reach 50% of goal calories from EN decreased by a median of 6 days (11 vs 5 days, *P*=0.012) without a change in NEC incidence after post-operative feeding. Conclusions: Feeding guideline implementation resulted in faster achievement of 50% goal EN calories and reduced IFALD without an increase in NEC.
Characteristic & Outcomes

	Pre-implementation N=57	Post-implementation N=33	P*
Baseline/Surgical Characteristics			
Gestational age, weeks median (IQR)	31.3 (27.2-36.9)	35.2 (31.4-37.1)	0.203
Diagnosis (%) Atresia Gastroschisis Hirschsprungs NEC Other SIP Volvulus	11 (19) 9 (16) 2 (4) 21 (37) 3 (5) 9 (15) 2 (3)	11 (33) 9 (27) 0 (0) 5 (15) 2 (6) 4 (12) 2 (6)	0.227
Initial procedure (%) Peritoneal Drain Resection/anastomosis Resection/ostomy Ostomy/no resection Abdominal wall closure	2 (3) 17 (30) 18 (32) 11 (19) 9 (16)	3 (9) 10 (30) 10 (30) 1 (3) 9 (27)	0.152
Nutrition Metrics			
1st post-op EN, days median (IQR)	13 (7-23)	8 (6-15)	0.048
Initial volume, ml median (IQR)	10 (6-14)	20 (10-20)	0.001
Bolus feeds initially (%)	43 (77)	14 (42)	0.001
50% EN, days median (IQR)	11 (5-21)	5 (3-12)	0.012
100% EN, days median (IQR)	21 (8-36)	11 (6-20)	0.089
IFALD & Other Outcomes			
IFALD (%)	40 (70)	16 (48)	0.041
Peak DB, mg/dl median (IQR)	5.6 (0.8 - 9.5)	2.3 (1.5-5.0)	0.011
Total PN, days median (IQR)	52 (31-99)	22 (14-49)	0.012
NEC after feeding (%)	3 (5)	1 (3)	0.620

IQR, interquartile range; NEC, necrotizing enterocolitis; SIP, spontaneous intestinal perforation; EN, enteral nutrition; PN, parenteral nutrition; DB, direct bilirubin
*Fisher's exact test or Wilcoxin rank-sum test

273 *THE NUTRITIONAL VALUE OF FOOD SERVICE MEALS TO HOSPITALIZED CHILDREN - NEED FOR IMPROVEMENT*

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Background: Many hospitals provide food to children as inpatients. While room-service meals may promote appetite and help maintain nutrition during pediatric hospitalization, it is unknown whether hospital-provided foods meet dietary guidelines. Pediatric obesity is a growing problem, and nutritional intake plays a key factor in obesity development.
Study Aims: To examine the dietary orders of hospitalized pediatric patients and to determine whether the nutritional content of ordered meals meet age-and-sex based nutritional guidelines.
Methods: Over Summer 2014 (June-August 2014), diet orders from all inpatients >=1y at a tertiary care pediatric hospital (3,148 hospitalizations) were collected. Among hospitalized youth receiving all nutritional intake by mouth, not on a clear liquid diet, and who stayed at least one calendar day where at least 2 meals were ordered, diet order data were analyzed for nutritional content. The nutritional content of meals ordered over a given calendar day was compared with daily dietary recommendations from the American Academy of Pediatrics based on age and gender - specifically caloric intake, fiber

intake, and consumption of sugar-sweetened beverages (SSB) (Current guidelines recommend no SSB). Among patients with >=2 calendar days where at least 2 meals were ordered, odds ratios for meeting dietary recommendations were calculated according to select demographic factors and hospital length of stay. Calculated odds ratios were adjusted for hospital length of stay.
Results: 968 diet orders from 269 patients [13 (1, 26) [mean (min, max)] years, 49% male, 47% Hispanic, 55% hospitalized <=7d] were reviewed. The majority of diet orders had no dietary restrictions imposed by care teams (66% "regular diet"). Just under half of diet orders (44%) over a given calendar day exceeded daily caloric recommendations. On days where diet orders exceeded caloric recommendations, daily caloric intake exceeded recommendations by 822 (685) [mean (standard deviation)] calories. Nine percent of diet orders met fiber recommendations and 53% of meals included SSB. Youth <13y, obese/overweight (OB/OW) youth, boys, and youth hospitalized <=7d were more likely to place diet orders exceeding daily caloric recommendations; girls, youth >=13y, and non-Hispanic youth were more likely to meet daily dietary fiber recommendations; and youth <13y, Hispanic youth, OB/OW youth, and youth hospitalized <=7d were more likely to order SSB than inpatient counterparts (Table).
Conclusions: Pediatric inpatient diet orders commonly do not meet fiber or SSB intake guidelines and often exceed dietary caloric guidelines. This may place hospitalized youth at risk for obesity. Hospitals should develop strategies to encourage families to order within nutritional guidelines to prevent additional health risk.
TABLE 1. Risk of meeting or exceeding nutritional guidelines by various demographic factors

	Exceeds Total Daily Caloric Recommendation	Meets Daily Dietary Fiber Recommendation	Exceeds Sugar Sweetened Beverage Recommendation
Age	<13Y v >=13 Y: 1.46 (1.13-1.89)	<13Y v >=13 Y: 0.29 (0.17-0.48)	<13Y v >=13 Y: 1.32 (1.02-1.71)
Weight Status	OB/OW v. Not: 1.80 (1.36-2.40)	OB/OW v. Not: 0.72(0.45-1.18)	OB/OW v. Not: 1.92 (1.43-2.59)
Ethnicity	Hispanic v. Non-Hispanic: 0.82 (0.63-1.06)	Hispanic v. Non-Hispanic: 0.59 (0.37-0.94)	Hispanic v. Non-Hispanic: 1.86 (1.43-2.44)
Length of Stay	<=7 days v. >7 days: 3.05 (2.12-4.26)	<=7 days v. >7 days: 0.79 (0.41-1.46)	<=7 days v. >7 days: 1.92 (1.37-2.69)

Values reflect Odds Ratio (Confidence Interval) adjusted for days of hospitalization where >=2 meals ordered.

274 *GUT MICROBIOME BIOMARKERS ARE ASSOCIATED WITH CLINICAL RESPONSE TO A LOW FODMAP DIET IN CHILDREN WITH IRRITABLE BOWEL SYNDROME*

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Background: A low fermentable oligosaccharides disaccharides monosaccharides and polyols (FODMAP) diet ameliorates gastrointestinal symptoms in many adults and children with IBS but 25% or more patients do not respond. One of the mechanisms of action of a low FODMAP diet is believed to be via changes in gut microbiome composition with decreased fermentation and gas production.
Objectives: We sought to determine if microbiome composition and/or metagenomic functional potential prior to starting the low FODMAP diet is associated with subsequent clinical response.
Methods: We previously reported the efficacy of a low FODMAP diet in 33 children with Rome III IBS (ages 7-17 yrs.) in a randomized, double blind trial. Following a one week baseline period, subjects were randomized to a low FODMAP diet (0.15 g/kg/day FODMAP content) or typical American childhood diet (TACD - 0.7 g/kg/day FODMAP content), followed by a 5-day washout period before crossing over to the other diet. A stool sample was collected during the baseline period for subsequent 16S rRNA gene sequencing following microbial DNA extraction per the Human Microbiome Project protocol. Gastrointestinal symptoms were assessed at baseline and during the dietary interventions with abdominal pain frequency being the primary outcome. Baseline gut microbial composition (16S rRNA sequencing of the V3-V5 region) sequences were quality controlled including chimera removal and closed-reference operational taxonomic unit (OTU - 97% similarity threshold) picking with QIIME 1.7.0 using Greengenes 13.5 as a reference database. Metagenomic KEGG ortholog predictions were generated using the PICRUSt package comparing Responders (≥50% decrease in abdominal pain frequency on low FODMAP diet only) versus Non-Responders (no improvement during either intervention). Linear Discriminant Analysis Effect Size (LEfSe) biomarker detection (Kruskal-Wallis rank-sum test ($P<0.05$), and linear discriminant analysis (log10 difference >2) were used to differentiate Responders from Non-Responders. Those who had a ≥50% decrease in abdominal pain frequency on the TACD, irrespective of their response to the low FODMAP diet, were considered to be a Placebo-responder and were not subsequently analyzed.
Results: Eight subjects were categorized as Responders (had significant improvement on the low FODMAP diet only), 15

as Non-Responders (did not have significant improvement on the low FODMAP or TACD), and 10 as Placebo-responders (improved on the TACD diet). Responders were enriched at baseline in 63 OTUs representing taxa with known greater saccharolytic metabolic capacity (e.g., *Bacteroides, Ruminococcaceae, Dorea, Faecalibacterium prausnitzii*) and 3 KEGG orthologs, of which two relate to carbohydrate metabolism. Non-Responders were enriched in 4 OTUs at baseline, of which two were uniquely assigned to be in the genus *Turicibacter*. Though limited information is available, other studies have found that *Turicibacter* does not have robust FODMAP saccharolytic potential.
Conclusions: Gut microbiome biomarkers are associated with low FODMAP diet efficacy. Children with IBS who significantly improve on the low FODMAP diet may have a gut microbiome with greater FODMAP carbohydrate saccharolytic potential.

275 *LOW FODMAP DIETARY FOOD LISTS ARE NOT ALL CREATED EQUAL*

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Background: A low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet ameliorates gastrointestinal symptoms in adults and children with irritable bowel syndrome. The best way to educate subjects on the low FODMAP diet is still being determined. However, food lists with guidance on which foods are allowed and which foods should be restricted are commonly provided during the education process. Whether readily available low FODMAP diet food lists provide consistent guidance has not been determined.
Aim: To determine the overlap and agreement of readily available United States based low FODMAP dietary guidance food lists.
Methods: Three low FODMAP dietary guidance food lists from sources affiliated with academic institutions within the United States were obtained from the internet for review. The lists were evaluated for the number of foods included, and specific recommendations regarding each listed food. Recommendations were classified into one of three general categories: full restriction, partial restriction, or no restriction. Where two or more lists provided information on the same food, agreement was assessed. Agreement was defined as two or more lists either allowing the food in some capacity (no restriction, partial restriction) or fully restricting the food. Disagreement was defined as one list recommending full restriction versus another list allowing the food in some capacity.
Results: Combined, the three lists provided recommendations for three hundred forty two different foods. List A provided guidance on 218 foods, recommending full restriction of 78 (35.8%), partial restriction of 24 (11%), and no restriction of 116 (53.2%). List B provided guidance on 203 foods, recommending full restriction of 85 (41.7%), partial restriction of 8 (2.2%), and no restriction on 110 (53.9%). List C provided guidance on 156 foods, recommending full restriction of 62 (39.7%), partial restriction of 20 (12.8%), and no restriction of 74 (47.4%). 180 (52.6%) foods were only listed on one of the evaluated lists, with List A having 77 unique foods, List B having 83 unique foods, and List C having 20 unique foods. Of the recommendations for the remaining 162 foods, 53 (32.7%) foods had absolute agreement with all 3 lists, 74 (45.7%) foods had agreement on two lists, and 35 (21.6%) foods had disagreement.
Conclusions: The evaluated low FODMAP dietary guidance lists differ from each other to a large extent with respect to the specific foods which are listed. When foods do overlap between lists, there is generally good agreement, though there are a sizable number of foods (21.6%) with discrepant recommendations. Further evaluation of low FODMAP food lists provided by United States based institutions in order to identify those which are most accurate and effective within an educational program are needed.

277 *INCIDENCE OF BACTEREMIA IN CHILDREN WITH REPORTED FEVER AND INTESTINAL FAILURE*

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Background: Intestinal Failure (IF) is a rare condition affecting approximately 3-4 people per million, but the precise prevalence in pediatric population is unknown. Patients with IF are dependent on parenteral nutrition to meet their daily fluid and nutritional needs. IF remains an important medical condition because of its significant mortality rate quoted as high as 25% in infants. Morbidity and mortality result most commonly from recurrent septicemia and parenteral nutrition-associated liver disease. Febrile children with IF are at high risk of septicemia from both central venous catheter infections and bacterial translocation caused by significant bacterial overgrowth in the gut. Furthermore, children with IF are more susceptible to infection as they can have underlying immune system deficiencies resulting from chronic liver disease and malnutrition with subsequent important vitamin and mineral deficiencies. Febrile children with IF therefore require prompt evaluation and treatment.
Methods: We retrospectively reviewed the health records of all patients with IF who presented with a history of fever by caretaker to Holtz Children's Hospital from 4/1/2009 to 6/30/2014. We regularly followed approximately 33 pediatric patients with IF during this time period and all patients presenting with a fever or a report of fever at home were included in the study. Data on gender, underlying etiology, white blood cell (WBC), C-reactive protein (CRP), and urine and blood cultures was collected.
Results: Twenty-six patients with IF presented to our institution with fever during the study period. A total of 246 febrile

episodes were evaluated and 245 of these had blood cultures drawn. The patients' ages ranged from 6 months to 22 years old, with 21 patients (81%) under 5 years of age, and 65% of patients were male. Diagnoses were gastrochisis (7, 27%), volvulus (5,19%), necrotizing enterocolitis (5, 19.%), atresias (3, 11.5%), aganglionosis (2, 8%), and other causes (4, 15%). Of the 25 patients who had blood culture drawn only a few patients (4, 15.4%) had all negative blood cultures, however a majority of patients (22, 88.4%) never tested positive for a urine infection. Evaluation of all 246 febrile episodes revealed an incidence of bacteremia of 55.04% (95CI, 42.3%-65.4%). Of those cultures that tested positive, 71.3% had gram-negative infections, 25% gram-positive and 8.9% fungal infections. CRP level and WBC count were not useful predictors of a positive blood culture, CRP (odds ratio 1.17; 95% CI 1.07-1.28, p<0.01) and WBC (odds ratio 0.95; 95% CI 0.90-1.0, p=0.07).
Conclusion: Children with reported fever and IF are at high risk for bacteremia. Few children presenting with fever and IF had urine infections which brings into question the usefulness of routine urine cultures on these patients. The CRP and WBC count on presentation to emergency room were poor predictors of bacteremia in this patient population. Children with IF are susceptible to both gram positive and gram-negative bacteremia. As such children with IF and a reported fever by caretaker should be treated with urgency with appropriate broad-spectrum antibiotics.

278 *ASSOCIATION OF SERUM 25-HYDROXYVITAMIN D LEVEL WITH METABOLIC CONTROL IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS*

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Objective. To demonstrate the association of serum 25- Hydroxyvitamin D level (25-OHD) with metabolic control in children and adolescents with type 1 diabetes mellitus (DM 1).
Methods. *Design:* Cross-sectional. *Setting*: A pediatric referral hospital. Sample: 74 patients with DM 1, age 6-15 years. *Variables*: a) Dependent. Metabolic control: HbA1c, glucose, total cholesterol (TC), triglycerides (TG), very low density lipoprotein (VLDL), low density lipoprotein (LDL), high density lipoprotein (HDL). b) Independent. Serum 25-Hydroxyvitamin D level. *Statistical Analysis*: Association of 25-OHD deficiency and metabolic parameters was estimated with chi square test.
Results. 37 males and 37 females, means age 11.7± 2.3 years; 58% (n=43) had HbA1c elevated 30% (n=22) TC >170mg/dL, 22% (n=16) LDL >100mg/dL, 13.5% (n=10) TG >150mg/dL, and 12% (n=9) HDL <35mg/dL. Mean concentration of 25-OHD was 26.8±7. Seventy percent (n=52) had insufficiency/deficiency of 25-OHD (≤ 29 ng/mL). TC and TG were associated with 25-OHD insuficiency/deficiency (p <0.05).
Conclusions. 25-OHD level showed no association with HbA1c; however, other parameters such as TC and TG, showed significant association. These findings differ from others probably because Mexican pediatric population with DM1 is exposed to different factors such as foods, sunlight and level of physical activity

*279 *BILE ACID TREATMENT OF TOTAL PARENTERAL NUTRITION (TPN) INFUSED ANIMALS INDUCES DIVERGENCE IN GUT MICROBIAL FLORA*

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Background: Total Parenteral Nutrition (TPN) is a lifesaving strategy providing all nutrition via the intravenous route. Unfortunately, it is associated with significant gut mucosal atrophy and inflammation. The TGR5 and FXR bile acid receptor agonists have been shown to modulate the intestinal barrier and immune responses. Recent evidence indicates that the mucosal barrier is also influenced by the gut microflora. We have previously published improvement in TPN induced gut atrophy with bile acid (BA) treatment. We hypothesize that BA treatment additionally induces alterations in the gut microbiota contributing to improved gut pathology.
Methods: Using our previously published ambulatory TPN animal model, piglets (n=10) were randomized to receive approximately two weeks of isocaloric enteral swine milk (EN) (n=3), TPN only (n=3), or TPN with an enteral BA receptor agonist Oleanolic Acid (OA) (n=4). Fresh stool samples were collected and stored at -80C for subsequent DNA extraction. Culture-independent identification of bacterial populations in feces was determined by 16S rRNA sequencing of the 5-809 nucleotide region of the E.coli genome and using a clone library-based method. Sequences were examined for quality and a total of 43-48 sequences per treatment were subjected to the un-weighted UniFrac metric. Statistical analysis was performed using Jackknife sample clusters, found in the UniFrac workflow. Additionally, bacterial sequences in each treatment were classified up to the genus level using the RDP-Classifier algorithm. Alpha-diversity was calculated at the phylum level using Shannon's diversity index.
Results: When subjected to the un-weighted UniFrac metric, clustering was noted based on the treatment. Branch points were supported by Jackknife analysis for TPN compared to other treatments but not well supported for the other branches (>95% for TPN only). Additionally, using the RDP classifier algorithm, we noted a shift towards the phylum *Bacteroidetes*

in piglets receiving only TPN. EN animals consistently showed a predominance of the phylum *Firmicutes*. Though no statistical difference between the *Bacteroidetes* phylum was noted in EN or TPN+OA animals, (p=0.4), a higher proportion of the phylum *Fusobacterium* was present with OA treatment . Furthermore, the alpha-diversity was 0.1351, 0.6403, 1.077 for TPN, EN, and TPN+OA respectively. The mean alpha diversity was significantly different between the three treatments (df=2, F=61.57 p<.0001).
Conclusion: We show that microbial communities diverge with TPN and overall microbial diversity is reduced in TPN treated animals. Additionally, a statistically significant expansion of the phylum *Bacterioides* was noted in TPN only animals. Though further mechanistic links are needed, the ability of the *Bacterioides* phylum to better utilize the essential host surface glycan may be a contributor to gut pathology. Additionally, a direct effect through bile acid receptor agonism remains plausible. Despite a rise in the phylum Fusobacterium in OA, this treatment clustered more closely with EN treatment. OA also resulted in the highest microbial diversity, indicating an overall preservation of gut microbiota that is significantly altered by TPN therapy.

281 *OBESITY: AN EMERGING CO-MORBIDITY OF AUTISTIC SPECTRUM DISORDER*

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Background: Contrary to previous reports associating feeding issues with failure to thrive (FTT) in children with Autistic Spectrum Disorders (ASD), current publications paradoxically now focus on the opposite trend. A recent study has documented a 30% prevalence of obesity among ASD patients, so that the North American Society for Pediatric Gastroenterology and Nutrition has posted a specific statement alerting parents of this emerging problem. It states that these children are at least as likely as those without autism to become overweight or obese. In addition, the Society offers advice for limiting abnormal feeding behaviors that might lead to weight gain.
Objective: To describe the nutritional status of inner city children with ASD and to compare that group with the general pediatric population at our institution
Design/Methods: As part of an ongoing QI project, we screened the medical records of all patients with ASD attending our public hospital general pediatrics clinic over a one-year period, 1/1/13-12/31/14. In addition to demographics, we determined the patients' BMIs. We further documented the nutritional status according to age (pre-school, school-aged, adolescent) to try to determine when the transition from normal BMI to overweight/obese was likely to occur. We then compared the rates of obesity and overweight among the ASD group to the known prevalence among our general clinic patients. The latter figures were retrieved from an internal data source which stratifies public city hospitals patients by age and BMI.
Results: Of the 722 who carried the diagnosis of ASD, 585 had complete nutritional measurements. Over half of our children with ASD were obese or overweight, which is markedly higher than the rates in our general pediatric clinic population (53 vs 38%, P<0.01). Elevated BMI or weight/ages was noted in all age groups, including 2-5 year-olds.
Conclusions: The current data suggest that the obesity epidemic has not excluded patients with ASD. Our review shows that the prevalence of obesity/overweight is actually higher in children with ASD, when compared to our general population. This is perplexing in view of the "conventional wisdom" that these children have known feeding issues associated with rigid, limited menus and dietary restrictions. In addition, we noted that the prevalence of overweight/obesity in ASD is increasing with age.
Further study is needed to determine which factors, such as breast feeding, the reliance on liquid nutrition, feeding/food preferences, as well as the effects of therapies, exercise, and medications, can explain our findings.
BMI Status of ASD Patients

Age (years)	FTT	Normal	Obese + Overweight
2-5	8 (6%)	63 (47%)	63 (47%)
6-10	7 (4%)	83 (45%)	93 (51%)
11-20	11 (4%)	102 (38%)	155 (58%)

282 *LONG-TERM EXPOSURE TO SMOFLIPID® IS NOT ASSOCIATED WITH SIGNIFICANT ELEVATIONS IN SERUM CONJUGATED BILIRUBIN LEVELS*

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Background: Long-term exposure to parenteral nutrition (PN) has been associated with the development of chronic liver disease. Lipid emulsions (LE), particularly soybean-based emulsions, have been implicated in this process. SMOFlipid® is a newer LE that has been studied primarily in the neonatal setting, as well as in clinically stable patients on home PN. The impact of long-term exposure to SMOFlipid® on hospitalized children with acute medical issues is not known. The aim of this study was to compare SMOFlipid® against Intralipid® (IL) in terms of their hepatic and metabolic effects in hospitalized children receiving prolonged courses of PN.

Methods: Prospective cohort study of hospitalized patients who received SMOFlipid® for ≥2 weeks. Patients with pre-existing liver disease were excluded. Anthropometric and biochemical parameters were compared against a historical cohort of children who had been exposed to IL during their hospitalization. Continuous data were compared using Student's t-test and χ^2 test was used for categorical data. Stata MP 13.0 (StataCorp, College Station, TX USA) was used for the analyses.

Results: Thirty-five patients (20 SMOFlipid®, 15 IL) with a median (range) parenteral nutrition (PN) exposure of 10 (4-38) and 6 (2-17) weeks, respectively, were included in this study. The median age was 1.3 (0.1-215.0) months and the most common indication for PN use was intestinal failure (24%). Baseline weight z-scores were not different between the groups (SMOFlipid®: -1.0 vs. IL: -1.1; p=0.926). Serum conjugated bilirubin (CB) levels at PN discontinuation had increased from baseline in 10% of those exposed to SMOFlipid® vs. 53% of those on IL (p=0.005). Mean CB was significantly different between the groups after Week 4, and that difference peaked at Week 10 (5 vs. 58 mmol/L, p=0.004; SMOFlipid® [n=9] vs. IL [n=4], respectively). Five patients were exposed to SMOFlipid® for >16 weeks; CB remained zero until PN discontinuation in all these patients. SMOFlipid® was associated with a significantly smaller increase from baseline to PN discontinuation in both alanine aminotransferase (ALT) and aspartate aminotransferase (AST) compared to IL (ALT: 3 vs. 68 U/L; p=0.04; AST: 1 vs. 61 U/L, p=0.006) and a more efficient lipid clearance measured with nephelometry (mean serum SMOFlipid® level: 0.3 vs. mean serum IL levels: 0.5 g/L, p=0.026). The change in weight z-scores during the time of PN exposure was not different between the groups (+0.1 vs. +0.3, p=0.521).

Conclusions: In contrast to IL, long-term use of SMOFlipid® is not associated with biochemical evidence of significant hepatotoxicity in hospitalized children. SMOFlipid® is also associated with more efficient serum lipid clearance than IL. Changes in weight z-scores over time are similar between the two LE studied.

283 *RELATIONSHIP BETWEEN DIETARY INTAKES AND HAIR MINERAL CONTENTS IN KOREAN CHILDREN*

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AIMS: This study was performed to analyze the dietary nutrient intake status and hair mineral content of the Korean young children (6 mo. ~ 5 years of age).

METHODS: A total of 55 children (56.4% male and 43.6% female) who visited the Seoul National University Bundang Hospital were included. The subjects were divided into three age groups: infants (0.5~1 year old), toddlers (1~2 year old), and preschoolers (3~5 year old). The 24 hour recall method was used to collect the food intake of young children. The hair mineral analysis was performed by using the Mass Spectrometer.

RESULTS: The mean energy intakes of the subjects were 730.3kcal, 994.3kcal, and 1,482.9kcal each by the age group. Mean percentage of recommended intake of the energy was 101.35% and was not different by the age group. Thirty-eight percentage and 55% of the toddlers and preschoolers consumed less than the estimated average requirement (EAR) of calcium. The number of children who consumed less than the estimated average requirement of iron was 28.6% at 0.5~1 year old infants, 10.8% at toddlers and 9.1% at preschoolers. In case of phosphorus, copper and selenium, only 3~5% of the toddlers had less than the EAR. In case of zinc, all the infants satisfied the EAR intake. The hair calcium content tended to decrease by the age, but was not significantly different by the age group. Meanwhile, hair iron content was significantly decreased with the age increment.

CONCLUSION: Dietary calcium, iron and potassium of young children were not enough to fill out the Korean DRI. Hair iron content also showed decreasing trend with age increment. Therefore, the mineral nutritional status of Korean young children, especially iron, may not be enough to fill out the requirement of the developmental stage.

284 *SERUM AND HAIR MINERAL LEVELS IN CHILDREN WITH FAILURE TO THRIVE ACCORDING TO THE TYPE OF FEEDING DIFFICULTIES*

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Purpose: The aim of this study is to investigate serum and hair mineral contents as well as other clinical and biochemical factors affecting physical growth and appetite in young children with non-organic failure to thrive (NOFTT) according to the presence or the subtypes of feeding difficulties.

Methods: Between August 2012 and July 2013, 136 children (77 boys, 59 girls) with NOFTT aged less than 6 years were included. NOFTT was defined when body weight was under the 5th percentile for age and gender on the growth chart without any organic causes. Feeding difficulties were diagnosed based on Wolfson criteria, and divided into 5 subgroups according to Chatoor's classification; infantile anorexia, sensory food aversion, reciprocity, posttraumatic type, and state regulation. Demographic, clinical data were reviewed and serum and hair mineral and trace elements levels were measured and analyzed in all subjects included.

Results: Out of all serum and hair minerals and trace elements, only hair sulfur contents out of all hair and serum minerals were significantly different between children with- and without feeding difficulties (3944.0 ± 217.9 *vs*. 4038.1 ± 272.7 mg%, $p = 0.047$). Regarding infantile anorexia type, hair sulfur contents were the only mineral that had significant differences (3939.2 ± 221.1 *vs*. 4033.2 ± 255.1 mg%, $p = 0.034$). There was no differences in all serum and hair mineral levels between children with- and without sensory food aversion, although serum prealbumin level was significantly lower in children with sensory aversion than those without sensory aversion (18.2 ± 3.4 *vs.* 19.9 ± 3.3 mg/dL, $p = 0.013$). Hair copper contents were significantly lower in children with reciprocity (1.23 ± 0.60 *vs.* 2.24 ± 2.51 mg%, $p = 0.049$) and hair zinc contents were also lower in children with reciprocity but not significant (4.92 ± 2.68 *vs.* 7.06 ± 4.10 mg%, $p = 0.055$). Regarding posttraumatic type, only hair manganese contents were significantly lower in children with fear of feeding (0.012 ± 0.004 *vs.* 0.026 ± 0.073 mg%, $p = 0.037$).

Conclusions: Most serum and hair minerals levels revealed no differences according to the presence or the subgroups of feeding difficulties in children with NOFTT, except for relatively lower levels of hair sulfur in infantile anorexia type, hair copper and possibly zinc in reciprocity type, and hair manganese in posttraumatic type.

285 *FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME ASSOCIATED WITH COW'S MILK PROTEIN ALLERGY IN CHINESE INFANTS*

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Background: Cow's milk protein allergy (CMPA) is the most common food allergy in infants and young children. It is also the most common cause of food-protein-induced enterocolitis syndrome (FPIES) in infants.

Aim: To examine the clinical features and treatment outcomes of Chinese infants with FPIES associated with CMPA.

Methods: We reviewed all infants ≤12 months of age who were diagnosed with food-protein-induced enterocolitis syndrome (FPIES) associated with cow's milk protein allergy (CMPA) between January 1, 2011 and August 31, 2014 in a tertiary Children's Medical Center in China. Patient's clinical features, feeding patterns, laboratory tests and treatment outcomes were reviewed.

Results: A total of 12 infants were diagnosed with FPIES and CMPA. The majority (83.3%) of infants presented at < 6 months of age. All infants presented with diarrhea from 5 to 20 times a day. Other common symptoms included low-grade fever, vomiting, bloody and/or mucus stools and irritability. Laboratory tests showed that all infants (100%) had hypoproteinemia (25.3 to 45.5g/L) and hypoalbuminemia (14.5 to 24.8g/L), with 75% of infants had lower serum globulin (10.8 to 19.5g/L). The course of disease before final diagnosis was from 10 days to 3 months. Five patients (41.7%) had misdiagnosis and delayed diagnosis before an evaluation by a pediatric gastroenterologist. All infants had clinical remission with resolution of diarrhea and normalization of serum albumin after elimination cow's milk protein (CMP). The majority (83.3%) of infants developed tolerance to CMP challenge test after 12 months of avoidance.

Conclusions: This is the first report of clinical features and treatment outcomes of 12 Chinese infants with FPIES associated with CMPA. The diagnosis relied on clinical presentation and resolution of symptoms after CMP avoidance. However, misdiagnosis and delayed diagnosis are common. It is important to be aware of FPIES associated with CPMA when evaluating an infant with chronic diarrhea accompanied by hypoprotenemia.

*286 *ASSESSMENT OF MACRONUTRIENT LOSSES IN STIMULATED MODELS OF CONTINUOUS TUBE FEEDS USING HUMAN MILK*

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Background: Even though early use of human milk is recommended in children with intestinal insufficiency, only 19% of infants at intestinal rehabilitation centers in the US receive human milk. One factor may be the observation from NICU-

based studies using syringe pumps that continuous tube feeds at low rates result in a loss of macronutrients. We sought to assess the macronutrient losses using human milk and elemental formula as continuous tube feeds as done in the inpatient and the home setting.
Methods: In-vitro continuous tube feeding simulations at rates of 5, 10, 20 and 30 mL/hr for 4 hours were created using the following equipment: EnteraLite Infinity pump, 500mL feeding bag and tubing (length=80 in., diameter=0.25 in., height at infusion=60 in.). Healthy volunteer donated term human milk was used. Aliquots for each simulation were labeled as control (borosilicate container), pre-infusion (feeding bag) and post-infusion (borosilicate containers) and were prepared based on the rate x 4 hours plus 30mL (for control and pre-infusion). 3mL hourly samples were drawn using a glass pipette, and 1mL was analyzed for lipid, carbohydrate, protein and caloric composition using the SpectraStar Near-Infrared Analyzer. Each simulation was run in triplicate and 273 samples were analyzed in total. Effects of continuous agitation and inversion of the feeding bag for delivery on the macronutrient composition were also investigated. Pairwise comparisons were performed using ANOVA, $p<0.05$ was considered significant.
Results: Mean composition of control human milk was as follows: fat 2.97 g/100 mL, protein 0.98 g/100 mL, carbohydrates 7.38 g/100 mL and total calories 18.04 kcals/oz. Significant losses of fat and total calories ($p<0.05$) were observed in the post-infusion samples at all rates at hours 1 to 4, highest losses being at 5mL/hr (65% and 28% respectively at hour 1, 77% and 37% respectively at hour 4; $p<0.01$). There were no significant carbohydrates and proteins losses. Surprisingly, there was a significant increase in the fat content/ hour in the pre-infusion aliquots, with maximum gains seen at 5mL/hr (17% at hour 1, 114% at hour 4; $p<0.01$). Additionally, the rate of infusion was negatively correlated to fat losses (Pearson correlation coefficient=0.56, $p<0.05$). No losses in macronutrients were observed with elemental formula feeds at 5mL/hr. When simulations were run with the feeding bag in an inverted position there were no significant fat or calorie losses between hours 2 to 4 at both 5 and 30 mL/hr, and lesser percent losses were observed (maximum losses 21% and 11% respectively at hour 1). Continuous agitation of a horizontally placed feeding infusing at 5mL/hr only partially limited the percent losses of fat and calories.
Conclusions: Continuous tube delivery of human milk using a feeding bag results in significant fat and calorie losses which can affect growth. In addition to adsorption of fats to the tubing, significant losses occur due to separation and resultant accumulation of fats in the feeding bag. Placing the feeding bag in an inverted position with infusion from the top enables early delivery of fats and significantly limits macronutrient losses.

287 *ANTIBIOTIC AND ACID SUPPRESSION MEDICATION PRESCRIPTIONS DURING INFANCY AND PEDIATRIC OBESITY*

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Background: Gut microbiome variations have been associated with obesity. Although the gut microbiome may vary temporally between infants, distinct patterns of the early gut microbiome persist longitudinally. The infant gut microbiome is highly influenced by early exposures which may include medications. We sought to investigate the association of infant antibiotics, proton pump inhibitors (PPI), and histamine-2 receptor antagonists (H2RA) with a diagnosis of obesity or overweight in later childhood.
Methods: A retrospective cohort study was performed using the Military Health System database. All infants with a birth record from October 2001 to September 2011 and who were followed for at least 2 years were included. Exposure in the first 180 days of life to any outpatient antibiotic, PPI, or H2RA was identified from pharmacy billing records. The two outcomes of obesity and overweight were identified using ICD-9-CM diagnostic codes. Single event survival analysis to the first diagnosis of obesity or overweight was performed using Cox proportional hazards regression with the medication exposures and sex as independent variables. Subjects were followed from age 2 years-old onward and were censored at healthcare disenrollment or on September 30, 2013.
Results: There were 755,055 children in the cohort representing 4,994,777 child-years. The median (interquartile range[IQR]) time children were followed in the cohort was 6.1 (4.1-9.0) years. 146,077(19.4%), 59,525 (7.9%), and 15,952 (2.1%) were prescribed antibiotics, H2RA, and PPI in the first 180 days of life. 14,393 (1.9%) children had a diagnosis of overweight and 24,346 (3.2%) had a diagnosis of obesity during the study period. The median (IQR) age at time of first diagnosis of overweight was 5.9 (4.0-8.1) years and for obesity was 5.7 (4.0-8.0) years. Antibiotics prescription and female sex were associated with both obesity and overweight (Table 1). PPI prescription was associated with a diagnosis of overweight. H2RA prescription was not associated with a diagnosis of obesity or overweight.
Conclusion: Antibiotics are associated with a pediatric diagnosis of obesity and overweight. PPIs are associated with a diagnosis of overweight during childhood. H2RAs were not associated with a diagnosis of overweight or obesity. These findings support the biological plausibility that microbiome-altering medications administered in early infancy can influence weight gain during the childhood years. The administration of these medications should be done judiciously during infancy, as these medications may have long-term implications. Future directions of this study will include the acquisition of BMI data for validation of primary findings.
Table 1 Hazard Ratios for a Diagnosis of Overweight or Obesity

	Hazard Ratio (95% CI) Overweight	Hazard Ratio (95% CI) Obese
Antibiotic	1.08 (1.03-1.12)	1.11 (1.07-1.14)
Proton Pump Inhibitor	1.19 (1.04-1.36)	1.06 (0.95-1.18)
Histamine-2 Receptor Antagonist	0.96 (0.89-1.04)	1.00 (0.95-1.06)
Female	1.11 (1.08-1.15)	1.04 (1.01-1.06)

CI= Confidence Interval

288 *DIETARY INTAKE AND ANTHROPOMETRICAL INDICATORS OF NUTRITIONAL STATUS IN CHILDREN AND ADOLESCENTS WITH CHRONIC KIDNEY DISEASE IN RENAL REPLACEMENT THERAPY.*

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Objective: To associate dietary intake with anthropometrical indicators of nutritional status in children and adolescents with chronic kidney disease (CKD) in renal replacement therapy.

Methods: *Design:* Cross-sectional. *Setting:* A pediatric referral hospital. *Sample: n*=55 patients with CKD, age 7-16 years old. *Independent variables*: energy and macronutrient intakes. *Dependent variables:* Nutritional status evaluated by anthropometrical indicators height for age (H/A), body mass index (BMI), triceps skinfold (TSK), mid upper arm circumference (MUAC), total arm area (TAA), fat arm area (FAA) and muscle arm area (MAA), mid arm fat index (MAFI). *Methods*. Conventional anthropometric technique and instruments, criteria of normality < > 2 SD. References: NCHS, *Frisancho. Statistics:* Frequencies, %, c^2, *Fisher* test, means, SD, *Student* test

Results: 22 patients were in peritoneal dialysis (PD) and 33 in hemodialysis (HD). Mean age was 14 years for HD children and 13.6 years for peritoneal dialysis (PD) patients. PD group had <-2SD HA 45%, 45% MUAC, 32 % MAA, 18% BMI, 4% TAA. In the HD group 54% had HA <-2SD, 21% BMI, 12% MUAC, 9% MAA. Energy intake was 1422±454 kcal in PD group and 1252±366 kcal in HD group (NS). The protein intake in PD group was 1.29g/kg and 1.3g/kg in HD, lipids 31.2 ±15.8g/d in PD and 41±19.1g/d in HD (p=0.032) and carbohydrates intake 174±74 g/d in PD and 177±52g/d in HD. Protein intake was associated with MAA (p=0.032) in PD. Protein intake was associated with MAFI (p=0.018), BMI (p=0.022); carbohydrates intake was associated with TSF (p=0.030) and BMI (p=0.029) in HD group.

Conclusions: Energy, protein and carbohydrates intakes were similar in both groups. Lipids intake was higher in HD group. Energy, protein, carbohydrates and lipid intake influences nutritional status indicators in both HD and PD patients.

289 *EARLY POST-DISCHARGE TELEMEDICINE VISIT: PILOT QUALITY IMPROVEMENT INITIATIVE TO REDUCE HOME PARENTERAL NUTRITION READMISSIONS*

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BACKGROUND: Home parenteral nutrition (HPN) provides improved quality of life and reduced medical expenses over prolonged hospitalizations for children with severe gastrointestinal disorders. Unfortunately, unplanned readmissions following discharge on HPN are common and often preventable. Telemedicine is a promising technology that has the potential to improve health-care outcomes. There is no data on its effectiveness when applied to pediatric HPN.

OBJECTIVE: To determine the impact of telemedicine visits on 30-day unplanned readmissions for children following initial discharge on HPN.

METHODS: We prospectively collected data from patients with ages 0-18 managed at a single HPN program from October 2011 to April 2015. Patients with prior history of HPN use excluded. We collected unplanned 30-day hospitalization information. Telemedicine visits were conducted using HIPAA compliant Vidyo software platform from March 2014 to April 2015. Continuous variables presented as median (min, max) or n (%). Fisher exact and Wilcoxon rank-sum was used to compare groups. Data analyzed using SAS edition 9.4.

RESULTS: Of patients initially discharged on HPN, 8 with and 56 without telemedicine visits were compared. There was no significant difference in age 0.7 (0.1, 18) vs. 3.1 (0.1, 17.2) years, male sex 4 (50%) vs. 34 (53%), diagnosis of short bowel syndrome in 6 (75%) vs. 30 (54%) and in-state residence was 5 (71%) vs. 33 (62%), *p*=0.5, 1, 0.45, 1.0 respectively. 6 (75%) of telemedicine visits were performed within 24 hrs post-discharge, and all were performed within 1 week post-discharge. Of 5 visits where time was electronically recorded, physician time spent on telemedicine was 37 (23-59) minutes. 30-day readmissions 1(13%) vs. 35 (61%), *p*=0.02.

CONCLUSIONS: In a small but well-represented pilot group, we observed a significantly lower rate of readmissions in pediatric HPN patients participating in telemedicine visit. More outcome data is needed to assess this potentially valuable application.

291 *AN EARLY INFANT RISK SCORE FOR CHILDHOOD OBESITY IN AN URBAN, LATINO POPULATION*

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Background: Early risk factors, such as maternal smoking and rapid infant weight gain, have been implicated in the increased rates of childhood obesity in the United States. However, a single prognostic model to predict an infant's risk of obesity in childhood is lacking. We hypothesized that using readily available pre-natal (maternal) and early infant (<6 months) information, a model could be developed that achieved adequate discrimination, calibration and accuracy in the prediction of childhood obesity at age 5, particularly amongst high-risk, urban populations.

Design/Methods: Data from ten known risk factors for childhood obesity were analyzed. Participants were from a cohort of 201 Latina women recruited during their pregnancy, who were followed longitudinally along with their infants. A logistic regression model (full model) included only readily available, objectively measured candidate predictors with documented association with childhood obesity. A second model was generated via stepwise backwards deletion applied at the 5% significance level (4 risk factors remained in this model). Discrimination and calibration were assessed via concordance index and Hosmer-Lemeshow test, respectively. Based on the data on each risk factor, an obesity risk score was generated for each patient using both models. Models were validated using a 5-fold cross validation technique, and predictive accuracy was assessed at multiple risk thresholds using sensitivity, specificity, positive and negative predictive value.

Results: Fifty-six of the 166 children (32%) followed through age 5 met criteria for childhood obesity (CDC BMI>95th%). Birth weight-for-age z-score and change in weight-for-age z-score between birth and 6 months were the strongest contributors, across both models, to the obesity risk score. Discrimination accuracy for both of the models was excellent (concordance index >0.8), and both models were adequately calibrated. While predictive capabilities varied depending on the level of the risk threshold (table 1), those <50th% risk threshold had an obesity probability of only 6% and negative predictive value in that group was nearly 95%.

Conclusions: Using objective, easily accessible candidate predictors, we were able to derive a prognostic obesity risk algorithm with excellent discrimination and calibration. Applied clinically, this algorithm could provide a simple filter for directing infants at low risk of obesity to standard weight monitoring, while reserving comprehensive prevention resources for those with scores above a set obesity risk threshold. Future study should be directed at further validation of this model and ultimately to direct, efficacious and cost-effective preventative interventions for those with high risk of obesity.

Predictive Accuracy of Full Model for Childhood Obesity Outcome

Risk Threshold	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
25th Percentile	95	35	40	94
50th Percentile	90	67	56	94
75th Percentile	51	85	61	79
90th Percentile	28	98	86	75

Proportion of population above risk threshold indicates positive prognostic test (likely to develop obesity at age 5)

292 *HEALTH BEHAVIORS OF ADOLESCENTS PRESENTING TO AN ADOLESCENT BARIATRIC SURGERY PROGRAM*

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Introduction: Modifiable health behaviors are associated with obesity and weight loss. Limited literature describes how prior weight loss attempts may be associated with health behaviors among adolescent bariatric surgery participants. The goal of this study is to examine the hypothesis that prior weight loss attempts are associated with healthier behaviors among adolescents seeking bariatric surgery.

Methods: We studied 41 patients presenting for bariatric surgery candidacy from 2014-15 at the Adolescent Bariatric Surgery Program at Boston Children's Hospital. The main exposure was self-reported prior weight loss attempts (number and maximum duration). Primary outcomes were self -reported breakfast eating (times/week), fast food consumption (times/week), exercise (times/week), sleep duration (hours/night), and screen time for leisure (hours/week). Statistical analyses included assessment of distributions, frequencies, Pearson's chi^2, and pairwise correlations. In multivariable regression models, we evaluated the association between weight loss attempts and health behaviors, adjusting for sex and race/ethnicity.

Results: Participants were mostly female (66%), and Latino/Hispanic (55%) or Caucasian (42%). The majority reported at least three prior weight loss attempts, and almost half (46%) reported engaging in weight loss for three months or less on any given attempt. For health behaviors, 61% ate fewer than five breakfasts weekly, 69% consumed fast food at least once

weekly, 30% slept fewer than 5 hours nightly, and 69% exercised fewer than three times weekly.
In unadjusted regression models, greater numbers of prior weight loss attempts were associated with more breakfast eating (ß = 0.74, p = 0.048). Longer duration of prior weight loss attempt was associated with more weekly exercise (ß = 0.84, p = 0.037). After adjusting for sex and race/ethnicity, these findings were attenuated for more breakfast eating (ß = 0.78, p = 0.07) and exercise (ß = 0.69, p = 0.11). Prior weight loss attempts were not associated with fast food consumption, sleep duration, or screen time for leisure.
Conclusions: In this sample of adolescents seeking bariatric surgery, participants reported multiple prior weight loss attempts of short duration and unhealthy behaviors were prevalent. Prior weight loss attempts were associated with less breakfast skipping and more frequent exercise, but not fast food consumption, sleep duration, or screen time for leisure. Opportunities exist to improve the health behaviors of adolescents prior to bariatric surgery.

293 *TOLERANCE AND GROWTH IN PRETERM INFANTS BY OPTIMIZING PROTEIN IN HUMAN MILK WITH HYDROLYZED LIQUID PROTEIN FORTIFIER*

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Background: Nutritional deficiencies in Very Low Birth Weight (VLBW,<1500 grams) infants contribute to suboptimal growth and poor outcomes.Despite use of human milk fortifiers, intake of protein remains below target levels. New strategies to improve protein fortification of human milk are available including a new extensively hydrolyzed liquid protein supplement (LP).
Objective: The objectives of this study were to evaluate the tolerance and growth outcomes in VLBW infants fed extensively hydrolyzed casein based liquid protein fortifier to optimize protein intake when added to fortified mother's milk or donor milk.
Methods: This is a prospective observational study on 30 VLBW infants, completed gestational age ≤ 32 weeks with birth weight > 3rd percentile on the Fenton growth curve receiving mother's own milk and/or donor milk. Enteral feedings were initiated using standard established feeding guidelines. LP fortification initiated when full enteral feeding volume of human milk fortified to 24 kcals/ounce breast milk using a standard powder fortifier was reached. LP was added at 1 mL/ 100 mL on a daily basis until at a goal of 6 mL/100 mL.This increased protein content by approximately 0.15 grams/100 mL daily to achieve the final goal of 2.7 grams protein/100 mL. Infants were weaned off LP fortification per donor milk transition guidelines.Data on weight, head circumference, feeding tolerance, serum biochemistry, enteral intake and presence of morbidities like necrotizing enterocolitis (NEC) and late onset sepsis were collected at the initiation of fortification and then weekly until discharge. The primary outcome was tolerance of LP fortification and the secondary outcome was growth, including weight gain and head circumference at discharge. Labs values, before and after fortification, were compared using a paired t-test. All statistical tests were two-sided and a p-value < 0.05 was considered statistically significant.
Results: Fifteen preterm infants have completed the study to date (11 females and 4 males). The mean gestational age was 27.8 ± 1.7 weeks, and the mean birth weight was 1031 ± 206.4g.There was no evidence of feeding intolerance as defined by enteral feedings held for 48 hours with presence of abdominal distention with no cases of NEC or late onset sepsis. The average weight gain on LP fortifier was 31grams/day. Weight and head circumference gain from initiation of LP to discharge were 18 g/kg/day and 0.88 cm/week, respectively. At discharge 53.3% had weight above the 10th percentile on the Fenton growth curve, while all of the infants had head circumference above the 10th percentile. LP addition did not elicit any statistically significant difference in infants creatinine levels (mean difference=-0.16, p-value=0.17), BUN (mean difference=0.25, p-value=0.80), or bicarbonate (mean difference=1.38, p-value=0.33) based on lab data collected weekly for all infants. A difference was observed for pH (mean difference=0.025, p-value=0.013), but this difference was not clinically relevant.
Conclusion: The addition of an extensively hydrolyzed LP fortifier was well tolerated in VLBW infants and goals for weight gain and head circumference were achieved with no evidence of acidosis or clinically relevant differences in blood chemistry parameters.

295 *EARLY CHILDHOOD GROWTH STANDARDS IN CYSTIC FIBROSIS: CDC CURVES PREDICT BETTER LONG-TERM OUTCOMES AND SURVIVAL*

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Background: Early nutritional status is strongly associated with long-term pulmonary function and prolonged survival in children with cystic fibrosis (CF). The CF Foundation (CFF) thus recommends that patients attain weight-for-length (WFL) >50th percentile by age 2 years, based on CDC growth references. However, most children under age 2 are now measured using WHO growth curves. We determined the correlation of WHO standards with CF outcomes in early adulthood and compared WHO with CDC standards in this population.

Methods: Prospective, observational cohort study using registry data for patients born 1989-1993 and diagnosed and treated at a CFF accredited center prior to age 2 (n=3014). Patients were categorized at age 2 as WFL <50th percentile based on both WHO and CDC measures; WFL>50th percentile on WHO but not CDC; and WFL>50th percentile on WHO and CDC. Patients were followed longitudinally into early adulthood. Primary outcome was FEV1 percent predicted (FEV_{1pp}); secondary outcomes included BMI, total hospital days, and overall survival.
Results: At age 2, 41.8% had WFL<50th percentile on both WHO and CDC curves, 15% had WFL>50th percentile on WHO but not CDC curves, and 43% had WFL>50th percentile on both WHO and CDC curves. In adjusted and unadjusted analyses, there was a stepwise increase with FEV_{1pp} at age 18 highest in those with WFL>50th percentile on both WHO and CDC and lowest in those <50th percentile on both ($p<0.001$) (Table). Patients achieving WFL >50th percentile at age 2 on the WHO scale showed significantly worse FEV1pp when compared with WFL >50th percentile on both WHO and CDC measures ($p<0.05$). Those reaching WFL >50th percentiles on both WHO and CDC also had significantly higher BMI and higher chance of lung transplant free survival, with rates >90% at age 18 (Table). Kaplan Meier analysis demonstrated 3 distinct survival trajectories for each category of WFL at age 2 with stepwise increase following increasing WFL category (Figure).
Conclusions: As a group, children with CF who reach WFL >50th percentile on the WHO scales alone had worse pulmonary, growth and survival outcomes compared with those with WFL >50th percentile on both CDC and WHO curves. CF care teams should continue to utilize CDC growth measures for patients < 2 years old. Future study should address whether nutritional intervention, prior to age 2 will improve growth in early childhood and subsequent pulmonary outcomes and long-term survival.
Outcomes at age 18 years for patients with CF born 1989 to1993, stratified by WFL at age 2 years

WFL percentile		BMI percentile	FEV1 % predicted	Hospital days	Survival
at age 2y	n(%)	(median)	(mean)	(per year median)	(%)
<50th WHO and CDC	1260 (41.8)	19.9	72.7	16	83.8
≥ 50th WHO not CDC	457 (15.2)	20.3	76.5	15	88.7
≥ 50th WHO and CDC	1297 (43)	21.2	79.5	15	92.3

PANCREAS/CELIAC/MALABSORPTION

296 *THE USEFULNESS OF ANTI TTG IGG IN THE DIAGNOSIS OF CELIAC DISEASE WHEN ANTI TTG IGA IS NEGATIVE*

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Guidelines for CD diagnosis recommend highly sensitive serologic testing like Anti tissue transglutaminase IgA (TTGA IgA) followed by confirmatory small bowel biopsies (SBB). When high probability of CD exists wherein the possibility of IgA deficiency is considered, total IgA should be measured. Alternative approach is to include both TTG IgA and IgG in high-probability patients without measuring the total IgA. We aim to assess the sensitivity of isolated TTG IgG in diagnosing CD.
Methods: We conducted a retrospective review of the Mayo Clinic electronic data for the period between 1997 - 2014. All patients (age 0-80 years) who had positive TTG IgG and negative TTG IgA were included. Patients who had other positive serologic testing (endomysial or deamidated gliadin peptides) were excluded. Demographic, clinical, presentation, diagnostic tests and biopsies results were recorded.
Results: We identified 242 patients 166 females (31 children and 211 adults), average age 43 years ± 17.6 SD. SBB was done in 186/242 (77%) patients. SBB was normal in 164/186 and 22 had histologic changes suggestive of CD (12 IEL and 10 partial villous atrophy). The 10 patients with partial atrophy were 2 IgA deficiency, 3 suboptimally oriented biopsies, 3 other diagnoses (dermatomyositis, collagenous sprue, autoimmune enteropathy) and 2 confirmed CD. Based on that TTG IGG sensitivity was low at 2/186 (1%) or (3%) if we consider the suboptimally oriented biopsies as confirmed CD. The indication for checking celiac serology was GI symptoms in 181 Patients, Iron deficiency/anemia in 13 and High risk screening in 48.
Conclusion: Almost all patients who had isolated positive TTG IGG had GI symptoms, but only 1% had confirmed CD. Hence isolated positive TTG IgG is associated with high rate of false positivity results. The serology testing cascade that starts with total IgA and proceed to TTG IgG only in deficient patients would effectively eliminate this issue.

297 *ASSESSING THE SENSITIVITY OF ANTI TISSUE TRANSGLUTAMINASE IN DIAGNOSING CELIAC DISEASE IN DIABETES MELLITUS TYPE 1 PATIENTS*

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Introduction: Patients with diabetes mellitus type1 (DM1) should be screen for celiac disease (CD) because of increased risk. A small bowel biopsy (SBB) is still required, but many are diagnosed without SBB. We aim to assess 1) number of new DM1patients with positive serology who had SBB, 2) If TTG is highly sensitive can SBB be omitted in new DM1 patients with highly positive celiac serology.

Methods: We performed a retrospective review of the Mayo Clinic electronic record between1980-2014. All patients age (1-60 years) with DM1 and CD were included. Demographics (Table1), clinical and histopathological parameters were recorded. This study was approved by the Mayo Clinic IRB.

Results: We identified 73 patients with DM1 and positive celiac serology. Sixty six had CD, while 7 with normal SBB were excluded. Average age at diagnosis of CD was 22.25 ± SD 2.82 years (range 2-53). Thirty patients (45%) were asymptomatic and 36 (55%) had gastrointestinal (GI) symptoms (Table2). Only 54/66 patients (82%) underwent confirmatory SBB (Table3).

Logistic regression suggested an association between highly positive celiac serology (10X UNL) and the presence of villous atrophy in both asymptomatic and symptomatic patients. The 7 excluded patients with normal SBB had symptoms and weakly positive serology (<2X UNL).

Conclusion: Despite the guidelines 18% of DM1 patients with positive serology were diagnosed with CD without SBB. Weakly positive serology is associated with false positive rate of 10%. Despite the suggested association between highly positive serology and villous atrophy, the decision of omitting the confirmatory SBB needs a prospective multicenter study.

Demographic of Patient with DM 1 and CD

DM1 and CD patients	Adults	Children	Female	Male	Average age
Total number= 66	35	31	47	19	22
Asymptomatic= 30	13	17	23	7	20
Symptomatic= 36	22	14	24	12	24

Gl symptoms in DM1 patients with CD

GI symptoms	Patients number= 36
Abdominal pain	24
Diarrhea	6
Vomiting	4
Bloating	1
Constipation	1

298 *CONSTIPATION AS A PRESENTATION OF CELIAC DISEASE*

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Introduction: Celiac disease (CD), a multifactorial, autoimmune disorder that occurs in genetically susceptible individuals and has varied presentation. While the typical CD presents with chronic diarrhea, steatorrhea, abdominal distention and failure to thrive, the atypical CD may has subtle presentation and can be easily missed or overlooked.

Constipation is one of the atypical presentations of CD and thus selected patients may need celiac screening for early diagnosis of disease. The aim of this study was to observe the atypical presentation of CD among Saudi children especially constipation as a first symptom of disease. Although classical CD was seen in most patients in the present study, clinical variability of the condition should be kept in mind.

Methods: It was a retrospective study conducted between the period of January 2013 to June 2014 at the Pediatric Gastroenterology clinics/ ward of the King Khalid University Hospital, Riyadh, KSA. The children included were less than 18 years of age of both sexes. The patients were selected with the Confirmed diagnosis of CD based on serology and small bowel biopsies were included. The data base included the presentation, duration of symptoms, description of bowel movements, associated abdominal pain, abdominal distension, blood stained stools and affect of medication.

Anthropometric measurements were also recorded. The data was analyzed by SPSS version 21.
Results: 100 cases of celiac disease were seen during the study period, diagnosed on basis of tissue transglutaminase antibodies (tTGA) and small bowel biopsy. There were 68 males and 32 females with a mean age of 7 years (range 9 months to 18 years). 54% presented with classic symptom and atypical disease was the feature in 46% of cases. Among the atypical presentation, constipation was found in 15% (N#15) of the cases. Mean±SD duration of constipation was 7±3 months. Describing severe constipation that is bowel opening once a week was observed in 8 (53.3%) and rest had mild to moderate constipation. Mild to moderate abdominal pain and distension was observed in the severe constipated children. None of the children had complete relief treated for 6-12 months period before final diagnosis of CD. Anthropometric measurements were not significant in the studied children. All the patients responded very well when put on gluten free diet with total resolution of symptoms and negative serology at 6 month follow up.
Conclusion: Celiac disease is common in Saudi Arabia. Mode of presentation is diverse ranging from classical to atypical. Atypical presentation of disease should be kept in mind especially constipation that can be easily overlooked. Early treatment and prompt treatment can make a difference in outcome of these patients.
Key Words
Celiac disease, constipation

299 *ANALYSIS OF VOLATILE ORGANIC COMPOUNDS IN THE EXHALED BREATH OF PATIENTS WITH CELIAC DISEASE*

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Background: Celiac disease (CD) affects an estimated 1-5% of the population. The diagnosis is based on positive serologies and confirmed with biopsies obtained during an upper endoscopy. Adherence to the gluten free diet (GFD) is associated with mucosal healing and normalization of serologies. Due to the high prevalence of CD and its non-specific symptoms, there is a need for noninvasive tests for diagnosing celiac disease in children. The aim of this study was to determine if CD is associated with unique changes in volatile organic compounds (VOCs) in the exhaled breath that are reversible with adherence to GFD.
Methods: We collected single exhaled breath specimens from patients aged 6-18 with new diagnosis of CD who are not on GFD (n=13) and those with an existing diagnosis of CD who are compliant with GFD (n= 27). Compliance with GFD was determined by normalization of celiac serologies. VOCs in breath specimens were analyzed per protocol with selective ion flow tube mass spectrometry.
Results: Mean age was 10.4 ± 2.9 and 11.9 ± 3.8 years in the new and existing diagnosis groups, respectively (p=0.22). 51 % were female. After adjusting for multiple confounders, significant changes in 35 mass scanning ion peaks were noted in newly diagnosed patients compared to those compliant with GFD. Stepwise discriminant analysis demonstrated that five mass scanning ion peaks can correctly classify patients into new vs existing disease with only 3 patients being misclassified.
Conclusions: Patients with newly diagnosed CD not on GFD have a unique pattern of VOCs in the exhaled breath that is different from those who are compliant with GFD. Larger sample size and comparison to controls are needed to validate this finding.

300 *OPTIMIZING BEHAVIORAL HEALTH AMONG ADOLESCENTS WITH CELIAC DISEASE*

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Background & Aims: Reduced quality of life has been reported among patients with celiac disease on a gluten-free diet. It has been shown that depression, anxiety and poor coping strategies, as opposed to gastrointestinal symptoms, account for such lower quality of life. We aimed to examine psychosocial functioning among adolescents with celiac disease, a particularly vulnerable population.
Material & Methods: This study was approved by the University of Chicago IRB for patients 12-18 years of age with celiac disease and their parents. Validated measures included the Pediatric Quality of Life Inventory (PedsQL), Child Symptom Inventory (CSI), Children's Attributional Style Questionnaire (CASQ) and Celiac Disease quality of life questionnaire (CDDUX). Surveys were available via a secure server, with data capture by the Research Electronic Data Capture (RedCap) program. Data generated include descriptive statistics and preliminary tests of association between dimensions of mental health, quality of life and adjustment to celiac disease.
Results: A total of 25 patients with biopsy confirmed celiac disease and corresponding parents have completed the surveys. Mean scores for the CDDUX in adolescent and parents were 29.4 (SD 6.3) and 28.5 (SD 7.4), respectively. Preliminary data indicate that parental report of their child's difficulties with celiac disease are significantly associated with impaired school functioning ($r = -.385$, $p = .032$), physical functioning ($r = -.345$, $p = .049$), and a trend toward a significant

association with emotional functioning (*r = -.325, p = 0.61)*. Parental report of their child's difficulties with celiac disease was also significantly associated with parental report of their child's depressive symptoms (*r = -.53, p =.004*). No statistically significant correlations between child's perception of celiac disease difficulties and emotional or behavioral problems or quality of life were observed.
Conclusions: These preliminary data suggest that parental perceptions of impairments related to celiac disease are significantly associated with their child's school functioning, physical functioning and perception of their child's depressive symptoms with a trend toward significance on their child's emotional functioning. This ongoing study will test the relative contribution of celiac related distress and quality of life on psychological functioning, and identify youth and family factors (e.g. coping strategies, parenting behaviors) that may attenuate these associations.

301 *CELIAC DISEASE INCIDENCE AND PRESENTATION IN HAMILTON COUNTY, OHIO*

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Background: Celiac disease (CD) is a common immune-mediated enteropathy triggered by dietary gluten and appears to be increasing in prevalence in the United States. Patients may not present with classical symptoms such as diarrhea and failure to thrive, and some children are obese at diagnosis. Some research indicates asymptomatic vitamin and mineral deficiencies may be present at presentation. Changes in nutritional status following diagnosis have not been reported in the US. Our center is the only one with pediatric gastroenterology services in Hamilton County. We aimed to determine the incidence and mode of presentation of celiac disease in Hamilton County, Ohio and to investigate if children experience catch-up growth with initiation of a gluten free diet (GFD).
Methods: We performed a retrospective review of electronic medical records of children residing in Hamilton County who were newly diagnosed with CD at our center from 2010 through 2013. Patients age 0-18 years who were assigned a new diagnosis of celiac disease, had biopsy proven disease and who had an address listed in Hamilton County were included. Patients diagnosed prior to 2010 or at a different center were excluded. Census data for Hamilton County were obtained online. Demographic, anthropometric, laboratory data and clinical symptoms were extracted from patient charts at the time of presentation and in follow up, if available. Z-scores and percentiles were calculated for weight-for-age (WFA), length-for-age (LFA), weight-for-length (WFL) and body mass index (BMI) based on recommended growth curves.
Results: Sixty-five Hamilton county residents (59% female) were newly diagnosed with celiac disease at our center in the 4-year period. 10 new diagnoses were made in 2010 out of the 189,640 children age 0-17 counted in the 2010 census, yielding an incidence of 5.27/100,000. The most common symptoms and associated conditions at the time of presentation were abdominal pain (48%), poor weight gain (26%), type 1 DM (23%), diarrhea (20%), nausea/vomiting (18%), hypothyroidism (9%), behavioral/psychological comorbidity (14%), short stature (9%), and constipation (6%). At presentation, median z-scores for WFA, LFA and WFL or BMI (over age 2) were 0.38, 0.05, and 0.46, respectively. Four (6%) patients had BMI >95th percentile, 9 (14%) had BMI >85th and <95th percentile, and 9 (14%) had BMI<15th percentile. Amongst patients seen 3-6 months after diagnosis, the mean BMI z-score change was -0.04 for the 9 patients with BMI>85%ile, and 0.61 for the 5 patients with BMI <15%ile at diagnosis. Of the 59 patients with elevated tissue transglutaminase IgA at diagnosis, 37 had a level checked after 12 months; 12/37 (28%) had normalized (<20U/ml), and another 12/37 (28%) had levels <30U/ml. At presentation, hypovitaminosis D and iron deficiency was seen in 11/15 (73%) and 1/7 (14%), respectively, for patients whose levels were checked.
Conclusions: We report an incidence of pediatric celiac disease in Hamilton County similar to other pediatric populations. Abdominal pain is a common presenting symptom, but no symptom was present in a majority of patients. Overweight status is common in patients with newly diagnosed CD, and patients with low and high BMI improved after diagnosis.

302 *ASSESSMENT OF GLUTEN EXPOSURES IN CHILDREN WITH CELIAC DISEASE*

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Background: Celiac Disease (CD) is one of the most common chronic diseases of childhood. A strict, lifelong gluten-free diet (GFD) remains the sole treatment for CD. Reports of accidental or intentional ingestion of gluten are common, but little is known about the sources or context of such exposures. We sought to ascertain the self-reported causes for gluten exposure for children with Celiac Disease.
Methods: Parents of children with biopsy-proven CD followed at McMaster Children's Hospital were asked to review a 22-item questionnaire listing sources, situations and causes of gluten exposure for their child. The questionnaire encompassed both intentional and unintentional gluten exposures and was developed through consultation with Registered Dietitians and Faculty in the Division of Pediatric Gastroenterology at McMaster Children's Hospital. Children independently completed a similar 21-item questionnaire adapted for pediatric use. Participants were invited to describe any additional sources or circumstances leading to gluten consumption not captured in the questionnaire.

Results: A total of 123 families participated in the study with a median of 32 months on a GFD. A minimum of one cause of gluten exposure was selected by 65% of parents and 60% of children. Restaurant dining was identified as a source of gluten consumption by 39% of parents, due to a lack of knowledge of the GFD by restaurant staff or poor labeling of menu items. Other commonly selected items on the parent questionnaire included: difficulty while traveling (13%), to avoid exclusion at social events (12%), and a lack of negative symptoms following gluten exposure (9%). Few parents identified cost (2%), or the availability of gluten-free food as a concern (5%). Children most commonly identified restaurant eating (32%), and the lack of any negative symptoms from eating gluten as the main causes of gluten exposure (14%). In this study population, 11% of children acknowledged consuming gluten because they felt left out at either home, school or with friends.
Conclusion: This study provides information about the common causes of gluten exposure for children with CD in Ontario, Canada. Restaurant dining and travel were the most commonly identified sources of gluten ingestion. Our study highlights the need for improved menu labeling and education of restaurant staff, requiring both policy changes and dialogue with food service industries. While availability of gluten-free products has greatly improved, exclusion from social activities remain a concern for both children and their parents. Further qualitative studies may build on these identified themes to better understand challenges families face with the GFD.

303 *ARE HIGH SERUM TITERS OF TTG SUFFICIENT TO DIAGNOSE CELIAC DISEASE IN CHILDREN?*

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Duodenal biopsies have been considered a mandatory step for the diagnosis of celiac disease in children. In recent years several reports suggested that high serum titers of tTG may be sufficient to make the diagnosis of celiac disease without the need for intestinal biopsies. Indeed the last European guidelines for celiac disease in children has supported this view. So far the American guideline has not supported this approach, probably due to the lack of clinical data from North America.
Aim: to compare between serum levels of tTG and intestinal biopsy results in North American children that were ultimately diagnosed with celiac disease.
Methods: Pediatric GI centers from North America were asked to participate in the study and provide their clinical data. Data included the initial serology results (tTG titers) and first biopsy results (Marsh criteria). High tTG titers were defined as levels greater than 3X the normal level per the local laboratory used in each center. Positive celiac histology defined as Marsh grade 3.0 or over. The study was approved by each institutional IRB individually.
Results: A total of 15 centers reported interest in the study of which 3 sent in their results at the time of the abstract submission including WV, Maryland and Connecticut. A total of 207 children participated, of which 53 were between 0-5 years, 85 between 5-10 years, and 69 were older than 10 years. The male/female ratio was 1:2.3 and the mean age ± SD was 8.7 ± 4.1. High tTG titer predicted celiac disease with a sensitivity, specificity, ppv and npv of 94.7%, 17.1%, 84.8%, 40%, and accuracy rate of 78.7%, respectively. In younger children (<5y/o) the results were 97.9%, 0%, 90.3%, 0%, and accuracy rate of 88.6%, respectively.
Conclusion: High titers of tTG (>3x UNL) demonstrated an acceptable sensitivity rate (>90%) for the diagnosis of celiac disease without the need of intestinal biopsies.

304 *NORMALIZATION TIME OF CELIAC SEROLOGY ON GLUTEN-FREE DIET PROLONGED IN CHILDREN WITH HIGHEST SEROLOGY AT DIAGNOSIS*

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BACKGROUND/AIMS: The ESPGHAN celiac guidelines propose that after the diagnosis of celiac disease, a child must be followed closely to ensure symptom and serologic improvement on a gluten-free diet (GFD). We evaluated the time to normalization of celiac serology in children adherent to a GFD at 6 mo, 1 yr, and 2 yr post diagnosis.
METHODS: All consecutive positive celiac serology (TTG > 20 kU/L) and biopsy results were obtained on children under age 18 yrs over a 3.5 yr period from the Calgary Laboratory Services Databases. Data were analysed if the child displayed at least one repeat celiac screen after biopsy diagnosis and complied with a strict GFD as documented on follow-up visits. Differences were calculated using independent t-tests with mean $\pm$ SE reported. Cumulative event rates were assessed by Kaplan Meier survival curves, and Log Rank test for comparison of survival curves.
RESULTS: During the study period, 348 children were diagnosed with celiac disease by biopsy. Of those, 123 patients were excluded because they had no repeat serology within 2 yrs after diagnosis (20.1%), or were not compliant with GFD based on history or serology (14.4%). The analysis was conducted on 225 children subdivided into three groups based on serology at diagnosis (Group A: TTG $\geq$ 10 x ULN and EMA $\geq$ 1:80, n = 91; Group B: TTG $\geq$ 10 x ULN and EMA $\leq$ 1:40, n=72; and Group C TTG < 10 x ULN, n=62). At six months post diagnosis, the cumulative proportion of patients with an elevated TTG was 96.4 $\pm$ 2.0%, 78.5 $\pm$ 4.9% and 64.5 $\pm$ 6.1% in Groups A, B, and C respectively. The mean TTG at 6

months was also highest in Group A (78.5 ± 9.3) compared to B (48.6 ± 7.2) or C (20.0 ± 3.5; A vs B or C, $p < 0.01$, B vs C $p < 0.001$). At one year post diagnosis, the cumulative proportion of patients with an elevated TTG was 76.5 ± 4.7%, 46.4 ± 6.4% and 29.0 ± 5.9% in Groups A, B, and C respectively. At one year, the mean TTG remained highest in Group A (65.9 ± 7.0) compared to B (24.4 ± 4.0) or C (14.6 ±1.9; A vs B or C, $p < 0.001$, B vs C $p < 0.05$). At two years, the cumulative proportion of patients with an elevated TTG was still 29.9 ± 5.8% in Group A, compared to 10.5 ± 4.3% in Group B and 1.7 ± 1.7% in Group C. The cumulative percentage of children with a normal TTG or EMA occurred later in Group A compared to groups B and C, with fifty percent of patients having normalized TTG at 1.7 ± 0.14 yr in Group A compared to 1.1 ± 0.1 yr in Group B and 0.8 ± 0.1 yr in Group C ($p < 0.001$, A vs B or C).
CONCLUSION: Over 75% of children with the highest serology values at diagnosis exhibited elevated serology at one year on a strict GFD and 30% failed to normalize serology after two years. In contrast, only 29% of children with a TTG < 10 x ULN at diagnosis displayed elevated celiac serology at one year and 2% after two years on a GFD. Serology level at diagnosis must be considered when interpreting subsequent serology results of a child on a GFD.

305 *ARSENIC LEVELS IN CELIAC PATIENTS: A PILOT STUDY*

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Background: Recent concerns regarding arsenic levels in rice have prompted the celiac community to question whether arsenic levels should be monitored in patients with Celiac Disease. Rice has the ability to concentrate environmental arsenic and sequester it so that it does not harm the rice plant. Children have a risk of dietary exposure 2-3 folds that of adults and are the most vulnerable category with special attention of those affected by Celiac Disease. Individuals with Celiac Disease may consume more rice and rice based products than in the typical western diet due to their inability to tolerate wheat, rye, and barley. Pediatric celiac patients therefore may be a high-risk category considering that rice and rice-based foods contain high levels of inorganic arsenic, as they substitute gluten foods for rice as their main dietary grain.
Objectives: High consumption of rice products in celiac patients prompted us to evaluate if they are truly at high risk for arsenic toxicity.
Methods: After IRB approval for retrospective chart review, we reviewed 60 charts from 7/1/2012 to 6/30/2014 at a pediatric tertiary care center. Thirty nine patients satisfied our inclusion criteria. The inclusion criteria were diagnosis of Celiac Disease by esophagogastroduodenoscopy with duodenal biopsies and available arsenic level results. We reviewed the serum arsenic levels and also compared the pediatric celiac patients to adult celiac patients to look for a difference between the two groups.
Results: Thirty nine patients, ages ranging from 5-68 years of age, met the inclusion criteria for review. Twenty-two patients were less than 18 years of age. The median age of reviewed patients was 10 years old for the pediatric group and 30 years old for the adult group. The duration of time between diagnosis to laboratory collection ranged from 4 months to 10 years. The mean duration period between diagnosis to laboratory collection was 2.35 years for the pediatric group and 3.31 years for the adult group. All of the patients had normal serum arsenic levels. Seven patients had rice exposure of greater than 6 years and the arsenic levels did not differ from the other patients with shorter exposure.
Conclusion: This pilot study did not demonstrate toxic levels of arsenic in patients who have been diagnosed with Celiac Disease eating a gluten-free diet. The results also did not indicate that longer exposure to a rice containing diet demonstrated an increased risk of arsenic accumulation for pediatric or adult celiac patients.

306 *IS MICRONUTRIENT DEFICIENCY AND BONE MINERAL DENSITY SCREENING NECESSARY IN CHILDREN WITH NEWLY DIAGNOSED CELIAC DISEASE?*

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Background: American College of Gastroenterology guidelines suggest adults with newly diagnosed celiac disease (CD) should undergo screening for micronutrient deficiencies and possibly for decreased bone mineral density. There is currently a paucity of data regarding the yields of these screening tests for children with newly diagnosed CD, which may differ from adults given they are in a different phase of growth and development.
Aim: To determine the yield of screening for micronutrient deficiencies and decreased bone mineral density in children with newly diagnosed CD.
Methods: A retrospective chart review was conducted in children (0-18 years) with newly diagnosed CD between 2011 and 2014. Data collected included baseline demographics, anthropometrics, MARSH scores, laboratory results (including tissue transglutaminase (tTG)-IGA, iron, 25OH vitamin D, iron and ferritin levels) and dual-energy x-ray absorptiometry (DEXA) scan results within 12 months of diagnosis. Chi^2 or Fischer's exact tests were used as appropriate to examine statistical associations between the factors examined.
Results: Of the 159 children identified, 39% were male and 61% were female; 16% were <5, 38% 5-9, 35% 10-14, and 11% >15 years. As expected, 93% at diagnosis had an elevated TTG IgA. In those tested, the percentage of abnormal

results for factors examined are summarized in Table 1.
Notably, on micronutrient screening, 45% of patients tested had Vitamin D insufficiency (40%) or deficiency (5%). There was no associations between a low 25 OH Vitamin D level with gender, marsh score, age, TTG IgA level, corrected calcium level, TSH, height<5th%, weight <5th% or BMI <5th%. 30% had a low ferritin at diagnosis, once again without any statistical association with the above factors.
In those who had a DEXA scan, 38% had an abnormal result with a z score <-1. A z score <-2 was significantly more common in those with weight <5th% (10% in those with normal z score >-1, 50% in those with z score <-2, p=0.009) and height <5th% (10% in those with normal z score >-1, 50% in those with z score <-2, p= 0.05) . There was no association between an abnormal DEXA scan result and other factors examined.
Conclusions: In this pilot study, there seems to be possible benefit of screening for certain micronutrient deficiencies and bone mineral density in children with newly diagnosed CD given the high percentage of children with abnormal Vitamin D levels and DEXA screening found. Apart from a modest association between decreased height and weight percentiles associated with abnormal DEXA results, there were no predictors found of which children would be most likely to have abnormalities. Larger prospective studies are needed to enable creation of guidelines for necessary screening tests for children with newly diagnosed CD.
Results of tests in children with newly diagnosed CD

	Normal (%)	Abnormal (%)
TTG-IGA at diagnosis	11/150 (7%)	139/150 (93%)
TTG-IGA at 6-12 months after diagnosis	42/94 (45%)	52/94 (55%)
Ferritin	26/37 (70%)	11/37 (30%)
Iron	38/43 (88%)	5/43 (12%)
25 OH Vitamin D Insufficiency Deficiency	46/83 (55%)	37/83 (45%) 33/83 (40%) 4/83 (5%)
DEXA Scan z<-1 z<-2	20/32 (62%)	12/32 (38%) 6/32 (19%) 6/32 (19%)

Denominators vary based on the number of children who had each test.

307 *IMPROVEMENT OF EXTRA-INTESTINAL MANIFESTATIONS OF CELIAC DISEASE ON A GLUTEN FREE DIET IN CHILDREN COMPARED TO ADULTS*

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BACKGROUND: Celiac Disease can be asymptomatic or present with classic (gastrointestinal) or atypical (extra-intestinal) symptoms.
OBJECTIVE: To evaluate extra-intestinal manifestations of celiac disease and symptom recovery on a gluten-free diet in a pediatric and adult celiac population at the University of Chicago.
METHODS: A retrospective chart review of the University of Chicago Celiac Center clinic charts was conducted. Demographics, serologic testing, intestinal biopsies, and extra-intestinal symptoms at presentation, 12, 24, and greater than 24 months were reviewed and recorded. Extra-intestinal symptoms included: abnormal liver enzymes, arthralgia/arthritis, dermatitis herpetiformis (DH), dental enamel defects, alopecia, fatigue, headache, anemia, stomatitis, myalgias, psychiatric disorders, rashes, seizures, neuropathy, short stature, delayed puberty, osteoporosis and infertility.
RESULTS: A total of 737 patients with biopsy confirmed celiac disease, TTG IgA >10 times normal with positive EMA in the absence of biopsy, and skin biopsy confirmed dermatitis herpetiformis were included. Patients not strictly adherent to a gluten free diet (GFD), lost to follow up, or who had insufficient data were excluded leaving a total of 328 patients (156 pediatric patients < 18 years of age). For pediatrics, the female to male ratio was 2:1 and the mean age at diagnosis was 8.9 years old. For adults, the female to male ratio was 4:1, and the mean age at diagnosis was 40.6 years old. Children (60%) and adults (62%) showed similar rates of extra-intestinal manifestations of celiac disease. Short stature (33%), fatigue (28%) and headache (20%) were the most commonly reported symptoms in children. Iron deficiency anemia (48%), fatigue (37%) and headache/psychiatric disorders (24%) were most common in adults. Overall children had higher rates of symptom resolution as compared to adults. Twenty-three percent of short stature children who failed to improve on a GFD were found to have other underlying comorbidities.
CONCLUSIONS: There are similar rates of extra-intestinal manifestations of celiac disease in children and adults. In children short stature, fatigue and headache were most common while anemia, fatigue and headache/psychiatric disorders were most common in adults. Overall children on a strict GFD showed higher rates of symptom resolution as compared to adults. Unresponsive children with short stature must be assessed for comorbidities.

308 *CELIAC DISEASE AND EPILEPTIFORM ACTIVITIES IN ELECTROENCEPHALOGRAPHY*

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BACKGROUND: To determine the presence of electroencephalograhic changes among patients diagnosed with celiac disease in order to define the association of celiac disease with epileptiform activities in electroencephalography. METHODS: A total of 307 children with the diagnosis of celiac disease (study group) and 197 age- and sex-matched healthy children as controls (control group) were included in this study. The study group was further divided into two as; new diagnosed celiac disease patients (n=216) and patients who were under gluten free diet (n=91) for at least six month. Medical histories of all children including age, gender, symptoms, weight, height, physical examination findings and laboratory data were all recorded. All patients underwent an electroencephalography in Pediatric Neurology EEG Laboratory with a 32 channeled electroencephalography for 30 minutes. RESULTS: Twenty-five patients were defined to have epileptiform discharges (spike/sharp-wave discharges) and 24 (7.8%) of those cases were in celiac disease group and 1 (0.5%) was in control group (p=0.001). Among those 24 cases 21 (9.7%) were in new diagnosed celiac disease group and 3 (3.3%) were in gluten free dietgroup (p=0.03). CONCLUSIONS: Patients diagnosed with celiac disease are prone to epileptiform activities in electroencephalography and should be evaluated for this purpose carefully. Moreover strict and early gluten free diet can be advised in those cases with epileptiform activities, since it may be effective in decreasing the prevalence of epileptiform activities.

General characteristics and laboratory findings of study participants

	Control (n=197)	New diagnosed celiac disease group (n=216)	Gluten free diet group (n=91)	p1*	p2**	p3***
Females (%) /Males (%)	109(55.3) / 88(44.7)	126 (58.3) / 90 (41.7)	54 (59.3) /37 (40.7)	0.12	0.13	0.87
Age (years)	10.29±3.5	10.15±3.7	9.88±4.2	0.69	0.21	0.19
Height Z score (cm)	-0.50±0.84	-1.3±1.3	-1.6±1.4	0.01	0.04	0.51
BMI Z score (kg/m2)	0.1±0.87	-0.36±1.0	-0.47±1.1	0.01	0.02	0.71
Hemoglobin (g/dL) (Mean±SD)	12.5±1.9	12.1±1.1	11.7±1.9	0.16	0.09	0.19
Serum Iron (µg/dL) (Mean±SD)	63.7±31.8	59.3±35.8	56.3±34.1	0.30	0.20	0.59
Serum Iron Bındıng Capacity (Mean±SD)	314.4±61.4	325.9±71.2	338.6±81.7	0.17	0.17	0.32
Vitamin B12 (pg/dL) (Mean±SD)	353.3±143.2	331.2±139.7	342.7±120.2	0.20	0.56	0.61
Folic Acid (ng/ml) (Mean±SD)	9.7±2.9	8.8±3.7	9.5±3.17	0.02	0.72	0.04

p1*: The p value between the control group and new diagnosed celiac disease patients
p2**: The p value between the control and gluten free diet groups
p3***: The p value between new diagnosed celiac diseas patients and gluten free diet group
Summary of EEG findings and assesment of patients

	Number of total cases	Control group (n=197)	New diagnosed celiac disease group (n=216)	Gluten free diet group (n=91)
Occipital focus	15	0	13	2
-- BOCE	9	0	8	1
-- Asymptomatic	6	0	5	1
Controtemporal focus	5	1	4	0
--BRE	3	0	3	0
--Asymptomatic	2	1	1	0
Generalized	5	0	4	1
-Epileptic	4	0		
---IGE	3	0	3	0
---JAE	1	0	0	1
-Asymptomatic	1	0	1	0

BOCE: Benign occipital childhood epilepsy
BRE: Benign rolandic epilepsy
IGE: Idiopathic generalized epilepsy
JAE: Juvenile absence epilepsy

309 *IS THERE UTILITY IS COLLECTING SEPERATE DUODENAL BULB BIOPSY CONTAINERS WHEN CELIAC DISEASE IS NOT SUSPECTED?*

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Background: No guidelines exist as to when duodenal bulb biopsies should be obtained in patients undergoing esophago-gastro-duodenoscopy (EGD). Previous studies have shown that obtaining biopsies from the duodenal bulb may improve the likelihood of detecting celiac disease in certain patients. However, there is an additional cost associated with each container of biopsy collected - approximately 700 dollars per container at Children's National Health System (CNHS).
Aim: To determine whether obtaining a separate duodenal bulb biopsy in a patient in which celiac disease is not suspected affects the final diagnosis.
Methods: A retrospective chart review was performed on patients who had undergone EGD at CNHS from November 1, 2013 to March 31, 2014. Patients were excluded from the study if they did not have duodenal bulb and distal duodenal biopsies collected in separate containers, they had a history of positive celiac titers, they adhered to a gluten free diet, or if they were diagnosed with other comorbid conditions that increased their risk for celiac disease. Clinical symptoms, erythrocyte sedimentation rate, albumin, hemoglobin, and histology from the bulb and distal duodenum were recorded for each patient. Results were dichotomized into two groups based on duodenal bulb biopsy results (positive versus negative). Fischer exact test was used to compare clinical symptoms and lab values between patients with positive bulb findings and those without.
Results/Discussion: 4 of the 70 patients included in this study had duodenal bulb biopsy findings that were different then the remainder of the duodenum. These findings were non-specific. These four patients were given clinical diagnoses of poor growth of unclear etiology, functional abdominal pain and non-specific abdominal pain, respectively. The fourth patient was lost to follow-up. No statistically significant differences were noted in baseline demographics, clinical symptoms, and lab values between patients with normal and abnormal duodenal bulb biopsy results. In this population of patients with a low pre-EGD suspicion for celiac disease, collection duodenal bulb biopsies in a separate container did not have an affect on the overall final diagnosis. Prospective, randomized controlled studies would be useful in determining the cost/benefit of obtaining bulb and distal duodenal biopsies in separate containers. Our study suggests the utility of doing so is low in this population.

310 *TEACH PROGRAM: THE IMPACT OF A NOVEL TEXTING EDUCATIONAL AUTOMATED COMPLIANCE HELP (TEACH) PROGRAM ON GLUTEN FREE DIET ADHERENCE AMONG ADOLESCENTS WITH CELIAC DISEASE*

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BACKGROUND: Adolescents are particularly vulnerable to nonadherence. The TEACH program is an automated text message intervention targeting this at-risk population within the existing mobile health (mHealth) self-monitoring

movement.
AIM: To determine the effectiveness of the TEACH automated educational text message reminder program in improving gluten-free diet adherence as measured by percent change in serum Tissue Transglutaminase IgA (TTG IgA) and Deamidated Gliadin Peptide IgA (DGP IgA), quality of life as measured by the NIH PROMIS tool, patient-reported dietary adherence as measured by the Celiac Dietary Adherence Test (CDAT), patient activation as measured by the Patient Activation Measure (PAM), and symptomatology as measured by the Celiac Symptom Index (CSI) among adolescents and young adults with celiac disease.
METHODS: We are currently performing a multicenter block-randomized, controlled study among patients 12-24 years of age with celiac disease from across the US. Participants are randomized to the TEACH program intervention group or the control group based on enrollment TTG IgA. The intervention group receives 45 validated, unique, partially bidirectional text messages created by our celiac disease team over the 3-month study period. All patient recruitment, data collection, longitudinal patient reported outcomes, and automated text message reminders are integrated using Stanford Bioinformatics' innovative REDCap system. Participants have serum TTG IgA and DGP IgA drawn and complete online questionnaires through the secure REDCap TEACH study website: http://j.mp/1zvLuBF (including NIH PROMIS QOL, CDAT, PAM, and CSI) at the beginning and end of the 3-month study period.
RESULTS: Approximately 1/3 goal recruitment is completed with 17 participants enrolled to date, and 40 participants in the process of completing enrollment. To date, the participants enrolled are 12-22 years of age, 10 female, with 5 randomized to the control group and 12 in the TEACH intervention group. Enrollment outcome measures include the following: TTG IgA <2-80 (mean 8, SD 19), DGP IgA 3-13 (mean 7, SD 4), NIH PROMIS raw scores 30-50 (mean 38, SD 6), CDAT scores 7-21 (mean 12, SD 4), PAM scores 14.5-100 (mean 71, SD 24), and CSI scores 17-51 (mean 31, SD 10). TEACH participants' satisfaction and engagement ratings are very high, and there has not been any drop out since the study began.
CONCLUSION: The novel TEACH program described above is the most comprehensive prospective automated interventional effort using an integrated mHealth platform among an at-risk adolescent patient population with celiac disease to date. When data collection is completed, we will have a comprehensive assessment of longitudinal patient reported outcomes and objective serum markers of adherence. If successful, the TEACH program has the potential to be applied broadly to a variety of chronic illnesses to improve adherence and disease self-management among adolescents.

313 *ISOLATED ANTI-GLIADIN IGG POSITIVE SEROLOGY WITH NON-SPECIFIC HISTOLOGIC FINDINGS MAY SUGGEST A NON-CELIAC DISEASE ASSOCIATED WITH MULTIPLE FOOD ALLERGIES INCLUDING WHEAT IN CHILDREN: A RETROSPECTIVE STUDY*

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Objectives: The gold standard for diagnosis of celiac disease (CD) is histology demonstrating villous blunting or atrophy. However, many patients with symptoms consistent with CD and positive serologic markers will have non-specific findings on histology. This has raised the question of whether these patients have early CD or other etiology such as wheat sensitivity. This distinction is important; given CD carries a risk of malignancy if untreated and treatment is life-long diet modification. We are interested in studying this population in pediatrics to investigate if a correlation with food allergy or a distinguished pattern in serological tests exists.
Methods: We reviewed 112 charts of pediatric patients that had CD serologic tests from 2002 - 2012 in an ongoing IRB-approved study. These tests included IgG and IgA antibodies against gliadin, deamidated gliadin, tissue transglutaminase, and endomysial antibody. In addition, IgA levels and genetic testing were included when available. Histology was categorized according to Marsh criteria. Food allergies, symptoms, and diet were documented.
Results: Eighty patients had serologic tests and histology available. The average age was 7.4±4.5 years and ranged from 20 months to 17 years. Of the 80 patients, 50 revealed Marsh 3 or 4 histology and had at least one positive serologic test, thus categorized in the CD group. Twenty patients had negative histology (Marsh 0-2) but had at least one positive serologic test. Comparing this histology negative, serologic test positive group (N=20) with the CD group (N=50), no differences were found in age, gender, symptoms or known CD associated conditions. However, in this non CD group 25% (5/20) had history of food allergy compared with 8% (4/50) in the CD group; the difference was borderline significant (p=0.102). Furthermore in the non CD group, the majority of positives were anti-gliadin IgG (N=10), in which 60% were only positive for that test. In contrast, in the CD population all anti-gliadin IgG positives (N=16) were concomitant with at least one other positive test (p=0.001). Nine of the non CD patients went on a gluten free diet and their symptoms improved.
Discussion: Our data suggests that this non CD group might represent a population characterized by a higher incidence of food allergy and a tendency to have only anti-gliadin IgG positivity on serological tests. A recent study in adults identified a non-celiac wheat sensitive population in which these findings were also described. Our results hint that a similar population exists in children. Many of the patients in the above group improved on a gluten free diet, which also supports wheat sensitivity as a possible etiology. However, an early stage of CD cannot be ruled out. Further studies with a larger sample size and longer follow up period are needed to explore this population.

LIVER

314 *RIP3 PROTECTS MICE FROM HIGH FAT DIET-INDUCED LIVER INJURY AND HEPATOCYTE APOPTOSIS*

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Background: Hepatocyte apoptosis plays a critical role in the development and progression of nonalcoholic fatty liver disease (NAFLD). RIP3-dependent necroptosis is a newly described form of programmed cell death that uses the same upstream activation pathways as apoptosis. There is significant crosstalk between apoptosis and necroptosis; therefore, we tested the hypothesis that blocking RIP3-mediated necroptosis may shift the balance of cell death toward more apoptosis contributing to liver injury mediated by high fat diet (HFD).

Methods: Wild-type (WT) and RIP3 knockout (RIP3 -/-) male mice were age-matched and randomized to chow (6% fat) or HFD (42% fat) for 12 weeks.

Results: Both WT and RIP3 -/- mice on HFD gained more weight than mice on chow diets and there was no effect of genotype on weight gain. HFD feeding to WT mice increased expression of RIP3 in liver, predominantly in peri-central zones. HFD also increased hepatic steatosis, plasma ALT/ AST activity and hepatocyte apoptosis, indicated by both increased TUNEL positive cells and accumulation of M30/CK18-cleavage products. Interestingly, RIP3-deficiency exacerbated HFD-induced liver injury; ALT/AST and triglyceride content were all higher in RIP3 -/- mice on HFD compared to WT. Expression of mRNA for the inflammatory chemokine MCP-1 and macrophage infiltration (Ly6C) were also increased in RIP3 -/- animals on HFD compared to WT. Finally, hepatocyte apoptosis assessed by TUNEL staining was increased in RIP3 -/- mice. Importantly, increased inflammation and injury was associated with increased liver fibrosis in RIP3-/- mice, assessed by expression of collagen-1α1, alpha-smooth muscle actin, matrix metalloproteinase 13 (MMP13) mRNA and Sirius red staining.

Conclusion: Absence of RIP3, a key mediator of necroptosis, exacerbated HFD-induced liver injury, associated with increased hepatocyte apoptosis, inflammation and fibrosis. These findings have great implications because the manipulation of hepatocyte cell death is being considered as a therapeutic target for NAFLD.

315 *NERVE GROWTH FACTOR (NGF) MAY PLAY A ROLE IN HEPATOCYTE APOPTOSIS AND DISEASE PROGRESSION IN CHILDREN WITH NASH*

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Background: Beyond its function in stimulating nerve growth and survival, nerve growth factor (NGF) plays a role in energy homeostasis and is expressed by hepatocytes during liver injury. Signaling through its p75 neurotrophin receptor (NTR), NGF can induce apoptosis. Hepatocyte apoptosis is thought to play a central role in nonalcoholic fatty liver disease (NAFLD) progression from the benign form of simple steatosis (SS) to the aggressive form of nonalcoholic steatohepatitis (NASH). The aim of the current study was to explore the role of NGF signaling in children with NAFLD.

Methods: Children with biopsy-proven NAFLD were divided into two groups according to pathologist diagnosis: SS (n = 12) and NASH (n = 7). Prior to immunostaining, the tissue was deparafinized. To visualize expression of NGF, p75, cytokeratin 18, activated caspase 3 in liver biopsies, tissue was pre-blocked for 20 minutes with anti-rat CD32 antibody and then stained with appropriate antibodies. Densitometry was acquired using NIH ImageJ software. NGF plasma levels were also measured using a commercial ELISA with intra- and inter-assay coefficients of variation < 10%.

Results: Immunohistochemistry staining for NGF was found in regions with significant damage and architectural distortion. This was significantly higher in children with NASH than SS as quantified by densitometry. Staining for cytokeratin 18 as a marker for hepatocytes showed colocolization of NGF to hepatocyte cytoplasm. P75 NTR staining demonstrated an increase in those with NASH compared to SS. Cleaved caspase 3, a marker of hepatocyte apoptosis, showed a significant increase in NASH and colocolized with NGF and p75 positive cells. Plasma levels of NGF were significantly higher in NASH group compared to SS group (140.5 ± 78 pg/mL vs. 82.6 ± 38.5, p value = 0.04).

Conclusion: Taken together, these findings provide evidence that in injured livers from children with NASH, there is increased expression of the NGF-p75 pathway which may play a role in hepatocyte apoptosis and disease progression to NASH.

316 *FEASIBILITY OF ACOUSTIC RADIATION FORCE IMPULSE (ARFI) IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)*

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Background: Nonalcoholic fatty liver disease (NAFLD) affects nearly 10% of children and adolescents in the U.S. Liver biopsy is the gold standard for assessing liver fibrosis stage. Acoustic radiation force impulse (ARFI) imaging presents a novel less invasive assessment method; however, few studies investigated its feasibility and accuracy in children with NAFLD.

Objective: The purpose of this study was to assess the feasibility of ARFI in diagnosing liver fibrosis stage in children with NAFLD.
Methods: The study included consecutive children with NAFLD who underwent ARFI at our institution. Ten measurements were taken in each patient and the median value was calculated. ARFI was successful if the interquartile range (IQR) of the 10 measurements was less than 30%. ARFI cutoff of 1.34 m/s was used to identify the presence of any fibrosis F1-F4 and a cutoff of 2.0 m/s was used to identify advanced fibrosis F3-F4.
Results: 21 patients with NAFLD underwent ARFI, ages 6 to 20, 12 males 9 females, all obese with a BMI percentile of 98.2 ± 1.5%. The mean ALT and AST were 52.8 U/L and 35.2 U/L respectively. A total of 14 patients had dyslipidemia (14 with HDL below 45 mg/dl, 5 with LDL above 110 mg/dl, and 8 with triglycerides above 150 mg/dl). Surprisingly, ARFI measurements were successful (IQR< 30%) in only 7 of the 21 children (33.3%). The median ARFI value of the 21 children measured was 1.63 m/s and 1.51 m/s in the 7 successful studies. Overall, 5/7 (71.4%) of children with successful ARFI had a value of 1.34 m/s or greater indicating the presence of liver fibrosis and one patient/ 7 (14%) had a value > 2.0 indicating advanced fibrosis.
Conclusion: ARFI measurements were successful in only one third of obese children with NAFLD indicating the need for further study to ensure the feasibility and accuracy of ARFI in diagnosing liver fibrosis in this population.

*322 *TNF-ALPHA PROMOTES PARENTERAL NUTRITION ASSOCIATED CHOLESTASIS IN MICE WITH INTETSINAL INJURY THROUGH SUPPRESSION OF BILE AND STEROL TRANSPORTERS*
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Background: Parenteral nutrition associated cholestasis (PNAC) is most severe and progressive in children and adults with underlying intestinal failure. In a mouse model of PNAC, endotoxin (LPS) absorbed from injured intestine induced TNFa transcription in hepatic macrophages (*Hepatology. 2012;55:1518*), which was associated with down regulation of hepatocyte bile and sterol transporters, with cholestasis and with retention of cholestatic PN-derived soy-lipid phytosterols. The aim of this study was to elucidate the mechanistic role of TNFa in the development of cholestasis in this model.
Methods and Results: Wild type C57/B6 mice were exposed to dextran sulfate sodium (DSS) (to induce intestinal injury and increased permeability) for 4 days followed by infusion of phytosterol-containing (soy lipid) PN solution through a central venous catheter for 14 days (DSS-PN mice). Cholestasis (increased serum bile acids and bilirubin) and hepatocyte injury (increased AST and ALT) developed in DSS-PN mice but not in DSS only, PN only, or untreated chow fed mice. DSS-PN mice displayed significantly reduced mRNA expression of hepatic *Abcb11* (BSEP), *Abcc2* (MRP2), and the heterodimeric sterol transporters *Abcg5*/*Abcg8* (sterolin-1 and -2). DSS-PN and control mice were then treated with Infliximab (Inflix), a monoclonal antibody against TNFα, 10 mg/kg IV, or saline on days 3 and 10 of PN. Inflix treatment significantly reduced AST, ALT, bile acids, and bilirubin to normal levels in DSS-PN mice. Inflix treatment also restored to normal the hepatic gene expression of *Abcb11*, *Abcc2*, and *Abcg5*/*8* in DSS-PN mice. Histology of colon and small intestine at 14d showed no evidence of inflammation in all treatment and control groups, suggesting that prevention of PNAC was unrelated to effects of Inflix on gut inflammation. To further determine the role of TNFa in suppression of these transporters, wild type mice were injected i.p. with recombinant TNFa (200ng/mouse) and liver sampled after 4 hrs. In addition, Huh7 and HepG2 cells (human hepatocyte cell lines) were incubated with TNFa (10-50ng/ml) for 4 hrs and gene expression was measured. Compared to controls, TNFa treatment significantly suppressed hepatic mRNA expression of *Abcb11*, *Abcc2*, and *Abcg5*/*8* in both the mice and the Huh7 and HepG2 cells. Incubation of these cell lines with LPS (100-1000ng/ml) had no effect on these transporters. Finally, using luciferase reporter assays in HepG2 cells, we demonstrated that incubation with TNFa antagonized LXR activation of the *ABCG5/8* promoter. Conclusions: TNFa signaling is a key mediator in the pathogenesis of PNAC in mice and promotes cholestasis through transcriptional suppression of hepatocyte *Abcb11* and *Abcc2*. In addition, TNFa mediated suppression of *Abcg5*/*8*, through antagonism of LXR signaling, may promote the hepatocyte accumulation of cholestatic phytosterols. Therefore, pharmacologic targeting of TNFa pathways may be a novel strategy for treatment of PNAC.

323 *CHRONIC HEPATITIS B IN A PEDIATRIC REFUGEE POPULATION*
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Background: Around the world approximately 240 million people are infected with hepatitis B (HBV) with an estimated 780,000 deaths each year. The likelihood of chronic HBV is inversely proportional to age of acquisition, with rates as high as 90% for newborns, 25-30% if acquired before the age of 5 and less than 5% if acquired during adolescence or adulthood. Chronic hepatitis B patients have a lifetime risk of hepatocellular carcinoma up to 25% and an incidence of cirrhosis of 2-3% per year. In Onondaga County, from January 2010 to December 2014, there was an influx of 4,950 people, mainly refugees from different parts of the world including Bhutan, Nepal, Burma, Iraq, Thailand, and Somalia. Of these 1,924 of them were under the age of 21. The aim of this study is to describe a unique refugee population of children with chronic

HBV and to create a database which can document and assesses disease activity and identify children with spontaneous seroconversion and those which may be amenable to treatment with antiviral medications.
Methods: Retrospective study from January 2010 to December 2014 that included all children under the age of 21 with the diagnosis of chronic hepatitis B. Information including laboratory and demographic data was collected from our pediatric gastroenterology and pediatric infectious disease clinics.
Results: A total of 44 patients were found to be hepatitis B surface antigen (HBsAg) positive, these patients had a mean age of 14.06 years, 23 (52%) were male and 21 (48%) were female. Thirty three (75%) were refugees, 6 (14%) of undocumented origin and 5 (11%) were adoptees (Vietnam and China). The refugee population is mainly from Burma (33%), Somalia (15%) and Nepal (15%), other countries were less represented with percentages between 3-6% (Thailand, Central Africa Republic, Congo, Kenya, Vietnam, China, Sudan, Liberia, Laos, Sierra Leone and Tibet). Twenty two (50%) had prior spontaneous seroconversion and hepatitis B e antigen (HBeAg) negative, 15 (34%) were in immune-tolerant phase and HBeAg positive and 3 (7%) did not have documented HBeAg status. Four patients (9%), mean age of 15 years, were in the immune-active phase for longer than 6 months and therefore they were started on antiviral therapy with good results.
Conclusions: As part of Onondaga County, our institution has a unique refugee population of children with chronic HBV who have emigrated from parts of the world with high HBV prevalence. Given the high percentage of chronic HBV in the pediatric population due to vertical transmission, identifying those children who are candidates for treatment could prevent future morbidity and mortality especially hepatocellular carcinoma and cirrhosis.

324 *ACCULTURATION AND OTHER PREDICTORS OF NAFLD AMONG AN ETHNICALLY DIVERSE SAMPLE OF CHILDREN AND ADOLESCENTS*

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Background: The prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) has been reported to range from 20% to 77% among obese children and adolescents, with ethnic minority groups being disproportionately affected. Specifically, Mexican Americans have a higher prevalence of NAFLD and more advanced disease versus their ethnic group counterparts. However, the prevalence estimates among other Hispanic groups is largely unknown, as are the reasons for these ethnic group disparities. As families assimilate or acculturate to the United States they may adopt unhealthy lifestyle habits or risk factors for NAFLD but this has been largely unexplored. We examined the relationship between the presence of NAFLD and level of acculturation in an ethnically diverse sample of pediatric patients.
Methods: A retrospective medical chart review is conducted on 130 overweight/obese patients who attended the University of Miami Pediatric Gastroenterology Clinics (July 2013-June 2014). Data included demographics, anthropometric measures, laboratory results, and imaging/pathology reports. Follow up telephone interviews were conducted to collect information on lifestyle habits (sleep, nutrition, physical activity) and level of acculturation using a modified Stephenson Acculturation Scale. NAFLD was defined as alanine aminotransferase (ALT) >24 IU/L in the absence of evidence for common causes of liver disease. Odds ratios (OR) and 95% confidence intervals (95%CI) are calculated by fitting logistic regression models to NAFLD.
Results: The overall prevalence of NAFLD was 34%. Hispanic males and patients with Central American (39%) and Caribbean (33%) ethnicities showed higher rates of NAFLD. Patients of Central American descent were more likely to have NAFLD than their American counterparts (OR=4.1; 95% CI: 1.25-13.51). Acculturation was evaluated in 63 patients and a higher prevalence of NAFLD was seen among Hispanic participants that accultured into their same ethnic subgroup. Higher rates of disease were also seen among patients with insufficient physical activity (86%), inadequate sleep hours (96%), and lower family income (43%).
Conclusions: The odds of NAFLD differ among Hispanic subgroups; present findings suggest that children of Central American and Caribbean descent, living in the United States have higher rates of disease, when compared to other Hispanics and Americans irrespective of race. Acculturation into minority ethnic groups could be a potential risk for the development of NAFLD. Other disparities can be explained by sociodemographic characteristics and lifestyle habits. In order to reduce the development of NAFLD and lessen the disparity among population subgroups healthcare providers should address modifiable risk factors among patients at risk.

325 *STABLE MIXED CHIMERISM AS A MARKER OF IMMUNOTOLERANCE IN NON-HUMAN PRIMATES*

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Background: Patients continue to face high morbidity and mortality after transplant, both from allograft rejection and from the toxicities associated with standard immunosuppressive regimens. The ultimate goal of transplantation research is the induction of immune tolerance after transplantation, in order to ensure graft survival and preservation of protective immunity without the need for lifelong immunosuppression. Previous work in murine models has shown that stable and full-spectrum mixed-chimerism (including significant T cell chimerism) can be induced with minimal pre-transplant

preparation. Our objective is to produce this tolerogenic state in a Rhesus Macaque model using a non-myeloablative regimen with busulfan and total body irradiation (TBI) along with costimulation blockade with mTOR inhibition.
Methods: After establishment of baseline immunological profile of donor and recipient, recipients receive nonmyeloablative conditioning with TBI (200-300cGy) and busulfan (9.5mg/kg) followed by donor peripheral blood stem cell transplant from an MHC-matched donor. Recipients receive post-transplant immunomodulation with CD80/86-directed costimulation blockade with belatacept, CD154-directed costimulation blockade with 5C8 antibody, and mTOR inhibition with sirolimus. Immunosuppression is gradually weaned post-transplant until all drugs have been discontinued after one year. At this time, immune tolerance is rigorously tested by placing both a donor and third-party skin allografts onto the recipient. In addition, longitudinal analysis of whole blood chimerism, lineage specific chimerism via multicolor flow-cytometric sorting of granulocytes, T, and B cells, and bone marrow chimerism will be assessed. Longitudinal flow cytometric analysis of the recipient is performed, evaluating for immune reconstitution/activation/regulation. Assessment for viral reactivation are also performed.
Results: Four Rhesus macaques have successfully undergone the transplant protocol, with three of the four completing the protocol (the fourth animal is currently day +165 post transplant). Results show stable whole blood chimerism of >80%, 50-75%, and <30%, and T cell chimerism of 40-70%, 20-40%, and <25%. Importantly, the survival of donor skin allografts have been directly related to the degree of stable T cell chimerism induced, with high-level chimerism yielding prolonged skin graft survival (>100 days post-skin graft without requirement for any immunosuppression).
Conclusions: Stable full-spectrum mixed-chimerism induction is possible by combining non-myeloablative pre-transplant conditioning and combining CD80/86-directed and CD154-directed costimulation blockade with sirolimus. Robust immune tolerance to both the bone marrow allograft and subsequently placed donor skin graft is achievable when significant T cell mixed chimerism is induced. This non-human primate model of immunotolerance is a further step towards the goal of inducible allograft tolerance in the absence of long-term immunosuppression

326 *PREVALENCE OF FOOD ALLERGY AFTER LIVER AND INTESTINE TRANSPLANTATION*
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Background: Food allergies are reported after transplantation of solid organs in children. While most reports are from liver transplants allergies are reportedly increased in other transplant groups suggesting that the phenomenon may be related to immunosuppression. We have recently reported an increase in the prevalence of esophageal eosinophilic disease in patients with intestine transplant. Here we examine food allergy in children who have undergone liver transplants and compared them to those who have undergone bowel transplant to ascertain whether either organ has a greater impact on development of food allergy.
Method: We reviewed the information from the database of the transplant institute of the MedStar Georgetown University Hospital which contains prospectively recorded data. Additional data were obtained from the patient records of the hospital. We compared prevalence of food allergy in pediatric patients who had undergone intestinal transplant versus those that undergone a liver transplant versus those that had a combined liver and intestine transplant. MINITAB software, (Minitab Inc. State College, PA) was used to analyze data using standard methodology.
Results : During the approximate period 2003 to 2014, pediatric transplants at our center included, 142 isolated liver transplants, 38 isolated intestinal transplants and 59 combined liver and intestinal transplants (data was not grouped by additional organs that may have been included). The respective mean ages, 4.8 ± 5.5, 5.4 ± 4.6, and 2.0 ± 2.2, were different ($p<0.05$). Though the proportion of females in each group was also different, 58%, 32% and 44%, the differences were not statistically significant. The proportion of patients with food allergies was, 14(9.9%), 5(13.2%) and 8(13.6%), in the respective groups, with the greatest increase in transplants containing an intestinal graft. There was however no statistical difference in the proportions patient s with food allergies between the respective groups ($p>0.05$).
Conclusion: Food allergies are increased amongst patients undergoing liver or intestinal transplant. Patients who have undergone a combined liver intestine transplant appear to have similar prevalence to the isolated intestine patients suggesting that immunosuppression rather than any particular organ confers a the risk for food allergy.

327 *RACIAL DISPARITIES IN INFANTS UNDERGOING LIVER AND INTESTINE TRANSPLANTATION*
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Background: We have previously shown a trend towards a reduction in infants on the liver-intestine transplant wait list over the past decade in the United States. We postulated this to be a result of improved care of infants with short bowel syndrome and in particular reducing the propensity for progressive liver disease. It is also known that the demographics of the United States are changing because of immigration and increased birth rates in non-white populations. Here we examine whether there is a racial component in the trend intestine transplantation in children.
Method: We reviewed data from the United Network of Organ Sharing (UNOS) database and the U.S. federal government national birth data. As per these databases racial groups were as follows: "White", "Black", "Hispanic" and for this analysis, "Asian" and "Other" did not represent a large enough number so were categorized under' "Other". Data was analyzed from 2004 to 2014 (11 years). MINITAB software, (Minitab Inc. State College, PA) was used to analyze data. As per UNOS

patients were grouped in the following age ranges in years: <1, 1-5, 6-10, and 11-17.
Results: A total of 817 transplants that included an intestine were performed in children aged up to 18 years of age during the study period. The majority where White (n=449) or less commonly Black (n= 170), Hispanic (n= 152) or Other (n= 46). The majority of transplants were either <1 year, or 1-5 years. The greatest change for number of annual transplants was in the White, infant group which achieved a maximal annual transplant rate in 2006 and dropping by 85% since then. However as a proportion of the total births in the United States the group of Black infants had the highest transplant rate 2.7/100,000 versus White 1.9/100,000 ($p<0.05$) and Hispanic individuals 1.5/100,000 ($p<0.05$). The biggest decrease in the number of transplants of infants as a proportion of the total births was also the greatest in the Black group. Up to and including 2013, the birth rates for the United States were overall stable throughout the decade.
Conclusion: There is a trend towards a reduction in infants undergoing intestine transplant and while the absolute reduction is greatest White newborns, newborns in the black category have shown the greatest drop as a proportion of births. These changes are not explained by changes in the demographics in the United States birth population.

332 *GENOME WIDE ASSOCIATION STUDY IDENTIFIES EFEMP1 AS A NEW CANDIDATE BILIARY ATRESIA SUSCEPTIBILITY GENE*

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Biliary atresia (BA) is a rare liver disease presenting within the first months of life. It is characterized by obliteration of the extrahepatic biliary tree in a progressive, necroinflammatory manner, leading to cholestasis, fibrosis, cirrhosis, and chronic liver damage, and accounts for 50% of pediatric liver transplantations in the US. The etiology of BA is not well understood, and environmental, inflammatory, and genetic components have been proposed as causative factors. A previously reported genome-wide association study (GWAS) in Chinese patients identified a signal on 10q25 upstream of the *ADD3* and *XPNPEP1* genes, which we later replicated in a Caucasian population. In this study, we performed a GWAS in 450 European-American non-syndromic BA patients collected through the Childhood Liver Disease Research Network (ChiLDReN) and 1981 genetically matched controls obtained from the Age-Related Eye Disease Study (AREDS). Genotyping was done with the Illumina Omni2.5 single nucleotide polymorphism (SNP) array. Adjusted logistic regression was carried out to test SNP association with BA. The most significant SNP was rs10865291 located on 2p16 (p-value = 2.7×10^{-7}; odds ratio 1.6; 95% CI (1.3 -1.9)), in the fifth intron of *EFEMP1*. *EFEMP1* encodes the EGF-containing fibulin-like extracellular matrix protein Fibulin-3 which has been implicated in tissue regeneration and organogenesis. It has also been reported to activate Notch signaling *in vitro*, although with less efficiency than *JAG1*. Droplet digital PCR performed on cDNA obtained from BA liver specimens collected at time of liver transplant, from healthy control liver, and from disease control liver (n = 5 for each group) revealed that *EFEMP1* expression was increased in the BA liver samples by 9.1 fold compared to the healthy control liver samples (P-value < 0.002), although no significant expression difference was detected between the BA and disease control groups. Immunohistochemistry showed that Fibulin-3 was specifically expressed in tubular structures around portal tracts in BA liver. Follow-up co-staining with CK-19, a marker of cholangiocytes, and alpha smooth muscle actin, a marker of blood vessels, will be performed to determine cell type-specific expression of Fibulin-3. Ongoing studies include replication of the GWAS results in additional BA cohorts of both European and African-American descent. In conclusion, we identified a locus on chromosome 2p16 within the *EFEMP1* gene as the second candidate region associated with susceptibility to BA using the GWAS approach. *EFEMP1* is highly upregulated in BA and disease control liver at time of transplant. In addition, the protein product Fibulin-3 is expressed in the portal regions. The identification of this new candidate susceptibility gene will facilitate characterizing the genetic basis of BA.

335 *THE ROLE OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) IN THE WORKUP OF BILIARY ATRESIA*

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INTRODUCTION: Biliary atresia accounts for approximately 30 percent of neonatal cholestasis. Due to the rapid progression of this disease, both prompt diagnosis and early intervention are required. Traditionally, a laparotomy and subsequent cholangiogram have been required to substantiate a diagnosis. ERCP, when available, is a less invasive

alternative in the evaluation and management of neonatal cholestasis. The use of neonatal ERCP, however is currently restricted to a few specialized centres worldwide. This study presents the findings from a Canadian paediatric centre utilizing ECRP in the workup of neonatal cholestasis.
METHODS: A retrospective chart review of our institution's early experience with the use of diagnostic ERCP in the work-up of neonatal cholestasis, non-secreting HIDA scan and non-conclusive liver biopsy was conducted.
RESULTS: Between June 2014 and May 2015, four patients (mean weight of 4.48kg (range 4.1-4.86 kg), had ERCP performed at a mean age of 58.5 + 17.14 days. Of these patients, biliary atresia was ruled out via ERCP in two patients while the other one was suspicious for biliary atresia and had intra-operative cholangiogram which confirmed biliary atresia. One ERCP was unsuccessful and the patient underwent intraoperative cholangiogram, ruling out biliary atresia.. The mean duration of ERCP procedure was 15.5 [W1] minutes and no post ERCP pancreatitis or complications occurred post procedure.
CONCLUSIONS: Our preliminary data regarding the use of ERCP in the diagnostic algorithm of neonatal cholestasis indicate it is a safe alternative to more invasive open or laparoscopic cholangiograms. ERCPs can be performed judiciously and expediently in the workup of neonatal cholestasis, allowing for timely diagnosis of biliary atresia

*336 *THE PREVALENCE OF TYPE 2 DIABETES AND PREDIABETES IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE AND THEIR ASSOCIATION WITH NONALCOHOLIC STEATOHEPATITIS*

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Objective: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children in North America. NAFLD is believed to be a risk factor for diabetes; however the prevalence rates and impact of type 2 diabetes in children with NAFLD are not well described. The study aims were to: 1) determine the prevalence of type 2 diabetes and prediabetes in children with NAFLD, and 2) assess diabetes and prediabetes as risk factors for nonalcoholic steatohepatitis (NASH) in children with NAFLD.
Methods: We included children age 2-17 years with biopsy-proven NAFLD who were enrolled in the NIDDK NASH Clinical Research Network. The presence of type 2 diabetes and prediabetes were determined by American Diabetes Association criteria using clinical history and fasting laboratory values. Liver biopsies were reviewed centrally by the Pathology Committee of the NASH CRN. Differences in demographic, clinical, and histopathologic features between children with normal glucose metabolism, prediabetes and diabetes were evaluated.
Results: The cohort consisted of 677 children with biopsy proven NAFLD whose mean age was 12.6 years and BMI 32.5 kg/m2. Among children with NAFLD, the estimated prevalence of diabetes was 6.6% (95% CI 4.8-8.5%) and of prediabetes was 23.3% (95% CI 20.2-26.5%). Overall, diabetes was more common among girls than boys with NAFLD (14.3% vs. 3.5%, $p < 0.001$). Children with diabetes had higher mean serum GGT levels (60 U/L) than those with prediabetes (47 U/L) or normal glucose (45 U/L) ($p= 0.02$) as well as higher serum triglyceride concentrations (diabetes 194 mg/dL, prediabetes 150 mg/dL, normal glucose 145 mg/dL) ($p= 0.02$). In contrast, there were no significant differences in ALT, AST, total cholesterol, LDL-cholesterol, or HDL-cholesterol levels across the 3 groups. Biopsy proven NASH was significantly more frequent in children with diabetes (44.2%) than those with prediabetes (32.2%) or normal glucose metabolism (21.9%) ($p<0.001$). After controlling for age, sex, height, weight, race and ethnicity among children with NAFLD, the odds of having NASH was significantly higher in those with diabetes (OR 2.6; 95% CI 1.3-5.0; $p<0.01$) and pre-diabetes (OR 1.8; 95% CI 1.2-2.7; $p<0.01$) compared to those with normal glucose regulation.
Conclusions: Impaired glucose metabolism was common in children with NAFLD. Among our cohort, the prevalence of children with type 2 diabetes and prediabetes was much higher than would be expected, based on contributions from obesity alone. Children with diabetes and prediabetes had a two to three fold greater odds of having NASH, which may convey greater long-term risk for adverse hepatic outcomes.

337 *THE INFLUENCE OF RACE, GENDER AND ETHNICITY IN BILIARY ATRESIA: A 12 YEAR RETROSPECTIVE REVIEW FROM A SINGLE U.S. CENTER*

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BACKGROUND: Racial and ethnic minorities are at risk for delayed diagnosis (Dx) and intervention for serious disease. Biliary atresia (BA) Dx may be delayed in African American (AA) and others with darker skin color. Some studies indicate gender differences in rates of BA in AA. We hypothesized that AA race and/or hispanic (H) ethnicity would delay BA Dx, hepatoportoenterostomy (HPE) and greater rate of transplantation (LTX) and increased death rates compared to caucasian/other (W) BA patients at our center. METHODS: A computerized chart review of all patients Dx with BA at Children's Healthcare of Atlanta (Egleston) from January 2002 to June 2014 was performed. The following data was

abstracted: Race (AA, W), Ethnicity (H, nonhispanic-NH), gender (F,M), age at diagnosis (AgeDx), age at HPE (ageHPE), HPE performance (HPE-YES, HPE-NO), surgeon performing HPE, total bilirubin (TB) at diagnosis (TBDx), TB at 3 months post HPE(TB3M), TB at LTx (TBLTX), status at 12 month post HPE (alive with native liver- ANL, alive LTX, death after LTX, death neither HPE or LTX), and miles from medical center by home postal code. Continuous data was analyzed with two tailed t-test, Categorical data by Fisher exact test. RESULTS: 70 patients had BA. 4/70 (5.7%) had BA splenic malformation (2 WHF, 1AAF) and 10/70 (14.2%) had cystic features in the biliary remnant (BACYS- 2AAM, 4 AAF, 3 WHF, 1 WNHF). Racial/ethnic/gender distribution for all BA was: AAM-14, AA 24, WHF-13, AHM-1, WNHF-7, WNHM-11. 58 had HPE, 3 had variant HPE procedures, 9 did not have HPE (AAM-2, AAF-4, WHF-2, WNHF-1). Of the 9 HPE-NO, 8 underwent LTX and are alive, 1 was ineligible for LTX and expired. 2 surgeons performed 34/58 (59%) of HPE. Overall ageHPE was 62+/- 26 days, n=58 (range 6-158). All AA HPE (n=30) and all W HPE (n=28) had similar ageHPE (62+/-24 vs 62+/- 29; p=0.9). No F-M differences were seen by racial category, but the ratio of F to M in H was different compared to NH (13:1 vs 31:25, p=0.01).CYSBA (n=9, 1 HPE not performed) were of similar ageHPE as BA HPE, n=49, (50+/-31 vs 64+/- 26; p=0.12). With HPE or equivalent, 33/57 or 58% (16 AA) are ANL and 24/57or 42% have had LTX (14 AA, 2 of which expired after LTX). There are no significant differences in survival in racial, ethnic or gender categories with either treatment. Furthermore, HPE-NO vs HPE-YES was not different across racial lines (AA 6:32 vs W 3:29; p=0.49). There were no racial differences for TBDx (AA 9.1+/-3, n=38 vs W 7.9 +/- 2.5, n=31; p=0.6), TB3M (AA 5.1 +/-5, n=29 vs W 3.0+/-5.6 n=29; p=0.15) or TBLTX (AA 11.7+/- 7.7, n=20 vs W 9.8 +/- 11.3, n =13, p=0.5). While distance from the medical center did not impact HPE or LTX performance along racial characteristics, death pre- or post- LTX was associated with greater distance from home to medical center (expired 105+/-64 miles, n= 6 vs 53 +/- 53 n= 62, p 0.03) and trended along racial lines (AA expired 96+/- 78 miles, n=4 vs AA Alive 48+/- 47 miles, n=34 p=0.07). CONCLUSION: At this center with many AA BA, BA Dx, HPE and LTX outcomes are similar by race and ethnicity. BA may be more common in WHF compared to WHM. Distance from treating medical center may be an impactful factor for adverse outcomes in minority populations and is an area for focused attention.

338 *INCREASING THE FRUCTOSE:GLUCOSE MOLAR RATIO PROMOTES IN VITRO HEPATOCYTE LIPOGENESIS.*
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Background: Ample clinical data suggest diets high in fructose promote hepatic steatosis and development of NAFLD in an insulin-dependent manner. Although underlying mechanisms are not fully elucidated, a recent *in vitro* study indicates fructose-mediated lipogenesis occurs without a change in lipogenic gene expression (PLoS ONE 6(11):e26583). Using a validated hepatocyte culture model, our prior report showed increasing culture media [glucose], up to 0.72mM, did not mediate further increases in triglyceride (TG) or cholesterol (C) biosynthesis. Here, we sought to determine whether increasing culture medium [fructose], while maintaining total monosaccharide and insulin content, effects enhanced lipogenesis.
Methods: Hepatocytes (huH17), demonstrating both glucose/fructose uptake and lipid biosynthesis, were incubated in standard culture media (Dulbeco modified Eagle's) containing isosomolar concentrations of monosaccharide (0.72mM), with the media fructose:glucose molar ratio ranging from 0.58-0.67. Following a 24 hr incubation, cells were harvested and analyzed for total protein, triglyceride and cholesterol content, using standard methodology.
Results: The table shows results of hepatocyte TG and C analysis at 24 hrs post-incubation.
Conclusion: 1. In an *in vitro* cultured hepatocyte model, both glucose and fructose + glucose in the culture medium support cell viability; 2. Compared to incubation with glucose alone, increasing the culture medium fructose:glucose molar ratio promotes enhanced lipogenesis for both TG and C. 3. Fructose-mediated, enhanced lipogenesis appears to occur via an insulin-independent mechanism. Speculation: These data provide further evidence that diets rich in fructose may increase the risk of hepatic steatosis and development of NAFLD.

Fructose:Glucose Ratio (mM:mM)	Triglyceride (ug/mg protein)	Cholesterol (ug/mg protein)
0.58	0.06	0.13
0.61	0.08	0.14
0.67	0.11*	0.18*

* $p<0.05$

*342 *PREDISPOSING FACTORS FOR SPONTANEOUS CLOSURE OF CONGENITAL PORTOSYSTEMIC SHUNTS*
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Background and aim: Congenital portosystemic shunts (CPSS) are rare vascular malformations associated with hepatic

encephalopathy, pulmonary complications and liver tumors in older children, adolescent and adults. Spontaneous closure of the CPSS is a rare event. Predictors of spontaneous closure of CPSS are unknown. Aim of this study was to assess whether spontaneous shunt closure is more frequent in children presenting with neonatal cholestasis.
Methods: We retrospectively reviewed medical charts of all consecutive patients with history of neonatal cholestasis and diagnosis of intrahepatic CPSS referred to 3 tertiary centers for pediatric hepatology from December 2009 to September 2014. We then reviewed all cases of CPSS published in the English literature from 1964 to October 2014 and classified the patients according to the type of shunt (intrahepatic vs. extrahepatic) and the presence or absence of neonatal cholestasis.
Results: A total of 392 patients from 209 articles were reviewed. Twenty-one patients were excluded because the information provided was incomplete. Of the 382 patients selected for the analysis (371 from the literature and 11 new patients; 161 women), 194 had an extrahepatic shunt and 188 had an intrahepatic shunt. Neonatal cholestasis was described in 55 patients (19 with extrahepatic and 36 with intrahepatic shunt, p=.014). A known cause of cholestasis was found in 12 patients (5 with intrahepatic shunt): biliary atresia in 8, neonatal hemochromatosis in 3, cytomegalovirus infection in 1. Spontaneous closure was observed in 27 (14.4%) patients with intrahepatic shunts, but in none of those with extrahepatic shunts (p<.0001). When only patients with intrahepatic shunts were considered, spontaneous shunt closure was observed in 15 patients with history of neonatal cholestasis (41.7%), as compared to 12 (7.9%) of those without cholestasis (p<.0001, odds ratio [OR] 8.3, 95% confidence interval [CI] 3.4-20.2). None of the patients with a known cause of neonatal cholestasis underwent spontaneous shunt closure. Among the patients with neonatal cholestasis that did not undergo spontaneous closure of the shunt, 15 had either a known cause of cholestasis, a follow-up shorter than 24 months or were treated before the 2 years of age. Accordingly, 71.4% of patients with intrahepatic shunt and shunt-related neonatal cholestasis, not treated or dead before the 24th month of life, underwent spontaneous shunt closure. The likelihood of spontaneous closure was higher in girls (p=.041), in patients whose intrahepatic shunt originated from the left or right distal portal branch (OR 6.1, 95% CI 2.4-15.8, p<.0001) and in those with multiple intrahepatic shunts (OR 3, 95% CI 1.1-8, p=.027). Patients with a patent ductus venosus were less likely to undergo spontaneous closure of the shunt (OR 0.1, 95% CI 0.03-0.36, p<.0001).
Conclusions: We found that presentation with neonatal cholestasis strongly predicts spontaneous closure of intrahepatic shunts. Spontaneous closure before the 24th month of age is more likely for distal or multiple shunts, while rare for patent ductus venosus. Such information might help avoiding the risk of early shunt closure procedures in infants with CPSS and neonatal cholestasis.

*343 *EFFICACY AND SAFETY OF ORAL CHOLIC ACID (CHOLBAM™) THERAPY IN BILE ACID SYNTHESIS DISORDERS DUE TO SINGLE ENZYME DEFECTS*

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Introduction: Bile acid synthesis disorders (BASD) can lead to cirrhosis and liver failure if untreated. We evaluated the long-term efficacy and safety of oral cholic acid (CA) in patients with BASD due to single enzyme defects (SEDs).
Methods: Data were obtained from 2 trials of oral CA at doses of 15 mg/day: Trial 1 was a Phase 3, nonrandomized, open-label, single-arm study of patients (n=50) treated over an 18-year period. Trial 2 was an extension trial with patients (n=21) from Trial 1 and new patients (n=10); data were available for 21 months of treatment. Enrollment was based on atypical urine bile acid metabolites measured using fast atom bombardment mass spectrometry (FAB-MS). Response criteria were: (1) serum ALT/AST <50 U/L, or baseline levels reduced by 80%; (2) serum total bilirubin values ≤1 mg/dL; (3) body weight (BW) increased by 10% or stable at >50th percentile; (4) survival for >3 years on CA or alive at end of Trial 2. (5) Reduction in urinary bile acid metabolites. Responders met ≥2 lab criteria and were alive at last follow-up; or met ≥1 lab criterion, had increased BW, and were alive at last follow-up.
Results: Among 44 evaluable patients (39 from Trial 1 and 5 new patients from Trial 2), mean age was 4 years (range: 3 wks - 36 y) at treatment start (avg. duration of treatment: 310 wks). *Efficacy:* On a scale of 0 to 3, 3 being highest, those with grade 3 metabolites decreased (Trial 1: 72.1% to 14.0%; Trial 2: 21% to 9%). In both trials, the % of patients with ALT/AST <50 IU/L increased. Mean serum direct bilirubin decreased significantly (3.5 to 0.6; P<0.001) in Trial 1 and was stable or decreased in Trial 2. Mean BW percentile increased significantly in Trial 1 (31.1 to 54.9; P=0.006). Overall, 28/44 patients (64%) were responders: 45% met 2 clinical criteria and 1-3 lab criteria and 55% met the BW criteria. 67% of patients (41/62) survived >3 y from trial entry; of these, 13 (32%) were long-term survivors, living 10-24 y on treatment. *Safety:* Adverse events were not collected systematically in either of the trials. Adverse reactions reported included: diarrhea (2%); gastroesophageal reflux , malaise, jaundice, skin lesion, nausea, abdominal pain, intestinal polyp, urinary

tract infection, and peripheral neuropathy (1% each). Five SED patients across both trials also experienced worsening serum ALT/AST or increased serum bilirubin, and one with cholelithiasis requiring cholecystectomy. In Trial 1, five patients died due to progression of underlying liver disease. In Trial 2, two patients died, both unrelated to CA or progression of underlying liver disease.
Conclusions: Oral cholic acid was well tolerated and reduced urinary bile acid metabolites, direct bilirubin, serum ALT/AST, and BW and prevented progression of liver disease in patients with BASD due to SEDs in compliant patients without end-stage liver disease.

346 *LOSS OF HEPATOCYTE-SPECIFIC VASCULAR ENDOTHELIAL GROWTH FACTOR ACCELERATES FIBROSIS IN NON-ALCOHOLIC STEATOHEPATITIS*

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Background: Inflammation, and vascular remodeling are important features of non-alcoholic steatohepatitis (NASH). Vascular endothelial growth factor (VEGF) mediates both of these processes and hepatocytes have been suggested as an important source of VEGF during various liver stresses. Our aim was to assess the role of VEGF in NASH and more specifically hepatocyte-derived VEGF in this context. To address these questions, we deleted the VEGF-A gene in hepatocytes.
Methods: We generated hepatocyte-specific conditional VEGF-knockout mice, crossing AlbCre with $VEGF^{flo/flo}$ in C57BL/6 genetic background. These mice were fed either a choline-deficient amino acid diet (CDAA) or choline-sufficient amino acid diet (CSAA) for 20 weeks in order to induce liver injury. $VEGF^{flo/flo}$ mice and wild-type mice served as controls. Liver tissue and blood samples were collected at the completion of the 20 week diet. Hepatocellular fibrosis and inflammatory activity were then assessed.
Results: Hepatocyte-specific VEGF knockout mice had significantly reduced formation of new blood vessels compared to wild-type mice. As expected, no marked difference in angiogenesis was noted in $VEGF^{flo/flo}$ mice and wild-type mice. When placed on the CDAA diet, $VEGF^{Dhep}$ mice were observed to have an increase in final liver weight (WT CDAA 3.89 grams, $VEGF^{Dhep}$ CDAA 4.10 grams; $p \leq 0.05$), as well as an increased overall final body weight (WT CDAA 41.82 grams, $VEGF^{Dhep}$ CDAA 43.39 grams; $p \leq 0.05$) when compared to wild-type mice.
Liver injury was also increased in these animals, assessed via serum transaminases (WT CDAA 324 U/L, $VEGF^{Dhep}$ CDAA 482 U/L; $p \leq 0.05$). Furthermore, mRNA levels of a-SMA (4.5-fold increase compared to wild-type/control, $p > 0.05$), TIMP-1 (3.12-fold increase compared to wild-type/control, $p \leq 0.05$), COL-1 (3.44-fold increase compared to wild-type/control, $p \leq 0.05$), and CTGF (2.1-fold increase compared to wild-type/control, $p > 0.05$), markers specific for fibrosis, were increased when compared to wild-type and $VEGF^{flo/flo}$ mice. These findings were accompanied by increased collagen production as seen in Sirius Red immunohistochemistry in $VEGF^{Dhep}$ mice when compared to control mice.
Conclusions: Our study demonstrates that in a diet-induced mouse model of NASH, deletion of VEGF-A in hepatocytes results in increased fibrosis and liver injury. These results suggest that angiogenesis, driven by the presence of hepatocyte-specific vascular endothelial growth factor, is key in mitigating fibrosis and tissue injury in fatty liver disease.

347 *CLINICAL SIGNIFICANCE OF LIVER HISTOLOGY ON OUTCOMES IN BILIARY ATRESIA*

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Background: Recent literature on biliary atresia (BA) has investigated the relationship of age at operation and centre experience with outcomes. This study investigates the influence of patient factors including liver histology at time of BA diagnosis and Kasai Procedure (KP) and post operative treatments on serum bilirubin at 6 months and 5 year native liver survival (NLS) at a single centre over a 15 year period.
Method: A retrospective chart review of all children diagnosed with BA from 1999-2014, identifying 29 patients. Primary outcome measures were serum bilirubin at 6 months and 5 year NLS. Secondary outcomes measured the incidence of cholangitis and portal hypertension (PHT).
Results: Bridging fibrosis in liver histology at KP was the only factor significantly associated with 5 year NLS. Age at KP, commonly been reported to have an influence on NLS post KP, was not found to significantly influence NLS at age 5 in this series. Independent assessment of other patient factors, treatment and complications post KP including biliary ductule size on liver histology, use of ursodeoxycholic acid post KP, normalisation of serum bilirubin at 6 months post KP, presence of PHT, episodes of ascending cholangitis all had no significant effect on 5 year NLS.
Conclusion: Liver damage in the form of bridging fibrosis at time of KP has a significant impact on long term NLS. Further investigation is warranted to determine the impact of postoperative management on the occurrence of complications, as well as short and long term outcomes post KP.

348 *IDENTIFICATION AND QUANTIFICATION OF TRANSMITTED/FOUNDER VIRUS IN MOTHER TO CHILD TRANSMISSION OF HEPATITIS C VIRUS BY SIGNLE GENOME SEQUENCING*

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Introduction: HCV affects approximately 1% of pregnant women globally. HCV mother-to-child transmission (MTCT) is the most common route of HCV infection in children. Acute community-acquired HCV infection in adults has been shown to result from low number of transmitted/founder (T/F) virus, with as low as one or more discrete low diversity viral lineages. Little is known about viral transmission and viral genetic diversity in MTCT. Here, we use single genome sequencing of viral half-genomes from plasma viral RNA of 5 mother-infant pairs to quantify T/F virus in infants that had HCV transmission from their mothers. Methods: Plasma samples from 5 mother-infant pairs, including one HCV mono-infected mother with two of her children and 3 HIV/HCV co-infected mothers each with singleton children were obtained. Single genome sequencing (SGS) were performed in the mothers around the time of delivery and two to three time points from each infant between 2 to 6 months of age. SGS is an amplification and direct amplicon sequencing technique that allows precise identification of T/F virus by providing viral sequences that are in proportion to their representation in plasma and avoiding template resampling and *Taq* polymerase errors. Sequence analysis and maximum-likelihood phylogenetic analysis were performed to delineate viral lineages and quantify T/F viral population. Results: 787 single-template derived 5' HCV half-genome amplicons from 5 mother-infant transmission pairs were sequenced. Phylogenetic analysis of viral sequences revealed that despite high maternal viral load (greater than 10^6 IU/ml) in each of the mothers at the time of delivery, low number of transmitted founder viruses led to viral transmission. Two children developed productive HCV infection from a single virus transmission; while three children were infected with two closely related viral lineages. All sequences from the children during the first 6 months of life clustered in one clade or two closely related clades suggesting low viral diversity in early infancy. Genetic distance analysis revealed mother's individual time point viral diversity ranging from 9.4x10^-4 to 9.1x10^-3 while infant individual time point viral diversity ranging from $7.4x10^{-4}$ to $2.5x10^{-3}$, with a standard error ranging from 10^{-4} to 10^{-5}. Infants have low viral diversity at birth and increases marginally overtime. Mother-infant sequence comparative analysis showed the difference of 1.8x10^-3 to 1.4x10^-2 between mother's viral sequences at the time of delivery versus infants' earliest time point with a standard error of 1.19 to $9.32x\ 10^{-5}$.Conclusion: For the first time, we are able to use SGS to identify viral sequence population in proportion to those circulating in the plasma and reveal T/F virus in MTCT. There is low number of T/F virus in both infants born to mono-infected or HCV/HIV co-infected mothers leading to productive infection. We also demonstrated that HCV on the half-genome level has low viral diversity during early infancy. These findings are critical to pave the steps necessary for future HCV MTCT prevention strategies and vaccine development.

APGNN

350 *PEDIATRIC LIVER ALLOGRAFT HEALTH WITH NORMAL LIVER FUNCTION TEST ,10 YEARS AFTER LIVER TRANSPLANTATION :ALL IS NOT WELL!!!*

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Purpose of the study: To evaluate the liver histology in children with normal tests of liver functions and radiology, 10 years after liver transplant.

Methodology:62 children,10years after liver transplant with normal liver functions(AST,ALT,GGT,Bilirubin,Albumin)who consented for liver biopsy,were studied prospectively. incidence and risk factors for abnormal graft histology were also evaluated.

Result:of the 62 children(32male),age being between 11years and 25years median age was 14(+/-2 years), at the time of biopsy,53(85.55)children had abnormal histology (fibrosis/steatosis/both). On Ishak staging stage 3 and 4 fibrosis was found in 23 (43.5%)children. 11(20.7%)had stage 1 fibrosis,17(32%) with stage 2. Recipient related risk factors evaluated were episodes of acute rejection,biliary and vascular complications,CMV infection,de novo autoimmune hepatitis and PTLD. Donor related risk factors evaluated were age,sex,CMV status,graft steatosis,Both donor and recipient risk factors were comparable with normal and abnormal histology groups.

Conclusion: Normal liver biochemistry does not reflect graft histology. Hence a caution has to be observed while predicting allograft health without liver biopsy

351 *CELIAC DISEASE AND HELICOBACTER HEILMANNII*

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Introduction: Celiac Disease is an immune-mediated response to the ingestion of wheat, rye or barley in genetically predisposed individuals. There are typical gastrointestinal symptoms associated with celiac disease, such as abdominal pain, constipation, diarrhea or other extra-intestinal symptoms. The surveillance of celiac disease is 1-133 and the general population. In pediatrics it is thought to be 1:104. Gold standard for diagnosis of celiac disease is a small intestinal biopsy while maintaining a regular diet. In 2012, the European Society of Gastroenterology, Hepatology and Nutrition guidelines

were modified and recommended that a diagnosis of celiac disease can be made without a small biopsy in symptomatic patients with a tissue transglutaminase IgA 10 times the upper limit of normal, positive for HLA DQ 2 and DQ 8. Positive anti-endomysial antibody at the same time tested for the HLA. Proceeding without a small intestinal biopsy may miss other conditions that can be the cause of symptoms such as in the following case.
Case Study GM is a 14 year old female who was healthy until 3 months prior to clinic visit. GM reports daily abdominal pain is epigastric in region, it can radiate to the side it's described as aching and twisting. Sleeping will improve her pain and eating makes her pain worse, especially with lunch which included wheat. GM does not wake up at night due to the pain or miss school. GM will occasionally complain of nausea and denies regurgitation, heartburn or vomiting. GM will have excessive burping. GM bowel movements occur daily to every other day, 1-2 times per month she will experience diarrhea without associated blood.
Lab evaluation
Total IgA = 108 (77-278)
DGP IgA = 165 (0-19)
DGP IgG = 73 (0-19)
TTG IgA - greater 100 (0-3)
TTG IgG = 21 (0-5)
Endoscopy
Esophagus- no pathological diagnosis
Antrum-minimally active chronic inflammation and organisms consistent with H. Heilmannii
Duodenum-mildly inflamed duodenal mucosa with villous blunting, focal plasmacellular expansion of the lamina propria and focal mild intraepithelial lymphocytes suggestive of Celiac disease
Celiac panel at time of biopsy
Total IgA = 89 (70-498)
TTG IgA - 145.9 (0-20)
EMA IgA- 1:320 (<1:5)
GM started the gluten free diet and was treated with Flagyl 250 mg three times per day (allergic to PCN) for 10 days ,Clarithromycin 7.5 ml (375 mg) twice per day for 10 days and Omeprazole 20 mg twice daily for 2 months.
After treatment of gluten free diet and for H. Heilmannii, presenting symptoms of abdominal pain and nausea improved.
Summary
Diagnosis for H. pylori can be made through non- invasive testing such as blood, stool or breath hydrogen tests. H. Heilmanni is only diagnosed through invasive test such as an Endoscopy.
European Guidelines for diagnosing Celiac Disease (TTG IgA 10 times the UNL, EMA positive, HLA positive and symptoms) without proceeding with a small intestinal biopsy may miss other causes of symptoms such as in this case. Following the gluten free diet may only partial treat the cause of symptoms and my pose further health issue. GM was seen in clinic 3.5 months after treatment and had symptoms of abdominal pain and nausea. GM was given another course of antibiotic therapy.

352 *ELEVATED BODY MASS INDEX IN THE PEDIATRIC PATIENT AT INITIAL DIAGNOSIS WITH CELIAC DISEASE*
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The spectrum of presenting symptoms of Celiac Disease (CD) is wide; from the classic presentation of an ill appearing, failure to thrive child to the child with abdominal pain, diarrhea, and/or constipation, to the asymptomatic child. Regardless of presenting symptoms, a common perception is that these children are not overweight or obese. The aim of this study was to assess the weight distribution of patients presenting to a tertiary medical clinic for evaluation and diagnosis of CD, and to identify what proportion could be categorized as overweight or obese based on body mass index.
Methods: Patients, aged 2 - 18 years, diagnosed between 2008 and 2014 at The Children's Hospital of Philadelphia were included in the analysis.
Data elements collected included: sex, medical history, and diagnostic investigations (CD specific serology and pathology reports).
BMI and BMI percentile were recorded at time of diagnostic biopsy or at time of positive serology.
Standard definition of BMI was applied: < 85%, normal weight; 85%-95%, overweight; >95% obese.
Results: 250 patient records met eligibility criteria and were included in the analysis of these, 97 (39%) presented with a normal BMI, 95 (38%) presented with a BMI between 85% and 95%, and 58 (23%) presented with a BMI > 95%. In the overweight category- 35 (37%) were male and 60(63%) were female. In the obese category - 31(53%) were male and 27(47%) were female.
Conclusion: In the general pediatric population, prevalence of overweight and obese ranges between 20.5 % and 34.5%. In this study, 61% presented with BMI greater than 85% at time of CD diagnosis. This finding is in contrast to the classic CD presenting symptoms. Clinicians should be mindful that an elevated BMI does not preclude a diagnosis of Celiac Disease in children.

353 *INSERTING AND CONFIRMING PLACEMENT OF TRANSPYLORIC FEEDING TUBES IN PEDIATRIC PATIENTS: EVIDENCE BASED REVIEW AND PRACTICE CHANGES*

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Problem: Medically complex, pediatric, patients often require post pyloric feedings to support their nutrition. At our institution there was a nursing procedure for inserting and confirming placement of transpyloric (TP) tubes using peristalsis to advance the tube. The information in the procedure on how to measure the insertion length of the tube for TP placement was limited. There was no procedure on how to confirm placement of TP tubes while receiving tube feedings.

Methodology: A literature search was conducted to find evidence on how to determine insertion length of TP tube and bedside methods to confirm placement of TP tubes while a patient is receiving feedings. The search was conducted using online databases CINAHL and PubMed. Research studies, clinical practice guidelines, continuing education, evidence based practice articles, and a practice alert by the American Association of Critical Care Nurses were found during the search. Benchmarking with other pediatric hospitals was conducted. The Johns Hopkins Nursing Evidence-Based Practice (JHNEBP) Rating Scale was used to evaluate the strength and quality of the evidence which ranged from Level IIA to Level IV B.

Results: Measuring tube insertion length for TP placement is most accurate when using the nose to earlobe to mid-umbilical span (NEMU) to right iliac crest technique. The most reliable bedside methods to confirm placement of TP tubes in patients receiving tube feedings are external length of the tube, pH, and residual feeding volume.

Conclusions: NEMU to right iliac crest technique should be used to measure tube insertion length for TP placement. Bedside methods to confirm placement of TP tube should be done at regular intervals while a patient is receiving continuous tube feedings and just prior to formula administration and medication administration if patient is receiving intermittent feedings.

The nursing standard and procedures on inserting and confirming placement of TP feeding tube were revised to reflect the evidence based recommendations found in the literature review. A procedure to confirm placement of a TP tube was created.

354 *STONE SOUP: A RECIPE FOR ACCESS AND DELIVERY OF PSYCHOSCOCIAL SUPPORT FOR CHILDREN WITH IBD*

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British Columbia Children's Hospital is the only tertiary care pediatric hospital in the province. The Gastroenterology clinic has more than 4000 patient visits per year and follows 450+ children diagnosed with IBD. Previously, the psychosocial needs of the IBD patients were met by GI nurses trying to link families to community resources or being placed on lengthy outpatient Medical Psychology waitlists. The GI team collaborated with a Medical Psychology service reconfiguration to pilot a stepped approach to care that asks children/youth what their psychosocial needs are early in their medical care with the goal of less intensive and proactive resources rather than waiting until psychosocial needs require more intensive care. In 2014 we devised an iPad self-assessment questionnaire based on the PCDAI and PUCAI as an educational tool for our population. To better understand their psychosocial needs we expanded our child/youth self-assessment process to include the Pediatric Quality of Life Questionnaire(PedsQL): Generic Core Scales, to screen for health related quality of life. The PedsQL is given to children 12 and over at GI clinic visits or during Infliximab infusions.

716 surveys were completed by 253 individuals. Fifty-seven (22.5%) children/youth (age 12 - 17years, 55% female) self-reported significant psychosocial concerns (Social/Feelings or Total PedsQl<50). Biweekly psychosocial rounds were instituted (nursing, psychology, co-op students) to review the ‘flagged' PedsQL self-reports. A range of follow-up actions, based on urgency of need included: GI nurse feedback to the family, a one-time psychology consult to children hospitalized for regular treatment, telephone consultation with the family to support the family in accessing community-based resources and outpatient Medical Psychology treatment.

Common themes emerged from the self-assessment, which resulted in the creation of the OMG:IBD (Oh My Guts:IBD) monthly support group for youth and parents, facilitated by the psychosocial rounds membership and a youth peer support volunteer. Families have provided excellent ratings of their experience. This initiative has increased child, family and IBD staff awareness of psychosocial issues and strategies for coping and resulted in the development of further educational and community-based resources. Next steps include refinement of our iPad tools and a formal assessment of the sensitivity of this self-assessment tool and subsequent psychosocial intervention.

355 *PRACTICE VARIATION IN PERFORMING 24-HOUR MULTICHANNEL INTRALUMINAL IMPEDANCE AND PH STUDIES*

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Since the Patient Protection and Affordable Care Act passed in 2010 and the development of accountable care organizations, balancing best practice and cost savings has become a priority in clinical practice. Gastroesophageal reflux disease (GERD) is a common problem that immensely impacts cost of medical care in the U.S. Studies in adults recently have determined that variation in provider practice affects cost and early pH measuring studies may decrease cost rather than empiric trials of proton pump inhibitors. In addition to the chronic medications, measuring GERD is costly as well. One such test is the combined 24 hour multichannel intraluminal impedance and pH (MII/pH) study which is a functional measure of GERD. In pediatric gastroenterology (GI), it is especially useful because it measures symptom association when children are not able to express themselves. There is no systematic assessment in the pediatric literature of the cost of practice variation in the evaluation and management of GERD. Objective: To assess in what setting the MII/pH study was done to determine the variation in practice and measure the number of Chest Xrays (CXRs) performed when placing MII/pH probes. Methods: We retrospectively reviewed charts of pediatric patients who had MII/pH studies done from Jan 2012 to Dec 2014. A pediatric GI nurse was responsible for placement of the probe at the request of up to 12 pediatric GI providers. We measured the setting for probe placement. Since CXRs were utilized to confirm placement, and contribute to cost, we recorded the number of CXRs per patient at time of probe placement. Results: We reviewed 96 charts. The number of probes placed at the time of EGD were 44/96 (45.8%), during hospitalization 24/96 (25%), and in the clinic 28/96 (29.2%). Some patients who had the probe as outpatient returned to clinic for it to be removed by a nurse for a total of 18/96 (18.8%) which causes an extra charge for the second clinic visit. The majority of the patients were hospitalized overnight 53/96 (55.2%). The rest (26%) were outpatient, removed the probe themselves, returned the equipment, and did not receive an extra charge in clinic. The number of confirmation CXR's ranged from 1 (80.2%) to 5 (1%) with 1 or 2 CXR's performed in 94.8% of patients. Summary: In this one clinical pediatric GI practice, there was significant variety for the process of performing 24 hour MII/pH studies including outpatient versus inpatient versus operating room placement. Conclusion: With MII/pH studies, finding a safe mechanism for shifting cost by performing more outpatient studies could significantly decrease cost to the organization. More in-depth, prospective studies that monitor outcomes are needed.

356 *COMPARISION OF WEEKLY TO DAILY VITAMIN D REPLACEMENT IN CHILDREN WITH IBD*

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Introduction: Vitamin D insufficiency (INSF) and deficiency (DF) are common in children with Inflammatory Bowel Disease (IBD). There are published recommendations for daily (*D*) and weekly (*W*) supplementation; it is unclear if either approach is better at improving 25-hydroxyvitamin D [25(OH)D] levels. The purpose of this randomized pilot study was to compare effectiveness & adherence of different Vitamin D_3 dosing regimens in children with IBD who were 25(OH)D INSF or DF.
Hypotheses: 1) *W* & *D* dosing with vitamin D_3 are equally effective at improving vitamin D 25(OH) in children with IBD who are25(OH)D INSF or DF. 2) There is no difference in adherence between *W* & *D* dosing of Vitamin D_3 in children with IBD who are 25(OH)D INSF or DF.
Study Design: Children (5 - 17 yrs) with IBD were screened during a routine lab draw that included a 25(OH)D level. If the screening level was < 32 ng/ml, the child was eligible. Subjects were classified as 25(OH)D INSF or DF and randomly assigned to *D* or *W* dosing for 8 weeks. All supplements were provided.
Vitamin D_3 dose was based on our standard practice & published guidelines
25(OH)D: 21 - 31 ng/ml (INSF): 2000 IU *D* or 14,000 IU once *W*
20 ng/ml or less (DF): 7000 IU *D* or 50,000 IU once *W*.
Demographic and disease specific data were recorded. Dietary calcium & vitamin D intakes were analyzed; those with a calcium intake below the DRI were counseled by an RD on ways to improve calcium intake. After 8 weeks, a 2nd blood sample was obtained. Both were analyzed in house using the same laboratory testing procedure (AB Sciex triple quadripole LCMSMS in Atmospheric pressure chemical ionization mode (APCI)). Unused medication was counted and compared with written log.
Results: 37 subjects enrolled; 31 completed study. Age range 9 - 17 yrs, M=13.9. 64.5% F, 61.3% Caucasian, 32.2% African American. 64.5% Crohn's, 29% UC.
Overall, participants on *D* therapy did not demonstrate a significant increase in 25(OH)D (M=16.30, SE=3.26) compared to those on a *W* dose (M=11.40, SE=2.94), [t (29) 1.118, p>0.5], SMD 0.403. Sub-group analysis revealed Vitamin D INSF subjects on *D* dosing demonstrated a greater but not statistically significant increase in 25(OH)D (M=15.84, SE=4.30) than those on *W* dosing (M=8.86, SE=3.50), [t (18) 1.274, p > 0.5], SMD .57 (medium effect size). There was little difference in DF participants on *D* dosing (M=17.14, SE =5.47) compared to those on *W* a weekly dose (M=16.07, SE =5.16),[t (9) 0.142 p > .05], SMD .09.
67.7% achieved 25(OH)D levels >31.5 ng/ml; including those who did not complete the study, this rate fell to 56.8%. 30/31 subjects were mostly adherent (at least 75% doses reported taken; written diary consistent with the medication count).

Conclusion and Recommendations: In this pilot study, there was no significant difference in improvement in 25(OH)D levels comparing *D* to *W* dosing regimens. However, INSF subjects had greater improvement with *D* dosing, with a moderate effect size, suggesting that this finding might be significant in a larger study.
A major limitation is sample size. While initial findings suggest that weekly or daily dosing is equally effective at improving vitamin D levels in clinical practice, further study is needed to develop stronger evidence for practice guidelines.

357 *VITAMIN D LEVELS IN CHOLESTATIC BILIARY ATRESIA PATIENTS*

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Background: In 2013 less than 40% of the Biliary Atresia patients followed at Children's Hospital Colorado liver center had normal vitamin D levels. Inadequate vitamin D can have significant clinical impact on bone health, bone fractures, and growth.
Objective: Global Aim: To improve serum vitamin D levels in Biliary Atresia patients presenting at Children's Hospital Colorado who are cholestatic.
SMART Aim (Specific, Measurable, Attainable, Relevant, Time bound):
Improvement in 70% of Biliary Atresia patients under the age of 2, with total bilirubin greater than 2 mg/dL and documented vitamin D deficiency. Vitamin D deficiency was defined as <30 for vitamin D 25 OH ng/ml or <16 pg/ml for vitamin D 1.25 from January - December 2014.
Methods: Identify vitamin D levels in all patients meeting above criteria by completing manual chart audits of patients within identified population. Email primary hepatologist alerting them to vitamin D deficiency and suggest change in supplementation for vitamin D. Monitor quarterly vitamin D levels to assess for improvement and give feedback to primary hepatologist if further supplementattion may be needed to increase serum vitamin D levels.
Results: Baseline data 2013 showed 38% patients had normal vitamin D levels within the identified population of Biliary Atresia, under the age of 2, with total bilirubin greater than 2 mg/dL and documented vitamin D deficiency.
First quarter data 2014 showed improvement in 74% of patients in this population with 57% having normal serum vitamin D levels.
Second quarter data 2014 noted improvement in 91% of patients in this population with 55% within normal serum vitamin D levels.
Third quarter data showed improvement in 92% of patients in this population with 77% within normal range for serum vitamin D levels.
Fourth quarter data demonstrated 92% of population with improvement with 75% within normal range for serum vitamin D levels.
Conclusion: Nursing monitoring and suggested changes in vitamin D supplementation improved the serum vitamin D levels in 92% of patients within the Cholestatic Biliary Atresia population under the age of 2.

358 *DEVELOPMENT OF A PEDIATRIC ENTERAL TUBE PROGRAM: A BASELINE NEEDS ASSESSMENT*

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Background: In recent years, both the type and frequency of enteral tube placements has increased in the pediatric patient population. This increase is likely attributed to longer survival rates of children with complex medical needs as well as general advances in medical technology. A 2011 nursing-led prevalence audit at Boston Children's Hospital (BCH) revealed that 40% of our inpatients had some type of enteral tube in place; of those tubes, 42% were identified as "troublesome" by the patient, staff, or caregiver. In addition, 34% of respondents reported that they would benefit from and desire additional enteral tube education. Therefore, as an institution, nursing, physician, case management, and hospital leadership began to recognize that enteral tubes represented a potential high-risk area for complications and resource utilization (prolonged hospitalizations, recurrent emergency room visits and readmissions), as well as an area for improving patient education and care coordination. These collaborative efforts led to the development of an Enteral Tube Program.
Aim: To perform a baseline assessment of hospital resource utilization of patients who underwent primary gastrostomy tube (G-tube or GJ-tube) placement, in order to develop future targeted quality improvement interventions.
Methods: A chart audit of patients who underwent primary gastrostomy tube placement between May 2013 and December 2014 was performed.
Results: 431 patients were included. 311 (72.5%) patients underwent general gastroenterology consultation prior to the decision for G-tube placement. Although 327 (76.9%) patients completed a recommended two week post-operative tube check, almost half (208, 48.3%) of patients did not return for a recommended 4-6 gastroenterology evaluation and only 250 (58%) had a nutritional reassessment during this time period. In addition, 149 (34.5%) completed follow-up with a feeding therapist within 2-months of their G-tube placement and 151 (35%) returned to their primary gastroenterologist for a 3-month re-evaluation. 13 (3%) patients required hospital readmission within 30 days of their initial tube placement, with the most common reason for readmission being cellulitis (23%) requiring intravenous antibiotics.
Conclusions: Primary enteral tube placement is commonplace with most patients being assessed by a gastroenterology

provider perioperatively. Although major complications requiring rehospitalization were minimal within the first month, a notable decline in subsequent gastroenterology, nutrition, and feeding reassessment was identified within the first three months following tube placement. Therefore, with the development of a multi-disciplinary Enteral Tube program, we will hope to optimize the quality of care of patients with enteral tubes by improving patient care coordination after tube placement, improving long term follow-up rates and monitoring of patients remaining tube dependent, and increasing patient and family education surrounding tube care and maintenance.

359 *MULTIDISCIPLINARY FEEDING TEAM APPROACH: USING A MEDICAL, MOTOR, AND BEHAVIORAL APPROACH*

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Introduction: Feeding difficulties in children are complex and result from both medical and behavioral problems. Given the multi-faceted causes of feeding difficulties, these children are most effectively served in a multidisciplinary clinic utilizing a team approach.

Background: The first three years of life are critical for the development of feeding skills. Approximately 20-30% of young children worldwide have feeding difficulties (Meadows, 2015). Traditionally feeding difficulties have been treated by therapists. This may not allow for medical or dietary evaluation and management. A multidisciplinary team is helpful to assess all aspects of why a child does not eat well. These teams are typically comprised of gastroenterology, speech pathology, and nutrition. The team approach enables evaluation by many specialists who work closely together to maximize care. There has been limited research in children with feeding difficulties and no research comparing a multidisciplinary with a more traditional approach. A multidisciplinary team from the University of Glascow found that 78% of 41 referrals to their program were no longer requiring tube feedings after utilizing the team approach. This typically took 1.7 years (Edwards et. al, 2015).

Case: 2 year old male presented to pediatric feeding team for complaints of limited oral intake, and gastrostomy tube dependence. Past medical history included congenital diaphragmatic hernia, GERD, constipation, underweight, and multiple formula intolerances. Oral intake consisted of a few bites of chewable foods with frequent episodes vomiting on a proton pump inhibitor (PPI) 1 mg/kg/day. He received five bolus feedings of Compleat pediatric formula daily. He was evaluated by a feeding team, including a speech pathologist, nutritionist, and pediatric nurse practitioner. At the first visit his PPI dose was increased to 2 mg/kg/day. The speech pathologist implemented a behavioral feeding program, with a goal of four ounces of puree three times per day. The nutritionist changed his gastrostomy tube feeding schedule from five bolus feedings daily to three small bolus feedings during the day, and slow continuous feedings overnight. As his vomiting improved, cyproheptadine (0.25mg/kg/day divided twice daily) was added, puree volumes were increased, and his gastrostomy tube feedings were decreased. He was weaned off all tube feedings four months from his initial visit and his gastrostomy tube was removed three months later.

Summary: Research is lacking regarding whether using a multidisciplinary approach is effective in treating children with feeding difficulties. This particular child had great benefit from this method and all members of the team contributed to the plan. Further research is needed to assess the effectiveness in children who are treated for feeding difficulties using a multidisciplinary approach.

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360 *ASSESSMENT OF A REGISTERED NURSE DRIVEN FECAL MICROBIOTA TRANSPLANTATION (FMT) PROCEDURE IN THE AMBULATORY SETTING*

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Background: The incidence of Clostridium Difficile (C. diff) in pediatric patients is on the rise. The current standard of care for the treatment of C. diff include Metronidazole as a first line therapy and Vancomycin for recurrent infections. Unfortunately, current antibiotic therapy is costly and often does not resolve the infection in pediatric patients. Use of Fecal Microbiome Transplant (FMT) has been studied for the treatment of recurrent C.diff infections with resolution of infection as high as 87-89%. FMT can be administered via colonoscopy or through a nasoduodenal or nasogastric tube (NGT). Here we describe a nurse-driven FMT program, developed using NGT FMT administration in an ambulatory setting, with the goal of reduced cost and improved patient outcomes.

Objective: To assess the efficacy of an RN driven NGT administration of FMT in pediatric patients with recurrent C.diff.

Methods: FMT was approved at the Childrens Hospital Colorado in February of 2015. Eligible patients include inpatient and outpatient pediatric patients, ages 1 year to 21 years with a diagnosis of recurrent C. diff infection , described as having failed 2 courses of antibiotics (including at least once course of oral Vancomycin), demonstrating continued symptoms and

a positive C. Diff PCR. Patients are evaluated for inclusion or exclusion criteria and consented by a provider from the pediatric gastroenterology or infectious disease .Premedication and procedures are ordered by provider. The FMT RN then confirms the procedure time and date, as well as premedication regimen with the family by phone. On the procedure day, the RN performs a time out, then places a NGT. NGT placement is confirmed by pH and X-ray. Once gastric positioning of the NGT is confirmed, the nurse administers the fecal microbiota solution (OpenBiome). Upon completion of the procedure, the NGT is removed and the patient is discharged. One week after the procedure, the RN performs a follow-up phone call to evaluate and assess response to the FMT procedure.
Results: A total of 7 patients, 4 females and 3 males, ages 2 to 18, have received a FMT in the ambulatory clinic at CHCO. 6 of the 7 patients became asymptomatic post procedure. 2 patient required retransplantation for recurrence of symptoms.
Conclusion: RN driven FMT procedure performed in an ambulatory clinic can provide a safe, effective, less invasive and less expensive alternative for the treatment of recurrent C.diff.

361 *AVOIDANCE OF MULTIPLE FOODS IN THE TREATMENT OF EOSINOPHILIC ESOPHAGITIS IS A CHALLENGE IN A CLINIC SETTING*

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Introduction: Eosinophilic Esophagitis (EoE) is an immunomodulated esophageal disease triggered by exposure to food allergens. Symptoms of EoE include difficulty swallowing, food impaction, vomiting, slow eating or pain with eating, which place children at risk of malnutrition. The current therapies for treating EoE are dietary elimination or swallowed steroids. Swallowed corticosteroids are an effective treatment, however, that does not identify the underlying food antigen and there are potential concerns with its long term use in children. The six food elimination diet (SFED) - avoiding dairy, soy, wheat, eggs, nuts, and seafood - as dietary management for EoE is an alternate strategy for long term treatment of EoE and in the identification of food allergens. This review was done to review our practice and the efficacy of the SFED in the treatment of EoE in the clinic setting outside of clinical trials.
Method: Retrospective chart review of cases EoE patients treated with SFED.
Results: Ten patients were identified from our EoE clinic who used food elimination strategies to treat their EoE. The mean age of diagnosis was 11 years old (range 3 to 17), there were 7 males and 3 females, and 9 out of 10 patients initially fulfilled our diagnostic criteria for EoE as having greater than 15 eosinophils per high power field (Eos/HPF), while on acid suppression. One patient had classical EoE changes and esophageal narrowing but Eos/HPF between 5 to 15.
Seven patients started the SFED and three are currently going through the diet elimination. Three patients who tried the SFED were non responders and went on to be treated with topical corticosteroids. Four patients completed the food elimination diet until they identifed their food triggers for EoE. One was found to react to dairy only after six scopes and remained in remission. Another was found to react to milk and egg. Two patients had normal endoscopies and biopsies after avoiding all six foods but relapsed while still avoiding 4 foods. They both eventually switched to topical steroids due to poor adherence to diet elimination. Of the three currently going through the SFED, all have responded to avoidance of all six foods and are all still in remission. So far, one has had had soy introduced, another has had egg and soy reintroduced successfully and the third patient has had wheat, soy, and baked egg reintroduced.
Conclusion: In our clinic setting, almost a third of our small cohort are primary nonresponders to the SFED. Those who reacted to multiple foods have difficulty adhering to the diet elimination. Alternative stragegies are needed to identify those who react only to 1 or 2 foods because they are more likely to adhere to food elimination as a treatment for their EoE.

362 *IMPROVECARENOW: A MODEL FOR COLLABORATIVE AND QUALITY CARE*

Alicia Smith. GI, Children's Hospital Colorado, Aurora, CO

Background: There is variability in the care of patients with pediatric Inflammatory Bowel Disease (IBD) across institutions and even among providers within the same institution. From the time of diagnosis, appropriate testing should be done in order to correctly classify disease based on location, extent and severity. Knowing this will guide treatment. Once diagnosed and treatment has begun, standardizing routine labs and medication dosing are recommended. Being a part of a multi-center collaborative where guidelines are followed can positively impact outcomes of children with IBD.
Objective: To improve remission rates of patients with IBD using guidelines endorsed by ImproveCareNow (ICN)
Methods: Patients are initially diagnosed and properly classified using lab work, biopsies and imaging to evaluate the disease phenotype, extent and severity in order to properly treat the patient. For each clinic visit, a Pre-Visit Planning form is generated to anticipate needs such as routine labs, dosage changes, frequency of visits, etc. The provider completes the ICN Smart Form, which allows for data to be uploaded. Every two weeks, we get reports back showing several metrics such as remission rate, disease classification bundle completion, growth and nutrition status and much more. On a quarterly basis, PDSA cycles are generated to ensure patient quality and safety. For example, we review steroid usage to ensure patients have a tapering plan and are on PPIs, calcium and vitamin D and that they have a follow up appointment if necessary. As an offshoot to this, we've developed and implemented an inpatient steroid use plan that is part of the discharge summary to ensure providers address this. We also review data regarding frequency of appointments. We review

patients who haven't been seen in 200 days and make phone calls to know if they still follow with us and if so, make an appointment. If they have transitioned to adult GI or moved, we remove them from ICN to ensure data accuracy.
Results: Disease classification bundle completion has increased from 71% in 2011 to 95% as of April 2015. Remission rate has also improved from 68% to 73% in the same time frame.
Conclusion: By being a part of a multi-center pediatric IBD collaborative, we have been more consistent in accurately classifying the diagnosis, thus ensuring proper therapeutic regimen. By assuring quality and safety measures related to medication use, reviewing data on a regular basis and making changes at either the patient level or for the whole population, remissions rates have improved.

363 *FAMILIAL PATTERNS OF NON-SYNDROMIC INTESTINAL FAILURE IN A LARGE PEDIATRIC PROGRAM*
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Background: Maldevelopment of the midgut may result in a variety of birth defects including intestinal atresia and malrotation. In contrast, defects in the formation of the anterior abdominal wall may result in birth defects such as gastroschisis. There has been much speculation about the etiology of these conditions, but a clear, causative factor has yet to be distinguished. There have been several case reports of familial intestinal failure due to intestinal atresia and gastroschisis. Furthermore, a recent whole exome sequencing study identified mutations in the *TTC7A* gene in a 5 patient cohort with multiple intestinal atresias. Since then, several other patients with multiple intestinal atresias and compromised immunodeficiency have been found to have *TTC7A* mutations. These early findings suggest that there may be a genetic etiology in certain types of intestinal failure.
Methods: We performed retrospective review of medical records and obtained detailed family history from 3 patients with familial intestinal failure. These included a parent-child dyad with gastroschisis, and a parent-child dyad and a sibling dyad with intestinal atresia.
Results:
Case #1: Parent-Child Gastroschisis
Patient #1 was diagnosed with gastroschisis at 20 weeks gestation and was born at 35 weeks' gestation with a closed abdomen, foreshortened intestine and jejunal atresia. His father was born with gastroschisis and underwent primary surgical closure in the neonatal period. His mother is healthy. He has no siblings. His only notable family history is a maternal half-aunt with Marfan syndrome.
Case #2: Parent-Child Intestinal Atresia
Patient #2 was born at 35 weeks' gestation with multiple atretic segments of jejunum beginning at 18 cm from the ligament of Trietz. She has additional medical history notable for multiple central venous catheter (CVC) associated thromboses. Her mother was born with intestinal atresia and a reported 25 cm of small bowel remaining. Her father has dyslexia and acquired traumatic brain injury sustained as an adult. She has no siblings.
Case #3: Sibling Intestinal Atresia
Patient #3 was born at 34 weeks gestation with malrotation and jejunal atresia. She has 10 cm of small bowel remaining plus her full colon. Her sister was born at 33 weeks gestation with malrotation and 2 proximal jejunal webs without break in serosal continuity. She has no other siblings. Her parents are both healthy.
Conclusion: Familial patterns of congenital intestinal failure have been described previously in the literature, and we have observed multiple cases of first degree relatives with either gastroschisis or intestinal atresia in our large, multidisciplinary pediatric intestinal rehabilitation program. Eliciting and documenting a thorough family history and referring patients with familial intestinal failure to clinical geneticists will help build on this knowledge base and will lead to an improved understanding about possible genetic contributions to these conditions.

364 *TEAM SUCCESS: DEVELOPING A COMPREHNSIVE EDUCATIONAL PROGRAM FOR PATIENTS DIAGNOSED WITH CONSTIPATION AND/OR ENCOPRESIS CONSIDERING HEALTH LITERACY RECOMMENDATIONS*
Jennifer J. Willoughby, Angela Turner. Gastro, Cincinnati Children's Hospital Medical Center, Aurora, IN
INTRO
"Nearly half of all American adults--90 million people--have difficulty understanding and using health information, and there is a higher rate of hospitalization and use of emergency services among patients with limited health literacy. Limited health literacy may lead to billions of dollars in avoidable health care costs."
"Health Literacy: A Prescription to End Confusion," Institute of Medicine, 2004
Annually over 1000 children are seen as new visits in our outpatient GI clinic at Cincinnati Children's Hospital for evaluation and treatment of constipation (ICD code 564.00) and/or encopresis (ICD code 787.6). A new visit patient is often allotted 30 minutes of time to include:
MD/APN evaluation
Physical exam

Establish treatment/plan of care
Education on diagnosis and treatment plan/goals
While education of our patients and families is a priority in care, clinic flow needs often dictate the amount of time providers can spend on the education of patients and their families. Families too may have distractions during the clinical consultation and do not retain all of the information that they receive during the visit. Supplementing verbal education with user-friendly written educational materials is essential to improving communication and helping patients and families retain education.
Internal and external customers have asked for written materials in the management of children with constipation. Referring community physicians look to CCHMC for educational materials to help educate patients and families. A focus group conducted by the CCHMC Patient/Family Education Program reported that families wanted more diagnosis specific information. During a review of types of educational materials needed within our GI practice, staff requested development of patient/family education materials addressing constipation/encopresis.
PURPOSE
Through the use of printed, health literacy approved educational materials, we aimed to:
Reduce literacy challenges associated with discharge instructions, medications and health education materials
Provide visual reinforcement strategies for patients and families for the management of constipation/encopresis
Improve accessability of educaitonal materials to health care providers (HCP)
IMPROVEMENT MODEL METHOD: Continuous Improvement Model
IRB Study #2014-6577
Worked with team of providers to create written educational materials that met hospital's reqirements for health literacy. Surveyed families/patients/community HCP on satisfaction of content of materials. Feedback utilized to change/improve educational materials.
FINDINGS
Have received 58% patient/family survey responses
100% read all or some of written the materials at home
100% found the material "easy to read"
85% would not make changes with the folder
92% reported inforamtion would help child's success
10% of surveyed HCP's responded to Survey Monkey
There was a distinct difference in what sections of the folders HCP and parents found most helpful
CONCLUSIONS:
Creating educational materials that meet helath literacy guidelines has been critical to:
Increasing knowledge of diagnoses
Reinforcing verbal edcuation
Providing home resource for review of education
Partnering with referring HCP's
Next steps include evaluating how the materials effect success of prescribed treatment

365 *INVESTIGATION OF OBESE CHILDREN EATING HABITS*
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Background and objectives: Childhood obesity is one of the most serious public health challenges of the 21st century. Obesity is defined as "abnormal or excessive fat accumulation that presents a risk to health". There are multiple factors (e.g., genetic, social, and environmental) that contribute to unhealthy weight gain. Obese children are likely to stay obese into adulthood and more likely to develop noncommunicable diseases like diabetes and cardiovascular diseases at a younger age. The aim of this study was to investigate the eating habits of obese patients.
Patients and Methods: : Of 30 obese patients (5-15 years old), analyzed with WHO Anthro-Plus, were included in this study. Anthropometric characteristics and frequency of food consumption were asked in the survey. BMI for age Z score above +2 SD value which is considered obese.
Results: Patients percent of the foods they consume every day: 88,5% bread, 76,9% fruits, 69.2% cheese, 61,5% milk, yogurt, 50% egg. Patients percent of the foods they consume every other day: 42,3% chocolate-candy, 30,8% toast-bagel, 53% meat, 38,5% rise-pasta.
42.3% of patients consumed legumes 1-2 times per month.
Conclusion: Obesity caused by a caloric intake greater than needed to meet the metabolic needs of the body. Changes in eating habits with genetic susceptibility factors are most emphasized in recent years. Individual adequate, balanced and healthy diet, especially to gain the right eating habits in childhood reduces the risk of cardiovascular diseases, diabetes, cancer and so on. It is important for the dietary habits acquired in childhood to increase in cognitive ability and. school performance. As a result, it determining has done to raise awareness of family about eating habits of obese patients

admitted to our clinic with this work, also in our region which food is considered to increase the risk of obesity.

366 *JAG1 - A BENIGN POLYMORPHISM OR ALAGILLE SYNDROME: AN 8 YEAR OLD MALE PRESENTING WITH FAILURE TO THRIVE*

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Introduction

JAG1 mutation is generally diagnostic of Alagille Syndrome (ALGS). Alagille Syndrome is a rare genetic disorder that affects bile flow from the liver secondary to fewer than normal bile ducts. In its most classic presentation, it affects the liver in the form of cholestasis, heart, eyes, spine and kidneys.

The Case

An eight year old male presented with failure to thrive and elevated liver enzymes. Initial workup did reveal elevation of AST (low 74U/L high 94U/L), ALT (low 400U/L high 549U/L) along with elevation of GGT low of 94 U/L high of 254U/L. Hyperbilirubinemia is not present. Ultrasound was normal with report of renal hypoplasia. Metabolic, autoimmune and infectious workup was negative. Esophagogastroduodenoscopy and liver biopsy revealed an H-Pylori infection and a virtually normal liver biopsy aside from small bile ducts. After 6 months of continued liver enzyme and GGT elevation a second liver biopsy was performed and it was without interval change and note of focal lobular inflammation.

Findings

Additional workup was requested for Jaundice Chip Resequencing Array. Results were consistent with: JAG1 Allele 1: c.2612C>G (p.P871R) that is considered a sequence variant that represents a benign polymorphism. Because of liver and kidney involvement we pursued further work up including: chest x-ray, echocardiogram and EKG, eye exam for posterior embryotoxin, fecal elastase and UA. Results revealed posterior embryotoxon, Pancreatic Elastase low at 109ug/g, chest x-ray without vertebral anomalies. ECG was normal and Echocardiogram revealed normal intracardiac structural anatomy no chamber enlargement, ventricular dysfunction, or pathologic flow disturbances.

Discussion

Initially, ALGS was diagnosed based upone 3 out of 5 criteria: (1) cholestasis, (2) evidence of cardiac disease (3) skeletal abnormalities, (4) ocular anomalies and (5) characteristic facial features until genetics came along. In this case, this boy was 8 years old at the time of presentation, cholestasis was present with elevation of the GGT and liver enzymes however no other obvious facial characteristics or paucity of intrahepatic bile ducts were present to suggest Alagille Syndrome. For diagnosis this case illustrates abnormal intrahepatic bile ducts, posterior embryotoxon, renal hypoplasia and pancreatic insufficiency with support of positive genetic findings consistent with ALGS. In summary, using genetic testing in clinically relevant cases may help to provide appropriate diagnosis, as recognition of this Syndrome is essential to provide appropriate management to improve the clinical care and quality of life for this young boy. This case also supports that the described mutation should not be considered a benign polymorphism.

367*IMPROVING THE AWARENESS OF SAFETY WITHIN A DAY HOSPITAL FEEDING PROGRAM: A TEAM APPROACH TO ESTABLISHING A FALLS RISK PREVENTION PROGRAM*

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The primary goal is to establish an interdisciplinary process for the assessment and prevention of falls within a day hospital feeding program. A secondary aim is to increase awareness of patient safety within the interdisciplinary team. Background: Pediatric safety remains a high priority. In an effort to support the National Patient Safety Goal, for establishing a Fall Reduction Program, strategies have been introduced to decrease falls risk among inpatient pediatric patients. Factors shown to contribute to falls in the hospital setting may not be transferable to other settings. Children in a day hospital setting face unique challenges, including: development, modulation/arousal level, degree of refusal behaviors, and environmental factors. Specific strategies for promoting a culture of safety through a focus on a falls risk prevention program will be addressed. Methodology: A review of the literature revealed a dearth of evidence in the area of ambulatory pediatric falls risk assessment and prevention. There are several pediatric validated screening tools for the inpatient setting and one for the home setting. A taskforce consisting of nursing, occupational therapy, psychology and feeding specialists identified gaps in safety knowledge and practice. A modified version of falls risk screening tool was created and had good inter-rater reliability between nursing and occupational therapy. A tiered-intervention approach was developed based on patient observation, chart review, and anedeotcal experience. Created standard, job aide, and patient family education script. Multiple avenues were employed for staff education. The results of the screen were incorporated in our biweekly rounds, as well as in daily communication. Conclusions: Implementing a modified falls risk prevention program within an ambulatory Day Hospital Feeding program is not only feasible, but necessary in order to establish an increased awareness of safety. By utilizing this framework as a screening process to identify safety concerns, a more uniform safety dialogue emerged. Each member of our team became safety champions. Team members reported increased confidence with implementing and discussing safety guidelines with parents and patients and an increased understanding of how to identify and modify scenarios that could eventually lead to injuries. In general, by identifying this emphasis of safety. The staff verbalized

awareness and confidence in implmenting procedures for patient transportation and parent education against falls. Future study is needed to evaluate the efficacy and establish validity of a modified falls risk screen within an ambulatory setting. Nursing implications: Changing the culture of safety within an ambulatory setting takes a team approach. Utilizing a standardized falls risk prevention program afforded staff to have a more consistent resource and uniform approach to patient safety and empowered staff to engage in a more purposeful exchange of dialogue centered on patient safety. Nursing is a key position to be the stimulus for change

Friday October 9, 2015

CONCURRENT SESSION 2 – INFLAMMATORY BOWEL DISEASE

368 *INFLIXIMAB DOSING STRATEGIES AND TROUGH EXPOSURE IN CHILDREN WITH CROHN'S DISEASE*
Adam Frymoyer, K. T. Park. Stanford University, Palo Alto, CA
Background: An infliximab (IFX) trough concentration < 1 μg/ml is associated with poor response and/or loss of response in Crohn's disease (CD). Dose optimization including dose escalation has proved beneficial. In children with CD, trough concentrations achieved after standard IFX dosing are not known. Large variations in the pharmacokinetics of IFX in pediatric CD suggest a one-size fits all approach may be inadequate. The objective of the current study was to evaluate trough concentrations in children with CD receiving IFX maintenance therapy.
Methods: Using published IFX pediatric population pharmacokinetic data, we constructed an analytic tree simulating maintenance dosing strategies at 5, 7.5, and 10 mg/kg in children aged 6, 10, and 14 years, assuming 50% weight-for-age. IFX clearance was predicted by weight (WT), serum albumin (ALB), and concomitant immunomodulator therapy. We applied Monte Carlo methods to simulate the pharmacokinetic profiles for 1000 children at various dosing strategies. Infliximab antibodies were assumed not to be present. ALB levels were varied at 3, 4, or 5 g/dL in a sensitivity analysis. IFX trough concentrations before each dose during maintenance therapy were analyzed. Maintenance strategies were examined at dosing intervals of every 4, 6, and 8 weeks to assess optimal trough level achievement.
Results: Based on our model for a 10 year old receiving concomitant immunomodulator therapy, an IFX dose of 5 mg/kg every 8 weeks resulted in a median (IQR) trough of 1.3 (0.5-2.7) mcg/ml, 2.4 (1.0-4.8) mcg/ml, and 4.1 (1.9-7.9) mcg/ml for ALB 3, 4, and 5 g/dl, respectively. The proportion of children achieving an optimal trough >1 mcg/ml at week 14 was 59%, 75% and 86% for ALB 3, 4, and 5 g/dl, respectively. The minimum dose required to achieve trough >1 mcg/ml at week 14 in ≥85% of children was 5 mg/kg every 6 weeks for ALB 4 mg/dl and 7.5 mg/kg every 6 weeks (or 5 mg/kg every 4 weeks) for ALB 3 g/dl. Higher doses were needed to consistently achieve a trough > 3 mcg/ml. Results were similar across other age groups.
Discussion: In children with CD and ALB ≤3, standard IFX maintenance dosing of 5 mg/kg every 8 weeks frequently results in suboptimal IFX trough concentrations < 1 mcg/ml. Personalized IFX dosing strategies including therapeutic drug monitoring may be more effective in achieving sufficient drug exposure during IFX maintenance therapy, decreasing drug tolerance and development of auto-antibodies to IFX

369 *INCREASED EXPRESSION OF LRRK2, A SUSCEPTIBILITY GENE OF IBD RESULTS IN SUPPRESSION OF AUTOPHAGY AND ENHANCED INNATE IMMUNE RESPONSES MEDIATING COLITIS*
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Background: Many genetic risk loci have been identified by genome wide association studies in recent years within inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis. LRRK2/MUC19 locus has one of the strongest association in IBD. LRRK2 gene has been studied as a causative and susceptibility gene of Parkinson's disease. However the immunological function and the mechanisms about how this locus affects the pathogenesis of IBD remain largely unknown. The aim of this study is to investigate the immunological role of LRRK2 in the pathogenesis of IBD.
Methods: We used LRRK2 BAC transgenic mice (LRRK2 Tg) in Dextran sulfate sodium (DSS)-induced colitis. Bone marrow derived dendritic cells (BMDC) from LRRK2 Tg and littermate control (CTL) were used to examine immunological function, through Immunoprecipitation and western blotting analysis to find the binding partners of LRRK2.
Results: LRRK2 Tg exhibited more severe DSS induced colitis than CTL. BMDC from LRRK2 Tg and CTL were stimulated with various TLR ligands including zymosan, a yeast wall extract. We found that TLR2 and TLR4 ligands did not show an increased response in LRRK2 Tg. However zymosan induced significant increase in TNF-a synthesis in LRRK2 Tg. As Zymosan can stimulate Dectin-1 we next stimulated BMDC with Dectin-1 agonists such as zymosan depleted (ZymD), a more specific ligand for Dectin-1, heat-killed Saccharomyces cerevisiae (HK-SC) and heat-killed Candida albicans (HK-CA). These stimulations significantly increased TNF-a production in LRRK2 Tg compared to CTL. To investigate the role of LRRK2 in Dectin-1 signaling, BMDC were stimulated with ZymD and the phosphorylation of NF-KB molecules were examined by western blotting. BMDC from LRRK2 Tg showed increased NF-KB signaling

compared to CTL. To identify the binding partners of LRRK2, HEK293T cells were transfected with TAK1, NEMO, TRAF6 and TAB2 expressing plasmids and the immunoprecipitants were subjected to western blotting. We found that these signaling molecules interacted with LRRK2. . In addition, we found that LRRK2 in synergy with TAB2 interacts with and causes Beclin-1 inactivation with subsequent inhibition of autophagy. Such inhibition led to a paracrine increased LRRK2 expression and augmented pro-inflammatory LRRK2 activity. Finally, LRRK2 inhibitors diminish pro-inflammatory cytokine production by Crohn's disease dendritic cells (DCs) and led to diminished DSS colitis.
Conclusions: These results indicate that increased expression of LRRK2 leads to increased inflammatory responses. LRRK2 through Dectin-1 signaling activates NF-KB signaling while decreasing autophagy. Patients with Crohn's disease express increased LRRK2 in the colonic mucosa and LRRK2 phosphorylation was increased during the course of DSS colitis leading to proinflammatory cytokines production in response to gut microbiota-derived innate immune stimuli. Finally, LRRK2 inhibitors diminished Crohn's disease dendritic cells (DCs) pro-inflammatory response and diminished DSS colitis. Thus LRRK2 is an emerging therapeutic target in IBD.

Friday October 9, 2015

CONCURRENT SESSION 2 – NEUROGASTROENTEROLOGY AND MOTILITY

370 *STUDY OF PEG 3350 IN PEDIATRIC POPULATION*

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Background: PEG 3350, widely used to treat constipation in children, may contain ethylene glycol (EG), diethylene glycol (DEG), or tri-ethylene glycol (TEG) that could be absorbed into the bloodstream. We examined blood levels of these 3 compounds in a cohort of control and PEG 3350 treated children.
Method: Nine children (7-12 y/o) with chronic constipation receiving 17 grams of PEG 3350 daily for ≥ 2 weeks were evaluated. Each participant brought the bottle of PEG 3350 that they had been using at home and measured out two doses. One dose was mixed in 6 ounces of tap water provided by a research nurse, and the other dose was stored for later analysis. A blood sample was drawn prior to drinking a morning dose. Subsequent blood samples were drawn every 30 minutes for 3 hours after the participant took their daily dose. Blood samples were also taken from 18 age and sex-matched controls to assess background levels of EG, DEG and TEG in the general pediatric population. To evaluate whether EG, DEG, and TEG found in blood samples could be from tap water, weekly random water samples were taken (n=8) from the water source used for the study. Levels were measured in blood, stored samples of PEG 3350, and tap water by liquid chromatography-mass spectrometry (LC-MS/MS) using multiple reaction monitoring.
Results: Baseline EG (514.3±270.8 ng/ml) and TEG (2.73± 2.54 ng/ml) levels in the 9 children on chronic PEG therapy did not differ from EG (537.0±446.1 ng/ml, p = 0.82) and TEG (10.3±12.5 ng/ml, p = 0.30) levels in the control group. Baseline DEG levels were lower in children receiving PEG 3350 than in controls (46.6±18.8 vs. 272.4±655.1 ng/ml, p=0.008). After ingestion of 17 grams of PEG 3350, blood levels of EG increased, peaked at 90 minutes (1102.2± 348.8ng/ml, p=0.006 vs baseline), and remained elevated at 180 minutes (970±222.2ng/ml, p=0.018). Blood levels of TEG increased over baseline at 30 minutes (15.69±9.70ng/ml, p=0.0057), peaked at 90 minutes (33.57±24.88ng/ml, p=0.0094) and remained elevated at 180 minutes (25.58ng/ml±19.1ng/ml, p=0.031). Blood levels of DEG never elevated significantly over baseline at any time point. Average levels of EG, DEG, and TEG in the PEG 3350 samples taken from study participants were 18.4±3.2, 2.5±0.4, and 1.6±0.2 µg/g, respectively. EG, DEG, and TEG levels in tap water were 29.8±26.1, 391.9±275.4, and 7.9±8.9 ng/ml, respectively.
Discussion: In our pilot study, chronic use of PEG 3350 in children with constipation did not result in sustained elevation of EG, DEG or TEG blood levels compared with matched controls not using PEG 3350. This suggests all children have exposure to these compounds from their environment. EG levels were the highest of the 3 compounds evaluated, but the amount of EG in a standard 17 gram dose of PEG 3350 is far less than the amount that the U.S. Department of Health and Human Services have adopted as the minimal risk level for EG (0.8mg/kg/day) from daily environmental exposure for intermediate-duration (15-364 days). Carefully controlled studies in additional experimental settings will be required to clearly understand the biological relevance of these compounds in infants and children not only from PEG 3350, but also from the environment.

Friday October 9, 2015

CONCURRENT SESSION 2 – NUTRITION

371 *THE BACTERIAL COMMUNITY OF THE SMALL INTESTINE IN CHILDREN WITH SHORT BOWEL SYNDROME*

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Small bowel bacterial overgrowth (SBBO) is among the most common infectious complications associated with Short Bowel Syndrome (SBS).[1] The human gastrointestinal tract contains hundreds of bacterial species, but only a small fraction can be identified by traditional culture methods.[2] Improved diagnostic tools are needed to improve detection and guide treatment of SBBO in these patients. In this prospective study, we used next generation sequencing (NGS) to characterize the microbiota of SBS patients who were undergoing endoscopies as part of routine management. We compared a cohort of stable SBS patients (ages 2-10 years) receiving parenteral nutrition (PN) to SBS patients who had transitioned to enteral feeds. The study population was composed of 8 SBS patients on PN, 11 SBS off PN and 3 controls. All patients had at least two weeks off antibiotics prior to sampling.

We found that the Shannon bacterial diversity scores between all jejunal and stool samples were significantly different (P-value 0.001), with the jejunal samples demonstrating greater diversity (Figure 1). Both jejunal and stool samples were dominated by the phyla Proteobacteria and Firmicutes (Figures 2,3). *Enterococcus sp*. and *Lactobacillus sp*. had the highest relative abundances in the Firmicutes phyla while *Klebsiella sp.* and *Escherichia coli* were the most abundant Proteobacteria. These results are in agreement with jejunal cultures taken at the time of sampling, which also were dominated by *K. pneumoniae* and *E. coli.* Patients without SBS had greater amounts of *Bacteroidetes sp*. of which *Bacteroides fragilis* and *Prevotella melaninogenica* were the most relatively abundant species.

Bacterial diversity scores between jejunal and stool samples in SBS patients receiving enteral feeds were significantly different (P-value 0.03). In patients receiving PN, there was less difference between jejunal and stool samples, suggesting a loss in bacterial diversity in the jejunal samples of patients receiving PN (P-value 0.065) (Figure 4). Patients without SBS had generally greater diversity scores, but low enrollment precluded further analysis. LEFSe analysis was performed, but did not identify a particular Operational Taxonomic Unit (OTU), or bacterial species, responsible for the difference between patients.

Although the colon is accepted to be the portion of the GI tract with the greatest quantity of micro-organisms, our results suggest that the jejunum is a rich environment with a complex microbial community. We found there is an overall loss in microbiota diversity in SBS, which is amplified in patients receiving PN. Further prospective studies are needed to determine more drastic changes in the microbiota are observed in association with clinical symptoms of SBBO. This study suggests that NGS assays could be developed to better diagnose SBBO.

References:

[1] Gutierrez et al. J Pediatr Surg. 2012 Jun;47(6):1150

[2] Manson et al. Adv Exp Med Biol. 2008;635:15-28.

PLEASE NOTE THAT GRAPHICAL REPRESENTATIONS OF OUR FINDINGS (FIGURES 1-4) ARE AVAILABLE, BUT COULD NOT BE UPLOADED INTO THE ONLINE ABSTRACT SUBMISSION FORM

Friday October 9, 2015

CONCURRENT SESSION 2 – UPPER GI TRACT

372 *EMPIRIC FOUR FOOD ELIMINATION DIET INDUCES REMISSION IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS AND SUBSEQUENT REINTRODUCTION IDENTIFIES FOOD TRIGGERS*

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, food protein-induced immune-mediated disorder of the esophagus. Empiric six food elimination diet (SFED) is effective for inducing clinical and histologic remission in children and adults with EoE. We previously identified milk, wheat, egg and soy as the most common food triggers for SFED-treated patients. In this prospective study, we tested the hypothesis that a four food elimination diet (4-FED) will induce remission in a majority of children with EoE.

Methods: Children diagnosed with EoE based on expert panel guidelines were enrolled in this prospective multicenter study and empirically eliminated milk, wheat, egg and soy from their diet. After 6-8 weeks of dietary intervention, clinical, endoscopic and histologic responses were assessed. The primary treatment endpoint was histologic remission defined as esophageal peak eosinophil count <15 eosinophils per high power field (eos/hpf). A secondary endpoint was identification of specific food triggers in those who responded to 4-FED.

Results: Fifty-five children (75% male, mean age 9.3 years, 78% white, 91% atopic) were treated with 4-FED. Abdominal pain (53%), slow eating (37%) and dysphagia (37%) were the most common presenting symptoms. Endoscopic findings

included: furrowing (82%), edema (74%), white exudates (62%) and rings (14%). Histologic remission was achieved in 39 (71%) subjects with pre and post treatment peak eosinophil counts of 66±11eos/hpf and 6±2 eos/hpf respectively ($p<0.001$). Thirty-nine of 55 (71%) subjects had a greater than 50% reduction in peak eos/hpf following 4-FED. In 82% of responders one or more of their presenting symptoms resolved following 4-FED. Improvement in the severity of endoscopic findings was seen in 83% of the responders with 34% completely normalizing. Specific food triggers identified based on histology in 26 (67%) children included milk in 14, egg in 7, soy in 5 and wheat in 3 children. A single food trigger was identified in 18 (69%), two foods in 4 (15%) and three foods in 1 (4%).
Conclusion: A majority of children treated with 4-FED achieved histologic, endoscopic and clinical improvement. 4-FED is an effective dietary treatment option to treat children with EoE and compares favorably with SFED.

373 *CHEMICAL AND MECHANICAL STIMULI DRIVE ESOPHAGEAL FIBROBLAST ACTIVITY: IMPLICATIONS FOR EOE FIBROSIS*

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BACKGROUND & AIMS: Eosinophilic esophagitis (EoE) is an immune-mediated allergic disease characterized by progressive esophageal dysmotility and fibrotic stricture associated with chronic esophageal fibroblast activation. In EoE, subepithelial fibroblast activation results in increased extra-cellular matrix deposition and stiffness. Fibroblasts have also been shown to activate on stiff substrates even in the absence of cytokines in models of liver and lung fibrosis, however it remains unknown how esophageal fibroblasts respond to matrix stiffness or inflammatory cytokines. In this study, we sought to determine how the EoE-associated microenvironment mediates fibroblast activation and fibrogenesis. METHODS: Primary esophageal fibroblasts from adult and pediatric patients with or without EoE were exposed to TGFβ to determine gene expression, collagen-matrix contractility, and cytoskeletal organization. The influence of matrix stiffness upon fibroblast behavior was assessed on the engineered surface of polyacrylamide gels with varying stiffness. Single cell fibroblast traction forces were measured using microfabricated-Post-Array-Detectors. RESULTS: TGFβ stimulation not only enhanced fibroblast-specific gene expression of α-smooth muscle actin (α-SMA) ($p=0.03$), collagen ($p<0.0001$), and fibronectin ($p=0.0001$), but also promoted fibroblast-mediated collagen-matrix contraction (13% increase, $p=0.01$), despite patient age or phenotype. Fibroblasts seeded on softer gels had quiescent morphology, decreased cell proliferation, and decreased activation as measured by α-SMA expression by qRT-PCR and immunofluorescence. Fibroblasts seeded on stiff gels had increased spindle morphology, increased proliferation, and increased α-SMA expression. Furthermore, fibroblasts seeded in a soft environment stimulated with TGFβ had little nuclear localization of phosphorylated SMAD3 compared to those on a stiff matrix. Fibroblasts from all phenotypes (EoE and non-EoE adults and children) exhibited consistent findings of proliferation and morphology when placed on matrices of similar stiffness. We found that fibroblasts seeded on softer posts generated traction forces on average of 4.8 nN/post whereas those on stiff posts generated 31.6 nN/post ($p=0.0001$). CONCLUSIONS: Esophageal fibroblasts are highly responsive to the stiffness of their environment. Fibroblasts transdifferentiate in a stiff environment despite the absence of cytokines or a proinlammatory mileu. Furthermore, matrix stiffness may critically influence TGFβ-mediated gene expression and functions of esophageal fibroblasts *ex vivo* independent of age and disease conditions. These findings provide a novel insight into the pathogenesis of fibrostenotic disease in EoE.

Saturday, October 10, 2015

PLENARY SESSION II

Fellow Research Award

374 *AN INNOVATIVE MUCOSAL IMPEDANCE DEVICE DIFFERENTIATES ACTIVE EOSINOPHILIC ESOPHAGITIS FROM INACTIVE DISEASE, NERD, AND CONTROLS*

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Introduction: Eosinophilic esophagitis (EoE) is a chronic pediatric GI disease that continues into adulthood. Assessment of disease activity and treatment success requires repeated endoscopies with biopsies. EoE compromises the epithelial barrier causing eosinophilia and spongiosis (dilated intercellular spaces (DIS) due to edema). Other than histologic assessment, no techniques accurately measure the mucosal effects of chronic esophageal exposure to injurious agents. A minimally invasive mucosal impedance (MI) device was developed to detect changes in electrical impedance as a result of DIS. The simple technique performed during esophagogastroduodenoscopy (EGD) adds about 3 minutes of procedure time. Adult studies validated the device's ability to detect conductivity changes between normal and inflamed esophageal mucosa. MI

validation in the pediatric EoE population could significantly reduce costs and risks of repeated endoscopies.
Methods: We evaluated esophageal MI in 85 patients (ages 1-18 yrs.) scheduled for routine EGD for GI complaints. Subjects included: 1) active EoE (n=16, esophageal biopsy with $\geq$ 15 eosinophils (eos) per high power field (hpf)), 2) inactive EoE (n=7, post therapy EoE with $\leq$ 15 eos per hpf in all biopsy specimens), 3) non-erosive reflux disease (NERD) (n=21, normal EGD with abnormal histology and/or pH-impedance), and 4) controls (n=26, normal EGD and histology). There were 14 patients that did not meet the criteria for any of the categories. MI measurements (in Ω) were obtained at 2, 5 and 10 cm above the squamocolumnar junction. Pathologists blinded to MI measurements reviewed biopsies from the 3 sites assessing epithelial changes, including inflammation, spongiosis and eosinophilia. Spongiosis was graded on an ordinal visual scale (normal, mild, moderate or severe). The Kruskal-Wallis test and proportional odds regression tested associations of MI with the four diagnostic groups, spongiosis severity, and eos counts.
Results: Esophageal MI measurements were significantly lower in active EoE at 2 cm, 5 cm and 10 cm [median 941 Ω; 1238 Ω; and 1653 Ω, respectively)] ($p< 0.001$) compared to inactive EoE [3599 Ω, 2979 Ω, and 3382 Ω], NERD [2686 Ω, 3115 Ω and 3794 Ω], and controls [3044 Ω, 3438 Ω and 3722 Ω] (Table 1). There was a statistically significant inverse correlation between MI measurements with both eos counts ($p< 0.001$), and spongiosis severity ($p< 0.001$).
Conclusions: 1) MI measurements provide immediate results of esophageal mucosal inflammation in pediatric patients. 2) Active EoE patients have significantly lower MI measurements than other patients. 3) MI measurements inversely correlate with eosinophil counts and spongiosis severity. 4) This novel device has the potential to provide immediate, less invasive disease monitoring in pediatric patients with EoE, thus significantly reducing costs and risks of repeated endoscopic evaluation.
MI Measurments by Diagnostic Category

	N	NERD N=21	Active EoE N=16	Inactive EoE N=7	Control N=26	P-value
2 cm	84	1800 [2686] 3322	634 [941] 1218	2458 [3599] 4150	1910 [3044] 3885	<0.001
5 cm	83	1957 [3115] 5230	1062 [1238] 1571	2480 [2979] 4232	2641 [3438] 4200	<0.001
10 cm	84	1926 [3794] 4795	1282 [1653] 2094	2392 [3382] 5320	2932 [3722] 4996	<0.001

a [b] c represent the lower quartile a, the median b, and the upper quartile c MI measurement in Ω for continuous variables.

YOUNG FACULTY INVESTIGATOR AWARD

375 *LOSS OF NUCLEAR RECEPTOR LRH-1 SENSITIZES INTESTINAL EPITHELIUM TO INFLAMMATORY INJURY*

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BACKGROUND. Current therapies for inflammatory bowel diseases (IBD) are aimed primarily at immune suppression. Targeting the multipotent intestinal stem cells (ISCs) that fuel the regeneration and healing of the intestine has the potential to enhance wound healing and reconstitution of the epithelial barrier that is compromised in IBD. Liver Receptor Homolog-1 (LRH-1, also known as NR5A2) is expressed in the intestinal crypts where the ISCs reside. This nuclear receptor interacts with the WNT/β-catenin pathway, drives intestinal corticosteroid production, and when absent exacerbates experimental colitis. We are investigating the role of LRH-1 in ISCs with respect to cell renewal, epithelial barrier function, and inflammatory response with the aim of developing a relevant intestinal tissue model system amenable to drug discovery.
Methods: To evaluate the contributions of LRH-1 to intestinal growth and epithelial integrity, we employed the intestinal organoid system utilizing mice harboring conditional LRH-1 knockout in ISCs (Lrh^{isc}) and intestinal epithelium (Lrh^{vil}). Lrh1 knockout was achieved by *in vitro* activation of an inducible Cre driver under control of the Lgr5 or Villin promoter for Lrh^{isc} and Lrh^{vil}, respectively. Following *Lrh1* knockout, the Lrh^{isc} and Lrh^{vil} organoids were evaluated for growth and viability using multiple metrics. To probe the effects of LRH-1 loss on organoid susceptibility to inflammatory injury, we treated intestinal organoids with TNFα and measured viability and epithelial integrity using MTT reduction, dextran exclusion, and immunofluorescence imaging. We complement our knockout studies with a novel use of the AAV system to humanize LRH-1 (hLRH-1) expression in the organoids and add-back LRH-1 function.
Results: LRH-1 ISC knockout reduces the rate of crypt proliferation and slows ISC-driven epithelial turnover as evidenced by diminished EdU incorporation and proliferative antigen Ki-67 staining. Epithelial tight junctions are distorted with LRH-1 knockout, resulting in increased epithelial permeability as demonstrated by dextran exclusion. Staining for Zona Occludens-1 suggests disordered tight junction formation following LRH-1 knockout. Moreover, intestinal organoids deficient in LRH-1 expression are more susceptible to TNFα-mediated inflammatory epithelial damage. AAV-mediated expression of hLRH-1 rescues viability in TNFα injury model and up-regulates corticosteroid producing enzymes Cyp11A1 and Cyp11B1.

Conclusions: LRH-1 intestinal knockout results in reduced epithelial cell growth, compromises epithelial integrity, and enhances susceptibility to inflammatory damage. Epithelial viability is rescued by AAV expression of hLRH-1. Our results suggest LRH-1 is a viable target for novel, epithelium-targeted IBD therapy. Intestinal organoids facilitate functional studies of epithelial integrity and may serve as a tool for evaluating and developing LRH-1 agonists. Finally, we demonstrate that the AAV system is a viable method to express controllable levels of target protein in the intestinal organoids.
Support: K12 HD07222, F32 CA163092, T32 DK007762

YOUNG FACULTY CLINICAL INVESTIGATOR AWARD

376 *PANTOPRAZOLE PHARMACOKINETICS IN OBESITY: WHERE GENES AND SIZE COLLIDE*

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Background: Overweight children (≈ 30% pediatric population) are at higher risk for gastroesophageal reflux disease (GERD). Yet, no guidelines exist on dosing proton pump inhibitors (PPIs), the mainstay of GERD therapy, in this growing patient population. The aim of this prospective study was to evaluate differences in the pharmacokinetics (PK) of pantoprazole (CYP2C19 substrate) in overweight vs. normal-weight children. Methods: Using TaqMan techniques, 52 children with GERD (6-17yrs) were genotyped for *CYP2C19* loss-of-function (**2, *3, *4*) and gain-of-function (**17*) alleles. After a single oral dose of pantoprazole [1.2mg/kg of Lean Body Weight (LBW)], plasma samples were collected at 10 time-points over 8hrs. Pantoprazole and its CYP2C19 catalyzed metabolites were measured in duplicate by HPLC with UV detection. Plasma data were analyzed via standard non-compartmental approach (Kinetica 5.0) to generate PK parameters of interest [e.g., apparent elimination rate constant (Lz), systemic exposure (AUC_{tot}), apparent clearance (CL/F) and apparent volume of distribution (VD_{ss}/F)]. Parameters were compared between overweight/obese (BMI $\geq 85^{th}$ percentile, n=24) and normal-weight (BMI 10-84^{th} percentile, n=25) children, using a 2-tailed unpaired t-test and Spearman's correlation ($\alpha=0.05$). Three subjects, homozygous for 2 loss-of-function or gain-of-function alleles, were excluded to avoid skewing of results. All subjects were included in a one-way ANOVA ($\alpha=0.05$) to examine the effect of *CYP2C19* genotype on drug disposition (**1*1*, n=24; **1*17*, n=15; **1*2*, n=7; **2*17*, n=3; **2*2*, n=2, **17/*17*, n=1). Results: No statistically significant differences were found in pantoprazole PK in overweight/obese vs. normal-weight children (Table). No differences were noted when data were normalized for LBW, ideal body weight or total body weight. A positive correlation emerged between AUC_{tot} and BMI ($r^2=0.4$; p=0.01). Independent of weight status, mean AUC_{tot} for pantoprazole was 2-fold greater in children with 1 loss-of-function vs. 1 gain-of-function allele (p=0.01). Except **2/*17*, CL/F was increased in children with one or two **17* alleles (p<0.03). In the wild-type group (*1/*1, n=24), CL/F was significantly reduced (0.25±0.1 vs. 0.41±0.23 L/h/kg; p<0.05) and AUC_{tot} increased (5.3±3.5 vs. 3.1±1.5 mg*h/L; p=0.05) in overweight/obese vs. normal-weight children. In a subset of obese children (BMI $\geq 95^{th}$ percentile), AUC_{tot} was significantly higher than normal-weight children (8.1±4.6 vs. 3.1±1.5 mg*h/L; p<0.05). Conclusions: *CYP2C19* genotype appears to be a primary determinant of pantoprazole PK in children, whereas BMI may explain individual variability within genotype groups. A CYP2C19 activity score, similar to that of TPMT for azathioprine/6-Mercaptopurine, may be advantageous in the dose-selection of pantoprazole; particularly, if long-term PPI therapy is anticipated.

PK Parameter	Normal Weight (n=25)	Overweight / Obese (n=24)	p-Value
Lz (1/hr)	0.90 ± 0.25	0.79 ± 0.27	0.15
CL/F (L/hr/kg)	0.43 ± 0.23	0.29 ± 0.17	0.05
VDss/F (L/kg)	0.61 ± 0.31	0.47 ± 0.33	0.19
AUCtot (mg/L*hr per 1mg/kg dose)	3.83 ± 2.66	4.24 ± 2.75	0.60

Table: Selected pharmacokinetic parameters for pantoprazole in overweight/obese vs. normal-weight children; parameters normalized to toal body weight.

BALISTRERI PRIZE

377 *SELECTIVE SEROTONIN REUPTAKE INHIBITORS HAVE CRITICAL AND LONG-LASTING EFFECTS ON ENTERIC NERVOUS SYSTEM DEVELOPMENT AND GASTROINTESTINAL FUNCTION*

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The use of selective serotonin reuptake inhibitors (SSRIs), the most common antidepressant used in pregnancy, has increased from 1.5% of pregnancies to 6.4% over the last decade. *In utero* SSRI exposure is associated with a two-fold

increased risk of congenital malformations though little is known about the effects of maternal SSRI use on gastrointestinal (GI) tract development and function in resulting progeny. A recent study, however, determined that these children require laxatives 10 times more often than children not exposed, demonstrating a likely impact of *in utero* SSRI exposure on intestinal motility.
SSRIs block the serotonin reuptake transporter (SERT) thus stopping inactivation of serotonin (5-HT) and resulting in enhanced serotonergic neurotransmission. Abnormal intestinal 5-HT signaling changes many parameters of GI physiology including enteric nervous system (ENS) development and GI motility. We thus hypothesized that SSRI exposure during neurodevelopment would affect these parameters.
Dams were administered the SSRI fluoxetine or vehicle from E1 to P21 (weaning from breastfeeding). Pups did not receive fluoxetine from P21 to time of testing at 6-8 weeks of age. Changes demonstrated were thus the result of developmental changes that occurred during early development. Whole mount immunocytochemistry was used to quantify total and late-developing neuronal subsets (which serotonin is known to affect). *In vivo* total, small intestinal, gastric and colonic transit was measured. To determine whether motility was the same without brain influence, colonic migrating motor complexes (CMMCs) were evaluated *in vitro* by spatiotemporal mapping. Additional mice underwent chemical sympathectomy with 6-hydroxy-dopamine (6-OHDA) to determine the role of sympathetic signaling in gut motility. Similar experiments were conducted in mice that congenitally lack SERT (SERT KO) to determine whether the consequences of fluoxetine exposure are due to SERT antagonism versus off-target effects of fluoxetine.
The ENS of fluoxetine-exposed mice contained significantly more total and late-born (CGRP-expressing, dopaminergic, gabaergic) neurons in both plexuses than that of vehicle-exposed mice. SSRI exposure thus increases the ability of early-born serotonergic neurons to promote development of late-born cells. Fluoxetine-exposed mice also demonstrated significantly longer colonic, small intestinal and total GI transit times. Paradoxically, the frequency and velocity of CMMCs were significantly increased in isolated colons of fluoxetine-exposed mice. 6-OHDA normalized *in vivo* transit time in fluoxetine-exposed animals; therefore, fluoxetine exposure enhances sympathetic outflow, which slows in vivo motility. Sympathetic input is eliminated when gut is isolated. Similar experiments on SERT KO mice emphasized that the defects induced by SSRI exposure are due to SERT antagonism rather than off-target drug effects.
These observations suggest that SSRI-exposure during development potentiates developmental actions of 5-HT, which leads to long-lasting abnormalities of the ENS and the GI functions it controls. These studies also provide insight into the potential pathogenesis of some congenital GI disorders and suggest caution in the use of an SSRI during pregnancy.

ODELL PRIZE

378 *HUMAN INDUCED PLURIPOTENT STEM CELL-DERIVED EXTRACELLULAR VESICLES REVERSE HEPATIC STELLATE CELL ACTIVATION*

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Background &Aim: Stem cells, and in particular induced pluripotent stem cells (iPSCs) represent a promising therapeutic approach for fibrotic diseases. However, their use is currently limited by issues such as scaling up production and eliminating cells with tumor-forming potential. Extracellular vesicles (EVs) are membrane surrounded structures released by cells, including iPSCs and contain a footprint of the cell of origin. Here we tested the hypothesis that iPSC-derived EVs (iPSC-EVs) have an anti-fibrogenic effect on hepatic stellate cells (HSC), the key cell involved in liver fibrosis. Methods: Human iPSC were generated as previously described (Israel MA et al., Nature, 2012). iPSC-derived EVs were isolated by differential centrifugation, quantified by FACS and characterized by dynamic light scattering and electron microscopy. Human HSC (LX2) were maintained in a quiescent-like phenotype by low-serum media and then treated with TGF-β (10ng/mL) in presence or absence of iPSC-EVs or EV-free media for up to 16h. Analysis of HSC phenotype, proliferation and chemotaxis were evaluated. Internalization of iPSC-EVs into HSC was assessed by fluorescent tracing techniques. Results: Characterization of EVs identified microparticles (MP) as the main extracellular vesicle population released by iPSC. The fluorescent tracing assay detected iPSC-EVs internalized in HSC particularly after 6h of incubation with EVs. The exposure of HSC to iPSC-derived EVs induced a 2-fold down-regulation of the pro-fibrogenic genes α-SMA, Collagen1α1 and TIMP-2 compared to cells treated with TGF-β and EV-free media (EV+TGF-β vs. TGF- β or vs. MP-free media+TGF-β, $p<0.005$). A further analysis of the HSC responses occurring during fibrogenesis, showed that iPSC-derived EVs reduced HSC proliferation and chemotaxis by 1.5-fold compared to TGF-β and MP-free media+TGF-β-treated HSC ($p<0.05$). Previous studies showed that activated HSC may revert to an inactive phenotype (iHSC), which is similar, but distinct from quiescence (qHSC). Based on this, we observed that HSC exposed to iPSC-derived EVs share some quiescence-associated genes such as PPAR-γ, Nr1d2 and Foxj1 but showed a greater up-regulation of inactivation-associated genes, such as IL7R, Csf2rb and Ly86 compared to TGF-β-activated HSCs. Conclusions: Our study uncovers iPSC-derived EVs as a potential anti-fibrotic therapeutic approach and demonstrates that they activate regenerative programs in HSCs by inducing a phenotypical switch from activated to their inactivated state.

379 *PEDIATRIC ERCP IN THE SETTING OF ACUTE PANCREATITIS: A REPORT FROM THE MULTICENTER PEDIATRIC ERCP DATABASE INITIATIVE*

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Background: Acute pancreatitis (AP) in children is not uncommon and can occur secondary to etiologies treatable by ERCP. The effect of active AP on safety and outcomes in pediatric ERCP is unknown. This abstract presents preliminary data from the first prospective multicenter database designed to evaluate indications and technical outcomes after ERCP in a pediatric population.

Methods: With IRB approval, six centers entered consecutive ERCPs on children < 18 years into an electronic database. Pre-procedural forms were filled out prospectively while post-procedural, 2-week follow-up and adverse event forms were completed following each ERCP. Standardized definitions were used to define procedure difficulty grade, adverse events (AEs), and acute pancreatitis. Cases performed between 5/1/14 and 5/27/15 were analyzed. Patient and procedural characteristics, procedural success rates and AEs were compared for patients diagnosed with AP within the week prior to the procedure (pre-AP) to those not diagnosed with AP in the week prior (no pre-AP). Variables were compared using two-sided Fisher's exact test for categorical variables and the student t-test for continuous variables.

Results: 178 ERCPs were entered over the 13-month time period. 26 (15%) ERCPs were in the pre-AP group. Indications for ERCP in the pre-AP group included therapy for suspected choledocholithiasis (11, 42%), therapy of biliary stricture (3, 11.5%), therapy of obstructed choledochal cyst (2, 7.7%), evaluation of biliary obstruction of unclear etiology (1,4%), therapy of chronic pancreatitis with goal of improving drainage (3, 11.5%), therapy of pancreatic duct leak (3, 11.5%), therapy of pancreatic pseudocyst with transpapillary drainage (1, 4%), and therapy of acute recurrent pancreatitis with plan for sphincterotomy (1, 4%). Table 1 compares patient characteristics, indications and adverse events for patients in the pre-AP and no pre-AP group. In addition, there were no significant differences in cannulation time, mean procedure time, or mean fluoro time between the two groups.

Conclusions: In this study, the presence of AP at the time of ERCP had no effect on procedure success, length of stay post-procedure, or adverse events suggesting that pediatric ERCP can be safely and effectively performed in this setting when appropriately indicated.

Characteristic	Pre-AP Group	No Pre-AP Group	P value
N	26	152	
Mean age, yrs (95% CI)	11.0 (9.5-12.5)	11.3 (10.6-12.0)	0.78
Mean weight, kg (95% CI)	48.5 (37.6-59.5)	47.2 (43.2-51.1)	0.80
Indication: Suspected Choledocholithiasis	11 (42.3%)	59 (38.8%)	0.83
Indication: Any Pancreatic	9 (35.0%)	38 (25.0%)	0.34
Difficulty grade 3 or greater	11 (42.3%)	41 (73%)	0.16
ASA class 3 or greater	13 (50.0%)	47 (27.0%)	0.07
Procedure considered a success	24 (92.3%)	141 (92.7%)	1.00
Length of stay after procedure, days (95% CI)	6.5 (4.2-8.7)	4.3 (2.7-5.8)	0.26
Adverse events	1 (3.8%)	13 (8.6%)	0.69
Pancreatitis	0	7 (6 mild, 1 severe)	
Pain not due to pancreatitis	0	4 (3 mild, 1 severe)	
Bleeding	0	1 (moderate)	
Cholangitis	0	1 (mild)	
Fever without a source	1 (severe)	0	

Table 1: Comparison of patient characteristics, procedural indications and adverse events based on presence or absence of pre-ERCP pancreatitis.

380 *FACTORS ASSOCIATED WITH INADEQUATE BOWEL PREPARATION FOR COLONOSCOPY IN CHILDREN - A PROSPECTIVE STUDY*

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Introduction: Inadequate bowel preparation (IBP) for colonoscopy leads to missed diagnosis, longer anesthesia time, higher chance of complications and increased costs. Adult studies have demonstrated that some patient characteristics like male gender and obesity are associated with IBP. Little is known about factors affecting bowel preparation in children, which can be a major determinant of Quality evaluation of colonoscopy.

Aim: To determine factors associated with IBP in children undergoing colonoscopy.

Methods: We enrolled children undergoing outpatient elective colonoscopy. All patients received standard weight-based PEG 3350 bowel preparation. Quality of bowel preparation was assessed using Boston Bowel Preparation Scale (BBPS) score. BBPS is a validated cleanout efficacy scale, based on a rating of 0 to 3 per colonic segment (right colon, transverse colon, and left colon); a total score from 0 to 9 is calculated. Data collected included patient demographics, indication for colonoscopy, total anesthesia time, cecal intubation time and type of insurance. Patients were divided into two groups based on BBPS score - adequate (BBPS score ≥ 5) and inadequate preparation (BBPS score < 5) - and groups were compared using Student's *t*-test and Chi-square test. Possible predictors of IBP were analyzed using multivariate logistic regression models.

Results: A total of 98 children (age range 2-18 years; mean age 12.3 years; 71.4% female; 80.6% Caucasian) were enrolled. The mean BBPS was 7 (SD of ±1.9). IBP was reported in 19.4%; while IBP was seen in 26.9% of obese children compared to 18.8% of normal weight patients, the difference was not statistically significant (p value > 0.05). Multivariable logistic regression analysis did not show statistical differences between the groups in other studied patient factors including age, gender, race, insurance type, total anesthesia time and cecal intubation time (p value= >0.05).

Conclusion: Contrary to several adult studies, preliminary results of our ongoing study do not show any relationship between examined clinical factors and IBP in children. Interestingly, IBP was less prevalent in our pediatric study compared to published adult data (19.4 % vs 30-40%). Possible explanations for these divergent data and the lack of correlation with obesity include use of weight-based bowel preparation regimen in children and possible parental supervision. Recognizing predictors of IBP in children is important as a more intense regimen could be used proactively in patients at-risk for IBP. These are important medical-care delivery interventions since quality outcomes in endoscopy are being increasingly discussed. We anticipate further refinement in our data as more patients are enrolled in this ongoing prospective pediatric study.

Saturday October 10, 2015

CONCURRENT SESSION 3 – LIVER

381 *SURVIVAL OUTCOME SCORES (SOFT, BAR AND PEDI-SOFT) ARE ACCURATE IN PREDICTING POST-LIVER TRANSPLANT SURVIVAL IN ADOLESCENTS*

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Background: Quantitative prediction of survival outcome following liver transplantation (LT) can improve decision making in graft allocation and risk stratification. Scoring systems such as the Survival Outcomes Following LT (SOFT) and Balance of Risk (BAR) Scores utilize recipient, donor and graft factors to predict the 3-month post-liver transplant survival in adults (≥18years). More recently, the Pediatric SOFT (Pedi-SOFT) score was developed to predict 3-month survival after LT in young children (≤12 years). These scoring systems have not been studied in adolescent patients (13-17 years).

Aim: Evaluate the utility and accuracy of SOFT, BAR and Pedi-SOFT scoring systems in predicting the 3-month post-LT survival in adolescents.

Methods: We performed a retrospective analysis of data from UNOS of 711 patients aged 13-17 years who received LT between 03/01/2002 and 12/31/2012. Recipients of combined organ transplants, donation after cardiac death, and those with missing details for BAR, SOFT and Pedi-SOFT scores were excluded. Kaplan-Meier curves were used to assess 3-month post-LT survival using these scoring systems. Receiver Operating Characteristic (ROC) curve was used to assess the accuracy of these scoring systems in prediction of 3-month post-LT survival.

Results: A total of 711 adolescent LT recipients were included with a mean age of 15.2 ± 1.4 and a mean MELD score at LT of 19.7 ± 12.7. A total of 100 patients died after LT including 33 within 3 months. SOFT, BAR and Pedi-SOFT scores were all found to be good predictors of 3-month post-transplant survival outcome with areas under the ROC curve of 0.81(CI 0.67-0.95), 0.80(CI 0.73-0.88) and 0.81(CI 0.73-0.89), respectively. The 3-month post-transplant mortality increased by 10%, 20% and 5% for each 1 unit increase in SOFT, BAR, and Pedi-SOFT scores respectively ($p<0.001$).

Conclusion: All three scores provided good accuracy for predicting 3-month survival post-LT in adolescents and may help clinical decision making to optimize survival rate and organ utilization.

382 *MIXED LINEAGE KINASE 3 MEDIATES RELEASE OF C-X-C MOTIF CHEMOKINE 10-BEARING EXTRACELLULAR VESICLES FROM LIPOTOXIC HEPATOCYTES*

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Backgrounds and aims: Genetic deletion of mixed lineage kinase 3 (MLK3) reduces macrophage associated-inflammation in a murine model of nonalcoholic steatohepatitis (NASH). However, the mechanistic links between MLK3 activation in hepatocytes and macrophage-driven inflammation in NASH are uncharted. Herein, we report that MLK3 mediates the release of C-X-C motif chemokine 10 (CXCL10), laden extracellular vehicles (EVs) from lipotoxic hepatocytes, which induce macrophage chemotaxis. Methods: Primary mouse hepatocytes (PMH) and Huh7 cells were treated with palmitate or lysophosphatidylcholine (LPC), a toxic metabolite of palmitate. Released EVs were isolated by differential ultracentrifugation, quantified by nanoparticle tracking analysis, and their protein content profiled by mass spectrometry (MS). Hepatocyte MLK 3 was inhibited using genetic models and pharmacological agents (CLFB-1134 and URMC-099) Results: LPC treatment of PMH & Huh7 cells induced release of EVs, which was prevented by either genetic knock down or pharmacological inhibition of MLK3. Mass spectrometry identified the potent chemokine CXCL10 in the EVs. CXCL10 was markedly enriched in EVs isolated from LPC treated hepatocytes versus untreated cells. Green fluorescent protein (GFP) tagged CXCL10 segregated into vesicular structures co-localizes with the red fluorescent protein (RFP) tagged EV marker CD 63 following LPC treatment of Huh-7 cells as visualized by total internal reflection microscopy (TIRF) and confocal microscopy. Either genetic deletion or pharmacological inhibition of MLK3 prevented CXCL10 enrichment in EVs. Treatment of mouse bone marrow-derived macrophages with lipotoxic hepatocyte-derived EVs induced macrophage chemotaxis, an effect blocked by incubation with CXCL10 neutralizing antibody. MLK3 deficient mice fed a high fat, fructose and cholesterol (FFC) diet had reduced concentrations of total plasma EVs, and CXCL10 containing EVs compared to the FFC diet-fed WT mice. In Conclusion: during hepatocyte lipotoxicity, activated MLK3 induces the release of CXCL10-bearing vesicles from hepatocytes which are chemotactic for macrophages. We speculate that these EVs mediate hepatic inflammation *in vivo* by inducing macrophages trafficking to the liver.

Saturday October 10, 2015

POSTER SESSION III

ENDOSCOPY/QI/EDUCATION

383 *SUFFICIENCY OF RECTAL SUCTION BIOPSIES AND USE OF CALRETININ IMMUNOSTAINING: A SINGLE CENTER REVIEW*

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Introduction: Hirschsprung's disease (HD) is characterized by the absence of ganglion cells in the myenteric and submucosal plexuses, extending proximally from the rectum. Adequate rectal suction biopsy (RSB) sampling requires at least a 3mm sample, with one third of it being submucosa, for evaluation of ganglion cells. In the past, acetylcholinesterase (AChE) staining was routinely performed but, due to variable interpretation between pathologists, there has been a shift towards calretinin immunostaining (CI). Calretinin is normally present in the muscularis mucosa and lamina propria and when absent is indicative of HD. A normal calretinin stain has been found to increase the yield and decrease previously inconclusive pathology results by 12%.

Aims: Primary: To determine how efficient a single center pediatric gastroenterology practice is in obtaining sufficient RSB samples for evaluation of HD. Secondary: To determine if CI may be used as a surrogate in cases when there is insufficient mucosa to evaluate for ganglion cells.

Methodology: Retrospective chart analysis of all patients who underwent rectal suction biopsy (RSB) between 11/2012-12/2014.

Results: A total of 144 RSB were performed in 140 unique patients. 40% of patients were younger than 1 year and were predominately male. 5 patients were identified to have new diagnosis HD and 6 patients had established HD. 66% of RSB were performed as an outpatient with the primary indication of constipation. When relying solely on abnormal H&E stain, our overall sufficiency rate was only 49%. When the sufficiency was based on if CI was performed, the yield increased to 68%. Notably, all patients found to have normal CI did not have HD. Sufficiency of sampling significantly decreased by age; sufficiency was found to be 88% if patients were under a year of age and this decreased to 40% if patients were older than 10. There was no difference in sampling with gun type used.

Conclusion: Overall sufficiency sampling was low in our single center practice but normal calretinin staining in an insufficient sample can increase yield by 19% and may prevent further unnecessary testing and cost. A proposed algorithm

in the evaluation of these patients was proposed by our team in order to decrease the need for further interventions.

385 *VARIABLE USE OF DISACCHARIDASE ASSAYS AMONG PEDIATRIC GASTROENTEROLOGISTS EVALUATING ABDOMINAL PAIN*

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Background: The compound heterozygosity of congenital sucrase-isomaltase deficiency (SD) is becoming better understood; however, the clinical significance of SD in children with GI symptoms has not been thoroughly investigated. Recent work suggests the frequency of lactase deficiency (LD) is 42% and SD is >9% upon disaccharidase testing at the time of upper endoscopy (Nichols *et al*., 2012). The goal of this retrospective study was to determine the relative frequency of sucrase deficiency in a large cohort of children undergoing esophagogastroduodenoscopy (EGD).

Methods: Endoscopic records from patients who underwent EGD and were biopsied for disaccharidases activity were reviewed. These EGDs were performed from 2010 to 2015 at a free-standing endoscopy center serving 13 pediatric gastroenterologists. The analyses compared the frequency of EGD, the number disaccharidase biopsies performed and assay results.

Results: Among patients undergoing EGD (N=5,362), disaccharidase testing was performed in 963 (18%). The primary indication for performing EGD was abdominal pain (N=3,344). Among the physicians who performed an EGD in patients with abdominal pain, the percent of disaccharidase assays performed varied widely among physicians, ranging from 1.6% to 64.5%. Regression analysis revealed significant correlations between the number of EGD performed (N) and the number of patients found with SD (p=0.019), and LD patients (p=0.003) and significant correlations between the numbers of disaccharidase assays performed (Tested) and the number of SD and LD patients (for each, p<0.0001).

Conclusion: This study revealed a large degree of inconsistency among a single group of pediatric gastroenterologists with respect to the use of disaccharidase assays as a diagnostic aid, and the resultant number of patients with SD and LD. There is a need for further prospective studies on the prevalence and significance of disaccharidase deficiencies and the best diagnostic procedures to establish the diagnosis.

Disaccharidase Assays in Patients with Abdominal Pain

	N	Tested	%Tested	Sucrase Deficient	%Sucrase Deficient	Lactase Deficient	%Lactase Deficient
Total	3,344	963	28.8	73	7.6	430	44.7
Range	27-645	4-419	4.4-64.5	0-23	0-50.0	2-199	0.7-30.1

392 *A QUALITATIVE ANALYSIS OF BARRIERS AND FACILITATORS TO AN EFFECTIVE BOWEL PREPARATION FOR COLONOSCOPY IN CHILDREN*

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Introduction and objective: A well-visualized colon has a direct impact on the success of the colonoscopy, the interpretation of the findings and the need for repeat procedure. Inadequate bowel preparation may be associated with missed diagnoses, procedure related complications and increased resource allocations. Studies have been conducted in the adult population to assess factors contributing to improved bowel preparation for colonoscopy. Telephone re-education, physician-delivered education with written instructions or cartoon visual aids have been effective. No such studies have yet to be conducted in children. Therefore, the primary aim of this study was to determine if there were any barriers or facilitators to good bowel preparation with our current bowel preparation protocol.

Methods: A qualitative interpretive description approach was utilized. Children aged 5-18 years old, who had undergone elective colonoscopy within the last six months, and their parents, were recruited from the McMaster University Medical Centre Gastroenterology Clinic. Each participant had used our standard bowel preparation protocol and had received both verbal and written information about it. Semi-structured interviews were conducted using an interview guide, with questions assessing the education provided about the preparation, the understanding of the preparation protocol, and the compliance and tolerability of the preparation itself. Interviews were audiotaped, transcribed, and coded using a constant comparative method. Microsoft Excel was used to manage the data. Sample size was established when no new additional themes were encountered.

Results: Seven parents and seven children were interviewed; seventy percent of the children were above the age of thirteen. Emerging themes focused on participants' need for information. Fifty percent of subjects were satisfied with their bowel preparation instructions, and the remainder identified the need for further information (particularly, clarification of details regarding mixing the medication, NPO status and clear fluid instructions). Teenagers reported an interest in additional educational resources such as videos or websites. Parents were satisfied with a written handout. All subjects reported

disliking the taste of the medicine, but continuing to drink it anyway. Facilitators to a successful bowel preparation included ease of obtaining the bowel preparation, ability to contact the gastroenterology staff with questions, and having few side effects of the medication.
Conclusions: This is the first qualitative study identifying the challenges children face when undergoing bowel preparation for a colonoscopy. Individuals focused most on their informational needs. Identifying the barriers and facilitators to this process will assist in the development of tools to improve the experience and quality of bowel preparation for future patients.

393 *UNDERSTANDING THE DIAGNOSTIC YIELD AND CLINICAL IMPACT OF UPPER ENDOSCOPY FOR AN INDICATION OF FAILURE TO THRIVE*

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Background: Failure to thrive (FTT) is a diagnosis used to describe inadequate weight gain or inability to maintain appropriate growth. It is a complex medical and social problem and commonly results in extensive medical testing and hospital admission. The vast majority of children with FTT do not have underlying enteropathic disease. Despite this, upper endoscopy (EGD) is a frequently used diagnostic tool in this population and FTT is among the most common indications for EGD. To fill a knowledge gap, this study characterizes the findings and impact of EGD in a large cohort of patients with FTT.
Aims: The primary aims were to characterize a cohort of children who underwent EGD for an indication of FTT, to determine clinical factors associated with abnormal EGD biopsy histology and to determine the proportion of cases in which biopsy histology resulted in a management change.
Methods: 685 children underwent EGD for an indication of FTT between 2007 and 2014. Clinical characteristics including demographics, anthropometric measurements, symptoms, laboratory and radiologic findings, upper endoscopy results, and subsequent changes in management were determined by retrospective chart review. Descriptive statistics were used to characterize the cohort. Chi-square and t-tests were used to determine clinical variables that were associated with abnormal endoscopy findings and changes in management. To assess clinical and demographic variables associated with abnormal histology, we implemented logistic regression models.
Results: Of the 103 patients analyzed thus far, the mean age of the cohort was 18.7 months (SD 7.7 months), 53% were female and 86% were outpatients. The mean WHO weight-for-age percentile was 9.4 (SD 14.3), mean BMI percentile was 20.0 (SD 21.9), and mean weight-for length percentile was 18.4 (SD 21.9). 68% of patients had weight-for-length z-scores between 0 and -2, 73% of patients had weight less than WHO 3rd percentile on more than one occasion, and 25% of patients had abnormal histology. 43% of these abnormal findings were non-specific esophagitis. 27% revealed esophageal eosinophilia (>15 eosinophils/hpf). CRP and albumin differed in those with abnormal vs. those with normal histology. Patients with abnormal histology had mean CRP of 1.33 vs. 0.42 mg/dL among patients with normal EGD histology ($p=0.01$, aOR elevated CRP 0.85, 95% CI 0.75-0.98). Patients with abnormal histology had mean albumin of 4.02 vs. 4.4 in those with normal histology ($p<0.001$, aOR hypoalbuminemia 1.13, 95% CI 0.96-1.34). There were no other significant demographic, clinical, or laboratory differences between patients with and without abnormal EGD histology. Medical management was directly changed based on 25% of upper endoscopy results. The most common change in management was the initiation or increase in dose of PPI therapy. 7 of 103 patients were treated for eosinophilic esophagitis.
Conclusions: The most common histologic EGD finding in the setting of FTT was non-specific esophagitis. Clinical characteristics were not able to reliably distinguish patients with and without abnormal EGD. The most common change in management following EGD was change in PPI therapy. Initiating PPI therapy prior to EGD should be strongly considered in children with FTT.

394 *AWARENESS AND CURRENT KNOWLEDGE OF EOSINOPHILIC ESOPHAGITIS AMONG COMMUNITY PEDIATRICIANS*

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Introduction: Though eosinophilic esophagitis (EoE) was first described in 1978, regular diagnosis in children began in the 1990s. The past decade has seen a dramatic increase in children with EoE among gastroenterologists. This was attributed to increased awareness of EoE, but studies show that the incidence of EoE has also increased over time. Given that EoE can mimic reflux, often managed by primary care pediatricians (PCPs), and the diagnostic importance of upper endoscopy, recognition of EoE among PCPs is vital. Since EoE gained recognition only in the last 20 years, we hypothesized that awareness of EoE is low among PCPs.
Objectives: To assess current knowledge of EoE among PCPs.
Methods: All 1567 members of the Illinois Chapter of the American Academy of Pediatrics (ICAAP) were e-mailed an

anonymous survey of 16 multiple choice questions. The survey evaluated knowledge and practice of EoE.
Results: 135 pediatricians completed the survey (8.6% of recipients with typical response rate of 2-3%). 67.9% identify as PCPs. 85.2% reported office-based practice. Years in practice: 17.7% reported <5yrs, 15.3% 5-10yrs, 20.0% 10-20yrs, 47.1% >20yrs. 89.5% have seen or suspected EoE in a patient. 58.6% believe EoE affects primarily whites; 64.8% believe both genders equally. 42.1% reported feeding dysfunction as the most common finding in toddlers. Dysphagia and food impaction was believed to be the most common symptom in both school-age children (38.4%) and adolescents (53.5%). 60.2% affirmed a strong association with atopy. 100% identified that EoE is diagnosed by upper gastrointestinal endoscopy. 37.9% noted that the diagnosis of EoE is best established after a trial of proton pump inhibitor use. 72.6% reported inhaled glucocorticoids are not a treatment. 67.5% noted that fluticasone is the most commonly used drug. 83.7% reported untreated EoE can lead to esophageal strictures. For specialists used as consultants in EoE, 98.8% reported pediatric gastroenterologist, 52.2% pediatric allergist, 26.7% dedicated EoE clinic, 5.8% pediatric otolaryngologist, and 2.3% pediatric pulmonologist. 0% of respondents noted that they do not refer EoE patients to a specialist.
Conclusions: 1. The survey response rate and the majority of PCPs having seen or suspected EoE in patients suggests awareness of EoE is high.
2. However, less than half knew the most common symptom in toddlers (feeding dysfunction) and school-age children (nausea and vomiting), and only slightly more than half in adolescents (dysphagia and food impaction).
3. PCPs have more knowledge regarding referrals, treatment and complications.
4. Among Illinois PCPs, there is awareness of EoE and the need for referral, but a general lack of knowledge surrounding epidemiology and symptomatology. This may represent a significant barrier to timely referral.
5. Further PCP education would be helpful.

395 *CLOSTRIDIUM DIFFICILE UNDER THE MICROSCOPE: RATES OF C DIFF TOXIN DETECTION AND CLINICALLY-SIGNIFICANT COLITIS FOUND AT TIME OF PEDIATRIC COLONOSCOPY*

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BACKGROUND: The frequency of Clostridium difficile (CD) infection has increased over the past decade, with peak incidence in 1-4-yr olds. Since positive tests for CD toxin (CDT) may be misleading in children, it is important to limit testing and treatment to cases with meaningful disease. Children younger than 1-2 yr old rarely have severe disease, and the probability of clinically meaningful disease is low in children 2-5 yrs old. However, the prevalence of pathogens found at the time of endoscopy, and their correlation with meaningful disease, is largely unknown.
METHODS: A retrospective chart review of colonoscopies of 392 children between 2006-2013 was performed. Sigmoidoscopy and ileoscopy were excluded. All colonoscopes used were sterilized following industry accepted and validated techniques. Stool was aspirated thru the colonoscope at the time of the study, collected in a sterile lukens trap, and sent for cultures including CDT, stool culture for enteric pathogens, ova/parasite preparation, and Giardia/Cryptosporidium antigen. Endoscopy and histology reports were reviewed for evidence of inflammation. For patients who were CDT positive (CDT+), further data was collected regarding first-time vs recurrent diagnosis, and if the infection was treated with antibiotics. Categorical variables were compared between age cohorts of CDT+ patients.
RESULTS: Of the 392 colonoscopies reviewed, 349 were tested for CDT, of which 61 were CDT+ (17.5%). The age range for the CDT+ group was 1-21 years, with an average of 11.25 years, and with a female predominance (34 vs 27 patients). This was a first time diagnosis for 54 of the 61 patients (88.5%). The vast majority of CDT+ patients were 5 years of age or older (82%). Of the 11 patients age 1-4 years that tested positive, none had evidence of colitis. For the CDT+ colonoscopies, 26.2% had visual evidence, and 21% had histologic evidence of colitis. Accurate data regarding CDT treatment was available for 18 of 61 patients (30%). Of these 18 patients 11 (61.1%) were treated, and 7 of the treated patients did not have evidence of colitis. Separately, only 3 of the 351 tested (0.85%) had positive stool cultures for enteric pathogens (Pseudomonas (2), Salmonella (1)); 10 of the 351 tested (2.8%) had positive ova/parasite preparations (Yeast (7), Blastocystis (2), Endolimax (1)); and 1 of the 124 tested (0.8%) had positive Giardia antigen. In CDT+, there was an increased relative risk of colitis in those who took PPI (RR 2.89, $p = 0.02$) or biologicals (RR 3.75, $p < 0.001$) within 90 days of colonoscopy. Antibiotics, H2-blockers, and steroids were associated with higher, but not statistically significant risk of colitis in the CDT + population.
CONCLUSIONS: Colonoscopy can be a useful tool for assessing gastrointestinal pathogens. Given the prevalence of CDT and meaningful disease in our CDT positive cohort, obtaining CDT and stool culture at the time of colonoscopy should be considered as part of the evaluation.

CDT RESULTS SUMMARY

AGE (yrs)	TOTAL IN STUDY (n=392), (%)	TESTED FOR CDT (n=349)	CDT + (n=61),(%)	VISUAL COLITIS (n=16), (%)	HISTOLOGIC COLITIS (n=13), (%)
1-4	52 (13.3)	45	12 (19.7)	0 (0)	0 (0)
5-9	67 (17.1)	54	9 (14.7)	4 (25)	3 (23.1)
10-14	111 (28.3)	104	17 (27.9)	2 (12.5)	2 (15.4)
15-21	162 (41.3)	146	23 (37.7)	10 (62.5)	8 (61.5)

397 *SAFETY AND EFFICACY OF ENDOSCOPIC ASSISTED PUSH GASTROSTOMY USING GASTROPEXY*

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Background: Most pediatric gastroenterologists use an endoscopic pull technique to place gastrostomy tubes. We assessed an endoscopic gastropexy technique for gastrostomy placement that allows immediate placement of a low profile gastrostomy tube or gastro-jejunostomy tube. The procedure uses endoscopy to place three T-fasteners through the skin into the stomach, plicating and securing the stomach to the abdominal wall. This plication secures a stable gastrostomy tract, and facilitates the immediate placement of a low profile gastrostomy button or gastro-jejunostomy tube. Serial dilators are then used to dilate the tract to the desired diameter of the ostomy for the tube placement. The gastropexy technique is often used with laparoscopic procedures for gastric volvulus repair or difficult fundoplications; little has been published investigating the outcomes of pediatric gastrostomy tube placement by the gastropexy technique.

Objective: To study the safety and outcomes following gastropexy placement

Methods: Patient charts were evaluated for the immediate complications of (pain, bleeding, and infection), the long term complications of (feeding problems, pain, death, infection, bleeding and granulation), and for readmissions within the 3 months following placement.

Results: We studied 13 patients, aged 1- 16 years (mean 7 years) requiring gastrostomy feedings . A low profile gastrostomy tube was placed in 9 patients, and a gastro-jejunostomy tube in 4 patients. Weights ranged from 9 - 52 Kg (mean 24 Kg). Procedure duration ranged from 14 - 48 minutes (mean 25, mode 21, median 21 minutes). There were no deaths, infections or gastrointestinal bleeds. Pain control was with acetaminophen in 11, morphine in 4, ketorolac in 3, ibuprophen in 2, hydromorphone in 1, acetaminophen/hydrocodone in 1, and topical in 3. Pain control was required for 24 to 48 hours. Time to start feedings ranged from 6 - 18 hours (mean 9 hours). All patients received 24 hours of an antibiotic following the procedure. Long term complications were gastrostomy care visit in 3, gastrostomy malfunction in 2, granulation tissue in 2, gastrostomy site irritation in 1, gastrojejunostomy pain in 1 and jejunostomy dislodgment in 1. There were no readmissions for gastrostomy tube related issues. All external T-fastener buttons fell off spontaneously in 1 - 4 weeks post procedure period.

Conclusion: Gastropexy assisted placement of gastrostomy and gastrojejunostomy appears to be a safe and effective procedure. Complications are similar to those of endoscopic pull technique. The patients did not require a second procedure for low profile gastrostomy change or initial gastro-jejunostomy placement. The advantage of this procedure versus other one step devices is the ability to use any low profile tube with a balloon type of internal bolster regardless of manufacturer. Because the gastric wall is attached to the abdominal wall by pexy, losing the tract with accidental dislodgement of the feeding device is less likely than with other procedures. Another advantage is avoiding naso-jejunostomy tubes that are often used in patients who require jejunal feedings while the gastrostomy tract matures. Further prospective case control studies are needed to identify other risks and safety.

400 *FOVEOLAR MORPHOLOGY IN NORMAL GASTRIC TISSUE AND IN H. PYLORI GASTRITIS*

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Background: Foveolar hyperplasia in adults has been defined as increased length and tortuosity of foveolae, combined with expansion of the proliferative compartment, in association with chemical and H. pylori gastropathy. However, morphologic descriptions of foveolar anatomy in pediatric gastric mucosal biopsies (both normal and diseased) have not been clearly elucidated, and the criteria for foveolar hyperplasia in children have not been defined. The present study sought to determine foveolar morphometric characteristics in a population of pediatric subjects undergoing routine upper endoscopy to evaluate possible gastric inflammatory disease.

Methods: Biopsy specimens were examined from 59 children (ages 2-19 yrs) undergoing endoscopy for dyspeptic symptoms. Included were 37 biopsies read as histologically normal and 22 biopsies demonstrating H. pylori infection. No

patients had received treatment with NSAIDs; and 6 subjects (all normal) had received treatment with PPIs for a maximum of 60 days prior to study. Gastric biopsies (hematoxylin-eosin stained) were evaluated for mucosal thickness (MT), foveolar height (FH) and the FH:MT ratio.
Results: Statistically significant increases, both in gastric body and in antral mucosal thickness, with parallel increases in foveolar height, were detected in association with H. pylori gastritis (see Table). However, a no significant, between-group differences were observed in FH:MT ratios.
Conclusion: 1. These data indicate parallel increases, both in mucosal thickness and in foveolar height, may be associated findings in pediatric subjects with H. pylori gastritis; 2. Foveolar lengthening, independent of increased MT as reported in adult subjects with gastric inflammatory disease, does not characterize H. pylori gastritis in children.
Speculation: Foveolar lengthening, in the setting of gastric mucosal thickening, supports a histopathologic diagnosis of H. pylori gastritis in pediatric subjects.

Gastric Measurements	Normal		H.pylori	
	Antrum (um)	Body (um)	Antrum (um)	Body (um)
Mucosal Thickness(MT)	507.1	710.92	694.3***	818.64*
Foveolar Height (FH)	143.72	127.18	212.48***	189*
FH:MT	0.29	0.18	0.31	0.22

*P-value: <0.05, ***P-value: <0.0001

404 *PEG TUBE PLACEMENT IS A SAFE AND EFFECTIVE OPTION FOR THE NUTRITIONAL SUPPORT OF INFANTS WITH CONGENITAL HEART DISEASE*
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Introduction: Percutaneous endoscopic gastrostomy (PEG) has been thoroughly described in different facets of pediatric and adult medicine as a safe alternative to operative gastrostomy tube placement. Infants with congenital heart disease are medically complex and frequently require gastrostomy tube placement for nutritional support, fluid, and/or medications. We describe a retrospective series of infants with congenital heart disease who underwent the PEG Ponsky pull procedure as an alternative to operative gastrostomy tube placement. Patients and Methods: Following Institutional Review Board approval, the medical records of 19 sequential children who underwent PEG tube placement from September 2014 - May 2015 were reviewed.
Results: The population was 79% male and ranged in age from 1-24 months (mean age 5.7 months) and weight from 3.1 - 9.9 kg (mean 5.8 kg). The primary indication was long-term caloric supplementation. Cardiac diagnoses included septation defects, tetralogy of Fallot, myopathy, and hypoplastic left or right heart. Four patients had single ventricle physiology, pre-Glenn shunting and 5 had orthotopic heart transplantation. All patients underwent PEG tube placement via standard Ponsky pull technique with 14 Fr MIC PEG tubes (Halyard Health) using an Olympus XP180N gastroscope; two gastroenterologists were present at all procedures. Drains and/or pacer wires were removed prior to PEG procedure. Average tube placement time was 3.9 minutes. All patients received preoperative antibiotics; aspirin was continued, but other anticoagulant medications were held for the day of the procedure. PEG tube placements were performed both in the endoscopy suite (15) and in the cardiac catheterization lab (4). Complications were to limited bleeding (aspirin-related oozing) (1) and mild leakage at the gastrostomy site (1). No bowel perforations, infections, or gastroperitoneal dehiscence were noted. Growth expectations from gastrostomy tube feeding were uniformly met. Conclusion: The Ponsky pull PEG tube approach is a safe and effective option for the nutritional support of small children with congenital heart disease, and has distinct advantages over operative gastrostomy tube placement, including limited exposure to anesthesia and no need for pneumoperitoneum.

FUNCTIONAL/MOTILITY

*408 *EFFECT OF ANESTHESIA ON COLON MOTILITY: A PROSPECTIVE STUDY OF CHILDREN WITH CHRONIC INTRACTABLE CONSTIPATION UNDERGOING COLON MANOMETRY*
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Background: Colon Manometry (CM) is a useful test to evaluate the pathophysiology of defecation disorders. However, there is no standardization on its performance with some centers doing the study after anesthesia and others 24 hours later.

Information on the effect of anesthesia on colon motility is limited, and its effect on CM interpretation is controversial. Therefore, we compared the effect of anesthesia on colon motility and CM interpretation between the day of catheter placement under anesthesia (day 1) and the following day (day 2).
Methods: this was a prospective study that included pediatric patients undergoing CM for the evaluation of chronic intractable constipation. All patients received an inpatient PEG bowel clean out. On day 1, a colonoscopy and CM catheter placement were performed under anesthesia. CM was done on day 1 and repeated on day 2. CM protocol consisted of a fasting, post-prandial and post-Bisacodyl phase. To evaluate the effect of anesthesia on colon motility, the motility index (MI) of all 3 phases were measured and compared between both days. The number, presence and quality of high amplitude propagating contractions (HAPCs) were assessed and compared between both days. CM was considered normal if there was presence of fully propagated HAPCs. The same observer analyzed all traces blindly.
Results: 60 patients were included, 53% were male. Mean age was 9.5 years (1.5-18.8). Sevoflurane was used in 52% and Propofol in 48% of the patients. There was a significant difference on the MI between both days during the fasting and post-Bisacodyl phases (Table 1). The mean number of HAPCs was significantly higher on day 2 when compared to day 1 (10.1 vs. 6.6, p=0.01) as well as the proportion of patients having HAPCs on day 2 than on day 1 (92% vs. 70%, p=0.002). On day 1, 37% of the patients had fully propagated HAPCs, 33% had partially propagated HAPCs and 30% had absent HAPCs. On day 2, 49% had fully propagated HAPCs, 43% had partially propagated HAPCs and 8% had absent HAPCs. The overall interpretation of the study also changed. On day 1, 22/60 (37%) of the patients had a normal study and 38/60 (63%) had an abnormal study. On day 2, all of the patients that had a normal study on day 1 remained normal and from the patients with an abnormal study on day 1, 18/38 (47%) had a normal study and 20/38 (53%) remained abnormal. The mean anesthesia time between patients who had an abnormal study on day 1 was significantly higher than the patients who had a normal study (106.5 vs. 87.7 min, p=0.03). There was also a tendency for the mean anesthesia time to be longer on patients whose study remained abnormal on day 2 when compared to those that changed to normal (115.5 vs. 96.7 min, p=0.08).
Conclusions: colon motility, HAPC number, presence and quality and CM interpretation can change between day 1 and day 2. Anesthesia time may be a predictive factor of CM interpretation change. We propose that patients with an abnormal study on day 1 need to be studied again on day 2.

Colon Manometry	Day 1*	Day 2*	P Value
Fasting	8.13±0.32	9.66±0.21	0.0001
Post-Prandial	9.26±0.25	9.89±0.25	0.10
Post-Bisacodyl	9.66±0.27	10.66±0.18	0.003

*Mean Motility Index (mmHg*cm*sec) ±SEM

*409 *EFFECT OF ANESTHESIA ON ANTRODUODENAL MOTILITY IN CHILDREN*
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Background: antroduodenal manometry (ADM) provides information about the motor activity of the upper gastrointestinal (GI) tract. However the timing of its performance is not well established and the effect of anesthesia on GI motility in children is unknown. Therefore, we evaluated the effect of anesthesia on gastric and duodenal motility and ADM interpretation between the day of catheter placement under anesthesia (day 1) and the following day (day 2).
Methods: this was a prospective study that included patients undergoing ADM for evaluation of upper GI symptoms. The ADM study was divided in 4 phases: fasting (3-hours), post-prandial (1-hour), IV erythromycin (EES) challenge (1-hour) and SC octreotide challenge (1-hour). Motility index (MI) was measured on all phases and results were compared between day 1 and day 2. The ADM phases were analyzed and compared between day 1 and day 2, as well as the overall interpretation of the study between both days. The ADM was considered normal if there was presence of the migrating motor complex (MMC) during fasting, gastric and small bowel post-prandial response, gastric response to EES (when absent post-prandially) and presence of small bowel MMC with octreotide (when absent during fasting). The same observer analyzed all traces blindly.
Results: a total of 17 patients were included, 59% were male. Mean age was 9.4 years (1-18). Diagnosis was idiopathic in 88% of patients and short bowel syndrome in 12%. There was a significant increase in the antrum and small bowel MI in both antrum and small bowel from day 1 to day 2 during the fasting, post-prandial and EES phase (P<0.05). Fasting phase was evaluated in all patients. We observed presence of MMC during fasting on both days in 10 patients, absent in both days in 3 and, absent on day 1 on 4 patients that then became normal on day 2. A total of 11 children received meal challenge, 4 of those had normal response on both days and changed from absent to present in 2 patients. A total of 12 patients received EES, antral response was normal on 11 of those 12 on both days and in 1 it was abnormal on day 1 and normal on day 2. Four patients received octreotide, 3 of those had a normal response on both days and 1 had an abnormal response on day 1 and normal on day 2. No parameter changed from normal on day 1 to abnormal on day 2. We found the overall ADM

interpretation was normal in 4 patients on day 1 and abnormal in the remainder 13 patients. Those 4 patients with normal ADM on day 1 remained normal on day 2 and of those 13 with abnormal ADM on day 1 a total of 6 were normal on day 2, so the overall change in interpretation from abnormal to normal by day 2 was 6/17 (35%) patients or 6/13 (46%) of the abnormal studies on day 1.
Conclusions: We observed a significant increase in MI for both antrum and small bowel from day 1 to day 2 suggesting an effect from anesthesia on GI motility. More importantly, we observed a change on ADM study interpretation in up to 35% of studies. Prospective and larger studies are needed to evaluate the overall effect of anesthesia on study interpretation with its potential implications on predicting response to therapy and overall outcome.

412 *INCREASED INCIDENCE OF CELIAC ARTERY STENOSIS IN PATIENTS WITH POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME*

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Background & Aim: Postural orthostatic tachycardia syndrome (POTS) has an estimated prevalence of 170 per 100,000 people. POTS is associated with signs and symptoms including but not limited to dizziness, inappropriate tachycardia with postural change, fatigue, headache and abdominal pain. Celiac artery stenosis (CAS) associated with extrinsic compression, has an estimated prevalence of 1.7%. The aim of the study was to consider the prevalence of CAS in patients with POTS versus a non-POTS population.
Methods: Data were collected retrospectively in pediatric patients (ages 1 day - 18 years) undergoing echocardiogram (echo) studies for general cardiac questions at Nemours Children's Hospital from January 1, 2014 to March 31, 2015. We routinely study the abdominal aorta and its proximal branch vessels, including the celiac artery, as part of our echo protocol. Diagnosis of CAS was made if the celiac artery flow velocity by pulse Doppler was $\geq$ 2 meters/second and turbulent flow was evident. Follow-up imaging included magnetic resonance angiography.
Results: Data from 634 patients were reviewed, of which 59 had diagnosis of POTS. CAS was diagnosed in 8 patients in 634 patients (total incidence 1.3%). Five (3 girls; age 14.8 +/- 2.5 years) of 59 POTS patients had positive echo findings for CAS (8.5%) while 3 of 575 non-POTS patients had positive echo findings (0.5%, p=0.0003). The mean celiac artery flow velocity in the POTS group was 2.5 m/s (range 2-2.9 m/s) and 2.4 m/s (range 2-2.7 m/s) in the non-POTS group.
Conclusions: The incidence of CAS was found to be greater in the patient subset with POTS than in the subset without POTS in this pediatric population. These findings suggest that POTS and CAS are associated. In addition, these findings support the screening of POTS patients for CAS when characteristic symptoms are present.

413 *THE UTILITY OF ESOPHAGEAL HIGH RESOLUTION MANOMETRY TO PREDICT ACHALASIA IN CHILDREN*

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Background: Esophageal High Resolution Manometry (eHRM) is a widely available technique to evaluate dysphagia symptoms in children. In adults, the 4 second integrated relaxation pressure (IRP4s) has been used to characterize lower esophageal sphincter function and esophageal obstruction. To date, no study has evaluated the utility of the IRP to predict achalasia in children.
Aims: To determine the utility of the IRP4s to predict achalasia in a cohort of children with achalasia.
Methods: Following IRB approval, records at New York Presbyterian Hospital-Weill Cornell Medical College were reviewed for pediatric patients undergoing eHRM. Manometric studies were performed using the Manoscan Eso System (Given Imaging, USA) and solid-state catheters. Children with greater than 80% normal peristalsis and complete esophageal emptying based on barium fluoroscopy, impedance or other clinical criteria were considered control subjects. Children with greater than 20% abnormal peristalsis and evidence of esophageal obstruction by fluoroscopic, impedance or clinical criteria were considered achalasia subjects. Categorical data was evaluated using chi-squared tests. Continuous variables were compared using the Student's t-test. Receiver operator curve (ROC) analysis was used to determine the best IRP4s cut-point to predict achalasia.
Results: 16 children (9M) were identified as controls and 12 children (8M) identified as having achalasia. All achalasia subtypes were identified in the cohort: type 1 (n=3), 2 (5) and 3 (1). Control children were older than achalasia children (13.9±3.6y vs. 9.92±5.0y, p=0.021), but there was no difference in gender distribution. Mean esophageal length (22.7±2.7cm vs 20.6±4.6cm, p=0.14) and basal LES pressure (23.6±11.7mmHg vs 23.0±12.9mmHg, p=0.91) were similar between groups. However, the IRP4s was significantly greater in the achalasia group vs. controls (17.9±8.9 mmHg vs 7.0±3.6mmHg, p=0.0002). ROC analysis predicted an optimal IRP4s cut-point of 12.3mmHg, (empiric AUC=0.844, sens=75%, spec=93.8%, accuracy=85.7%, PPV=90%, NPV=83.3%, LR(+)=12, LR(-)=0.27). Based on this cut-point, 3 false negative results occurred in children with achalasia type 2 based on morphologic appearance of eHRM and esophageal obstruction on fluoroscopy. The single false positive case had normal fluoroscopy and 100% peristalsis eHRM

morphology.
Discussion: This study suggests that an IRP4s greater than 12.3mmHg is predictive of achalasia in children, particularly when used in conjunction with other clinical signs such as esophageal obstruction on barium fluoroscopy and abnormal peristalsis on eHRM. This finding is limited to studies performed using the Manoscan Eso platform and solid-state eHRM catheters, as adult studies suggest variation in absolute pressure measurements occur among motility platforms and catheter types. While this study reports on a large cohort of children with achalasia, this study may be limited due to its overall small sample size and difference in age ranges between groups.
Conclusions: IRP4s is a useful eHRM measure to aid in the identification of children with achalasia. Multi-center studies will provide additional support for the use of the eHRM measurements best suited to categorize esophageal outlet obstruction in children.

415 *MANOMETRIC FINDINGS DURING ATTEMPTED DEFECATION IN PEDIATRIC PATIENTS WITH CHRONIC CONSTIPATION*

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BACKGROUND: Chronic constipation is a common concern in children, accounting for 3% of general health visits and 35% of referrals to pediatric gastroenterologists. Up to 95% of the cases of constipation are functional. Dyssynergic defecation and inadequate defecatory propulsion may play a role in the etiology of chronic constipation and retentive fecal soiling in adults. No adequate investigation has being conducted to evaluate dyssynergic defecation in pediatric patients. Ano-rectal manometry (ARM) can be a useful study to investigate the etiology of constipation and to evaluate for abnormal physiology.
METHODS: A retrospective chart review was conducted in 20 patients, ages ranging 3 to 16 years, who were able to attempt defecation during the ARM and had an adequate intrarectal pressure. The mean sphincter pressure, residual anal pressure, percent anal relaxation and rectoanal pressure differential were analyzed using the Manoscan 360 by Given Imaging. Dyssynergic defecation was defined as inappropriate contraction of the pelvic floor or less than 20% relaxation of the basal resting sphincter pressure with adequate propulsive forces during attempted defecation.
RESULTS: A total of 5 patients had an anal relaxation that was less than 20 % (average percent anal relaxation of - 4.5%). The remaining 15 patients had a normal anal relaxation that was greater than 20% (average percent anal relaxation of 46%). The rectoanal pressure differential (residual anal pressure - intrarectal pressure) was higher in the group with adequate defecation compared to the group with dyssynergic defecation (44.3 vs. 4.52 mmHg, respectively). Thirty five percent of our patient population was found to have a negative rectoanal pressure differential (inability to generate a rectal pressure higher than the anal pressure during defecation). Encopresis was more frequently associated with dyssynergic defecation (42%) than to an abnormal rectoanal pressure differential (14%).
CONCLUSION: Inadequate relaxation of the sphincter pressure during defecation attributed to 20% of our manometric studies, correlating with the adult literature. Interestingly, patients with manometric findings of dyssynergic defecation were also found to have a decreased rectoanal pressure differential. Both of these findings together could then exacerbate symptoms of constipation and ineffective defecation.

420 *DISTRIBUTION OF T-TYPE α1H CA^{2+} CHANNELS (CAV3.2) IN THE RAT MODELOF HIRSCHSPRUNG'S DISEASE*

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Background: Hirschsprung's disease (HD) has been shown to be associated with abnormal distribution and function of interstitial cells of Cajal (ICC). It has been shown that T-type α1H 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 establish HD rat model and observe the distribution of Cav3.2 in abnormal colon of HD rat model and to further explore the role of Cav3.2 in the pathogenesis of Hirschsprung's disease.
Methods Microinjection catheters were carefully placed into the rectum of neonatal SD rats of 6-8 days old, and 0.2% benzalkonium chloride (BAC) solution was injected to establish HD rat model. The distribution of Cav3.2 in abnormal colon of HD rat model was assessed by immunohistochemical staining and the co-localization of Cav3.2 and c-kit receptors was examined by double immunofluorescent staining.
Results After 8 weeks of BAC treatment, the HD rat model was successfully established. The distribution of Cav3.2 was detected by immunohistochemical staining. In the normal colon, Cav3.2 were mainly distributed between circular muscle and longitudinal muscle and showed continuous distribution. However, in the narrow segment of HD rat model, the expression of Cav3.2 was decreased significantly and its continuity was disrupted. Similarly, in the normal colon, the co-localization of Cav3.2 and c-kit were distributed between circular muscle and longitudinal muscle, and showed continuous

distribution. By contrast, the co-localization of Cav3.2 and c-kit were significantly reduced or vanished in the narrow segment of HD rat model.
Conclusion Compared to the normal colon, the distributions of Cav3.2 and c-kit receptors were both decreased significantly in the narrow segment of HD rat model. The abnormal alteration of Cav3.2 probably mediates the functional change of ICCs in the Hirschsprung's disease, resulting in the intestinal dysfunction of HD.

421 *ASSESSMENT OF FUNCTIONAL DISABILITY IN CHILDREN BASED ON FDA AND EMA GUIDLINES FOR IMPROVED ABDOMINAL PAIN SEVERITY*

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Background: Pediatric functional abdominal pain (FAP) in children is associated with school absenteeism, disability and overall poor quality of life. The FDA and European Medicines Agency (EMA) have recommended ≥30% improvement in pain intensity as one of the responder criteria in clinical trials for adults with IBS. It is unclear if these recommendations correlate with improvement in functional disability or if they are applicable in children. Pediatric pain endpoints based on a broader assessment of functioning and validated disability tools are necessary to make adequate future recommendations.
Objectives: To examine the relationship between improvement of ≥30% in abdominal pain (using a combined visual analog numeric scale and faces scale) and improvement in functional impairment using a validated disability tool (PedMIDAS).
Methods: 235 patients, 6-18 years of age, presenting to an outpatient pediatric gastroenterology clinic with FAP, prospectively completed a detailed symptom and medical history questionnaire. This included (1) average level of pain intensity in the previous 2 weeks as measured by a combined visual analog numeric pain rating scale (graded 0-10) and a faces scale, and (2) the PedMIDAS tool, an instrument measuring functional limitations by number of days that common activities are compromised at school, home and social activities due to pain. The disability from initial visit (T1) to follow-up (T2) was categorized as improved, not changed or worsened and the relationship to change in pain severity was analyzed.
Results: 189 children (mean age 11.8 ± 2.9 years) had baseline PedMIDAS scores. Sixty-eight percent were female. Eighty-four percent had abdominal pain at least 2-4 times per week with a minimum of 2 months duration. Of those subjects, 64 had pain intensity scores and PedMIDAS for both T1 and T2. The mean (SD) pain intensity at T1 was 6.26 ±2.1. Interventions from T1 to T2 varied and included reassurance and/or pharmacological therapy. From T1 to T2, 45% of subjects showed ≥30% improvement in pain intensity. For the subjects with ≥30% compared to those with <30% improvement in pain, the PedMIDAS change score showed a significantly greater degree of improvement in disability (mean change score -20.4 ± 35.5 vs. 5.1± 43.3) ($p=0.018$). Pain intensity was significantly correlated with disability with a stronger correlation at T2 compared to T1 ($r=0.49$, $p<0.01$ vs. $r=0.2$, $p=0.01$). Improvement in disability did not differ between those who had longer duration of pain (>1 year) compared to shorter duration (2-12 months) ($p > 0.05$).
Of those with ≥30% improvement in pain at T2, 13/25 (52%) had improved disability and 12/25 (48%) had no improvement. The sensitivity and specificity for improved disability at T2 with ≥30% improvement in pain was 46.4% and 66.6%, respectively.
Conclusion: In children with FAP, a ≥30% improvement in pain rating correlates well with improved ability to function but has very low sensitivity and specificity.

422 *HIGH PREVALENCE OF NAUSEA AMONG SCHOOL CHILDREN IN LATIN AMERICA*

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Background: The prevalence of functional gastrointestinal disorders (FGIDs) varies by region. Chronic nausea is highly prevalent in North American children. We hypothesized that nausea is also common among children in developing countries. Our aim was to evaluate the prevalence of nausea and its association with FGIDs in a large scale, population-based study of Latin American school children.
Methods: A Spanish version of the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III (QPGS-III) was administered to school children in Central and South America. Subjects were classified into FGIDs based on Rome criteria (QPGS-III). Students from four public and four private schools in the countries of El Salvador, Panama and Ecuador participated in this epidemiologic study.
Results: A total of 1137 school children (mean 11.5±1.9 years, range 8-15 years) completed the QPGS-III (El Salvador n=399; Panama n=321; Ecuador n=417). Nausea was present in 15.9% of all school children. Two hundred and sixty-eight

(24%) children met criteria for at least one FGID. By country, 20.3%, 28.7% and 22.8% of school children had a FGID in El Salvador, Panama and Ecuador respectively. Constipation and incontinence was the most common FGID category with nearly all of these representing functional constipation. Nausea was significantly more common in children with FGIDs compared to those without: El Salvador 38% vs. 15% (p<0.001); Panama 22% vs. 7% (p<0.001); Ecuador 25% vs. 13% (p=0.004). Among children with FGIDs, those with functional constipation had a higher prevalence of nausea. Nausea was significantly more common among girls than boys (OR 0.58; 95% CI 0.41-0.82, p=0.0016) and in children from private versus public schools (OR 1.98; 95% CI 1.41-2.81, p<0.0001)
Conclusion: Nausea is commonly present in Latin American school children. FGIDs are frequently associated with nausea.

423 *EVALUATION OF GASTROESOPHAGEAL REFLUX BY COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE AND PH MONITORING AND ESOPHAGEAL MOTILITY PATTERNS IN CHILDREN WITH ESOPHAGEAL ATRESIA*

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Background: gastresophageal reflux disease (GERD) and esophageal dysmotility are common in patients with esophageal atresia.
Aims: To evaluate GERD and esophageal motility patterns in children with EA using pH-impedance (pH-MII) monitoring and high resolution esophageal manometry (HREM) respectively. Reflux patterns and distal baseline impedance (DBI) in EA patients were also compared with those of normal children with suspected GERD
Methods: A retrospective chart review was done on 35 EA patients and 35 age and sex matched normal controls with suspected GERD. 24 hour pH-MII monitoring was done on all patients. For patients on proton pump inhibitor (PPI) therapy, it was continued during the study. 8 EA patients also underwent HREM. Data was also collected on patient demographics, endoscopy and clinical symptoms.
Results: In the EA cohort, the median age was 53 months, with 21 males and the majority (71.4%) had Type C EA. 85.7% of the EA cohort and 40% of the control group were on PPI therapy during the pH-MII study. pH-MII testing showed a total of 1457 retrograde bolus movements (RBMs), of which only 14.3% was acidic in the EA cohort. In the control group there were 1482 RBMs of which 46.3% was acidic. There was no significant difference in the total RBMs between the two groups. Acidic RBMs was significantly lower in the EA group (208) compared to the control group (689), p =0.0008, and non-acid reflux index (NA RI) was significantly higher in EA children 1.1(0.0-7.8) compared to controls 0.6(0.0-5.7),p=0.0046. There was no significant difference in total RBM, acid reflux index (ARI), and number of proximal reflux episodes between EA patients with and without fundoplication, long gap, esophagitis on biopsy and those on or off PPI. In EA patients out of total 1183 total reported symptoms, only 335 (28%) were associated with a RBM. The mean DBI was significantly lower in EA 1029.6 (410.9SD) Ω compared to controls 2998.2 (1028.8SD) Ω with suspected GERD, p<0.0001. By logistic regression only PPI use had a significant effect on DBI, p<0.0001. None of the GER (ARI, NARI, or RBM) or bolus transit (mean acid clearance time (MACT), and bolus clearance time (BCT)) parameters or age had a significant effect on DBI. HREM was abnormal in all EA patients and demonstrated either aperistalsis, pressurization, weak peristalsis with small or large breaks or distal peristalsis in those studied. 4 out of 8 EA patients had different peristaltic patterns for their solid swallows compared to their liquid swallows in HREM.
Conclusions: pH-MII testing allowed increased detection of non-acid reflux events in EA patients which would have been missed with standard pH monitoring alone. NARI was the only reflux parameter which was significantly higher in the EA cohort compared to the control group with suspected GERD, but the clinical significance of NAR in EA patients remains to be determined. Majority (72%) of gastrointestinal symptoms in EA patients were not temporally related to RBMs in pH-MII testing. DBI was significantly lower in EA patients compared to controls, however its clinical relevance remains to be determined. Esophageal motility as determined by HREM was abnormal in all EA patients.

*424 *AN INTERVENTION TO REDUCE PROCEDURAL DISTRESS AND IMPROVE EFFICIENCY IN PEDIATRIC ANORECTAL MANOMETRY PROCEDURES: A RANDOMIZED TRIAL*

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BACKGROUND: Pediatric procedural anxiety and behavioral distress commonly occurs across medical procedures and can result in significant stress to children and their families and impact the success of the medical procedure. In an anorectal manomentry procedure, children are awake and the procedure itself requires the child be able to relax for optimal findings; therefore, identifying strategies at reducing procedural distress in this population is especially important. This study examined whether an intervention of psychoeducation and distraction opportunity decreases levels of procedural distress in children and their parents when undergoing an anorectal monometry and improved clinical outcomes of the procedure.
METHODS: Children undergoing an anorectal manometry procedure in an outpatient Gastroenterology clinic were randomly assigned to the intervention or control group. The intervention group received pre-procedural psychoeducation and distraction tools during the procedure whereas the control group received treatment-as-usual without psychological

intervention. Procedural distress was assessed through physiological arousal measurements (HR and SBP), an observational scale of procedural distress (PBCL), self-reported anxiety by participants over age 8 (STAIC-S), and parent report of parental anxiety (STAI-S) and child distress. Completion time of the procedure, number of balloon inflations to produce rectoanal inhibitory reflex (RAIR), and medication use for anxiolytic effects were also measured.
RESULTS: A total of 63 children (57% male) were enrolled and completed the study, with ages ranging from 2 through 12 (Mean 6.7; SD 2.49). Children in the intervention group demonstrated significantly less observed distress (PBCL, $p<0.001$), parent-rated distress ($p = 0.01$), and child self-reported anxiety (STAIC-S, $p = 0.04$). Self-reported parental anxiety was also significantly less in the intervention group (STAI-S, $p = 0.02$). Physiological measures of anxiety demonstrated decreased SBP compared with baseline for the intervention group compared with the control group ($p = 0.02$), but no differences between the two groups for HR changes ($p = 0.43$). Total completion time for the procedure was significantly decreased for the intervention group ($p = 0.01$), as was the number of balloon inflations required to ellicit RAIR ($p = 0.03$). The proportion of participants from the intervention who received anxiolytic medication as 0.226, whereas the proportion of participants from the control who received anxiolytic medication was 0.344; however this difference was not significant ($p = 0.41$).
CONCLUSIONS: Results expand on previous research finding benefits of psychological intervention in reducing distress during medical procedures. In the anorectal manometry procedure, patient distress and parent anxiety were both reduced with psychoeducational and distraction interventions and the procedure itself was more efficient and effective. Understanding and utilizing psychological methods that decrease distress for patients and their caregivers is imperative to improving medical care standards.

*425 *SACRAL NERVE STIMULATION FOR TREATMENT OF CONSTIPATION IN CHILDREN RECEIVING ANTEGRADE ENEMAS*

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Background: Antegrade continence enemas (ACEs) are an effective treatment option for children with severe constipation refractory to medical and behavioral treatment. However, up to 31% of children do not respond adequately to ACEs and subsequent medical options are limited. Sacral nerve stimulation (SNS) has been shown to be safe and effective in the treatment of adults with constipation and fecal incontinence (FI). Recent studies suggest that SNS may be beneficial for children with constipation and FI, but no studies have focused on children with symptoms severe enough to require ACEs. The aims of our study are to evaluate the efficacy of SNS for children with constipation dependent on ACEs and describe the time course of response. Methods: We included patients up to 21 years old treated with ACEs who initiated SNS between 2012 and 2014. We reviewed the medical record and patient-reported questionnaires for ACE and medication usage, symptom assessment, Fecal Incontinence Quality of Life Scale (FIQL), Fecal Incontinence Severity Index (FISI), and Vancouver Dysfunctional Elimination Syndrome Score (DES). Encounters were selected at baseline and 1, 3, 6, 9, 12, 18 and 24 months after SNS initiation. Wilcoxon rank sum tests were used for comparison. P-values<0.05 were considered statistically significant. Results: Twenty-one children (57% male, mean age 14.3 years, range 8-21 years) were included: 13 subjects (62%) had FI, 12 (57%) had urinary symptoms, and 10 (48%) were born with an anorectal malformation. Prior to SNS initiation, ACEs had been used for a mean of 5.3 years. Subjects received a median of 7 antegrade enemas/week at baseline and this steadily decreased to 0 at 12 months ($p<0.0001$). Ten patients (48%) had their appendicostomy or cecostomy closed and half of closures occurred within 12 months. Oral laxative use did not change significantly. All components of the FIQL showed some improvement at 1 month but remained stable afterwards. Changes were not significant at 1, 12 and 18 months. Median FISI scores improved from 33 to 15 in the first 6 months and then subsequently increased. Median DES showed a non-significant decline from 11 to 8 at 18 months ($p=0.777$). Four subjects (19%) required SNS removal within 24 months of SNS, 3 for wound infection and 1 for lead migration. Two of the 4 had their SNS replaced. Another subject required SNS repositioning due to lower extremity numbness. Conclusion: SNS is a promising therapy for children with constipation dependent on ACEs, a population that is challenging to manage and with limited medical options. Subjects were able to steadily decrease ACE frequency over the first year after SNS and nearly half had their appendicostomy or cecostomy closed within 2 years. We did not detect significant long-term changes in FI or DES-specific scores. Further studies are needed to determine the impact of SNS on constipation-specific symptom scores in this population and to identify predictors of response.

*426 *THE IMPACT OF MENARCHE ON FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS): RESULTS OF THE LARGEST POPUATION-BASED STUDY OF CHILDREN IN THE WESTERN HEMISPHERE*

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Background: The pathophysiology of FGIDs is incompletely understood. The two most common FGIDs, irritable bowel syndrome (IBS) and functional constipation (FC), are 2-3 times more common in females. No clear gender predominance has been found in children. Hormonal differences are often thought to contribute to the female predominance in adults. Studies show gender differences in visceral sensitivity. Estradiol can modulate pain perception in rats. In adults, IBS symptoms vary with menstruation, pregnancy and menopause. The precise age when IBS and FC become more prevalent in females has not been described. If hormonal differences are responsible for the female predominance among adults with IBS and FC, we would expect to find a change in gender composition and prevalence after menarche. Aim: To evaluate the impact of menarche on gender composition and prevalence in children with IBS and FC. Hypothesis: The prevalence of IBS and FC will increase in females after menarche and no changes will be seen in males of similar age. Methods: Cross-sectional study. Children without organic diseases from 12 schools in 9 Colombian cities completed the Questionnaire on Pediatric Gastrointestinal Symptoms - Rome III. Studies in Colombia report mean age at menarche of 12.7 years. Subjects were divided into premenarchal (PRE) and postmenarchal (PST) age groups with menarche cutoffs at 13 and 14 years (PRE1=8-12y, PST1=13-18y and PRE2=8-13y, PST2=14-18y) and groups were compared. Results: 4267 of 4751 (89.8%) invited children agreed to participate. After excluding those with organic disease, 3891 (47.0% F, mean 12.0y) completed the study. 939 (24.1% of total) met criteria for a FGID. 187 (4.8% of total, 51.9% F) met criteria for IBS. Children with IBS in PRE1 and PRE2 were 56.0% (70/125) and 53.4% (75/140) female and in PST1 and PST2 were 43.5% (27/62) and 46.8% (22/47) female. Differences between PRE1/PST1 and PRE2/PST2 were not significant. Prevalence of IBS among females was higher in PRE1 and PRE2 (6.4%, 70/1099; 5.7%, 75/1327) than PST1 and PST2 (3.7%, 27/730; 4.4%, 22/502), but this was only significant comparing PRE1/PST1 ($p<0.05$). Overall prevalence of IBS was higher in PRE1 and PRE2 (5.4%, 125/2327; 5.0%, 140/2798) than PST1 and PST2 (4.0%, 62/1564; 4.3%, 47/1093), but this was only significant comparing PRE1/PST1 ($p<0.05$). 494 (12.7% of total, 48.0% F) children met criteria for FC. There was no difference in gender composition between PRE1/PST1 (47.6%, 161/338 vs. 48.7%, 76/156 F) or PRE2/PST2 (47.7%, 187/392 vs. 49.0%, 50/102 F). Prevalence of FC among females was higher in premenstrual than postmenstrual groups (14.6%, 161/1099 in PRE1 vs. 10.4%, 76/730 in PST1, $p<0.01$; 14.1%, 187/1327 in PRE2 vs. 9.9%, 50/502 in PST2, $p<0.05$). Overall prevalence of FC was higher in premenstrual than postmenstrual groups (14.5%, 338/2327 in PRE1 vs. 10.0%, 156/1564 in PST1, $p<0.0001$; 14.0%, 392/2798 in PRE1 vs. 9.3%, 102/1093 in PST2, $p<0.0001$). Conclusion: There was no significant female predominance in children with IBS or FC. IBS and FC prevalence did not increase after menarche, suggesting that pubertal hormonal changes may not play a primary role in the development of IBS and FC. IBS and FC prevalence was lower in adolescents than younger children.

427 *A NEW INSIGHT INTO COLON MOTILITY USING HIGH RESOLUTION MANOMETRY*

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Background: Conventional colon manometry with 8 pressure sensors catheters uses gastrocolic response (GCR) and high amplitude propagating contractions (HAPCs) as the main parameters for defining normality. High resolution manometry studies have challenged this approach and suggested features other than GCR and HAPCs may be clinically relevant. Methods: We retrospectively reviewed charts of 30 patients with chronic constipation, 6 patients (2F) with normal oro-anal transit and normal colon motility (CM) were defined as the disease controls; remaining 24 patients (9F) had slow transit (>50% of sitz markers in right colon at 72 hrs) or abnormal CM defined by lack of GCR or regional or pan-colonic absence of HAPCs. The study protocol used: fasting 1 hr, post prandial 1 hr and post-bisacodyl 30 mins. We used a 36 sensor HRM catheter with 20 sensors 4 cm apart and 16 distal sensors 2 cm apart. HAPCs were defined as amplitude ≥75 mmHg, propagating ≥15 cm; Low amplitude propagating contractions (LAPC) amplitude <50 mmHg and propagating for ≥ 15 cm (antegrade or retrograde); Bursts: amplitude >8 mmHg, frequency ≥ 3 per min and duration ≥ 3 min; Isolated pressure waves: amplitude ≥ 5 mmHg, duration ≥ 30 sec. The contraction pattern were evaluated for the transverse colon (TC), descending (DC), recto-sigmoid colon (RS), insufficient data to analyze ascending colon (AC). Mann Whitney U test was used for group comparisons, p values < 0.05 was considered significant. Results: At the end of the study catheter tip was in the AC:4, TC:22, DC:4. Five patients had slow transit, 14 had lack of HAPCs in at least 1 region and 6 had absence of GCR. The p value for differences in contraction pattern between controls and patients are shown in the Table. Area under the curve (AUC) for pre and post prandial period was not significant between the two groups. Conclusion: Our results suggest that colon contraction patterns such as LAPCs, isolated waves and burst waves may be important in clinical evaluation of children with chronic constipation. Evaluating bisacodyl response is important but it is the least informative in differentiating colon contractions other than HAPCs. Using a more comprehensive approach to evaluate colon motility in addition to the GCR and HAPCs may help improve the diagnostic usefulness of colon motility studies.

Table

Variable	Fasting period	Post prandial period	Post bisacodyl
HAPC-TC	NS	<0.001	NS
HAPC-DC	0.001	<0.001	NS
HAPC-RS	0.001	NS	NS
LAPC-TC (Antegrade)	NS	0.04	NS
LAPC-DC (Antegrade)	0.01	0.01	NS
LAPC-RS (Antegrade)	0.01	0.02	NS
LAPC-TC (Retrograde)	NS	NS	NS
LAPC-DC (Retrograde)	NS	0.03	NS
LAPC-RS (Retrograde)	NS	NS	NS
Bursts-TC	NS	NS	NS
Bursts-DC	NS	NS	NS
Bursts-RS	NS	0.001	NS
Isolated Waves-TC	NS	0.01	NS
Isolated Waves-DC	NS	0.01	NS
Isolated Waves-RS	<0.001	0.04	NS

TC: Transverse colon; DC: Descending colon; RS: Recto sigmoid colon; NS: p value was not significant

*428 *TRENDS IN CHOLECYSTECTOMIES FOR BILIARY DYSKINESIA IN PEDIATRIC POPULATION IN THE UNITED STATES*

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Background: Diagnostic criteria for biliary dyskinesia are not well established in the pediatric age group. The outcomes of conservative medical management and surgery for biliary dyskinesia are similar. In recent studies, the reported incidence of cholecystectomy for biliary dyskinesia varies from 14% to 60% suggesting variation in patient selection criteria for surgery. We used a national inpatient database to evaluate the trends in cholecystectomies performed for biliary dyskinesia in children less than 18 years of age. We hypothesized that there will be a significant increase in number of cholecystectomies performed for biliary dyskinesia in the United States based on recent reported data.

Methods: We performed a retrospective review of NIS HCUP data for 2002 and from 2007 to 2011. To identify children who had cholecystectomy, we used ICD 9 codes 51.22 (open procedure) and 51.23 (laparoscopic) for cholecystectomy. To identify the reason for cholecystectomy we queried the following diagnostic ICD 9 codes: calculous of gall bladder with cholecystitis (574.0, 574.1, 574.2, 574.3, 574.4, 574.5, 574.6, 574.8, 574.9), biliary dyskinesia with other specific disorders of gall bladder (575.8), cholecystitis without calculous (575.1) and chronic cholecystitis without calculous (575.11). We used chi-square test to compare group differences.

Results: The number of cholecystectomies performed as primary procedural diagnosis on weighted analysis and the indication for the surgery are shown in Table 1. Procedures performed specifically for the diagnosis of biliary dyskinesia in 2002 and 2007-2011 along with gender, ethnicity, hospital stay and health care expenditure for the admission are shown in Table 2. Between 2007-2011, 79% of cholecystectomies were performed in females and also compared to the pre-adolescent age group, the number of cholecystectomies performed in adolescent patients was significantly higher ($p<0.001$).

Conclusion: An increasing number of cholecystectomies are performed for the diagnosis of biliary dyskinesia in children in the United States. On average, we found almost 40% increase in this procedure over a 10 year period. It is important that consensus guidelines for the diagnosis and management of this clinical entity are developed in children.

Table 1

	2002	2007-2011	p value
Number of cholecystectomies/year	5446	6981*	0.03
Laparoscopic procedure	91.0%	94.8%	0.03
Calculous cholecystitis	79.0%	73.6%	NS
Chronic cholecystitis without calculous	5.6%	5.5%	NS
Acalculous cholecystitis	1.4%	1.8%	NS
Biliary dyskinesia	6.5%	10.8%	0.03
Other indications	7.5%	8.3%	NS

* = average surgeries/year, NS = p value not significant

Table 2

	2002	2007-2011	p value
Number of cholecystectomies for biliary dyskinesia (%)	6.5	10.8	0.03
Age (%): ≤ 12 yrs 13-17 yrs	48.4 51.6	25 75	NS
Female (%)	80.4	79.0	NS
Ethnicity(%): Caucasian African American Hispanic	76 6.1 17.4	73.5 4.7 17.2	NS
Mean length of hospitalization (days)	3.16	3.43	NS
Hospital charges/admission (\$)	17,661	27,350	<0.001
Insurance (%): Private Insurance Medicaid	66.5 29.0	59.4 33.8	NS

NS = p value not significant

*429 *PREOPERATIVE EVALUTION DOES NOT PREDICT RISK OF CONVERSION TO TRANSPLYORIC FEEDING IN GASTROSTOMY DEPENDENT PEDIATRIC PATIENTS*

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Background: Prior literature suggests that a proportion of pediatric patients undergoing gastrostomy tube (GT) placement, especially those with underlying neurologic disability, will require coversion to gastrojejunal (GJ) feeds. Limited literature exists as to whether preoperative assessments may predict which patients will go onto require GJ feeding. The goal of this study was to compare the preoperative evaluations between patients sucessfully maintained on gastrostomy feeds ("GT" patients) versus patients who failed GT feeds and required conversion to transpyloric feeding ("GJ" patients).

Methods: We identified patients at Boston Children's Hospital who underwent GT placement and ultimately required GJ feeding between 2006-2013. These patients were matched according to age, neurologic, and cardiac status with a cohort of patients who remained GT dependent. Preoperative characteristics of both groups were compared in order to identify risk factors for conversion to GJ feeding. Proportions were compared using Chi-square analyses.

Results: 81 GJ patients (median (IQR): age 14 (4, 57.5) months; weight 8.8 (4.6, 15) kg) were matched with 81 GT patients (median (IQR): age 14 (4.5, 57) months; weight 8.5 (5.2, 14.3) kg). Median time from GT to GJ conversion was 8 (IQR 3, 16.5) months. No differences in comorbidities (neurologic or cardiac disease, prematurity, cancer, metabolic/genetic disorder, oropharyngeal malformations, or pulmonary disease) were found. No differences in preoperative gastrostomy evaluations were seen. Both groups had similar rates of nasogastric feeding trials (GT (60, 74.1%) vs GJ (58, 71.6%), p=0.7), upper GI series (GT (47, 58%) vs GJ (45, 55.6%), p=0.75), and modified swallow studies (GT (38, 46.9%) vs GJ (46, 56.8%), p=0.21). No differences in aspiration were seen with 22 GT patients (27.2%) having abnormal modified swallow studies compared to 29 GJ patients (35.8%, p=0.4). There were no differences found in success of preoperative nasogastric feeding trials (GT (50, 61.7%) vs GJ (48, 59.3%), p=0.9) or frequency of abnormal upper GI series (GT (4, 0.05%) vs GJ (3, 0.04%), p=0.4). Only 1 GT patient (1.2%) vs 6 GJ (7.4%) patients underwent impedance probe testing prior to GT tube placement. 4 GT patients (4.9%) vs 8 GJ patients (9.9%) had prior gastric emptying studies (p=0.19) with

no differences in median percent gastric residual at 1 hr (GT 52% (IQR 39, 52) vs GJ 63% (45, 66.8), p=1.00).
Conclusions: No differences in preoperative patient characteristics, including presence of aspiration or tolerance of nasogastric feeds, were seen in patients with successful gastric feeding as compared to those requiring conversion to GJ feeds. More prospective studies are needed to determine whether additional preoperative reflux or motility testing may help decipher which gastrostomy patients will need future transpyloric feeding.

432 *OPTOGENETIC INVESTIGATION OF THE COLONIC EPITHELIUM IN THE GENERATION OF ACTION POTENTIALS*

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Introduction/Aims: Visceral pain in functional gastrointestinal disorders is thought to be caused by mechanosensory information that normally produces non-noxious sensations, but has been altered such that it produces pain. Before we can determine why non-noxious stimuli become painful, we need to identify the cells that are responsible for transducing mechanical stimuli (e.g., colonic distension) into visceral afferent action potentials. Previously, it has been assumed that transduction occurred primarily in visceral afferents themselves. However, recently, it has been shown in the skin that activation of epidermal keratinocytes expressing channelrhodopsin (ChR2) alone produced sensory neuron stimulation similar to natural stimuli. Thus, the epithelium may have a role in pain sensations. Using a novel optogenetic mouse model, we investigated the role of the colonic epithelium in the generation of action potentials in colon sensory neurons.
Methods: Transgenic mice were isolated that expressed ChR2-yellow fluorescent protein (YFP) in colonic epithelium via a *Cre*-recombinase driven by the villin promoter or in colon afferents via a transient receptor potential vanilloid receptor-1 (TRPV1)-*Cre.* An *in vitro* mouse colon preparation was used by isolation of the distal colorectum with the pelvic nerve attached for single-fiber electrophysiological recordings. Colorectal afferent endings were characterized by blunt probing, mucosal stroking, and stretch. Once a mechanosensitive fiber was found, the intestinal epithelium was directly stimulated in the afferent fiber's receptive field using a 480 nanometer blue light.
Results: Villin-*Cre* produced ChR2-YFP expression selectively in colonic epithelium. Activation of the colonic epithelium via ChR2 resulted in generation of action potentials in 13/47 mechanosensitive fibers (28%). Epithelial activation often produced complex, robust, high frequency firing patterns. In most cases, there was a significant delay (2-30 seconds) between light onset and the first action potential. This was in contrast to the response when the ChR2 was expressed in the afferents themselves (TRPV1-*Cre*), where firing was virtually instantaneous with light onset. In some cases, light activation of the epithelium was able to potentiate the response to stretch (12/22 fibers).
Conclusions: These results demonstrate for the first time that intestinal epithelial activation contributes to the transduction and modulation of mechanosensitive colon afferents and may have important implications to the mechanism of visceral pain. The relatively long delay in action potential generation indicates that chemical communication is responsible and that additional cell types (e.g., innate immune cells) may be involved.

434 *SINGLE CENTER EXPERIENCE WITH HYDROXYZINE IN THE TREATMENT OF CYCLIC VOMITING SYNDROME*

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Background: To this date, there has been no specific therapy proven to be effective for cyclic vomiting syndrome (CVS) in controlled trials. Multiple regimens have been proposed including: cyproheptadine, propranolol, amitriptyline, and phenobarbital. These medications are not without major side effects. The aim of this study is to describe the author's experience with hydroxyzine in children with CVS.
Patients and methods: This was a systematic retrospective review of charts from March 1st 2012 till December 31st 2014. Patients diagnosed with CVS and treated with hydroxyzine were included in this study. Demographic criteria as well as response to therapy were reviewed.
Results: Forty-eight patients were diagnosed with CVS during the period of two years and nine months. Female to male ratio was 2:1. The average age at diagnosis was 10.4 years. Fifteen patients were treated with hydroxyzine. Overall success rate was 86.7%. Of those, 61.5% had a dramatic resolution of symptoms and 38.4% had a slower rate of improvement. Only 2 patients failed to respond.
Conclusion: Hydroxyzine seems to be a safe and effective alternative prophylactic treatment in children with CVS. Further randomized controlled studies are needed to support this specific indication for prescribing hydroxyzine.

436 *SACRAL NEUROMODULATION - A NEW TREATMENT MODALITY FOR CHILDREN WITH CHRONIC CONSTIPATION AND FECAL INCONTINENCE*

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Background: Sacral Neuromodulation (SNS) for fecal incontinence (FI) in adults has been approved by the FDA since 2011. In a 3-year follow-up of a large cohort, the success rate was 86% with significant improvement in quality of life indicators. We present our initial experience with SNS for treatment of chronic constipation and FI in children.

Methods: Retrospective chart review of 7 patients who underwent SNS procedure since 2014 was performed. All patients were evaluated in the GI Motility program and had anorectal and colon manometry evaluation. None of the patients responded to conservative treatment and 3 had failed antergade cecostomy enemas. SNS implantation was staged with the first being a test trial: a temporary lead was placed in the third sacral foramen, adjacent to the nerve root and connected to an external stimulator. Defecation diary was recorded over a period of 2 weeks. If the patient experienced > 50% success, an internal permanent subcutaneous stimulator was substituted for the external in a second stage procedure. This study was approved by IRB.

Results: The age range of patients was 7 to 15 years (median 8 years). Median follow up was 16 months. In one patient the test trial was not successful and therefore, 6 patients had a permanent implant. Motility evaluation revealed dyssynergia in 2, lack of high amplitude contractions in the left colon in 2 and low resting anal pressure in 1 patient. None of the patients had an identifiable underlying neurogenic cause for their symptoms. The first function to emerge during the trial period was the sensation of urgency to defecate. All patients had improvement in frequency of bowel movements and fecal incontinence. In two, associated daytime urinary incontinence also resolved. All patients were able to reduce or eliminate oral medications. One underwent reversal of the irrigation channel and in the other two, reversal is pending. One patient experienced partial superficial separation of the surgical wound, which subsequently healed completely.

Conclusions: Our preliminary data suggests that SNS can be considered in children with chronic constipation and FI, who do not respond to conservative treatment. The staged approach allows patient selection for success, is completely reversible if unsuccessful, and may increase the overall success rate.

437 *FREQUENCY OF FOOD HYPERSENSITIVITY IN CHILDREN WITH CHRONIC CONSTIPATION*

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Background: Alimentary allergy has different presentations in children, one of them could be functional bowel symptoms such as chronic constipation.

Objective. The aim of this study were to determine the frequency of food hypersensitivity in patients with chronic constipation.

Methods: *Design.* Cross-sectional. *Setting*: A pediatric referral hospital. Sample: 81 patients with chronic idiopathic constipation (define as Rome III criteria), age 5-16 years, all subjects had previously been treated with laxatives for at least 3 months without succcess. *Protocol*: All 81 patients performed skin prick test. *Statistics:* median, chi square.

Results: n= 81, 50% male, median age 9.7 years $\pm$ 2.8 SD, 37 (46%) cases had food hypersensitivity, ratio F:M 1.6:1 p= 0.046, 32 cases had relatives with atopy. The top 10 allergen more frequent were: 8.6% egg withe, coffee; 7.4% milk, peanut; 6.2% strawberry, apple; 4.9% shrimp, corn, bean and cumin.

Conclusions: The frequency of food hypersensitivity is high in patients with chronic idiopathic constipation, more than a pediatric population, this finding could reflect the relation between allergy and constipation, but is necessary more study for confirm that.

438 *INCREASES IN PLASMA CITRULLINE LEVELS FOLLOWING TEDUGLUTIDE TREATMENT IN CHILDREN WITH SHORT BOWEL SYNDROME*

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Levels of plasma citrulline, an amino acid produced by enterocytes, correlate with remnant bowel mass in pediatric patients with short bowel syndrome (SBS).[1] In addition, plasma citrulline levels increase with greater enteral tolerance and may predict independence from parenteral support (PS) in children with SBS.[1,2] We sought to assess changes in plasma citrulline levels in response to teduglutide (TED) treatment in pediatric patients with SBS aged ≥1 year.

This 12-week, open-label, multicenter, safety and pharmacokinetic/pharmacodynamic study enrolled children aged 1–17 years with a history of SBS ≥12 months who had reached a plateau in intestinal adaptation (ie, PS could no longer be reduced in a clinically significant way) and showed minimal or no advance in enteral nutrition (EN; ie, specialized nutrition provided via feeding tube or orally) for ≥3 months. Patients were enrolled sequentially into 3 dosing cohorts: 0.0125

mg/kg/day (n=8), 0.025 mg/kg/day (n=14), and 0.05 mg/kg/day (n=15); a fourth observational cohort received standard of care (SOC; n=5). Plasma citrulline was assessed at baseline, Week 12 (end of treatment), and Week 16 (4-week follow-up) in the 3 TED dosing cohorts but not in the SOC cohort.
At Week 12, mean prescribed PS volume was reduced by 32% from baseline and mean patient-reported EN volume was increased 49% from baseline in the combined TED dosing cohorts (n=37). These changes were accompanied by an increase in mean ± SD plasma citrulline levels in all 3 TED dosing cohorts (0.05 mg/kg/day, 15.8±9.3 mmol/L at baseline to 24.7±20.7 mmol/L at Week 12 [84% increase]; 0.025 mg/kg/day, 15.5±7.9 mmol/L at baseline to 22.7±10.9 mmol/L at Week 12 [42% increase]; 0.0125 mg/kg/day, 14.7±7.3 mmol/L at baseline to 22.1±13.3 mmol/L at Week 12 [30% increase]). At 4 weeks after withdrawal of TED (Week 16), mean ± SD citrulline levels decreased toward baseline values (0.05 mg/kg/day, 15.5±14.6 mmol/L; 0.025 mg/kg/day, 17.4±8.8 mmol/L; 0.0125 mg/kg/day, 20.5±15.2 mmol/L).
The increases in plasma citrulline observed in this analysis likely reflect intestinotrophic changes that contribute to improved absorption and enhanced EN tolerance with TED in children with SBS who have reached a plateau in intestinal adaptation.
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INFLAMMATORY BOWEL DISEASE

439 *EFFICACY AND SAFETY OF ATTENUATED LIVE VACCINES IN CHILDREN TAKING IMMUNOSUPPRESSANTS: A PROSPECTIVE TRIAL*

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Background: Attenuated live vaccine is contraindicated for use in patients taking immunosuppressants (IS) because of its risk of infection by vaccine strain. However, infection by measles or varicella may results in serious complication in immunocompromised host, and several case series have shown the relative safety of live attenuated vaccine in immunosuppressed children.
Objective: To evaluate the efficacy and safety of attenuated live vaccines in children taking IS.
Design/ Methods: This is a prospective trail to evaluate for the efficacy and safety of attenuated live vaccines (mumps, rubella, varicella, and mumps) in children taking IS. Patients whose antibody titers were negative or borderline for at least one of the above viruses, and revealed defined cellular and humoral immunity (CD4 $\geq$500/mm^3, normal lymphocyte blast transformation by phytohemagglutinin, and serum IgG $\geq$300 mg/dl) were included in this study. Patients received vaccines for the insufficient antibodies. Antibody titers at 2 months and 1 year after vaccination were measured. Adverse events were also monitored.
Results: Seventy-two children (nephrotic syndrome (50), inflammatory bowel disease (10), Systemic lupus erythematosus (3), post kidney transplantation (3), others (6)) has received total of 128 vaccinations (measles/rubella (38), measles (2), varicella (59), mumps (29)). IS at the time of evaluation were calcineurin inhibitor only in 35 (27%), antimetabolite only in 59 (46%), and both calcineurin inhibitor and antimetabolite in 32(25%). Twenty-four (19%) were taking low-dose corticosteroids in addition to IS. Antibody titers were converted to positive in 71% of vaccinations (mumps 89%, rubella 100%, varicella 61%, and mumps 48%) at 2 month. Antibodies had remained positive for 1 year in 72% of responders. Eighty-seven percent of patients with antibody titer $\geq$10.0 at 2 months had persistent positive antibody titers at 1 year, compared to only 42% of patients with antibody titer < 10.0 (p=0.001). Adverse events possibly related to vaccination were observed in 25 (20%) vaccinations including one vaccine related varicella infection. However, none of them were critical.
Conclusions: Attenuated live vaccines in children receiving IS appeared relatively safe and effective if they were given after the evaluation of their immunological status.

442 *PREDICTORS OF POUCHITIS AFTER ILEAL POUCH-ANAL ANASTOMOSIS IN CHILDREN*

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Objectives: No previous studies have examined predictive factors for development of pouchitis after ileal pouch-anal anastomosis (IPAA) in children. In this retrospective study, we evaluated the risk factors that predict pouchitis in children with IPAA.
Methods: The records of patients who underwent IPAA surgery at Children's Hospital of Wisconsin between January 2000 and December 2013 were retrospectively reviewed. Patients with clinical, endoscopic and histological findings consistent with pouchitis were identified. Antibiotic-responsive pouchitis was defined as an episode of pouchitis that responded to a 2-week course of antibiotics. Antibiotic-dependent pouchitis was defined as pouchitis which required long-term, continuous

antibiotic therapy to maintain remission. Antibiotic-refractory pouchitis was defined as pouchitis that failed to respond to antibiotics requiring oral or topical 5-aminosalicylates, corticosteroid therapy, or oral immunomodulator therapy. Antibiotic-dependent and antibiotic-refractory were categorized as chronic pouchitis. The groups of patients with and without overall or chronic pouchitis were compared to determine which demographic, pathological, or disease characteristics may serve as predictive factors for the development of overall or chronic pouchitis.
Results: Of the 60 patients who underwent IPAA, 40 had ulcerative colitis (UC), 17 had familial adenomatous polyposis (FAP) and 3 had Crohn's disease (CD). Pouchitis was identified in 22 (55%) patients with UC and 2 (11.8%) patients with FAP. Subgroup analysis of patients with UC revealed that antibiotic-dependent pouchitis occurred in 4 (10%) patients and antibiotic refractory pouchitis in 9 (22.5%) patients. The mean age at diagnosis of UC was 10.8 years and the mean age at colectomy was 13.9 years. In UC patients, the median duration from construction of IPAA to first episode of pouchitis was 9.51 (range 0.52 to 41.57) months and to chronic pouchitis was 10.98 (range 0.92 to 69.57) months. In UC patients, the median follow-up period from construction of IPAA was 35 (range 4.59 to 87.67) months. Study analysis revealed that higher PUCAI score at the time of diagnosis was a significant predictive factor for overall pouchitis ($p = 0.0002$) as well as chronic pouchitis ($p = 0.02$).
Conclusions: Patients with UC and a higher PUCAI score at the time of diagnosis have a higher risk for developing pouchitis.
Comparison of predictive factors in patients with and without pouchitis

Perioperative factors	Pouchitis (N = 22)	No pouchitis (N = 18)	P
Male/Female	13/9	10/8	0.82
Mean age at diagnosis (yr)	11.29	10.39	0.47
Mean age at colectomy (yr)	13.89	14.08	0.53
IPAA - Two stage/Three stage	2/20	4/14	0.38
Mean cumulative dose of steroids (mg)	10660	5828	0.06
Immunomodulators	17	12	0.5
Biologics	19	11	0.14
Extent of colitis - Pancolitis/left sided	17/5	12/6	0.74
Mean PUCAI score at diagnosis (SD)*	70.4 (8.99)	46.9 (19.49)	0.0002
Extraintestinal manifestations	3	0	0.24
Colectomy - open/laparoscopic	6/16	4/14	0.9
Postoperative complications	14	15	0.9

IPAA - Ileal Pouch-Anal Anastomosis; *Significant predictor

443 *SEASONAL VARIATIONS IN ONSET AND EXACERBATION OF INFLAMMATORY BOWEL DISEASES IN CHILDREN*

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Background: Inflammatory bowel diseases (IBD) are clinically characterized by exacerbations and remissions with no known triggering factors for either onset or exacerbation. Some studies have suggested that IBD follow a seasonal pattern with regard to their onset and exacerbations. Conflicting data has also been reported for the seasonal variation in births of patients with IBD. The aim of this study is to determine if there is any seasonal pattern to the onset and exacerbation of IBD in the pediatric population and if the birth of children diagnosed with IBD follows a seasonal pattern.
Methods: Patients between the ages of 1 and 21 years and with a diagnosis of IBD established between July 1992 and July 2012 were investigated concerning the onset of symptoms, exacerbations and their season of birth. The seasons were defined as winter (December - February), spring (March - May), summer (June - August) and fall (September - November). Data were collected by identifying and reviewing hospital charts and records of patients with established diagnosis of IBD using ICD codes. To assess the seasonality of IBD onset, exacerbation and birth cases within our study cohort we pooled the data from all IBD patients to evaluate its general distribution with respect to the season. In addition, we also compared the individual data for the first, second and third exacerbations to assess any seasonal pattern. Data were analyzed using the Chi-square test and statistical significance was set at a p value of 0.05.
Results: A total of 170 children were included in this study; Of the patients, 58% were male, 78% were Caucasians, 74% were outpatients, and 52.9% had CD. The mean age at the onset of symptoms was 13.3 ± 4.6 years (mean ± SD), and the mean age for first exacerbation was 14.3 ± 3.9 years (mean ± SD). 34% of patients had their onset in the fall and 19% of

them had their onset in the summer (p = 0.021). When breaking down the study group to UC and CD categories, the onset of the diseases continued to be more frequently in fall but with no statistical significance. The total number of documented exacerbations was 358 and the median number of exacerbations was two, with a range of 1 to 11. IBD exacerbations were generally uniformly distributed throughout the year and no difference was detected in seasonality between the observed and expected pattern of IBD exacerbations for the first three exacerbations experienced by patients (p values were 0.066, 0.250, and 0.17 respectively). Patients with either CD or UC did not appear to follow any seasonal pattern with their exacerbations. We did not observe any specific season where children with IBD tended to be born.
Conclusions: Our data suggests that the onset of symptoms of IBD tends to have a seasonal trend with the highest incidence in the fall. However, we did not observe any association between seasonality and exacerbations in the pediatric population. Moreover, there was no specific season in which children with IBD tended to be born in greater numbers.

444 *NATURAL HISTORY OF INFLAMMATORY BOWEL DISEASE IN MANITOBAN CHILDREN*

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Background: Improving knowledge of the natural history and clinical course of inflammatory bowel disease in children will provide better understanding of prognostic outcomes in these children.
Aim: To determine any possible change in diagnosis, disease progression and frequency of surgery in a cohort of children with IBD in Manitoba, Canada over a long follow-up period.
Methods: The Pediatric Gastroenterology Clinic at the Children's Hospital in Winnipeg, Canada has provided care for nearly all children resident in the province of Manitoba and for most of the children living in Nunavut and Northwestern Ontario since 1978. The database of this clinic from January 1978 to December 2007 was reviewed and medical charts of children diagnosed with IBD were examined. Changes in diagnosis, disease behaviour, distribution and surgical rates were determined
Results: During the 30-year study period, 397 patients with IBD, of whom 221 (56%) were boys, were diagnosed with IBD. A total of 233 (59%) had Crohn's disease (CD), 141 (35%) had ulcerative colitis (UC), and 23 (6%) had unclassified IBD (IBD-U). 103 children (mean age at diagnosis 12.9 y; range 6.3-17 y, 63 boys) with IBD had complete medical records and were followed for mean duration of 14.3 y; range 2.1-34.5 y. Sixty two (60.2%) had CD, 37 (35.9%) had UC and 4 (3.8%) had (IBD-U). Ten patients (9.7%) had their diagnosis changed from either UC to CD or CD to UC. Disease distribution and behaviour changed in 31 (30%) and 33 (32%) children respectively. Seven (18.9%) out of 37 patients with UC had colectomy while 36 (58%) out 62 patients with CD had CD-related surgery with mean number of surgeries/person of 0.97 (range 1-7) surgeries. No disease-related mortality was encountered.
Conclusions: Disease progression occurred in about one third of Manitoba children with IBD. Up to 10% may have their diagnosis changed over time.

445 *ENTERAL FEEDING THERAPY FOR MAINTAINING REMISSION IN CHILDREN WITH CROHN'S DISEASE: A SYSTEMATIC REVIEW*

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Background: Enteral nutrition (EN) therapy as primary treatment for Crohn's disease (CD) is considered the first-line of treatment in children, especially in Europe and Japan. The efficacy of EN for maintaining remission in children with inactive is unclear
Aim: To systematically identify, review and critically appraise the evidence of the efficacy and safely of EN in maintaining remission for children with inactive CD.
Methods: We searched PubMed/MEDLINE (National Library of Medicine), EMBASE (Ovid), and Cochrane Central Register of Controlled Trials (CENTRAL, Wiley) from inception till April 2014 for relevant citations of published randomized controlled trials (RCT) and cohort studies using individualized search strategies prepared for each database. The primary outcome was relapse rate for children < 17 years with inactive CD who have been in remission and subsequently started or maintained on EN for maintaining remission. Quality assessment for cohort studies was performed using *Newcastle-Ottawa Quality Assessment Scale.*
Results: No RCT was found. Only two observational studies that included 95 children fulfilled the inclusion criteria and were considered to be of a good quality. One study showed a relapse rate 42% in the EN group compared to 78% in the non-EN group at the end of 12 month-follow up period (P< 0.02). The other study showed a relapse rate of 40% in the EN group compared to 85% in those on no treatment (P=0.001) and 35% in patients on azathioprine (P=0.14) at the end of one year-follow up.

Conclusions: The current evidence, although insufficient, suggests that EN may be of benefit in maintaining remission for children with inactive CD. Large properly-designed randomized controlled studies are needed to confirm this conclusion.

446 *SIEVING ENTEROPATHY: A NOVEL FORM OF PROTEIN LOSING ENTEROPATHY ASSOCIATED WITH MUTATIONS IN PLASMALEMMA VESSICLE ASSOCIATED PROTEIN (PLVAP)*

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Background & Aims: Severe intestinal diseases observed in very young children are often the result of monogenic defects. Protein losing enteropathy (PLE) is categorized into two main etiologies: mucosal injuries (such as infection and Inflammatory Bowel Disease), and abnormalities of the lymphatic system (as seen in primary intestinal lymphangiectasia). We used whole exome sequencing (WES) to examine the genetic etiology in a patient with a distinct severe form of protein losing enteropathy (PLE) characterized by selective hypoproteinemia, hypoalbuminemia, and hypertriglyceridemia. Investigations using electron microscopy with ultrathin sections and immunohistochemistry confirmed mouse model findings in our patient.

Methods: WES was performed at The Centre for Applied Genomics, Hospital for Sick Children, Toronto, Canada. Exome library preparation was performed using the Ion Torrent AmpliSeq RDY Exome Kit. Functional studies were carried out based on the identified mutation.

Results: At 8 days of life, our patient (of consanguineous Afghan descent) presented with lethargy, poor feeding, severe metabolic acidosis, hyponatremia, secretory diarrhea and seizures. Laboratory examinations showed undetectable albumin (<10 g/L), low ceruloplasmin, elevated TSH, low free T4, low IgG, IgA, IgE and IgD with markedly elevated triglyceride level (4.3-10.3 mmol/L). IgM was noted to be normal and he had no proteinuria. Endoscopy showed an edematous duodenum and stomach with normal colon. He developed pericardial effusion requiring pericardial drain after developing a *Klebsiella oxytocia* urinary tract infection. He decompensated after Coagulase negative *Staphylococcus aureus* sepsis and died at 136 days old.

Using whole exome sequencing, we identified a homozygous nonsense mutation (1072C>T; p.Arg358*) in the *PLVAP* (plasmalemma vesicle associated protein) gene which truncated the protein by 84 amino acids. PLVAP is expressed in endothelial cells and plays a critical role in the formation of essential diaphragms of calveolae and fenestrae, maintaining microvascular permeability. Ultrathin sections of intestinal biopsies were examined using electron microscopy, showing identical findings of disruption of endothelial fenestrated diaphragms as is seen in the *Plvap* -/- mouse. Studies were performed *in vitro* with immortalized endothelial cells transfected with the mutated *PLVAP* construct (1-357) which showed proper homodimerization, glycosylation and trafficking to the plasma membrane. In tissue biopsies from our patient, immunohistochemistry showed an absence of PLVAP in CD31 positive vessels, and RNAscope multiplex assay showed an absence of *PLVAP* mRNA. These findings suggested a lack of expression in patient biopsy tissues, likely secondary to nonsense-mediated mRNA decay.

Conclusions: *PLVAP* p.Arg358* mutation resulted in the loss of PLVAP expression with the subsequent absence of endothelial fenestral diaphragms. This led to a selective plasma protein extravasation of proteins <200 kDa (or 30 nm) with resulting sieving protein-losing enteropathy and ultimately death. The endothelial barrier defect demonstrated in our patient suggests a novel category of protein losing enteropathy, which prompts further investigations into novel interventional strategies.

447 *A GENOMIC/TRANSCRIPTOMIC APPROACH TO IDENTIFY CANDIDATE ADHERENT-INVASIVE ESCHERICHIA COLI SIGNATURE TRANSCRIPTS*

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Introduction: Adherent-invasive Escherichia coli (AIEC) strains are abnormally abundant in lesions of patients with Crohn's disease (CD). The AIEC phenotype includes adherence and invasion of intestinal epithelial cells and survival of these bacteria within macrophages in vitro.

Our aim was to identify candidate transcripts that distinguish AIEC from non-invasive E. coli (NIEC) strains that can be applied for rapid and accurate identification of AIEC by culture-independent technology.

Methods: Pure cultures of the reference AIEC strain LF82 and the NIEC strain HS were grown. We performed comparative RNA-Sequence (RNASeq) analysis using RNA that was isolated during exponential and stationary growth to examine different phases. Coding sequences were analyzed for uniquely expressed and differentially expressed genes (DEG). To identify CDS specific to AIEC we sequentially incorporated the genomes of 10 phenotyped NIEC and 13 additional AIEC strains by subtractive genomics. Reverse transcriptase polymerase chain reaction assays for 6 genes were conducted on fecal and ileal RNA samples from 22 inflammatory bowel disease (IBD), and 32 patients without IBD (non-IBD) to determine if expressed genes are detectable in clinical samples.

Results: Differential expression analysis revealed that 224 and 241 genes had increased and decreased expression, respectively, in LF82 relative to HS. Pathways with DEGs in LF82 compared to HS included transition metal transport, siderophore metabolism, glycogen metabolism, oxidation-reduction, chemotaxis related transcripts and flagellum-dependent motility genes. CDS that mapped only to the LF82 genome accounted for 747 genes. Using subtractive genomics that incorporated the genomes of 10 previously phenotyped NIEC, 166 CDS mapped to the LF82 genome and lacked homology to 11 human NIEC strains. We compared these CDS across 13 additional AIEC, but none were homologous in all AIEC. Four LF82 gene loci belonging to clustered regularly interspaced short palindromic repeats region (CRISPR) - CRISPR-associated (cas) genes were identified in 4 to 6 AIEC and absent from all non-pathogenic bacteria. AIEC strains were enriched for pdu operon genes. One CDS, encoding an excisionase, was shared by 9 AIEC. The expression of Cas loci was detected in a higher proportion of CD than non-IBD fecal and ileal RNA samples ($p < 0.05$).

Conclusion: These results support a comparative genomic/transcriptomic approach towards identifying candidate AIEC signature transcripts.

448 *INFLIXIMAB THERAPY IN PEDIATRIC ULCERATIVE COLITIS: A SINGLE-CENTRE EXPERIENCE*

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Background/Aim: In a single centre pediatric cohort of 195 children with luminal inflammatory Crohn's disease (CD), primary non-response to infliximab (IFX) was uncommon (<10%), and subsequent durability of response enhanced by concomitant immunodulation with thiopurine or methotrexate therapy. (Church P et al, Inflamm Bowel Dis 2014) Pediatric long-term data in ulcerative colitis (UC) remain sparse. We aimed to review the real-world effectiveness of IFX in inducing and maintaining clinical remission in UC in the same singlecentre.

Methods: The records of pediatric UC patients aged <18 years old treated with 3 doses of IFX between July 2002 and March 2013 at The Hospital for Sick Children, Toronto, Canada were retrospectively reviewed. Responders to IFX induction continued to receive scheduled maintenance treatment. Remission and response were assessed at week 8, 6 months, and annually thereafter using physician global assessment (PGA) and pediatric ulcerative colitis activity index (PUCAI). Clinical response was defined by PUCAI decrease ≥20, and clinical remission by PUCAI <10 and PGA quiescent, provided no increase as steroids tapered. Factors associated with response and remission were assessed with multivariable logistic regression. Durability of response was explored using survival analysis.

Results: 95 children (57% male; median age 13.9 yrs (IQR 10.9-16.1), median UC duration 9.9 months (IQR 1.9-19.9)) received IFX treatment for steroid-refractory (n=55) or steroid-dependent (n=40) UC. Induction regimen was standard (5 mg/kg at weeks 0, 2, 6) in 59 (62%) and intensified (≥7mg/kg and/or dosing at weeks 0, 1, 4 or 5) in 36 (38%). Overall 35 (37%) of 95 were primary non-responders. Among the 60 (63%) who achieved clinical response, 50 (53% of total 95) achieved clinical remission. Multivariable analysis revealed an improved chance of clinical response for patients with steroid refractory disease (OR 9.81, 95% CI 2.18-44.12), male gender (OR 2.83 (1.10-7.26), and lower PUCAI (OR 1.03, 95% CI 1.06-1.01) when controlling for disease duration, steroid dose and intensified induction regimen. Steroid-free clinical remission was more often achieved in steroid-refractory (34/55, 62%) compared to steroid-dependent (16/40, 40%)

patients. During first year of follow-up dose escalation and/or interval shortening based on symptoms was implemented in, respectively, 15 (25%) and 14 (23%) of 60 responding patients. Complete loss of responsiveness among initial complete remitters occurred in 15% by one year, and in a total of 20% by two years. Adverse events included psoriatiform skin lesions in 3(3%); profound neutropenia in 1; systemic CMV infection in 1; infusion reactions in 7 (7%); transient elevation of liver transaminases in 37 (39%).
Conclusion: At this single pediatric centre primary non-response to IFX induction appears more common in UC than in CD. Clinical remission when achieved is durable.

449 *IBD DETERGENT SOFT WATER HYPOTHESIS - POSTULATING A RELATIONSHIP OF MUNICIPAL SOFT WATER AND HIGH CROHN'S DISEASE INCIDENCE*

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Objectives and Study: An increased incidence of Crohn's disease has been associated with more hygienic elements of modern urban life, greater exposure to air pollution, artificial preservatives in processed foods, and antibiotics[1]. Global mapping also indicates higher rates of Crohn's Disease in northern latitudes located in alluvial flood plains with municipalities delivering soft water. We explored the relationship of soft water in potentiating post treatment emerging contaminants in municipal water.
Methods: Using published figures of Crohn's disease incidence in 62 community health districts from the province of Quebec, Canada, we identified units with high or very high incidence of Crohn's to those with low or very low Crohn's disease incidence[2]. We mapped disease specific data on 57 health units to government published description of water quality in these administrative areas segregating units with high or very high water hardness (greater than 170 ppm of total mineral content) to those with low or very low soft water (less than 50 ppm of total mineral content). Data were compared by Fisher's Exact T-Test with significance defined as < 0.05.
Results: Thirteen of 30 administrative units were characterized as having soft water and high incidence of Crohn's Disease vs. 5 of 30 units with soft water and low levels of Crohn's, significant at a level of $p< 0.0004$.
Conclusion: This analysis suggests an association between municipalities with soft or very soft water and health units with a high incidence of Crohn's disease among adults. Because of their intrinsic diversity, larger urban municipalities with >100,000 populations do not figure in the calculation. The majority of the municipalities with soft water and high Crohn's disease incidence lie in the St. Lawrence alluvial flood plain. We are exploring the role of soft water in potentiating the influence of synthetic detergents on intestinal microbiota and/or intestinal permeability as a predisposing factor to the development of Crohn's disease. Alternative agents could include antibiotics, heavy metals among other emerging water contaminants.
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450 *TRANSITION OF YOUNG ADULTS WITH IBD: A 10-YEAR POPULATION BASED COHORT STUDY OF HEALTH SERVICES UTILIZATION*

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Most studies of adolescent's transition to adult care are clinic based involve small sample size. Population level health services utilization, costs of care and outcomes over time for transitioning adolescents with chronic diseases are becoming available. The aim of this population-based study was to evaluate health services utilization, costs and selected outcomes trended over time, comparing gender differences based on 10 cohorts of adolescents who turned 17 in each baseline year from 1996- 2011 in British Columbia (BC).
Background. Kappelman et al., identified 8.1 percent of a total US population of 9,056 with Crohn's Disease including patients < 20 years of age. Results were not presented by age group however, the authors concluded that in the US patients with IBD consume "substantial" healthcare resources. Benchimol et al., reported on surgical and hospitalization rates for children <18 diagnosed with IBD between 1994 - 2004 in Ontario, Canada.[4] Changes in treatment approaches over the time period affected surgical rates.
Methodology: Administrative data was obtained for the BC population aged 1 - 65+ for Medical Service Plan (MSP), acute care Discharge Abstract Data (DAD), and Pharmanet. The data was anonymized and a workID created for each administrative file allowing linkage to the files for the unique individuals. For this study only information related to patients who turned 17 in each year from 1996 to 2011 was included. 15 unique cohorts for each year was created with a total of 1,397 unique patients based on an algorithm used by the BC Ministry of Health.
Results: Utilization of fee-for-service primary and specialist care services, diagnostics services (MSP), acute care and

pharmaceutical data will be presented including total services, costs and standardized based on per person year. In addition, total events for endoscopic procedures, laboratory and radiology events all of which will be trended over time for each study cohort will be included. Patients using any health care services in each service event year will be computed in order to identify any differences in utilization over the period from transition to adult care at age 17. This analysis will explore the tendency of transitioning adolescents with chronic diseases who fail to comply with treatment immediately after transition to adult care. All health utilization information (costs, visits, hospitalizations, number of individuals) will be trended over the study period. Trends will be differentiated by gender and show distinct patterns over each cohort's trajectory. These results will provide important population based results of transition of youth and will address some of the post-transition issues.

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*451 *ANALYSIS OF DE NOVO VARIANTS IN VEO-IBD IDENTIFIED BY WHOLE EXOME SEQUENCING*

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Background: The severe phenotype and young age of patients with very early-onset IBD (VEO-IBD) suggest a more pronounced genetic susceptibility and dysregulated immune response than older onset IBD. We hypothesized that rare or novel coding variants were enriched in patients with severe VEO-IBD and could be detected by whole exome sequencing. We previously demonstrated the role of multigenic and autosomal recessive (AR) inheritance in disease development. Here we looked for *de novo* variants in genes involved in primary immunodeficiencies (PID), IBD and in the whole exome of VEO-IBD patients to further evaluate this hypothesis.

Methods: IBD patients 5 years and younger and their parents were recruited. Exome capture was performed by Agilent SureSelect V4, and sequencing was accomplished with Illumina HiSeq platform. Following functional annotation, single base substitutions likely to alter protein function were kept for subsequent analysis. We then evaluated complete trios under a *de novo* model of inheritance defined by the presence of a single base substitution or copy number variation in the proband that was not inherited from either parent

Results: We analyzed a total of 69 trios for analysis. Patients' age ranged from 3 weeks to 4 years. Candidate variants were identified under the *de novo* model. Examples include a whole gene deletion of *XIAP* in a male who presented at 3 weeks of life with severe failure to thrive and bloody diarrhea refractory to medical and surgical therapy. A novel *de novo* variant in *MUS81* (p.E226Q) was detected in heterozygosity in a female patient with VEO-IBD who presented at 17 months. Immunophenotyping was significant for low CD8 T cells. MUS81, critical in DNA replication, is important for genomic integrity. A *de novo* novel variant in *GPR35* was detected in a male diagnosed at 6 months of life with severe ileocolonic VEO-IBD. This G coupled protein receptor (GPCR) is expressed on immune cells and intestinal epithelial cells, and has been implicated in IBD. It has been associated with gut homeostasis through regulation of metabolism and subsequent anti-inflammatory T cell regulatory response.

Conclusions: *De novo* variants in genes involved in PID, IBD and pathways not previously associated with IBD may be important for a subset of patients with VEO-IBD. It is likely that for some patients with VEO-IBD, additional defects in the same pathway, involving both the innate and adaptive immune response, result in the specific phenotype.

453 *INFLAMMATORY BOWEL DISEASE SPARES THE POOR BUT AUTOIMMUNE HEPATITIS DOES NOT: SOCIOECONOMIC FACTORS IN IMMUNE-MEDIATED DISEASE IN UTAH*

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Background: Pediatric-onset inflammatory bowel disease (IBD) and autoimmune hepatitis (AIH) are heterogeneous immune-mediated disorders. The etiologies of both are complex and only partially explained by genetic factors. Environmental influences likely play a larger role in the pathogenesis of both IBD and AIH but are poorly quantified in children. Our objective was to quantify how the prevalence of IBD and AIH varied in neighborhoods with low and high socioeconomic status (SES).

Methods: US Census tracts are pre-defined, geographically contiguous subdivisions ("neighborhoods") of a county containing 1,200-8,000 residents each, that collectively cover the entire population of a state. Each of these neighborhoods is connected to detailed demographic and SES data collected from the 2010 US Census survey. We identified all known cases of pediatric IBD and AIH in Utah in a population-based fashion. Each patient's residential address at diagnosis was

linked to its corresponding United States Census tract, and the associated SES data. We ranked all Utah tracts from 1-588 for each of six SES variables, grouped them into deciles, and calculated the age and race-adjusted prevalence of IBD and AIH in each decile. We used linear regression to quantify trends.
Results: We identified 465 patients with pediatric IBD and 44 patients with pediatric AIH amongst 775,561 children. The prevalence of IBD was correlated with the general SES of each neighborhood. The prevalence of IBD varied between 31 and 101 cases per 100,000 children in neighborhoods within the lowest and highest decile of SES, respectively. Neighborhoods with the most IBD had the highest median family income (R-squared 0.74, p=0.001), highschool graduation rate (R-squared 0.58, p=0.011), and urbanization (R-squared 0.96, p=0.019), and the lowest foodstamp usage (R-squared 0.61, p=0.007), poverty rate (R-squared 0.68, p=0.003), and childbirths per 1000 women (R-squared 0.46, p=0.03). In contrast, the prevalence of AIH was approximately 8 per 100,000 children in all deciles, regardless of a low or high SES.
Concusions: Pediatric IBD is more common in Utah neighborhoods with a higher SES, and more rare in neighborhoods with a low SES. Pediatric AIH affects children of high and low SES equally. Unknown environmental factors related to the general SES of a child's neighborhood likely explain most of a patient's risk for IBD. The relationship between specific environmental risk factors that tend to differ between high and low SES groups such as antibiotic usage, dietary quality, smoking, and rates of vaginal delivery, should be studied further.

456 *IMPACT OF ROTAVIRUS INFECTION ON RELAPSES IN CHILDREN WITH IBD*

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Introduction: Relapse in inflammatory bowel disease (IBD) is not predictable. Bacterial infections are well recognized triggers but little is known on enteric viruses. In areas where rotavirus diarrhea still causes up to 40% of hospitalizations in pediatric population, this may be an important factor to consider.
Aim: To analyze the role of rotavirus in the occurrence of relapses in children with IBD.
Methods: Retrospective, descriptive analysis of patients diagnosed with IBD in a Pediatric Gastroenterology Unit between 2004 and 2014. The following variables were considered: classification of IBD, severity of relapse (PUCAI, PCDAI), isolation of rotavirus in stool during a relapse (immunochromatography), treatment performed and its efficacy.
Results: Fifty one children were evaluated: ulcerative colitis (UC) n=36, Crohn's disease (CD) n=11 and indeterminate colitis n=4. 26 presented relapse episodes (5 requiered colectomy). 15% (4/26) rotavirus rescue in stool (UC n=3, CD n=1, mean age:10.76 yrs (r 7.58-14 ys). All patients had PUCAI/PCDAI score >40 at time of relapse which occurred in a median follow up time of 13 months. They were all admitted to hospital (mean stay:18 days) and required a step-up treatment: the addition of azathioprine in 1 CU, and the other 3 received biological treatment with infliximab. Two patients under infliximab induction (UC both) had poor outcome, and required total colectomy, with subsequent reconnection after 5 and 11 months.
Conclusion: Treatment escalation and even the need of colectomy were observed after relapses due to rotavirus infection .These observations occurred before the vaccine was included in public health calendar. Reducing the circulation of rotavirus may prevent the devastating effects in patients on inmunosuppression.

457 *CHANGE IN FECAL ASCA MEASUREMENTS MAY DIFFERENTIATE PATIENTS WITH CROHN DISEASE FROM THOSE WITH ULCERATIVE COLITIS*

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Background: Measurement of serum Anti-Saccharomyces cerevisiae antibody (ASCA) levels has been used to help assess patients with known or suspected inflammatory bowel disease (IBD). Previous studies have demonstrated that fecal ASCA are present in the stool of patients with IBD. Fecal lactoferrin (FLA) has been shown to be a sensitive biomarker for mucosal inflammation in patients with both UC and CD. We now assess whether absolute change in fecal ASCA levels can help clinicians differentiate patients with Crohn disease (CD) from those with ulcerative colitis (UC).
Aim: To compare absolute change in paired fecal ASCA and FLA levels obtained from children and adolescents with CD and UC during periods of active and convalescent disease activity.
Methods: Paired stool samples obtained from individual patients during periods of active and inactive disease were collected and measured for fecal ASCA and lactoferrin by enzyme-linked immunoassays (ASCA-CHEK and IBD-CHEK respectively). Disease activity was determined by Physician Global Assessment (PGA). The absolute change in paired fecal measurements was calculated as the absolute value of the difference between clinic visits, and reported as median (IQR) and assessed by Wilcoxon rank-sum test. The ability of fecal measurements to predict disease type was determined by receiver operator characteristics and area under the curve (AUC).
Results: 47 patients (age 3-20 years; 53% female; 72% CD) were included in this study. Paired stool samples were obtained within 13 months (median 6.5) of one another. Absolute change in fecal ASCA levels between periods of disease activity and clinical remission were higher in patients with CD than those with UC (0.136 (0.009, 0.520) vs. 0.002 (0.001, 0.020);

P=0.001). The reverse was true for FLA, with lower FLA in CD than those with UC (0.279 (0.129, 0.847) vs. 1.026 (0.564, 1.078) by IBD-CHEK; *P*=0.02). Optimal cut-points for predicting disease type from absolute change in fecal ASCA and FLA were determined. The sensitivity and specificity for absolute change in fecal ASCA > 0.004 was 0.82 and 0.69, respectively, with an accuracy of 0.79 (AUC=0.84). The operating characteristics for absolute change in FLA >1.078 were very poor, with sensitivity 0.18 and accuracy 0.34 (AUC=0.27).
Conclusions: Consistent with previous studies, we found FLA to be a sensitive marker for mucosal inflammation. However, the absolute change in FLA was a poor discriminant of disease type. In contrast, absolute change in fecal ASCA > 0.004 was a sensitive and accurate predictor of disease type. Larger prospective studies are warranted to assess if changes in the level of fecal ASCA represent a novel, and more specific, metric for determining disease phenotype in children and adolescents with IBD.

459 *QUALITY IMPROVEMENT IN PEDIATRIC INFLAMMATORY BOWEL DISAESE: THE MANITOBA EXPERIENCE*

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Background: Quality improvement (QI) in medicine is defined as the efforts to change care using an evidence-based approach in order to make meaningful positive changes to the healthcare. Efforts to improve quality of care to children with chronic disease such as inflammatory bowel disease (IBD), could result in better outcomes. In January 2012, several QI measures were implemented to the Pediatric IBD Program of Manitoba, Canada
Objective: The aim of this study was to examine whether implementations of healthcare measures for children with IBD has led to improvement in disease outcomes
Methods: A comprehensive chart review of children with IBD, who were diagnosed prior to January 2012, and continued to be followed after QI measures were implemented, was performed. Quality indicators were measured and compared before and after January 2012. Those indicators included; number of clinical relapses as defined by activity indices, number of steroid courses, IBD-related emergency room (ER) visits, and IBD-related hospital admissions. Within subjects pre and post-intervention differences were
calculated using generalized estimating equation (GEE) approach. A negative binomial regression model with the duration of follow-up as an offset was utilized to calculate relative risks for the indicator. A relative risk of less than 1 indicated that the post-intervention rates are lower than the pre-intervention rates.
Results: A total of 76 children, (mean age 10.35±3.45, 38 boys) with IBD (45 Crohn's disease and 31 ulcerative colitis) who were followed for a mean duration of 2.45 ± 1.04 years before and for 1.96 ± 0.7 years after QI measures were implemented.
Relative risks, 95% Confidence Intervals (CI), and P values are provided in table 1
Conclusions: QI measures resulted in significant improvement in healthcare outcomes of Manitoban children with IBD. This may well improve overall outcome with subsequent savings in healthcare costs. More evidence is required on validating and linking individual health indicators to specific quality improvement interventions.
Table 1

Indicator	Relative Risk	95% CI	P Value
Clinical relapses	0.30	0.21 - 0.42	<0.0001
Steroid courses	0.20	0.13 - 0.29	<0.0001
IBD-related ER visits	0.24	0.14 - 0.39	<0.0001
IBD-related hospital admissions	0.13	0.06 - 0.29	<0.0001

*461 *THE EFFECT OF FENNEL ON INFLAMMATORY MEDIATORS AND BARRIER FINCTION IN T84 INTESTINAL EPITHELIAL CELLS AND A DSS-INDUCED COLITIS MOUSE MODEL*

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Background: *Foeniculum vulgare* (*F. vulgare*), commonly known as fennel, has been used for thousands of years as an alternative treatment for digestive disorders. *F. vulgare* has been found to have multiple beneficial effects, such as antifungal, antithrombotic and anti-inflammatory actions. It is unknown whether *F. vulgare* has an effect on inflammatory mechanisms prominent in inflammatory bowel disease (IBD). Our aim is to study the effect of *F. vulgare* on inflammatory mediators and barrier function in T84 intestinal epithelial cells and a dextran sodium sulfate (DSS) induced colitis mouse model.
Methods: T84 cells were treated with *F. vulgare* extract and then interferon gamma (IFNg). Quantitative PCR (qPCR) was performed to evaluate expression of inflammatory mediators, STAT1 and STAT3, and the tight junction-associated

proteins, zonula occludens 1 (ZO-1) and occludin. For the *in vivo* study, six-week old C57BL/6 mice were given drinking water that contained DSS for 5 days, with or without the addition of *F. vulgare* extract. Treatment with *F. vulgare* or plain water continued for 3 days. Mice receiving no DSS with or without *F. vulgare* served as controls. Distal ileal and proximal colonic tissues were collected for immunohistochemistry, qPCR and western blotting.
Results: Expression of STAT1 induced by IFNg in T84 cells was significantly decreased by treatment with *F. vulgare*. There was a trend towards increased expression of ZO-1 and occludin, with no significant effect of *F. vulgare* on expression of STAT3 (n=4). *In vivo* histologic analysis of colonic mucosa revealed decreases in crypt distortion and inflammatory infiltrates in DSS/*F. vulgare vs.* mice treated with DSS alone. Increased transepithelial electrical resistance, a measure of intercellular permeability, in the proximal colon was revealed in mice treated with *F. vulgare* vs controls, and in mice co-treated with DSS and fennel vs DSS alone (n=3). Decreased total STAT1 and phosphorylated STAT1 (pSTAT1) protein expression was also seen in mice treated with DSS/*F. vulgare* vs DSS alone.
Conclusions: Our studies show that *F. vulgare* decreases STAT1 expression and decreases pSTAT1 in response to inflammatory agents, which adds to our understanding of the basis for *F. vulgare*'s anti-inflammatory effects. STAT1 is a major inflammatory mediator in IBD, thus our study could indicate a potential therapeutic role for fennel in IBD. The barrier function of the gastrointestinal tract may also be improved by *F. vulgare* based on the trends in the expression of tight junction proteins, tissue resistance, and histology of intestinal epithelial cells and tissues.

462 *DURABILITY OF INFLIXIMAB IS RELATED TO DOSE AND DISEASE EXTENT*

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Background: Anti tumor necrosis factor alpha is an established treatment of Inflammatory Bowel Disease (IBD). Primary non-response or secondary loss of response remains a critical issue. There is a rising concern that suboptimal dosing in extensive disease may predispose to poor response and/or duration of response to infliximab (IFX) therapy. However data supporting this notion is limited.
Aim: To determine if IBD patients with extensive disease require a higher dose of IFX than patients with limited disease.
Methods: We retrospectively reviewed the records of 105 pediatric patients who received IFX between 2012 and 2014. Patients who continued on 5mg/kg q8 weeks of IFX therapy were compared to patients who needed IFX dose escalation to 10mg/kg or shorter infusion interval. Patients started at 5mg/kg were then compared to those who were started at 10mg/kg IFX. Patients with pancolitis were classified as "extensive"; those with limited or patchy colitis were classified as "moderate"; those with proctitis, ileitis or scattered colonic aphthae were classified as "limited". We compared the duration of IFX maintenance and dose escalation among the various groups.
Results: A total of 98 patients were eligible for the study, 87/98 (89%) of the patients were started at 5mg/kg of IFX and 11/98 (11%) of patients were started at 10mg/kg. Of the patients started at 5mg/kg, 52/87 (60%) remained well and continued on the same dose and 35/87 (40%) needed dose escalation due to poor response. All patients started at 10mg/kg IFX continued on the same therapy. Further analysis showed that 70%, 58 % and 26% of patients with extensive, moderate and limited disease respectively who were started at 5mg/kg of IFX required therapy escalation. The average time to escalation of therapy in extensive, moderate and limited disease were 7.1, 10.7 and 11 months respectively. All patients with extensive and moderate disease started at IFX 10 mg/kg continue on the same therapy as of a mean of 9 and 11 months respectively. All patients with limited or moderate disease who required escalation of IFX therapy remain on the escalated therapy. Among patients with extensive disease whose therapy was escalated, 3/7 (43%) continue on the escalated dose and 4/7 (52%) discontinued IFX due to non response or infusion reaction.
Conclusion: Durability of response to IFX is related to the dose and extent of disease. None of our patients (n=11) started at IFX 10 mg/kg/dose have required discontinuation. 40% of patients begun on 5mg/kg/dose (n=35) required dose escalation. Patients with extensive disease who were started at 5mg/kg/dose of IFX were more likely to require dose escalation than patients with limited disease (70% vs 26%). Optimal IFX dosing in a timely fashion is crucial in enhancing the durability of IFX therapy. Larger scale studies are needed to further confirm this notion.

VARIABLE	NUMBER(%)
Total chart reviewed Patients included Patients excluded	105 98 7
Male Female	52(53) 46(47)
Ulcerative Colitis Crohn's disease Indeterminate	11(11) 85(87) 2(2)
Extensive disease Moderate disease Limited disease	18(18.4) 27(27.6) 53(54)
Patients on 6MP Patients on Methotrexate	48(48.9) 17(17.4)
Patients started at 5mg/kg Patients started at 10mg/kg Escalated IFX therapy from 5mg/kg q 8week	87(88.8) 11(11.2) 35(40.2)
IFX discontinued	7(7.1)

465 *INCLUSION OF HISTOLOGIC ABNORMALITIES CHANGES THE PARIS CLASSIFICATION OF PEDIATRIC CROHN'S DISEASE PHENOTYPE*

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Introduction: The Montreal classification scheme for adult inflammatory bowel disease (IBD) phenotype does not include histologic findings. The Paris modification for pediatric IBD adapts the model using only radiologic and endoscopic findings to describe disease location in these patients. We hypothesize that Crohn's disease classification will change with inclusion of microscopic findings.

Methods: A random subset was selected from a cohort of patients with Crohn's Disease diagnosed before 18 years of age between 2001-2014 at the IBD Program at University of California, San Francisco Benioff Children's Hospital (UCSF). Patients were included if they had confirmed diagnosis of Crohn's Disease, had no history of surgical resection, and underwent complete upper endoscopy (EGD) and colonoscopy with biopsies at UCSF. Endoscopic and radiologic (macroscopic) findings were reviewed independently by two physicians to create a macroscopic classification for each patient. A second classification including combined macroscopic and microscopic findings was created for each patient. Interobserver agreement between the macroscopic and microscopic classifications of disease extent were independently evaluated using a kappa statistic. The raters jointly reassessed and determined a "true" diagnosis in all discordant cases. Data are expressed as mean±SD.

Results: The records of 60 randomly selected patients were reviewed; 61.7% were male (mean age of diagnosis 10.88±0.56 years). Mean follow up was 6.02±0.46. The interobserver variability of the classification of ileocolonic disease (L1, L2 and L3) improved with inclusion of microscopy (weighted kappa= 0.73, 95% C.I. 0.65-0.82), in contrast to macroscopic findings alone (weighted kappa =0.58, 95% CI 0.5-0.71). In upper gastrointestinal tract disease (L4a), macroscopic changes alone were sufficient (k=0.51) and had less interobserver variability compared with inclusion of microscopic findings (k=0.38). Inclusion of microscopic findings significantly changed classification of colonic disease in pediatric IBD, with more patients classified to have more extensive (ileocolonic; L3) disease.

Conclusion: Agreement on classification of colonic involvement in pediatric Crohn's disease improved by including microscopic findings. Further studies are needed to justify inclusion of histologic abnormalities in establishing Crohn's disease phenotype.

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Macroscopic vs Microscopic Disease Location

Location according to the Paris Criteria	Macroscopic† Findings N (%)	Macroscopic+ Microscopic Findings N (%)	p-value
L1	9 (15)	6 (10)	<0.001
L2	17 (28.33)	9 (15)	
L3	26 (43.33)	41 (68.33)	
L4a	28 (46.67)	51 (85)	0.111

† Macroscopic findings including radiologic tests.

466 *CORRELATION OF ERYTHROCYTE SEDIMENTATION RATE AND C-REACTIVE PROTEIN WITH CLINICAL, RADIOGRAPHIC, AND HISTOLOGIC ACTIVITY IN FOLLOW-UP OF CHILDREN WITH IBD*

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Introduction: Inflammatory bowel disease (IBD) activity and severity are assessed by clinical evaluation and diagnostic tools such as laboratory, radiographic and histological abnormalities. The most common diagnostic serum biomarkers in use are ESR and CRP. In this retrospective study we examined the correlation of those biomarkers with clinical, radiographic, and histological findings in children with IBD during follow-up.

Methods: We reviewed the medical records of all children with IBD evaluated in our hospital between the years 2011 and 2014. Demographic data and disease information were collected on all patients during follow-up. ESR and CRP (performed within 2 weeks of event) were assessed at the last clinic visit, last imaging study and at the last colonoscopy. Clinical activity was assessed as active or inactive based on physician global assessment. Active colitis by histology and abnormal small bowel imaging results were noted. ESR > 20 mm/hr and CRP > 3 mg/L were considered as abnormal according to lab standards. Statistical analysis included examination of the markers as dichotomous variables (normal vs. abnormal) and as continuous variables.

Results: We studied 135 children (75 boys; mean age 12.5 years) with IBD. 58% of the children had Crohn's disease and 42% had ulcerative colitis. Elevated ESR and CRP were seen in 60% and 67% of children at diagnosis. ESR and CRP were available in 128 patient at the last clinic visit, 79 patients at colonoscopy and 41 patients at the last imaging study during follow-up. By utilizing the inflammatory markers as continuous variables we found a trend of positive correlation between ESR and clinical activity (P =0.07) and strong correlation with histological colitis (p=0.005 , see Table). CRP was only useful in detecting active clinical disease (p=0.002). There was no correlation between elevation of ESR or CRP with abnormal small bowel imaging study. When utilized as a dichotomous variable, abnormal ESR correlated with clinical activity, but abnormal CRP did not.

Discussion: This study helps differentiate the use of ESR and CRP in detecting disease activity during follow-up of children with IBD. ESR correlated well with clinical disease activity and histological colitis while CRP was useful only with clinical disease activity. ESR and CRP are not useful to predict radiographic abnormalities of small bowel.

Univariate logistic regression results assessing capability of ESR and CRP as continuous markers in predicting disease activity

		Active disease by PGA score at clinic visit	Histologic active colonic disease at colonoscopy
ESR	10 mm/hr	15%	1%
	20 mm/hr	19%	1%
	40 mm/hr	28%	5%
	60 mm/hr	41%	40%
	80 mm/hr	54%	72%
	P value	0.07	0.005
CRP	1 mg/L	13%	67%
	3 mg/L	15%	68%
	10 mg/L	23%	70%
	30 mg/L	58%	76%
	50 mg/L	86%	81%
	P value	0.002	0.203

467 *CHARACTERIZATION OF NAILFOLD CAPILLAROSCOPY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE*

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Background: Inflammatory Bowel Disease (IBD) is a chronic intestinal inflammatory disorder with a variety of clinical and biomarker indices that attempt to monitor disease activity and predict disease course. To date, no combination is consistently successful. Nailfold capillaroscopy (NFC) is a non-invasive technique validated and utilized in children with rheumatologic conditions, including juvenile dermatomyositis (JDM). NFC analyzes nailfold capillaries using digital photography to assess microvacular abnormalities. Previous studies have demonstrated specific nailfold capillary patterns of JDM patients correlate with disease severity, may predict prognosis, and improve with therapy. Given that vasculitis is a well described phenomenon in IBD, we hypothesize that NFC will provide a novel, non-invasive assessment of microvacular abnormalities in IBD, reflect disease activity and provide insight into prognosis and treatment efficacy.
Aims: The aim of this study was to characterize NFC patterns in patients with Crohn's disease (CD) and ulcerative colitis (UC) compared to healthy controls and identify a link to disease activity.
Methods: Children ages 2 to 22 years with a diagnosis of CD or UC as well as healthy children were recruited for onetime data collection. Exclusion criteria included IBD-Unclassified, any other causes of intestinal inflammation, or any other chronic disease. Records were reviewed for demographics, medications, and medical history. Disease activity using Pediatric Crohn's Disease Activity Index or Pediatric Ulcerative Colitis Activity Index along with serum inflammatory markers was recorded at time of enrollment. NFC was assessed using a Sony Cyber-shot camera equipped with DermLite® II Pro. Digital photographs of 8 digits were collected from each participant and Adobe Photoshop® was used to analyze the subpapillary venous plexus (SVP) and End-Row Loops (ERL). An ERL was counted as a capillary terminating in the distal nailbed. The SVP was defined as the plexus of vessels feeding the ERLs. Statistics performed using Fisher's exact test or χ^2 test as appropriate.
Results: Nailfold pictures were collected from 16 patients with IBD (9 CD/7 UC) and 10 healthy controls. NFC demonstrated significant SVP drop-out (68.9% vs 0%; $P<0.01$) and SVP branching (37.5% vs 0%; $P<0.05$) in IBD patients compared to healthy controls. SVP drop-out was more prominent in patients with active IBD vs IBD in clinical remission (88.9% vs 42.9%; $P=0.077$). Patients on steroids had a four-fold increased relative risk of branched SVP compared to patients on immunomodulator or biologic therapy (100% vs 25%; $P< 0.05$). There was no difference in the number of ERLs in patients with IBD vs healthy controls (5.6 vs 6.84; $P =0.104$). There was no difference in ERLs, SVP drop-out, or SVP branching in patients with CD vs UC.
Conclusion: IBD induces prominent changes in the both SVP density and SVP branching compared to controls. Worse clinical disease activity and active use of corticosteroids correlated with the degree of SVP abnormality. These changes within the SVP have not been described in patients with rheumatologic conditions. This data suggests NFC may serve as a useful, non-invasive tool to monitor disease activity in IBD.

468 *PROHIBITIN 1 IN INTESTINAL HEALTH AND INJURY*

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Prohibitin 1 (PHB1), a highly conserved, ubiquitously expressed protein, has been implicated in the regulation of cell proliferation, apoptosis, transcription, mitochondrial protein folding, and a cell-surface receptor. This diverse array of functions of PHB1 is attributed to the cell type studied and its subcellular localization. The expression of PHB1 mRNA and protein were decreased in patients with inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis as well as animal models of colitis. Transgenic mice overexpressing PHB1 were protected from Dextran sodium sulfate (DSS)-induced colitis as well as colitis-induced colon cancer. The goal of our research is to study the role of Prohibitin1 in healthy and injured intestine. Phb1loxP/loxP mice were developed and intestine-specific Phb1 KO mouse has undergone the development by serial breeding Phb1loxP/loxP mice with Villin-Cre mice as well as tamoxifen-inducible Villin-Cre mice. Knockdown of PHB1 in murine young adult mouse colonic epithelium (YAMC) cells Slowed down cell proliferation and increased apoptosis. It also raised Proto-oncogene serine/threonine-protein kinase (Pim-1) expression and decreased B-cell lymphoma 2 (Bcl-2) and long noncoding RNA H19 gene expression. Knockdown of PHB1 did not affect the NFκB pathway in YAMC cells. Intestine specific knock out mouse model of Prohibitin1 will serve as an important tool to understand the function of PHB1 in intestinal health and injury. The functions of PHB1 in regulating cell proliferation and apoptosis make it a potential therapeutic target in inflammatory bowel disease.

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LIVER

469 *PREVALENCE OF EXTRAHEPATIC COMPLICATIONS OF NONALCOHOLIC FATTY LIVER DISEASE IN CHILDREN*

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Background: Recent data in adults suggest that nonalcoholic fatty liver disease (NAFLD) is independently associated with extrahepatic complications such as cardiovascular disease and diabetes. The aim of the current study was to evaluate the prevalence of these complications in a group of children with NAFLD seen at a tertiary center.

Methods: Consecutive children who presented to our pediatric metabolic liver disease clinic from April 2014 to October 2014 for evaluation of NAFLD were included. Anthropometric measures, blood pressure, family and medical history, examination findings, laboratory and imaging results were prospectively entered in our database. Data on the following complications were collected: hypertension, dyslipidemia, metabolic syndrome, diabetes, hyperinsulinemia, polycystic ovarian syndrome, and obstructive sleep apnea.

Results: Fifty-six children were included with a mean age of 12.89 $\pm$ 1.0 year, a mean BMI percentile of 98.2 (range 73.4 - 99.9), 66.1% were male and 58.6% were Caucasian. In terms of cardiovascular complications, hypertension was present in 20.4% of patients, dyslipidemia (either HDL <40, LDL >110, Triglyceride > 150 or Total cholesterol > 200) in 67.9%, and metabolic syndrome in 47%. Evidence of hyperinsulinemia/pre-diabetes or diabetes was present in 48.2% (N=27) of patients and polycystic ovarian syndrome was present in 11% of female patients (2/18). In addition, we found that 17.8% (N=10) of patients had evidence of sleep apnea (AHI > 1.5). Analysis of total number of extra-hepatic complications showed that 83.9% of children with NAFLD had at least one of these complications (N=47). 19.6% (N=11) had one complication, 35.7% (N=20) had two, 16.1% (N=9) had three and 12.5% (N=7) had four.

Conclusion: Extrahepatic complications are exceedingly common in children presenting with NAFLD. We recommend aggressive investigation and management of these complications in conjunction with the management of NAFLD.

470 *ETIOLOGY OF LIVER FAILURE IN NEONATES AND YOUNG INFANTS*

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Background: Liver failure in neonates and young infants carries a poor prognosis. Establishment of an etiological diagnosis remains the key for treatment. Aim: To identify the etiologies of liver failure in the neonatal period and early infancy, in an attempt to manage treatable causes and provide genetic counseling for inherited disorders. Methods: All neonates and infants (< 24 months of age) presenting to Cairo University Pediatric Hospital, over a 2-year period, with acute liver failure were enrolled. Investigations and initial management went hand-in-hand; acyclovir and lactose-free formula (in neonates) were started after drawing samples for Herpes simplex virus and Galactose-1-phosphate testing. Investigations were further performed on a patient-to-patient basis. Our workup included the molecular diagnosis of DGUOK-related mitochondrial DNA depletion syndromes. Results: Acute liver failure was diagnosed in thirty-seven cases. Twelve patients (32.4%) had a definitive etiological diagnosis including; hemophagocytic lymphohistiocytosis (4 patients), tyrosinemia (2 patients), DGUOK-related mitochondrial DNA depletion syndrome (2 patients), herpetic hepatitis (1 patient), acetaminophen toxicity (1 patient), galactosemia (1 patient) and neuroblastoma (1 patient). Diagnosis was probable but inconclusive in 10 cases because they succumbed before completion of investigations. The diagnosis remained indeterminate in 15 patients (40.5%).

Patients with indeterminate etiology presented at a younger age (p = 0.037), had significantly lower ALT, AST (p = 0.035, p = 0.026 respectively) and lower serum albumin (p = 0.028). Conclusion: Inspite of exhaustiveness of the performed workup, a considerable portion remained indeterminate. Inherited disorders need to be intensively explored using advanced techniques as next generation sequencing.

471 *FREQUENCY OF DIAGNOSED GASTROINTESTINAL & LIVER DISEASES IN PAEDIATRIC OPD (OUT PATIENT DEPARTMENT) AT A TERTIARY CARE HOSPITAL OF KARACHI, PAKISTAN*

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OBJECTIVE: To assess the frequency of diagnosed gastrointestinal diseases in the paediatric outpatient patients of Abbasi Shaheed Hospital.

METHODS: A retrospective cohort study was conducted at Paediatrics unit-II of Abbasi Shaheed Hospital (from February 2013 to March 2015), which is a tertiary care hospital; sample size of the study was 101, and age was between 1 month to 11 years. Patient admitted from emergency have been excluded. All analysis was performed using SPSS 20.

RESULTS: Out of 101 patients, there were 43(48.8%) males & 45(51.2%) females, of which age range was 3.019 ± 0.99, 16 patients were referred to other hospitals (including those for liver transplantation) & 13 were lost to follow up.

CONCLUSION: The study concludes that Celiac disease & Hep B and C were the most prevalent disease in our set up where as TTG, endoscopy, liver biopsy & PCR are the most frequent investigation performed (other than the routine).

Frequency of diagnosed gastrointestinal diseases in the paediatric outpatient patients of Abbasi Shaheed Hospital

Disease	Number of Patients	Significant investigations(other than routine)
Celiac disease	18(20.45%)	Tissue transglutaminase & endoscopy with biopsy in all patients
Hepatitis B	14(19.4%)	PCR (quantitative), HDV
Hepatitis C	13(18.1%)	PCR quantitative and genotype
Others (including Biliary atresia, hereditary tyrosinemia, GSD, cryptogenic cirrhosis), PFIC	43(48.8%)	HAV (IgM, IgG), HDV, HEV, HIDA scan, liver biopsy with special stains.

473 *THE ROLE OF LIVER BIOPSY IN INVESTIGATION OF CHOLESTATIC LIVER DISEASE IN INFANCY*

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Objectives: To assess the diagnostic yield, and impact on clinical management of liver biopsy in infants with cholestatic jaundice.

Methods: This is a retrospective cohort study of children presenting under one year of age with cholestasis, who underwent liver biopsy between December 2002 and December 2013 at the Montreal Children's Hospital. Charts of 70 subjects were reviewed and data extracted regarding antenatal, family and patient history, laboratory data, pre-biopsy working diagnosis, post biopsy diagnosis, and change in treatment or management. A blind assessment by two independent gastroenterologists was done to assess biopsy utility, defined as presence of one of three possibilities: establishment of a diagnosis, exclusion of an important diagnosis, or change in management or treatment based on biopsy result.

Results: Seventy-nine biopsies were performed within the time frame outlined, with 21 meeting the exclusion criteria. Twenty biopsies were excluded as they were done for an indication other than cholestasis and one was excluded due to incomplete data. Assessment by both gastroenterologists of the remaining 58 biopsies showed that the biopsy was useful in 11/58 (19.0%) cases. There were no significant differences between patients in whom the biopsy was useful compared to those in whom it was not in terms of severity of direct hyperbilirubinemia, age at biopsy, age at admission, co-morbidities, stool color and TPN exposure. Twenty-three of the 58 patients also had a percutaneous cholangiogram as part of the workup of which 14 were percutaneous and 9 were performed intra-operatively. Of these 23 patients, liver biopsy failed to add useful information in 22 cases. Of the 58 biopsies performed, 4 had documented complications including bleeding, hypovolemic shock, and accumulation of free fluid in the perihepatic area.

Conclusions: Liver biopsy is an invasive test used in combination with other clinical modalities to determine the etiology of neonatal cholestasis. Data collected suggests that biopsy was useful in less than 20% of cases with a complication rate of 6.9%. Consequently, the role and timing of liver biopsy needs to be reassessed to determine which patients would most benefit from this procedure.

475 *PATIENTS AFTER THE FONTAN PROCEDURE ASSOCIATE WITH ELEVATED LIVER STIFFNESS ACCORDING TO TIME SINCE SURGERY*

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Background: The Fontan procedure is an effective palliative operation for patients with congenital heart malformation. Patients who undergo this procedure have been reported to develop liver dysfunction, cirrhosis, and liver tumors as long-term complications, but post-surgical liver involvement is not fully understood.

Objective: We aimed to elucidate liver stiffness and hepatic fat deposition in patients who had undergone the Fontan procedure.

Method: Twenty six patients (median age 12.0 years, range 4.2 to 24.9 years) who had undergone the Fontan procedure (median time since surgery 10.3 years, range 2.8 to 17.6 years) were examined for liver fibrosis (as liver stiffness measurement, LSM) and hepatic fat deposition (as a controlled attenuation parameter, CAP) by using FibroScan transient elastography. As a control group, 142 patients (median 11.7 years, range 1.3 to 17.7 years) without liver dysfunction, liver disease, or obesity were examined. The FibroScan results were compared with clinical and laboratory data.

Results: LSM was significantly higher in the Fontan group than in the controls (16.5±8.7 kPa vs. 4.0±1.0, *P*£ 0.001), whereas there was no difference in CAP between the two groups (177.6±47.8 dB/m vs. 182.9±43.8, $P = 0.44$). Age at time of examination was highly correlated with LSM ($\rho = 0.70$) in the Fontan group but not in the control group ($\rho = 0.35$). Time since surgery was also correlated with LSM ($\rho = 0.57$) in the Fontan group. On the other hand, age at time of surgery didn't show a significant correlation with LSM in the Fontan group ($\rho = 0.34$). LSM in the Fontan group showed no correlation with AST, ALT, hyaluronic acid, type 4 collagen, and the AST to platelet ratio index.

Conclusion: Fibrosis without fat deposition is a feature of liver involvement in post-Fontan patients. Because of the correlations between liver stiffness and time since surgery, it is important to follow up these patients non-invasively by using FibroScan.

476 *HEPATOTOXICITY OF STATINS AS DETERMINED BY ALT IN A PEDIATRIC COHORT WITH DYSLIPIDEMIA*

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Background: Statins are approved therapy for children and adolescents with familial hypercholesterolemia. Statins have low but measurable rate of hepatic side effects, ranging from asymptomatic liver enzyme elevation to liver failure. Although use of statins has increased in children, there are few studies examining statin hepatotoxicity in youth

Objective: To evaluate the hepatotoxicity of statins, as determined by serum ALT, in children and adolescents.

Methods: We analyzed data collected prospectively as part of a quality improvement initiative (Standardized Clinical Assessment and Management Plans; SCAMP®) in a Preventive Cardiology Clinic from September 2010 to March 2014. Study sample included patients (≤ 21 years of age) who had ALT measured during clinical care. Exposure of interest was statin initiated during or prior to the observation period. Patients were divided into two groups: 1) non-statin user before or during the observation period; and 2) statin user, started on statins before or during the study period. Secondary analysis compared the same individuals before and after starting statins. We used multivariable linear and logistic mixed effect regression models accounting for repeated measures with ALT as the outcome, statin use as the independent variable of interest, and adjusted for age, sex and race. An additional model also adjusted for overweight/obesity.

Results: Over the 3.5-year observation period, there were 1521 unique patients, of whom 943 had at least 1 ALT measurement (total 2704 ALT measurements - mean 2.9/ patient). Median (IQR) follow-up after first ALT was 18 (9-30) months, totaling 11,564 patient-months follow-up. There were 203 pediatric patients on statin therapy (71% were on simvastatin and 25% on atorvastatin), of which 97 initiated statins during the observation period. In the non-statin and statin groups, respectively, mean age was 13.9 (SD 4) and 14.5 (SD 4) years, 46% and 47% were female, 59% and 73% were white, and 52% and 29% were obese. Mean ALT was higher in non-statin than statin users (28 [SD 28] mg/dL vs. 23 [SD 20] mg/dL). In adjusted models, the non-statin users had an ALT 2.1 mg/dL (95% CI 0.1, 4.4; p=0.04) higher than statin users; which was attenuated after additionally adjusting for weight status (1.3 mg/dL [95% CI -0.9, 3.5], p=0.24). In comparing the same individuals pre and post-statin initiation, we found no difference in adjusted mean ALT (0.9 mg/dl, 95% CI -5.2, 3.4; p=0.7). No significant differences were found among statin users using dichotomous cutoffs for elevated ALT. We observed no clinically relevant hepatotoxic events.

Conclusion: In this pediatric cohort, there was no evidence of statin-induced hepatotoxicity. Higher ALT among children not on statins is likely explained by more obesity. Adult guidelines have recommended less frequent monitoring of liver enzymes for statin users; our results suggest this change might also be appropriate in pediatric patients.

*477 *PREDICTORS OF POOR OUTCOME IN PEDIATRIC PRIMARY SCLEROSING CHOLANGITIS: A MULTICENTER COLLABORATION*

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Background: Knowledge about which children with primary sclerosing cholangitis (PSC) will have progressive liver disease is lacking. Our objective was to establish the natural history of pediatric PSC and to identify clinical risk factors for poor liver outcomes in a multicenter collaboration.
Methods: We created a retrospective cohort of all available cases of pediatric-onset PSC at multiple institutions. Patients were followed from time of PSC diagnosis to the development of portal hypertension, liver transplantation, or death. Observations were censored at the date of last known follow-up. A multivariate Cox regression analyzed the association between five predictors: male gender (vs. female), large duct (vs. small duct) disease, cholestasis at diagnosis (total bilirubin (Tbili) > 2.0mg/dL), overlap with autoimmune hepatitis (AIH) (vs. PSC without overlap), and inflammatory bowel disease (IBD) (vs. no IBD) with two separate outcomes: portal hypertension, and liver transplantation/death.
Results: We identified 72 patients with PSC, with mean age 12.8yr (range 1.1-17.8), 60% (43/72) male, followed for mean time of 5.2yr (range 0.1-16.4). AIH was present in 29% (21/72). Cholangiography was performed in 86% (62/72), with large duct involvement identified in 75% (47/62). The remaining patients were diagnosed on the basis of liver biopsy. IBD was present in 86% (62/72). Mean Tbili at diagnosis was 1.2 (range 0-13.4), with 13% (10/72) of patients presenting with a Tbili >2.0. Survival with native liver 5 years after diagnosis of PSC was 86% [95%CI 72-93]. Cholestasis at diagnosis (hazard ratio (HR) of 7.6 [95%CI 1.6-35]) was associated with death or liver transplant. Survival free of portal hypertension 5 years after diagnosis of PSC was 70% [95%CI 55-80]. Male gender (HR 4.3 [95%CI 1.4-12.6]), large duct disease (HR 5.4 [95%CI 1.3-22.5]) and cholestasis at diagnosis (HR 4.3 [95%CI 1.6-11.9]) were associated with development of portal hypertension.
Conclusions: 30% of pediatric PSC patients will progress to portal hypertension within 5 years of diagnosis. Male gender, large duct disease and elevated Tbili at diagnosis are risk factors for progressive PSC. These risks and outcomes are being further evaluated in a larger, international collaboration.

479 *STEATOSIS IN LIVING RELATED DONOR: IS A PREDISPOSING FACTOR FOR NASH IN THE RECIPIENTS?*

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Introduction: Living related donor (LRD) increases the supply of organs for liver transplantation (LTx), decreasing waiting list mortality. The presence of fatty liver in the potential donor is found frequently in evaluations, and sometimes becomes an obstacle for donation
Objectives: Analyze the presence of fatty liver (FL) in the population evaluated for related living donor (LRD).
Evaluate if the presence of fatty liver in the donor is a predisposing factor for the development of steatosis in the recipients.
Methods: A retrospective and descriptive study of our population was done. 173 patients were evaluated for LRD in our Center between 2005- 2015, 129 patients were included .They were separated into 2 groups: D1: Donors without FL on the biopsy and D2: donors with FL on the biopsy. The recipients group were separeted in the same way: R1: donor with history of FL and R2: donor without history FL.
Results: 129 pac were included.D1: 78 pac had not steatosis on biopsy, 26 of them were selected as LRD(33%),X age: 27.7, 18F/8 M , X Cholesterol: 176.81 X AST: 21 X ALT:26. D2: 51 pac had steatosis on biopsy, 17 of them were selected as LRD (33%),X age: 33.2, 9F/8M , X cholesterol: 189.5,X AST: 25, X ALT:30. At recipients groups we found. R1: 17 recipients of LRD with steatosis, X age: 19.5 m,10F/7M, 4 pac (23.5%) present FL in the post transplant evolution (2/4 Moderate: 1 associated with acute cellular rejection and 2/4 cases severe : 1 associated with acute cellular rejection . R2: 26 recipients of LRD without steatosis, X age: 19.3m ,17 F/9M. 8 pac (30.7%) presented steatosis in the post transplant evolution (4 cases Moderate: 3/4 associated to acute cellular rejection and 4 cases severe : 1/4 associated to acute cellular rejection, 1/4 associated with hepatitis).In both groups FL was presented between the first and third month after transplant. There were not significant differences (p: 0.863) between these two groups.
Conclusions: In our experience, a properly selected donor, the history of fatty liver in the donor is not a predisposing factor for the development of NASH in the recipients.

482 *NOVEL ASSOCIATION OF LGR5 WITH A PROGENITOR CELL PHENOTYPE IN PEDIATRIC ALPHA-1 ANTITRYPSIN DEFICIENCY*

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Background: Alpha-1 antitrypsin deficiency (A1ATD), the most common inherited pediatric liver disease, can progress to cirrhosis and hepatocellular carcinoma; however, not all patients are susceptible to severe liver disease. One possible disease-modifying mechanism involves recruitment of liver progenitor-like cells to rescue hepatocytes rendered dysfunctional by the intracellular accumulation of misfolded mutant ATZ globules.

Methods: We analyzed expression of liver progenitor cell markers in both human A1ATD and PiZ transgenic mouse liver tissues.

Results: By immunohistochemistry, we identified LGR5 (leucine-rich repeat-containing G-protein coupled receptor 5) as a novel progenitor biomarker in early and late regenerating hepatocytes in 15 pediatric A1ATD cases, as well as in repopulated zones of PiZ mouse livers. We further compared our findings to other pediatric liver explants, including acute liver failure (n=7), progressive familial intrahepatic cholestasis (n=10), and biliary atresia (n=4). Overall there was reduced LGR5 expression in bile ducts compared to hepatocytes. The histologic pattern in humans suggested transdifferentiation, with LGR5-expressing hepatocytes adjacent to proliferating EpCAM+ biliary cells in advanced liver disease. Affymetrix analysis on isolated PiZ primary mouse hepatocytes also revealed gene expression profiles related to stress, survival, and progenitor cell phenotype.

Conclusions: Similar to adults, liver progenitor-like cells are a common feature of pediatric liver disease. These studies are the first to support a potential role for LGR5 in hepatocyte regeneration in A1ATD, suggesting its usefulness as a biomarker in children. We have now generated a PiZ/LGR5-eGFP reporter mouse line, and studies are underway to investigate critical cellular pathways that can induce this progenitor cell phenotype and support hepatocyte rescue, as a means to exploit hepatic regenerative capacity for therapeutic benefit.

483 *BILIATRESONE CAUSES LOSS OF CHOLANGIOCYTE POLARITY, MICROTUBULE INSTABILITY, AND DECREASED SOX17*

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Background: Biliary atresia (BA) is a rapidly progressive disease of unknown etiology causing cholestasis, fibrosis and obliteration of the extrahepatic bile duct. It is typically diagnosed in the first few months of age and is the most common indication for pediatric liver transplantation. We previously isolated a novel isoflavanone from a plant implicated in outbreaks of BA in livestock; this toxin causes selective disruption of the extrahepatic bile duct in zebrafish, mimicking BA. We characterized the effect of biliatresone on mammalian cholangiocytes in 3-D culture.

Methods: We used cholangiocytes in 3-D culture; they form spheroids, with external basement membranes (basolateral surface) and lumens (apical surface). Spheroids were treated with biliatresone or vehicle at times when lumens were well formed and were stained for cell polarity and basement membrane markers and analyzed by confocal microscope. A microarray was carried out to determine gene expression changes after treatment with biliatresone.

Results: Spheroids treated with biliatresone demonstrated instability of cellular tubulin within 3 hours. This was followed by loss of polarity (disruption of the apical F-actin ring) and lumen closure at around 12 hours. Biliatresone treatment caused a decrease in Sox17, and knockdown of Sox17 mimicked the sequence of events observed with biliatresone treatment, including microtubule instability.

Conclusions: We show that a toxin that causes BA in livestock and zebrafish results in microtubule instability followed by loss cholangiocyte polarity and luminal integrity in mammalian cholangiocyte cultures. A decrease in Sox17 is implicated in this process.

485 *THE ROLE OF RACE AND PAYOR ON AGE OF KASAI PORTOENTEROSTOMIES FOR BILIARY ATRESIA IN THE UNITED STATES: A STUDY FROM A NATIONAL INPATIENT DATABASE 2007-2011*

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Background: Biliary atresia is a progressive cholangiopathy of unknown etiology in newborns. Kasai portoenterostomy

remains the primary surgical procedure to enhance enteric biliary flow and improve patient survival. Age at Kasai has been shown to be the most critical determinant of outcome with best results when the procedure is performed at ≤60 days of life (DOL). Large US centers have individually reported data on outcomes of the Kasai. The most recent nation-wide analysis reported in 1990 did not include effect of race or payor on age of Kasai. We aimed to investigate the association between race and payor on average age of Kasai procedure in the United States using a national database.
Methods: Retrospective review of NIS HCUP, the largest publicly available all-payer inpatient health care database in the US, 2007-2011 was performed. ICD 9 codes 51.37 (Kasai portoenterostomy) and 751.61 (Biliary atresia) were used to identify cases. SAS 9.4 software was used for statistical analysis. A p-value of <0.05 was considered statistically significant.
Results: 706 Kasai portoenterostomies performed for biliary atresia were identified using weighted analysis. 43.4% of surgeries were performed at ≤ 60 DOL, 43.8% at 61-90 DOL and 12.8 % at >90 DOL. Mean age of procedure was 67.2 DOL (95% CI 62.7-71.6). Patients were mostly female (53.7%) and Caucasian (53.2%), with an equal mix of payor (Medicaid 49% and private insurance 47%). (further analysis in Table 1)
Conclusions: Despite the recommendation to perform Kasai portoenterostomy for biliary atresia at ≤60 DOL since outcomes are improved with earlier intervention, the age of procedure is unchanged since previously reported national data from the 1970s. Furthermore, more than half of the patients were >60 days at the time of intervention. African American patients in particular were more likely to be older at the time of Kasai, suggesting there may be a delay in diagnosis in this population. No significant difference was found among patients with private versus Medicaid insurance.
Table 1

	Kasai ≤ 60 DOL	Kasai > 60 DOL
Mean age at Kasai (days)	46.9 (95% CI 43.5-50.4)	82.6 (95% CI 76.6-88.7)
Race (%): Caucasian	57.8	45.6
African American	5.2	20.5*
Asian/Pacific Islander	18.3	9.6
Hispanic	10.8	13.1
Gender (%): Male	55.6	39.5
Female	44.3	60.4
Payor (%): Medicaid	46.7	48.8
Private Insurance	48.1	46.8

*p-value <0.025

486 *FAMILY FUNCTIONING AS A PREDICTOR OF WEIGHT LOSS IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE*

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Background & Aims: Non-alcoholic fatty liver disease (NAFLD) is the most common pediatric chronic liver disease in industrialized countries. The primary objective of this study was to assess whether family functioning was associated with increased BMI and response to life style modification. Methods: Parents and overweight (BMI>85%), and obese (BMI>95%) children with NAFLD (ages 8-18) were recruited from a pediatric liver clinic. Children and parents were consented to complete the General Functioning subscale of the McMaster Family Assessment Device (GF-FAD). The GF-FAD consists of 12 questions where higher scores indicate poorer family functioning. Only parents completed the Family Health Behavioral Scale assessment (FHBS). The FHBS assesses the family's diet and exercise practices. BMI and laboratory measurements were recorded 6 months pre- and post-assessment and at the time of assessment completion. All patients received counseling by the hepatologist and nutritionist encouraging life style modifications. Results: A total of 39 families were recruited. The sample consisted of 13 females and 26 males with an average age of 13.29 (SD= 3.2) years old. The sample included 60% Latino, 20% Caucasian, 8% Native American, and 8% Bi-racial patients. The average percentile BMI for age and gender was 96.52 with a range of 85th to 99th percentile. Internal consistency (alpha) for GF-FAD father report was 0.82, FAD mother report was 0.78, FAD child report was 0.84. The internal consistencies for the FHBS mother and father report were 0.82 and 0.87, respectively. The alphas indicated that every test item was in fact measuring the construct they intended to measure lending support for the reliability of this measure in this setting. A parent GF-FAD total score was created by averaging the mother and father score on the GF-FAD. BMI at baseline was positively and significantly correlated with BMI at time of assessment and 6 months post-assessment (r = 0.982, 0.918, respectively) indicating a high level of stability in BMI across time. The child GF-FAD total score was significantly correlated with parent GF-FAD total score (r= 0.473, p<0.05). The parent FAD total score was also significantly correlated with BMI 6

months post-assessment (r= 0.464, p<0.05). While controlling for baseline BMI, parent GF-FAD total score significantly and positively predicted BMI 6 months post-assessment (β = 0.199, p <0.05). Child FAD total and parent FHBS total did not significantly predict BMI 6 months post-assessment. Conclusions: Poor family functioning was found to be related to higher BMI. Parent GF-FAD is a promising method to evaluate patients who may be at greater risk for disease progression in terms of BMI that will require more intense therapy to elicit non-obesogenic behavioral change. Interestingly, the child GF-FAD and parent FHSB was not predictive.

489 *FREQUENCY AND IMPACT OF SEVERE HEPATOPULMONARY SYNDROME ON LIVER TRANSPLANTATION IN CHILDREN*

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Background: Resolution of hypoxemia after liver transplantation (LTx) for hepatopulmonary syndrome (HPS) is expected. Limited data on time to resolution, or impact of HPS on surgical outcomes in children is available. The aim of this study was to determine if oxygen therapy negatively impacts outcomes and describe time to resolution of hypoxemia in children.
Methods: We conducted a single center, case control study of all LTx recipients with HPS and hypoxia who required oxygen pre-LTx between 2002 and 2015. Controls were LTx recipients matched on age, diagnosis, and LTx date who did not require oxygen. We collected data from electronic medical record.
Results: Of 135 LTx recipients 47(35%) underwent bubble echocardiogram and 32/47(68%) had positive studies. We identified 9/135 (6.7%) patients with HPS who required oxygen therapy pre-LTx; 7/9 cases underwent LTx from 2011-2013 with only 2/9 prior (2003 and 2008). Bubble echocardiogram occurred more after 2008, 35/75 (47%) v. 12/60 (20%) (from 2002-2008) (p<0.05).
Mean age at LTx was 8 (0.8-18years) vs 7.8 (range:0.9-18.8years), p=0.9 in cases v. controls. Biliary atresia was the most common liver disease in 6/9(67%) cases 11/17(65%) controls. Other case diagnoses included alpha-1 antitrypsin deficiency, non-cirrhotic portal hypertension, and congenital hepatic fibrosis (n=1 each).
Each case had (+) bubble echocardiogram, with PaO_2 obtained in 7/9; median 58 (IQR: 42-67mmHg) and 6/17 controls had (+) bubble studies, none of which had hypoxia. 5 cases had abnormal sleep studies in which desaturations were noted and non-infant cases (n=7) received 0.5-5LPM of FiO_2 pre-LTx.
Varices occurred in 7/9 cases; only 2 experienced bleeding; 2/9 cases had ascites v. 14/17 controls (p<0.01), and overt encephalopathy occurred in 2 cases.
Cases had lower mean M(P)ELD scores at listing (4 (range:-8-12) v. 16 (range: -2-34), p<0.01), but similar M(P)ELD scores at LTx (32 (range:-11-38) v. 27 (range: 7-45), p=0.6) as exceptions were granted to 7/9 patients for HPS with 1 case transplanted as status 1B for intubation and hepatic encephalopathy. Median wait time was 123 vs. 180days (p=0.8) for cases v. controls.
Transplant utilized deceased donor grafts in all but 1 control; cold-ischemia time, estimated blood loss, and transfusion requirement were also similar (p>0.05). Median length of stay post-LTx was similar (13 (IQR: 11-21)v.12 (IQR:10-19)), with similar intubation and ICU time (P>0.05 for all variables). Cases were intubated 0-2days.
Cases received additional respiratory support: CPAP (n=1), High-Flow Nasal Cannula (n=4), NO_2 (n=1), and iloprost (n=1). At ICU transfer 8/9 cases required oxygen and 4/9 at hospital discharge. Cases required oxygen median 11 (range: (2-270 days) post-LTx. Case mortality rate was 0/8 (0%) with 0% in controls.
Conclusions: Hepatopulmonary syndrome, diagnosed by positive bubble echocardiogram, occurs commonly in LTx recipients with chronic liver disease or portal hypertension; most cases are mild and do not require oxygen. When oxygen is required, resolution can be expected, but may require substantial time without negatively impacting surgical outcomes. Survival was excellent in all cases despite low PaO_2 levels.

490 *AUTOIMMUNE HEPATITIS AFTER LIVER TRANSPLANTATION: IS IT ALL THE SAME?*

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Introduction: Following liver transplantation (LT), autoimmune hepatitis (AIH) can be seen as recurrent disease (rAIH) or de novo occurrence (dAIH). Differentiating clinical and histological features and patient predictors for development of AIH post LT are as yet unknown. Objective: The aim of this study was to identify differences in demographics, clinical presentation and outcomes of patients with rAIH and dAIH post LT. Methods: A retrospective review of LT recipients from 1997- 2014 was conducted. AIH post LT was diagnosed by the presence of autoantibodies and suggestive histology. Results: Out of 387 pediatric LTs conducted, rAIH was seen in 23 %(7/30) of the patients and de novo AIH in 2.2 % (8/357). Patients with dAIH were younger at transplant (1-5 years) as compared to rAIH (10-17 years). African-Americans constituted 85% of the rAIH group and 50% of dAIH group. Additionally, rAIH occurred in the allograft earlier than dAIH (41.4 m ±13.6 vs 112.5 m ± 22.4; p = 0.02). Mean GGT was higher in dAIH (398.9U/L ± 73.8 vs 206 U/L ± 48.7; p =

0.05). Autoantibodies were seen more commonly in rAIH vs dAIH (SMA: 57%vs 25%; LKM: 42% vs 0%; ANA 28% vs 25%) In addition to steroids, most rAIH required dual immunosuppression (i/s) (70% vs 50%). More than 2 episodes of acute cellular rejections were seen in 70% of rAIH (5/7) vs 37 % of dAIH(3/8) patients prior to diagnosis. Conclusions: Post LT, rAIH is seen earlier than dAIH with an aggressive phenotype requiring more immunosuppresion. Increased number of rejections in rAIH may predispose to recurrence of disease. Autoantibody markers in either group are unreliable for screening. Future research should be directed towards identifying non-invasive biomarkers for diagnosing these conditions.

491 *BLOCKADE OF RIP KINASE PATHWAY EXACERBATES ISCHEMIA REPERFUSION INJURY IN A STEATOTIC LIVER*

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Background: Steatotic livers undergoing ischemia reperfusion injury (IRI) demonstrate significant hepatocellular dysfunction and cell death leading to increased morbidity and mortality in obese individuals with fatty liver. Necroptosis is a form of regulated cell death, which is triggered by death domain receptors and mediated through receptor interacting protein kinase (RIP). Though well studied in renal IRI, it's role in steatotic liver IRI is largely unknown. Aim: The aim of this study was to investigate the role of the necroptosis pathway in steatotic mice undergoing IRI. Methodology: C57BL/6 mice were fed a high fat diet (HFD) for 12 weeks and subjected to 40 minutes of hepatic ischemia, followed by 24 hours of reperfusion. They were pretreated with necrostatin, a RIPK1 inhibitor and hepatocellular injury was assessed by serum ALT, necrosis by H&E and propidium iodide (PI) staining. Western blot (WB) and RTPCR were done. RIP3$^{-/-}$ / Caspase8$^{-/+}$; TNF α $^{-/+}$ / TRAF2 $^{-/-}$, and RIP KD (kinase dead) mice were fed a HFD and subjected to IRI. Hepatocellular injury was assessed as above along with evaluation of the NF-kβ survival pathway. Results: After IRI, HFD fed mice treated with necrostatin showed substantially increased necrosis (76.6 ± 6.6 vs 30 ± 1.2 %; $p<0.0005$) and serum ALT (2040 ± 0.5 vs 706.7 ± 49.2 IU/l; $p<0.0003$) as compared to saline treated HFD fed mice. This was confirmed by presence of increased PI staining ($p<0.05$), signifying increased cell membrane permeability and necrotic death. Similarly, after IRI, RIP3 $^{-/-}$ / Caspase8 $^{-/+}$; TNF α $^{-/+}$ / TRAF 2 $^{-/-}$, and RIP KD mice fed a HFD, showed increased necrosis and serum ALT as compared to WT HFD fed mice. Compared to lean mice, HFD fed mice showed reduced expression of RIP 3 as demonstrated by mRNA ($p<0.001$) and WB ($p<0.002$). Interestingly, there was a concomitant decrease in level of NF-kβ ($p<0.04$) in HFD fed mice compared to lean mice. Conclusion: Our results indicate that RIP kinase pathway, which is an established cell death pathway in IRI of other organs is not the principle mechanism of hepatocellular injury in IRI of a steatotic liver. In fact, blockade of this pathway leads to increased hepatocellular injury, which is likely a combination of unmasking of other death domain pathways such as FAS and TLR4; and mitigation of the survival NF-kβ pathway. This provides critical therapeutic targets for developing therapies specifically aimed at mitigation of hepatocellular death after IRI of a steatotic liver, which is a burgeoning clinical problem.

492 *VARIABILITY OF THE ANATOMY OF THE HEPATIC ARTERY AND ITS IMPACT ON LIVING DONOR LIVER TRANSPLANTATION*

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Introduction: The hepatic artery has numerous anatomical variables in healthy adults (45%)
This information is not known in children and especially in patients with chronic liver disease.
Recognizing different presentations of the hepatic artery may have impact on living donor surgery.
Objective: Determining the conformation of the hepatic artery in patients candidate to living donor transplantation, and evaluating the implications of this variability in complications at surgical time.
Material - Methods: Retrospective descriptive analysis from February 2009 to May 2014. 59 patients were studied, of whom 24 were women of a median age of 22 months (R 13 -34m), with average weight of 12 kg (IQR 9-15 Kg), PELD 17.
Toshiba Aquilum 64, ALARA radiation dose, nonionic iodinated contrast -
Angio multidetector CT was performed.
Results: Out of the 59 patients, 35 were selected to receive living donor liver transplantation, median age being of 21 months (r 14.27 m), average weight of 11 kg (r 9-13 k.).
The hepatic artery study showed that 24 patients had classic conformation of hepatic artery (group 1) and the remaining 11 (31%) showed configuration variables (group 2)
We have compared Group 1 with Group 2; and observed that:
Group 1 (24)
Group 2 (11)
Total complications
postoperative
13 (54%)
10 (90%)

Operating time
360 '(r 290-420)
390' r (345-420) p <0.35
Cold ischemia
89 '(r 60-120.)
150 `(r 100-240.) p <0.40
Positive Predictive Value, PPV, variability artery and complications are 90%.
Negative Predictive Value, NPV is 45%.
Conclusion: The variability of the hepatic artery is not a contraindication for transplantation, it causes increased graft ischemic time and it also increases surgical time, but there are not of significance difference with classical artery hepatic.

493 *DIAGNOSIS OF BILIARY ATRESIA: A 40-YEAR SINGLE CENTER EXPERIENCE. ARE WE MOVING IN THE RIGHT DIRECTION?*

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Introduction: Biliary atresia is a fatal perinatal obliterative cholangiopathy of unknown etiology managed by Kasai portoenterostomy and supportive care. Literature shows that clinical outcomes of these patients depend primarily on the age of surgery, which is linked to the age at referral to Pediatric Hepatology.

Aims and Methods: To determine whether there has been any improvement in age at referral or age at Kasai over time, we performed a 40-year retrospective chart analysis of biliary atresia patients managed at our institution.

Results: Our cohort included 89 patients with biliary atresia over 40 years. Of these, 4 patients had minimal data and 20 patients had some missing data due to unavailable or limited old records. Over the last 40 years, the mean age of referral to our institution has increased somewhat from 52 days to 58 days when averaged over 10 year intervals. Additionally, the median age of referral has increased over the last 10 years from 51 days to 64 days (Table 1). The mean age of Kasai has remained unchanged and the median age has increased minimally despite an increase in age at referral. Approximately 1/3 of patients underwent a Kasai ≤ 60 days throughout this time period. However, the number of infants undergoing Kasai at ≤ 90 days decreased over time from 91% prior to 1995 to 81% in the last decade.

Conclusions: The recent increase in median age at referral is concerning for a lack of awareness of biliary atresia and the importance of timely intervention among referring physicians. Despite the older age at referral, we managed to maintain the age at Kasai relatively unchanged. However, there is a worrisome trend towards fewer patients undergoing the Kasai at ≤ 90 days over the last decade. Unfortunately, there has been no improvement in age at referral and, therefore, age at diagnosis of biliary atresia over the last 40 years. Hence, to improve our outcomes for these patients, we need widespread primary care provider education to help identify and refer these patients earlier for definitive surgical intervention.

TABLE 1

	Ante 1995	1995-2004	2005-2014	Total
Mean age at referral (days)	52	54	56	54
Median age at referral (days)	54	51	64	57
Mean age at Kasai (days)	68	67	69	68
Median age at Kasai (days)	67	66	71	68
Kasai ≤60 days N (%)	8/22 (36)	13/30 (43)	10/31 (32)	31/83 (37)
Kasai ≤90 days N (%)	20/22(91)	26/30(87)	25/31(81)	71/83(86)

494 *AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DIEASE: NOT JUST A RENAL DISEASE*

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Introduction: Autosomal Recessive Polycystic Kidney Disease/Congenital Hepatic Fibrosis (ARPKD/CHF) is an inherited hepatorenal fibrocystic disease with a wide spectrum of dual organ developmental abnormalities, secondary to *PKHD1* mutations. These patients have CHF of varying severity, independent of renal disease progression. Improved care and longer survival of these patients has resulted in increased incidence of lethal clinical complications of CHF.

Renal pathophysiology of ARPKD/CHF is well understood and clinical trials targeting the renal disease are near. But pathophysiology of CHF is not well studied and hence warrants investigation, given independent disease progression in the two organs.

We hypothesize that aberrant signaling pathways are similar in renal and hepatic cystic disease of ARPKD/CHF. However, differences in organ specific disease progression may affect results of potential therapies.

Aim and Methods: PCK rat, an orthologous model with *PKHD1* mutation, consistently develops dual organ abnormalities

as in human disease, providing the best model for our investigation. We performed a systematic characterization of morphological changes in development and progression of CHF in PCK Rats, correlating them with biliary ductal ectasia, proliferation, apoptosis and periportal fibrosis at progressive stages of disease. Our goal was to identify ‘critical stages' of the disease to develop liver specific therapies.
Five male rats each at 0, 30, 60, 90, 120 and 150 days of age were evaluated and physiologic data (body, liver, kidney, intestine and spleen weights) was collected. From this cohort, 3 livers each at ages 30, 90 and 150 days were randomly selected to undergo histopathological analysis. Serial sections were stained with Masson's Trichrome stain to score fibrosis and immunohistochemistry (IHC) was done to mark cholangiocytes, proliferation and apoptosis correlating it with degree of ductal ectasia, and progression of fibrosis. Morphometric analysis was performed using *ImageJ* to quantitate disease burden at different time points.
Results: Liver weight to body weight ratio's increased as disease progressed and was profound in sick animals. Morphometric analyses of liver tissues show consistent enlargement and deformation of biliary ducts with increasing age. A 50% increase in cyst numbers and cyst area per surface area of the liver with increased proliferation of cholangiocytes and mesenchymal cells was observed between ages of 30 and 90 days. Thereafter, proliferation gradually decreased to negligible by day 150. Periportal fibrosis index increased to 39% at day 90 and thereafter by 8% to 150 days. Fibrosis score increased from 0 to 2 between 30 and 90 days and to 4 at 150 days. Fibrosis was more prominent in hilum around larger cysts. Apoptosis increased steadily with age.
Conclusion: Increase in proliferation upto day 90 and decrease thereafter suggest that proliferation is not a major factor in the disease once fibrosis begins and the ‘critical stage' of the disease is before 90 days. Given the difference in organ specific rate of disease progression, therapies aimed at the proliferation of renal tubular epithelia require a histopathological assessment of the liver disease to provide maximum benefit.

495 *EFFICACY AND SAFETY OF SEBELIPASE ALFA IN CHILDREN AND ADULTS WITH LYSOSOMAL ACID LIPASE DEFICIENCY: RESULTS OF A PHASE 3 TRIAL*

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Lysosomal Acid Lipase (LAL) Deficiency is a progressive multisystem disease that is an underappreciated cause of cirrhosis, severe dyslipidemia and early onset atherosclerosis.
A phase 3, double-blind, placebo-controlled trial (NCT01757184) randomized affected children and adults (N=66) to placebo or sebelipase alfa 1 mg/kg every other week for 20 weeks. Primary endpoint was ALT normalization. Secondary endpoints included additional important efficacy assessments, safety and immunogenicity. Medically important abnormalities were common at baseline including fibrosis (100%), bridging fibrosis (Ishak score 3 or 4; 47%) and cirrhosis (31%) in biopsied patients (n=32) and a median LDL-C of 204.0mg/dL (range 70-378mg/dl). Mean age of biopsied patients was 12 yr. LDL-C was ≥190mg/dL in 58% (38 of 66 of patients, including 24% (9 of 38) who were on lipid lowering medications.
After 20 weeks, ALT normalization (ULN range 34-43 U/L) was achieved in 31% of the sebelipase alfa group and 7% of the placebo group. Multiple secondary efficacy endpoints were also met including relative reduction in LDL-C, non-HDL-c, and triglycerides and relative increase in HDL-C. Over 350 infusions of sebelipase alfa were given during the double-blind period. The number of patients with AEs was similar in each arm. During the double-blind period, most AEs were mild and unrelated to sebelipase alfa; 6 patients experienced infusion-associated reactions (4 placebo; 2 sebelipase alfa). Dosing was paused in 1 patient after an atypical infusion-related reaction following sebelipase alfa treatment.
Sebelipase alfa for 20 weeks demonstrated statistically significant improvements in ALT normalization and in a number of other important disease related abnormalities including marked reductions in LDL. The safety profile appears favorable and infusions were generally well tolerated.

496 *IMPACT OF SEBELIPASE ALFA ON SURVIVAL TO 2 YEARS OF AGE WITH RAPIDLY PROGRESSIVE LYSOSOMAL ACID LIPASE DEFICIENCY*

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Lysosomal Acid Lipase Deficiency (LAL D) in infants, historically known as Wolman Disease, is a medical emergency with rapid disease progression and death occurring within the first 6 months of life. In a natural history study, failure to thrive, liver complications, massive hepatomegaly, and mortality were confirmed in LAL D infants. Disease progression was frequently accompanied by rapidly progressive liver failure. In addition to steatosis and foamy histiocytes, fibrosis was prominent and seen in 4 infants before 6 months of age and in 1 infant as early as 1.5 months of age. In infants with evidence of growth failure who did not undergo transplant, the K-M estimate (95% CI) of survival ≥1 year of age was 0 (0, 0). Those treated with HSCT or liver transplant survived slightly longer but died at <1 year of age (median = 8.6 months). A phase 2/3 trial (LAL-CL03) assesses the safety and efficacy of sebelipase alfa in 9 LAL deficient infants with growth failure in the first 6 months of life. All subjects had diarrhea/vomiting, hepatosplenomegaly, failure to thrive and adrenal calcification. Median baseline liver function tests reveal significant underlying liver dysfunction: ALT (145 IU/L) and AST (125 IU/L).

As of January 2015, 6 subjects have met the primary endpoint (survival at 12 months of age) and 5 have survived to 2 years of age (mean time in trial 21.5 months) and continue to receive sebelipase alfa. Deaths (n=4) were unrelated or unlikely related to sebelipase alfa. Deaths were deemed to be related to underlying disease or due to complications of an abdominal paracentesis (n=1). Three died after receiving ≤4 doses. In addition to improved survival relative to the historical cohort, all subjects demonstrated improved weight gain, improvement of GI symptoms, and reductions in hepatosplenomegaly. Rapid improvements in biochemical and hematological markers including ALT, AST, and hemoglobin were observed. One subject experienced sebelipase alfa infusion-related SAEs, which included tachycardia, pallor, chills, and pyrexia. These SAEs all resolved. The most common treatment-emergent AEs: diarrhea (6 subjects), vomiting (6), pyrexia (5), nasopharyngitis (5), rhinitis (5). Anti-sebelipase alfa antibodies were detected in 4 of the 7 with available data. Two positive for anti-sebelipase alfa antibodies also developed neutralizing antibodies to enzyme activity and cellular uptake; they remained positive in January 2015. All 4 seropositive subjects continue weekly infusions of sebelipase alfa.

Analysis suggests that sebelipase alfa rapidly improves weight gain and many of the disease activity parameters observed in infants with LAL D. These improvements appear to be accompanied by a substantial survival benefit compared to a matched historical control group.

497 *COMPARISON OF NON INVASIVE MARKERS AND LIVER BIOPSY FOR ASSESSMENT OF SEVERITY OF HEPATIC FIBROSIS IN CHILDREN WITH BILIARY ATRESIA*

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Biliary atresia (BA) is an idiopathic neonatal obstructive cholangiopathy characterized by a progressive obliteration of the large bile ducts. It is the most common cholestatic liver disorder requiring liver transplantation in infants and children. Hepatic fibrosis is a universal and prominent feature of BA even after a portoenterostomy. Therefore assessing the stage of fibrosis is an important tool to predict the course of biliary atresia.

A liver biopsy is the gold standard for diagnosis, but is associated with certain risks. Currently available non-invasive markers for fibrosis have not been validated in children. Several authors, using routine laboratory data have constructed a simple model: the AST (aspartate transaminase) to platelet ratio index (APRI), to predict fibrosis in chronic viral hepatitis and in BA (1,2).

Objective: Previous investigators have suggested that non-invasive markers such as APRI serve as a useful tool which ameliorates the need to perform a liver biopsy and thereby eliminates significant procedural risks. A key series was published by Kim et al. (1) for use of APRI was associated with positive predictive values in excess of 95%. We sought to validate the efficacy of APRI, to predict histological staging of hepatic fibrosis in children with BA using the staging system by Batts & Ludwig

.APRI was calculated as follows: APRI=AST/ULN X100 / Platelet count (10^9/L)

Methods: A retrospective chart review study of 31 patients with BA over a 10 year period, who had initial liver biopsies at diagnosis was performed. Age at liver biopsy, laboratory data including serum AST and ALT, total bilirubin (TB), platelet count and INR at the time of biopsy were obtained. Data were analyzed using Matlab™ (Statistics Toolbox, Natick, MA). Descriptive statistics were first obtained by calculating mean, range and standard deviation of each variable. A Pearson correlation analysis was then performed comparing APRI and stage of fibrosis. Both r and *p*-values were calculated. Multivariate analysis of variance (MANOVA) was also calculated to determine if the group of biomarkers predicted histologic grading when used together.

Results: The mean age at biopsy was 61 ± 30 days (mean ± SD). The histologic changes in 31 biopsies included portal

fibrosis (stage 1, 2) in 18 (58%), bridging fibrosis (stage 3) in 11 (35.5%) and cirrhosis (stage 4) in 2 (6.5%). 28/31 underwent a Kasai procedure (77%). All descriptive statistics are listed in Table 1. 17/31 patients received a liver transplant (55%). Correlation of APRI with biopsy staging was not significant (r = 0.24 and $p = 0.44$.) MANOVA analysis showed that the overall use of biomarkers did not predict histological grading ($p = 0.24$). Interestingly, APRI was not significantly elevated in children who underwent a liver transplant ($F_{1,29} = 0.17$ and $p = 0.69$, ANOVA).
Conclusion: The progression of fibrosis in BA is unpredictable and varied. Based on our retrospective review we did not find APRI to be a useful surrogate non-invasive marker for fibrosis. Since our sample size was small, further study of a larger cohort is necessary to ascertain the value of APRI or similar markers as a screening tool for fibrosis in BA.

498 *ROLE OF PARAOXANASE 1 AS AN ANTIOXIDANT IN NON-ALCOHOLIC STEATOHEPATITIS*

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Background and Aims: Non-alcoholic steatohepatitis (NASH) is a leading cause of chronic liver disease in children. Oxidative stress plays a role in the pathophysiology of NASH. The activity of the enzymatic mechanisms like Paraoxanase 1 (PON1) that counteract the oxidative stress may be altered in NASH. We have previously reported that PON1 expression is elevated in NASH livers at both mRNA and protein levels, but its presence in circulation was not elevated. The aim of this study is to investigate the role of PON1 as an intracellular antioxidant in liver.
Methods: HepG2 cells were transfected with PON 1 and control plasmid for 48hours. Western blot was performed to confirm the overexpression of the PON1 gene in the transfected cells. Oxidative stress was measured in the transfected cells using flow cytometry. HepG2 cells were incubated with 10 mM of chloromethyl-2', 7'-dichlorodihydroflurescein diacetate, acetyl ester (CM-H2DCFDA; Invitrogen) in the dark for 30 minutes at 37°C. The CM-H2DCFDA exhibit bright fluorescence upon oxidation by reactive oxygen species. The fluorescence signals were collected immediately in the FL-1 (530 nm) channel on BD LSR Fortessa flow cytometer. Mean fluorescence intensity was analyzed by the BD FACS Diva software. Mean fluorescence intensity was compared in PON 1 overexpressed Hep G2cells and control cells.
Results: Western blot analysis showed the overexpression of PON 1 in the transfected HepG2 cells. Mean fluorescence intensity was significantly decreased (p-value <0.05) in PON 1 overexpressed cells compared to control cells, indicating reduction of intracellular oxidative stress in the cells transfected with PON1.
Conclusion: Our results demonstrated that elevated expression of PON 1 decreases the oxidative stress in HepG2 cells. This mechanism may play a protective role in the liver cells affected by oxidative stress in diseases like NASH.

499 *THE EFFECT OF NEUROPSYCHIATRIC MEDICATIONS ON PEDIATRIC NAFLD*

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Background: Obesity affects more than 30% of children in the United States. Obese and overweight children are at risk of developing non-alcoholic fatty liver disease (NAFLD). A subset of these patients will progress to steatohepatitis (NASH), which can lead to cirrhosis and the need for liver transplantation. Neuropsychiatric conditions also affect an increasing proportion of children. Many of these disorders require long term pharmacotherapy that may associate with drug induced liver injury. We sought to evaluate the role that neuropsychiatric medication (NPM) use might play in the severity of NAFLD with the hypothesis that these medications would exacerbate NAFLD.
Methods: Patients with NAFLD were retrospectively identified in the Liver Care Center at Children's Mercy Hospital between 2000 and 2013 based on ICD9 codes as well as radiographic and histologic reports. Demographics, vital signs, medications, co-morbities (both psychiatric and non-psychiatric), radiology and laboratory reports were collected and entered into a REDCap database. Patients were then grouped into those who were taking NPM and those who were not and results were analyzed. Data was analyzed from an initial visit and a visit 18-36 months later.
Results: Of the 148 patients with NAFLD evaluated, 38 used NPM while managed by the Liver Care Center. Patients were predominantly male in both groups with insulin resistance the most common comorbidity. Initial mean BMI at presentation was higher in the NPM group (33.2 compared to 31.6 in the non-NPM group). Initial mean ALT was lower (101.8 IU/L versus 124.4 IU/L in the non-NPM group). The most common medication used was anti-depressants (22) followed by ADHD stimulants (19). Over 18-36 months, mean ALT improved in the non-NPM group, going from 129.8 IU/L to 113.1 IU/L, while the mean BMI z-score also improved, going from 2.33 to 2.28. Interestingly, in the NPM group, the mean ALT also improved, going from 105.4 IU/L to 76.2 IU/L despite the mean BMI z-score worsening from 2.3 to 2.4. This trend was not expected especially given NPM group had statistically worsening BMI ($p = 0.0067$) but no significant change in ALT ($p = 0.0559$).
Conclusions: NPM use does not worsen liver injury in the setting of NAFLD. We wonder if NPM use may in fact be hepatoprotective, though this study was not powered to assess this idea more clearly. Further study is needed, but providers should not unduly fear NPM use in the setting of NAFLD.

*500 *EARLY COMPENSATORY MECHANISM OF THE LIVER AFTER THE INITIAL ACCUMULATION OF FAT IN A DIET-INDUCED NAFLD MODEL*

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Background: Nonalcoholic fatty liver disease (NALFD) is the most common chronic liver disease in both adults and children. Several studies have shown a clear association between increased time of exposure to high fat diet and progression to the various stages of disease. However, early and potentially critical changes in the liver and extrahepatic tissues during high caloric feeding remain incompletely characterized. Based on this, we *aimed* to elucidate the early events in NAFLD progression that may be targeted to prevent development of liver inflammation and fibrosis. Methods: C57/B6 mice were fed a high fat diet (HFD) or control diet (normal chow) for 3 days, 7 days, and 2 weeks to reproduce a physiologically relevant model of early NAFLD. The extent of liver steatosis, along with markers of lipid metabolism, inflammation, and cell death were assessed by histological, molecular, and immunofluorescence analyses. Results: Mice fed with HFD for 3 days showed a significant large and small droplet liver steatosis accompanied by an increase in adipocyte diameter, whereas mice fed with HFD for 7 days showed resolution of liver steatosis (Steatosis score: HFD 3 days vs HFD 7 days, $p<0.023$) and attenuation of adipocyte size (HFD 3 days vs 7 days, $p<0.028$), independent of liver/body weight ratio. Interestingly, hepatic fat accumulation reappeared after 2 weeks on HFD (Steatosis score: 3 days 1(±0.7) vs 7 days 0 (±0) vs 2 weeks 0.6 (±0.5)). Findings from molecular analysis of lipid export, uptake, oxidation, and storage in liver tissue mirrored histological changes, with increases in expression of Fatty acid binding protein (FABP1), Stearyl-CoA desaturase-1 (SCD1), and Carnitine palmitoyltransferase 1 (CPT1) at 3 days with attenuation of expression at 7 days. The link between liver steatosis and inflammation was investigated using markers of macrophage recruitment, as shown by F4/80 staining, and neutrophil activation indicated by increased level of of myeloperoxidase (MPO). Analysis revealed that the expression of both markers was up-regulated with increased exposure to HFD. Additionally, the expression of the inflammatory marker IL6 mirrored the early changes observed in liver histology. Conclusion: These findings suggest that the liver activates a compensatory response to early fat accumulation during NAFLD progression, which is later compromised following continued exposure to a HFD.

501 *ABLATION OF INSULIN AND IGF1 SIGNALING IN FAT INDUCES LIPODYSTROPHY AND PROGRESSIVE NAFLD WHICH INCLUDES INFLAMMATION, FIBROSIS AND HAPATOCELLULAR CARCINOMA*

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Obesity, characterized by excessive adipose tissue mass and lipodystrophy, regarded as a marked reduction in adipose tissue mass, are the two seemingly opposite forms of adipocyte dysfunction, but surprisingly share many similar metabolic derangements such as insulin resistance, dyslipidemia and fatty liver disease.

To study the role of adipocyte dysfunction on metabolism we created mice lacking either the insulin receptor (IR), IGF-1 receptor (IGF1R), or both receptors specifically in adipose tissue using Cre-recombinase driven by the adiponectin promoter.

Mice lacking IR (F-IRKO) or both IR and IGF1R (F-IR/IGFRKO) developed profound lipodystrophy with >95% reduction in both perigonadal and subcutaneous white fat depots, while mice lacking IGF1R (F-IGFRKO) exhibited only a 25% reduction in white adipocyte mass. Lipodystrophic mice at 12 weeks of age demonstrated fed blood glucose levels of >500 mg/dl and insulin levels 10 to 15-fold increased over control mice. Serum TG, FFA and cholesterol levels were also significantly elevated, while adipokines such as leptin, resistin and adiponectin were markedly reduced. Lipodystrophic F-IRKO and F-IR/IGFRKO mice developed profound fatty liver disease with progressive increase in liver weights, 6.5 to 9 times above controls, due to excessive triglyceride accumulation, secondary to increased lipogenic gene expression, *ACC1*, *FAS* and *SCD1*. By one year of age fatty liver disease progressed to include inflammation with increased CD68, TNF-α, and F4/80, pericellular fibrosis with elevated TGF-β, α-SMA and Col1a1, as well as inversion of ALT to AST ratio. Fibrosis, as scored by an independent pathologist, reached grade 3 interstitial fibrosis in F-IR/IGFRKO mice and stage 1 fibrosis in F-IRKO mice. Livers of both lipodystrophic mice also exhibited nodular morphology with increased markers of proliferation (Ki67), as well as increased tumor markers β-*catenin*, *AFP* and *Cyclin D1*. The hepatocytes in these nodules compressed the surrounding liver parenchyma and showed atypical nuclei and increased mitotic figures, while additional liver findings included tumor-like malformations of bile ducts, segments of bone with bone marrow elements and areas of extramedullar hematopoiesis. Liver glycolysis was increased as assessed by increased expression of the rate limiting glycolytic enzyme, PKM2, and a dramatic increase in global resting energy expenditure, further indicative of increased glycolysis. Insulin signaling in the liver revealed decreased PTEN protein levels and increased PIP_3 levels, a well-known signaling event in hepatocellular carcinogenesis.

In summary, we have developed a mouse model of fatty liver disease associated with lipodystrophy which progresses to include liver inflammation, fibrosis and hepatocellular carcinoma.

502 *EPIDEMIOLOGY OF PATIENTS PRESENTING WITH HYPERBILIRUBINEMIA TO A PEDIATRIC EMERGENCY DEPARTMENT OVER A THREE-YEAR PERIOD*

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Background: There is a surprising lack of scholarly reports on pediatric emergency department (PED) exposure to hyperbilirubinemia (HB). Obtaining epidemiologic data about this condition in the PED would be valuable to emergency medicine providers, pediatric gastroenterologists, and general pediatricians. Such information might lead to more refined evaluations and treatment strategies that physicians could employ when addressing patients with HB in the PED.

Methods: This was a retrospective observational study, completed at an urban tertiary academic PED. Patients were included in the study if they presented to the PED from 2010 to 2012, were 0-18 years in age, and had an elevated serum bilirubin. A review of these charts was completed to determine the incidence of HB, presenting signs and symptoms, morbidity, mortality, and, when possible, the etiology. For the purposes of this study, "pathologic HB" was defined as that arising from any significant disease process known to cause HB. Non-pathologic HB was attributed to those with only minor infections, minor dehydration, benign neonatal HB, or mild elevations without a clear cause.

Results: We identified 1,534 total visits (1,236 unique patients) where a patient was found to have HB, which represented 0.8% of total patient visits (190,079) over the three-year period. In 48% (732) of the patients HB was determined to have arisen from an identifiable pathologic etiology. First time diagnosis of pathologic HB occurred in 14% (211) of HB visits, and 0.001% of all visits. The five most common etiologies for any visit with identifiable pathologic HB were sickle cell disease (202), acute lymphoblastic leukemia (72), sepsis (58), TPN associated cholestasis (52), and pancreatitis (38). The five most common etiologies for first time identifiable pathologic HB were choledocholithiasis (23), urinary tract infection (19), sepsis (18), pancreatitis (16), and neonatal blood type incompatibility (12). We demonstrated a bimodal incidence, noting a significant increase of HB in patients less than 6 months and those greater than 9 years as well as a male predominance throughout all age ranges. 15 patients went on to have a liver transplant with the most common etiology being autoimmune hepatitis (4). Of these liver transplant patients, only 4 were first time pathologic HB patients identified in the PED (1.9% of all such patients). 21 patients with pathologic HB have since expired, either as a result or a complication of their underlying etiologies, with the most common cause of death being sepsis (10). First time pathologic HB patients identified in the PED had a mortality rate of 1.4% for their immediate hospitalization.

Conclusion: Though a seemingly common laboratory finding with a myriad of possible etiologies, hyperbilirubinemia was encountered rarely in our PED. The incidence of HB presenting to the PED exhibited a bimodal age distribution and a male predominance throughout all age ranges. A new discovery of pathologic HB and progression to liver transplant or death during the initial presentation was extremely rare.

503 *CLUES TO THE DIAGNOSIS OF BILIARY ATRESIA IN NEONATAL CHOLESTASIS*

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Aim: Differential diagnosis of neonatal cholestasis can be difficult for many physicians. Some cases may still remain uncertain, despite history, physical examination, laboratory findings, liver biopsy and radiological scanning, especially in diseases such as biliary atresia (BA) in which early diagnosis can be life-saving. The purpose of this study was to identify important clues in differentiating BA from other causes of neonatal cholestasis (nonBA) and to establish the reliability of tests.

Method: Thirty-four patients (M/F; 15/19) with BA under monitoring at the Çukurova University Medical Faculty Pediatric Gastroenterology, Hepatology and Nutrition Department and Pediatric Surgery Department between 2009 and 2015 and 27 nonBA cases of cholestasis (M/F; 14/13) were assessed retrospectively in terms of history, physical examination and laboratory and radiology findings. Syndromic babies, premature babies, septic babies and those receiving parenteral nutrition were excluded.

Results: No difference was determined between BA and nonBA cases in terms of age, sex, number of pregnancies, number of births and birth weight. Jaundice was identified at an earlier age in cases with BA (p=0.02) while parental consanguinity was greater in the nonBA group (p=0.01). At physical examination, splenomegaly was more marked in the nonBA group (p=0.02). Presence of pale stool was significantly high in cases with BA (p=0.001). Only GGT value was significantly higher in cases with BA compared to the nonBA group (p=0.001), and there was no difference between the groups in terms of other laboratory tests. Radiologically, gall bladder contraction at abdominal USG was significantly higher in subjects diagnoses with BA compared to the other group (p=0.002). The highest specificity in diagnosis of BA was observed in GGT elevation + pale stool and gall bladder contraction at abdominal USG. The finding with the highest sensitivity was presence of pale stool (97%).

Conclusion: Pale stool + GGT elevation and gall bladder contraction at abdominal USG are the most reliable tests for the diagnosis of BA, and early period intraoperative cholangiography can be performed in these cases before investigating

other cholestatic diseases.
Specificity and sensitivity of tests used in diagnosis of biliary atresia

	Specificity (%)	Sensitivity (%)	p
GGT (>200 IU)	62	79.4	0.001
Pale stool	37	97	0.000
Abdominal USG	74	70	0.000
GGT + USG	85.1	67	0.000
GGT + pale stool	85.1	76.4	0.000
GGT + pale stool + abdominal USG	96	67	0.000

506 *SAFETY, COMPLICATIONS AND OUTCOME OF LARGE VOLUME PARACENTESIS WITH OR WITHOUT ALBUMIN THERAPY IN CHILDREN WITH TENSE ASCITES DUE TO CIRRHOSIS AND BUDD-CHIARI SYNDROME*

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Aims

There is no published data on post-paracentesis circulatory dysfunction (PPCD) or its prevention in children. Our study was aimed to analyse the safety and complications of large volume paracentesis (LVP) in children with tense ascites due to cirrhosis and Budd-Chiari syndrome with or without albumin therapy.

Methods

A prospective longitudinal observational study enrolled children with tense ascites who underwent single time LVP at admission. They were divided into albumin infused (AI) and albumin non-infused (ANI) groups. Hemodynamic monitoring and laboratory parameters including plasma renin activity (PRA) were compared between baseline, 48 hours and day 6 of LVP. Their outcome at 3 months and maximal follow-up were noted.

Results

32 children (AI, n=17; ANI, n=15) had comparable baseline characteristics and 90.6% had high PRA at the onset. Albumin infusion given in AI group (n=17) was 0.9 ± 0.2 g/kg dry weight or 7.0 ± 3.5 g/L of ascitic fluid extracted. The incidence of PPCD was 37.5% (ANI: 67%; AI: 12%, p=0.003), occurred if ascitic fluid extraction was >197.5mL/kg (sensitivity: 90%; specificity: 50%, area under curve: 77%, p=0.01) and if flow rate was higher in ANI group (1224 ± 476 vs. 678 ± 214 mL/h, p=0.009). Of the 13 variables in binary logistic regression analysis (age, pedal edema, height and weight Z-scores, duration of ascites, volume and velocity extracted, diuretic use, INR, serum albumin, PELD score, Child-Pugh grade and albumin non-infusion), only albumin non-infusion was found to be the determinant for PPCD (p=0.006, OR: 45.5; 95% CI: 4.7-442.5). ANI patients were susceptible to asymptomatic, persistent hyponatremia (baseline vs. day 6, 131 ± 4 vs.128 ± 6 mEq/L; p=0.04) and had higher rates of recurrent ascites (42%) and hospital readmission (67%) within 3 months. Over a follow-up of 11.1 ± 7.8 months, 10 patients died. Kaplan Meier survival curve showed that the AI group survived marginally longer than ANI group (19.7 ± SE 1.8 vs. 16.6 ± SE 2.4 months; p=0.18).Similarly those with PPCD compared to those without had similar survival rates (18.4 ± SE 2.3 vs. 17.9 ± SE 2.0 months; p=0.98). No independent predictor of mortality was identified in logistic regression analysis either at 3 months or at maximal follow-up.

Conclusions

LVP is safe in all age groups, best performed under albumin cover to overcome the problems of PPCD and hyponatremia. It is prudent to restrict volume extraction to less than 200 mL/kg actual dry weight for all, and flow rate of 680 mL/h in albumin non-infused. Those who did not develop PPCD also showed a benefit in the 3 month follow-up outcome in terms of lower ascites recurrence and hospital readmission

Comparison of plasma renin values (ng/mL/h) between albumin infused (AI) and albumin non-infused (ANI) groups (n=32)

	AI (n=17)	ANI (n=15)	p
Overall PRA value at baseline	27.5±18.4	24.1±24.7	0.65
Overall PRA value on day 6	28.3±21.2	53.1±28.8	0.01
Folds elevation from baseline*	1.1±0.5	5.4±6.3	0.02
Number of subjects with PPCD	2	10	0.003

Note: values expressed as mean ± SD, PRA: plasma renin activity, PPCD: post-paracentesis circulatory dysfunction, * calculated as ratio of PRA values at baseline and day 6 (Day 6 value/ baseline value= fold elevation)

MICROBIOLOGY/INFECTIONS/PROBIOTICS

508 *USE OF PROCALCITONIN FOR THE PREDICTION OF BACTEREMIA IN CHILDREN PRESENTING WITH FEVER FROM POSSIBLE CLABSIS (CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTIONS) IN HOME TPN PATIENTS*

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BACKGROUND: Unnecessary use of broad spectrum antibiotics in hospitalized children with possible central line associated bloodstream infections (CLABSIs) is an increasing problem. Our current protocol for a patient who presents with a central line and fever is to obtain a blood culture from the central line and start inpatient broad spectrum antibiotics pending results of the blood culture. A retrospective chart review at Lucile Packard Children's Hospital at Stanford (August 2013-August 2014) revealed that forty five percent (45%) of these children had a negative blood culture. An early biomarker for predicting bacteremia in a pediatric patient with a fever and a central line has the potential to reduce unnecessary antibiotic exposure and the development of multi-drug resistant organisms in this population.
AIM: To determine if Procalcitonin (PCT) is a useful biomarker for early prediction of bacteremia in children and to determine the best cutoff point of PCT (ng/ml) for identifying bacteremic patients.
METHODS: We evaluated PCT in 31 patients who presented to the Emergency Room or clinic with fever and a central venous catheter from August 2014 to May 2015. Seventeen patients (54%) had a positive blood culture (16 bacterial and 1 fungal). The range of PCT levels was found to be between <0.1 and >20 ng/ml. The mean value of PCT in bacteremic patients was 6.45ng/ml. Higher cutoff PCT values were associated with worse clinical presentation and faster growth of positive blood cultures. Two of the positive blood cultures were excluded from the study because they showed a common contaminant of blood cultures (Coagulase negative staph with late growth). Both excluded patients had a PCT value of < 0.1.
RESULTS: A PCT level of > 0.3ng/ml produced a sensitivity of 93.3 % and positive predictive value of 87.5%. The specificity of a PCT level ≤0.3 ng/ml was 85.7 % with a negative predictive value of 92.3 % One patient with PCT level <0.1 ng/ml still yielded a positive fungal culture 48 hours after being drawn. Given the small sample size, further studies are needed to assess the clinical utility of PCT for the early detecting of CLABSIs, especially fungal infections.
DISCUSSION: In conclusion, PCT represents a promising biomarker in the early detection of bacteremia in children, although more studies are needed to validate sensitivity and specificity and to determine an optimal PCT cutoff value for highest diagnostic yield.

509 *CHOOSING THE NUMBER ONE NUMBER TWO: METHODOLOGY FOR SELECTION OF A COMPETITIVE UNIVERSAL MICROBIOTA DONOR FOR FECAL MICROBIOTA TRANSPLANT*

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Background: *Clostridium difficile* infection (CDI) is a serious cause of morbidity in pediatrics for the over 17,000 pediatric patients who are diagnosed per year in the United States. Oral antibiotics, the current standard of care, fail nearly 1/3 of patients, who develop relapses due to gut dysbiosis. Fecal Microbiota Transplant (FMT) is a promising therapy with over 90% efficacy whereby stool from a healthy donor is transplanted to correct this dysbiosis; the optimal microbiota for transplantation, however, has not been defined. The common method of donor selection is to utilize a related donor (often parent), without any assessment of the *quality* of the microbiota being transplanted.
In response to the challenge of providing excellent quality transplanted microbiome, our team has established a competitive donor protocol which uses a multi-step process to identify one single universal donor to provide the bacterial milieu for transplantation.
Methods: In our observational prospective cohort study, a universal competitive microbiota donor was selected after

meticulous screening of potential donors from Palo Alto and from our Boston-based collaborators, OpenBiome. The multi-tiered process to identify the universal donor began with the initial step of screening potential donors with standardized questionnaires to assess for risk factors for infectious disease and focused recruitment on those following an agrarian diet. Next, the donors with negative first screenings progressed to the second tier to screen for risk factors for dysbiosis (antibiotic use, diarrheal illness, inflammatory bowel disease, obesity). Those without identified risk factors underwent a third tier of serum and stool screening for infectious etiologies based upon the consensus guidelines. Finally, those with negative serum and stool screening underwent 16s microbiota sequencing and the samples were assessed for markers of gut health including: SCFA concentration with a focus on the concentration of butyrate, *Bacteroidetes/Firmicutes* ratio, and overall bacterial diversity (alpha diversity by both phylogenic diversity (PD), and observed species via utilization of Shannon and Simpson Diversity Indices).
Results: Based on the donor screening process described above, 9 potential donors were selected (3 from Palo Alto and 6 from OpenBiome). All 9 potential donors had negative serum and stool screening for infectious agents and met the requirement of having a *Bacteroidetes/Firmicutes* ratio >1. The universal donor was methodically selected based on the following parameters: a superior butyrate concentration of 4.2 micromol/mL of stool slurry (range 2.5 - 5.1 micromol/mL), a Shannon Index of 6.07 (range of samples from 4.00 to 6.48), a Simpson Index of 0.93 (range of samples from 0.77 to 0.96), and high PD on rarefaction curves.
Conclusions: We have identified a standardized approach to assuring the delivery of the best quality microbiota for future FMT treatments; we venture that this bacterial milieu will optimize repopulation of the dysbiotic gut. Our future directions include performing optimized FMT with our competitive donor in pediatric and young adult patients with recurrent CDI and assessing the evolution of the gut microbiota post-transplant.

511 *THE PREVALENCE OF SMALL BOWEL BACTERIAL OVERGROWTH IN CHILDREN WITH SHORT BOWEL SYNDROME AND ITS ASSOCIATION WITH CATHETER-RELATED BLOODSTREAM INFECTIONS*

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BACKGROUND: Small bowel bacterial overgrowth (SBBO) is a common complication in patients with short bowel syndrome (SBS). Though the implications are not completely understood, it is recognized that patients with SBBO are at higher risk of morbidity from malnutrition, enterocolitis, bacterial translocation, and gut-derived sepsis. The literature is limited regarding the prevalence and significance of SBBO in children with SBS.
OBJECTIVES: Our aim was to examine the prevalence of SBBO in a cohort of patients with SBS. We also sought to identify the most common organisms implicated, the prevalence of resistant organisms, and the association between SBBO and catheter-related blood stream infections (CRBSI).
METHODS: We performed a retrospective chart review of 101 patients with SBS treated in our Intestinal Rehabilitation Program at Children's National Health System in Washington, D.C., from 2007 to 2014. Patients were identified who had jejunal cultures obtained at various intervals to evaluate for SBBO. Cultures reviewed were obtained by direct aspiration either during endoscopy or through a newly-placed gastrojejunostomy tube. SBBO was defined as the presence of at least 10^5 colony-forming units per mL of a single organism. Jejunal aspirates with fewer organisms or without any growth were considered negative for SBBO. CRBSI was assessed as the presence of a positive blood culture in patients with an indwelling catheter. Statistical analysis was performed using Fisher's exact test.
RESULTS: 65 children (62% male, median age 1.5 years, range 0.1-18.3 years) had jejunal aspirate data and 36 of these were found to have SBBO (55%). The most common organisms implicated were gram-negative bacteria (74%), with *Klebsiella pneumoniae* as the most frequently identified (26%). *Escheria coli* was the next most common bacterium (21%). Gram-positive bacteria comprised 26% of the total, with *Enterococcus spp.* being the most common (19%). 6 resistant organisms (*Klebsiella pneumonia* carbapenemase and Vancomycin-resistant *Enterococcus*) were identified (4%). Associations were found between the absence of an ileocecal valve and SBBO (OR 1.7, 95% CI 0.61-4.47, P=0.45), as well as between intestinal length less than 40cm and SBBO (OR 1.6, 95% CI 0.57-4.21, P=0.45), but neither was statistically significant. 44 of these 65 patients had at least one CRBSI (68%), and 25 of 44 (57%) also had SBBO. CRBSI was associated with SBBO, but this was not statistically significant (OR 1.6, 95% CI 0.58-4.47, P=0.44). 12 (48%) of the 25 patients with SBBO and evidence of CRBSI had the same organisms identified in their jejunal fluid and in their bloodstream.
CONCLUSIONS: SBBO is common in children with SBS and may be associated with CRBSI. Gram-negative bacteria were the most common organisms identified in jejunal aspirates in our study. The further characterization of risk and possible therapeutic implications requires additional prospective study.

512 *COST IMPLICATIONS OF METHOD OF DELIVERY AND DONOR SOURCE IN FECAL MICROBIOTA TRANSPLANTATION*

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Background: Clostridium Difficile infection (CDI) represents an significant healthcare burden for both adult and pediatric patients. Oral antibiotics are first line therapy for CDI, but the recurrence rate of infection is between 14-21% and patients can experience multiple recurrences. Fecal Microbiota Transplantation (FMT) has emerged as a promising treatment for recurrent CDI with efficacy rates as high as 87-89%.There are multiple methods of FMT delivery, including via colonoscopy, nasoduodenal tube, and nasogastric tube. The FMT donor has historically been a first-degree relative of the patient, but costs of donor screening are considerable. Donor stool banks have emerged, with unrelated stool donation achieving FMT efficacy rates equivalent to related stool donors in treatment of CDI. With the goal of developing a cost-effective protocol for FMT delivery for recurrent CDI in our institution, we modeled charge data for potential FMT administration techniques and donor sources.

Methods: We assessed hospital and professional charge data for the following scenarios: 1. FMT delivery via colonoscopy; 2. FMT delivery via fluoroscopy-guided, radiology-placed nasoduodenal tube; 3. FMT delivery via RN-placed nasogastric tube. We assessed laboratory charge data from a standard commercial laboratory for standard screening tests for FMT donor and compared these to procurement and administration charges for an unrelated stool banked FMT donor source.

Results: Utilizing unrelated stool bank donation, total charges (hospital/facility and professional charges) for FMT via colonoscopy were $7,766.95, for FMT via nasoduodenal tube were $4,997.50, and for FMT via nasogastric tube were $ 1,138.50. Standard commercial laboratory charges for donor screening were $1,154. Charges for unrelated stool bank donation (procurement and pharmacy charge for storage/administration) were $627.50. Based on these comparative charge data, our institution developed an Registered Nurse-driven FMT protocol using NG administration and an unrelated stool bank donation. A total of 7 patients have successfully been administered FMT using this protocol without complication.

Conclusion: Compared to FMT via colonoscopy and nasoduodenal tube, FMT administration via nurse-placed NG tube decreases total health care charges by 85% and 78%, respectively. The use of a stool bank donor reduces health care charges by at least 50% compared to use of a related donor for FMT. The use of nurse-driven FMT administration and unrelated stool donation presents an opportunity for large reduction in healthcare expenditures for treatment of recurrent CDI.

516 *SECRETED METABOLITES OF BIFIDOBACTERIUM INFANTIS AND LACTOBACILLUS ACIDOPHILUS PROTECT AGAINST IL-1β-INDUCED INTESTINAL BARRIER DYSFUNCTION*

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Background Necrotizing enterocolitis (NEC) is characterized pathologically by submucosal edema, mucosal ulcerations, hemorrhage, and necrosis of the distal ileum and proximal colon.[1] The disturbanced epithelial integrity and increased intestinal permeability in preterm infants is associated with the pathogenesis of NEC.[2] A recent report showed that increased intestinal permeability precedes NEC onset using a neonatal mouse model.[3] An association between tight junction integrity and NF-κB pathway activation has been previously described. Some probiotic strains have been reported to protect the intestinal barrier function by stabilizing TJ structures, and may protect against NEC through a maturational affect on the intestinal barrier.

Methods Using a transwell model, Caco-2 cells were apically pretreated with probiotic conditioned media from either B. infantis or L. acidophilus (PCM) then stimulated with 10 ng/mL of IL-1β in the basolateral chamber. The transepithelial electrical resistance (TEER) was measured after 72 hours. After FITC-dextran was added to the apical transwell chamber, fluorescence in the basolateral supernatant was determined as a measure of FITC-dextran flux. Caco-2 cells or H4 cells were cultivated in cell culture medium to 90% confluence, pretreated with PCM, then stimulated with 10 ng/mL of IL-1β. The cell culture media and IL-1β stimulation alone were used as negative and positive controls, respectively. Each experimental condition was completed in triplicate. Following the incubation period, Western blot analysis and immunoflourescence (IF) of tight junction protiens were performed. Using the same experimental design in Caco-2 cells, protein levels of NF-κB and IκBα in the nuclear and cytoplasmic compartments were evaluated using western blot analysis.

Results Conditioned media from both B.infantis and L.acidophilus increased the transepithelial electrical resistance (TEER) of Caco-2 monolayers, in a dose-dependent manner ($p < 0.01$), decreased transepithelial FITC-dextran transport, and prevented IL-1β induced TEER reduction ($p < 0.01$). PCM normalized the IL-1β induced protein expression changes of claudin-1 and occudin in Caco-2 cells, shown by western blot analysis and IF. Similarly, in fetal H4 cells, PCM normalized the IL-1β induced changes of claudin-1 protein expression, however no signficant IL-1β induced change in occludin protein

expresssion was noted. PCM pretreatment successfully reduced the nuclear translocation of NF-κB p65 in IL-1β stimulated CaCO2 cells, shown by western blot analysis, however did not prevent the decrease of cytoplasmic IκBα expression. Conclusion Conditioned media from B. infantis and L. acidophilus has beneficial effects on intestinal barrier function, which may partly explain the mechanism by which these products decrease the incidence and severity of NEC in preterm infants. The PCM showed different modulatory effects on tight junction complexes between mature and immature enterocytes, suggesting a developmentally regulated response.

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*517 *CITROBACTER RODENTIUM-INDUCED COLONIC INFLAMMATION LEADS TO DOWNREGULATION OF SHORT CHAIN FATTY ACID RECEPTORS AND ENHANCED INFLAMMATORY CYTOKINE PRODUCTION*

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Background: Inflammatory bowel disease (IBD) includes Crohn's disease and ulcerative colitis that causes chronic inflammation of the gastrointestinal track. Dietary and environmental factors, such as exposure to stress, have been suggested to impact the severity of IBD, but the mechanisms by which this occurs are not yet clear. One possible mechanism involves changes in the composition of the commensal gut microbiota. For example, nondigestible polysaccharides are not broken down by the small intestine and are fermented by colonic bacteria that produce the most abundant microbial metabolite short-chain fatty acids (SCFAs) acetic, propionic, and butyric acid. SCFAs are produced by Firmicutes and Bacteroidetes phyla, and induce an anti-inflammatory response via G-protein-coupled receptors and histone deacetylases. Exposure to stressors has also been shown to impact the composition of the gut microbiota, and exacerbate colonic inflammatory responses. Whether stressor-induced changes in the microbiota, colonic inflammation, and SCFA production are related is not yet known.

Aim: Determine the impact of a murine social stressor and infectious colitis on SCFAs, SCFA receptor expression and inflammatory cytokines in the colon.

Methods: Male specific pathogen-free (SPF) C57BL/6 mice 6-8 weeks old were fed standard laboratory chow. Mice were either infected with *C. rodentium* or left uninfected as a control. In addition, mice were either exposed to a social stressor known as called Social Disruption (SDR) or left undisturbed as an additional control group. The SDR involves repeated social defeat over a 2 hr period beginning one day prior to infection and repeated on 6 consecutive days (i.e., repeated until 5 days post infection). Mice were either sacrificed on Day 6 or Day 12 post infection. Semi-quantitative real time PCR was performed on colonic tissue to assess the expression of inflammatory cytokines (including TNF-α, and iNOS) and anti-inflammatory cytokines (TGF-β). Semi-quantitative real time PCR was also performed to assess SCFA receptors GPR41, GPR43, and SLC5A8 mRNA from proximal colonic tissue. Fecal samples taken from the colon on the day of the sacrifice were extracted to quantify SCFA levels (acetic, butyric, and proprionic acids) by gas chromatography-mass spectrometry (GC-MS.

Results: Mice exposed to *C. rodentium* infection had decreased TGF-β mRNA levels ($p < 0.05$), and increased iNOS and TNF-α mRNA levels ($p < 0.05$). Exposure to the SDR stressor also increased iNOS and TNF-α mRNA ($p<0.05$). Interestingly, only colonic infection resulted in reduced GPR41 and GPR43 receptor mRNA expression ($p<.05$). Stressor exposure did not impact these SCFA receptors. Levels of proprionic acid were statistically increased in infected mice (an effect that tended to be exacerbated by stressor exposure).

Conclusion: Mice infected with C. rodentium induced reductions in SCFA receptors were associated with higher levels of inflammatory cytokines and lower levels of anti-inflammatory cytokines. This supports the contention that SCFA have anti-inflammatory effects and suggests that infection-induced reductions in SCFA receptors exacerbate colonic inflammation.

521 *RESPONSE RATE COMPARISONS FOR NITAZOXANIDE AS PART OF AN EMPIRIC MULTI-DRUG REGIMEN IN TWO AGE GROUPS OF CHILDREN WITH SUSPECTED H. PYLORI INFECTION*

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Helicobacter pylori (*H. pylori*), a gram-negative bacterium found in the human stomach, is often present in patients with chronic gastritis. Traditional treatment for *H. pylori* includes metronidazole or clarithromycin; both being associated with development of resistance. We have previously described our clinical experience using a multi-drug treatment regimen for pediatric *H. pylori* that included nitazoxanide, a newer nitrothiazole benzamide compound used in treating intestinal protozoa infections (Ramos-Soriano A.G. Black J.*Case Rep Gastroenterol* 2015;9:36-42). In this report we assess the response rate to this combination in various age groups to determine comparability. Charts were identified for patients who were treated between January 1, 2008 and December 31, 2013 with an ICD-9-CM code 041.86 (Helicobacter pylori [*H.*

pylori]) and who underwent elective endoscopy. All patients were exposed to nitazoxanide for 3 days plus azithromycin, and cefixime (or another 3rd generation oral cephalosporin) for 7-10 days, plus a proton pump inhibitor for 30 days. The clinical cure criteria were predefined. There were 127 individual occurrences or cases identified for inclusion in the review with 88 occurrences meeting the inclusion criteria for this specific analysis. The success rate or clinical cure for the new therapy combination in patients from 1 to 12 years of age inclusive was 83.9% (47 of 56) as defined prior to the chart review. The success rate or clinical cure rate for the same therapy was 89.3% (25 of 28) in patients 13 to 20 years of age inclusive. While the cure rate was slightly better for the 13 to 20 year old group, there was no statistical difference between the groups. There were no serious adverse events observed or reported during the treatment of any patient in either group. Approximately 10% of patient charts reflected minor complaints of nausea, vomiting, or abdominal cramps during the time that active drug therapy would have occurred. Nitazoxanide appears to be an effective and well tolerated option for use in combination with other agents to treat *H. pylori* induced gastritis regardless of age.
Response Rate to Multi-drug Therapy

	Number Included	Percent (%)		Number Included	Percent (%)
Cases for patients 1-12 years old	56		Cases for patients 13 - 20 years old	28	
Clinical Cure	47	83.9	Clinical Cure	25	89.3
Clinical Failure	9	16.1	Clinical Failure	3	10.7

527 *COMPREHENSIVE ASSESSMENT OF ACUTE GASTROENTERITIS IN CHILDREN USING MULTIPLEX NUCLEIC ACID-BASED TESTING IN THE ROTAVIRUS VACCINE ERA*

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Background: Acute gastroenteritis is one of the most common illnesses in children and is associated with substantial morbidity in the United States even after introduction of rotavirus vaccine. However, the comprehensive etiological profile of acute gastroenteritis in children is poorly defined.
Methods: We collected stool specimens from pediatric patients (< 6 years of age) presenting with vomiting and/or diarrhea to a tertiary care children's hospital in Nashville, TN from 2008-2011 as part of active population-based viral gastroenteritis surveillance. Stools from these patients and age-matched healthy controls were tested using Luminex's Gastrointestinal Pathogen Panel and realtime RT-PCR for astrovirus and sapovirus.
Results: Of the 219 stool samples from patients with AGE, 158 (72%) tested positive for at least one pathogen with norovirus genogroup (G) II (34.7%) and *Clostridium difficile* (16.4%) being the most predominant. A pathogen was identified in 4/36 (11%) of the healthy control specimens with *Clostridium difficile* present in 3 (8.3%) and norovirus GII in one specimen (2.7%). A large subset of the AGE cohort (14%) tested positive for more than one pathogen. Patients with co-infections did not differ clinically from those with a single etiology or no identified etiology.
Conclusions: Using a multiplex nucleic acid-based testing platform, which allows for simultaneous testing for multiple enteric pathogens, we detected norovirus GII or *Clostridium difficile* in more than 50% of the samples tested. However, the clinical utility of results from such platforms needs to be further defined, particularly in light of the detection of pathogens in asymptomatic children, and the relative clinical significance of co-infections further interrogated.

Demographic and clinical characteristics of patients with acute gastroenteritis by pathogen

	Subjects with Viral Pathogen Identified n=110	Subjects with Bacterial Pathogen Identified n=18	Subjects with Co-infection Identified n=30	Subjects with No Pathogens Identified n=61	P value
Age in months, median (IQR)	19 (9-29)	11.5 (5-18)	10 (6-16)	16 (3-26)	0.03
Gender (% male)	61 (56%)	6 (33%)	17 (57%)	36 (59%)	0.28
Race White Black Other	39 (35%) 38 (35%) 33 (30%)	3 (17%) 12 (66%) 3 (17%)	11 (37%) 13 (43%) 6 (20%)	14 (23%) 24 (39%) 23 (38%)	0.092
Hospitalized	29 (26%)	7 (39%)	10 (33%)	25 (41%)	0.24
Length of hospitalization, median days (IQR)	1 (1-2) n=29	1 (1-2) n=7	1 (1-2) n=10	2 (1-3) n=25	0.094
Fever during Illness	64 (58%)	14 (78%)	19 (63%)	42 (69%)	0.62
Highest temperature, median °F (IQR)	102.45 (101-103) n=52	101.9 (101-102.3) n=11	102 (101.15-103.4) n=16	102.2 (101.9-103.2) n=37	0.41
Vomiting during Illness	100 (91%)	13 (72%)	26 (87%)	51 (84%)	0.14
Days of diarrhea prior to presentation, median (IQR)	3 (2-5) n=91	5 (2-6) n=13	3 (2-4) n=25	2 (2-3) n=49	0.046
Maximum number of diarrheal episodes in 24 hours, median (IQR)	6 (4-10) n=87	7 (4-12.5) n=12	5 (3-10) n=26	4 (2-7) n=47	0.03
Days of illness prior to presentation, median (IQR)	3 (2-5)	4.5 (3-6)	4 (3-5)	3 (2-6)	0.06
Rotavirus vaccine status Yes No Unknown	79 (72%) 25 (23%) 6 (5%)	12 (67%) 5 (28%) 1 (6%)	26 (87%) 4 (13%) 0 (0%)	34 (56%) 23 (38%) 4 (6%)	0.09

Continuous variables were compared using Kruskal Wallis Test.
Categorical variables were compared using Pearson's Test.

528 *VSL #3 AS A POTENTIAL MODIFIER OF ENTEROTOXIGENIC BACTEROIDES FRAGILIS INDUCED COLITIS IN WILD TYPE MICE*

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Introduction: Probiotics have been studied as a potential therapy in inflammatory bowel disease (IBD) in humans as well as various colitis animal models. Enterotoxigenic *Bacteroides fragilis* (ETBF) is an opportunistic pathogen that persistently colonizes humans and mice, induces persistent colitis in mice and has been suggested to have increased prevalence in patients with IBD. In murine models, ETBF induces colonic tumorigenesis; in humans, ~90% of colorectal cancer patients are colonized with ETBF (Boleij A, Clin Infect Dis 2015). VSL #3 is a probiotic mixture that has been shown to induce and maintain remission of colitis in IBD as well as in several mouse models of colitis. One model, in which VSL #3 has not been studied, is ETBF induced colitis. Our study aim was to determine whether probiotic administration with VSL #3 would attenuate colitis induced by ETBF in wild type mice.

Methods: Twenty specific pathogen-free C57BL/6 wild type mice were divided equally into 4 groups. Mice were either inoculated with ETBF in phosphate buffered saline (PBS) (~1 x 10^8 bacteria) or PBS alone. Subsequently, VSL #3 in PBS (~1.7 x10^9 CFU/mouse/day) or PBS alone was administered daily by gavage for 7 days to mice inoculated with ETBF and healthy mice. Stool was collected on days 4 and 7. Histologic grading by a blinded pathologist was performed on the proximal and distal colon using a previously published grading scale. Statistical analysis was performed using a two tailed unpaired t-test. Expression of interleukin-17 (IL-17), an important pro-inflammatory cytokine in ETBF-induced colitis, was

assessed from colonic tissue by Real-time PCR. Relative gene expression was calculated by the $\Delta\Delta C_T$ method.
Results: Stool colony counts of ETBF demonstrated adequate colonization and no statistically significant difference between the ETBF groups on day 4 and 7 (2.23×10^8 - 3.10×10^{10} CFU/g). Mice inoculated with ETBF and treated with VSL #3 had attenuation of colitis on histopathology compared to mice inoculated with ETBF alone that was statistically significant (p=0.0481). This difference was most prominent in the distal colon (p=0.0165). IL-17 expression in mice inoculated with ETBF but treated with VSL #3 was less than mice inoculated with ETBF alone (p=0.0556).
Discussion: We have demonstrated that mice inoculated with ETBF had less severe colitis when treated with VSL # 3 compared to those mice inoculated with ETBF alone, a result that reached statistical significance. This difference was most prominent in the distal colon, which is biologically plausible given ETBF colitis is most severe in the distal colon. Our results suggest that IL-17 expression is reduced in mice inoculated with ETBF and treated with VSL #3 compared to those mice inoculated with ETBF alone. Our results suggest that administration of VSL #3 after ETBF exposure can attenuate the severity of the subsequent colitis induced by this bacterium. Further studies could determine if probiotic treatment after or prior to ETBF inoculation decrease the likelihood of long-term sequelae of ETBF infection such as chronic colitis and colonic tumor formation.

NUTRITION

530 *COMPARISON OF VITAMIN D 25 HYDROXY LEVELS TO THE LENGTH OF TIME PATIENT WAS TAKING PROTON PUMP INHIBITOR TO ASSESS FOR PROTON PUMP INHIBITOR ASSOCIATED VITAMIN D DEFICIENCY*

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Routine use of proton pump inhibitors (PPIs) have been used for gastroesophageal reflux disease (GERD) in infants and children since the early 2000's. There have been reports in adults of decreased bone mineral density associated with increased fracture risk in adults who have taken PPIs for many years. However, in children the same observation has not been documented. The etiology to the decreased bone density has not been clearly elucidated in the literature. One possible mechanism is related to the fact that elevating the pH in the stomach and proximal small bowel affects vitamin D absorption. We check vitamin D 25 hydroxy levels for health maintenance in various GI conditions. Objective: The hypothesis is that patients with longer treatment by PPI will have lower vitamin D 25 hydroxy levels. Methods: We collected charts for patients with ICD9 codes for GERD, abdominal pain, and esophagitis and reviewed charts of subjects that also had a vitamin D 25 hydroxy level documented between Jan 2011- Dec 2014. The chart was reviewed to measure how long the patient had been taking the PPI. Other data were collected such as age, whether or not they were fed by Gtube, anthropometrics, and vitamin supplements. Results: Of 746 patients with the ICD9 codes, 131 had a vitamin D 25 hydroxy level. Secondary medical diagnoses included congenital heart disease, neurodevelopmental disorder, genetic disorders, kidney disease, GI inflammatory disease, and GI functional/motility disorder. Other demographics include: Male 52%, female 48%, G-tube fed 35%, Mean age 8.31 years, median age 7.25 years, range age was 4 days old to 21.33 years old. In formula-fed subjects, there was a difference in Vitamin D 25-Hydroxy levels with low vitamin D 25 hydroxy levels after PPI was taken for greater than12 months ($p < 0.02$), but in those with regular diet, there was no difference in Vitamin D 25 hydroxy levels for those who took PPI greater than 12 months compared to less than 12 months (p=0.14). As the table depicts,there was no difference in Vitamin D 25-hydroxy levels between patients who were taking PPI when compared at intervals less than or equal to 3 months, 12 months, or 24 months based on Chi square analysis; p values were 0.55, 0.83, 0.72 respectively. Summary: In general, Vitamin D 25 hydroxy levels were not significantly lower than normal after taking PPI for up to 24 months. Surprisingly, there were more low vitamin D 25 hydroxy levels in those fed strictly formula by G-tube who took PPI greater than 12 months compared to those subjects who took it less than 12 months. Conclusion: More studies are needed to evaluate whether there are longterm affects on bone density in children with medical conditions requiring long term treatment with PPI and vitamin D 25 hydroxy levels is likely not an adequate marker.
Comparison of Months on PPI to Vit D 25 OH Level

	PPI ≤3 mon	PPI > 3mon	PPI ≤ 12 mon	PPI > 12mon	PPI ≤ 24 mon	PPI > 24 mon
Vit D normal	26	29	37	18	44	11
Vit D low	28	24	36	16	43	9
p	0.55		0.83		0.72	

Chi square analysis. p= p-value. Significance of 0.05 was not met.

531 *ROLE OF DIETARY NITRATE AND NITRITE IN ORTHOSTATIC INTOLERANCE*

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Background: Orthostatic Intolerance (OI) is defined by symptoms including dizziness, lightheadedness, headache, sweating, nausea and abdominal pain that occur in the upright posture and relieved by recumbency. The acute form of OI is called vasovagal syncope or simple faint and the chronic form is called POTS (Postural Tachycardia Syndrome). Preliminary data suggests that in these patients with OI, there is enhanced production of nitric oxide which by its role of diminishing adrenergic vasoconstriction, can lead to splanchnic hyperemia and thus orthostatic intolerance. Nitric oxide can be produced endogenously in the tissues as well through the enterosalivary circulation. Dietary nitrate is reduced to nitrite by commensal bacteria in the mouth, nitrite in turn is subsequently reduced to nitric oxide. Approximately 80% of dietary nitrates are derived from vegetable consumption, particularly lettuce, beets, spinach and celery; sources of nitrites include vegetables, fruit, and processed meats.We therefore hypothesize that patients with OI ingest greater amounts of nitrate and nitrite containing foods when compared to healthy controls.

Methods: We studied 10 patients with orthostatic intolerance and 10 healthy subjects aged 14-29 years. Dietary nitrate and nitrite intake was assessed using the NIH-AARP Diet and Health study validated 124 food frequency questionnaire. A finometer was used to measure beat-to-beat BP and EKG for heart rate and rhythm.

Results: There was no difference in the age or sex ratio between healthy subjects and patients with OI. Patients with OI had a significantly higher resting heart rate and a significantly lower mean arterial pressure as seen in table 1. Subjects with orthostatic intolerance consumed more than twice the total nitrite and nitrate than controls (121.1 vs 54.4 mg/day) largely as a result of intake of significantly greater plant containing nitrate.

Conclusions: The results show that subjects with OI consumed twice the total nitrate and nitrite content than healthy subjects. This may be a result of dietary preferences in the Orthostatic intolerance group. Thus, increased dietary nitrate and nitrite intake may lead to increased endogenous production of NO, leading to increased peripheral vasodilatation, thus contributing to OI. Hence modifications of dietary nitrate and nitrite intake may therefore mitigate the effects of orthostasis in patients with OI.

Table 1

	MAP	HR	BMI
Controls	86.5 ± 5.7	61.6± 4.2	25.4± 3.8
Orthostatic Intolerance	78.3±7.2 *	71.8±12.4 †	22.0± 4.6

MAP=Mean Arterial Pressure (mmHg), HR=Heart Rate (beats/minute),
BMI=Body Mass Index (kg/m2). Values shown are mean±SEM.
*P<0.01, †P<0.05, comparing controls to subjects with OI.

Table 2

Dietary Nitrite (NO2-) and Nitrate(NO3-) in mg/day							
CONTROLS (n=10)				ORTHOSTATIC (n=10)			
NO2- Plant	NO3- Plant	NO2- Animal	NO3- Animal	NO2- Plant	NO3- Plant	NO2- Animal	NO3- Animal
0.7±0.1*	49.4±6.2†	0.5±0.1†	3.9±0.0	1.4±0.2	116.9±27.1	0.3±0.1	2.5±0.5

Values shown are mean±SEM. *P<0.01, †P, 0.05, comparing controls to subjects with OI.

532 *SHORT -TERM OUTCOMES USING BLENDERIZED TUBE FEEDINGS AMONG GASTROSTOMY TUBE DEPENDENT CHILDREN*

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Background: Families of children transitioned from enteral feedings of commercial formulas by gastrostomy tube (g-tube) to blenderized tube feedings (BTF) report increased feeding tolerance, decreased vomiting, and improved stooling. The purpose of this study was to evaluate the effectiveness of BTF in improving g-tube tolerance while maintaining adequate growth.

Methods: A retrospective chart review was completed for 29 g-tube dependent patients who initiated blenderized tube feedings at CHOC Children's hospital from 2013 to 2015. Twelve patients were excluded due to pending follow up with the gastrointestinal clinic. Data collected included pre and post medication use, vomiting and reflux, stooling patterns, gastrostomy tube tolerance and anthropometric z-scores. Data was analyzed using paired samples t tests.

Results: Seventeen patients on BTF (7 female, 10 male), with an average age of 6 years (±4.8) were included. Nine out of 17 patients remained on a combination of commercial formula and BTF at the conclusion of the study. Half of the participants had the diagnosis of constipation and one third were diagnosed with reflux. No significant changes in medication use, stooling frequency, and only a slight improvement in stooling consistency were reported after initiating BTF. After BTF initiation, 41% and 29% of patients reported improvements in vomiting and g-tube tolerance, respectively. Thirteen patients out of 17 remain on BTF at the conclusion of the study. BMI z scores pre and post BTF were 0.05 and -0.12, respectively.
Conclusions: Pediatric patients who are dependent on gastrostomy tube feedings can benefit from partial BTF for the management of vomiting and g-tube tolerance, and may not demonstrate significant changes in stooling patterns and medication use. Pediatric patients on BTF are able to maintain adequate growth.

535 *FIRST NATIONAL COLLABORATIVE STUDY (US-COLOMBIA) OF THE NUTRITIONAL STATUS OF CHILDREN AND ADOLESCENTS IN COLOMBIA*

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Background: Anthropometric monitoring of children is highly important. Previous studies in Colombia showed a high index of malnutrition. Economic conditions in the country have changed. Over the past decade, the GDP (gross domestic product) has more than tripled. Colombia is a vast country with diverse climate and regional income. We conducted the first collaborative (US-Colombia universities) survey of the nutritional status of children in the entire country. To account for regional variables we selected private and public schools of mixed socioeconomic and racial composition representative of all Colombian regions.
Methods: Between 2/1 and 10/31/14 we interviewed and measured all children (5-18 years) in 12 schools of 9 geographically dispersed cities across Colombia. Demographic variables included sex, school type, age and geographical region were obtained. Anthropometric measures of weight, height and BMI were obtained following World Health Organization (WHO) guidelines. Subjects were classified based on BMI percentile for age and sex as: at risk for overweight (between > 1SD and ≤ 2 SD), overweight (between > 2 SD and ≤ 3 SD), obesity (> 3 SD), thinness (between > -2 SD and ≤ -3 SD), and severe thinness (> -3 SD). We evaluated under-nutrition variables including stunting, wasting and underweight by using height for age, weight for height and weight for age <2 SD below the mean respectively.
Results: The total number of participants was 5717. 2423 were school-aged children (5-12yo) and 3294 were adolescents (13-18 yo). 52% female. Participants by region and cities: Pacific (Cali, Santander de Quilichao, n=2076), Andean (Cúcuta, Pereira, La Unión, n=1744), Atlantic (Cartagena, San Andrés de Sotavento, Soledad, n=1508), Amazonian (Florencia, n=393). Stunting (low height for age) was found in 454 (8%). Public school-age (OR 0.29, 95%CI 0.19-042) and adolescent age (OR 0.29, 95%CI 0.19-042) had higher odds of stunting. 4002 (70%) children had normal BMI. 1719 (30%) had abnormal BMI. Distribution of children with abnormal BMI: 1112 (19%) at risk for overweight, 398 (7%) overweight, 47 (1%) obese, 125 (2%) mild/moderate thinness, and 37 (1%) severe thinness. Private school students (OR 0.29, 95%CI 0.19-042) and adolescents (OR 0.67, 95%CI 0.59-0.75) had higher odds of abnormal BMI.
Conclusions: 30% of children had abnormal BMI. When compared with previous data, nutritional status of Colombian children is changing. There is lower prevalence of stunting, now 8%. However there is an increasing trend for over-nutrition. Socioeconomic status and age appear to play an important role in nutritional status.

536 *DISACCHARIDASE ACTIVITY IN CHILDREN UNDERGOING UPPER ENDOSCOPY AND THEIR CLINICAL CHARACTERISTICS*

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Background: The genetic basis of congenital sucrase-isomaltase deficiency is well-described. However, the epidemiology and clinical significance of sucrase deficiency in children with GI symptoms has not been thoroughly investigated. Recent work suggests the frequency of lactase deficiency is 42% and sucrase deficiency is >9% when disaccharidase biopsies are obtained (Nichols *et al*., 2012). The goal of this retrospective study was to assess the prevalence of disaccharidase deficiencies in children undergoing diagnostic EGD for various clinical indications and the clinical and demographic characteristics of sucrase deficiency.
Methods: Endoscopic records from patients undergoing EGD and biopsies for disaccharidases activity were reviewed. The EGDs were performed over a 5-year period (2010-2015) at a free-standing endoscopy center serving 13 pediatric gastroenterologists. Symptoms, clinical and histological diagnosis, treatment, disaccharidase assay results and demographic variables were obtained from the medical records of patients with sucrase deficiency.
Results: Among patients undergoing EGD (*N*=5,362), disaccharidase testing was performed in 963 (18%). The most common indications for performing EGD included abdominal pain (*N*=3,344) and diarrhea (*N*=529). Of those tested, 73 (7.6%) were found to have sucrase deficiency (<25 μmol/min/gm) and 430 patients (45%) had lactase deficiency. Among the 73 patients with sucrase deficiency, their age was 12 ±4.6 years and 45 (61.6%) were male. Presenting symptoms

included abdominal pain (n=49;78%), diarrhea (27;43%), constipation (21;33%), nausea (n=19;30%), vomiting (15;24%), weight loss/FTT (15;24%) flatulence (10;14%) and bloating (8;11%).Abnormal biopsies were found in 33 patients (52%) and eight patients (11%) had blood in their stools Those with abnormal biopsies were significantly younger (130±48 vs 156±59 months), had a lower BMI percentile (46 ±32 vs. 63 ±34) and had more episodes of weekly diarrhea (20 vs 13) (for each, $p<0.05$). Primary diagnoses attributed after endoscopy included disaccharidase deficiency (n=20; 28%), celiac disease (16; 22%), duodenitis/ulcer (7; 10%), IBD (7; 10%), esophagitis/EoE (7; 10%), gastropathies/ulcers (9;12%), and other diagnoses (7; 21%). A significant correlation was found between sucrase assay results and the maltase and palatinase assay results.
Conclusion: This study's results are similar to previous reports of sucrase deficiency in the pediatric population as 7.6% of our cohort of children undergoing disaccharidase testing during EGD were sucrase deficient. Our findings imply that testing for sucrase and other disaccharidase deficiencies among patients with chronic diarrhea and/or abdominal pain should be considered during diagnostic EGD. Additional research focused on optimal methods (invasive and non-invasive) to test for sucrase deficiency is needed. There should be an effort to establish relative prevalence of sucrase deficiency in the pediatric population, and to understand its clinical significance.
Results from Patients with Complete Disaccharidase Panels

Laboratory Interpretation	N	Mean Activity (SD)	95% CI
Pan-Disaccharidase Deficiency	44	15.8 (5.5)	14.1, 17.4
Both Lactase & Sucrase Deficiency	15	16.9 (4.3)	14.5, 19.3
Lactase Sufficient & Sucrase Deficient	4	5.5 (6.0)	-4.1, 15.1

537 *DAILY 5,000IU VS. WEEKLY 50,000IU VITAMIN D SUPPLEMENTATION TO VITAMIN D DEFICIENT OBESE CHILDREN: A HEAD TO HEAD COMPARISON*

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Vitamin D deficiency is a common finding among American children especially those with obesity. Vitamin D deficiency has been associated with obesity related complications including NAFLD and metabolic syndrome. The dose of Vitamin D supplementation recommended for normal healthy children has been reported but there are no guidelines aimed towards children with high risk conditions to develop Vitamin D deficiency such as: obesity, ethnicity, low sun exposure and others. Aim: to compare between 2 doses of Vitamin D supplementation in a cohort of obese Caucasian children from West Virginia.
Methods: Obese children who attended the pediatric gastroenterology clinic were prospectively recruited. Exclusion criteria included children who have malabsorption conditions for any medical condition or children with endocrine pathology involving the parathyroid system. Serum Vitamin D levels were measured in obese children and those with Vitamin D deficiency (defined as level <20ng/ml) were randomly assigned by computer to one of two Vitamin D supplementation groups: 5,000 IU/daily (Group A) and 50,000 IU/once weekly (Group B). Vitamin D supplementation was provided free to all participants for the duration of the study. Compliance was assessed by weekly telephone calls and pill counts at 1 month and the completion of the study. Repeat Vitamin D levels were checked upon completion of the treatment at 2 months.
Results: Serum Vitamin D level was measured in 52 obese children, of whom 4 (8%) had normal levels (>30ng/ml), 12 (23%) were Vitamin D insufficient (20-30ng/ml), and 39 (69%) were Vitamin D deficient (<20ng/ml). To date a total of 26 children composed our study (14 - Group A; 12 - Group B). Ten children declined participation or were non-compliant with study protocol and were terminated from the study early. So far, all 26 children (14 - Group A; 12 - Group B) have completed the full course of treatment. Twenty-three of the children achieved adequate serum levels of Vitamin D (>30ng/ml) and 3 children (2 - Group A; 1 - Group B) did not reach adequate levels. None had Vitamin D toxicity or abnormal serum calcium levels. Adequate serum levels of Vitamin D were achieved in both groups but the mean level of Group B was higher compared to Group A after 2 months of treatment (Table).
Conclusion: Vitamin D supplementation at a dose of 5,000IU/d is comparable with 50,000IU/wk. Both doses are safe and should be recommended to obese children.
Vitamin D supplementation in obese children

# Patients	Vitamin D (5,000IU/d) mean ± SEM	# Patients	Vitamin D (50,000IU/wk) mean ± SEM	p-value
14	39.50 ± 2.861	12	50.32 ± 4.091	P = 0.0365

538 *EXAMINING WHERE FAMILIES WITH YOUNG CHILDREN SHOP AND WHY*

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Background: Although many obesity interventions aim to improve a child's diet most interventions do not seek to understand where families purchase food for their child and why. By understanding the context in which nutritional choices are made we can better support families in dietary behavior change.

Objective: To examine 1) the places were families with children with overweight and obesity purchase food 2) why they choose to shop in particular places and 3) whether the type of food establishment or frequency with which they shop at that location is associated with children's BMI z-score or intakes of sugar-sweetened beverages or fresh fruit and vegetables.

Design/Methods: We studied baseline data of 721 children ages 2-12 years with overweight or obesity participating in Connect4Health, a childhood obesity randomized controlled trial. Using telephone surveys we asked parents to list the top 3 places where they purchase food for their family, how frequently and why they go there. Using linear regression adjusted for child age, sex, race/ethnicity, household income, parental BMI and parental education we then examined whether the type of food establishment where they shopped most often was associated with baseline BMI z-score or intakes of sugar-sweetened beverages or fresh fruit and vegetables.

Results: Mean (SD) age of the participants was 7.7 years (2.9). 34% identified as white, 22% as Hispanic, 32% as Black, 5% as Asian, and 6% as Multiracial/other. 58% lived in households where the annual income was ≤$70,000. 51% of parents were college educated. 44% of parents were obese. Mean (SD) BMI z-score at baseline was 1.87 (0.55), mean (SD) sugar-sweetened beverage intake was 1.23 (1.38) servings per day and mean (SD) fresh fruit and vegetable intake was 2.50 (1.59) servings per day. Parents reported they most frequently purchased food at a supermarket (87%). 9% purchased food for their families most often from a wholesale market such as Costco and 1% at fast-food restaurants. 44% shopped 2-3 times per week at the food establishment they visited most often, 43% shopped there 1-2 times per month. Families chose to shop where they did because it was close to home (47%), they offered low prices (30%) and had a high quality of food selection (20%). 93% drove to their most frequented food establishment.

Type of food establishment (e.g. supermarket, wholesale, fast-food) frequented most often was not associated with BMI z-score or fresh fruit and vegetable intake. In adjusted models, children whose families purchased food most often at a fast-food restaurant consumed 1.22 (95% CI: 0.27, 2.17) more servings of sugar-sweetened beverages per day compared to those families purchasing foods at a supermarket. Frequency with which families went to the food establishment was not associated with BMI z-score, sugar-sweetened beverage intake, or fresh fruit and vegetable intake.

Conclusion: Families purchased food most often at supermarkets. Children whose families most often purchased food at fast-food restaurants consumed more sugar-sweetened beverages. With the knowledge of where families shop and why, we can tailor obesity interventions to help families make healthy nutrition choices where they are shopping.

539 *THE BLEND STUDY: A FEASIBILITY STUDY LOOKING AT CHILDREN TRANSITIONING ONTO BLENDERIZED TUBE FEEDS*

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Background: Literature studying the effects of homemade blenderized gastrostomy tube (G-tube) feeds on children's health and well-being is limited. Many caregivers are asking for this form of feeding as an alternative to commercial formula. Preliminary data suggests blenderized feeds may have medically important benefits in children, including better tolerance of G-tube feeds. The aim of this study was to assess the feasibility of transitioning medically stable children from commercial formula to blenderized G-tube feeds.

Methods: The BLEND (BLenderizedENteral Nutrition Diet) Study is a prospective, 6 month-long, feasibility study. Children who are medically stable and received ≥75% of their nutrition enterally via a G-tube were included. Children were transitioned onto the blenderized diet using an energy appropriate diet prescription and were followed closely by a Registered Dietitian throughout the study period. Food records, gastrointestinal symptoms, feeding behaviour scores and exit interviews were collected throughout. Transition from formula to a blenderized diet was considered successful if ≥75% of goal calories were provided by the blenderized diet at the time of the exit interview.

Results: Fourteen patients with complex medical histories and a mean age of 3.3 years (female =10, male =4) were included in the study. At enrolment, acid suppression was used in 79%, promotility agents in 43% and laxatives in 29% of patients. At the end of the study, the proportion of patients reporting lack of emesis went from 36% to 56% ($p=0.64$). Frequency of stools did not change, however Bristol scores did change from 5 to 3.5 ($p<0.02$). Anthropometric percentile parameters, z-scores and body composition remained unchanged. The energy and protein intakes were significantly higher with the

blenderized feeds than with commercial formula feeds (calories: 98 kcal/kg/d vs. 66 kcal/kg/d; protein: 4.1g/kg/d vs. 2.3g/kg/d, both $p<0.05$). At this time 77% of participants have completed the study and of these participants 90% met goal blenderized feeds. Out of all 14 patients only one patient discontinued the diet and one patient transitioned to 100% oral feeds. At study completion 70% of caregivers found the diet more time consuming and 60% found the diet more expensive compared to commercial formula,but 100% were satisfied with the blenderized diet and planned to continue using the blenderized diet long-term.
Conclusion: Blenderized feeds can be used successfully via the G-tube in children who are medically stable instead of commercial formula. Increased calorie and protein intakes are required to maintain the same anthropometrics. Caregivers unanimously agreed upon the perceived benefits of this diet.

540 *UNDERSTANDING BREASTFEEDING: THE STRUGGLE BETWEEN CHALLENGE AND SATISFACTION.*
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Introduction. Breastfeeding practice is a highly effective strategy in reducing infant morbidity and mortality. Its compliance is inadequate among different populations. Exploring breastfeeding (BF) at an individual and community level is important to identify factors related to the low prevalence of this practice.
Objectives: To describe BF experiences, duration and factors associated with exclusive breastfeeding (EBF) for 6 months in a population of mothers from a low-income community in Bogotá, Colombia.
Methods: Mixed methods research design. A cohort of 114 mothers of term newborns was recruited at the postpartum period and followed up at 6 months after childbirth. Two structured interviews were performed to the mothers during the hospital stay and at 6 months with a telephone conversation. Logistic regression analysis was used to identify factors associated to EBF; Kaplan-Meier curves were used to determine EBF time. Three focus group sessions were developed with the original cohort of mothers. BF experiences were discussed and classified within five main domains. A semantic web analysis was developed to understand the construct of BF experience.
Results: Sixty one mothers were lost at follow-up. The mean time for EBF was 4.4 months. Associated factors contributing to EBF for 6 months were not having problems with BF *OR 27.56 (IC 95%: 4.23 - 179.0)* adjusted by having a vaginal delivery *OR 7.50 (IC 95%: 1.38 - 40.82)*. BF experience is satisfying though challenging, family and medical support is needed throughout the process. Child well being is the predominant condition for decision making in BF practice.
Comments: Community-based strategies for mother and child companionship during BF practice must be developed. The construct of BF is complex and multi-influential. Child well being is its beginning and its finality.

541 *ACCURACY OF PARENTALLY REPORTED WEIGHTS AND HEIGHTS AT 12 MONTHS OF AGE AS ESTIMATES OF WEIGHT-FOR-LENGTH PERCENTILES*
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Background: Many studies examining obesity in children rely on parentally reported anthropometrics and there is concern regarding the reliability of such data. No studies to date have looked at the reliability of this data for very young children at 12 months of age, which may differ from older children for many reasons.
Aim: To determine the accuracy of parentally reported weights and lengths at 12 months of age compared with measured weights and lengths obtained from a pediatrician's visit, and to examine factors associated with parentally reported inaccuracies.
Methods: 185 children enrolled in a longitudinal genomic study had parentally completed surveys returned at 12 months of age including weight and length. Measured weights and lengths were recorded for the same children from their 12 month pediatrician visit. Weight for length percentiles were calculated using WHO gender specific growth charts. Pearson's correlation coefficient was calculated to determine association between reported and measured values. The interquartile outlier rule was used to detect potential outliers. Chi-squared testing was used to assess for factors associated with outlying data.
Results: Parentally reported weight was strongly associated with measured weight at 12 months (Pearson's r=0.90). However there was only a moderate correlation between parentally reported and measured lengths (r=0.52) and calculated weight for length percentiles (r=0.65).When the interquartile outlier rule was used to remove outliers from parentally reported data 16 outliers were detected; importantly all these outliers had parentally reported lengths or weights far outside the entire range of measured lengths and weights and were also outside 3 standard deviations of national reference data (WHO). With outliers removed, there was as increase in correlation between parentally reported and measured data for weight (r=0.93) and length (0.69) and now a strong correlation for weight for length percentiles (r=0.76). Outliers removed compared to children included were more likely to have maternal education less than a bachelor's degree (p=0.008); there was no difference in other factors including participant gender, maternal ethnicity and household income.
Conclusions: At 12 months of age, parentally reported weights appear to be accurate, but parentally reported lengths and

hence calculated weight for length percentiles are less accurate. However after removal of clear outliers from parentally reported data using the interquartile outlier rule, there is a strong correlation between calculated parentally reported and measured weight for length percentiles suggesting this may be an effective method to use to increase accuracy in obesity studies in young children using parentally reported data.

		Pearson's Correlation Coefficient*
Raw Data		
Reported weight	Measured weight	0.90
Reported length	Measured length	0.52
Reported weight for length	Measured weight for length	0.65
Outliers removed (interquartile range rule)		
Reported weight with outliers removed	Measured weight	0.93
Reported length with outliers removed	Measured length	0.69
Reported weight for length with outliers removed	Measured weight for length	0.76
* Strong correlation considered r>0.70		

542 *BEING OVERWEIGHT AT 12 MONTHS OF AGE IN HISPANIC VERSUS NON-HISPANIC CHILDREN: COMPARING CLINICAL, SOCIAL, AND ADMIXTURE FACTORS*

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Background: Childhood obesity is disproportionately high in Hispanics, yet there is a paucity of data comparing factors associated with being overweight in Hispanic vs. Non-Hispanic populations.
Objective: To compare clinical and social factors as well as ancestral proportions from genomic data associated with being overweight in Hispanic vs.non-Hispanic children at 12 months of age.
Methods: >2000 children recruited in a longitudinal study of genomics and child health had clinical and social data collected perinatally and through surveys every 6 months. Currently 515 children have clinical, social and genomic data at age 12 months. Weight for length at 12 months was calculated using WHO gender specific growth charts and overweight was defined as weight for length ≥85th percentile. Factors associated with being overweight among Hispanics vs. Non-Hispanics were analyzed using Chi^2 and t-tests. Genomic data was generated and self-reported ethnicity was validated with estimated ancestral admixture proportions (ASIAN, EUROPEAN, AFRICAN, AMERICAS).
Results: Of the 515 children, 12% were Hispanic and 88% Non-Hispanic; 144 (28%) in total were overweight. Of those overweight, 23(16%) were Hispanic. Clinical and social factors significantly associated ($p<0.01$) with being overweight in Hispanic vs. Non-Hispanic children were 1)early solid food introduction 2)juice and sugar sweetened beverage consumption 3)lower maternal education. Factors significantly associated ($p<0.01$) with being overweight in the Non-Hispanic population were 1)increased weight gain during pregnancy 2)lower maternal confidence scores 3)higher perceived stress score. Admixture proportion of individuals showed strong congruence to self-reported ethnicity.
Conclusions: Different clinical and social factors may be associated with being overweight at 12 months in Hispanic vs. Non-Hispanic children. Knowledge of these differential factors can allow targeted anticipatory guidance to different populations at an early age for modifiable factors such as dietary interventions, to possibly reduce obesity later in life. This is preliminary data from a large longitudinal study that will examine how clinical, social, genomic and microbiome data are associated with childhood obesity over time.

Variables	Hispanic +Overweight N=23	Non-Hispanic + Overweight N=121	p-value
Maternal age	30	33	0.008
Maternal BMI	27.6	25.4	0.07
Weight gain in pregnancy	51.8%	60.2%	<0.001
Maternal education<Bachelor's	82.8%	10.8%	<0.001
Gestational diabetes	11.8%	5.9%	0.3
Maternal confidence score	60.3	57.4	<0.001
Perceived stress score	11	14	0.001
Paternal BMI	28.8	27.5	0.2
Prematurity	12.9%	9.7%	0.58
Birth Weight(g)	3309	3423	0.33
Gender(Male)	41.9%	56.9%	0.11
AAP guidelines for solid food introduction(met)	0%	25%	0.001
Ever breast fed	68%	53%	0.1
Juice consumption/week	7.8	2.1	<0.001
Sugar sweetened beverages/week	1.2	0.08	<0.001
Sleep >4 hour stretch	100%	97.5%	0.85
TV and Video time Ever	91%	84%	0.4
Admixture proportion			
AMR	0.79	0.057	<0.001
EUR	0.14	0.82	<0.001

543 *CLINICAL, SOCIAL AND GENOMIC FACTORS ASSOCIATED WITH OBESITY AT 12 MONTHS OF AGE*

Nancy Gilchrist[3], Yvonne Yui[3], Sahel Hazrati[4], Wendy Wong[4], Kathi Huddleston[4], Suchitra K. Hourigan[1,2], John Niederhuber[4,2]. [1]Pediatric Specialists of Virginia, Greatfalls, VA; [2]Johns Hopkins School of Medicine, Baltimore, MD; [3]Inova, Fairfax, VA; [4]Inova Translational Medicine Institute, Fairfax, VA

Background: Childhood obesity is increasing rapidly, with contributing social, genomic and clinical factors. Although many genomic risk factors are associated with obesity, there have been few prospective studies in very young children, where potentially genomic factors may have a more influential role.

Objective: To examine genomic, social and clinical predictors of being overweight, obese and severely obese at 12 months of age.

Design/Methods: >2000 newborns have been recruited in a longitudinal genomic study. Currently 367 have clinical and genomic data available at age 12 months. Infant blood was collected for whole genome sequencing. Clinical and social data was collected perinatally and through parental completed surveys at 6 and 12 months. Weight for length at 12 months was calculated using WHO gender specific growth charts. Overweight was defined as weight for length ≥85th percentile, obese as weight for length ≥95th percentile, and severely obese as weight for length ≥99th percentile.

A supervised genetic analysis was conducted using the SKAT for the association of rare variants (MAF<=0.1) from overweight, obese and severely obese compared to normal weight children. Gene-set level p-values were computed for 363 obesity related genes from the human obesity gene map while adjusting for sex as a covariate. Association of clinical and social factors with obesity at 12 months was analyzed using SAS 9.3 and R 3.0.3.

Results: Of the 367 infants, 31% were overweight, 20% obese and 13% severely obese.

After adjusting for multiple testing with Bonferroni correction, only two genes were significant at the 0.1 level, namely, WT1 (P=0.0033) and CNR1 (P=0.090), for the severely obese group. None of the genes were significant after Bonferroni correction for the overweight or obese groups.

Clinical and socials factors that were significantly associated (p<0.05) with being overweight and obese in all 3 groups were Hispanic origin, lower maternal education and any juice consumption at 12 months (Table 1).

Conclusions: Clinical, social and genomic risk factors are associated with obesity at 12 months; pilot data suggests genomic

factors may play an important role in those who are severely obese at this age.
This is preliminary data from a longitudinal study following a large cohort of infants to potentially find novel genetic variants associated with childhood obesity and how they influence weight over time.
Factors significantly associated with being overweight, obese or severely obese at 12 months.

	Overweight (≥85th%)	Obese (≥95th%)	Severely Obese (≥99th%)
Variables	p-value		
SOCIAL AND CLINICAL FACTORS			
Hispanic origin	0.003*	0.0008*	0.0001*
Maternal education<Bachelor's	0.03*	0.023*	0.006*
Gestational diabetes	0.05*	0.28	0.26
Greater paternal BMI	0.12	0.025*	0.05*
Greater birth weight	0.026*	0.14	0.56
AAP guidelines for solid food (not met)	0.16	0.01*	0.05*
Juice consumption ever	0.03*	0.009*	0.02*
Not having reported feeding difficulties	0.006*	0.05*	0.097
Sleeping<4 hour stretch	0.3	0.06	0.03*
Any TV and video time	0.05*	0.08	0.85
GENOMIC FACTORS			
WT1	1.0	0.647	0.003*
CNR1	1.0	1.0	0.090

* = significant, p <0.05

544 *TRACKING PATIENT PROGRESS AND OUTCOMES IN A TRANSDISCIPLINARY PEDIATRIC INTENSIVE FEEDING PROGRAM*

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Background: Pediatric feeding problems are common, with incidence rates between 25-45% (Lukens & Silverman, 2014). Negative health outcomes associated with feeding disorders include placement of feeding tubes, which may hinder the development of oral feeding behaviors by limiting hunger drive and exposure to stimulation associated with eating (Byars et al., 2003). The primary route of treatment is often outpatient feeding therapy, which is effective for a substantial portion of the population; however, some children are unsuccessful in this setting or of too high medical/psychiatric complexity for outpatient treatment. In these cases, a transdisciplinary approach (medical, oral-motor, and behavioral) is often required. There is a paucity of research regarding children who participate in such programs as only a handful exist in the United States. This study provides clinical outcomes and progress data for a sample of such children treated using an intensive transdisciplinary approach.
Method: All 238 children who have participated in the Intensive Feeding Program (IFP) since the adoption of electronic medical records in 2011 were eligible for the current study. Two patients were excluded from preliminary analyses due to a large amount of missing data (over 50%). IFP includes 3 treatment meals per day, 5 days per week, across 6-8 weeks. A behavioral protocol is used as well as oral-motor exercises for desensitization and oral-motor strength/coordination. Data on oral intake, acceptance and disruptive behaviors are collected each session. Data are tracked using a secure access database and used primarily for clinical purposes. Parents sign a release form for inclusion of treatment data into the ongoing research registry.
Preliminary Results: Non-parametric tests demonstrated significant improvement in nutritional and behavioral outcomes from intake to discharge (see table). Average daily caloric intake increased from 538 kCal per day to 1087 kCal per day (p<.001). For children who entered the program with enteral feedings (N=158), mean percentage of daily enteral calories was 78% at intake and 21% at discharge (p<.001). Behavioral coding has been completed on approximately 1/3 of our sample and results indicate significant improvement in behavioral outcomes as well, including acceptance of bites and drinks (72% at intake to 96% at discharge) and reduction in disruptive behaviors (55% to 9%). Further coding is currently

in progress that will allow for week by week tracking of progress on these outcomes as well as behavioral data to determine the typical course of treatment.
Conclusion: Preliminary results demonstrate the effectiveness of the transdisciplinary IFP model for treatment of feeding disorders by increasing oral intake and decreasing G-tube reliance. Further analyses in progress will help to reveal week-by-week behavioral outcomes in regards to acceptance and disruptive behaviors.

Variable Name	Intake	Discharge	*p-value*
Average Oral Calories Per Day	538	1087	< .001
Average percentage of enteral calories per day (N=158)	78%	21%	< .001
Mean acceptance of bite/drink trials	72%	96%	< .001
Mean percentage of disruptive behaviors	55%	9%	< .001

p-values based on Wilcoxon Signed-Rank tests.

545 *CLINICAL AND NUTRITIONAL STATUS MAINTAINED WITH TEDUGLUTIDE TREATMENT IN PEDIATRIC PATIENTS WITH SHORT BOWEL SYNDROME*

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The aim of treatment with teduglutide (TED), an analog of the intestinotrophic factor glucagon-like peptide 2, is to decrease parenteral support (PS) requirements by increasing the absorptive capacity of remnant intestine in patients with short bowel syndrome (SBS). We sought to determine whether clinical and nutritional status could be maintained despite reductions in PS in children with SBS aged ≥1 year during treatment with TED.
A 12-week, open-label, multicenter, safety and pharmacokinetic/pharmacodynamic study was carried out in children aged 1–17 years with a history of SBS ≥12 months who had reached a plateau in intestinal adaptation (ie, PS could no longer be reduced in a clinically significant way) and showed minimal or no advance in enteral nutrition (EN; ie, specialized nutrition provided via feeding tube or orally) for ≥3 months. Patients were enrolled sequentially into 3 dosing cohorts: 0.0125 mg/kg/day (n=8), 0.025 mg/kg/day (n=14), and 0.05 mg/kg/day (n=15); a fourth cohort received standard of care (SOC; n=5).
Pooled data for the TED dose cohorts showed that mean prescribed PS volume decreased by 32% at Week 12 in the combined TED cohorts (n=37), with the greatest decrease (39%) in the 0.05-mg/kg/day cohort. Patient diary data indicated that EN volume increased by 49% in the combined TED cohorts; the greatest improvement (58%) was observed with the 0.05-mg/kg/day dose. Parameters of clinical and nutrition status were maintained across all dosing cohorts (Table) despite clinically meaningful reductions in PS during TED treatment. At Week 12, median values for liver function analytes (serum alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, bilirubin, blood urea nitrogen, gamma glutamyl transferase) were stable or decreased slightly in the SOC and all TED cohorts. Median pancreatic enzymes (amylase, lipase) were stable in all treatment cohorts.
In pediatric patients with SBS aged 1–17 years, treatment with TED resulted in clinically meaningful reductions in PS without detrimental effects on nutrition or clinical status, indicating effective absorption from EN feedings.
Mean Clinical and Nutritional Parameters at Baseline and Week 12 in Pediatric Patients With SBS

Mean	0.0125, n=8*	0.025, n=14†	0.05, n=15‡	SOC, n=5
Weight, kg BL Wk12	20.0 22.4	18.9 20.3	17.0 17.3	13.1 13.6
Albumin, g/L BL Wk12	39.5 38.7	39.2 37.5	39.7 38.4	38.4 36.4
Calcium, mmol/L BL Wk12	2.3 2.3	2.4 2.3	2.3 2.3	2.4 2.3
Magnesium, mmol/L BL Wk12	0.8 0.8	0.8 0.8	0.8 0.8	0.8 0.8
Phosphate, mmol/L BL Wk12	1.7 1.6	1.6 1.5	1.6 1.6	1.7 1.6

BL=baseline; SOC=standard of care; TED=teduglutide; *Wk 12 n=7; †Wk 12 n=13 (n=12 for weight); ‡Wk 12 n=13

546 *GASTROINTESTINAL COMPLICATIONS MANIFESTING IN PATIENTS WITH AICARDI SYNDROME*

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Introduction: Aicardi Syndrome is a rare disorder, classically defined by the triad of agenesis of the corpus collosum, chorioretinal lacunae, and infantile spasms. Gastrointestinal (GI) dysfunction is found in over 90% of children with Aicardi Syndrome and is the second most common complication after seizures. Symptoms include constipation, reflux, abdominal pain, and diarrhea, significantly impairing quality of life. There is a paucity of data regarding the frequency with which these symptoms occur. As such, we intend to characterize the type and frequency of GI symptoms suffered by children with Aicardi Syndrome.

Methods: A 2 page questionnaire describing GI symptoms was distributed to parents of children with Aicardi Syndrome at the 2014 Aicardi Syndrome Family Conference in Bloomingdale Illinois. Results were compiled and analyzed for trends. The IRB at Lurie Children's Hospital approved this study.

Results: A total of 22 patients were included in the study. Of these 22 patients, 2 (9%) were deceased. The average age of living patients included in this study was 5.4 years (range 4 months to 12 years). 20 patients (91%) were Caucasian, 1 patient (4.5%) was Native American, and 1 patient (4.5%) was Hispanic. The most common gastrointestinal symptom described was constipation, occurring in 17 (77%) of patients. 1 patient had been hospitalized and 2 had been seen in an emergency room for constipation. 5 patients (23%) reported normal stools. Diarrhea occurred in 3 patients (14%) however all of these reported alternating between constipation and diarrhea. None of the patients in this study were toilet trained. 10 patients (45%) had enteric tubes and of these 10 patients 7 were exclusively tube fed. The remaining study patients were fed orally. Of the 10 patients with an enteric tube, 9 had permanent gastrostomy tubes and 1 used a nasogastric tube. 3 of these patients were on continuous gastric feedings, 5 on bolus feedings, and 2 on some combination of both. Patients receiving tube feedings were older than patients who were orally fed (8.45 years versus 3.75 years). 4 patients (36%) were on a ketogenic diet whereas the remainder used a variety of either polymeric and hydrolyzed formulas. Twelve patients (65%) were on some form of acid suppression for reflux. Eleven patients (50%) had undergone previous esophagogastroduodenoscopy (EGD). Gross findings were noted in 2 patients, 1 with a gastric ulcer and another with esophagitis. 4 patients (18%) had undergone fundoplication for refractory reflux.

Conclusion: This is the first study to characterize GI complaints in patients with Aicardi syndrome. Constipation, treatment with acid suppressant medications and use of enteric tube feedings for nutrition were noted frequently in this population. Diarrhea and gross pathologic findings on EGD were much less frequent. This study will help clinicians anticipate GI complaints in patients with Aicardi Syndrome and allow for anticipatory guidance of common GI problems. Future prospective studies will be useful to characterize these symptoms further.

547 *THE BITTERSWEET TRUTH ABOUT SUGAR: MEASUREMENT OF SUGAR LITERACY IN PARENTS OF OVERWEIGHT/OBESE CHILDREN*

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Background and Aims: The link between added sugar overconsumption and pediatric obesity, dyslipidemia, and non-alcoholic fatty liver disease is well-established. Despite increasing public health messaging about its dangers, sugar overconsumption remains prevalent. Previous education efforts assume that individuals have a baseline level of sugar knowledge, which they may not have. This lack of knowledge makes counseling difficult and often ineffective. The purpose of this study was to develop a novel test to measure sugar knowledge (sugar literacy) and test if an individual's overall health literacy is predictive of their sugar literacy.

Hypothesis: Sugar literacy is independent of an individual's health literacy.

Methods: A sugar literacy test was developed through informal focus groups with key stakeholders including pediatric obesity, nutrition, and health literacy experts. The brief test measures knowledge of sugar content in foods and beverages, interpretation of food labels, and the health sequelae of sugar overconsumption. Twenty-eight parents of overweight/obese children were administered the sugar literacy test and The Newest Vital Sign (NVS), a validated health literacy instrument. Comparisons between NVS and sugar literacy scores and socioeconomic factors were made using Pearson's analyses.

Results: A strongly positive relationship existed between health literacy and education (r=0.73, p=1.26E-05) in our population. A similar correlation was seen when using English as a primary language (r=0.60, p=0.00069) and income (r=0.43, p=0.02) for comparison. Our data, however, suggests that no relationship exists when comparing health literacy and sugar literacy (r=0.115, p=0.56).

Conclusions: Our preliminary data suggests that health literacy may not be predictive of sugar literacy. This study brings to light unrecognized gaps in nutrition knowledge which may sabotage counseling efforts if they go unaddressed. The results obtained in our study will be used to develop more tailored education materials that will hopefully lead to decreasing sugar overconsumption.

Health Literacy versus Sugar Literacy and Socioeconomic Factors

	Health Literacy
Education	r=0.73, p=1.26E-05
English as Primary Language	r=0.60, p=0.00069
Annual Household Income	r=0.43, p=0.02
Sugar Literacy	r=0.115, p=0.56

548 *INTRAVENOUS OMEGA-3 FATTY ACID EMULSION (OMEGAVEN ™) IN PARENTERAL NUTRITION RELATED LIVER DISEASE AND LONG-TERM OUTCOME ON RETINOPATHY OF PREMATURITY AND NUERODEVELOPMENT.*

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Objective: To assess short and long-term outcomes in patients with severe parenteral nutrition-associated liver disease (PNALD) treated with Omega -3 Fatty Acid Emulsion compared to gestational and chronological age matched controls with mild PNALD.

Background: Parenteral nutrition (PN) is a life-saving therapy for patients with intestinal failure syndromes, including patients with short bowel syndrome due to a variety of congenital or acquired gastrointestinal illnesses. PNALD is a common problem in the neonatal intensive care unit.Long-term PN carries significant morbidity and mortality, with 30% to 60% of patients developing PNALD. Omega-3 fatty acid emulsion (OmegavenTM) has been demonstrated to be safe and effective in treating PNALD, and may reduce mortality and organtransplantation rates. However long-term outcome data on Omegaven™ is limited.

Methods: Data was collected on a cohort of 36 patients who developed cholestasis while receiving PN Soybean lipid emulsions that received Omegaven™ under a compassionate treatment protocol at Golisano Children's Hospital, from September 2007 until September 2014 compared to a matched cohort. The primary efficacy end-point was time to reversal of cholestasis (direct bilirubin < 2 mg/dL) and secondary outcomes were neurodevelopmental assessment at 12 months assessed by Bayley Scales of Infant Development III / Bayley Infant Neurodevelopmental Screener, and incidence and severity of retinopathy of prematurity (ROP) at discharge from NICU compared with gestational age controls who developed more mild cholestasis while receiving soybean oil-based lipid.

Results: Cholestasis and transaminitis reversed for all 36 patients who received Omega-3 Fatty Acid Emulsion. No subjects required liver transplantation for PNALD over last 8 years since the introduction Omega-3 Fatty Acid Emulsion (data not

shown). A subset of patients developed essential fatty acid deficiency. Subjects that were restarted or transitioned to soybean lipid emulsion did not have reoccurrence of parenteral nutrition-associated liver disease. No difference was detected in neurodevelopment assessment of competency by Bayley Scales of Infant Development III (2007-2011) /Bayley Infant Neurodevelopmental Screener (2012-2014) for patients receiving Omega-3 Fatty Acid Emulsion compared to soybean lipid emulsion who received routine follow-up as per NICU routine. However subjects with prolonged NICU course, who received prolonged administration of Omegaven™ trended to be less competent in their neurodevelopment assessment. No difference was detected in retinopathy of prematurity between premature infants receiving an intravenous fat emulsion containing fish oil compared to premature infants who receive fat emulsion containing soy oil.
Conclusion: Fish oil-based emulsion appears safe, and effective in treating PNALD, and might decrease organ transplantation rates in children requiring long term PN. Essential fatty acid supplementation is sometimes needed for patients supported with Omegaven™ .

549 *INDIAN PEDIATRICIAN'S PERSPECTIVE OF COW'S MILK PROTEIN INTOLERANCE, A SURVEY*

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Little is known about cow's milk protein intolerance (CMPI) in developing countries where alternate formulas are sparse. We report a survey of Indian pediatricians on their attitudes and practices with CMPI.
Methods :- 15,000 members of the Indian Academy of Pediatrics were invited to take an online survey on their opinions about association of CMPI with different clinical conditions as well as their response to a clinical scenario of a healthy infant with rectal bleeding. The data was compiled and statistically analyzed.
Result :- 165 responses, 26 partial were obtained (1.1%). 5 were in general practice while rest were pediatricians, 73.68% practiced in urban or suburban settings. Common manifestations of CMPI noted in practices were Diarrhea (85.9%), Colic (83.9%), abdominal pain (73.6%), vomiting (73.4%), Asthma (66.6%), hematochezia (64.2%), constipation (63.6%) and atopic dermatitis (63.6%).
In infants with colic 48.4% of Pediatricians considered (50% of more times) CMPI as the cause, 70% were likely (50% of more) to change formula or diet and 50% or more success were reported by 75.7%. Similar figures for gastro esophageal reflux were 44.9%, 63% and 62.1% respectively. For diarrhea 54.3% physicians were likely to consider CMPI, 68.9% changed diet and 74.5% reported 50% or more success rate.
In a healthy infant under 6 months with hematochezia, 63.5% considered CMPI as the cause. In breast fed infants, 91% would have continued the infant on breast feed, half of them would have taken milk out of the mother's diet. In formula fed babies, 65.9% were likely to change formula; 58.7% preferred soy based formula while 45.5% used rice based liquid or diet. Only 4.8% considered elemental or semi elemental formulas. The physicians collectively reported a median percentage of 30% of such hematochezia resolving spontaneously, 50% with treatment, 10% continuing without complications and 5% had complications. There was no statistically significant difference in responses from physicians practicing in urban/suburban and rural/mixed settings.
Conclusion: Indian physicians were aware of CMPI as the cause of various GI and non GI symptoms. Though they less readily considered CMPI as the cause of infantile hematochezia, management with locally sourced diets was successful. Population based studies are indicated to provide cost effective guideline for management of CMPI in this environment.

550 *METHYL DONOR DEFICIENCY INDUCES SMALL INTESTINAL CRYPT HYPERTROPHY IN MICE AND MURINE ENTEROIDS*

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Background & Aims: Highly prevalent in low- and middle-income countries, environmental enteropathy (EE) is a subclinical intestinal condition characterized, in part, by malabsorption, intestinal villous atrophy, and crypt hypertrophy. The pathogenesis of EE remains unclear, however supplementation with folate (a key source of one carbon units for DNA methylation) is an effective adjunct therapy for tropical sprue, i.e., persistent diarrhea on a background of EE. To determine the extent to which methyl donor deficiency (MDD) provokes features of EE in mice, we evaluated mechanistic links between dietary methyl donor deficiency and intestinal crypt hypertrophy in mice and in mouse small intestinal crypt cultures (enteroids).
Methods: We randomized dams to a standard diet or an isocaloric MDD diet lacking folate, choline, and betaine when pups were 10-days-old. We then randomized weanlings to their dams' diet on day of life 21. Mice were sacrificed and the jejunum was harvested at 6 weeks of age for both histology (n=6/group) and generation of enteroids.
Results: Histological comparisons of the jejunum revealed longer crypts in MDD versus control mice, moreso in the distal (85.6 +/- 13.7 μm vs. 69.3 +/- 7.2 μm; P<0.0001), vs. proximal (88.8 +/- 17 μm vs 80.7 +/- 10.7 μm; P=0.04) portions of the small intestine. Enteroids from control and MDD mice were both viable in standard minigut media; however, all enteroids maintained in MDD media displayed alterations in crypt morphology and decreased epithelial proliferation.

Enteroid crypt neck width was 1.3-fold greater in standard vs. MDD media (P<0.001). The number of crypt buds per enteroid was 1.6-fold higher in standard media vs. MDD media (p = 0.0007). The ratio of EdU-positive, or proliferating, cells to Hoechst-positive cells was 2.2-fold higher in standard media vs. MDD media (P<0.0001). Qualitatively, enteroids in MDD media displayed longer crypt domains relative to lumen size vs. enteroids in standard media.
Conclusions: Complementary *in vivo* and *in vitro* findings of altered small intestinal crypt morphology in the setting of methyl donor deficiency (MDD) suggest that MDD plays a role in the pathogenesis of environmental enteropathy. Further studies are needed to determine whether prolonged MDD promotes megaloblastic changes of epithelial cells and epigenetic changes of intestinal stem cells and whether methyl donor supplementation prevents or reverses these changes to promote intestinal epithelial homeostasis in global settings of poverty.

551 *TRANSITION TO A REAL FOOD ENTERAL FORMULA IN PEDIATRIC PATIENTS WITH INTESTINAL FAILURE*

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Background: Children with intestinal failure (IF) pose a dietary challenge as they age. Traditionally in IF, amino acid based formulas are used initially due to concerns for malabsorption and possible allergic reactions to intact proteins. The use of real food enteral formula (RFEF) via gastrostomy tube has been reported to improve feeding tolerance in pediatric populations on long term enteral nutrition therapy, and studies in animals with IF suggest that intact macronutrients stimulate intestinal adaptation. We hypothesized that children with IF in enterocolonic continuity would have improved stool consistency and frequency when transitioned from an elemental formula to a RFEF (Pediatric Compleat, Nestle Health Science).
Methods: Data were collected in a retrospective chart review from January 2012 to October 2014 of children with IF, over one year of age, who were receiving enteral nutrition either via continuous infusion, bolus feeding, or a combination of both methods. All patients were independent of TPN. Indications for RFEF trial were *diarrhea,* defined as greater than three large, loose, liquid stools per day and *constipation associated with dysmotility* defined as less than 3 stools per week .
Results: Ten children with mean small bowel length of 48.25cm (range: 34-64cm, median 46.5cm) were trialed on RFEF. Nine of ten (90%) children tolerated the transition to 100% RFEF of which 7/9 (78%) patients had their entire colon in continuity, and 2/9 (22%) had part of the colon in continuity. The average age at successful transition was 29.2 months (RANGE: 12 -72 /median 30 months). Average length of time to transition to 100% RFEF was 67.3 days (RANGE: 2-322 /median 18 days). The indication for transition to RFEF was diarrhea in 7/9 (78%) patients and constipation related to dysmotility in 2/9 (22%). In the diarrhea group, all parents (7/7) reported an improvement in stool consistency, changing from "loose, liquid, large" to "semi-formed" or "formed" and a decrease in the total number of stools, changing from >3 per day (Range: 3-8, median 5), to < 3 per day (range being QOD - 2 x per day). For the 2 patients in the dysmotility group, parents reported an overall improvement in stool frequency, changing from 1-3 times weekly with straining, to once daily or every other day. Additionally, stool consistency changed from "large" and/or "hard" to "soft" and/ or "formed". Supplemental fibers (Nutrisource, Pectin) were discontinued in 100% of patients transitioned to RFEF. Total cost savings with transition to RFEF was noted, as the average cost for elemental formula per month with added pectin is approximately $710/month compared to $375/month for RFE (difference equal to $11.00/1,000 calories). All children transitioned to RFEF maintained age appropriate weight gain.
Conclusion: In children with IF, a RFEF may decrease diarrhea and constipation associated with dysmotility. A commercially available RFEF is a cost effective and nutritionally adequate means of providing nutrition to this patient population greater than one year of age.

552 *LONG-TERM OUTCOMES OF CHILDREN HOSPITALIZED WITH FAILURE TO THRIVE*

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Background: Much is known about the causes of failure to thrive (FTT) in children and its effect on cognitive development. There is general agreement that children require nutritional supplementation in order to reduce neurodevelopmental risks, but the approach to treatment is not standardized, nor have the outcomes of various treatment modalities been well-studied. There is some data to suggest that among smaller children there is a tendency for early "catch-up" growth and limited studies demonstrate an association between nonorganic failure to thrive and obesity; however, there exist no systematic reviews explicitly addressing long-term anthropometric outcomes of children hospitalized with FTT. Our study aimed to 1) describe children hospitalized for FTT and their growth over time and 2) characterize children with persistently poor growth and those whose growth normalized or exceeded expected weight gain.
Methods: We conducted a retrospective study of patients aged 0 to 7 years admitted to Hasbro Children's Hospital between 12/31/2006 and 10/31/2014 and discharged with ICD-9 diagnosis codes for FTT. Using electronic medical record search, we compiled a database of eligible subjects. Patients with FTT as a result of congenital and acquired malabsorptive bowel conditions or metabolic disorders were excluded. We collected data on demographics, initial anthropometric measures and

approach to nutrition rehabilitiation including types and routes of supplementation. Follow-up data available in our EMR were collected for up to 48 months post-admission.
Results: Preliminary data review included a total of 94 subjects found to have the selected ICD-9 diagnoses. A total of 27 were excluded according to above criteria or if they were found to have transient systemic disease requiring temporary IV hydration due to decreased feeding during acute illness, but did not have weight loss or require nutritional evaluation during their hospitalization. A total of 52/67 (78%) of subjects had follow-up data available in our EMR.
Mean age at time of admission was 14.7 months, with range 0.16 to 78 months. Majority (93%) were children below 5 years old. Only 4% had a history of prematurity. Presence of maternal psychiatric condition was recorded for 9 % of patients and almost 20% had involvement with department of children and family services. Table 1 describes the nutritional status of patients at admission and by final follow-up. Table 2 characterizes patients according to routes of supplementation.
Conclusion: The major findings of our study were that the majority of children with FTT were otherwise healthy and did not require long-term or enteral supplementation. The presence of comorbidities may be helpful in predicting long-term need for NG or GT supplementation.
Analysis of nutritional status

	Severe malnutrition (z score <-3)	Moderate (-3 to -2)	Mild (-2 to -1)	Normal (-1 to 2)	Overweight (>2)
Admission	12 (24%)	8 (16%)	4 (8%)	21 (43%)	3 (6%)
Final follow-up	1 (2%)	5 (10%)	8 (16%)	35 (71%)	0 (0%)

*1 patient had no admission height. 3 subjects had no available heights at follow-up visits.
Analysis of routes of supplementation

	0 comorbidities	1 comorbidity	2 or more
Subjects requiring only oral feeds	22 (65%)	8 (24%)	4 (12%)
Subjects eventually on oral-only feeds	6 (46%)	5 (38%)	2 (15%)
Subjects requiring G-tube	1 (5%)	8 (42%)	10 (53%)

*553 *DIETARY FRUCTOSE IMPAIRS HEPATIC MITOCHONDRIAL FATTY ACID OXIDATION AND ACCELERATES THE DEVELOPMENT OF FATTY LIVER DISEASE.*

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Non-alcoholic fatty liver disease (NAFLD) is a frequent complication of obesity and insulin resistance. In the present study we assessed the effects of high carbohydrate diet and/or high fat diet (HFD) on obesity, insulin resistance and NAFLD development in C57Bl6 mice using 6 different diets. Three groups were on normal chow, one with regular drinking water (Chow + H2O), the second with 30% fructose in drinking water (Chow + Fruct), and the third group with 30% glucose in drinking water (Chow + Gluc). The next three groups were all on high-fat diet and again on regular water (HFD + H2O), fructose (HFD + Fruct), or glucose (HFD + Gluc).
While on chow diet, both glucose and fructose supplemented mice gained more weight than mice on regular water, they did not develop diabetes or fatty liver disease. Both HFD+H2O and HFD + Gluc group gained more weight than all chow controls, but the HFD + Fruct fed-mice gained the most weight over the 10 week study period. The difference in body weight was primarily due to increased liver and visceral adipose tissue weights in HFD + Fruct mice. They also developed the most severe hyperglycemia and insulin resistance and on a molecular level had decreased Akt phosphorylation and decreased overall tyrosine phosphorylation of insulin signaling molecules. Liver specific metabolic derangements included reduced mitochondrial size, decreased ATP and increased uric acid production. *De novo* lipogenesis was increased as exemplified by increased triglyceride content per mg of liver and increased mRNA levels of *Srebp1c*, *Acly*, *Acc1*, *Fas* and *Scd1* from 2 to 12-fold over Chow+H2O group. Furthermore, fatty acid oxidation was decreased as assessed by increased liver acyl-carnitine profile, decreased global oxygen consumption and decreased oxygen consumption in cultured hepatocytes. By contrast, the HFD + Gluc group was protected from insulin and glucose intolerance in spite of gaining as

much weight as insulin resistant HFD+H_2O mice. Liver fat metabolism was increased in HFD + Gluc group and correlated with increased mRNA expression of *ChREBP, Cpt1α, Pgc1α,* and *Acad9*. Overnight fasted HFD + Gluc mice had the most robust elevation if free fatty acids and corresponding beta hydroxybutyrate levels. Serum fibroblast growth factor 21 (FGF21) levels were increased on fructose, but much more robustly with glucose supplementation, both on chow and HFD. Additionally, serum adiponectin levels were elevated only with glucose, but not fructose supplementation.
Thus, dietary fructose, but not glucose, impairs mitochondrial fatty acid metabolism and supports lipogenesis, contributing to the development of a more severe fatty liver disease and insulin resistance.

554 *THE ROLE OF DIAGNOSTIC UPPER ENDOSCOPY IN THE MANAGEMENT OF INFANTS WITH FAILURE TO THRIVE*

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Background: Failure to thrive (FTT), weight for age below the 5th percentile or weight deceleration that crosses two major percentile lines on a growth chart, is a state of under-nutrition due to inadequate caloric intake, inadequate caloric absorption, or excessive caloric expenditure and is seen in 5- 10 % of children. Management guidelines and differential diagnoses of FTT are vague and greatly dependent on clinical presentation. As such, there are no standardized diagnostic algorithms for the diagnosis and treatment of FTT.
Aims: To evaluate the utility of diagnostic Upper Endoscopy (EGD) in the management of infants with FTT.
Methods: We retrospectively evaluated medical records that recorded symptoms, presenting diagnoses and treatment outcomes of 37 consecutive patients over a two year period from 2012 to 2014 with FTT secondary to feeding refusal. All patients were defined as having FTT as they weighed below the 5th percentile for age without associated symptoms such as vomiting, diarrhea or constipation. Laboratory and imaging evaluations were unremarkable for all. All patients had EGD performed with biopsies of the esophagus, stomach and duodenum. Weight for age Z-scores before and after EGD were calculated (CDC/NCHS weight for age percentile calculator) according to the mean of 50th percentile for weight and age. Data are reported as mean ± SD.
Results: Subjects were between 2 and 24 months of age (14.0±5.5 months); F: M- 9: 28. Fifteen of the 37 patients were <1 year of age. The occurrence of mucosal disease was significantly different comparing patients with FTT younger than and older than 1 year of age (60% vs 22.7%, $p<0.001$). Endoscopic findings comparing the two groups of patients (< 1 year vs > 1year age) showed normal EGD (40% vs 73%), eosinophilic esophagitis (33% vs 9%), and celiac disease (9% vs 6%). In children < 1 year of age, the average z-score for weight prior to treatment was -3.1±0.9 (SD). After evaluation and treatment, the mean z-score for weight decreased significantly ($p<0.001$) to -1.7±0.9 (SD) indicating an improvement in weight gain.
Conclusions: Findings from EGD showed the incidence of mucosal disease was significantly different when considered in relation to age. In children <1 year of age, 60.0 % had mucosal disease in comparison to 22.7% in children >1 year of age. At follow-up, patients <1 year of age, had a mean increase in weight from 0.6 to 8.1%; in patients >1 year of age weight increased from 1.2 to 9.4%. There is a higher incidence of treatable mucosal disease in patients < 1 year of age as compared to patients >1 year of age as diagnosed by EGD. Therapeutic choices guided by this information resulted in increases in weight in our patients, thus suggesting the utility of EGD in this patient population for the diagnosis and treatment of FTT.

555 *GROWTH AND TOLERANCE OF INFANTS FED FORMULA WITH PRE- AND PROBIOTICS*

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Background: Pre- and probiotics beneficially affect the host by improving the survival and establishment of live microbes from dietary sources in the gastrointestinal tract. We have previously demonstrated adequate growth in healthy infants receiving a cow's milk-based formula with either a prebiotic blend of polydextrose (PDX) and galactooligosaccharides (GOS)[1], or the probiotic *Lactobacillus rhamnosus GG* (LGG) added to extensively hydrolyzed formulas[2].
Objective: The objective of this study was to compare the growth rate from 14-120 days of age between an investigational study formula containing both pre- and probiotics to the currently marketed formula containing prebiotics alone.
Methods: In this multi-center, double-blind, controlled, parallel-group, prospective study, infants received one of two formulas from 14-120 days of age: a currently marketed routine infant formula containing PDX/GOS (Control, n = 171), or an investigational formula containing PDX/GOS and LGG (10^6 CFU/g powder) (Investigational, n = 177). The primary outcome for this study was rate of weight gain (g/day) from 14-120 days of age. Growth rates and weight-for-length z-scores were analyzed using ANOVA. Formula tolerance was evaluated by parental-reported stool characteristics, gassiness and fussiness and analyzed using the CMH test.
Results: A total of 275 infants completed the study (Control, n = 131; Investigational, n = 144), with no differences in study completion rates between the groups. There were no significant differences in the rate of weight gain (g/day) from 14 to 120 days of age between the two formula groups. Weight-for-length z-scores were similar at 30, 60, 90, and 120 days.

Relative to normal, there was less parental-reported fussiness in the investigational group at 60 and 90 days of age compared to the control group ($p < 0.05$; Table 1). No significant differences were detected between study groups for infant gassiness or stool characteristics.
Conclusions: Results of this study demonstrated that the investigational formula containing pre-and probiotics was well-tolerated and associated with normal growth when fed to healthy infants from 14 to 120 days of age.
References: [1]Ziegler E, Vanderhoof JA, Petschow B, et al: J Pediatr Gastroenterol Nutr 2007;44:359-64.
[2]Scalabrin DM, Johnston WH, Hoffman DR, et al: Clin Peds 2009;48(7):734-44.
Infant fussiness relative to normal at days 30, 60, 90, and 120

		Study Group				
		Control		Investigational		
Age (Days)	Fussiness Relative to Normal	n	(%)	n	(%)	p-value
30	Less fussy than normal	15	(10)	8	(5)	0.228
	About the same level of fussiness	113	(74)	124	(78)	
	More fussy than normal	24	(16)	28	(18)	
60	Less fussy than normal	7	(5)	14	(10)	0.017*
	About the same level of fussiness	104	(76)	117	(80)	
	More fussy than normal	26	(19)	15	(10)	
90	Less fussy than normal	8	(6)	16	(11)	0.009*
	About the same level of fussiness	100	(74)	110	(78)	
	More fussy than normal	28	(21)	15	(11)	
120	Less fussy than normal	14	(11)	18	(13)	0.134
	About the same level of fussiness	90	(73)	109	(78)	
	More fussy than normal	20	(16)	12	(9)	

*Statistically significant, p-value <0.05

556 *ASSESSMENT OF NUTRITION EDUCATION AMONG PEDIATRIC GASTROENTEROLOGISTS: DEVELOPING A PEDIATRIC NUTRITION CORE CURRICULUM EDUCATION PROGRAM AT EMORY UNIVERSITY*
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Background: Pediatric nutrition is a rapidly changing area of scientific and clinical significance.
The need for greater nutrition training among pediatric gastroenterologists is becoming increasingly evident. Recognizing the importance of nutrition education, NASPGHAN has published guidelines providing a core curriculum defining the minimum knowledge/skills required of graduating fellows. These distinguish between a Level 1 Nutrition Curriculum which is the basic training required for all trainees, and Level 2 which defines advanced objectives for the fellow aiming to become an "Expert in Nutrition". For completion of Level 2, the guidelines suggest a minimum of one year of advanced training at an academic center under the supervision of a full time nutrition faculty. However, even minimum Level 1 requirements are not consistently covered in most fellowships.
Aim: To develop a program fulfilling Level 1 requirements to provide a short period of concentrated nutrition study within the current three year pediatric gastroenterology fellowship. Our goal was to develop a 4-month Pediatric Nutrition Core Curriculum Education Program featuring competency-based goals and objectives for second- and third-year GI fellows.
Methods: We did extensive literature and peer review to summarize nutrition programs available online and national opportunities for additional clinical nutrition training.
Results: Our proposed program consists of time spent with dieticians, local nutrition advocates, national nutritional education opportunities and self-study from reliable on-line modules/ textbooks. Current challenges in Nutrition Education with proposed solutions are highlighted in Table 1. We suggest a similar curriculum outline be adopted by NASPGHAN for use as a template for use by pediatric gastroenterology fellows who wish to achieve their nutritional competency regardless of advance nutritional programs developed at their institution.
Conclusion: We suggest a core curriculum comprised of time with dieticians, national nutritional education exposure, and self-study through online learning modules and textbooks to help structure and bring consistency to the methodology of nutrition education during gastroenterology fellowship training.
Table 1: Current challenges in Nutrition Education with proposed solutions.

Challenges and Barriers	Proposed Solutions
Lack of faculty expertise in nutrition in medical schools and teaching hospitals leading to inadequate role modeling and insufficient resources for curriculum development and implementation	Seek out time with RDs Seek out time with Clinical PharmDs that may be involved with TPN management in your local hospital Reach out to any MDs in your local area interested in nutrition Reach out to MD's in geographic region with interest in nutrition
Lack of nutrition education in medical schools and residency programs	Self study via online modules: • UNC Chapel Hill teaching modules • ASPEN teaching modules Seek out additional educational opportunities: • N2U sponsored by NASPGHAN • Dannon Nutrition Leadership Institute National organizations and meetings: • ASPEN • NASPGHAN • ASN • Pittsburgh Annual Intestinal Rehab Conference
Inadequate practice and low self-efficacy toward diet and lifestyle intervention in treating patients with obesity, T2D, hypertension, and CVD	• Spend time with RDs to develop partnerships that are effective in patient counseling and intervention • Self-education through on-line modules and textbooks
Minimal or lack of reimbursement for nutrition and behavior services for medical and allied health care professionals	Familiarize self with proper coding and billing nuances based definitions of nutritional diagnoses
Failure to recognize nutrition experts in the training of medical students and residents	• Develop partnerships with RDs to assist with training and experience • Seek out additional nutrition experts on the national level
Inadequate time in ambulatory setting and lack of confidence to address nutrition issues	• Familiarize self with available patient education material • Develop partnerships with RDs to provide time effective care • Self-education through on-line modules
Inadequate attention to nutrition support of hospitalized patients	Help develop protocols through partnership with RDs and monitor progress through quality improvement modules

Note: Barriers are listed from American Journal of Clinical Nutrition Ref: 'Residency and specialties training in nutrition: a call for action. Carine M Lenders, Darwin D Deen, Bruce Bistrian, Marilyn S Edwards, Douglas L Seidner, M Molly McMahon, Martin Kohlmeier, and Nancy F Krebs'.

558 *ASSOCIATION OF VITAMIN E INTAKE DURING EARLY CHILDHOOD WITH ALANINE AMINOTRANSFERASE LEVELS DURING MID-CHILDHOOD*

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BACKGROUND: Vitamin E supplementation improves the severity of liver disease and reduces alanine aminotransferase (ALT) levels in children with nonalcoholic steatohepatitis (NASH). The extent to which dietary vitamin E intake early in childhood is associated with ALT levels later in childhood is unknown.

OBJECTIVE: To test the hypothesis that lower vitamin E intake during early childhood is associated with higher ALT level during mid-childhood.

METHODS: We prospectively studied 534 children in Project Viva cohort, a pre-birth cohort of mother-child pairs in eastern Massachusetts. Mothers reported child dietary intake at early childhood research visits (median 3.1 years) using a validated food frequency questionnaire. At mid-childhood (median 7.6 years), we collected child blood and anthropometric data. The main outcome was elevated mid-childhood ALT level, defined as ≥25.8 units/liter for males and ≥22.1 units/liter for females. In multivariable logistic regression models, we assessed the relationship of energy-adjusted dietary vitamin E intake in early childhood with ALT levels in mid-childhood, adjusting for child age, sex, race/ethnicity, and BMI z-score.
RESULTS: 48% of children were female, 63% non-Hispanic white, 18% non-Hispanic black, and 4% Hispanic/Latino. In early childhood, median vitamin E intake was 3.6 mg/day (IQR 1.2, range 1.4-9.2). At mid-childhood, median ALT was 19 units/liter (IQR 8, range 8-76) and 22% of children had an elevated ALT level. In multivariable-adjusted logistic regression models, children with the lowest quartile of energy-adjusted vitamin E intake during early childhood had higher odds of elevated mid-childhood ALT (1.78 [1.11,2.87]) compared to those in higher quartiles of vitamin E intake.
CONCLUSIONS: In this cohort, low early childhood dietary intake of vitamin E was associated with elevated ALT level in mid-childhood.

559 *INFANTS FED WITH AN INNOVATIVE NUTRITION SYSTEM MANIFEST HEALTHY GROWTH*

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Purpose: Human milk (HM) composition evolves over the course of lactation presumably to match the changing nutritional needs of developing infants. An innovative infant nutrition system, including a dispenser and single-serve capsules of powdered formulas, was designed to precisely deliver hygienic reconstituted formula of varying composition, analogous to the evolving composition of HM. This study tested the hypothesis that infants fed with the nutrition system grow comparably to the WHO growth standards. Exploratory analysis was also conducted on weight gain pattern in the first year, which has been shown to correlate with obesity risk later in life.
Methods: Healthy term infants ≤14 days of age, whose parents had voluntarily elected exclusive formula feeding, were enrolled in this single-arm study from four hospitals in Switzerland. Over a 12-month period, infants consumed study formulas tailored to infants' nutritional needs at 1, 2, 3-6, and 7-12 months of age. Protein content for example among other differences compared to conventional formula was 2.26, 2.01, 1.88, and 1.86 grams/100kcal in these four formulas, respectively, reflecting the declining protein content in HM. Infants consumed study formulas exclusively until at least age 4 months. Primary outcome was weight-for-age z-score (WAZ) at age 4 months, which was compared to a clinically relevant non-inferiority margin of -0.5 SD (equivalent to a 3 grams/day weight gain difference from age 0-4 months) based on American Academy of Pediatrics recommendations.
Results: Of 33 enrolled infants, 29 completed the 12-month study. Per-protocol analysis (n=30) [preferred over intention-to-treat (n=32) for non-inferiority analysis] showed that mean (95% CI) WAZ at age 4 months was 0.12 (-0.15, 0.39); the lower bound of the 95% CI was above the pre-defined -0.5 cutoff. Similarly, the means (95% CIs) for length-for-age (LAZ), weight-for-length (WLZ), BMI-for-age (BMIAZ) and head circumference-for-age z-scores (HCAZ) at age 4 months were 0.05 (-0.19, 0.30), 0.16 (-0.16, 0.48), 0.11 (-0.20, 0.43), and 0.41 (0.16, 0.65), respectively; the lower bounds of the 95% CIs were all above the -0.5 cutoff. Notably, the changes in WAZ (mean±SD) from birth to 6 months (0.25±1.1) and from birth to 12 months (0.49±1.2) were <0.67 SD. Changes in WAZ >0.67 SD are defined as a clinically significant threshold for rapid weight gain, which has been shown to be associated with an increased risk for later obesity. No safety or gastrointestinal tolerance concerns were noted by study pediatricians.
Conclusion: Infants fed with an innovative nutrition system, which provides well-tolerated formulas with varying nutritional composition similar to changes in HM composition during lactation, grow comparably to the WHO growth standards. Moreover, the findings on WAZ changes suggested a healthy weight gain pattern during the first year of life. Additional studies are needed to investigate potential long-term benefits of consuming formulas with evolving composition vs. conventional formula.

560 *DISTURBED BILE ACID HOMEOSTASIS IN PATIENTS WITH SEVERE MALNUTRITION*

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Background: Severe malnutrition (SM), in the form of marasmus and kwashiorkor, is a major cause of mortality in children under 5 years. SM has been associated with hepatic steatosis, especially in kwashiorkor, suggesting liver dysfunction. Bile acids are synthesized by the liver and play a major role in intestinal lipid absorption. In addition, bile acids can be

hepatotoxic. This study aimed to investigate whether SM was associated with changes in BA homeostasis.
Methods: Upon receiving ethics approval, 40 children (6 months-5 years old) hospitalized for SM were recruited from Queen Elisabeth Central Hospital, Malawi. Both children with edematous malnutrition (kwashiorkor) and wasting (Marasmus) were included. Clinical characteristics were collected throughout the duration of hospital stay. Fecal and blood samples were collected upon admission and close to discharge. Serum and fecal bile acids and serum 7α-hydroxy-4-cholesten-3-one (C4) were quantified using LC-MS. Serum FGF-19 levels were determined using a sandwich ELISA kit.
Results: Serum unconjugated BA were found to be higher at admission 0.30 μmol/L (0.10, 0.70) (median and interquartile range) compared to levels measured at the time of clinical recovery 0.15 (0.04-0.35 μmol/L; P<0.05). Fecal conjugated BA were decreased at admission 21.5 (6.7-174.3 pmol/mg dry stool) compared to recovery 147.8 (17.4-992.2) pmol/mg dry stool (p< 0.05), without any changes in total fecal BA content. Fecal secondary/primary BA ratio was significantly lower at discharge with lower secondary BA while similar primary BA content (p<0.01). Intestinal BA signaling was upregulated during admission and was associated with decreased C4 concentrations, indicating suppressed BA synthesis. There was no significant difference in the BA profile between kwashiorkor and marasmus patients.
Conclusions: SM is associated with increased intestinal BA signaling and suppressed hepatic BA synthesis associated with accumulation of unconjugated BA in the serum. Function of bacteria to produce secondary BA appears to be enhanced in children with SM, potentially contributing to liver toxicity in SM.

Saturday, October 10, 2015

CONCURRENT SESSION 4 - MALABSORPTION

561 *EARLY ENTERAL NUTRITION AND AGRESSIVE FLUID RESUSCITATION ARE ASSOCIATED WITH IMPROVED CLINICAL OUTCOMES IN ACUTE PANCREATITIS*

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Objectives: The management of acute pancreatitis (AP) in children varies given the lack of specific guidelines. We sought to determine whether recommendations extrapolated from the adult literature would impact the outcomes of pediatric AP.
Study design/methods: Recommendations based on adult guidelines regarding early management of AP were implemented through an admission order set at Cincinnati Children's Hospital Medical Center (CCHMC) at the beginning of January 2014. Recommendations included administering high rates of intravenous fluids (IVF) within 24 hours of admission and enteral nutrition (EN) within 48 hours of admission. Nine months after implementing these measures, we performed a retrospective chart review of AP admissions before and after the implementation of "the standard of care" management, specifically between November 30 2009 and September 30, 2014. The treatment groups were the following: NPO (nil per os) for the first 48 hours + IVF low (lo) within 24 hours, NPO for 48 hours + IVF high (hi) within 24 hours, enteral nutrition within 48 hours (PO) + IVF lo within 24 hours and PO within 48 hours + IVF hi within 24 hours. Data analysis for outcomes was conducted. Outcomes studied were: hospital length of stay (LOS), intensive care unit (ICU) transfer rates, development of severe pancreatitis (SAP), pulmonary complications, and readmission rates post discharge from the hospital. Results: Our cohort included 201 patient encounters. The best outcomes occurred in patients who received feeds within the first 48 hours and received greater than maintenance IVF within 24 hours. Those patients had a shorter LOS mean 3.2 days in group PO +IVF hi compared to 7.1 days if they were in the NPO + IVF lo (p <0.001). There were significantly less ICU and SAP rates in the groups that were managed by the standard of care protocol compared to the other groups. ICU admission rate was 20% vs 1% and SAP rates was 35% vs 4.2 % in groups NPO + IVF lo compared to PO + IVF hi respectively (p<0.01). The readmission rate within 72 hours post discharge was not different between the treatment groups. Conclusion: Our data support early EN and early aggressive IVF to improve outcomes of pediatric AP. Future multicenter studies are needed to further our understanding of AP management in this patient population.
Summary of treatment group responses

Response Variable	NPO + IVF lo (a)	NPO + IVF hi (b)	PO + IVF lo (c)	PO + IVF hi (d)	Overall F-test	Significantly different pairs
LOS geometric mean in days (SE)	7.1 (1.01)	5.0 (0.58)	2.8 (0.24)	3.2 (0.22)	<0.001	ad, bd, bc, ab
SAP Rate (SE)	35% (10.7)	17% (6.80)	9.1% (3.88)	4.2% (2.04)	0.0026	ad, bd, ac
ICU Transfer Rate (SE)	20% (8.94)	13% (6.21)	1.8% (1.80)	1.0% (1.04)	0.0043	ad, bd, ac
Re-Admission Rate (SE)	10% (6.71)	3.3% (3.28)	5.5% (3.06)	4.2% (2.04)	0.8384	

NASPGHANPANCREAS PRIZE

562 *TARGETING PANCREATIC CALCINEURIN TO PREVENT POST-ERCP PANCREATITIS*

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Pancreatitis is the most common and burdensome iatrogenic complication after endoscopic retrograde cholangiopancreatography (ERCP). It occurs in children with at least the same frequency as in adults, and despite current preventative approaches, the problem still exists. In recent work, we unraveled for the first time that a fundamental mechanism for post-ERCP pancreatitis (PEP) is the activation of aberrant Ca^{2+} and calcineurin (Cn) pathways through a combination of radiocontrast (RC) exposure to the pancreas and increased intra-pancreatic ductal pressure. However, Cn is expressed in a variety of cells and tissues, and it is unclear which source of Cn is necessary to transduce PEP. We hypothesized that Cn within the pancreatic acinar cell was a central node for PEP and, in this study, we generated acinar cell-specific conditional knockout (CKO) mice by crossing an elastase-Cre-ERT line with mice containing LoxP sites flanking an exon within the critical Cn subunit CnB1. Upon tamoxifen induction at 6-8 weeks of life, PCR confirmed an acinar-specific deletion of CnB1. PEP was induced by briefly infusing RC at high pressure within the pancreatic duct. Compared with littermates without the deletion and relative to sham-operated saline-infused controls, acinar Cn CKOs were more protected against PEP than mice with a global Cn knockout ($CnA\beta^{-/-}$). Surprisingly, a single, brief intra-ductal application of the Cn inhibitors FK506 or cyclosporine A (1-10 μM), along with the RC infusion, protected against PEP more potently than giving multiple systemic doses for 24 hours, and there were no adverse effects with the former. These data demonstrate that acinar cell Cn is necessary for PEP, and they support therapies for PEP that target Cn within the pancreas.

Saturday, October 10, 2015

CONCURRENT SESSION 4 – GUT MICROBIOME

563 *STOOL BILE ACID PROFILES IN PEDIATRIC PATIENTS WHO RECEIVED FMT FOR CLOSTRIDIUM DIFFICILE INFECTION*

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Background: Fecal microbiotal transplant (FMT) is considered a recent triumph for the treatment of *C. difficile* infection (CDI), an antibiotic-associated diarrheal disease. *C. difficile* has both high morbidity and mortality, and conventional antibiotic therapy can fail in up to 30% of cases. FMT has remarkable efficacy and is thought to work by restoration of a healthy microbiome. Recently, bile acids have been found to play an important role in *C. difficile* pathogenesis. Taurocholate, glycocholate and cholate are germinants of *C. difficile* and Chenodeoxycholic acid (CDCA) and secondary bile acids are inhibitors of germination.

Adult studies have shown that FMT can restore a healthy microbiota in patients with CDI. Additionally in adults, FMT is able to restore stool bile acid profiles to resemble that of the donor's, a profile that is unfavorable for *C. difficile* germination.

Pediatric CDI is more complex than adult CDI as many pediatric asymptomatically carry of *C. difficile*. However, recurrent infection can occur along with it associated morbidities. Due to differences in pediatric disease, we examined stool bile acid profiles pediatric patients who received FMT for recurrent CDI.

Methods: Pediatric patients were recruited for an IRB-approved protocol for FMT for recurrent CDI. A healthy screened donor was used as a universal donor. Stools samples were obtained prior to and after FMT. Stool samples from patients with CDI (n=3) as well as the universal donor were sent for global metabolomics. Stool bile acid data was extracted from this data.

Results:

Prior to FMT, pediatric CDI patients had expansion of the primary bile acid cholate, tauro- and glyco- conjugated bile acids, and noticeable lack of secondary bile acids compared to the healthy universal donor, a stool bile acid profile favorable for *C. difficile* germination. This profile was markedly different than that seen in healthy children. After FMT, CDI patients had restoration of the secondary bile acids and depletion of cholate, glyco- and tauro-conjugated bile acids, suggesting functional restoration of the microbiome and its metabolic byproducts post FMT.

Conclusions: Stool bile acids profiles in pediatric recurrent CDI patients show similar characteristics to adult patients with CDI: their profiles are ones that are favorable for *C. difficile* germination. FMT in these pediatric patients results in restoration of bile acid profiles to that of the healthy donor, suggesting FMT creates functional restoration of the microbiome, at least in respect to fecal bile acids.

564 *IMPACT OF TREATMENT ON THE ESOPHAGEAL MICROBIOTA AND BACTERIAL RECEPTOR EXPRESSION IN EOSINOPHILIC ESOPHAGITIS*

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Amir F. Kagalwalla[3], Angelika Zalewski[4], Ikuo Hirano[4], Nirmala Gonsalves[4], Kathryn A. Biette[1], Joanne C. Masterson[1], Steven J. Ackerman[5], Glenn Furuta[1]. [1]Pediatrics Gastroenterology, University of Colorado Denver, Aurora, CO; [2]Pediatrics, University of Colorado Denver, Aurora, CO; [3]Pediatrics, Northwestern University Chicago, Chicago, IL; [4]Gastroenterology and Hepatology, Northwestern University, Chicago, IL; [5]Biochemistry and Molecular Genetics, University of Illinois at Chicago, Chicago, IL

Background: Eosinophilic Esophagitis (EoE) is an allergic disease characterized by upper intestinal symptoms found in association with chronic inflammation and eosinophil infiltration. Few studies have determined the esophageal microbiota in health or disease and those have utilized mucosal biopsies. We have previously reported that the minimally invasive Esophageal String Test (EST), a swallowed Enterotest™ capsule containing a nylon string, can be used to sample the esophageal microbiome in a manner comparable to esophageal biopsies.

Objectives: The overall goal of this study was to identify the esophageal microbiota in EoE and determine whether treatment (proton pump inhibitor, steroid or diet) changes this profile. We hypothesized that clinically relevant alterations in bacterial populations are present with esophageal inflammation in EoE. The approach was to identify the esophageal microbiota in well-defined patients with EoE and determine the impact of treatment on the microbiota and bacterial receptors.

Methods: In this prospective study, ESTs were collected from subjects with EoE, and normal mucosa. Bacterial communities were determined by 16S rRNA gene amplification, 454 pyrosequencing and MiSeq, and compared between health, disease and treatment. ESTs were collected from EoE (n=49) and controls (n=43), half the subjects in both groups were treated with proton pump inhibitor (PPI). All subjects had upper intestinal symptoms with further diagnostic criteria including EoE $\geq$ 15 eos / high power field (HPF) and other causes excluded; and normal esophageal mucosa. To determine the impact of treatment on bacterial receptor expression, human esophageal epithelial cells (EPC2-hTERT) were stimulated with the proton pump inhibitor Omeprazole (50μM) or Fluticasone propionate (1μM) in the presence of a Th2 (IL-13 and IL-5) and Gram - (LPS) micromilieu. Bacterial receptor expression was determined by western blot.

Results: *Haemophilus* was present in all subjects independent of diagnosis; however subjects on PPI (n=42) had a 50% increase in *Haemophilus* relative abundance compared to untreated subjects (n=15) $p<0.01$. *Haemophilus* relative abundance was slightly decreased by 25% in subjects treated with steroids (n=23) compared to untreated (n=15). No significant differences in bacterial genera (with a relative abundance >1%) were observed between the microbiota on biopsies and matching ESTs in EoE subjects (n=7). Expression of the bacterial receptor for *Haemophilus,* ICAM-1, was increased by PPI treatment and decreased by steroid treatment in esophageal epithelial cells.

Conclusions: The microbiota is altered in EoE from that found in the normal mucosa. Moreover, the bacterial composition and bacterial receptor expression in the esophageal epithelium is altered by treatment.

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Saturday, October 10, 2015

CONCURRENT SESSION 4 – NEUROGASTROENTEROLOGY AND MOTILITY

NASPGHAN MOTILITY PRIZE - BASIC

565 *IBUPROFEN SLOWS MIGRATION OF ENTERIC NERVOUS SYSTEM PRECURSOR CELLS INCREASING THE RISK OF HIRSCHSPRUNG-LIKE DISEASE IN ANIMAL MODELS*

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Background: Intestinal motility disorders are common and debilitating, but disease mechanisms remain poorly understood. Among the best understood motility disorders is Hirschsprung disease, a problem where the enteric nervous system (ENS) is completely missing from the distal bowel. Hirschsprung disease is generally considered to be a genetic disorder, but inheritance is non-Mendelian, multigenic, and partially penetrant. Because of the complex cellular and biochemical pathways needed to form the ENS, we hypothesized that some specific maternal medicines might affect ENS development or alter Hirschsprung disease risk.

Methods: We used zebrafish to test the effect on ENS development of medicines used by more than 0.5% of women during early pregnancy. Fish were treated during the period of bowel colonization by ENS precursors and then stained to visualize enteric neurons. Additional studies tested ibuprofen in developing chick colon organ culture, WT and mutant pregnant

mice, fetal mouse gut slice culture and dissociated cell culture. After drug treatment, the effect on the developing ENS was determined using immunohistochemistry and quantitative analysis methods.
Results: Ibuprofen slowed mouse ENS precursor migration *in vitro*, reduced bowel colonization by ENS precursors in fish and in *Ret+/-* mice *in vivo*, and dramatically reduced bowel colonization by ENS precursors in chick gut organ culture. Doses of ibuprofen needed to reduce the migration of ENS precursors can be achieved with one to three over the counter tablets. Ibuprofen also reduced ENS precursor neurite growth *in vitro*, reduced lamellipodia formation in migrating ENS precursors, and reduced RAC1/CDC42 activation. Interestingly ibuprofen did not affect migration of NIH3T3 cells or fetal mouse gut mesenchymal cells, suggesting special sensitivity of the developing ENS to ibuprofen. Current data suggest that ibuprofen effects are not due to COX inhibition, and *in vivo* effects vary markedly in different species.
Conclusions: Ibuprofen slows migration of ENS precursors *in vitro* and slows colonization of fetal bowel by ENS precursors in zebrafish, mice and chick. These data raise concern that ibuprofen use during early pregnancy may increase Hirschsprung disease risk in genetically susceptible individuals. Together with prior work suggesting that vitamin A deficiency and some other medicines may increase Hirscshsprung disease risk, these data suggest that human epidemiologic studies are now appropriate to identify potentially preventable causes of Hirschsprung disease.

NASPGHAN MOTILITY PRIZE - CLINICAL

566 *PARENT-ONLY INTERVENTION REDUCES SYMPTOMS AND DISABILITY IN ABDOMINAL PAIN PATIENTS*
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Background and Purpose: Abdominal pain is the most common recurrent pain complaint of childhood. Medical evaluations rarely yield evidence of an organic disease etiology, resulting in a diagnosis of functional abdominal pain. It is associated with considerable disruption of normal activity, including school attendance, and emotional distress in both children and parents. It also has a significant impact on health-care costs, accounting for more than 50 % of visits to pediatric gastroenterology practices. Previous research by our group and others has shown that the ways parents think about and respond to their child's pain are associated with the severity and impact of abdominal pain in children. Thus, the purpose of the present study was to investigate whether an intervention targeting parental cognitions and responses would reduce the level of symptoms and disability in children with abdominal pain of functional origin. Additionally, we sought to determine if this intervention could be effectively delivered remotely to parents via the telephone. Methods: Parents of 312 children ages 7-12 years old with a physician diagnosis of abdominal pain of functional origin, verified by Rome III criteria, were randomly assigned to one of three conditions: 1) in person CBT for 3 sessions; 2) telephone delivered, remote CBT (CBT-R) for 3 sessions and 3) a telephone delivered attention placebo condition (Education Support/ES). Children and parents completed the Child Symptom Inventory (CSI) to obtain GI symptom before and immediately following treatment, as well as 3 and 6 months post treatment. Parents also completed health care and school attendance questionnaires at the same time points. Results: Participating parents were 96% female, 84.6% Caucasian, and their mean age was 40.3 years. Treatment groups were compared on reduction in symptoms from baseline through six month follow-up with linear mixed models adjusting for mean changes from baseline. Parents in the CBT-R treatment reported significantly reduced child symptoms on the CSI compared to the ES group ($p < .05$). Log-linear regressions showed that CBT and CBT-R groups differed significantly from the ES group in reducing health care visits for abdominal pain($p<.05$) and the CBT-R group also showed a significant reduction in missed school days for abdominal pain over the ES group ($p<.05$). Conclusion: A very brief telephone intervention delivered to parents alone reduced reported symptoms, as well as both health care utilization and children's disability, as measured by missed school days, in children with abdominal pain of functional origin. This low cost intervention should be considered as a useful addition to the clinical treatment of these children.

Saturday, October 10, 2015

CONCURRENT SESSION 5 – INFLAMMATORY BOWEL DISEASE

567 *GENETIC VARIATION IN VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE*
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Background: Inflammatory bowel disease (IBD) is a chronic inflammatory gastrointestinal disorder. Genome-wide association studies (GWAS) have identified 163 single nucleotide polymorphisms (SNPs) associated with adult IBD risk and many play a role in adolescent-onset IBD. Very early onset IBD (VEO-IBD) is a unique IBD subset that is diagnosed in the first 6 years of life and whose incidence is rising quickly. Some of these cases are ultimately diagnosed as a well-defined primary immunodeficiency. Select VEO-IBD cases have been redefined as Mendelian IBD due to loss of function genetic mutations (e.g. *IL-10RA, XIAP*). We hypothesized that VEO-IBD pathophysiology is driven by a combination of high burden of common IBD risk SNPs and rare gene variation especially in immune-mediated genes.

Methods: DNA samples were obtained from VEO-IBD patients (who were diagnosed in the first 6 years of life) and their parents when available. Probands were genotyped for 163 IBD risk SNPs on the Immunochip. A genetic risk score (GRS) was calculated by assigning a weight to each SNP based on the overall IBD odds ratio from GWAS meta-analyses. The GRS distribution was compared to GRS of cohorts of adult-onset Crohn's disease (CD) and ulcerative colitis (UC) and healthy adult controls seen at Massachusetts General Hospital. Whole exome sequencing was performed on probands and parents. Whole Exome SureSelect kit was used and sequencing was performed on Illumina HiSeq. Sequences were processed by Picard pipeline and aligned with GRCh37, h19. Variant calling was performed using the GATK toolkit. Variants were filtered for a minor allele frequency (MAF) <0.5% in the Exome Aggregation Cohort (ExAC) controls for individual analysis. The cumulative rate (per individual gene) of essential splice site, frameshift, and missense variants (predicted to affect gene function by PolyPhen-2) in 50 genes implicated in VEO-IBD as well as the 163 genes implicated by IBD GWAS was compared to ExAC healthy controls by Fisher's exact test. The Partners Healthcare IRB approved this study.

Results: The cohort included 95 probands (36 with UC, 35 with CD, 24 with IBD-U) including 46 full proband-parent trios. Average age of IBD onset was 2.6 years (IQR 1.3-4). The genetic risk burden of common IBD SNPs in VEO-IBD was slightly lower than adult-onset CD($p=0.02$) and similar to adult-onset UC (0.2) but substantially higher than healthy adult controls ($p=1x10^{-7}$). Top individual candidate variants associated with VEO-IBD (as compared to healthy controls) were found in *IL6ST* (rs146226365, p=0.000163), *CD48* (rs150735389, p=0.000836), and *DOCK8* (rs200899164, p=0.001757). Rare variants in *NFIL3* were slightly increased in VEO-IBD subjects compared to controls (2.1% vs. 0.4%, p=0.049).

Conclusions: Common adult IBD risk SNPs play a similar role in VEO-IBD. The earlier presentation cannot be explained by an increased burden of common IBD risk SNPs. Rare genetic variants appear to play an evolving role in VEO-IBD.

Saturday, October 10, 2015

CONCURRENT SESSION 5 – LIVER

568 *MICRORNA-181 PROMOTES GRAFT PROLONGATION BY PLASMACYTOID DENDRITIC CELLS BY INCREASING T REGULATORY CELLS AND DECREASING B CELLS AS REVEALED BY MASS CYTOMETRY (CYTOF)*

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Liver allografts are well tolerated and other solid organ allografts, when transplanted concurrently with livers, show improved outcomes. However, the mechanisms underlying "hepatic tolerance" have yet to be elucidated. Previous data show that hepatic dendritic cells (DC) have diminished antigen presentation and immune stimulatory function compared with DC in lymphoid tissue. Immature plasmacytoid (p) DC have been shown to induce graft prolongation and we have previously shown miR-181a1b1 is increased in pDC as compared to conventional DC. Wild-type (WT) BALB/c mice were transplanted with allogeneic (C57BL/6) vascularized heterotopic heart grafts. Animals received either no treatment (n=3) or were injected i.v. with 0.5×10^6 hepatic pDC (n=5) or miR-181a1b1$^{-/-}$ (KO) pDC (n=3) at day (D)−7 from transplant. Recipients with no treatment rejected their allograft by D7 while recipients pre-treated with hepatic pDC had significantly prolonged allograft survival to D15-21 ($p<0.01$). However, recipients pre-treated with hepatic KO pDC rejected their allografts by D7-9. To determine the mechanism of graft prolongation, splenocytes were obtained at D7 and cytometry by time-of-flight (CyTOF, mass cytometry) was utilized to comprehensively characterize the immune response post-transplant. Correlation analyses of molecular features derived from mass cytometry data were performed using Citrus, a method for unsupervised identification of significant cellular populations. Cells were clustered on the basis of the expression of 17 surface and three intracellular markers with significant changes in cell frequency inferred with the "glmnet" package in R that fits a generalized linear model via penalized maximum likelihood. B cells were elevated in the rejecting mir-181a1b1$^{-/-}$ group, while CD4$^+$ T regulatory cells were elevated in the group that received WT pDC and had prolonged graft survival. Further analysis of B cell subsets by flow cytometry revealed a significant increase in marginal zone B cells and plasmablasts in the absence of miR181 as compared to WT. These data demonstrate that CyTOF is a powerful new technology to identify immune cell populations post-transplant. Our findings that graft prolongation by miR-181-expressing pDC is associated with a decreased in B cells and an increase in Treg cells.

*569 *PROSPECTIVE ANALYSIS OF PRESENTING FEATURES OF NEONATAL CHOLESTASIS - LIMITATIONS IN PREDICTIVE MODELS OF BILIARY ATRESIA*

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Introduction: Optimizing outcomes in biliary atresia (BA) requires timely diagnosis. Cholestasis is a presenting feature of BA as well as other diagnoses (nonBA). Identification of clinical features of neonatal cholestasis that would expedite decisions to pursue subsequent invasive testing to correctly diagnose BA would enhance patient outcomes. The goal of this analysis was to develop a predictive model for BA using data available at initial presentation.

Methods: Infants at presentation with neonatal cholestasis (direct/conjugated bilirubin > 2 mg/dl) were enrolled prior to surgical exploration in a prospective observational study (PROBE - NCT00061828). Clinical features (physical findings, laboratory results and gallbladder sonography) at enrollment ("presentation") were analyzed. BA was defined by cholangiographic and surgical findings at laparotomy with confirmatory bile duct remnant pathology. NonBA required an alternative specific diagnosis or a total bilirubin $\leq$ 1.0 mg/dl at $\geq$ 120 days of age for those infants with idiopathic neonatal hepatitis (INH) or idiopathic cholestasis (IC). Initially, 19 clinical features were selected as candidate predictors. Two approaches were used to build models for diagnosis prediction, including a classification and regression decision tree (CART) and a logistic regression model using a stepwise selection strategy. For the latter, we have explored potential nonlinearity functional forms in continuous predictors and interaction terms to develop the best prediction model.

Results: In PROBE between April 2004 and February 2014, 428 infants met criteria for BA and 309 met criteria for nonBA (A1AT 37, Alagille 31, CMV 11, PFIC 6, CF 6, choledochal cyst 5, bile acid synthesis defect 4, other 67, INH 64, IC 78). Univariate analysis identified 11 features of BA and nonBA that were significantly different. Using CART for a predictive model of BA vs nonBA (significant factors - acholic stools, wt z-score, facial features, palpable liver span, gGTP and albumin), the ROC AUC was 0.83. 14% of BA infants were misclassified as nonBA, while 25% of nonBA infants were misclassified as BA. Stepwise logistic regression identified 7 factors (gender, acholic stools, facial features, ALT, alkaline phosphatase, gGTP and sonographic gallbladder absence) in a predictive model with an ROC AUC of 0.87. Using this model, a predicted probability of >0.8 (n=245) yielded a 90% true positive rate for BA (i.e. 24 cases of nonBA) while <0.2 (n= 118) yielded a 7% false negative rate (i.e. 8 cases of BA).

Conclusion: Despite the relatively good accuracy of our optimized prediction models, the high precision required for differentiating BA from nonBA was not achieved. Accurate identification of BA in infants with neonatal cholestasis requires further evaluation and BA should not be excluded based only on presenting clinical features.

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Saturday, October 10, 2015

CONCURRENT SESSION 5 – UPPER GI TRACT

570 *CLAUDIN-7 DYSREGULATION IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS: A ROLE FOR TGF-β1 IN ESOPHAGEAL EPITHELIAL BARRIER DYSFUNCTION*

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Background: Altered barrier function has recently been implicated in the pathophysiology of eosinophilic esophagitis (EoE). Transforming growth factor beta (TGF-β1), a potent pleiotropic growth factor and cytokine involved in fibrosis and remodeling, is increased in EoE, but its role in esophageal barrier function is not certain. We hypothesized that TGF-β1 leads to esophageal epithelial barrier dysfunction. The purpose of this study was to determine mechanism(s) by which TGF-

β1 alters epithelial barrier.
Methods: To examine the impact of TGF-β1 on esophageal epithelial barrier, we used a 3-dimensional air-liquid interface model (3D-ALI) that induces stratification and differentiation of epithelial cells *in vitro*. Non-transformed immortalized human esophageal epithelial cells (EPC2-hTERT) were exposed to rhTGF-β1 (5-10 ng/mL) during the 3D-ALI process of differentiation and stratification. Functional assays of barrier were performed using transepithelial electrical resistance (TEER) and 3kDa FITC-dextran paracellular flux (FITC-Flux). Epithelial barrier (occludin, claudin-1, -4, -7, E-cadherin, ZO-1, desmoglein-1, -2, and -3) molecule expression was analyzed using real time RT-PCR. Selected molecules were then evaluated in human esophageal biopsies from control and pediatric EoE subjects. Claudin-7 (CLDN7) stable knockdown cells were generated by lentiviral delivery of sh-RNA interfering constructs. Knockdown was verified by western blot and RT-PCR, and these cells were then subjected to assessments of barrier function *in vitro*.
Results: TGF-β1 exposure throughout 3D-ALI-induced epithelial differentiation and stratification resulted in barrier dysfunction with 40% decreased TEER ($p<0.05$) and 1.8-fold increased FITC-Flux ($p<0.05$). TGF-β1 significantly attenuated CLDN7 mRNA expression in an establishing epithelial barrier (55% decrease; $p<0.01$) compared to unstimulated control cells. TGF-β1 also significantly attenuated claudin-7 protein expression in EPC2-cells (77% decrease $p<0.05$, TGF-β1 5ng/ml; 72% decrease; $p<0.05$, TGF-β1 10ng/ml) compared to unstimulated control cells. Furthermore, knockdown of CLDN7 in esophageal epithelial cells resulted in barrier dysfunction with 37% decreased TEER and 1.6-fold increased FITC-Flux compared to sh-control cells. Finally, CLDN7 expression was also significantly decreased in human esophageal biopsy specimens from EoE subjects with active disease compared to those with inactive EoE (68.7% decrease; $p<0.05$) and control subjects (69.6% decrease; $p<0.01$).
Summary: TGF-β1 contributed to esophageal barrier dysfunction, inhibiting the establishment of a stratified and differentiated epithelial barrier. TGF-β1 exposure attenuated the expression of the tight junction molecule claudin-7, whose expression is also dysregulated in active EoE subjects.
Conclusion: TGF-β1 plays a role in esophageal epithelial barrier dysfunction at least in part, through claudin-7 dysregulation. We anticipate that further investigations will permit identification of TGF-β1 and claudin-7's mechanisms in inducing barrier dysfunction in EoE.

571 *NON-INVASIVE MONITORING OF INTESTINAL PERMEABILITY AND INFLAMMATION IN A PROSPECTIVE SEROLOGICAL DIAGNOSIS STUDY OF PEDIATRIC CELIAC DISEASE*

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Introduction: In 2012, the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) endorsed a serological diagnostic (SD) approach for pediatric celiac disease. This study applied modified ESPGHAN diagnostic criteria in a prospective manner and non-invasively monitored mucosal healing: using gastro-intestinal permeability and fecal calprotectin, at diagnosis and one year on a gluten-free diet (GFD). We hypothesized that symptom improvement, dietary adherence and mucosal recovery would not be impacted by SD vs endoscopic biopsy diagnosis (ED).
Methods: At the Stollery Children's Hospital Multidisciplinary Celiac Clinic, SD was offered if patients had an anti-tissue transglutaminase (aTTG) level ≥200 U/ml, provided confirmatory repeat aTTG and at-risk HLA haplotypes. Patients with aTTG <200 U/ml had ED. In both CD diagnostic groups and in healthy controls gastrointestinal permeability was assessed using sugar probe tests containing lactulose, mannitol and sucrose. Mucosal inflammation was assessed using fecal calprotectin (FC), comparing to a laboratory normal cut-off value of ≤50 ug/g of stool. Statistical analysis used Kruskal-Wallis one-way analysis of variance (significance set as 0.05). Data shown in Table 1 is presented as medians and range.
Results: 117/170 (69%) patients were recruited: 42 SD, 50 ED. 26 healthy children were recruited as controls for gastrointestinal permeability testing. As expected, aTTG was significantly higher in SD compared to ED ($p<0.001$). Lactulose:mannitol ratio (L/M), fractional excretion of sucrose (FESucrose) and FC were all elevated at diagnosis in CD patients (n=67) compared to controls ($p<0.05$) and in SD vs controls ($p<0.005$). In the ED group, L/M was elevated vs controls ($p<0.001$), but FC and FESucrose were not different vs controls ($p>0.05$). L/M and FC were significantly higher in SD compared to ED at diagnosis ($p<0.05$). At one year follow up, SD (n=33) and ED (n=43) reported equal symptom improvement (100% vs 92%; $p>0.05$) and GFD adherence (94% vs 93%; $p>0.05$). There were no significant differences in L/M, FESucrose or FC between all CD patients and controls, nor between SD and controls ($p>0.05$). In the ED group, L/M remained significantly higher than controls ($p=0.049$), while FESucrose and FC were not different ($p>0.05$).
Conclusion: A serological diagnostic approach had no adverse impact on symptom improvement or dietary adherence. All CD patients had mucosal disease at diagnosis evidenced by altered permeability and inflammation. After one year on a GFD, all CD patients showed improved intestinal permeability and inflammation, regardless of diagnostic strategy. Specifically tailored to our local population, this is the first prospective study that supports serological diagnosis for pediatric CD in North America.
Table 1.

		N (SD;ED)	Serological Diagnosis (SD)	Biopsy Diagnosis (ED)	Control
aTTG (U/ml)	Baseline	46;45	595 (200-4100)	29 (7.8-190)	≤7.0
	12 months	36;36	11.5 (1.0-98.0)	2.95 (1-420)	
Lactulose:Mannitol	Baseline	42;25	0.049 (0.022-0.292)	0.033 (0.011-0.155)	0.022 (0.010-0.072)
	12 months	37;16	0.022 (0.012-0.317)	0.025 (0.011-0.042)	
% Fractional Excretion of Sucrose	Baseline	42;25	0.086 (0.011-0.448)	0.061 (0.003-0.270)	0.045 (0.010-0.530)
	12 months	37;16	0.039 (0-0.259)	0.046 (0-0.878)	
FC Calprotectin (ug/g)	Baseline	41;26	81.6 (6.0-3068.1)	50.0 (4.9-1755.4)	≤50
	12 months	32;16	37.1 (5.7-736.5)	13.0 (1.1-418.2)	