

27th ANNUAL NASPGHAN-MEAD JOHNSON RESEARCH FORUM FOR PEDIATRIC GASTROENTEROLOGISTS March 19-22, 2009

The NASPGHAN-Mead Johnson Research Forum for Pediatric Gastroenterologists is the final in a series of annual conferences designed to contribute to career development of subspecialty residents in pediatric gastroenterology, hepatology and nutrition. The three goals for the conference are to:

- ◆ Provide a forum for presentation of research abstracts by subspecialty residents that encourages constructive feedback and analysis by a team of experienced researchers;
 - ◆ Instruct, coach and mentor the attendees in academic career development by didactic presentation and individual interaction with faculty;
 - ◆ Facilitate intellectual and social interchange among all attendees.
-



NASPGHAN MISSION:

The mission of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition is to *advance* understanding of normal development, physiology and pathophysiology of diseases of the gastrointestinal tract and liver in children, *improve* quality of care by fostering the dissemination of this knowledge through scientific meetings, professional and public education, and policy development, and *serve* as an effective voice for members and the profession.



CDHNF MISSION:

- ◆ To fund and promote research and educational programs that will advance the creation, application, and dissemination of knowledge of gastrointestinal, hepatobiliary, pancreatic and nutritional disorders in children.
- ◆ To identify, encourage, support, and coordinate scientific research and professional study of these pediatric disorders.
- ◆ To strengthen the role of pediatric gastrointestinal and nutritional scientists as leaders in research and education in these medical and health care fields.
- ◆ To evaluate and improve the quality and availability of medical care for children with digestive disorders.
- ◆ To support the research and educational programs of NASPGHAN.

FACULTY

Course Director:

Brent Polk, MD

Dean's Professor of Pediatrics and Cell & Developmental Biology
Chief, Pediatric Gastroenterology, Hepatology & Nutrition
Director, Digestive Disease Research Center of Vanderbilt University & Children's Hospital
Vanderbilt University
Nashville, TN

Faculty:

David Gremse, MD, FAAP, FACG

Professor and Chair of Pediatrics
University of Nevada School of Medicine
Las Vegas, NV

Cara Mack, MD

Associate Professor of Pediatrics
Section of Pediatric Gastroenterology, Hepatology and Nutrition, The Children's Hospital
University of Colorado Denver School of Medicine
Aurora, CO

Judith Podskalny, PhD

Director, Research Fellowship & Career Development and Digestive Disease Centers Programs
Division of Digestive Diseases and Nutrition, NIDDK
Bethesda, MD

Elyanne M. Ratcliffe, MD, FRCPC

Assistant Professor of Pediatrics
Division of Gastroenterology and Nutrition
McMaster University
Hamilton, Ontario

David Rudnick, MD, PhD

Assistant Professor of Pediatrics and Developmental Biology
Washington University School of Medicine
St. Louis, MO 63110

Margaret Stallings

Executive Director
NASPGHAN/CDHNF
Flourtown, PA

Attendees

Orhan Atay, MD
Cleveland Clinic Foundation
Pediatric Gastroenterology, A111
9500 Euclid Avenue
Cleveland, OH 44195
atayo@ccf.org

Chad Best, MD
U of MN Children's Hospital, MMC 185
Dept of Ped Gastroenterology
420 Delaware Street SE
Minneapolis, MN 55455
bestx051@umn.edu

Gilberto Bultron, MD
Yale University Dept of Pediatrics
FMP 408
333 Cedar Street
New Haven, CT 06520
Gilberto.Bultron@yale.edu

Megan Butler, MD
Univ of Miami School of Medicine
1601 NW 12th Ave. (D-820)
Mailman Ctr Rm 3005A
Miami, FL 33136
mbutler@med.miami.edu

Ninfa Candela, MD
North Shore-LIJ Health Systems
Schneider Childrens Hospital #234
269-01 76th Ave.
New Hyde Park, NY 11040
ncandela47@hotmail.com

Rebecca Cherry, MD
Children's Hospital Los Angeles
Div of GI
4650 Sunset Blvd. Mailstop #78
Los Angeles, CA 90027
rcherry@chla.usc.edu

Jason Dranove, MD
Riley Hospital for Children
702 Barnhill Drive
Room ROC 4210
Indianapolis, IN 46202
jdranove@iupui.edu

David Dunkin, MD
Mt. Sinai Med Center
Div of of Ped GI
One Gustave Levy Place, Box 1656
New York, NY 10029-6504
david.dunkin@mssm.edu

Kristin Fiorino, MD
Children's Hospital of Philadelphia
Division of GI and Nutrition
34th & Civic Center Blvd
Philadelphia, PA 19104
fiorino@email.chop.edu

Joel Friedlander, DO, MBe
Children's Hospital of Philadelphia
Division of GI & Nutrition
34th & Civic Ctr Blvd.
Philadelphia, PA 19104
friedlander@email.chop.edu

Orlee Guttman, MD
University of Toronto
Hosp for Sick Children/Div GI & Nutrition
555 University Ave
Toronto, ON M5G 1X8
orlee.guttman@sickkids.ca

Ryan W Himes, MD
Texas Children's Hospital
Ped GI and Nutrtrition
6621 Fannin St, MC 10.10
Houston, TX 77030-3608
rwhimes@texaschildrenshospital.org

Leonardo R Hormaza, MD
University of Chicago
5839 S. Maryland Avenue
MD 4065
Chicago, IL 60637
lhormaza@peds.bsd.uchicago.edu

Seamus Hussey, MD
The Hospital for Sick Children
Div GI and Nutrition
555 University Ave.
Toronto, ON M5G 1X8
seamus.hussey@sickkids.ca

Ajay Kumar Jain, MD
Texas Children's Hospital
Ped GI & Nutrition
6621 Fannin St, MC CC101000
Houston, TX 77030-2399
akjain@bcm.edu

Folashade Jose, MD
UCSF
Div of Ped GI, Hepatology & Nutrition
500 Parnassus Avenue, MU4E
San Francisco, CA 94143-0136
josef@peds.ucsf.edu

Judith Kelsen, MD
Children's Hospital of Philadelphia
Division of GI and Nutrition
34th & Civic Center Blvd
Philadelphia, PA 19104
kelsen@email.chop.edu

Kyle Kusek, MD
Nationwide Children's Hospital
Div of GI
700 Children's Drive
Columbus, OH 43205-2696
KusekK@chi.osu.edu

Daniel Leung, MD
Children's Hospital of Philadelphia
Division of GI and Nutrition
34th & Civic Ctr Blvd
Philadelphia, PA 19104
leungd@email.chop.edu

Ying Lu, MD
Children's Hospital, Boston
300 Longwood Avenue
GI Cell Biology, Enders 720
Boston, MA 02115
yinglet@yahoo.com

Louai Manini, MD
Mayo School of Graduate Medical Education
Pediatric Gastro & Hepatology
Mayo Clinic East 19B, 200 First Street SW
Rochester, MN 55905
Manini.MhdLouai@mayo.edu

Tejas Mehta, MD
Emory Univ School of Medicine
Ped GI & Nutrition
2015 Uppergate Drive, NE
Atlanta, GA 30322
tejas_mehta@oz.ped.emory.edu

Katrina Nguyen, MD
Children's Hospital at Downstate
Ped Gastro, Hepatology & Nutrition
445 Lenox Road, Box 49
Brooklyn, NY 11203-2098
mdkatrina@earthlink.net

Paulina Ordonez, MD
UCSD Medical Center
U of California San Diego
200 West Arbor Drive
San Diego, CA 92103-8450
mordonez@chsd.org

Sujal Rangwalla, DO
University of Michigan
Department of Pediatrics/Communicable
Diseases
1500 E. Med Ctr. Dr, D5200 MPB
Ann Arbor, MI 48109-0718
sujal@med.umich.edu

Melanie Rhue, MD
Cincinnati Children's Hosp Med Center
Ped GI, Hep & Nutrition
3333 Burnet Avenue, MLC 2010
Cincinnati, OH 45229-3039
melanie.rhue@cchmc.org

Michael J Rosen, MD
Vanderbilt Children's Hospital, DOT
2200 Children's Way, Room 9112
Nashville, TN 37232-9175
michael.rosen@Vanderbilt.Edu

Nasim Sabery, MD
Children's Hospital, Boston
300 Longwood Avenue
GI Cell Biology, Edners 720
Boston, MA 02115
nasim.sabery@childrens.harvard.edu

Shaista Safder, MD
Case Western Reserve University/University
Hospitals of Cleveland
111000 Euclid Avenue
Cleveland, OH 44106
shasandmanju@yahoo.com

Charles Samson, MD
Cincinnati Children's Hospital Med Centre
Ped Gastro/Hep/Nutrition
3333 Burnet Avenue, MLC 2010
Cincinnati, OH 45229-3039
charles.samson@cchmc.org

Meghana Sathe, MD
Southwestern Med Ctr/Children's Medical
Center
Dept of Pediatrics
1935 Medical District Drive
Dallas, TX 75235
meghana.sathe@childrens.com

Wael Sayej, MD
Women & Children's Hospital of Buffalo
Digestive Diseases & Nutrition Center
219 Bryant Street
Buffalo, NY 14222
wsayejmd@yahoo.com

Marc Schaefer, MD
Brown Sch of Medicine-Hasbro Children's
Hospital
Ped Gastro, Nutrition & Liver Diseases
593 Eddy Street MPH-131
Providence, RI 02903
mschaefer1@lifespan.org

Mary Sherlock, MD
University of Toronto/Hospital for Sick Children
Div GI/Nutr
555 University Ave
Toronto, ON M5G 1X8
mary.sherlock@sickkids.ca

Catharine Walsh, MD
University of Toronto
Hospital for Sick Children/Div of GI &
Nutrition
555 University Ave.
Toronto, ON M5G 1X8
catharine.walsh@utoronto.ca

Samantha Woodruff, MD
The Children's Hospital, B290
13123 East 16th Avenue
Aurora, CO 80045
woodruff.samantha@tchden.org

Matthew Wyneski, MD
Cleveland Clinic Foundation
Pediatric Gastroenterology, A111
Cleveland, OH 44195
mwyneski@neuoucom.edu

Desale Yacob, MD
Nationwide Children's Hospital/Ohio State
University
Div of Gastroenterology
700 Children's Dr
Columbus, OH 43205-2696
YacobD@chi.osu.edu

Thursday, March 19, 2009

5:30 P RECEPTION

6:00 P WELCOME, ORIENTATION and INTRODUCTIONS

BEGINNING THE FIRST JOB IN YOUR CAREER

MODERATOR: Brent Polk

6:15 P FACULTY PRESENTATION: **David Rudnick**
Thinking about your career strategically

6:35 P PANEL DISCUSSION: *Making the transition from fellowship to your first job*
PANELISTS: **David Gremse, Cara Mack, Judy Podskalny, Elyanne Ratcliffe, and David Rudnick**

ABSTRACT SESSION I
MODERATOR: Brent Polk

6:45 P **Samantha A Woodruff**
ESOPHAGEAL FIBROSIS IS INCREASED IN CHILDREN WITH EoE
Reviewer: Ying Lu

7:00 P **Kim Doan Katrina Nguyen**
EFFECT OF EOSINOPHIL GRANULE PROTEINS ON p27 EXPRESSION IN ESOPHAGEAL EPITHELIAL CELLS
Reviewer: LR Hormaza

7:15 P **David Dunkin**
THE EFFECT OF THE ROUTE OF SENSITIZATION IN THE INDUCTION OF A COW'S MILK ALLERGIC RESPONSE
Reviewer: Mary Sherlock

7:30 P DINNER

Friday, March 20, 2009

7:00 A CONTINENTAL BREAKFAST

ABSTRACT SESSION II
MODERATOR: **David Rudnick**

- 8:00 A **Catharine M Walsh**
GASTROINTESTINAL ENDOSCOPY SIMULATION TRAINING: WHAT TYPE OF FEEDBACK IS MOST EFFECTIVE?
Reviewer: Folashade Jose
- 8:15 A **Tejas Mehta**
INCREASED PREVALENCE OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) AND ITS COMPLICATIONS IN HOSPITALIZED U.S. CHILDREN
Reviewer: Matthew J Wyneski
- 8:30 A **Gilberto Bultron**
SEVERE PAINLESS GASTROINTESTINAL BLEEDING: AN UNUSUAL PRESENTATION OF HELICOBACTER PYLORI ASSOCIATED DUODENAL ULCER ON CHILDREN OF SOUTHEAST ASIAN ORIGIN
Reviewer: Kyle Kusek
- 8:45 A **Kristin Fiorino**
EVALUATION OF THE RELATIONSHIP BETWEEN UPPER AIRWAY DISEASE AND GASTROESOPHAGEAL REFLUX DISEASE USING DIAGNOSTIC TESTING
Reviewer: JR Kelsen
- 9:00 A **Mhd Louai Manini**
FEASIBILITY AND APPLICATION OF 3-DIMENSIONAL ULTRASOUND FOR MEASUREMENT OF GASTRIC VOLUMES IN HEALTHY ADULTS AND ADOLESCENTS
Reviewer: Ninfa Candela
- 9:15 A BREAK
- 9:30 A **Shaista Safder**
POSTURAL TACHYCARDIA SYNDROME (POTS) AND FUNCTIONAL GASTROINTESTINAL DISORDERS (FGID): A ROLE FOR ALTERED ELECTRICAL ACTIVITY OF THE STOMACH?
Reviewer: Orhan Atay
- 9:45 A **Jason Dranove**
THE EFFECT OF ERYTHROMYCIN ON THE COLONIC MOTILITY OF CHILDREN AND YOUNG ADULTS DURING COLONIC MANOMETRY
Reviewer: Sujal Rangwalla

- 10:00 A **Desale Yacob**
RESPIRATORY FAILURE, COMPARTMENT SYNDROME, COLONIC PERFORATION AND COLECTOMY: CONSTIPATION TO THE HIGHEST DEGREE
Reviewer: Charles Samson
- 10:15 A **Chad Best**
A PRE-POST RETROSPECTIVE STUDY OF PATIENTS WITH CYSTIC FIBROSIS AND GASTROSTOMY TUBES
Reviewer: Michael J Rosen
- 10:30 A **Wael N Sayej**
BIOMARKERS IN CHILDREN WITH NON-ALCOHOLIC STEATOHEPATITIS
Reviewer: Seamus Hussey
- 10:45 A BREAK

ABSTRACT SESSION III
MODERATOR: Elyanne Ratcliffe

- 11:00 A **Nasim Sabery**
LONG TERM EFFECTS OF VITAMIN SUPPLEMENTATION OF HIV-INFECTED MOTHERS ON CHILDHOOD MORBIDITY AND MORTALITY IN TANZANIA
Reviewer: Joel Friedlander
- 11:15A **Megan Butler**
ASSOCIATION OF VITAMIN D RECEPTOR (VDR) IN PARKINSON DISEASE: A GENETIC RISK FACTOR FOR NEURODEGENERATION
Reviewer: Meghana Sathe
- 11:30 A **Ajay Kumar Jain**
ROLE OF CHENOXYCHOLIC ACID (CDCA), FXR (FARNESOID X RECEPTOR) AND FIBROBLAST GROWTH FACTOR 19 (FGF19) IN PARENTERAL NUTRITION ASSOCIATED LIVER DISEASE
Reviewer: Samantha Woodruff
- 11:45 A **Ryan W Himes**
Tlr2 DEFICIENCY PROTECTS MICE FROM DIET-INDUCED OBESITY AND INSULIN RESISTANCE
Reviewer: Orlee Guttman
- 12:00 P **Rebecca Cherry**
HEPATIC FAT FRACTION IS ASSOCIATED WITH ABDOMINAL FAT DISTRIBUTION AND FASTING INSULIN IN OVERWEIGHT LATINO ADOLESCENTS
Reviewer: Kim Doan Katrina Nguyen
- 12:15 P MORNING WRAP UP
- 1:00 P LUNCH

5:00 P RECEPTION

ABSTRACT SESSION IV
MODERATOR: Cara Mack, MD

5:30 P **Orlee Guttman**
BILIARY ATRESIA AT THE HOSPITAL FOR SICK CHILDREN: A 33-YEAR EXPERIENCE
Reviewer: David Dunkin

5:45 P **Daniel Leung**
THE CHEMOKINE Cxcl10 PROMOTES CHOLESTASIS AND HEPATIC INFLAMMATION IN EXPERIMENTAL BILIARY ATRESIA
Reviewer: Catharine M Walsh

6:00 P **Melanie Rhue**
THERAPEUTIC EFFECT OF INCREASED HEPATIC LYSOSOMAL ACID LIPASE IN A MURINE MODEL OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)
Reviewer: Tejas Mehta

6:15 P **Meghana Sathe**
DYNAMIC ATP-ENRICHED VESICULAR COMPARTMENTS IDENTIFIED IN CHOLANGIOCYTES BY LIVE CELL IMAGING
Reviewer: Desale Yacob

6:30 P **Paulina Ordonez**
HUMAN EMBRYONIC STEM CELLS AS A RESEARCH MODEL FOR CELL BIOLOGY IN HEALTH AND DISEASE
Reviewer: Gilberto Bultron

FUNDING AND BUDGETING FOR YOUR CAREER PATH
MODERATOR: Cara Mack, MD

6:45 P FACULTY PRESENTATION: **Judy Podskalny**
NIH Support for career development (Ks, R03s and ESIs)

7:15 P FACULTY PRESENTATION: **Brent Polk**
Other Funding Sources

7:35 P PANEL DISCUSSION: *How to pay for what you want to do*
PANELISTS: **David Gremse, Judy Podskalny, Brent Polk, Elyanne Ratcliffe, and David Rudnick**

8:00 P DINNER

Saturday, March 21, 2009

7:00 A CONTINENTAL BREAKFAST with the NASPGHAN/CDHNF Leadership

ABSTRACT SESSION V
MODERATOR: David Gremse

- 8:00 A **Matthew Wyneski**
SAFETY AND EFFICACY OF ADALIMUMAB IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE
Reviewer: Kristin Fiorino
- 8:15 A **Kyle Kusek**
HUMAN ALPHA DEFENSIN 5 mRNA LEVELS ARE DECREASED IN CHILDREN WITH UNTREATED, NEWLY DIAGNOSED CROHN DISEASE
Reviewer: Mhd Louai Manini
- 8:30 A **JR Kelsen**
RATE OF RECURRENCE OF CLOSTRIDIUM DIFFICILE IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE
Reviewer: Shaista Safder
- 8:45 A **Ninfa Candela**
CLINICAL OUTCOME OF CHILDREN WITH IBD AND PREFERENTIAL MMP METABOLISM: ALLOPURINOL VS. ALTERNATIVE THERAPY
Reviewer: Jason Dranove
- 9:00 A **Orhan Atay**
PLASMA CITRULLINE LEVELS IN PEDIATRIC PATIENTS WITH SMALL BOWEL CROHN'S DISEASE: A NOVEL BIOMARKER OF INFLAMMATION
Reviewer: Paulina Ordonez
- 9:15 A BREAK
- 9:30 A **Sujal Rangwalla**
EVALUATION OF INTESTINAL FIBROSIS IN THE TNBS RAT MODEL OF CROHN'S DISEASE USING ULTRASOUND ELASTICITY IMAGING (UEI)
Reviewer: Chad Best
- 9:45 A **Charles Samson**
GRANULOCYTE-MACROPHAGE COLONY STIMULATING FACTOR IS REQUIRED FOR HOMEOSTATIC RESPONSES TO INTESTINAL INJURY IN THE CARD15 DEFICIENT HOST
Reviewer: Wael Sayej

- 10:00 A **Michael Rosen**
STAT6 ACTIVATION IN ULCERATIVE COLITIS: A TARGET FOR PREVENTION OF IL-13-INDUCED COLONIC EPITHELIAL CELL DYSFUNCTION
Reviewer: Nasim Sabery
- 10:15 A **Seamus Hussey**
THE ROLE OF ATG16L1 IN BACTERIAL-INDUCED AUTOPHAGY
Reviewer: Megan Butler
- 10:30 A **Joel Friedlander**
Foxp3-DEPENDENT BENEFICIAL EFFECTS OF DNA METHYLTRANSFERASE INHIBITOR THERAPY ON MURINE COLITIS
Reviewer: Ajay Kumar Jain
- 10:45 A BREAK

ABSTRACT SESSION VI
MODERATOR: Brent Polk, MD

- 11:00 A **Ying Lu**
IMMUNE RESPONSE TO INFLUENZA VACCINE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE
Reviewer: Ryan W Himes
- 11:15 A **Marc Shaefer**
SURGERY IN A PROSPECTIVELY FOLLOWED COHORT OF PEDIATRIC PATIENTS WITH CROHN'S DISEASE (CD)
Reviewer: Rebecca Cherry
- 11:30 A **LR Hormaza**
THE ROLE OF LECTIN-LIKE TRANSCRIPT 1 (LLT1) IN CELIAC DISEASE
Reviewer: Orlee Guttman
- 11:45 A **Mary Sherlock**
INFLIXIMAB-INDUCED PSORIASIS IN PEDIATRIC CROHN DISEASE; EXPERIENCE OF THIS PARADOXICAL EVENT AT A TERTIARY CENTRE
Reviewer: Daniel Leung
- 12:00 P **Folashade Jose**
DEVELOPMENT OF EXTRAINTESTINAL MANIFESTATIONS IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE
Reviewer: Melanie Rhue
- 12:15 P LUNCH
- 1:15 P FREE TIME
- 4:30 P Individual 15-minute meetings with **Dr. Judith Podskalny** to discuss NIH career development award process (sign up on site on a first come, first served basis)

5:45 P RECEPTION

CAREER DEVELOPMENT PLANNING
MODERATOR: David Rudnick

6:15 P FACULTY PRESENTATION: **Cara Mack**
Career development in academics

6:35 P FACULTY PRESENTATION: **David Gremse**
Continuing research outside an academic medical center

6:45 P PANEL DISCUSSION: *Balancing your various roles*
PANELISTS: **Cara Mack, MD, Judy Podskalny, and Brent Polk, Elyanne Ratcliffe,**
and NASPGHAN Council Member

7:30 P DINNER

Esophageal Fibrosis is Increased in Children with EoE

Samantha A Woodruff¹, Vincent A Mukkada¹, Kelley E Capocelli², Mark Lovell², Glenn T Furuta¹.

1. Pediatric Gastroenterology, Hepatology and Nutrition, University of Colorado Aurora, CO, USA 80045

2. Pediatric Pathology, University of Colorado Aurora, CO, USA 80045

Background: The only long term known complication of Eosinophilic Esophagitis (EoE) is stricture formation. However, the pathogenesis and natural history of this complication is unknown. Eosinophils (eos) are associated with tissue remodeling and fibrosis in other organ systems. Fibrosis has historically been difficult to assess in the GI tract due to technical limitations of mucosal biopsies.

Hypothesis: Children with EoE have increased esophageal fibrosis compared to children with normal esophageal biopsies.

Aim: To determine if esophageal eosinophilia increases esophageal collagen deposition and fibrosis in EoE.

Materials and Methods: Archived esophageal mucosal biopsies from Children's Hospital Denver Jan–Dec 2006 were screened for esophageal lamina propria. Of 890 esophageal biopsies, 290 (33%) demonstrated >2mm of lamina propria when observed under 40X magnification. A subset of well-defined patients (65) was studied as follows EoE (20), GERD (7), normal (21), and indeterminate esophagitis (16). Biopsies were studied in a blinded fashion recording the number of eos/HPF and fibrosis. Fibrosis was characterized by amount of collagen deposition along the basal lamina with 0=loose individual collagen fibrils lacy pattern, 1=tighter collagen deposition with some individual fibrils and 2=densely packed collagen fibrils. Pathologic findings were then unblinded and correlated with clinical data.

Results: Children with a clinicopathologic diagnosis of EoE have increased fibrosis compared to GERD and normal controls. (Fibrosis score 2 EoE vs GERD $p < 0.001$, EoE vs Normal $p < 0.001$ Fisher's Exact test) Figure 1. Increased fibrosis scores correlated with higher numbers of eos per HPF. Figure 2.

Conclusion: Eosinophilic inflammation is associated with increased collagen deposition.

Figure 1. Fibrosis Scores among all patients

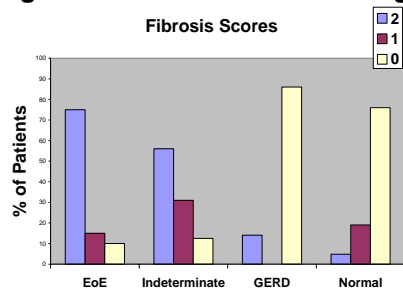
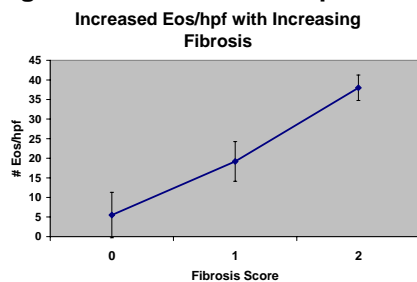


Figure 2. Increased Eos/hpf with increasing Fibrosis among all patients



Effect of Eosinophil Granule Proteins on p27 Expression in Esophageal Epithelial Cells

Nguyen, Kim-Doan Katrina¹; Blain, Stacy W²; Gress, Frank³; Treem, William R¹

1. Pediatrics, Division of Gastroenterology, Hepatology, and Nutrition, SUNY Downstate Medical Center, Brooklyn, NY, USA. 2. Pediatrics, Anatomy and Cell Biology, SUNY Downstate Medical Center, Brooklyn, NY, USA. 3. Medicine, Division of Gastroenterology, SUNY Downstate Medical Center, Brooklyn, NY, USA.

INTRODUCTION: p27, a tumor suppressor that regulates the G1 to S phase transition of the cell cycle, is reduced or mislocalized in Barrett's associated adenocarcinoma (BAA). Mislocalization of p27 from the nucleus to cytoplasm disrupts its normal function, and has been associated with poor prognosis in BAA. We have shown that bile acids and hydrochloric acid (HCl) cause mislocalization of p27 from the nucleus to the cytoplasm in normal squamous esophageal epithelial cells (HET-1A) in culture, without affecting total cell p27 levels. Both bile and acid reflux have been associated with an increased risk for development of Barrett's esophagus (BE), but not every patient with BE has a history of GERD. Many patients with symptoms mimicking GERD are later found to have eosinophilic esophagitis (EoE). Eosinophil granule proteins implicated in EoE [major basic protein (MBP) and eosinophil peroxidase (EPO)], have been shown to damage human pneumocytes and guinea pig tracheal epithelium. We sought to determine whether MBP or EPO affects p27 expression in HET-1A cells similar to bile acids and HCl. **METHODS:** HET-1A cells were incubated with MBP at 5-100µg/ml or EPO at 0.8-80µg/ml for 24 hours. Cells were harvested for cytotoxicity studies and immunoblot analysis to determine p27 expression. Indirect immunofluorescence (IF) was performed to determine the subcellular localization of p27. Flow cytometric analysis was used to study the MBP and EPO effects on cell proliferation. **RESULTS:** Exposure of HET-1A cells to MBP or EPO at various concentrations did not affect total cell p27 levels. When HET-1A cells were treated with either MBP or EPO, increased p27 was detected in the cytoplasm, along with reduced but not absent p27 nuclear staining. Flow cytometric profiles were similar for untreated cells and cells treated with MBP or EPO. **CONCLUSIONS:** 1) Exposure of HET-1A cells to MBP or EPO results in increased cytoplasmic p27. 2) The presence of p27 in the cytoplasm may disrupt its normal cell cycle inhibitory function and be an important early marker of dysplasia.

The Effect of the Route of Sensitization in the Induction of a Cow's Milk Allergic Response

David Dunkin, Cecilia Berin, Franziska Roth-Walter and Lloyd Mayer. Immunology Institute, Mount Sinai School of Medicine, New York, NY, USA, 10029.

INTRODUCTION: We have previously shown that naturally particulate milk allergens (casein - CAS) are preferentially taken up into the Peyer's patch and induce greater sensitization compared to soluble allergens (α -lactalbumin - ALA) taken up through IECs. However, emerging clinical evidence suggests that other sites such as the skin or the airways may be more likely inductive sites of allergic sensitization to food proteins. As initial antigen exposure is likely to play an important role in food allergy induction, we examined the effect of different routes of exposure using aggregated versus soluble milk proteins on sensitization.

METHODS: C3H/HeJ mice were exposed weekly for six weeks to an aggregated or a soluble cow's milk antigen, CAS or ALA respectively, with the adjuvant cholera toxin. Sensitization routes included oral, cutaneous (skin), intranasal (IN), sublingual (SL), and intraperitoneal (IP). Mice were then challenged orally with the sensitizing antigen at increasing doses, followed by an IP challenge if anaphylaxis was not induced. Anaphylaxis severity was assessed by symptom score and body temperature and antigen specific immunoglobulins in serum (IgE, IgA, IgG1 and IgG2) as determined by ELISA.

RESULTS: All groups of mice exposed to CAS via mucosal routes responded to CAS challenge with anaphylaxis. Percent anaphylaxis was as follows: oral: 87.5%(n=8), skin: 20%(n=5), IN: 100%(n=10), SL: 60%(n=5), IP: 60%(n=5). Mice with more severe symptoms showed a significant decrease in core body temperature: control: 36.3C(Standard error (SE) =0.11), oral: 33.3C(SE=.31), skin: 34.4C(SE=0.76), IN: 33.0C(SE=0.3), SL: 33.2C(SE=0.8), IP: 35.7C(SE=0.11). CAS specific immunoglobulins were elevated at 6 weeks in all groups when compared with controls. Identical experiments using the soluble allergen ALA induced allergic symptoms upon challenge in all groups except controls: oral: 78%(n=9), skin: 80%(n=5), IN: 100%(n=9), SL: 100%(n=5), IP: 80%(n=5). Again, mice with more severe symptoms showed a significant decrease in core body temperature: control: 37.6C(SE=0.24), oral: 36.1C(SE=0.3), skin: 33.9C(SE=0.7), IN: 34.6C(SE=0.3), SL: 34.0C(SE=0.4), IP: 35.5C(SE=0.18).

CONCLUSION: Our data show that allergic sensitization to food proteins can occur through a variety of mucosal routes. In addition, it appears that aggregated food proteins require mucosal sites for sensitization whereas soluble proteins can readily sensitize via the skin. These data suggest that non-oral routes of food allergen exposure may be clinically important in the development of food allergy.

GASTROINTESTINAL ENDOSCOPY SIMULATION TRAINING: WHAT TYPE OF FEEDBACK IS MOST EFFECTIVE?

Catharine M Walsh,^{1,2} Simon C Ling,^{1,2} Charlie Wang,² and Heather Carnahan.² Hospital for Sick Children,¹ University of Toronto,² Toronto, Ontario, Canada

BACKGROUND: Feedback has been identified as the most important feature of simulation-based medical education that leads to effective learning. However, the most effective feedback conditions for endoscopy skill acquisition in a simulated setting have yet to be determined.

PURPOSE: This study sought to determine the optimal timing of expert feedback (concurrent versus terminal) in promoting skill acquisition and retention in novices learning to perform colonoscopy in a simulated setting.

METHODS: Thirty novice endoscopists were pre-tested on a bench model colonoscopy simulator task which involved navigating a real colonoscope through a series of marked targets as quickly and accurately as possible. Participants were then randomly assigned to receive feedback either during (concurrent) or after (terminal) each practice trial. All participants underwent 12 trials of practice in their assigned training condition. The effectiveness of training was assessed using an immediate post-test and one week later using both a retention test and a transfer test to a novel path through the simulator. Performance measures included execution time and blinded expert assessment of performance (checklist and global rating scores). In addition, novices were asked to rate the quality of feedback received.

RESULTS: Both groups performed similarly at pre-test ($p > .05$). There was no significant difference in the time to complete the practice session for the concurrent versus terminal feedback group (34.1 min vs. 38.5 min, $p > .05$) and both groups performed similarly during the post-test and retention test ($p > .05$). On transfer testing, however, the terminal feedback group performed significantly better as measured by execution time, checklist and global rating scores ($p < .05$). In addition, performance of the concurrent feedback group decreased significantly on the transfer test as compared with the post-test and retention test ($p < .05$). Students in both groups rated the feedback they received as equally useful, clear and timely ($p > .05$).

CONCLUSIONS: The results of this study show that not all feedback conditions are equally effective. While the performance of participants in both the terminal and concurrent feedback groups improved, the use of terminal feedback resulted in better learning as demonstrated by superior performance on transfer testing. Incorporation of terminal feedback into technical skills training curricula may therefore help to greatly enhance the educational benefits of endoscopy simulation technology, while ensuring effective utilization of faculty time.

Investigator's statement (check all that apply):

This research involves human subjects research.

The IRB approval #: 22179 (University of Toronto IRB)

This research involves the use of laboratory animals. IACUC # is _____.

Name: Catharine M Walsh

Email address: catharine.walsh@utoronto.ca

Objective: GERD in children results in significant complications and morbidity. Though adult studies have shown an increase in GERD and its sequelae, studies in children are lacking. We aimed to describe the epidemiology of GERD in hospitalized U.S. children.

Methods: We used the Pediatric Hospital Information Survey database encompassing initially 32 and now 46 U.S. children's hospitals. We analyzed clinical and financial data of hospitalized children from 1995-1999 and 2002-2006. ICD-9 codes for esophageal reflux and complications were used for data queries. Collected data included age, gender, race, and discharges/year. Discharge rates were calculated per 10,000 hospital discharges.

Results: The percentage of hospital discharges with a diagnosis of GERD increased from 3.5% of 1,848,349 discharges in 1995-1999 to 4.3% of 2,128,205 discharges in 2002-2006. The rate of discharges with a diagnosis of GERD increased from 1995-1999 and from 2002-2006(table 1). For the 2 time periods, there were 2 and 6 cases of esophageal adenocarcinoma, respectively. From 2002-2006, there were 56 cases of Barrett's esophagus. The rate of funduplications performed increased from 1995-1999, but decreased from 2002-2006(table 1). Total hospital charges for patients with a primary diagnosis of GERD increased yearly from 1995-2006(table 1).

Conclusion: The hospitalization rate for GERD and its sequelae in U.S. children is rising. The total cost of hospitalization is increasing, as are complications of GERD, including esophageal cancer. However, surgical management has decreased. Overall, the burden of GERD and its complications is rising in hospitalized U.S. children.

	1995	1996	1997	1998	1999	p-value	2002	2003	2004	2005	2006	p-value
Hospital discharge rate for children with discharge diagnosis of GERD (per 10,000 discharges)	377.3	448.5	474.9	503.6	543.66	p<0.001	366.8	365.2	413.4	430.6	446.9	p<0.001
Rate of fundoplication for children with primary discharge diagnosis of GERD	26.8	27.3	28.3	29.5	30.5	p<0.001	36.2	31.8	31.3	25.7	23.8	p<0.001
Total adjusted charges (in millions) for children with primary discharge diagnosis of GERD	28.41	30.408	36.086	50.077	54.319	p<0.001	58.963	65.152	80.561	85.523	88.057	p<0.001

TITLE: Severe Painless Gastrointestinal Bleeding: An unusual presentation of Helicobacter pylori associated Duodenal Ulcer in Children of South East Asian Origin.

AUTHORS (LAST NAME, FIRST NAME): Bultron, Gilberto¹; Benjamin Gold²; Pashankar, Dinesh¹

INSTITUTIONS (ALL): 1. Pediatric Gastroenterology, Nutrition and Hepatology, Yale University School of Medicine, New Haven, CT, USA. 2. Emory University, Atlanta, GA.

ABSTRACT BODY:

Introduction: Children with Helicobacter pylori associated duodenal ulcer usually present with abdominal pain and vomiting. Severe gastrointestinal bleeding due to duodenal ulcer is rare in children. We report three children of South East Asian origin who presented with severe painless gastrointestinal bleeding due to helicobacter pylori related duodenal ulcer.

Case Reports: All three children (Table) were of South East Asian origin. All of them were previously healthy and did not have prior history of abdominal pain or vomiting. They presented acutely with symptoms of gastrointestinal bleeding. The examination in all was remarkable for pallor and signs of hypovolemia resulting in tachycardia and orthostatic hypotension. They required fluid resuscitation for hypovolemic shock and two of them received blood transfusions in the local hospital prior to referral. Endoscopy showed nodular gastritis with large duodenal ulcers and no active bleeding. All of them received combination therapy of two antibiotics and proton pump inhibitor. They all did well.

Conclusion: We report an unusual presentation of helicobacter associated duodenal ulcer in children. This phenotype is characterized by severe gastrointestinal bleeding without any prior gastrointestinal symptoms and is seen in children of South East Asian origin.

Patient	Age (years)	Gender	Race/Nation	Presentation	Hemoglobin at Presentation	Endoscopic Findings	Blood Transfusion
1	11.5	M	Asian/ Vietnamese	Pallor, melena, dizziness	8.1 g/dl	Duodenal ulcer Helicobacter gastritis	Yes, 1 unit
2	14	F	Asian/ Chinese	Pallor, dizziness	8.9g/dl	Two Duodenal ulcers, Helicobacter gastritis	No
3	12	F	Asian/ Korean	Pallor, hematemesis	6g/dl	Gastritis, Duodenal ulcer Helicobacter gastritis	Yes, 2 units

Evaluation of the Relationship between Upper Airway Disease and Gastroesophageal Reflux Disease Using Diagnostic Testing

Context: Brief episodes of gastroesophageal reflux (GER) are part of the normal physiologic maturational changes of the nervous and musculoskeletal systems. Complications of GER are classified as GER disease (GERD). GERD is often suspected of being associated with respiratory or otolaryngology conditions such as laryngomalacia, subglottic stenosis, recurrent pneumonia, asthma, laryngeal edema and acute life threatening events in addition to esophagitis. Unlike adults, pharyngeal regurgitation is more common in infants, placing them at an increased risk of supraesophageal complications.

Objectives: Evaluate the relationship between upper airway disease and GER using diagnostic modalities, including pH probe, scintigraphy, histology and visual assessments. Evaluate the efficacy of pharmacological acid blockade.

Study Design/Setting/Participants: Retrospective chart review at The Children's Hospital of Philadelphia and satellites from January 1, 2004 to December 31, 2007. Inclusion criteria include ages 0 to 18 years, all races and ethnicities, referral for clinical suspicion of GERD, and airway disease. Exclusion criteria include eosinophilic esophagitis, known esophageal motor abnormalities, connective tissue disease, esophageal malignancy, or pregnancy.

Results: (Preliminary data, 17 of 157 subjects evaluated) A Reflux Finding Score (RFS) >8 has a 95% certainty to correlate with laryngopharyngeal reflux. The Cotton Meyer grading scale for subglottic stenosis (SGS) was not statistically associated with the reflux index ($r^2 = 0.02$, $p=0.7$, CI = -3.2 to 2.2). The degree of esophageal inflammation did not statistically correlate with the reflux index, $r^2 = 0.02$, $p=0.7$, CI = -0.3 – 0.2. There was not a statistically significant association between the RFS and an increase in reflux index, $r^2 = 0.2$, $p=0.2$, CI = -1.2 to 0.3.

Conclusions: The degree of SGS by Cotton Meyer or inflammation by histology are not associated with the severity of GER by reflux index. The RFS may not provide a statistically significant grading scale for GERD.

Kristin Fiorino

The Children's Hospital of Philadelphia

Title: Feasibility and Application of 3-Dimensional Ultrasound for Measurement of Gastric Volumes in Healthy Adults and Adolescents

Mhd Louai Manini, MD^{1,3}, Duane D Burton¹, Duane D Meixner², Deborah J Eckert¹, Matthew Callstrom, MD², Grant Schmit, MD², Mounif El-Youssef, MD³ and Camilleri Michael, MD¹.
¹CENTER Program, Mayo Clinic, Rochester, MN, United States; ²Department of Radiology, Mayo Clinic, Rochester, MN, United States and ³Division of Pediatric Gastroenterology, Mayo Clinic, Rochester, MN, United States.

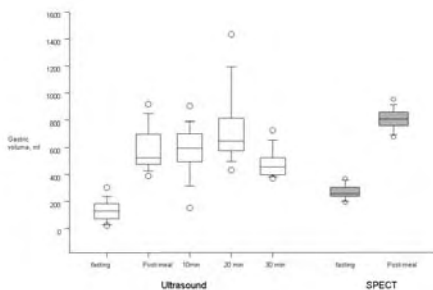
Purpose: Abnormal gastric accommodation to a meal results in dyspepsia. Current methods to measure gastric volume (GV) are invasive or involve ionizing radiation.

The aims of this study were: 1. To compare fasting and postprandial (PP) GVs measured by 99mTc-SPECT and 3-Dimensional Ultrasound (3D-US) in adults; 2. To assess the performance characteristics of 3D-US measurement of GV during fasting and postprandially; 3. To develop normative data of GVs in 24 healthy adolescents.

Design/Methods: The study included two healthy groups: **1.** 11 adults underwent SPECT and 3-D US simultaneously to measure GV; each adult also underwent a second 3-D US within a week from the first study **2.** 24 adolescents (age 13-17 years[®]) underwent one 3-D US measurement. Each 3-D US study included fasting, 300 mL Ensure[®] meal, and 0-30 min PP GV measurements. 3-D US, was performed by one operator with a stationary external probe (1.4-5.8 MHz) and a mechanized volume data acquisition.

Results: Adults fasting and PP GVs by 3-D US and SPECT are shown in [figure1]. Mean delta (PP-fasting) GV was 462±134 mL for 3-D US and 530±49 mL for SPECT (p=0.15). There were larger inter-individual COV for GVs by 3-D US (60.3% fasting, 21.3% PP) compared to SPECT (19% fasting, 9.2% PP). Intra-individual COV for two 3-D US measurements were 84% fasting and 44% average PP. Estimated GVs for the adolescent group (median, 25th-75th IQR) were: Fasting 33 (18-53mL), 30 min PP 330 (284-357mL), and delta GV 281 (240-324mL).

Conclusions: 3-D US is a promising method to measure GV accommodation to a meal. Large COVs reflect, in part, the learning stage in development of this promising technique.



Postural Tachycardia Syndrome (POTS) and Functional Gastrointestinal Disorders (FGID): A role for altered electrical activity of the stomach?

Shaista Safder , Thomas Chelimsky, Bethany Braunstein, Elizabeth Heller, Mary ORiordan, Gisela Chelimsky

Background: The cause of abdominal pain in patients with orthostatic intolerance is unclear. Children can be divided in sub-groups based on whether upright tilting replicates symptoms. We investigated whether the electrical activity of the stomach also changes with tilt position.

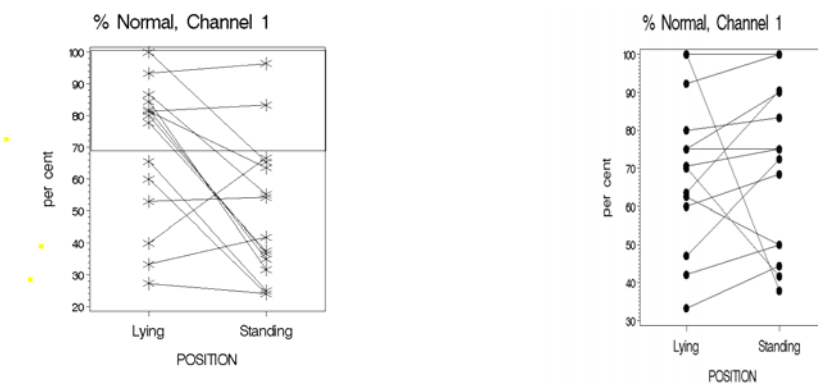
Hypothesis: Children with FGID and POTS have changes in the electrical activity of the stomach during the upright portion of the tilt.

Methods: All children undergoing autonomic testing were enrolled in this IRB approved prospective study. EGG was recorded 10 minutes in supine position and during the upright portion of tilt. EGG findings were correlated with autonomic diagnosis using Wilcoxon Rank Sum test. For the purpose of statistical analysis children were divided into two groups: 1) POTS and or vasodepressor syncope (VDS) 2) Non-POTS group include normal subjects and subjects with autonomic neuropathy.

Results: 30 patients participated (20 females). Mean age 14 ± 3.5 years. 20 had POTS/VDS, 5 autonomic neuropathy, 5 were normal. 11 subjects with POTS replicated symptoms during upright portion of the tilt. When evaluating Channel 1 of EGG, subjects with POTS/VDS, but not those without POTS, showed a tendency for an increase in % arrhythmia ($p=0.02$) and a decrease in % normal gastric activity ($p=0.02$) in the upright position in relation to the supine position.

Conclusion: This exploratory study suggests that the electrical activity of the stomach changes during the upright position in children with POTS/VDS, but not in children without this diagnosis. These changes could reflect abnormal autonomic control of gastric electrical activity and bear some relationship to the chief complaint of pain which worsens in the upright position. Further studies are needed to corroborate these findings.

Legend to Figures Changes in % normal gastric electrical activity lying vs standing. (Stars:POTS subjects; dots: non-POTS subjects) $p= 0.02$



Title: The Effect of Erythromycin on the Colonic Motility of Children and Young Adults During Colonic Manometry

Jason Dranove MD, Debra Horn RN, and Joseph Croffie MD
Division of Pediatric Gastroenterology, Hepatology, and Nutrition
Riley Hospital for Children
Indiana University School of Medicine
Indianapolis, IN, USA

Introduction: Erythromycin, a motilin receptor agonist, is successfully used as a gastro-duodenal prokinetic agent. Its effects on colonic motility have been studied in adults with conflicting results. Given the limited available treatments for colonic dysmotility, further investigation into erythromycin's effects on colonic motility are warranted.

Aims: To study the effect of erythromycin on colonic motility in pediatric patients with recalcitrant chronic constipation/encopresis and other suspected colonic motility disorders.

Methods: Patients referred for colonic manometry were eligible for enrollment. After appropriate bowel cleanout, a colonic manometry catheter was inserted endoscopically. A colonic manometry study was conducted on the next day. Fasting motility was recorded for 1 - 2 hours, then erythromycin lactobionate (EL) 3 mg/kg was administered intravenously, and colonic motility was monitored for 1 – 2 hours following erythromycin. Manometry was then continued per routine, including manometric evaluation after a meal and after intra-colonic administration of Bisacodyl. Colonic pressure tracings were recorded and transferred to a personal computer system (RedTech-GiPC Gastrointestinal System). The Motility Index (MI) (average area under the curve) of pressure tracings at each pressure transducer was calculated for each patient for a period of 15 and 60 minutes before and after EL infusion. Change in MI was compared by Wilcoxon Signed Rank test. A $p < 0.05$ was considered statistically significant.

Results: Twenty patients were enrolled (50% male, mean 10.7 years). The most common indications were constipation with encopresis (60%) and suspected pseudo-obstruction (20%). 70% of patients had normal colonic manometry, and 30% of patients demonstrated a neuropathy. No patients had a true myopathy. Average MI for the 60 minute period prior to and after EL infusion were 254 mm Hg/hr +/- 74 (95% CI 216-293) and 253 mm Hg/hr +/- 94 (95% CI 214 – 291) respectively ($p=0.55$). Average MI for the 15 minute period prior to and after EL infusion were 64 mm Hg/15 min +/- 23 (95% CI 51 – 76) and 69 mm Hg/15 min +/- 32 (95% CI 57 – 82) ($p = 0.45$). On subanalysis, EL did not increase MI in either the normal manometry group or the neuropathy group.

Conclusion: Administration of intravenous EL resulted in no changes in colonic motility index in pediatric patients referred for colonic manometry. Further studies on potential colokinetic agents are warranted in this population of patients.

Respiratory Failure, Compartment Syndrome, Colonic Perforation and Colectomy: Constipation to the Highest Degree

Yacob, Desale; Balint, Jane P; Erdman, Steven H; Mousa, Hayat M; Di Lorenzo, Carlo.

Nationwide Children's Hospital, Columbus, OH, USA.

It is believed that 5% to 20% of the general pediatric population suffer from constipation. The majority of children with constipation are believed to have a functional disorder and are successfully managed on an outpatient basis. However, there are times when functional constipation may lead to significant morbidity and requires immediate intervention. We report three cases of neurologically and cognitively normal adolescents who presented with life threatening fecal impaction. 1) 16 year old male who presented to the Emergency Department with abdominal distension, respiratory distress and bilateral pedal edema. He had an emergent manual disimpaction under general anesthesia. His post-disimpaction recovery was complicated by an ICU stay, foot drop and limp. 2) 15 year old male who presented to the Emergency Department in septic shock with severe abdominal distension and pain. He had an emergent exploratory laparotomy which revealed a megacolon, a perforated cecum, and abdominal compartment syndrome. He had a subtotal colectomy, an ileostomy, and a postoperative period complicated by intraabdominal abscesses, decubitus ulcers, neuropathic lower extremity pain and a temporary tracheostomy. 3) 15 year old male with a long standing history of constipation who presented with a severe impaction and respiratory difficulties and developed cardiopulmonary arrest during an attempt at a clean-out. He required emergent bedside exploratory laparotomy for a perforated colon. These patients were not known to have any underlying disorders predisposing them to severe, life threatening constipation. Hirschsprung's disease was ruled out in all after their acute presentations. They have now all recovered completely. These cases document that although rare, serious complications can occur with constipation. Therefore, it is important to be vigilant in the care of these patients, to educate patients and parents about the dangers of untreated constipation, and to proceed thoughtfully in the management of severe impactions.

A pre-post retrospective study of patients with cystic fibrosis and gastrostomy tubes.
Best C, Dunitz J, Phillips J, Holme B, Gaillard P, Schwarzenberg S.
Division of Pediatric Gastroenterology, Hepatology, and Nutrition, University of Minnesota,
Minneapolis, Minnesota.

Background: The impact of inadequate nutrition on the progress of cystic fibrosis (CF) is well documented and gastrostomy tube (GT) feedings appear to be a valuable adjunct in the care of such patients. It is not known whether delivery of GT feedings results in improvements in pulmonary status, an essential factor in increasing lifespan in CF. We conducted a retrospective review utilizing the Minnesota Cystic Fibrosis Center Database. Our hypothesis was that GT feeds would improve weight gain and this improvement would be accompanied by improved pulmonary function.

Methods: Subjects were identified by presence of a GT. Primary outcomes were body mass index (BMI)-percentile, and National Health and Nutrition Examination Survey (NHANES) FEV1-percent-predicted (ppFEV1). For adults ≥ 18 , BMI-percentile was computed using the age of 18. Patients were included if they had at least 5 ppFEV1 observations and at least 1 BMI-percentile calculation before and after GT placement. Patient-wise regression analysis was conducted with modeling of each patient's ppFEV1 measurements separately as a linear function of time with both a step change and slope change. BMI-percent values were compared during four time periods: the two years immediately before GT placement and the first, second, and fourth year after GT placement. The hypotheses were tested using t-tests. The possibility that the changes in lung function may be correlated with the level of lung function at GT placement was tested by regressing the estimated step changes and the estimated slope changes for the 46 patients against their ppFEV1 levels at GT placement and testing whether ppFEV1 at placement was a significant predictor.

Results: 46 CF patients with a GT and at least 5 ppFEV1 observations and at least 1 BMI-percentile calculation before and after GT placement were identified. A total of 3091 ppFEV1 measurements and 3086 pBMI calculations were obtained. The mean estimated step and slope changes in ppFEV1 at GT placement were +0.0861% ($p = 0.9527$) and GT +3.725% per year ($p = 0.0007$). On subgroup analysis, the mean estimated step and slope changes at placement for adults were +1.1138% ($p = 0.5043$) and +7.1593%/yr ($p = 0.0085$) and -0.319% ($p = 0.8691$) and +2.3722% /yr ($p = 0.0278$) for children. The estimated coefficient for the ppFEV1 level at placement was -0.07 (p -value = 0.4291).

For BMI-percentile analysis, 46 patients had at least 1 measurement both in the two years before placement and in the 1st year after GT placement. The change in mean BMI-percentile was +4.2407% ($p = 0.0387$). 39 patients remained a year 2 and 29 at year 4 with mean percentile differences of +13.226%, ($p < 0.0001$) +10.93% ($p = 0.0067$).

Conclusion: Aggressive nutritional management of patients with cystic fibrosis using GT feedings results in significant improvement in their growth. Improvement in growth after GT feedings in this patient population is associated with significant improvement in pulmonary function and this improvement does not appear to depend on the level of lung function at the time of GT placement.

Biomarkers in Children with Non-Alcoholic Steatohepatitis

Wael N. Sayej, MD

Background: Non-Alcoholic Steatohepatitis (NASH) represents a serious form of fatty liver disease, characterized by hepatic steatosis associated with evidence of inflammatory changes and variable degrees of fibrosis. It has been estimated that up to 20% of the population may have fatty liver disease and up to 3% have NASH. Liver biopsy continues to be the main method of diagnosing NASH. This study is aimed at identifying diagnostic and prognostic markers for NASH, which we hope will eventually allow designing a reliable framework for the screening, staging, differential diagnosis and prediction of response to therapy. **Methods:** blood samples were collected from patients undergoing liver biopsies. The blood samples were collected in EDTA tubes and serum was separated, aliquoted, and stored at -80°C for the purpose of this study. Patient demographic data and laboratory test results were collected from their medical records. Enzyme linked immunoassays were performed to check for levels of inflammatory markers that we hypothesized could be potential markers including: Leptin, IL-6, IL-8, TNF, TNFr1, TNFr2, IP-10, IGFBP-1, and TRAIL. Interleukin-1 β and β -NGF were used as negative controls. Statistical analysis (ANOVA, Kruskal-Wallis test, and TTests) was performed using Graphpad Prism software v.5.00. **Results:** A total of 76 patients with blood samples were enrolled in the study, only 62 had liver biopsies. The groups included: NASH BMI \geq 30 (n=19), NASH BMI 25-30 (n=4), NASH BMI<25 (n=3), NASH + Diabetes (n=5), NASH + hepatitis B or C (n=2), hepatitis B (n=8), hepatitis C (n=7), AIH (n=3), hepatitis NOS (n=6), other liver disease (n=4), Obese patients with no liver biopsy (n=8) and Controls (normal liver biopsy or normal weight and LFT's) (n=7). Leptin levels were significantly higher in the NASH and obese patients compared to all other groups, $p < 0.0001$. Levels correlated with the degree of obesity, $p < 0.0001$. However, Leptin did not correlate with the degree of steatosis, inflammation, or fibrosis. Leptin in NASH BMI \geq 30 patients correlated with insulin resistance (IR), $p < 0.0001$. IGFBP-1 levels were lower in NASH patients with IR and obese patients compared to NASH patients with no IR, $p = 0.0386$ and 0.0436 . IP-10 was significantly higher in patients with AIH and hepatitis C infection, $p < 0.0001$ and $p < 0.0342$. TNFr1 levels were higher in NASH patients, $p = 0.0327$. It was also higher in NASH patients compared to obese patients with no liver biopsies, $p = 0.0039$. TNFr2 was also higher in NASH BMI \geq 30 than the other groups, $p = 0.0157$; obese with no biopsies, $p = 0.0128$; and controls, $p = 0.0189$. There was no significant difference in serum levels of IL-6, IL-8, TNF, TRAIL. Interleukin-1 β and β -NGF. **Conclusion:** Leptin is a good marker to measure in the evaluation of NASH. However, it does not give any insight as to the degree of steatosis, inflammation or fibrosis. Obese patients with normal liver enzymes also have higher leptin levels, which might indicate that leptin is only a marker of obesity and not liver disease. TNFr1 and TNFr2 might serve as potential markers for evaluating inflammation in patients with NASH. IGFBP-1 is a good marker to evaluate for insulin resistance in NASH and obese patients. IP-10 is a possible marker to evaluate for acute inflammation thus differentiating AIH or acute infections of the liver from other liver diseases. Further studies are required with larger population numbers to expand on these results and conclusions.

Investigator's statement (check all that apply):

This research involves human subjects research. The IRB approval # is DB#745.

This research involves the use of laboratory animals. IACUC # is _____.

Name: Wael N. Sayej, M.D.

Email address: wsayejmd@yahoo.com

