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Scientific Abstracts
GROWTH IMPROVEMENT IN ADALIMUMAB-TREATED PEDIATRIC PATIENTS WITH CROHN’S DISEASE: DATA FROM IMAGINE 1.

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Introduction: Children with Crohn's disease (CD) often have impaired growth. The IMAGINE 1 trial demonstrated the safety and effectiveness of adalimumab (ADA) on inducing and maintaining remission in children with moderately to severely active CD1. The impact of ADA therapy on growth in patients with delayed growth at trial entry is analyzed.

Methods: In IMAGINE 1, patients aged 6-17 years with baseline (BL) PCDAI >30 received open-label induction of ADA at weeks 0/2 according to body weight (≥40kg, 160/80mg; <40kg, 80/40mg). At week 4, patients were randomized to double-blind higher-dose (HD) ADA (≥40kg, 40mg every other week [EOW]; <40kg, 20mg EOW) or lower-dose (LD) ADA (≥40kg, 20mg EOW; <40kg, 10mg EOW) to week 52. Patients were allowed to escalate to blinded weekly therapy for flare or non-response, followed by open-label HD ADA weekly for continued flare or non-response. Change from BL in height velocity z-score was measured at weeks 26 and 52 in patients with and without growth delay (defined as height velocity z-score ≤ -1.0) in all ADA patients regardless of treatment group.

Subgroup analyses by BL corticosteroid use, disease severity (based on median BL PCDAI of study population (PCDAI < 40, moderate CD; PCDAI ≥ 40, severe CD), and prior infliximab (IFX) use were performed.

Results: Overall, statistically significant improvement in growth was observed at weeks 26 and 52 with ADA maintenance therapy in patients with growth delay (median height velocity z-score at BL -2.9 and median change from BL at weeks 26 and 52; 2.4 and 3.3, respectively, each p<0.001), but not in patients with normal growth (BL median 0.2; median change from BL=0 at weeks 26 and 52). No statistically significant differences between LD and HD ADA were observed. Growth improvement trended to be larger in patients with ADA therapy than in patients with IFX naïve patients (Table).

Conclusion: ADA treatment significantly improved growth in children with moderately to severely active CD and growth delay. The pronounced effect of ADA on growth in children with concomitant corticosteroid use or severe disease by PCDAI requires confirmatory studies.


Median BL height velocity z-score values and change from BL at weeks 26 and 52 in patients with growth delay (height velocity z-score ≤ -1.0 at BL)

<table>
<thead>
<tr>
<th>Group</th>
<th>BL</th>
<th>ΔWeek 26</th>
<th>ΔWeek 52</th>
</tr>
</thead>
<tbody>
<tr>
<td>LD</td>
<td>-3.0 (N=47)</td>
<td>2.5* (N=47)</td>
<td>3.4* (N=30)</td>
</tr>
<tr>
<td>HD</td>
<td>-2.8 (N=42)</td>
<td>2.3* (N=42)</td>
<td>3.3* (N=29)</td>
</tr>
<tr>
<td>IFX naïve</td>
<td>-3.1 (N=54)</td>
<td>2.7* (N=54)</td>
<td>3.8* (N=41)</td>
</tr>
<tr>
<td>IFX experienced</td>
<td>-2.3 (N=35)</td>
<td>1.7* (N=35)</td>
<td>1.4* (N=18)</td>
</tr>
<tr>
<td>Corticosteroid use at BL</td>
<td>-2.8 (N=38)</td>
<td>2.5* (N=38)</td>
<td>4.3* (N=23)</td>
</tr>
<tr>
<td>No corticosteroid use at BL</td>
<td>-2.9 (N=51)</td>
<td>2.3* (N=51)</td>
<td>2.3* (N=36)</td>
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<td>Moderate CD</td>
<td>-3.2 (N=26)</td>
<td>2.7* (N=26)</td>
<td>3.0* (N=22)</td>
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<tr>
<td>Severe CD</td>
<td>-2.7 (N=63)</td>
<td>2.3* (N=63)</td>
<td>3.8* (N=37)</td>
</tr>
</tbody>
</table>

*p<0.001 change from BL using Wilcoxon signed rank test
2 MATRIX METALLOPROTEINASE 9 (MMP-9) EXPRESSION IN THE PROGRESSION OF PEDIATRIC INFLAMMATORY BOWEL DISEASE. Valentina Shakhnovich1,2, Craig A. Friesen1, Nancy Neilan1, Julie Bass1
1Gastroenterology, Children's Mercy Kansas City, Kansas City, MO; 2Clinical Pharmacology, Children's Mercy Kansas City, Kansas City, MO

Introduction: Matrix metalloproteinase-9 (MMP-9), an enzyme involved in epithelial extracellular matrix degradation, has been shown to be increased in the intestinal mucosa, as well as the serum, urine, and stool, of patients with Inflammatory Bowel Disease (IBD). It is thought to contribute to disease pathogenesis via proteolytic effects, resulting in tissue damage, as well as, through mediation of inflammation. In a murine model, upregulation of MMP-9 activity precedes initiation of the inflammatory cascade and the development of colitis. We evaluated colonic MMP-9 distribution in a group of patients with initial non-diagnostic endoscopies who subsequently went on to develop IBD.

Methods: Histopathologic and immunohistochemical evaluations were performed on previously obtained intestinal biopsy specimens from 16 pediatric patients with IBD (7 Crohn's disease; 8 ulcerative colitis; 1 indeterminate colitis) comparing rectosigmoid specimens obtained during the initial non-diagnostic endoscopies (normal gross appearance with biopsies not fulfilling histologic criteria for IBD) and subsequent rectosigmoid specimens obtained from the same children at the time of diagnosis (mean time to diagnosis 23.2 months). Tissue specimens underwent immunohistochemical staining with purified polyclonal mono-specific rabbit anti-human-MMP-9 and were evaluated for staining in the lamina propria (LP) and crypt epithelium (CE)) in a blinded fashion, with a semi-quantitative method defining MMP-9 staining as absent, focal, or diffuse. Pre- to post-diagnosis staining frequencies and patterns of expression were compared utilizing the Fisher's exact test, with a statistical significance level set at p<0.05.

Results: Positive staining occurred in a higher proportion of specimens obtained during the diagnostic endoscopies as compared to the initial non-diagnostic endoscopies in both the LP (88% vs. 31%, p=.003) and the CE (50% vs. 0%, p=.002). LP staining was diffuse in 12 and focal in 2 of the 14 MMP-9-positive diagnostic specimens. LP staining was diffuse in 2, and focal in 3, of the 5 MMP-9-positive initial non-diagnostic specimens. CE staining was diffuse in 7 of the 8 positive diagnostic specimens, and none of the initial non-diagnostic specimens. There were no differences in the frequency of positive staining between patients with Crohn's disease and those with ulcerative colitis.

Conclusions: Diffuse positive staining for MMP-9 was observed frequently (>85%) in the rectosigmoid mucosa of children at the time of IBD diagnosis. Positive MMP-9 staining was detected in a greater proportion of biopsy specimens obtained at diagnosis compared to biopsies obtained from the same children prior to detection of overt, gross or histologic disease, suggesting a possible pathogenic role of MMP-9 in IBD development. As such, MMP-9 may be a useful early marker of disease progression in a subset of patients with IBD.

Will be presented in Oral Abstract Session 2 – Basic IBD

3 DECREASED PREGNANE X RECEPTOR (PXR) EXPRESSION IN CHILDREN WITH CROHN'S DISEASE. Valentina Shakhnovich1,2, Carrie Vyhlidal1, Craig A. Friesen1, Amber Hildreth4, James Daniel2, Vivekanand Singh1, Gregory L. Kearns2, J S. Leeder3, Singha1, Gregory L. Kearns2, J S. Leeder3
1Pathology, Children's Mercy Kansas City, Kansas City, MO; 2Gastroenterology, Children's Mercy Kansas City, Kansas City, MO; 3Clinical Pharmacology, Children's Mercy Kansas City, Kansas City, MO; 4Pediatrics, Children's Mercy Kansas City, Kansas City, MO

Background: Human pregnane X receptor (PXR) is a xenobiotic nuclear receptor responsible for transcriptional regulation of specific drug metabolizing enzymes (e.g., CYP3A4) and transporters (e.g., ABCB1). PXR dysregulation has also been implicated in IBD pathogenesis in a well-established mouse model, as well as some human studies. Data on PXR expression in intestinal tissue of pediatric patients with Crohn's disease (CD) remain limited, with no conclusive information regarding PXR expression in healthy vs. inflamed mucosa. The primary objective of this single center pilot study, utilizing archived pediatric biopsy samples, was to test the hypothesis that PXR expression is decreased in actively inflamed small intestinal tissue from pediatric patients with CD.

Methods: RNA was extracted from archived formalin-fixed paraffin-embedded intestinal biopsy samples obtained during routine EGD/colonoscopy in pediatric patients, aged 7 to 18 years, with a diagnosis of CD (n=18) and age- and sex-matched Controls without IBD (n=12). Tissue samples with adequate mRNA quality, as determined by 3;5' GAPDH ratio <10, were included in the analysis of relative mRNA expression of PXR and its target genes (e.g., CYP3A4) in the duodenum (duod) and the terminal ileum (TI) of all children. Quantitative real-time reverse-transcription polymerase chain reaction (RT-qPCR) was used to determine relative mRNA expression normalized against GAPDH, an established reference gene in the small intestine. All data were log transformed. Presence of inflammation in the TI of CD, but not the duod of CD or any of the Control tissues, was confirmed by histopathology and IL-8 expression. Epithelial cell integrity was assessed via Villin expression. Differences in relative mRNA expression were explored via two-tailed paired Student t-test, two-tailed Spearman's correlation, and linear regression analysis; α=0.05.

Results: GAPDH expression did not differ with age, sex, or location along the small intestine (i.e., TI vs. duod) in the CD or the Control group. In the cohort of children with CD, a statistically significant decrease in PXR expression was
observed in the inflamed TI vs. non-inflamed duod (TI=1.88±0.89 vs. duod=2.5±0.67; p=0.0003). In contrast, no difference in PXR expression was observed between non-inflamed TI vs. non-inflamed duod in Controls (TI=2.11±0.41 vs. duod=2.26±0.61; p=0.52). Likewise, villin expression was decreased in inflamed TI of children with CD (TI=3.80 ± 0.94 vs. duod=4.61 ± 0.52; p<0.001), but not in Controls (TI=4.30 ± 0.35 vs. duod=4.47 ± 0.40; p=0.29). Significant correlation was observed between PXR and villin expression across all samples (r²=0.780, p=0.01).

Conclusions: PXR expression is decreased in the inflamed TI, but not the non-inflamed duod, of children with CD. The observed difference in PXR expression is not due to regional differences in PXR expression, as no difference was observed between the TI and duod in sex- and age- matched Controls. Our data suggest that PXR may play a role in disease phenotype expression in Crohn's and that the observed coordinate downregulation of PXR and villin is disease- or inflammation-specific, which may have significant implications for drug-disposition and response in children with IBD.

Celiac/EoE/Allergic Enteropathy

7 MODE OF DELIVERY DETERMINES NEONATAL PHARYNGEAL BACTERIAL COMPOSITION AND EARLY INTESTINAL COLONIZATION. David Brumbaugh1,2, Jaime Arruda3, Kristen Robbins4, Diana Ir4, Daniel Frank4 1Pediatrics, University of Colorado, Aurora, CO; 2Digestive Health Institute, Children's Hospital Colorado, Aurora, CO; 3Obstetrics and Gynecology, University of Colorado, Aurora, CO; 4Medicine, University of Colorado, Aurora, CO

Introduction: Initial bacterial colonization of the human intestinal tract is an important early-life process that shapes development of immune function. Mode of delivery is a critical determinant of colonization dynamics. Cesarean delivery has been associated with up to a 20% increased risk of childhood asthma and was recently found to contribute to an increased odds of celiac disease, suggesting that early bacterial colonization may impact lifelong immune tolerance. We sought to determine whether cesarean delivery alters the types of bacteria present in the infant pharynx at the time of first swallow, potentially impacting the course of early intestinal colonization.

Methods: We conducted a prospective observational cohort study of 12 infants born by planned cesarean section (CS) and 11 infants born vaginally (VB). Maternal vaginal (VAG) and rectal (REC) swabs were obtained just prior to delivery, a pharyngeal aspirate (ASP) was collected from the infant at the time of parturition, and infant stool samples were collected prior to nursery discharge, at 2 weeks, and 6 weeks of life. Bacterial 16S rRNA genes were amplified by PCR, sequenced using Illumina MiSeq, and grouped into Operational Taxonomic Units.

Results: A median of 117317 (IQR, 83240 to 172512) high-quality 16S sequences were generated per sample. The infant aspirate microbiome was more similar to maternal vaginal and rectal microbiomes in VB than in CS infants. Differences in phylum-level relative abundance by delivery mode were observed in ASP and stool samples at all time points. Increased Firmicutes (62.6% vs. 30.1%, Wilcoxon p=0.0013), primarily lactobacilli, was found in aspirates of VB infants compared to CS, whereas aspirates of CS were enriched in Actinobacteria (20.1% vs. 3.8%, p=0.045). Stool was enriched in Bacteroidetes in VB compared with CS infants in the first days of life as well as at 2 and 6 weeks (p=0.017, 0.0001, 0.006, respectively). Significant differences in phylum-level relative abundance by delivery mode were observed in ASP and stool samples at all time points. Increased Firmicutes (62.6% vs. 30.1%, Wilcoxon p=0.0013), primarily lactobacilli, was found in aspirates of VB infants compared to CS, whereas aspirates of CS were enriched in Actinobacteria (20.1% vs. 3.8%, p=0.045). Stool was enriched in Bacteroidetes in VB compared with CS infants in the first days of life as well as at 2 and 6 weeks (p=0.017, 0.0001, 0.006, respectively).

Conclusions: This is the first study to show that mode of delivery influences bacterial composition of the offspring pharyngeal aspirate at birth. In a vaginal delivery, this first aliquot of swallowed bacteria contains organisms derived from maternal vaginal and rectal sources and is the initiator of bacterial colonization of the intestine. The aspirates of VB infants were enriched in lactobacilli, whereas CS aspirates were enriched in skin-associated bacteria. This difference in pharyngeal lactobacilli exposure did not, however, influence lactobacilli recovery from infant stool. Exposure to higher densities of lactate-producing organisms in a vaginal delivery may impact later bacterial succession through their modification of the intestinal microenvironment, as bacteroidetes were relatively less dense in the stool of CS infants. These findings further our understanding of early intestinal bacterial colonization and may guide future interventions to restore physiologic intestinal colonization in infants born by cesarean delivery.

8 EOSINOPHILIC OESOPHAGITIS: A 10-YEAR REVIEW. Valerie Marchand, Gastroenterology, Sainte-Justine UHC, Montreal, QC, Canada

Eosinophilic oesophagitis (EO) is an emerging condition characterised by endoscopic, histologic and clinical features. Recently published guidelines have proposed diagnostic criteria. The aim of this study was to look at the characteristics of patients diagnosed with EO over a 10-year period. METHODS: The medical chart of all patients who had > 15 eosinophils per high power field (eo/hpf) on esophageal biopsy between 2003 and 2012 were reviewed. Patients were considered to have EO if they had an eosinophil-predominant inflammation in the esophagus on biopsy (> 15 eo/hpf), with no secondary causes of esophageal eosinophilia. RESULTS: 234 patients (168 M; 66 F) had a biopsy report mentioning >15 eo/hpf. Median age at diagnosis was 12.3 years. Seventy-three cases were diagnosed from 2003 to 2007 and 138 cases from 2008 to 2012. Diagnosis was made because of acute food impaction in 25 patients (10.7 %). Endoscopic findings included furrows (74%), trachealization (34%), exudate (39%). Three patients had eosophageal stenosis, 7 had gastric ulcer and 7 had duodenal ulcer. Food allergy was present on skin test and/or RAST in 61 % of patients. The most common allergies were eggs (72), milk (68) and wheat (63). Weight Z-score at diagnosis was < 2 SD.

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in 10.7% of patients. Only 114 patients had a second endoscopy. Of those 5/30 had normal biopsies on PPI alone.

**CONCLUSIONS:** EO is an emerging disease and its incidence is increasing. Food allergy is found in a majority of patients and growth may be affected. The recently published criteria will help to better define this disease and their application will standardize the management of patients with EO.

**9 EOSINOPHILIC ESOPHAGITIS: ARE THERE DIFFERENCES AMONG RACE, AGE, AND GENDER?**

Erika V. Smith, T. Prescott Atkinson, Mary Lynch, Suzanne Hammett, Reed Dimmitt

1Pediatric Gastroenterology, Children's of Alabama, Birmingham, AL;
2Pediatric Gastroenterology, University of Alabama, Birmingham, AL;
3Pediatric Allergy and Immunology, University of Alabama, Birmingham, AL;
4Psychology, University of Alabama, Birmingham, AL.

**Background:** The incidence of Eosinophilic Esophagitis (EO) has increased dramatically over the past decades. While the exact pathophysiology is still unknown, an alteration in the innate and adaptive immune systems is theorized. Several studies have reported a strong male Caucasian predominance. The University of Alabama at Birmingham/Children’s of Alabama established a Gastrointestinal Eosinophilic Disorders Program in 2012. The purpose of our retrospective review was to identify the demographics of our patient population and determine any significant differences in presentation among race, age, and gender.

**Methods:** Our study was an IRB approved retrospective review from December, 2000 to January, 2014 of 144 patients with EO. The patients were analyzed by demographics, symptomatology, hematologic and histologic findings, and atopic manifestations. The results were analyzed with Fisher’s exact test, significance determined as p ≤ 0.05.

**Results:** Race: Our EO population had a greater percentage of African American (AA) children (25.5%) when compared to other studies. This corresponds to the percentage of AA children in Alabama (26.5%). AA patients with EO were more likely to have atopic disease including asthma and food allergies, but they were significantly more likely to have eczema and allergic rhinitis. They were also more likely, although not significant, to have vomiting and failure to thrive at presentation. In contrast, Caucasians were significantly more likely to have abdominal pain and a family history of dysphagia. AAs were diagnosed at a significantly younger age than Caucasians (6.5 years vs 8.5 years), and were more likely to have peripheral eosinophilia (89% vs. 66%). Although not significant, AAs were more likely to have a positive skin prick test to Aeroallergens (60% vs. 37.7%). Age: Patients with EO aged 0-3 years were significantly more likely to have eczema, weight loss, vomiting, poor appetite, and failure to thrive. They also had a higher number of elevated proximal esophageal eosinophils and positive patch testing. In comparison, patients aged 12-18 years were more likely to present with abdominal pain and food impactions. Gender: We saw little difference in the clinical presentation based on gender. Males were significantly more likely to have a family history of dysphagia when compared to females.

**Conclusions:** In review of our population, there is little variation in phenotypic presentation among gender. In contrast, there were several differences in presentation by race, including AAs presenting at a younger age. This would argue against access to care as an explanation for the small percentage of AA patients with EO. Our elevated AA percentage reflected our baseline population rather than a true Caucasian predominance. Differences by race may be associated with unknown genetic variations and/or allergen exposures within the environment. EO patients less than 3 years of age had more signs and symptoms than their older counterparts. Perhaps, more aggressive disease presents at a younger age. Given these findings, continued research into immune dysregulation and environmental triggers is pivotal into better understanding EO.

**10 EOSINOPHILIC ESOPHAGITIS (EOE): DYSPHAGIA PREDOMINANT AND ABDOMINAL PAIN PREDOMINANT. IS THE ESOPHAGEAL HISTOLOGY DIFFERENT IN THESE TWO GROUPS?**

Christopher Chu, Nemencio R. Ronquillo, Rohini Chennuri, Brian P. Adley, Kristina R. Borgen, Alan Schwartz, James Berman, Thirumazhisai S. Gunasekaran

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2Pathology, University of Illinois, Chicago, IL;
3Department of Pathology, Advocate Lutheran General Hospital, Park Ridge, IL;
4Department of Pediatrics, University of Illinois Medical Center, Chicago, IL;
5Department of Pediatrics, Loyola Medical Center, Chicago, IL;
6Center for Children's Digestive Health, Park Ridge, IL;
7Pediatric Gastroenterology, Advocate Children's Hospital, Park Ridge, IL.

EOE in children and adolescents can present with a variety of symptoms. Consequently, we grouped EOE patients into EOE-dysphagia (D), abdominal pain (AP), gastroesophageal reflux (GER), and failure to thrive (FTT) based on recent EOE Consensus recommendations. We previously reported that EoE-AP patients have suboptimal outcomes with standard treatment compared to EoE-D1. We postulate that EoE-D and EoE-AP may be different conditions and may have different histopathology. AIM: Compare the esophageal histopathology in patients with EO-E and EoE-AP to see if there is a difference that may help us to understand the pathogenesis of two potentially distinct disease processes.

**METHOD:** Data from children with EO seen between 1/2010 and 12/2012 has been maintained in a database. The patients are cohort into four groups as above. Physical findings, CBC, CMP, upper gastrointestinal endoscopy, and findings of the biopsies of the duodenum, antrum, distal and mid esophagus were captured. Treatment included dietary
modification and/or topical steroids. In some patients, PPI was continued. For this study, an equal number of patients from the EoE-D and EoE-AP cohorts were analyzed. The pathologists reviewing the histology were blinded as to symptom cohort. Biopsies of the esophagus at time of diagnosis were reviewed for the following criteria; eosinophilic microabscesses (MAB), superficial layering of eosinophils (SLE), epithelial desquamation (ED), basal zone hyperplasia (BZH), rete peg elongation (RPE), spongiosis (SP), subepithelial fibrosis/LP fibrosis (FB), diffuse involvement if eosinophils present (DFE), eosinophils diffuse but not confined to rete pegs (E-Dist _), degranulation of eosinophils (DE). Differences in proportions of patients in each group whose biopsies included each finding were compared with Fisher's exact test (2-sided). RESULTS: There were a total of 67 patients in both groups, males 59 (88%) age 2 - 17, mean 11.68 years, and the primary presenting symptom was dysphagia or abdominal pain in the respective groups. CONCLUSION: The frequency of eosinophilic microabscesses, superficial layering of eosinophils, and epithelial desquamation found in biopsies for patients with EoE-D were twice as frequent compared to those in EoE-AP and statistically significant. The remainder of histologic findings was also higher in EoE-D patients, with the exception of rete peg elongation, but overall were not statistically significant. We found that the epithelial structure of the esophagus in EoE-D has more histological evidence of inflammation compared to EoE-AP. This inflammation can produce dysmotility of the esophagus and/or remodeling of the submucosa leading to dysphagia. This finding, along with differences in treatment outcomes, suggests that EoE-D and EoE-AP may represent different diseases.

Histological Findings for EoE-Dysphasia vs. EoE-Abdominal Pain

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>Eosinophilic Microabscesses (p = 0.003)</th>
<th>Superficial Layering of Eosinophils (p = 0.003)</th>
<th>Epithelial Desquamation (p = 0.004)</th>
<th>BZH (p = 0.055)</th>
<th>Rete Peg Elongation (p = 1.00)</th>
<th>Spongiosis (p = 0.27)</th>
<th>Subepithelial Fibrosis/LP Fibrosis (p = 0.60)</th>
<th>Diffuse involvement, if eos are present (p = 0.67)</th>
<th>Eosinophils diffuse; not confined to rete pegs (p = 0.016)</th>
<th>Degranulation of eosinophils (p = 0.46)</th>
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</thead>
<tbody>
<tr>
<td>EoE-D N = 67</td>
<td>56.7%</td>
<td>44.8%</td>
<td>50.7%</td>
<td>97%</td>
<td>97%</td>
<td>92.5%</td>
<td>61.2%</td>
<td>82.1%</td>
<td>92.5%</td>
<td>71.6%</td>
</tr>
<tr>
<td>EoE-AP N = 67</td>
<td>29.9%</td>
<td>19.4%</td>
<td>25.4%</td>
<td>86.6%</td>
<td>98.5%</td>
<td>85.1%</td>
<td>55.2%</td>
<td>77.6%</td>
<td>76.1%</td>
<td>64.2%</td>
</tr>
</tbody>
</table>

Patients in the EoE-Dysphagia group showed a statistically significant increase of eosinophilic microabscesses, superficial layering of eosinophils and epithelial desquamation compared to EoE-Abdominal Pain group of patients.

11 INCIDENCE OF EOSINOPHILIC ESOPHAGITIS IN CHILDREN; IS THERE A TRUE INCREASE IN INCIDENCE; IS THERE A MONTHLY/SEASONAL VARIATION? Alissa Mayer1, Vaishali Bothra1, Thirumazhisai S. Gunasekaran1,2, Alan Schwartz3, Kiranmai Gorla1, James Berman1,3, 1Pediatric Gastroenterology, Advocate Children's Hospital, Park Ridge, IL; 2Pediatrics, University of Illinois Hospital, Chicago, IL; 3Pediatrics, Loyola Medical Center, Chicago, IL

Most literature show that the incidence of EoE is increasing. It is unclear if this is due to a true increase or because of increased awareness resulting in an increase in the EGD + BX done. A previous study did not find a true increase in the incidence of EoE, but the total numbers of children diagnosed with EoE has increased from more BX done. In addition, it appears unclear whether there are monthly and seasonal variations in the diagnosis of EoE. Aim: Review the total EGDs done over a long period to examine the percentage of BX positive for EoE over time and to see if there is a monthly and seasonal variation in the incidence of EoE. Methods: This retrospective study included all EGDs done in children, age 18yrs or younger, from 01/2003 to 12/2012, at Advocate Children's Hospital-Park Ridge, IL. Pathology reports of EGD were re-reviewed. Monthly incidence was mean of all 10 years. Inclusion: esophageal biopsy containing ≥15 eosinophils in any one of the esophageal biopsies. Results: Total 4761 (mean 476.1) EGDs done in this period and increased steadily from 436 in 2003 to 529 in 2012. During this period 362 patients were diagnosed with EoE based on the above criterion. See Table. Conclusion: With the gradual increase in number of EGDs performed there is a true increase in the incidence of EoE, but this increase was not steady. Monthly incidence showed the least in February followed by June and highest in July followed by September and November. Fall had the highest and Winter the lowest incidence. More long term prospective studies are required to confirm these findings.
Annual Incidence

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Endoscopies</th>
<th>Percentage of EoE Positive (95%CI)</th>
</tr>
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<tbody>
<tr>
<td>2003</td>
<td>436</td>
<td>6.19</td>
</tr>
<tr>
<td>2004</td>
<td>410</td>
<td>7.51</td>
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<tr>
<td>2005</td>
<td>430</td>
<td>4.86</td>
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<tr>
<td>2006</td>
<td>471</td>
<td>8.25</td>
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<td>2007</td>
<td>490</td>
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<tr>
<td>2008</td>
<td>508</td>
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<tr>
<td>2009</td>
<td>510</td>
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<td>2010</td>
<td>484</td>
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<tr>
<td>2011</td>
<td>527</td>
<td>9.26</td>
</tr>
<tr>
<td>2012</td>
<td>529</td>
<td>7.11</td>
</tr>
</tbody>
</table>

Except 2010 there has been a steady increase in the total EGDs. EoE incidence also increased steadily; It was lowest in 2005 (4.86%) and highest 2010 (10.29%). These two years were significantly different than the overall mean incidence.

Monthly Incidence

<table>
<thead>
<tr>
<th>Month</th>
<th>Percentage of EoE Positive (95%CI)</th>
</tr>
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<tbody>
<tr>
<td>January</td>
<td>8.23</td>
</tr>
<tr>
<td>February</td>
<td>4.99</td>
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<tr>
<td>March</td>
<td>6.51</td>
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<td>April</td>
<td>6.82</td>
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<td>May</td>
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<td>September</td>
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Monthly incidence of EoE is highest in July, followed by September and November and the lowest in February followed closely by June. EoE incidence for the seasons are: Fall 9.07%, Summer 8.07%, Spring 6.95% and Winter 6.44%.

12 CHILDREN WITH AUTISM SPECTRUM DISORDER ARE MORE LIKELY TO BE DIAGNOSED WITH CELIAC DISEASE. Cade M. Nylund, Elizabeth Hisle-Gorman, Christine Erdie-Lalena, Gregory H. Gorman, Pediatrics, Uniformed Services University, Bethesda, MD

**Background:** A Swedish nationwide study found that children with autism spectrum disorder (ASD) had 4.6 times the odds of having a positive celiac disease (CD) serologic test. However, the same study, along with others, found no association between ASD and a diagnosis of CD. We sought to evaluate an association between ASD and the diagnosis of CD in a large ambulatory U.S. population.

**Methods:** A retrospective matched cohort study included children ages 0-18 years old enrolled in the Military Health System (MHS) between Oct 2000 and Sept 2013. The MHS database includes all military and civilian providers billing data for child beneficiaries of U.S. uniformed service members. The cohort was created by matching children with ASD to children without ASD in a ratio of 1:5 by birthdate (within 45 days), sex, and period of enrollment time. ASD was defined as any patient with 2 or more International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnoses for ASD. A diagnosis of CD was defined by the combination of the ICD-9-CM diagnostic code "579.0" and any previous Current Procedural Terminology code for esophagogastroduodenoscopy (EGD).
Poisson regression was utilized to calculate rate ratios for EGD and for CD and adjusted rate ratio for CD.

**Results:** There were 48,810 subjects with ASD and 244,050 controls representing a total of 2,588,813 person-years. A total of 4,385 subjects had an EGD and 236 of these had CD. Patients with ASD were more likely to have an EGD (1,884; 3.9 per 100) than controls (3,501; 1.4 per 100; rate ratio [RR] 2.69; 95% confidence interval [CI], 2.54-2.86; \(P <0.001\)) and children with ASD also had slightly increased absolute number of EGDs (RR 1.13; 95% CI, 1.05-1.09; \(P<0.001\)). The rate of CD was higher among the ASD group (107; 22 per 10,000) than the controls (129; 5 per 10,000; RR 4.15, 95% CI, 3.21-5.36; \(P <0.001\)). After adjusting for the number of EGD, children with ASD continued to have a significantly increased rate of diagnosed CD (adjusted RR 1.53; 95% CI, 1.19-1.98).

**Conclusions:** Children with ASD are more likely to have a diagnosis of CD compared to sex and age adjusted controls. Children with ASD are also more likely to have an EGD performed. The increased rate of CD persists after adjusting for the increased rate of EGDs in the ASD population suggest an association between ASD and celiac disease. Further studies are needed to evaluate this association.

13 EPIDEMIOLOGICAL DETERMINANTS OF ESOPHAGEAL FOOD IMPACTION AND PREVALENCE OF ESOPHAGEAL EOSINOPHILIA IN CHILDREN WITH ESOPHAGEAL FOOD IMPACTION REQUIRING ENDOSCOPIC REMOVAL: A RETROSPECTIVE STUDY. Girish Hiremath\(^1\), Fatimah Hameed\(^1\), Ann Pacheco\(^1\), Sridevi Devaraj\(^3\), Carla Davis\(^2\), Robert Shulman\(^1,4\), Anthony Olive\(^1\), \(^1\)Pediatric Gastroenterology, Hepatology and Nutrition, Texas Children's Hospital, Baylor College of Medicine, Houston, TX; \(^2\)Pediatric Allergy and Immunology, Texas Children's Hospital, Baylor College of Medicine, Houston, TX; \(^3\)Pathology, Texas Children's Hospital, Baylor College of Medicine, Houston, TX; \(^4\)Children's Nutrition Research Center, Houston, TX

**BACKGROUND:** Esophageal food impaction (EFI) requiring emergent endoscopic removal (EFI-ER) is a common gastrointestinal emergency. Esophageal malformation with/without corrective surgery and esophageal dysmotility are known risk factors for EFI-ER. Recent evidence suggests that eosinophilic esophagitis (EoE) may possibly be a risk factor for EFI. EoE is a chronic, clinicopathological condition characterized by intense eosinophilic infiltration in the esophagus (EE) which is normally devoid of eosinophils. To-date there is limited information regarding EFI-ER and EE among children.

**AIMS:** To examine the epidemiological determinants of EFI in children, and to investigate the prevalence of EE in children presenting with EFI-ER to an emergency center in a tertiary care hospital.

**METHODS:** Using ICD-9 (935.1) and CPT codes (43215, 43247, 31511) we screened our electronic medical (EPIC) and endoscopy (CORI) records and identified 985 children presenting to Texas Children's Hospital Emergency Center (TCH EC) with esophageal impaction between Jan 2007 and Dec 2013. Demographics, clinical information, endoscopy data, biopsy rates and EE rates were analyzed using Stata 10.2.

**RESULTS:** Forty-seven (5%) children had EFI-ER and contributed towards 59 EFI events, with 9 (19%) children experiencing ≥2 EFI's. The median age was 10 years (range:1-17) with the majority being male (79%), Caucasian (59%) children. Difficulty in swallowing was the most common presenting symptom, and meat was the most common impacted food. Prior history of esophageal corrective surgery and/or dysmotility was noted in 17 (36%) children of whom 4 (24%) had ≥2 impactions. Of the remaining 30 (64%) children with EFI-ER, abnormal endoscopic features were noted in 18 (60%) children. Esophageal biopsies (median=2; range=1-9) were obtained from 18 (60%) children at the time of EFI removal, and biopsies obtained from 13 (72%) children revealed EE (median eosinophils/high power field=18; range=1-70). The endoscopic removal was performed by Gastroenterology (GI), Surgery (SX) or Otolaryngology (ENT) sub-specialities based on a pre-determined schedule. The endoscopic removal and biopsy rates were significantly higher in GI (53% and 84%, respectively) compared to the SX (23% and 3%, respectively; \(P=0.04\)) or ENT (23% and 1%, respectively; \(P=0.02\)) sub-specialities. The EE rates in children presenting with EFI increased from 46% in Jan 2007-Dec 2010 to 53% in Jan 2011-Dec 2013 in the setting of comparable overall biopsy rates (50%) during these time frames.

**DISCUSSION:** Our data suggest that esophageal scarring and/or dysmotility accounts for about 1 in 3 children utilizing emergency services for EFI. EE is likely a major contributor of EFI-ER in children without any esophageal scarring and/or dysmotility. The rates of EFI at our center have increased over 6 years and this could be related to increasing prevalence of EE in children. Efforts to educate physicians to obtain multiple esophageal biopsies during endoscopic disimpaction and a follow-up upper endoscopy with biopsies after 8 weeks of high-dose acid blockage therapy to exclude other causes of EE (e.g. reflux esophagitis) to determine precise relationship between EoE and EFI-ER are warranted.
QUALITY OF EVIDENCE FOR EOSINOPHILIC ESOPHAGITIS AS A RISK FACTOR FOR ESOPHAGEAL FOOD IMPACTATION REQUIRING ENDOSCOPIC REMOVAL IS LIMITED: A SYSTEMATIC REVIEW AND POOLED ANALYSIS. Girish Hiremath1, Fatimah Hameed1, Ann Pacheco1, Sridevi Devaraj4, Anthony Olive1, Carla Davis2, Robert Shulman12, 1Pediatric Gastroenterology, Hepatology and Nutrition, Texas Childrens Hospital, Baylor College of Medicine, Houston, TX; 2Children’s Nutrition Research Center, Houston, TX; 3Pediatric Allergy and Immunology, Texas Children’s Hospital, Baylor College of Medicine, Houston, TX; 4Pathology, Texas Children's Hospital, Baylor College of Medicine, Houston, TX

BACKGROUND: The 2011 Updated Consensus statement describes eosinophilic esophagitis (EoE) as a clinicopathological condition, characterized by eosinophil-predominant mucosal inflammation localized to the esophagus due to an underlying allergen/immune process, and not due to other conditions also known to cause esophageal eosinophilia (e.g. reflux esophagitis). EoE affects all ages, worldwide. There is growing concern that EoE is a risk factor for esophageal food impaction requiring endoscopic removal (EFI-ER).

AIMS: To critically review existing literature and perform pooled-analysis of evidence linking EoE and EFI-ER.

METHODS: MEDLINE and SCOPUS databases were searched using a combination of terms - 'esophageal impaction' ‘food bolus impaction’ ‘esophageal eosinophilia' and ‘eosinophilic esophagitis', from inception until April 2014. We included publications in English which provided the number of EFI-ER, proportion biopsied during the procedure, and proportion of biopsied patients diagnosed with EoE - as defined by each author in the included studies. Fixed and random effects models were designed for overall and sub-group analyses [age (children vs. adult); location of the study (USA vs. non USA)] of proportions. All analyses, including the test for heterogeneity among the studies were performed using MedCalc 12.5.

RESULTS: In all, 458 publications were identified during our initial search. Of these, 9 publications met our inclusion criteria [9 retrospective studies, 8 prospective study], with research period ranging between 1988 and 2010. Two publications accounted for 5 independently analyzable reports resulting in a total of 12 analyzable studies. Measures taken to exclude other causes of esophageal eosinophilia were not adequately described in any of the included studies. Given marked heterogeneity (≥75%), results from random effects model are provided. The overall biopsy rates during EFI removal (Cases: N=953) was 44% (95% CI: 30-59%) and the overall EoE rate among those biopsied (N=363) was 47% (37-57%). In sub-group analyses, the biopsy rates between children (N=182) and adults (N=784) were comparable [50% (43-57%) vs. 50% (27-72%)], while the EoE rates among children (N=86) were higher compared to adults (N=281) [50% (33-66%) vs. 44 (31-59%)]. Although biopsy rates were lower in the studies conducted in USA (N=519) compared to those conducted outside USA (N=447) [39% (24-55%) vs. 50% (27-72%)], the EoE rates were higher in studies conducted in the USA (N=146) compared to those conducted outside USA (N=234) [58% (50-66%) vs. 33% (18-50%)].

DISCUSSION: Using the author's definition, it appears that low biopsy rates during EFI-ER may result in underestimation of the relationship between EoE and EFI-ER, and EoE may be the most frequent reason for EFI-ER in USA. However, the quality of existing evidence is limited by small observational studies, significant variability between the studies, and lack of clarity on measures taken to exclude other causes of esophageal eosinophilia. Prospective studies designed to obtain multiple esophageal biopsies during EFI-ER and to acquire follow-up biopsies ruling out other causes of esophageal eosinophilia would allow us to understand the precise relationship between EoE and EFI-ER.

PEDIATRIC CELIAC DISEASE TRENDS - SHOULD WE HAVE NEWER GUIDELINES? Mohini G. Patel, Artik Alper, Anthony F. Porto. Yale University, New Haven, CT

Objective: Celiac Disease (CD) is now recognized as a common genetically determined disease in childhood. With the rise in the incidence in the last decade attributed to better and more prompt screening, we continue to find varying practices between different providers in diagnosing and monitoring CD patients at our institution. We created a survey and sent it to the pediatric GI community to learn more about trends in the evaluation and care of children with CD.

Methods: An 18 question survey was sent to members of the pediatric GI community via the webmail list server. Questions looked at demographics, markers used for diagnosing patients, number of biopsies taken at endoscopy, monitoring patients after a diagnosis is made, screening for family members and screening for other high risk populations. We had 239 responders.

Results: Of the 239 responders, 148 (61.9%) were in academic practice, 62 (25.9%) were in a hospital-based practice, 4 (1.7%) were solo practitioners, and 25 (10.5%) were in private practice. 185 (78.1%) responders were attending's, and of them 92 (48.7%) were in practice more than 10 years. We found that most people will diagnose CD on biopsies. However, 82 people (34.7%) will diagnose patients on laboratory markers only, with most of these practitioners doing this if the TTG level is 10 times the upper limit of normal. However, some practitioners will diagnose patients based only on serology if the parents refuse endoscopy even when the TTG level is not 10 times the upper limit of normal. When evaluating a patient for CD, most people will obtain between 5-6 duodenal biopsies (53.81%), with 21.19% obtaining >6 duodenal biopsies. When obtaining biopsies in the duodenum, most people will biopsy the second portion
of the duodenum and duodenal bulb, however 85 (35.9%) will biopsy distal to the ampulla as well. When screening children under 2 years of age for CD, the majority of practitioners continue to use total IgA (209 people, 89.3%) and TTG IgA (212 people, 90.6%) with only 113 practitioners (48.3%) using deamated anti-gliadin IgA and 88 practitioners (7.7%) using deamated anti-gliadin IgG. For IgA deficient children, 26 practitioners (12%) would proceed directly to an endoscopy without any further laboratory investigations. Sixty-one providers (28.2%) indicated that they check celiac genetic markers, HLA DQ-2 and 8, and in IgA deficient children while approximately 10% check for genetic markers in routine screening of children and family members. Once a patient is diagnosed with CD, there is no consensus on how frequently to monitor TTG levels and vitamin levels. Conclusions: Our survey findings show that the diagnosis, treatment and monitoring of patients with CD vary among practitioners. The last NASPGHAN guidelines were published in 2005. Newer guidelines would likely improve diagnostic accuracy and decrease the impact burden on patients and their families.

16 physical growth evaluation in patients with rectal bleeding as a form of presentation of cow milk protein allergy (CMPA), comparison between amino acid formula (AAF) and extensively hydrolyzed protein formula (eHF), Cecilia Tennina, Maria Anabel Tilli, Christian G. Boggio Marzet, Pediatric Gastroenterology & Nutrition Section, Hospital Gral. de Agudos "Dr. Ignacio Pirovano", Buenos Aires, Argentina

Introduction: Isolated rectal bleeding in childhood is a presentation form of CMPA, usually has a benign course and responds satisfactorily to exclusion diet and the use of hypoallergenic formulas. Several studies showed a decrease in growth indicators, both weight and height for age in children with CMPA. Aim: To evaluate if there are any differences in physical growth in children with confirmed diagnosis of CMA who were treated with either AAF or eHF.

Methods: All children from 2009-2013 who presented to the Pediatric Gastroenterology Section at Pirovano Hospital with a diagnosis of CMA with rectal bleeding as a first manifestation were included. Treatment was provided depending on the treating physician. Measurements of height and weight at the moment of diagnosis were obtained as well as 3, 6 and 9 months after treatment was initiated.

Results: 38 patients were included. Treatments provided were AAF (n=8), eHF (n=7) and AAF plus maternal exclusion diet (n=23). The basal median for height and weight were similar for the three groups initially (p=0.79 y p=0.49 Kruskall Wallis Test). After 9 months of treatment, the AAF group had a statistically significant increase median weight different from the other groups (p=0.03 Kruskall Wallis Test).

Conclusion: The use of AAF in patients with CPMA whose first manifestation was rectal bleeding resulted in a statistically significant increase in median weight after 9 months compared with the other two treatments evaluated.

17 esophageal dilation is an effective and safe treatment of pediatric eosinophilic esophagitis-associated stenosis. Abdulrahman A. Al-Hussaini, Pediatric Gastroenterology and Hepatology, King Fahad Medical City, Riyadh, Saudi Arabia

Background and objective: Esophageal narrowing resulting from eosinophilic esophagitis (EoE) presents management challenges because several case series in adults have suggested an increased risk of complications associated with esophageal dilation. Data on management of esophageal narrowing associated with EoE in children are scanty. We report the largest pediatric case series with the aim to assess the safety and effectiveness of esophageal dilation in pediatric EoE.

Patients and Methods: Children diagnosed as having EoE, during the period from 2004 to 2013, were reviewed for presence of esophageal narrowing. An esophageal narrowing limited to one portion of esophagus defined a short segment narrow caliber, a narrowing involving two or more portions defined a long segment narrow caliber, while a very short stenosis (< 1cm in length) defined esophageal stricture. The characteristics of the narrowed esophagus, therapeutic approach, clinical outcome, and complications were reviewed.

Results: Of the 47 pediatric EoE cases diagnosed during the study period, 10 cases (8 males; median age 9 years, range 4-12) were identified with esophageal narrowing (21%), which constituted 14% of the total cases of esophageal stenosis presenting to our center (10/70). All 10 cases presented with dysphagia/ intermittent food impaction. Six had short segment narrow caliber esophagus and 4 had long segment narrow caliber esophagus (median length of the narrowing was 4 cm, range 3-14 cm). Three cases with narrow caliber esophagus also had esophageal stricture 2-3 cm below upper esophageal stricture. Nineteen dilation sessions were performed in all cases using Savary dilator. Esophageal diameter improved from median 7 mm to median 13.4 mm. Good response was obtained in all cases. Following the dilation procedure, longitudinal esophageal mucosal tear occurred in all cases without esophageal perforation or chest pain.

Conclusions: Esophageal dilation using Savary dilator is safe and highly effective in management of esophageal narrowing associated with EoE in children.
18 HOW DOES ESOPHAGUS LOOK ON BARIUM ESOPHAGRAM IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS? Abdulrahman A. Al-Hussaini1, Amany Abozeid2, Abdul Hai1, 1Radiology, King Fahad Medical City, Riyadh, Saudi Arabia; 2Pediatric Gastroenterology and Hepatology, King Fahad Medical City, Riyadh, Saudi Arabia

Background and objective: The clinical, endoscopic and histologic findings of EoE are well characterized, however there have been limited data regarding the radiologic findings of eosinophilic esophagitis in children. In this retrospective study, we report the radiologic findings of eosinophilic esophagitis on barium swallow study and correlate them with the endoscopic findings.

Methods and materials: We identified children diagnosed with EoE in our center from 2004 to 2013. EoE was defined as esophageal mucosal infiltration with a peak eosinophil count ≥ 15 eosinophils/high-powered field in biopsies obtained from multiple levels of esophagus. EoE cases who underwent barium swallow study within 1 week prior to upper endoscopy, were included in the study. The radiographs were independently reviewed by 2 pediatric radiologists, blind to clinical information. Clinical and endoscopic data were collected by retrospective chart review.

Results: During the study period, 47 pediatric EoE cases were diagnosed; 22 cases had barium swallow study done as part of the diagnostic approach (median 8 years; age range 4-12 years). All children presented with dysphagia. Twelve children had abnormal radiologic findings of esophagus (34.5%): rings formation (n=4), diffuse irregularity of mucosa (n=8), fixed stricture formation (n=3), and narrow-caliber esophagus (n=10). Barium swallow study failed to show ring formation visualized on upper endoscopy in 10 patients.

In conclusion: The sensitivity of barium contrast radiography as a diagnostic test for EoE appears to be low. With the exception of stricture formation and narrow-caliber esophagus, our data show poor correlation between radiologic and endoscopic findings.

19 ZONULIN RELATED HAPTOGLOBIN 2-2 GENOTYPE INCREASES SUSCEPTIBILITY TO INTESTINAL INFLAMMATION IN A MOUSE MODEL. Craig Sturgeon1,2, Jinggang Lan1, Shu Yan1, Alessio Fasano1, 1Pediatrics, Massachusetts General Hospital, Charlestown, MA; 2Graduate Program in Life Sciences, University of Maryland, Baltimore, Baltimore, MD

Background: An increase in intestinal permeability has recently been proposed to be the third element, along with genetic makeup and environmental triggers, in the pathogenesis in allergic, inflammatory and autoimmune disorders. Zonulin is a protein that has been discovered to regulate intestinal permeability through reversible disassembly of tight junctions. We recently have identified human zonulin as the precursor to haptoglobin (HP)-2. HP has two genotypes: HP-1 and HP-2 arising from duplication of the HP alpha chain that occurs only in humans. It has been reported that HP2 is linked to a series of immune mediated diseases and that HP2 homozygosis is associated to a more severe clinical outcome. Aim: To use a murine model to establish whether HP2 homozygosis increases susceptibility to inflammation.

Methods: We acquired mice that have an artificial mutation to replicate the human HP2 gene. We administered DSS to these HP2 mice and C57Bl/6 to replicate the HP1-1 and HP2-2. We administered 3% DSS for 7 days and either euthanized after 7 days or switched the animals to water for 7 days of recovery. Animals were weighed daily and after euthanasia tissue was fixed in 4% paraformaldehyde, paraffin embedding and H&E stained for analysis. Results: After 7 days the C57Bl/6 animals on DSS had an average weight of 90.5% their starting weight and the HP2 an average of 86.5% (p>0.05). Histological analysis of the intestinal tissues showed no difference in the ileum between DSS and water or between HP2 and C57Bl/6 animals. The colon of the HP2 animals had a trend towards more damage and inflammation but did not reach statistical difference due to high variance of samples. After the 7 days of DSS treatment and 7 days of recovery the C57Bl/6 animals showed good recovery with a final weight of 92.1% their starting weight after a low of 78.8% on day 9 (day 2 of recovery) while the HP2 mice saw a final weight of 81.5% after a low of 66.9% on day 12 (day 5 of recovery). One of the HP2 mice, which received the DSS treatment, died on day 13. Histological analysis of the intestinal tissues showed no statistical difference in the ileum or the colon. But the colon of one of the two HP2 mice treated with DSS did not recover. Therefore we can conclude that HP2 mice are more susceptible to DSS treatment, they show a decrease in body weight and worse histology after 7 days as well as do not recover as efficiently as C57Bl/6 animals. Two-thirds of our HP2 recovery animals did not recover; one died after 12 days and the other while body weight did recover their colon was absent of crypts, which will never be able to recover. Conclusions: We show, using a knock-in HP2 mouse model, that HP2-2 genotype is associated to increase susceptibility to intestinal damage following DSS treatment.

20 EVERY OTHER DAY DOSING OF ORAL VISCOUS Budesonide IS NOT EFFECTIVE IN THE MANAGEMENT OF EOSINOPHILIC ESOPHAGITIS. Eitan Rubinstein, Peter Ngo, Douglas McDonald, Elizabeth J. Hait, John J. Lee, Boston Childrens Hospital, Boston, MA

Introduction: Eosinophilic esophagitis (EoE) is a clinicopathologic disorder characterized histologically by esophageal eosinophilia (>15 peak eosinophils/high power field). Daily topical steroids have been shown to be an effective
Eosinophilic esophagitis (EoE) is an emerging chronic inflammatory disease characterized by eosinophil infiltration of the esophageal tissue. Management options include attempts to decrease the dose of topical steroids delivered on a daily basis, but this approach has not been successful in maintaining remission. We examined if reducing frequency of oral viscous budesonide (OVB) to alternate day regimens would be effective in controlling esophageal eosinophilia.

Methods: Retrospective review of patients followed in the Boston Children's Hospital Eosinophilic Gastrointestinal Disease program was performed. Patients were selected if they had been diagnosed with EoE based on consensus statement guidelines and shown adequate healing on standard OVB dosing (1 or 2 mg based on age). Patients selected for review had been offered and accepted a reduction in frequency of their standard daily dose to a Monday, Wednesday and Friday (MWF) regimen.

Results: Eight patients diagnosed with EoE based on consensus statement guidelines with peak eosinophil counts ranging from 20 to 120 eosinophils/high power field (HPF) were identified. Seven patients demonstrated healing of previously demonstrated EoE on daily dosing of OVB with peak eosinophils from 0 to 10 eosinophils/HPF (median 0 eosinophils/HPF). Six of the 7 had recurrence of eosagastitis with peak eosinophils ranging from 25 to 115 per any HPF (median 40) on MWF dosing. One patient showed partial response to MWF OVB dosing with maximum eosinophils of 14 per HPF. One additional patient who started on MWF dosing of budesonide, had healing on this regimen, but had never been trialed on daily OVB.

Conclusion: Reduced frequency dosing of OVB does not seem to be an effective management strategy for treatment of EoE. Prospective studies with larger number of patients may be necessary to confirm our observation.

21 IMPACT OF HUMAN MATURATION UPON ESOPHAGEAL FIBROBLAST FUNCTION IN EOSINOPHILIC ESOPHAGITIS. Amanda B. Muir1, Kara Dods1, Alain Benitez1, Yuli Noah1, Maureen DeMarshall2, Gary Falk2, Mei-Lun Wang1, Rebecca Wells1, Hiroshi Nakagawa2, 1GI, Children's Hospital of Philadelphia, Philadelphia, PA; 2GI, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

Background/Aims: Eosinophilic esophagitis (EoE) is an allergic disorder that universally leads to dysphagia and esophageal fibrosis characterized by excessive deposition of extracellular matrix (ECM) components such as collagen. Current treatments, including corticosteroids, are aimed at reducing eosinophil burden and symptoms of esophageal dysfunction. Variability in EoE symptoms, ranging from GERD symptoms and abdominal pain in children to recurrent esophageal food bolus impactions in adolescents and adults may reflect the natural history of the disease, though mechanisms by which esophageal fibrosis progresses in EoE are unknown. It has been shown that TGFβ-activated esophageal fibroblasts are effector cells in EoE-associated fibrosis. In other models, others have also shown that fibroblast contraction is irreversibly enhanced by increased extracellular matrix stiffness, reflecting observations that reversal of fibrosis is difficult to achieve in vivo. We hypothesize that aging esophageal fibroblasts have enhanced activation, extracellular matrix production, and contractility and that the differences between pediatric and adult fibroblasts will be further altered in EoE. Methods/Results: Following informed consent, primary esophageal fibroblasts were isolated from esophageal biopsies from EoE and control subjects ranging from 6-52 years of age, and were used at passages 3-7. Following 7 days of TGFβ stimulation, all fibroblast cohorts had enhanced αSMA and collagen mRNA expression, suggesting activation of myofibroblasts, essential in fibrosis. Interestingly, adult EoE fibroblasts had enhanced collagen expression compared to control adult fibroblasts and both pediatric cohorts. Fibroblasts from subjects with a history of food impaction had enhanced constitutive collagen expression compared to subjects without. To investigate contractility, esophageal fibroblasts were embedded in collagen gels, and the diameter of floating gels was measured over 7 days. Pediatric control (n=7) and pediatric EoE (n=5) fibroblasts contracted by 23.6% and 25.5% respectively, while TGFβ-stimulated gels containing pediatric fibroblasts had enhanced contractility [33% (control), 32.5% (EoE)]. Interestingly, adult control fibroblasts (n=4) had enhanced contractation (40%) in the unstimulated state and this effect was enhanced with the addition of TGFβ (48.7%). However, adult EoE subjects (n=7) exhibited significantly less baseline contraction than their control counterparts (21.3%). Co-culture with budesonide enhanced gel contraction, leading to 50.5%(adult control), 34.5%(pediatric control), 36.2%(adult EoE), and 40% (pediatric EoE) contraction compared to day 0 gels. Conclusions: Esophageal fibroblasts become more contractile during human maturation. Adult EoE fibroblasts have increased collagen expression and secretion compared to normal controls. Fibroblast contraction was decreased in adults with EoE, which may reflect irreversible fibroblast alterations induced by progressive tissue stiffness in EoE. Paradoxically, budesonide enhanced fibroblast contractility. Our results implicate maturational changes in esophageal fibroblast contractility in the pathogenesis of EoE fibrosis, and suggest that corticosteroids may play a role in tissue remodeling in EoE.

22 BIOLOGICAL ASSAY TO CHARACTERIZE ESOPHAGEAL LAVAGE FLUID FROM CHILDREN WITH EOSINOPHILIC ESOPHAGITIS. Anu Maharjan2, Wael N. Sayej1,2, Antoine Menoret2, Marina Fernandez1, Francisco Sylvester1, Jeffrey Hyams1, Anthony Vella1, 1Digestive Diseases, Hepatology and Nutrition, Connecticut Children's Medical Center, Hartford, CT; 2Immunology, University of Connecticut Health Center, Farmington, CT

Background: Eosinophilic esophagitis (EoE) is an emerging chronic inflammatory disease characterized by eosinophil...
inflammation. In our preliminary work, we have identified a cytokine network that includes IL-8, which distinguished EoE patients or active inflammation from those in remission or normal controls. In this study, the collection of esophageal lavage fluid from EoE active, EoE remission, and normal patients allowed us to examine the molecular factors that are unique for each patient group.

**Aim:** To identify molecular factors associated with EoE that initiate inflammation in the esophageal epithelium.

**Method:** Esophageal lavage fluid (ELF) from 1 EoE active, 2 EoE remission, and 2 controls were fractionated by FPLC using anion-exchange chromatography (HQ column). The monocyte cell line, MonoMac6 was cultured in the presence of the collected lavage fractions for 24 hours. After incubation, the supernatants were analyzed for the presence of IL-8 by ELISA.

**Results:** There was a distinct pattern of IL-8 production from ELF of patients with EoE remission versus EoE active or control. Esophageal lavage fluid fractions tested had decreased secretion of IL-8 in remission patients when compared to patients with active EoE or normal controls.

**Conclusion:** The decreased secretion of IL-8 in remission patients when compared to EoE active or normal shows the dampening of immune stimulation under the current EoE treatment. This study shows that it is possible to obtain specific cellular activity from patient esophageal lavage fluid and identify potential factors that trigger esophageal inflammation.

### Clinical/Translational Inflammatory Bowel Disease

#### S1P SIGNALING IN INFLAMMATORY BOWEL DISEASE AND COLITIS-ASSOCIATED CANCER: PRECLINICAL STUDY RESULTS AND PRELIMINARY FINDINGS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS. Emile Degagne, Yasmin Ahmed, Elizabeth Gleghorn, Alexis Rodriguez, K. T. Park, Takiyah Wilson, Ashish Patel, Ginny Gildengorin, Julie Saba, Lucile Packard Children's Hospital at Stanford University, Palo Alto, CA; UCSF Benioff Children's Hospital Oakland, Oakland, CA; Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX

**INTRODUCTION:** S1P lyase (SPL) irreversibly degrades the bioactive sphingolipid S1P. SPL is highly expressed in enterocytes but downregulated in colon cancer. We hypothesize that in an inflammatory environment, SPL downregulation in intestinal epithelial cells acts as an early event leading to colitis-associated cancer (CAC) and that plasma S1P levels and expression of S1P-related genes could serve as new biomarkers. METHODS: We generated conditional SPLGutKO mice and treated them with AOM/DSS to promote CAC and determined the disease activity index, tumor number, STAT3 and STAT3-related targets activity. We treated WT mice with sphingadienes, as chemotherapeutic agent, and measured disease activity index, tumor number, STAT3 activity and S1P levels. We recruited patients undergoing endoscopy and collected plasma and biopsie from colon. We measured plasma S1P, S1PR1-5, Sphk1-2, Sgpp1-2, SPL and ORMDL3 mRNA expression. RESULTS: SPLGutKO mice exhibited more severe colitis and higher tumor incidence than controls. Activation of STAT3 and its transformation-inducing cell signaling pathway was augmented in SPLGutKO mice. Oral sphingadiene treatment induced colonic SPL expression and reduced STAT3 signaling, colitis and colon cancer. In a preliminary analysis of 50 IBD patient and control blood and tissue samples (out of a projected recruitment of 150 total), plasma S1P levels were found to increase with disease severity, and Sphk1, S1PR1, S1PR2, S1PR4 and ORMDL3 mRNA expression are increased in IBD colon tissue compared to controls. CONCLUSION: Our results provide a molecular basis for S1P-induced transformation, specifically through activation of STAT3-dependent signaling. Further, our data establish that SPL is a critical modulator of inflammation-associated colon carcinogenesis that can be targeted for therapeutic benefit. Our results suggest that dietary sphingolipids may augment or prevent colon cancer, depending upon their ability to be metabolized to S1P. Finally, we showed that plasma S1P levels and S1P-related genes expression in colon tissue can be used as novel biomarkers of IBD.

#### DUODENITIS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE. Arik Alper, Danilo Rojas-Perez, Steven Hardee, Sandra Escalera, Raffaella Morotti, Dinesh S. Pashankar, Yale University, New Haven, CT

**Introduction:** Duodenitis is not uncommon in children with inflammatory bowel disease (IBD). Previous studies report a prevalence of duodenitis of 31-33% and 3-23% in children with Crohn's disease (CD) and ulcerative colitis (UC), respectively. However, there is a lack of information about specific histological features of duodenitis in children with IBD, particularly regarding differences from duodenitis due to other causes and associated esophagitis or gastritis. Aims: 1. To assess the prevalence and pathological characteristics of duodenitis in children with IBD and to compare those with non-IBD duodenitis. 2. To assess esophageal and gastric pathology associated with duodenitis in children with IBD. METHODS: We retrospectively studied all children who had an upper endoscopy and biopsies in our institution from 2008 to 2012. We reviewed all histopathology reports for duodenitis, gastritis and esophagitis, defined by the presence of an inflammatory infiltrate. We selectively reviewed the medical charts of all the patients with IBD and duodenitis, and collected demographic, clinical and endoscopic data. We reviewed few randomly selected biopsies and compared the histological features of duodenitis in children with IBD to children without IBD. RESULTS: The study included 3064 endoscopies that were performed over a 5-year period. Overall, 362 (12%) children had duodenitis.
review showed that 315 children with IBD had an upper endoscopy performed during this period of time, and 58 (18%) had histological evidence of duodenitis. There were 209 children with CD and 106 children with UC. Duodenitis was noted in 47 patients (22%) with CD and 11 patients (10%) with UC (P=0.009 for the difference). The mean age of these children with duodenitis was 13.1 ± 3.8 years and 57% were boys. Most common indications for endoscopy included abdominal pain (40%) and diarrhea (36%). In 62% of the endoscopies, the mucosa appeared macroscopically normal despite histological evidence of duodenitis. The table below shows the presence of associated gastritis and esophagitis in children with CD and UC. We compared the histological findings of randomly selected 27 IBD cases (22 with CD and 5 with UC) with an age matched control group (39 with celiac disease and 47 with non specific duodenitis). IBD and celiac patients had relatively similar pathological findings such as villous blunting and intra epithelial lymphocytes. Cryptitis was most frequently seen in patients with IBD compared to the control group (P<0.0001), with no significant difference between UC and CD. Duodenal eosinophilia (>20 eosinophils/hpf) was most frequently seen in patients with UC compared to other groups (P=0.001). Conclusions: Although less frequent than in patients with CD, duodenitis has a prevalence of 10% in children with UC (vs. 21% with CD). Correlation between macroscopic appearance of the duodenum and the histological findings is relatively poor. Gastritis was seen in both UC and CD, but esophagitis was seen only in children with CD. Cryptitis was seen equally in both CD and UC. Duodenal eosinophilia was more common in UC.

<table>
<thead>
<tr>
<th></th>
<th>Crohn’s (n=47)</th>
<th>UC (n=11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagitis</td>
<td>13 (28%)</td>
<td>0 (0%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Gastritis</td>
<td>41 (87%)</td>
<td>10 (91%)</td>
<td>0.736</td>
</tr>
</tbody>
</table>

29 A HISTOLOGICAL SCORING SYSTEM FOR ILEITIS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE. Benjamin Sahn1, Vera De Matos2, Eduardo Ruchelli1, Samuel Masur1, Andrew Klink1, Robert Baldassano1, David Piccoli1, Pierre Russo1, Petar Manu01, 1The Children's Hospital of Philadelphia, Philadelphia, PA; 2CS Mott Children's Hospital - University of Michigan, Ann Arbor, MI

Introduction: Pediatric Crohn disease (CD) and ulcerative colitis, (UC) may present with a confluent colitis and ileitis without clear distinction between CD ileitis and backwash ileitis (BWI). Differentiating between these has medical and surgical implications. The primary aim of the study was to determine the probability of ileitis representing CD based on clinical and histological features. Secondary aims were to describe the association of various biopsy features with Crohn ileitis or BWI and to demonstrate reproducibility of a semi-quantitative scoring system for ileitis.

Methods: A retrospective review of 100 newly diagnosed patients with IBD between 2000 and 2010 was performed. Inclusion criteria were: (1) age 1-18 years, (2) histologic left-sided, extensive or pancolitis, (3) histologic ileitis, (4) diagnosed and followed at our center for minimum of 2 years. Exclusion criteria included: (1) identification of a co-existing alternative cause of ileitis at diagnosis and (2) use of any medication to treat IBD at time of diagnosis. Two pathologists designed a scoring system for ileitis (table) and reviewed ileal specimens blinded to clinical information.

Results: The IBD phenotypes at diagnosis were CD (n=84), UC (n=13), IC (n=3). Pancolitis was present in 88% and left sided colitis in 12%. The findings of crypt distortion, lamina propria (LP) expansion by mononuclear cells, and acute LP inflammation combined with four clinical variables in multivariate regression analysis had adequate discriminative validity when comparing the mean probability of a final CD diagnosis between CD and not-CD groups (0.90 vs. 0.59, p value < 0.001). In univariate analysis, the presence of crypt distortion had an odds ratio (OR) of 11.7 (p = 0.024, 95% CI 1.4-88.1) and LP expansion had an OR of 8.6 (p = 0.007, 95% CI 1.8-40.7) for the diagnosis of CD. Pyloric metaplasia and erosions / ulcers were seen in 9/86 (11%) and 21/86 (24%) of CD ileitis respectively, and not seen in those without CD. The inter-rater and intra-rater agreements for the presence or absence of each histologic feature had kappa coefficients ranging from 0.24 - 0.59 for most features and 1.0 for granulomas.

Conclusions: The described statistical model incorporating a novel histological scoring system for ileitis in IBD and clinical variables adequately discriminates between the presence and absence of Crohn disease in children who present with confluent colitis and ileitis. Ileal crypt distortion and LP expansion were associated with CD. Pyloric metaplasia and focal erosions or ulcers were only observed in CD. Fair to moderate observer agreement was found between two pathologists grading the presence or absence of histological findings, with perfect agreement for granuloma detection.
### Histological Scoring System for Ileitis

<table>
<thead>
<tr>
<th>Histological Feature</th>
<th>Grading</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crypt distortion</td>
<td>None / Moderate / Severe</td>
</tr>
<tr>
<td>Villus blunting</td>
<td>None / Mild / Moderate / Severe</td>
</tr>
<tr>
<td>Acute inflammation in LP</td>
<td>None / Focal / Diffuse</td>
</tr>
<tr>
<td>Acute inflammation in epithelium</td>
<td>None / Surface / Cryptitis / Crypt abscess</td>
</tr>
<tr>
<td>LP expansion by mononuclear cells</td>
<td>Normal / Moderate / Marked</td>
</tr>
<tr>
<td>Erosions/ Ulcers</td>
<td>Absent / Present</td>
</tr>
<tr>
<td>Pyloric metaplasia</td>
<td>Absent / Present</td>
</tr>
<tr>
<td>Granulomas</td>
<td>Absent / Present</td>
</tr>
</tbody>
</table>

30 **ASSOCIATIONS BETWEEN DISEASE ACTIVITY, PARENT DEPRESSIVE SYMPTOMS, AND HEALTH-RELATED QUALITY OF LIFE AMONG YOUTH WITH INFLAMMATORY BOWEL DISEASE.** Bonney Reed-Knight1,2, Ronald L. Blount1, Jeffery D. Lewis3,4, 1Transplant Services, Children's Healthcare of Atlanta, Atlanta, GA; 2Emory University School of Medicine, Atlanta, GA; 3Children's Center for Digestive Health Care, Atlanta, GA; 4Children's Healthcare of Atlanta, Atlanta, GA; 5Psychology, University of Georgia, Athens, GA

**PURPOSE:** Health-related quality of life (HRQOL) is a multidimensional construct, influenced by disease, individual, and environmental factors. Greater disease activity has understandably been demonstrated to predict poorer HRQOL, though disease status alone does not fully account for HRQOL.

**METHODS:** Participants include 89 adolescents ages 11-18 (M = 14.68, SD = 2.30) diagnosed with IBD and their caregiver. Fifty-six percent of the sample is male, and 74% are diagnosed with Crohn's disease. Adolescents completed the IMPACT-III (Otley et al., 2002), a disease-specific measure of HRQOL for youth with IBD. Parents rated their own depressive symptoms using the Symptom Checklist-90-Revised (SCL-90-R; Derogatis, 1994). Physicians rated disease activity using the Pediatric Crohn's Disease Activity Index (PCDAI; Hyams et al., 1991) and the Pediatric Ulcerative Colitis Activity Index (PUCAI; Turner et al., 2007).

**RESULTS:** Disease activity was negatively associated with patients' HRQOL (r = -.38, p < .01). Similarly, parents' self-reported symptoms of depression were negatively associated with IBD patients' HRQOL (r = -.45, p < .01). A multiple regression model was tested to examine whether the association between disease activity and HRQOL depends on the level of parents' depressive symptoms. The interaction between disease activity and parents' depressive symptoms was significant, (b = .03, SEb = .02, p = .05), suggesting that the relationship between disease activity and HRQOL depended on the severity of parents' depressive symptoms. Simple slope tests revealed a significant negative association between disease activity and HRQOL at low levels of parents' depressive symptoms (b = -.82, SEb = .22, p < .01) and moderate levels of parents' depressive symptoms (b = -.53, SEb = .17, p < .01), though the relationship was no longer significant at high levels of parents' depressive symptoms (b = -.25, SEb = .17, p > .05). In other words, at high levels of parents' depressive symptoms, patients' HRQOL was consistently poorer and not dependent upon disease activity.

**CONCLUSIONS:** Youth with greater disease activity whose parents report lower or moderate levels of depressive symptoms are more likely to report poorer HRQOL. Youths whose parents self-report higher levels of depressive symptoms consistently report poorer HRQOL regardless of disease activity. HRQOL is a multidimensional outcome measure, likely influenced by multiple systems including parent psychological functioning. Interventions to improve HRQOL in youth with IBD should target disease activity as well as patient and family psychological functioning.

31 **LACTOSE-FREE MILK FORMULA USEFULNESS SUPPLEMENTED ADDED WITH PECTIN IN OLDER INFANTS WITH NOT COMPLICATED ACUTE GASTROENTERITIS (LFP).** Carlos I. Oyervides, Isabel Torres, Alma R. Paredes, Gastroenterología, Hospital del Niño "Federico Gómez", Saltillo, Mexico

**Background:** Diarrheal diseases are one of the most important causes of morbidity and mortality in children under 5 years of age. In the second year of life, milk continues to be essential part of a child’s diet. Providing a milk formula designed to improve its intestinal tolerability and to maintain an adequate nutritional intake, have an effect on enteral symptom duration.

**Objective:** To evaluate LFP effectiveness in children 1-2 years of age with not complicated acute gastroenteritis.

**Materials and methods:** All patients at admission underwent a complete medical history and examination, stool test and Rotatest. Patients were randomized into two groups: The first group (control) received an anti-diarrhea diet and 45 mEq/Lt rehydration solution (RS). Group 2 received the same treatment plus LFP. Evaluations at start, third and fifth day were performed. Body weight, number and consistency of bowel movements, number of peristaltic movements, duration of diarrheic symptoms, duration of oral rehydration therapy, and anti-diarrhea diet were assessed at beginning
and end of the study. SPSS Statistics (v 17.0) was used for statistical analysis. $X^2$ or Fisher’s exact test and Student’s t-test were used. Significance value was 0.05.

**Results:** At the beginning, 32 patients without dehydration were included, with a mean age of 17.2 months, of which 2 were excluded. In the 30 patients who completed the study, there were no differences in demographic characteristics. 1 due to dysentery and 1 due to treatment failure the day of admission. Only one patient had documented rotavirus infection and was added to test group. The duration of diarrheic symptoms was 3.41 days in group 1, and 2.43 in group 2 ($p=0.038$, CI 0.316-1.952). Bowel movements on third day in group 1 were 2.64, and 1.81 in group 2 ($p=0.02$, CI 0.027-1.081), on fifth day there was no difference ($p=0.89$). Children in group 2 at the beginning of the study had more watery bowel movements than group 1 ($p=0.001$). On third day, there was no difference, and at the end of the study showed more formed stools ($p=0.001$). RS was administrated for 3.41 days in group 1, and 2.43 in group 2 ($p=0.025$, CI 0.177-1.733). The days of using diet had no difference between the two groups. Number of peristaltic movements improved faster in children receiving LFP ($p=0.005$) and were similar at the end of the study. Body weight of group 1 had an average of -230 g at the end of the study with regard to that at admission, and group 2 had an average of +230g with respect to that at admission ($p=0.43$).

**Discussion:** Use of LFP shortened disease duration in one day. Bowel movement pattern significantly improved on third day when using LFP. This effect was also reflected in normalization of peristaltic movements. Need of oral rehydration therapy was shorter with LFP, but with no effect on diet need. LFP use prevented not only loss of weight, but contributed to its increase. Evidence obtained in the study is limited by test group size. Therefore, it is concluded that the use of LFP demonstrated to be more effective than traditional management. Of note, shortening of symptom duration is similar to that observed with other drugs. Studies with a larger number of children comparing different therapeutic options are recommended.

**32 MALNUTRITION AND ELECTROLYTE ABNORMALITIES IN PATIENTS WITH CEREBRAL PALSY AND GASTROINTESTINAL DISORDERS.** Catalina Jaramillo, Abi Johnson, Tetyana Vasylyeva, Ruchi Singh, Pediatrics, Texas Tech University Health Science Center, Amarillo, TX

**Introduction:** Undernutrition and growth failure are common findings in studies on neurologically impaired children and seem to be related to inappropriate caloric intake, altered nutrient needs, inability to self-feed and oral motor dysfunction. Up to one-third of pediatric patients have associated growth disorder and nutritional deficits. Malnutrition affects the quality of life and is associated with increased health care use. Although in the past undernutrition was considered as a natural spectrum of disease of neurologically impaired children, it is now recognized that adequate nutrition in these patients is essential. The objective of this retrospective study is to determine the prevalence of malnutrition and electrolyte abnormalities in children with cerebral palsy and gastroesophageal reflux.

**Materials and Methods:** A retrospective review of the 268 medical records of pediatric patients under 18 years of age with diagnosis of cerebral palsy was done. A total of 96 patients were excluded due to lack of CP diagnosis or inaccurate/insufficient data. Out of the remaining 172 patients: 45 subjects did not have GI problems, 69 patients had constipation and 58 patients had either GERD, esophagitis, gastrostomy and feeding difficulties. Data collected included: weight, length and BMI percentiles (%), pre-albumin, albumin, Sodium (Na), Potassium (K), Chloride (Cl), Bicarbonate (HCO3), Calcium (Ca), Magnesium (Mg), Phosphorus and Vitamin D. The data for patients with and without GI disease were compared. Subgroup analysis by GI diagnosis was also done: Constipation vs. GERD, Esophagitis, Gastrostomy and Feeding difficulties vs. no GI diagnosis. Normality was checked and the variables that meet normality were analyzed by parametric t-Test; the rest of variables were analyzed by non-parametric tests (Mann-Whitney).

**Results:** The initial results suggest a significant difference ($p=0.0126$) in the values of albumin in children with CP without vs. with gastrointestinal disorders. A subgroup analysis, a significant difference ($p=0.0129$) was found in magnesium levels between CP children with constipation vs. GERD/esophagitis/ feeding issues/ gastrostomy.

**Conclusions:** Our results suggest that children with CP and GI disorders have decreased levels of albumin possibly secondary to GI losses and/or insufficient intake. Protein losing enteropathy might also explain GI losses. Lower levels of Mg levels in children with CP and constipation might be secondary to the use of laxatives. Further prospective studies might help determine the etiology behind our findings. This could enhance the pharmacological and nutritional care of this patient population.
Comparison of variables between the GI and Non-GI diagnosis groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>GI Dx (Mean ± SEM)</th>
<th>Non-GI Dx (Mean ± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na (mM/L)</td>
<td>138.7 ± 0.4</td>
<td>138.6 ± 0.5</td>
</tr>
<tr>
<td>K (mM/L)</td>
<td>4 ± 0.1</td>
<td>4.2 ± 0.1</td>
</tr>
<tr>
<td>Cl (mM/L)</td>
<td>116.4 ± 13.6</td>
<td>105.4 ± 0.5</td>
</tr>
<tr>
<td>HCO3 (mM/L)</td>
<td>24.4 ± 0.4</td>
<td>23.5 ± 0.4</td>
</tr>
<tr>
<td>Ca (mg/dL)</td>
<td>9.6 ± 0.05</td>
<td>9.6 ± 0.1</td>
</tr>
<tr>
<td>Mg (mg/dL)</td>
<td>2.1 ± 0.03</td>
<td>2.1 ± 0.06</td>
</tr>
<tr>
<td>Phos (mg/dL)</td>
<td>4.7 ± 0.1</td>
<td>5.1 ± 0.2</td>
</tr>
<tr>
<td>Vit D (mg/dL)</td>
<td>40.4 ± 2.9</td>
<td>33 ± 2.7</td>
</tr>
<tr>
<td>Albumin (mg/dL)</td>
<td>3.9 ± 0.05</td>
<td>4.1 ± 0.06</td>
</tr>
<tr>
<td>Prealbumin (mg/dL)</td>
<td>19 ± 0.9</td>
<td>18.4 ± 1</td>
</tr>
</tbody>
</table>

33 EFFECTIVENESS OF NUTRITIONAL AND ANTI-TNF THERAPY IN NORTH AMERICAN CHILDREN WITH ACTIVE CROHN'S DISEASE. Dale Lee3, Robert Baldassano3, Charlene Compher3, Lindsey Altenberg2, Anthony Otley2, Anne Griffiths4, Frederick Bushman6, Gary D. Wu1, James D. Lewis1,2, 1Gastroenterology, University of Pennsylvania, Philadelphia, PA; 2Pediatric Gastroenterology, IWK Health Centre, Halifax, NS, Canada; 3Pediatric Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 4Pediatric gastroenterology, Hospital for Sick Children, Toronto, ON, Canada; 5School of Nursing, University of Pennsylvania, Philadelphia, PA; 6Microbiology, University of Pennsylvania, Philadelphia, PA; 7Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, PA

Intro: The goal of treatment in pediatric Crohn's disease (CD) has moved beyond symptom control to mucosal healing. The comparative effectiveness of partial enteral nutrition therapy (PEN), vs. exclusive enteral nutritional (EEN), and anti-TNF-alpha therapy in achieving mucosal healing has not been prospectively assessed.

Aim: In a prospective study of the effects of enteral nutrition on the intestinal microbiota, we compared fecal calprotectin (FCP) changes and clinical responses achieved with enteral nutritional therapy and anti-TNF-alpha therapy.

Methods: PCDAI, FCP, and diet (prompted 24 hour recall) were measured at baseline and 8 weeks in children with active CD initiating treatment with PEN, EEN, or anti-TNF. Enteral nutritional therapy was administered per participating institution.

Results: Data were available for 90 children with active CD (age 13.0 +/- 3.1 yrs; 60% males; PCDAI 33.7 +/- 13.7; and FCP 976 +/- 754), 52 were treated with anti-TNF; 38 with enteral nutritional therapy (22 EEN, 16 PEN with ad lib diet). Children starting enteral nutritional therapy had shorter disease duration (0.04 vs 0.72 yrs; p<0.001). At week 8, PCDAI clinical remission (PCDAI <=10) was achieved by 47% on PEN, 68% EEN, and 74% anti-TNF (p=0.30 PEN vs EEN; p=0.07 PEN vs anti-TNF; p=0.77 EEN vs anti-TNF). A final FCP<250 was achieved with PEN in 14%, EEN 45% and anti-TNF 62% (p=0.08 PEN vs EEN; p=0.004 PEN vs anti-TNF; p=0.29 EEN vs anti-TNF).

Conclusion: Although PEN improves clinical symptoms, EEN and anti-TNF were more effective for mucosal healing.

34 CORRELATION BETWEEN INFlixIMAB LEVELS (IFX) AND ANTIBODY TO INFlixIMAB (ATI) IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD) WITH THE COMMERCiALLY AVAILABLE ASSAY USING ELECTROCHEMILUMINESCENCE. Edgardo D. Rivera Rivera1, Chuanhong Liao2, Kathleen Van’t Hof3, Thomas Mangatu1, Stacy Kahn1, Ranjana Gokhale1, Barbara S. Kirschner1, 1Pediatrics; Division of Gastroenterology, Hepatology and Nutrition, University of Chicago, Chicago, IL; 2Department of Statistics, University of Chicago, Chicago, IL

Background: Immunogenicity against infliximab (IFX) is well established. Antibodies to infliximab are often associated with loss of effect which can be an important limiting factor in the treatment of patients with moderate to severe IBD. However, a recent meta-analysis with adult population demonstrated that ATI formation can be overcome by infliximab dose optimization (Nanda, KS, et al. Am J Gastroenterol 2013; 108:40).

Aim: This study was designed to determine whether there is a relationship between IFX levels and ATI formation in a pediatric population utilizing a newly available commercial assay which uses electrochemiluminescence (ECL) methodology.

Methods: We performed a prospective observational study of pediatric patients receiving infliximab as part of the
medical regimen for IBD (UC, CD, and IC). Trough IFX and ATI levels were obtained in 69 consecutive patients: 54 patients as part of their maintenance regimen and 15 patients at the end of induction, with a commercially available assay using ECL methodology (Esoterix Endocrinology, Calabasas Hills, CA). Study population: 69 consecutive patients of whom 67% were <18 years of age and 33% were 18-22 years old. Gender: 52% male, 48% female. Diagnosis: 85% CD, 12% UC, and 3% IC. The median dose of IFX was 5.98 mg/kg (level of detection is ≥ 0.4 mg/mL). Concomitant therapy in 35 patients: thiopurines (33%) or methotrexate (67%).

Results: Of 69 consecutive patients who had IFX and ATI levels assessed using the ECL assay, ATIs were detected in 28/69 (41%) of patients with median level of 113 ng/mL. Comparison of median IFX levels in patients with detectable vs non detectable ATIs using the Spearman correlation showed a coefficient (Spearman's rho) of -0.4240, thus demonstrating an inverse relationship between IFX and ATI levels (p value of < 0.001). In addition, IFX levels were compared based on the phase of therapy (induction vs maintenance). Median trough levels were higher during the induction phase compared to maintenance phase (p value of < 0.001).

Conclusion: This study is to our knowledge the first analysis of IFX levels and ATI in pediatric patients with IBD utilizing the newly-available commercial electrochemiluminescence assay. Our results show a statistically significant inverse relationship between IFX and ATI levels. As expected, IFX levels were higher during induction compared to maintenance. In our population only 51% were on concomitant thiopurine or methotrexate, reflecting the concern of pediatric gastroenterologists for increased malignant potential. Patients with elevated ATI are being studied longitudinally to determine whether ATI levels can be reduced by increasing IFX levels. No financial support from Esoterix has been received to conduct this study.

Infliximab levels based on phase of therapy and antibody positivity status

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Median trough IFX level (mg/mL)</th>
<th>range</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction phase</td>
<td>15</td>
<td>28.0</td>
<td>(0.9 - 43.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Maintenance phase</td>
<td>54</td>
<td>4.3</td>
<td>(0.0 - 40.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Antibody positive (≥ 23 ng/mL)</td>
<td>28</td>
<td>1.8</td>
<td>(0.0 - 30.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Antibody negative (&lt;22 ng/mL)</td>
<td>41</td>
<td>9.0</td>
<td>(0.9 - 43.0)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>


Background: The importance of mucosal healing in inflammatory bowel disease (IBD) has been well recognized, especially when considering long term complications. Different tools to evaluate this have been developed: the Crohn's Disease Endoscopic Index of Severity (CDEIS) and the Simple Endoscopic Score for Crohn's Disease (SES-CD) have been used for Crohn disease (CD) and the Mayo Endoscopic Score (MES) has been used for ulcerative colitis (UC). Fecal calprotectin (FC) has also been utilized in IBD to help select those patients warranting endoscopic procedures and potentially reducing the overuse of endoscopies.

Aim: This study was designed to determine if there is a correlation between the FC levels and the degree of mucosal inflammation as derived from endoscopic activity score systems in patients with CD (SES-CD) and UC (MES), both of which are currently used in clinical practice.

Methods: We performed a retrospective observational study of pediatric IBD patients who had recorded measures of FC values and colonoscopy within a period of 2 months: CD patients mean interval was 15 days and UC patients mean interval was 45 days. To investigate the association of FC value with SES-CD and MES, in CD and UC patients, respectively, Pearson's correlation or Spearman's correlation was performed as appropriate. All analyses were conducted with Stata version 13 with significance levels set at p < 0.05.

Results: A total of 24 pediatric patients were identified who met the criteria for the study (18 CD patients and 6 UC patients). For the CD patients the mean (SD) FC was 1133.2 (881.4) mcg/g and the mean (SD) SES-CD was 17.6 (10.3). For the UC patients the mean (SD) FC was 1700.0 (1240.5) mcg/g and the mean (SD) MES was 2.3 (1.0). In both cohorts there was a positive correlation and statistical significance with a p value of < 0.01 and Pearson's correlation coefficient of 0.6209 for the CD patients and Spearman's rho of 0.9798 for the UC patients respectively, therefore, demonstrating a positive and direct relationship between FC values and endoscopic scores.

Conclusion: This study demonstrates a direct relationship between fecal calprotectin and two of the most commonly used scoring systems for endoscopic mucosal inflammation. These findings highlight the potential role for FC in predicting the severity of endoscopic mucosal damage and inflammation since higher FC levels correlated positively with higher SES-CD and MES. Fecal calprotectin could be particularly helpful in pediatric patients, especially in
situations when the need of colonoscopy is unclear and as an emerging tool for predicting the degree of mucosal healing in the management of CD and UC.

Table 1. Patients Characteristics

<table>
<thead>
<tr>
<th>Baseline General Characteristic</th>
<th>CD</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>18.0 (75.0%)</td>
<td>6.0 (25.0%)</td>
</tr>
<tr>
<td>Age, years Mean (SD)</td>
<td>15.1 (2.9)</td>
<td>15.9 (5.6)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>10.0 (55.6%)</td>
<td>5.0 (83.3%)</td>
</tr>
<tr>
<td>Male, N (%)</td>
<td>8.0 (44.4%)</td>
<td>1.0 (16.7%)</td>
</tr>
<tr>
<td>Age at diagnosis, years Mean (SD)</td>
<td>11.7 (4.3)</td>
<td>11.1 (7.1)</td>
</tr>
<tr>
<td>Time between Scope and FC Test, days Median (range)</td>
<td>15.0 (0.0-60.0)</td>
<td>45.0 (5.0-60.0)</td>
</tr>
</tbody>
</table>

36 EXAMINATION OF A HOME INFLEXIMAB INFUSION PROGRAM IN PEDIATRIC INFLAMMATORY BOWEL DISEASE. Elaine Barfield, Aliza Solomon, Robbyn Sockolow, Pediatric Gastroenterology and Nutrition, New York Presbyterian-Weill Cornell Medical College, New York, NY

Objectives: Inflammatory bowel disease is a chronic disease of the gastrointestinal tract characterized by an unpredictable course of relapsing and remitting symptoms often treated with infliximab. Historically infliximab was administered in the hospital setting, however recently some providers have prescribed infliximab via home infusions under nursing supervision. The goal of this study was to compare health-related quality of life (HRQOL), health care maintenance, cost of infliximab, and school absenteeism in pediatric patients receiving home infusions of infliximab versus those receiving infliximab in our hospital infusion center.

Methods: Inclusion criteria were age 9-17 years, confirmed diagnosis of IBD, and compliance with infusions. At subsequent visits, subjects (home infusions) and controls (hospital infusions) completed the IMPACT III, a self-administered HRQOL questionnaire. Health care maintenance data was collected via retrospective chart review. Explanation of benefits and school attendance records were reviewed to evaluate cost of infliximab and school absenteeism, respectively.

Results: 38 patients were included - 18 subjects and 20 controls. Thirty-three had Crohn's, 3 had UC and 2 had indeterminate colitis. The median age at diagnosis was 11.5 years. Sixteen (42.1%) patients were male and 35 (92.1%) were Caucasian.

Across the 6 domains assessed by the IMPACT III, there were no significant differences in HRQOL between subjects and controls. There were also no differences in frequency of surveillance endoscopy/colonoscopy, annual dermatology and ophthalmology visits, vaccination status, surveillance of vitamin levels, or reaction frequency between the groups. There were no significant differences in the cost of infliximab; the median cost per vial (100mg) for subjects was $828 versus $844.40 for controls (p=0.45). Over one semester, the median number of missed school days in subjects was 1 versus 5 in controls (p=0.008). Infliximab was administered on 46.4% of the days missed by the control group and on zero of the days missed by subjects (p<0.001).

Conclusions: HRQOL is a valuable tool enabling clinicians to screen for poor functionality across important life domains. Incorporating measures of HRQOL into clinical visits may allow physicians to identify and work to improve the functional and health status of their patients. Interestingly, while home infusions allow patients to receive therapy in comfortable settings at convenient times, location of infusions did not affect HRQOL. However because health care maintenance and cost did not differ between the groups and given that there was less school absenteeism in the home infusion group, we suggest that clinicians consider and discuss this safe and convenient alternative location for infliximab infusions with patients and families.
Median Scores for IMPACT III Questionnaire

<table>
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<tr>
<th></th>
<th>Subjects</th>
<th>Controls</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Score</td>
<td>145.5</td>
<td>151.5</td>
<td>0.49</td>
</tr>
<tr>
<td>Bowel Symptoms Score</td>
<td>29.5</td>
<td>31</td>
<td>0.17</td>
</tr>
<tr>
<td>Systemic Symptoms Score</td>
<td>13</td>
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<td>Emotional Functioning Score</td>
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<tr>
<td>Social Functioning Score</td>
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<td>54</td>
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<tr>
<td>Body Image Score</td>
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<td>0.19</td>
</tr>
<tr>
<td>Treatment/Interventions Score</td>
<td>11.5</td>
<td>12.5</td>
<td>0.57</td>
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</tbody>
</table>

37 SICKLE CELL DISEASE IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A CASE SERIES OF SIX PATIENTS. Elizabeth C. Maxwell, Judith Kelsen, GI, Children's Hospital of Philadelphia, Philadelphia, PA

Background: A variety of comorbid disease processes have been described in inflammatory bowel disease (IBD), however concurrent sickle cell disease (SCD) and IBD has only rarely been reported in the adult literature. Due to the recent increase in prevalence of this overlap seen in our pediatric IBD practice, we hypothesized that children with dual diagnosis of SCD and IBD have more severe disease, in both presentation and disease course.

Methods: A retrospective chart review of pediatric patients followed at the IBD Center at the Children's Hospital of Philadelphia identified six patients with dual diagnosis of SCD and IBD between 2010-2014. Gender, age at presentation, disease location, disease severity at presentation and at one year of therapy, and initial and current therapies were assessed for each patient.

Results: Six patients with SCD and IBD were identified. Three were male. There were three cases of Crohn disease, two with indeterminate colitis, and one with ulcerative colitis. Three patients had ileocolonic disease, two had colonic disease, and one had upper tract and colonic disease. Four patients were diagnosed at the age of 8 years or younger. Four met criteria for failure to thrive at the time of diagnosis. Disease at presentation was severe as measured by Patient Global Assessment (PGA) score in four patients. Five patients were classified as moderate to severe at one year of therapy. Four of the six patients have required biologic therapy with anti-TNF. Two have been refractory to dual therapy with immunomodulator and anti-TNF, and one has been refractory to monotherapy with anti-TNF.

Conclusions: Children with IBD and SCD at our institution appear to have more severe disease at presentation and require aggressive therapy. We hypothesize that chronic anemia, transient tissue ischemia, and vascular occlusions described in SCD may contribute to disease severity and symptomatology in this cohort. Potential mechanisms for disease potentiation in our cohort may also include alteration of the gut microbiota secondary to hypoxia and reperfusion, resulting in a dysbiotic bacterial community. Though our sample size is small, thus limiting our ability to draw statistically significant conclusions regarding these relationships, these trends suggest that additional larger studies are needed to further explore these associations.

38 THE PHARMACOKINETICS OF ANTI-TNFα THERAPY: CORRELATION WITH DISEASE ACTIVITY AND DRUG-INDUCED IMMUNOGENICITY IN CHILDREN WITH IBD. Emily Shin1, Lindsay Wilson7, Carmen Cuffari1, 1Pediatrics, The Johns Hopkins University, Lutherville, MD; 2The Johns Hopkins Hospital, Baltimore, MD

Introduction: Although anti-TNFα therapy has proven efficacy in the induction and maintenance of disease remission in children with ulcerative colitis and Crohn's disease, not all patients respond, and a high proportion of patients lose response over time. One factor associated with loss of response is the production of anti-TNFα antibodies that enhance drug clearance. This presumed influence on the pharmacokinetics of serum anti-TNFα levels has been shown to influence patients' maintenance of clinical response to drug therapy. Our aim is to evaluate the relationship between trough serum anti-TNFα drug levels and other potential factors influencing drug clearance, including serum albumin, and C-reactive protein (CRP) in pediatric patients with IBD.

Methods: 14 trough anti-TNFα drug levels were performed in 12 patients (6M;6F) with a median (range) age of 14.5 (6-21) years. All patients had received at least five consecutive infusions or injections of infliximab (9) or adalimumab (3), respectively. Just one patient was on concomitant immunosuppressive therapy (MTX). Presumed therapeutic infliximab (>3mg/mL) and adalimumab (>5mg/mL) drug levels were correlated with serum albumin (N>3.5gms/dL), CRP (N<1mg/mL), antibodies to anti-TNFα drugs and patient gender.

Results: Table

Conclusions: The pharmacokinetics of anti-TNFα therapy is strongly influenced by factors related to enhanced drug clearance, including disease activity as measured by serum albumin and CRP. These measures of disease activity may
reflect accelerated drug clearance by the reticuloendothelial system known to be enhanced in patients with systemic inflammation. Future prospective studies are needed to determine if males in general and patients with more severe tissue inflammation require higher than conventional dosing strategies to either induce or maintain disease remission.

DETERMINANTS OF ANTI-TNF α DRUG LEVELS

<table>
<thead>
<tr>
<th></th>
<th>*Therapeutic anti-TNFα</th>
<th>non-therapeutic anti-TNFα</th>
<th>p-value</th>
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<tbody>
<tr>
<td>CRP (&lt;1mg/mL)</td>
<td>9/14</td>
<td>1/14</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Albumin (&gt;3.5gms/dL)</td>
<td>9/14</td>
<td>2/14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>absent antibodies to drug</td>
<td>11/14</td>
<td>0/14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>females</td>
<td>5/6</td>
<td>1/6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>males</td>
<td>3/6</td>
<td>36</td>
<td>NS</td>
</tr>
</tbody>
</table>

*infliximab (>3μg/mL); adalimumab (>5μg/mL)

39 THE DAILY ULCERATIVE COLITIS SCALE (DUCS): A NOVEL OUTCOMES MEASURE FOR PEDIATRIC ULCERATIVE COLITIS, Emuella Flood1, Debra G. Silberg2, Beverly Romero1, Kathleen Beusterien1, M. Haim Erder2, Carmen Cuffari4, 1ICON Commercialisation and Outcomes, Bethesda, MD; 2Shire, Wayne, PA; 3ORS Health, Washington, DC; 4Division of Pediatric Gastroenterology and Nutrition, The Johns Hopkins University School of Medicine, Baltimore, MD

INTRODUCTION: This study was conducted to test and refine the Daily Ulcerative Colitis Scale (DUCS), an electronic daily sign and symptom diary in pediatric patients with ulcerative colitis (UC).

METHODS: This was a 2-visit cognitive debriefing interview study involving children aged 8-17 y with mild to moderate UC (patient-reported outcomes [PRO] version), and caregivers of children aged 5-10 y (observer-reported outcomes [ObsRO] version). UC severity was based upon Pediatric Ulcerative Colitis Activity Index (PUCAI) score at the time of the interviews. The interviews involved open-ended questions on the signs, symptoms, and impact of UC to confirm findings from a previous concept elicitation study. This was followed by cognitive debriefing of the DUCS, along with items to assess global health and to examine device usability and sample characteristics. The Visit 1 interview (~1 hr) was held in person. For the next 3 days, participants completed the DUCS using a hand-held device in the morning and before bedtime, after which the Visit 2 interview (~25 min) was conducted via phone to explore feasibility and usability. Sample characteristics were analyzed using descriptive statistics (mean, SD, median, range for continuous variables; N, % for categorical variables). Interview transcripts were analyzed using MAXqda qualitative analysis software, in which codes were applied to allow focused review of responses across the sample. Findings were used to refine the DUCS to ensure clarity, relevance and comprehensiveness.

RESULTS: The PRO sample consisted of 38 participants (22 females); 2 participants completed interviews for 2 different diary versions, resulting in 40 completed interviews. Mean age at enrollment was 12.8 y (SD, 2.4; range, 8-17; median 13). Mean PUCAI score at Visit 1 was 12.3 (SD 14.2; range 0-45). Seven caregivers participated in the ObsRO cognitive debriefing interviews; 1 tested 2 different versions of the eDiary, resulting in 8 completed interviews. Mean caregiver age was 41.5 y (SD 6.4; median 42) and mean age of the caregivers' children was 8.5 y (SD 1.7; median 9). Findings from the Visit 1 concept elicitation questions were consistent with those of the initial concept elicitation study. Four rounds of revisions were made to the PRO and ObsRO DUCS based on patient/caregiver interview feedback, as well as feedback from the US Food and Drug Administration (FDA). The FDA suggested amending the response scales and adding questions to capture overnight symptoms. Patient input influenced changes such as clarification of text and graphics and the selection of the optimal pain scale. Both child and adult participants found the device easy to navigate and use.

CONCLUSION: The DUCS eDiaries, developed with input from patients, caregivers, physicians, and the FDA, are content valid instruments capturing signs and symptoms of pediatric UC, appropriate for measuring treatment benefit. Despite potential bias from caregivers reporting on behalf of young patients, the instruments revealed good concordance with disease activity. This novel index of disease activity can provide a valid and reliable measure of signs and symptoms that may allow physicians to better judge the merits of proposed therapies for pediatric patients with UC.

40 CLINICAL, HISTOPATHOLOGICAL AND LABORATORY FEATURES OF CASES OF FMF WITH IBD, Gokhan Tumgor, Mehmet Agin Ped. Gastroenterology, Cukurova University Medical Faculty, Adana, Turkey

Aim: Familial Mediterranean Fever (FMF) is a genetic disease characterized by recurring febrile attacks and inflammation of the serous membranes. Various studies have shown an increase in FMF accompanied by inflammatory bowel disease (IBD) in recent years. The purpose of this study was to analyze the clinical, endoscopic, histopathological, genetic analysis and laboratory characteristics of cases of FMF with accompanying IBD.
**Method:** Twenty-eight patients attending the Çukurova University Faculty of Medicine Gastroenterology Clinic between 2012 and 2014, diagnosed with FMF, receiving colchicine therapy and with symptoms of abdominal pain, diarrhea, indigestion, swelling, fever, nausea, vomiting, burping, weight loss or joint pain were included in the study. The cases were assessed in terms of demographic and clinical characteristics, hemogram, biochemistry, sedimentation, CRP, fibrinogen, P-ANCA and ASCA, genetic analysis, imaging techniques and endoscopic and colonoscopic procedures. Eye examination was performed on all patients. Upper GI endoscopy alone was performed in 12 of the 28 cases and upper GI endoscopy + colonoscopy in the other 16. Five cases with histopathological inflammation determined at colonoscopy (Group 1) and 11 cases without inflammation (Group 2) were compared in clinical and laboratory terms.

**Results:** No significant difference was observed in terms of clinical findings between Group 1 and Group 2. There was no family history, perianal lesion, rectal bleeding or bloody diarrhea in either group. Hemoglobin and MCV values in Group 1 were low (p<0.05), while sedimentation values were significantly elevated (p<0.05). Histopathological examination of biopsy specimens from the colon and terminal ileum in Group 1 was compatible with IBD. Endoscopic appearance of the colonic mucosa was normal in all cases; while occasional multiple ulcer areas were observed in the terminal ileum in two cases. Homozygous M694V mutation was more common in Group 1 than in Group 2 (80% and 18%, respectively). Clinical findings of Group 1 cases resolved with mesalazine therapy within 1 week.

**Conclusion:** The prevalence of IBD in cases of FMF has risen. Even though colonoscopic appearance in cases with FMF is normal, it is still important for biopsies to be taken in terms of showing histopathological inflammation. IBD should be borne in mind in patients with homozygous M694V gene mutation. Elevated sedimentation and low hemoglobin and MCV in patients with FMF with abdominal pain and dyspeptic symptoms may be a good marker of IBD.

**Endoscopy/Potpourri**

**41 NOVEL INTERMITTENT DISACCHARIDASE DEFICIENCIES DISCOVERED AMONG VARIATIONS OF DUODENAL BIOPSY ACTIVITIES OBTAINED FROM REPEATED ENDOSCOPIES, Bruno P. Chumpitazi1, Susan S. Baker2, Bridget Adams3, Roberto Quezada-Calvillo3, E. O. Smith4, Buford L. Nichols5,6, Pediatrics, Baylor College of Medicine, Houston, TX; 2Pediatrics-N&GI, SUNY, Women and Children's Hospital, Buffalo, NY; 3CIEP-Facultad de Ciencias Quimicas, Universidad Autonoma de San Luis Potosi, San Luis Potosi, Mexico; 4USDA ARS Children's Nutrition Research Center, Houston, TX**

In a previous report, the mean percentage coefficient of variation (CV%) for replicate biopsy disaccharidase activities was computed from 4 adjacent endoscopic biopsy specimens obtained from the duodenum. Maltase and lactase displayed CV% of 18-20% whereas sucrase showed variation of 27%. **Objective:** the CV% of duodenal activities was determined from biopsies obtained from replicate endoscopies obtained in clinical care of Eosinophilic Esophagitis patients. **Methods:** Signed informed consents were obtained as approved by institutional review boards at Baylor College of Medicine (H-1320) and Women and Children's Hospital at the State University of New York at Buffalo (DB 817). Lactase, sucrase and maltase activities were assessed by Dahlqvist methods in individual biopsies. The CV% for each patient was calculated for each substrate and then averaged as CV% for group activity. **Results:** 57 patients were studied. Ages ranged from 106 to 6934 days. Three groups were identified: all normal activities (N=35); always lactase deficient (L=5); and intermittent enzyme deficiency (I=17). Histology was normal from 90% of endoscopies. Mean lactase CV% was for N: 28±15; L: 31±27; and I: 61±25. Mean sucrase CV% was for N: 22±15; L: 26±19; and I: 41±18. Mean maltase CV% was for N: 18±9; L: 20±17; and I: 36±16. ANOVA for each substrate revealed CV% differences between groups (p<0.05) but not between N and L. The CV% was doubled in the intermittent (I) group. **Conclusions:** 1. There was no correlation with histologic mucosal inflammation in any group. 2. In Eosinophilic Esophagitis patients in N or L groups the mean CV% of disaccharidase activities from replicate endoscopies was comparable to that we reported from replicate biopsies obtained at the same endoscopy. 3. A novel group with intermittent enzyme deficiency (I) was detected in 17 patients (30%); 7 had isolated lactase deficiency; 4 had lactase with pandisaccharidase deficiencies; and 6 had other deficiency patterns.

**42 CLINICAL CLASSIFICATION OF LACTASE DEFICIENCIES BASED ON SUCRASE ACTIVITIES AND AGE AT DUODENAL BIOPSY, Bruno P. Chumpitazi1, Bridget Adams3, Derick Cooper1, Roberto Quezada-Calvillo2, E. O. Smith2, Buford L. Nichols3, Susan S. Baker1, Pediatrics, Baylor College of Medicine, Houston, TX; 2USDA ARS Children's Nutrition Research Center, Houston, TX; 3QOL Medical, Vero Beach, FL; 4CIEP-Facultad de Ciencias Quimicas, Universidad Autonoma de San Luis Potosi, San Luis Potosi, Mexico; 5Pediatrics-N&GI, SUNY, Women and Children's Hospital, Buffalo, NY**

Lactase deficiency (LD) makes up 71% of all deficient activities detected from clinically indicated duodenal biopsies. Conventional LD <10 mm/min/g protein = U) diagnosis requires presence of normal sucrase (> 25 U) activity. **Hypothesis:** Lactase and sucrase activities, reviewed by age at biopsy, can be informative for recognizing adult-type LD. The standard of duodenal biopsy lactase deficiency is <10 U. **Methods:** Complete sets of lactase and sucrase assays were obtained on 27,261 clinically indicated biopsies that were assayed between 2005 - 2010 using Dahlqvist methods.
Activities were classified by age at biopsy. Sucrase deficiencies (SD) were stratified by severity: mild: >15 - <25 U, moderate: >10 - <15 U, and severe: <10 U. **Results:** SD accompanied 45% of all LD (<10 U) in 2 year olds but at four years and thereafter LD with normal sucrase (>25 U), increased to 83% of all LD biopsies. The remaining LD had SD (<25 U). Severe SD (<15 U) with LD (<10 U) activities suggest pandisaccharidase deficiency (PD). **Discussion and Conclusions:** 1. Recognized by age pattern, severe LD (<10 U) without SD accounts for most of increased frequency observed after 4 years and can be interpreted as adult-type LD. 2. Mild to moderate SD (>10 - <25 U) with LD (<10 U) does not support diagnosis of adult-type LD. 3. Patients combining severe LD (<10 U) with SD (<25 U) at any age also should be investigated for sugar and starch malabsorption due to PD or Congenital Sucrase-Isomaltase Deficiency (CSID). 

**Age on % of LD with different SD levels**

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
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<tr>
<td>SD &lt; 10 U</td>
<td>19</td>
<td>9</td>
<td>7</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>5</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>SD &gt; 10 - &lt; 15 U</td>
<td>13</td>
<td>8</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>SD &gt; 15 - &lt; 25 U</td>
<td>23</td>
<td>13</td>
<td>13</td>
<td>14</td>
<td>11</td>
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<td>76</td>
<td>79</td>
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<td>83</td>
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<tr>
<td>LD % &lt; 10 U</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
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</table>

LD = lactase deficient; SD = sucrase deficient

**43 CLINICAL RECOGNITION OF CONGENITAL SUCRASE-ISOMALTASE (CSID) VARIANTS BASED ON LACTASE ACTIVITIES AND AGE AT DUODENAL BIOPSY**

Bruno P. Chumpitazi1, Bridget Adams2, Derick Cooper3, Roberto Quezada-Calvillo4,5, E. O. Smith4,1, Buford L. Nichols4,1, Susan S. Baker2, 1Pediatrics, Baylor College of Medicine, Houston, TX; 2Pediatrics -N&GI, SUNY, Women's and Children's Hospital, Buffalo, NY; 3QOL Medical, Vero Beach, FL; 4USDA ARS Children's Nutrition Research Center, Houston, TX; 5CIEP-Facultad de Ciencias Quimicas, Universidad Autonoma de San Luis Potosi, San Luis Potosi, Mexico

Sucrase Deficiency (SD) makes up 2.5% of total duodenal disaccharidase deficiencies. Conventional diagnosis of congenital sucrase deficiency (CSID) requires that lactase activities be normal ( >15 mm/g protein, = U). **Hypothesis:** Lactase and sucrase patterns, reviewed by age at biopsy, can be informative for recognizing CSID variants. The statistical standard for sucrase deficiency (SD) is <25 U but for clinical CSID diagnosis is <15 U. **Method:** Complete sets of lactase and sucrase assays were obtained on 27,261 duodenal biopsies assayed between 2005 - 2010 using Dahlqvist methods. Activities were classified by age at biopsy. Lactase deficiency (LD) was stratified as mild: >10 - <15 U; moderate: (>5 - <10 U); and severe: <5 U). **Results:** From birth to age of 4, SD with normal or mild lactase decreased. SD (<15 U) was frequent among moderate LD (>5 - <10 U). The most frequent SD was associated with severe LD (<5 U) in 55% of 2 year olds but by 10 years increased to 80% of all SD biopsies. These are classed as pandisaccharidase deficiencies (PD). **Discussion and Conclusions:** 1. Recognized by age pattern, mild to moderate LD (>5 -15 U) is common among CSID (<15 U) patients. 2. SD is less common than LD and may fail to be investigated clinically when associated with moderate LD (>5 - <15 U). 3. The frequent severe SD (<15 U) with LD (<5 U), at any age, should be investigated for sugar and starch malabsorption due to PD.

**Age at biopsy on % of SD combined with LD levels**

<table>
<thead>
<tr>
<th>Age in Years</th>
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<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
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<th>16</th>
<th>18</th>
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<tbody>
<tr>
<td>LD &lt; 5 U</td>
<td>56</td>
<td>62</td>
<td>65</td>
<td>69</td>
<td>83</td>
<td>76</td>
<td>75</td>
<td>79</td>
<td>75</td>
<td>72</td>
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<tr>
<td>LD &gt; 5 - &lt; 10 U</td>
<td>19</td>
<td>26</td>
<td>17</td>
<td>21</td>
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LD = lactase deficient; SD = sucrase deficient
44  **DISACCHARIDASE ACTIVITY IN CHILDREN UNDERGOING ESOPHAGOASTRODUODENOSCOPY.**
Kalpesh Thakkar, Baylor College of Medicine, Houston, TX
**Background:** The occurrence of disaccharidase deficiency in children has been understudied. The relationship between intestinal mucosal histology and disaccharidase activities is not well defined.

**Methods:** We conducted a retrospective study to explore disaccharidase activity in children undergoing EGD with duodenal biopsy analysis of disaccharidase levels. We collected demographic features (age, gender), histopathological characteristics, and disaccharidase activity levels (e.g., lactase, sucrase, maltase, palatinase) for each patient enrolled in the study.

**Results:** We reviewed 53 patients (mean age 6.9; SD 2.1) including 23 (42%) females. Most (34, 63%) children had a normal disaccharide panel (i.e., all 4 disaccharidase were within normal range). Among subjects with disaccharidase deficiency, 11 (20%) had lactase deficiency only, 2 (3.7%) had maltase deficiency, 2 (3.7%) had combined lactase/maltase deficiency, 1 (1.9%) had combined lactase/palatinase deficiency, and 3 (5.7%) subjects had deficiency of all 4 enzymes. Sex was not associated with disaccharidase deficiency, however older age was associated with lactase deficiency (5.6y vs 9.9y; p=0.01). Duodenal histopathology showed chronic inflammation in 11 patients, increased eosinophilic infiltrate in 9 patients, and villous blunting in 3 patients. Overall, the majority of these histopathologic features were not associated with disaccharide deficiency or activity levels. Specifically, inflammatory changes were not associated with lactase deficiency (p=0.27), sucrase deficiency (p=0.58), maltase deficiency (p=0.62), or palatinase deficiency (p=0.82). However, patients with increased eosinophilic infiltrate had significantly lower lactase levels than those without (15.1 uM/min/g vs. 31.5 uM/min/g; p=0.03).

**Conclusions:** Duodenal histology is generally not associated with disaccharidase deficiency, however the presence of eosinophils may be predictive of lower lactase activity. Further analysis of current data is needed to examine clinical characteristics and histologic features associated with disaccharidase deficiency and compare disaccharidase levels across patient groups based on clinical morphology.

45*  **FACTORS AFFECTING ILEUM INTUBATION IN PEDIATRIC PATIENTS UNDERGOING COLONOSCOPY.** Kalpesh Thakkar1, Jennifer Holub2, Mark Gilger1, Douglas S. Fishman1, 1Baylor College of Medicine, Houston, TX; 2Oregon Health & Science University, Portland, OR
**Background:** With limited indications for screening, children typically undergo colonoscopy for diagnostic purposes to evaluate symptoms including abdominal pain, diarrhea, and lower gastrointestinal bleeding. Therefore, inspection of the terminal ileum is crucial for the evaluation of possible IBD. The consortium of the Pediatric Endoscopy Database System-Clinical Outcomes Research Initiative (PEDS-CORI) use a structured computerized endoscopy report generator, which includes fields recording the extent of colonoscopy examination.

**Methods:** We conducted prospective data collection using a standard computerized report generator and central registry (PEDS-CORI) to examine factors affecting examination of the ileum during colonoscopies performed in 14 pediatric centers between Jan 2000 and Dec 2011. Procedures with and without examination of the ileum were compared with regards to demographic and clinical features in practices with more than 100 colonoscopy procedures during the study period.

**Results:** We analyzed 21, 807 colonoscopy procedures performed in patients with mean age of 11.9 (SD 4.8). Overall, 15,130 (69%) of colonoscopies included examination of the ileum. Patients in which the ileum was not examined were younger, had higher ASA class, and were more likely to have procedures performed under intravenous sedation. Procedures done under general anesthesia were associated with intubation rate of 76%, while other sedation types (intravenous sedation) had a significantly lower intubation rate of 63% (p<0.001).

Procedures done in male patients achieved an intubation rate of 68%, significantly lower than the 71% rate seen in female patients (p<0.001). The presence of a fellow was not associated with ileal intubation (p=0.072). Colonoscopies done with an adequate bowel prep reported a higher rate of intubation than those without (94% vs. 82%; p<0.001).

Of the 21, 807 reports received during the study period, 56% did not document bowel prep quality, 31% did not include duration of procedure, and 12.7% did not include ASA classification.

**Conclusions:** Approximately, 30% of colonoscopy procedures in children did not include complete examination (i.e., reach the ileum). Several factors including age, sedation method, ASA class, and quality of bowel prep are associated with examination of the terminal ileum during colonoscopy in children.

46  **GASTROINTESTINAL MANIFESTATIONS OF BARDET-BIEDL SYNDROME: A SYSTEMATIC REVIEW.** Vikram J. Christian, Pediatrics, Marshfield Clinic, Marshfield, WI
**Introduction:** Bardet-Biedl syndrome (BBS) is a genetic disorder characterized by retinal dystrophy, obesity, polydactyly, cognitive impairment, male hypogonadism, and renal abnormalities. In most of North America, prevalence is thought to be between 1 in 140,000 to 1 in 160,000. In recent years, Marshfield Clinic has become a referral center for children affected with BBS.
Hyperphagia and obesity have been well described as part of BBS. Isolated case reports and studies show the incidence of other gastrointestinal manifestations as well. This review aims at unifying these reports into a useful resource for pediatric gastroenterologists who may encounter these patients in their practice.

Methods: Given the low prevalence of BBS, this review was largely limited to case reports. Articles were obtained from online resources such as OMIM and Pubmed. Reported gastrointestinal manifestations were summarized, classified and tabulated based on anatomic site of involvement and level of evidence available.

Discussion: This review shows that various case reports link BBS with gastro-esophageal reflux, peptic ulcer disease, non-alcoholic steatohepatitis, hepatic fibrosis, cirrhosis, portal hypertension, bile duct proliferation, dilatation of biliary tract, elevated liver enzymes, primary sclerosing cholangitis, gall stones, Crohn's disease, colonic dysmotility, anal stenosis and Hirschprung's disease.

The majority of articles reviewed provided Level V evidence. The generally low quality of evidence means that these associations must be interpreted with caution. However, the low prevalence rate of BBS limits this review and future reviews to case report and case study data. Thus the evidence summarized in this review is likely to serve as a foundation on which future case report data may be built on.

47  **STANDARDIZING PEDIATRIC INPATIENT CLEAN OUTS WITH NG PEG 3350 WITH ELECTROLYTES IMPROVES COLONOSCOPY PREP.** Katherine Sturgeon, Pediatric Gastroenterology, Children's Mercy Hospital, Parkville, MO

Colonoscopy preparation is fraught with challenges, especially in the pediatric population. The inpatient clean out relies on patient compliance and is highly dependent on nursing staff's knowledge, availability and persistence in ensuring the clean out is adequate. By standardizing and simplifying the process, we predicted that the percentage of inpatients unclean at time of colonoscopy would be reduced. This would have both safety and diagnostic advantages. Our hospital has historically utilized oral Polyethylene glycol 3350 powder (PO) or nasogastric Polyethylene glycol 3350 with electrolytes (NG) for our colonoscopy preparations. The prep quality of each colonoscopy is documented on a colonoscopy database sheet. Upon review of our inpatient colonoscopy database sheets over 6 months, I found that the PO population is unclean 19% more of the time than the NG group. The total percentage of unclean patients at time of colonoscopy using both PO and NG clean outs was 8% over the 6 month period. NG clean out is simpler for patients and nursing staff alike. Knowing that these patients are statistically better prepped, we advocated that all inpatients undergo colonoscopy prep with NG. The data was evaluated over the 3 months following this change. The number of inpatient PO clean outs was reduced by 12%. Despite this reduction, the total number of patients unclean at time of colonoscopy increased by 12%. Nearly half of the PO cleanouts during this time period were unclean at colonoscopy time (14% of the NG group). This significantly affected the total number of patients unclean. Based on this QI project, it is made clear that a standardized protocol using NG is superior to PO for inpatient colonoscopy preparation. We cannot expect the percentage of inpatients unclean at time of colonoscopy to be reduced if PO clean out continues to be utilized.

48  **JEJUNAL VARICES DIAGNOSED BY CAPSULE ENDOSCOPY IN PATIENTS WITH POST LIVER TRANSPLANT PORTAL HYPERTENSION.** Lee M. Bass1, Stanley Kim1, Riccardo Superina1, Saeed Mohammad2, 1Department of Radiology, Northwestern University Feinberg School of Medicine, Chicago, IL; 2Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL; 3Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL

BACKGROUND: Portal vein obstruction due to portal vein stenosis or thrombosis occurs in about 5 -10% of children following technical variant liver transplants. Portal hypertension secondary to this is a major cause of morbidity and mortality in these children. Patients present with chronic anemia as well as with portal gastropathy, esophageal, gastric and rectal varices. However, jejunal varices are uncommon and have heretofore not been well described. We present a cohort of children with significant GI blood loss, negative upper endoscopy and jejunal varices detected by capsule endoscopy (CE).

METHODS: Retrospective chart review of patients with at our institution with portal hypertension and severe anemia who had CE for Chronic GI blood loss following liver transplantation.

RESULTS: Three patients were identified at our institution presenting at a median age of 8 yrs. of age (Range 7-16 yrs.). All three patients had their initial transplants as infants at a median age of 7 mos. (Range 5-18 mos.) for biliary atresia. One patient had heterotaxy syndrome associated with BA. Two patients had portal vein stenosis with a history of portal venoplasty. One patient had portal vein obstruction and had received a meso-rex bypass. The patients were admitted to the hospital with a median hgb of 2.8 g/dl (Range 1.8-6.8 g/dl). Upper endoscopy was negative for significant esophageal varices, gastric varices and bleeding portal gastropathy in all three children. After continued blood loss was noted, CE was performed to further investigate the etiology of the GI bleeding. All three patients had significant jejunal varices noted on capsule endoscopy in mid-jejunum. Jejunal varices were described as large prominent bluish vessels underneath visualized mucosa. One varix demonstrated evidence of recent bleeding. The CE
results led to further investigation and venoplasty of the portal vein in two patients. In the patient with previous meso-
rex bypass, a decompressive shunt directing an obstructed splenic vein into the bypass was performed. Two of the
patients have not required further intervention while one has required a repeat venoplasty and been asymptomatic for six
months.

CONCLUSION: This is the first series describing jejunal varices on CE in pediatric patients with portal hypertension
after liver transplant. All patients had further investigation and intervention as a result of the results of the CE study.
While jejunal varices are uncommon, they remain an important cause of GI blood loss particularly in patients with
portal vein complications. Capsule endoscopy is a useful tool to diagnose intestinal varices in children with portal
hypertension and GI bleeding following liver transplant.

49 INTESTINAL ANASTOMOTIC ULCERS IN CHILDREN WITH SHORT BOWEL SYNDROME AND
ANEMIA DETECTED BY CAPSULE ENDOSCOPY. Lee M. Bass1, Jessica Zimont1, Joshua Prozialeck1, Riccardo
Superina2, Valeria Cohran1, 1Department of Pediatrics, Northwestern University Feinberg School of Medicine,
Chicago, IL; 2Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL

BACKGROUND: Anastomotic ulcers are a known cause of anemia in children with a history of intestinal resection.
The etiology of these ulcers may be secondary to ischemia or small bowel bacterial overgrowth (SBBO). Surgical
resection may be required in the setting of anemia requiring multiple blood transfusions. Colonoscopy can be used to
diagnose these ulcers. However, following serial transverse enteroplasty procedures (STEP), the area of involvement
may be difficult to visualize with standard endoscopic techniques. We describe a cohort of patients with short bowel
syndrome (SBS) and anemia who had anastomotic ulcers detected by capsule endoscopy (CE).

METHODS: Retrospective chart review of patients with SBS at our institution that had CE for chronic GI blood loss.

RESULTS: Four patients who underwent a total of 5 CE studies were identified. The underlying diagnoses included
Necrotizing Enterocolitis (N=2), Gastrochisis (N=1), and Jejunal Atresia (N=1). Two patients had undergone STEP
procedures. All patients had their ileo-cecal valve resected during previous surgeries. The median hemoglobin within
one month prior to CE was 8.0 g/dl (Range 6.8-14). Two patients were receiving IV Iron infusions. In 4 of 5 CE studies,
patients had received blood transfusions within the previous several months. The median age at time of CE was 5.5
years (Range 4-14). The median weight of the patients was 18.4 kg (Range 15.6-43.6). Endoscopic placement using
AdvanCE introducer and Real-Time (RT) viewer was performed in 4 / 5 CE studies. One patient had an ulcer noted
within the area of the STEP. Enterocolonic anastomotic ulcers were noted in the remainder of studies denoted as a wide,
flat circumferential ulcer with a white base (Fig 1 & 2). The surgical suture line was noted in 3 of 5 CE studies. The CE
results guided a change in medical management in all 4 patients, including a change in antibiotic regimens for SBBO
and one has persistent anemia and has been scheduled for a repeat evaluation by CE.

CONCLUSION: CE may be a helpful adjunctive tool at detecting anastomotic ulcers in patients with SBS and chronic
GI blood loss. All patients had a change in management as a result of findings on CE. The use of the AdvanCE
introducer device and RT viewer enabled us to perform the procedure on small children with altered anatomy due to
surgical resection. We recommend use of CE in patients with short bowel syndrome and recurrent anemia or GI blood
loss.

50 HISTOLOGICAL INFLAMMATORY PATTERN OF GASTRIC BIOPSIES IN CHILDREN VERSUS
ADULTS INFECTED WITH HELICOBACTER PYLORI IN NORTH-EAST MEXICO. Jesus Nares-Cisneros3,
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Mexico, Mexico; 2Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de
Guadalajara, Guadalajara, Mexico; 3Servicio de Gastroenterología y Nutrición Pediátrica, UMAE, Hospital de
Especialidades No. 71,IMSS, Torreón, Coahuila., Torreon, Mexico; 4Servicio de Anatomía Patológica Hospital General
de Zona No. 16, Instituto Mexicano del Seguro Social, Torreon, Mexico

AIM: To compare the gastric inflammatory pattern of gastric biopsies in children and adults infected with Helicobacter
pylori.

PATIENTS AND METHODS: Gastric biopsies obtained by endoscopy in 100 children and 100 adults infected by
Helicobacter pylori are reported. The indication of endoscopy and biopsy was recurrent abdominal pain in children and
suspicion of peptic ulcer disease in adults. In both cases indications and procedures were performed according their
Department's study protocols. Biopsies were stained with Hematoxilin/eosin and Giemsa techniques and were
reviewed by two independent pathologists. The Sidney classification was used to define the histological variables. The
protocol was authorized by the Research of Ethics Committees of both hospitals.

RESULTS: Mean age of children was 8.4 (3.7 SD) years. Adults mean age was 41.8 (16.5 SD). Gastric colonization
density by Helicobacter pylori, follicular gastritis and infiltrate of mononuclear cells and neutrophils was significantly
higher in adults with respect to children (p<0.001 for these 4 variables); when these variables were analyzed as dichotomous, ORs showed a significant increased risk of adults of having higher colonization, follicular gastritis and inflammatory infiltrates. Atrophy of gastric mucosa and intestinal metaplasia were identified in a few adult cases. Gastric adenocarcinoma was found in one adult patient.

**DISCUSSION:** The differences found between the histological patterns of children and adults infected by *Helicobacter pylori* are remarkable. These findings may be related to host age-dependent characteristics, differential virulence of the agent for each group or to a combination of both factors.

51 **CLINICAL PROFILE OF 29 SAUDI CHILDREN WITH HELICOBACTER PYLORI GASTRITIS.** Anjum Saeed1,2, Asaad Assiri1,2, Syed Z. Zaidi1, Ahmed Al Sarkhy1, Hamad Aljaedi1, Mohammad El Mouzan1, Yassin Hamid1, 1Pediatric, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia; 2Prince Abdullah Bin Khalid Celiac Disease Research Chair, King Khalid University Hospital, King saud university, Riyadh, Saudi Arabia; 1Histopathology, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia; 4Pediatric, Dr. Suleman Al-Habib Medical Group, Riyadh, Saudi Arabia

**Introduction:** Helicobacter Pylori (H. pylori) is a gram negative, spiral gastroduodenal pathogen that infects 50% of the world population, more prevalent in developing countries because of overcrowding and poor hygienic conditions as transmission is primarily by feco-oral route. Although infection is acquired during childhood but disease manifestations appear decades after the acquisition of infection and may lead to serious consequences like gastritis, ulcers and gastrointestinal malignancies. Presentation is variable but its association with recurrent abdominal pain, gastroesophageal reflux, iron deficiency anemia and asthma is still controversial. Despite the lack of evidence, trend is to screen children for H Pylori and treat those found to have the infection. This study was conducted to review the clinical profile of Saudi children with H. pylori gastritis. **Material & Methods:** It was a retrospective study conducted at pediatrics division of a private tertiary care hospital, Riyadh. A total of 202 Saudi children both males and females between 1 to 16 years of age who underwent oesophage gastroduodenoscopy (OGD) from Jan 2009 to Jan 2012 were included in the study. Out of these, 29 children were found to have H Pylori gastritis. The diagnosis was confirmed with histopathology. Clinical profile of these patients including age, gender, clinical presentation, association with gastroesophageal reflux disease (GERD), iron deficiency anemia, food allergy, asthma, endoscopic and histopathological findings were reviewed. **Results:** Mean age of presentation was 10 years. 52% presented between 11-16 years, 44% between 5-10 years and 3% before 5 years of age. 42% were males and 58% were females with male to female ratio of 1:1.8. 84% patients presented with abdominal pain, 28% with heartburn whereas vomiting and growth failure were the chief complaint in 8% and 16% of the patients respectively. Iron deficiency anemia, asthma, food allergy and family history of PUD and GI malignancies were not found in any of the patients. Reflux esophagitis was the feature in 24% (n=7). Sydney system was used for the classification and grading of gastritis. Atrophic gastritis was a feature in 17% while rest had non atrophic gastritis. All patients had chronic active gastritis. None of the patients showed metaplastic, dysplastic or malignant changes. Villous atrophy was found in 17%. All the patients were put on eradication therapy. 82% responded well to treatment. **Conclusion:** H. pylori infection is not an uncommon entity and is an important cause of gastritis in Saudi children. Majority of the patients presented with abdominal pain but it has no clear association with GERD, iron deficiency anemia or allergies. **Key Words:** Helicobacter Pylori, Gastritis, Children.

68 **USE OF DOCUSATE SODIUM MINI-ENEMAS TO ACHIEVE FECAL CONTINENCE IN CHILDREN WITH ANORECTAL MALFORMATIONS.** Rinarani Sanghavi1, Jasmine McElhany2, 1UT Southwestern Medical Center, Dallas, TX; 2Children’s Medical Center Dallas, Dallas, TX

**Introduction:** Children with anorectal malformations (ARM) continue to suffer from fecal incontinence episodes (FIE) even after corrective surgery, negatively affecting their quality of life. We report a series of children with ARM in whom docusate sodium mini enema (DSME) was used as part of a bowel management program to achieve stool continence (SC).

**Methods:** Charts of patients referred to our program over 13 months were retrospectively reviewed. Fecal incontinence episodes at baseline and at the most recent visit were assessed by parent recall.

**Results:** Twenty patients were prescribed DSME as part of their bowel management program. Ages ranged from 3 months to 18 years. Malformations included imperforate anus (n=14), and Hirschsprung disease (n=6). All patients had 2-5 large FIE per day. Frequency of use of DSME was daily (n=15) and 2-5 times a week (n=5). At follow up (mean 23.45 months) 10 patients or 50%, reported improvement. Fecal incontinence episodes were reduced to less than 2 times a week for 10 patients. Seven of the non-responders admitted poor compliance with DSME therapy. Volume of FIE decreased in all patients. Complaint of burning sensation to the bottom caused discontinuation of therapy in one patient. No major complications were noted.

**Conclusions:** Docusate sodium mini enemas were effective in reducing frequency and volume of FIE in 50 % of children with surgically repaired ARM. This therapy may be helpful in achieving social continence in these children as part of a bowel management program. Compliance may be challenging.
DEXLANSOPRAZOLE MR IS SAFE AND EFFECTIVE FOR HEARTBURN RELIEF IN ADOLESCENTS WITH SYMPTOMATIC NON-EROSEIVE GASTROESOPHAGEAL REFLUX DISEASE. Benjamin D. Gold, Thirumazhisai S. Gunasekaran, Betsy Pilmer, Barbara Hunt, Reema Mody, Maria C. Perez. 1Children's Center for Digestive Healthcare, LLC, Atlanta, GA; 2Center for Children's Digestive Health, Park Ridge, IL; 3Takeda Development Center Americas, Inc., Deerfield, IL; 4Takeda Pharmaceuticals International, Deerfield, IL

Objective: To assess the safety and effectiveness of oral dexlansoprazole MR 30 mg capsules in adolescent subjects with symptomatic non-erosive gastroesophageal reflux disease (GERD).

Methods: This multicenter study enrolled males and females aged 12 to 17 years with a ≥3-month history of GERD and heartburn for ≥3 of any 7 screening days to receive open-label oral dexlansoprazole MR 30 mg QD for 4 weeks. Main exclusion criteria included history or endoscopic evidence of coexisting esophageal disorder(s) (eg, varices or stricture). Non-erosive GERD was confirmed by endoscopy at baseline, and subjects received an electronic diary to record presence and severity of heartburn. The primary endpoint was treatment-emergent adverse events occurring in ≥5% of subjects; additional endpoints included heartburn frequency and severity, the Pediatric Gastroesophageal Symptom and Quality of Life Questionnaire-Adolescent-Short Form (PGSQ-A-SF), and investigator assessment of GERD symptoms.

Results: Ninety-five (91.3%) of the 104 enrolled subjects were white and 73 (70.2%) were female; 34 (32.7%) were aged 12 to 14 years and 70 (67.3%) were aged 15 to 17 years. A total of 102 subjects completed the treatment period. Adverse events of diarrhea and headache met the primary endpoint threshold, each occurring in 7 (6.7%) subjects. Measures of heartburn frequency and severity showed substantial improvement over the 4 weeks of treatment (Table); all values were improved from baseline. The mean (SD) PGSQ-A-SF symptom subscale score, assessing days with symptoms in the past week (on a scale of 1=0 days to 5=7 days), was 1.8 (0.76) at week 4, an improvement of -0.7 (0.76) from baseline. The impact subscale measured 4 impact questions (didn't feel like doing anything, couldn't eat what I wanted, couldn't drink what I wanted, and was in a bad mood) on a scale of 1 (never) to 5 (always). The mean (SD) week 4 score was 1.9 (0.96), an improvement of -0.7 (0.97). In investigator assessments, 70 subjects (74%) experienced a ≥1-grade improvement in heartburn from Baseline to Week 4. Adverse events occurred in 38 (36.5%) of subjects; most were mild in severity. Two subjects withdrew due to adverse events (worsening GERD and dizziness).

Conclusion: Administration of dexlansoprazole delayed-release capsules for 4 weeks was well tolerated and effective in relieving daytime and nighttime heartburn and in improving health-related quality of life in adolescent subjects with symptomatic non-erosive GERD. The results are consistent with those of a previous study in adults.

Method: We conducted a retrospective review of the Mayo Clinic data between 2005 and 2013. Children age (0-18) years diagnosed with gastroparesis, who underwent a 2 hour GE study, followed by 4 hour GE study were included. Children with history of gastric surgery (including gastric neurostimulator devices), diabetes, or on prokinetic medications were excluded. GE study was considered abnormal if GE was < 7% at 1 hour.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (range)</th>
</tr>
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<tbody>
<tr>
<td>% of days without heartburn</td>
<td></td>
</tr>
<tr>
<td>Daytime</td>
<td>59.3 (0-100)</td>
</tr>
<tr>
<td>Nighttime</td>
<td>80.5 (0-100)</td>
</tr>
<tr>
<td>Daytime or nighttime</td>
<td>47.3 (0-100)</td>
</tr>
<tr>
<td>Mean degree to which heartburn hurt (a)</td>
<td></td>
</tr>
<tr>
<td>Daytime</td>
<td>0.64 (0-2.4)</td>
</tr>
<tr>
<td>Nighttime</td>
<td>0.30 (0-2.4)</td>
</tr>
<tr>
<td>Daytime or nighttime</td>
<td>0.49 (0-2.3)</td>
</tr>
</tbody>
</table>

(a) 0=none, 1=did not hurt very much, 2=hurt some, 3=hurt a lot.

TWO HOUR GASTRIC EMPTYING RADIONUCLIDE SCINTIGRAPHY IS ASSOCIATED WITH FALSE DIAGNOSIS OF GASTROPARESIS IN CHILDREN

Imad Absah, Lawrence A. Szarka. 1Department of Pediatric Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; 2Department of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN

Introduction: Gastroparesis is a disorder of the stomach resulting in delayed gastric emptying in the abdominal pain, and weight loss. There is a paucity of data about gastroparesis in children. Etiology includes post-viral, idiopathic and autonomic dysfunction disorders. Four hour radionuclide scintigraphic gastric emptying (GE) study is the recommended diagnostic study but many centers perform 2 hour GE study. There have been no comparison studies between these two methods in pediatric patients.

Methods: We conducted a retrospective review of the Mayo Clinic data between 2005 and 2013. Children age (0-18) years diagnosed with gastroparesis, who underwent a 2 hour GE study, followed by 4 hour GE study were included. Children with history of gastric surgery (including gastric neurostimulator devices), diabetes, or on prokinetic medications were excluded. GE study was considered abnormal if GE was < 7% at 1 hour.
31% at 2 hours and 81% at 4 hours. Demographic, symptoms and GE results were recorded. The study was approved by the Mayo Clinic IRB. Results: 13 children (7 females, average age 12 years) were identified. Indications for GE at the time of both studies were abdominal pain (63%), nausea/vomiting (38%), and bloating/abdominal distention (16%). Patients discontinued any prokinetic before the 4 hour GE study. Out of 11 patients with gastroparesis by 2 hour GE study, only 2 (18%) had abnormal 4 hour GE study. Median time between studies was 6 months. None of the patients with normal 2 hour study had an abnormal 4 hour study. Discussion: Most of the patients (82%) had normal 4 hour GE study, despite persistence of their symptoms. These patients could have functional or other motility disorders (impaired accommodation). The improved GE results could be due to regression toward the mean, or true improvement in the gastric emptying function during the time elapsed between the two studies. Conclusion: The 2 hour radionuclide scintigraphic GE test is unreliable, and can result in false diagnosis of gastroparesis in children. Four hour GE radionuclide scintigraphy testing should be the standard practice.

71 NON ACID REFLUX AS A CAUSE OF ESOPHAGITIS FOLLOWING REPAIR OF ESOPHAGEAL ATRESIA ASSESSED BY MULTICHANNEL INTRALUMINAL IMPEDANCE. Judith Cohen Sabban1, Romina Mehaudy1, Silvia Christensen1, Pablo Lobos2, Marina Orsi1, 1Hospital Italiano, Buenos Aires, Argentina; 2Hospital Italiano, Buenos Aires, Argentina

Gastroesophageal reflux (GER) and dysmotility are common findings in children with esophageal atresia (EA). Despite less aggressive laparoscopic procedures and frequent PPI use, it seems that esophageal damage cannot be prevented. Impedance studies may detect unrecognized underlying mechanisms which could explain this complication. Objective: To evaluate the dynamic and chemical characteristics of GER in children with EA using Multichannel Intraluminal Impedance-pH24hs (MII/pH) and determine the presence or not of esophagitis on biopsies obtained by upper endoscopy regardless of previous PPI history. Materials and methods. Retrospective analysis of patients studied between 2003 and 2013. Fourteen children (1-3 ys) operated for EA soon after birth, and 20 controls of similar age evaluated for extraesophageal symptoms with normal MII/pH recordings. All patients with EA had received PPIs. The medication was discontinued 10 days prior to the study. Upper endoscopy and esophageal biopsies were performed followed by a 24 hr MII/pH to determine longest reflux (LR), all reflux percent time (RPT), and median bolus clearance time (BCT). Results: A total of 34 children (16 girls), median 1.78 years (r 1-3 ys). Variables analyzed showed. LR 24.82 ± 20.3 sec vs 1.62 ±0.57 sec (p = 0.003), RPT 7.79 ± 7.07% vs 0.94 ± 0.45% (p = 0.0001) and BCT 28 ±18.3 sec vs 16.95 ± 4.9 sec (p = 0.014). Acid reflux: 20.43 ± 17.47 vs 15.85 ± 12.45 (p = 0.378), non acid reflux: 29.79 ± 20.35 vs 11.2 ± 6.05 (p = 0.0001). In patients with EA, 64.2% (9/14) had biopsies with mild/moderate esophagitis. Conclusion: Untreated non acid reflux may explain persistence of esophagitis in patients with EA. The MII/pH study also shed some light on the dynamic disorders in these surgically repaired esophagus.

72 OBESITY IS NOT ASSOCIATED WITH INCREASED REFLUX EPISODES OR ESOPHAGITIS IN AN UNSELECTED POPULATION OF CHILDREN. Meenakshi Ganesh1, Rachel L. Rosen1, Carly Milliren2, Samuel Nurko1, 1Pediatric Gastroenterology, Boston Children’s Hospital, Boston, MA; 2Boston Children's Hospital, Boston, MA

Introduction: Reflux and obesity are increasing in prevalence in children. Numerous studies have examined the association between obesity and reflux in adults, suggesting that obese adults have increased reflux burden. However, the data in children is limited. Aim: To compare the reflux burden of obese versus non-obese children.

Methods: We identified Multichannel Intraluminal (MII) impedance studies of unselected patients referred to our Institution for evaluation of reflux. We excluded patients with acid blocking medication during the study, eosinophilic esophagitis, enteral tubes, prior esophageal or gastrointestinal surgeries, structural abnormalities of the GI tract, severe systemic disease, cystic fibrosis and patients with prior transplants. We defined obesity as BMI ≥95th percentile. The primary outcome was comparison of total, nonacid, acid and pH only episodes between obese and non-obese individuals. Secondary outcome included comparison of prevalence of esophagitis in the 2 groups.

Results: A total of 477 patients with impedance studies were identified and 273 met criteria for inclusion in the study. The mean age of the population was 8.1±5.4 years, and was not significantly different between the obese and non-obese groups. Fifty-three patients (19%) were obese, and, of those, 43% were females (p=0.61). We found that total, non-acid, acid and pH episodes were not significantly different between obese and non-obese individuals (Figure 1, Median reflux episodes per 24hrs of obese vs non-obese: Total: 43 vs 43 p=0.90, Non-acid: 16 vs 13 p=0.61, Acid: 22 vs 25 p=0.96, pH: 6 vs 7 p=0.63). We found no significant difference using BMI cutoffs of 99 percentile (morbidly obese) as well. Furthermore, there was no difference in prevalence of esophagitis in obese individuals compared to the non-obese (29% vs 21%, p=0.3). After adjusting for age, sex, GI symptoms, and PPI before or during test, obese patients had on average 2.6 more total reflux episodes compared to non-obese, however this difference was not significant.

Conclusion: This is the first study looking at the objective assessment of reflux in an unselected population of obese children. Our data suggest that, unlike adults, obesity is not associated with increased reflux burden in children.
Table 1: Comparison of Reflux Episodes and Esophagitis in Obese versus Non-Obese

<table>
<thead>
<tr>
<th></th>
<th>Obese (N=53)</th>
<th>Non-Obese (N=220)</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>Reflux Episodes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Reflux</td>
<td>43 (30-64)</td>
<td>43 (25-70)</td>
<td>0.9</td>
</tr>
<tr>
<td>Non-acid</td>
<td>13 (6-35)</td>
<td>16 (8-35)</td>
<td>0.6</td>
</tr>
<tr>
<td>Acid</td>
<td>25 (8-39)</td>
<td>22 (10-38)</td>
<td>1.0</td>
</tr>
<tr>
<td>pH-only</td>
<td>7 (4-14)</td>
<td>6 (3-13)</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Esophagitis</strong></td>
<td></td>
<td></td>
<td>0.2</td>
</tr>
<tr>
<td>(N=225)</td>
<td>13 (28%)</td>
<td>33 (18%)</td>
<td></td>
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73 CHARACTERIZATION OF CHILDREN WITH FEEDING DIFFICULTIES IN A UNIQUE MULTIDISCIPLINARY CLINIC. Barbara McElhanon1, T. L. Burrell2,3, Kathryn Holman2,3, Haley E. Hughes4, William G. Sharp2,3, 1Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Emory University School of Medicine, Atlanta, GA; 2Marcus Autism Center, Atlanta, GA; 3Department of Pediatrics, Emory University School of Medicine, Atlanta, GA; 4Children's Healthcare of Atlanta, Atlanta, GA

**Background:** In a one week sample, 35% of patients seen at an outpatient gastroenterology clinic associated with a tertiary pediatric hospital required enteral feeds to achieve 100% of their caloric and nutritional needs. These high numbers are a result of the feeding problems that more commonly affect medically compromised children (Kerwin, 1999) and/or children with developmental disabilities (Field, et al., 2003). The etiology of feeding disorders may include organic problems that contribute to painful feeding experiences (Sharp et al., 2010) such as metabolic dysfunction, structural abnormalities, oral motor dysfunction, and gastrointestinal problems. While 40% of caregivers report feeding problems in early childhood (Manikam & Perman, 2000), approximately 3 to 10% develop chronic feeding problems (Kerwin, 1999) that likely persist over time (Lindberg et al., 1991). There are risks associated with enteral tubes which include surgical and anesthesia risks (Bankhead, 2009); 73 to 83% of children will have at least one complication (Naiditch, 2010) as well as impairment to their quality of life.

There is no evidence-based systematic approach to weaning children off enteral feeds. Many of the methods for tube feed weaning described in the literature focus on inpatient and day treatment settings. Due to the limited number of these programs, as well as the large expense of these programs, many children reliant on tube feedings are not able to access this level of service. Behavioral interventions are effective in treating severe feeding problems to increase oral intake (Sharp et al., 2010), but many children may not require this intensive intervention if identified early.

Our clinic includes evaluation by a gastroenterologist, dietitian, and behavioral psychologist with expertise in feeding disorders to create an interdisciplinary treatment plan for patients. Therefore, this study characterizes the patients on initial evaluation who require either intensive behavioral feeding intervention, consultative level services, or have successfully transitioning to oral feeds with little professional support.

**Methods:** A retrospective chart review was performed including visits from November 2013 to April 2014 including psychologist's assessment, nutritional assessment, and medical evaluation. The included 29 participants were at least 9 months old and either receiving enteral feeds or at risk for initiating enteral feeds.

**Results:** Presenting problems included gastrostomy dependence (65.6%), nasogastric tube dependence (17.2%), and feeding problems (e.g. problem behaviors during meals, limited solid intake)(17.2%). 83% of patients receiving enteral feeds exhibited problem behaviors interfering with oral consumption.

Problem behavior is one of the most frequently reported concerns with transitioning from enteral to oral feeds with head turning (54%) being the most commonly reported problem behavior exhibited during meals in this sample. Oral motor concerns are also commonly reported specifically with transition from puree to higher texture foods.

**Conclusions:** Characterizing patients who are able to safely wean from enteral feeds will inform the development of a systematic approach to weaning patients from feeding tubes.
suggesting strong ongoing improvement after discharge. Degree of improvement did not correlate with time since rumination was completely resolved), on average, patients rated their progress since discharge as a 6.7 (SD = 3.3),

Fifteen percent of patients required one re-admission to the hospital, and each time this was due to stress or illness. Anticipatory guidance related to improve coping with stress and close follow-up after discharge may be needed to maintain improvement.

The current study is the first to determine the course of post-treatment progress in a sample of patients with ARS treated receiving enteral feedings at the time of admission, all of whom were able to discontinue use of those feedings by

On a scale of -10 to +10 (with "0" indicating no improvement in rumination since discharge and "10" indicating that rumination was completely resolved), on average, patients rated their progress since discharge as a 6.7 (SD = 3.3), suggesting strong ongoing improvement after discharge. Degree of improvement did not correlate with time since discharge. Thirty-one percent of patients reported that their rumination had stopped completely and had not returned. Fifty percent of patients reported ongoing improvement in rumination with the behavior occurring less often and the rumination less intense. Nineteen percent reported that rumination had improved but then worsened. Rumination had

A follow-up questionnaire was mailed to 44 patients who were admitted to the inpatient ARS treatment program from 2009-2013. The questionnaire inquired about multiple aspects of the patient's rumination and health since discharge, including degree of perceived improvement, changes in rumination and vomiting, and hospitalizations. Questionnaires were received from 26 patients (92% female, mean age = 15.8 years). Average duration of rumination prior to treatment in our program ranged from 3 to 96 months (mean = 22.2 months, SD = 20.4). Sixty-two percent of patients were longer require supplemental feedings. While patients have been shown to improve considerably by the end of inpatient treatment in our program, little is known about their progress and the course of rumination after discharge.

The current study is the first to determine the course of post-treatment progress in a sample of patients with ARS treated receiving enteral feedings at the time of admission, all of whom were able to discontinue use of those feedings by

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Anticipatory guidance related to improve coping with stress and close follow-up after discharge may be needed to maintain improvement.

In this study we investigated the association between IC and 3 types of social support: maternal social support, partner involvement in caring for the newborn, and the happiness of the relationship between the mother and partner.

**Results:** Infant colic was reported by 11.5% of the new mothers. High social support was protective for infant colic (odds ratio (OR), 0.48, 95% confidence interval (CI), 0.37-0.64) in comparison to low social support; as was high partner involvement with newborn care (OR, 0. 58, 95% CI, 0.43-0.78) in comparison to low; and high relationship happiness (OR, 0.20, 95% CI, 0.11-0.36) in comparison to low.

**Objective:** In this study we investigated the association between IC and 3 types of social support: maternal social support, partner involvement in caring for the newborn, and the happiness of the relationship between the mother and partner.

**Design/Methods:** 3,006 women aged 18 to 36 years were enrolled during the 3rd trimester for a prospective study examining the associations between delivery mode and subsequent health outcomes. Participants were interviewed by telephone 1 month after first (singleton) childbirth, and asked if their baby had a variety of problems during the previous 4 weeks, including "colic - crying/fussiness 3 or more hours a day". Logistic regression equations were used to measure the association between each type of social support and infant colic, controlling for potentially confounding factors including maternal age, race/ethnicity, education, poverty, insurance, marital status, smoking, mode of delivery and breastfeeding.

**Background:** Maternal psychological factors like depression, anxiety, and stress have been associated with infant colic. However, little research has investigated the extent to which positive factors such as social support and the happiness of the mother-partner relationship are protective for infant colic.

**Methods:** The questionnaire included 19 questions regarding the mother-partner relationship, focusing on the happiness of the relationship, partner involvement with newborn care, and the extent to which each type of social support (maternal social support, partner involvement, and relationship happiness) were received. Logistic regression equations were used to measure the association between each type of social support and infant colic, controlling for potentially confounding factors including maternal age, race/ethnicity, education, poverty, insurance, marital status, smoking, mode of delivery and breastfeeding.

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76 GASTROESOPHAGEAL REFUX AND RESPIRATORY PROBLEMS AFTER LONG-GAP ESOPHAGEAL ATRESIA REPAIR. Khalid Khan1, Vishal Shah1, John E. Foker2, 1MedStar Georgetown University Hospital, Washington, DC; 2University of Minnesota, Minneapolis, MN

Background: Few data exist on the outcome of long-gap esophageal atresia (LG-EA) in part because of the few patients managed at any individual center. Of particular concern are gastroesophageal reflux (GER) as a result of upward tension on the gastroesophageal junction and respiratory problems related to poor clearance of the esophagus.

Method: We surveyed parents of children with LG-EA who underwent primary repair after traction applied to the esophageal ends the University of Minnesota.

Results: Of 20 patients who underwent LG-EA repair all the patients had undergone a Nissen fundoplication after repair. At the time of the survey 10/20 patients were on anti-acid, 9/10 with a proton pump inhibitor and 9/10 had a diagnosis of GER and one additional patient had symptoms but not a diagnosis or medication. Symptoms were reported in all 9 patients who had a diagnosis of GER, heartburn, n=5, regurgitation n=4, and bad breath, n=3. Respiratory symptoms included a night time cough in 9/20 individuals, of whom 8/9 were also diagnosed with GER. A diagnosis of chronic chest, lung or breathing problems were reported in 9/20 individuals which included night time cough in 6/9, wheezing in 5/9, 6/9 had a diagnosis of GER. Pneumonia had been reported in the recent history of 7/20 individuals of whom 5 were admitted to hospital, 5/7 had a diagnosis of GER and all 7 were described as having a chronic chest problem.

Conclusion: Almost half of children undergoing LG-EA with traction have either respiratory problems and or gastroesophageal reflux in the long term. Gastroenterologist should be prepared to manage reflux in these children despite having had a Nissen fundoplication.

77 ASSESSMENT OF CYP2C19 PHENOTYPE IN CHILDREN USING THE 13C-PANTOPRAZOLE BREATH TEST. Valentina Shakhnovich1,2, Susan M. Abdel-Rahman2, Megan Buri3, Jaylene Weigel4, Robin E. Pearce2, Andrea Gaedigk2, Gregory L. Kearns2, 1Gastroenterology, Children's Mercy Kansas City, Kansas City, MO; 2Clinical Pharmacology, Children's Mercy, Kansas City, MO; 3Creighton University Medical School, Omaha, NE

Background: The 13C-Pantoprazole breath test (PTZ-BT) has been used in adults as a non-invasive approach to assess activity of CYP2C19, a drug metabolizing enzyme (DME) important for the biotransformation of many therapeutic compounds, including proton pump inhibitors (PPIs) and several serotonin reuptake inhibitors. We applied PTZ-BT to a pediatric population, where traditional, more invasive methods of DME genotyping/phenotyping may be unacceptable to patients or parents.

Methods: In this single center, prospective, open label study of PTZ-BT in 24 children (6-17 yrs old) with gastroesophageal reflux disease, participants received a single oral dose (~1 mg/kg) of 13C-pantoprazole. Breath samples were collected at baseline and at 16 time-points over an 8-hr study period. 13CO2 and 12CO2 concentrations were measured by infrared spectrometry, and enrichment of 13CO2 expressed as the increase in 13CO2/12CO2 relative to baseline (DOB). DOB vs. time data were curve fit using a model-dependent pharmacokinetic approach (Kinetica v. 5.0).

Subjects were genotyped for CYP2C19 *1 (wild-type), *2, *3, *4, (loss of function) and *17 (gain of function) allelic variants. The apparent terminal elimination rate constant (lz) and mean residence time (MRT) were compared between genotype groups using a two-tailed, student t-test (a=0.05).

Results: Twenty-two children (12F, 10M) were included in the analysis; nine had *1/*1, six had *1/*17 and seven had *1/*2 or *2/*17 genotypes, respectively. A significant increase in lz was observed in the *1/*17 (0.011 ± 0.007 min⁻¹) vs. the *1/*1 (0.004 ± 0.004 min⁻¹) group (p=0.04), while MRT was significantly decreased in the *1/*17 (135 ± 84 min) vs. the *1/*1 (395 ± 271 min) group (p=0.04). No differences were observed in the *1/*1 vs. *1/*2 or *2/*17 groups.

Conclusion: This preliminary study suggests that PTZ-BT is a safe, non-invasive CYP2C19 phenotype test, suitable for use in children, and potentially useful in discriminating *1/*1 from *1/*17 individuals. Knowledge regarding CYP2C19 genotype/phenotype can be used to individualize drug treatment regimens, making treatment safer and more effective for children.

78 CANDIDA IS AN IMPORTANT PATHOGEN IN SMALL INTESTINAL MICROBIAL OVERGROWTH. Nishant H. Patel, Timothy Hadley, Janet Conrad, Chirajyoti Deb, Karoly Horvath, Devendra I. Mehta, Pediatric Gastroenterology, Center for Digestive Health and Nutrition, Arnold Palmer Hospital for Children of Orlando Health, Orlando, FL

Aim: The duodenum is relatively sterile and the bacterial colony count is considered normal if it is below 10⁵CFU/ml. The normal count for the Candida species is unknown. We aimed to analyze clinical data of children diagnosed with small intestinal fungal overgrowth during a 10 month period.

Method: The duodenal mucosal surface was brushed twice using two separate brushes during upper GI endoscopy in all 4 segments. The brushes were cut, placed in special media and transported to our Laboratory for quantitative culture.
**Results:** Eighty-six (86/243 = 35.4%) children had overgrowth based on colony counts of >10⁴ CFU/ml. Seventeen of these 86 (19.8%) patients had overgrowth with *Candida albicans* (n=10), *C. glabrata* (n=4), *C. krusei* (n=2) and *C. tropicalis* (n=2). The colony count varied from 1 to 100 x 10³ CFU/ml. There was no age difference between the positive, negative and *Candida* overgrowth groups. Thirteen patients had mixed yeast and bacterial flora and 4 had purely *Candida* overgrowth. Six patients (6/13) had PPI therapy, which is a possible risk factor. Six of the 17 had G- or GJ-tubes. Four patients received antibiotic therapy in the previous 6 months. The main clinical symptoms were abdominal pain, reflux and constipation. Three patients had associated *Candida* esophagitis. One had polyglandular autoimmune syndrome type 1, who had recurring fungal overgrowths. Thirteen patients underwent anti-fungal therapy and 7/13 (54%) showed improvement with their symptoms.

**Conclusions:** Duodenal brushing during endoscopy provides samples for a novel diagnostic test that allows more efficient diagnosis of small intestinal microbial overgrowth (SIMO) than aspirate culture. Fungal overgrowth is an important causative factor for SIMO symptoms. Fungal overgrowth measured at a 10 times lower frequency (10³ CFU/ml) than the threshold value (10⁴ CFU/ml) of bacterial overgrowth is capable of producing SIMO related symptoms. Patients with chronic underlying disease are at-risk for colonization with fungal species.

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**79* DEFINING NORMAL IMPEDANCE PARAMETERS IN CHILDREN.** Meenakshi Ganesh¹, Rachel L. Rosen¹, Carly Milliren², Samuel Nurko¹, ¹Pediatric Gastroenterology, Boston Children’s Hospital, Boston, MA; ²Boston Children’s Hospital, Boston, MA

Multichannel Intraluminal Impedance (MII) with pH is the gold standard for diagnosis of reflux, however, normal impedance parameters for children have not been defined. Positive Symptom Index (SI) has been used as a criterion for pathologic reflux although the impedance characteristics of patients with positive SI are not known. **Aim:** 1. Define impedance parameters in children without reflux. 2. Compare those with patients with reflux, defined by reflux index (RI)>6%. 3. Determine if patients with positive SI have increased number of reflux episodes.

**Methods:** We identified all impedance studies performed in our institution, a tertiary referral center, till the end of 2013, and excluded patients with acid blocking medication during the study, enteral tubes, GI surgeries, and severe systemic diseases. For aim 1, we included patients with RI <6%, no GI symptoms, and normal esophageal biopsies (controls). For aim 2, GERD patients were defined as those with RI >6%. For aim 3, patients with positive SI were divided into those with and without a high RI.

**Results:** We identified 463 patients, of which, 31 patients fulfilled criteria to be included as controls. The indications for impedance studies in controls were persistent cough, dental erosion, hoarseness, and chest pain. 55% were female with mean age of 6±5 yrs. The 95th percentiles for total, nonacid, acid and pH only episodes were 80, 38, 41, and 20 respectively, similar to previously published adult values (Table 1). Sixty-eight patients met criteria to be included as ‘GERD’. Comparing GERD patients with controls, the two differed significantly in all reflux parameters, thereby validating the values for normal impedance (Table 1, Median episodes for controls vs GERD:Total: 21 vs 58, Non-acid: 9 vs 15, Acid: 12 vs 39, pH only: 4 vs 17, p <0.05 for all groups). 129 patients had positive SI of whom, 92 had a normal RI. Patients with positive SI and normal RI had higher acid and nonacid episodes than controls (Median episodes for positive SI versus controls: Total: 54 vs 21 p<0.01, Non-acid: 27 vs 8 p<0.01, Acid: 25 vs 13 p<0.05, pH: 5 vs 4 p=0.2). They had similar total and nonacid episodes but lower acid episodes than patients with positive SI with high RI (Median episodes per 24 hrs for positive SI with and without acid burden: Total: 54 vs 63 p=0.1, Non-acid: 27 vs 18 p=0.3, Acid: 25 vs 43 p<0.05, pH 5 vs 17 p<0.01). The theme of high nonacid episodes in patients with positive SI regardless of RI raises the possibility that the symptoms in these individuals were due to nonacid reflux.

**Conclusion:** We are reporting normal impedance parameters in children using a cohort with no GI symptoms. Our numbers discriminate well from patients with abnormal acid index. Our data also suggest that patients with positive SI have high nonacid reflux that may be contributing to their symptoms.
### Table 1: Reflux Episodes in Normal and GERD patients

<table>
<thead>
<tr>
<th></th>
<th>Total Reflux Episodes</th>
<th>Acid Reflux Episodes</th>
<th>Non-acid Reflux Episodes</th>
<th>pH only Episodes</th>
</tr>
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<tbody>
<tr>
<td>Adults N= 60</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Median (25th,75th)*</td>
<td>30 (18, 45)</td>
<td>28 (7, 31)</td>
<td>9 (6, 15)</td>
<td>0 (0, 1)</td>
</tr>
<tr>
<td>95th</td>
<td>75</td>
<td>55</td>
<td>26</td>
<td>3</td>
</tr>
<tr>
<td>Child without reflux N=31</td>
<td>21 (14, 36)</td>
<td>12 (7, 22)</td>
<td>9 (4, 12)</td>
<td>4 (1, 7)</td>
</tr>
<tr>
<td>Median (25th,75th)</td>
<td>80</td>
<td>41</td>
<td>38</td>
<td>20</td>
</tr>
<tr>
<td>95th</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child with GERD N= 68</td>
<td>58 (36,90)†</td>
<td>39 (25, 61)†</td>
<td>5 (6, 27)†</td>
<td>17(11,26)†</td>
</tr>
<tr>
<td>Median (25th, 75th)</td>
<td>213</td>
<td>166</td>
<td>96</td>
<td>62</td>
</tr>
</tbody>
</table>

† Reflux episodes in GERD patients were significantly different from those of patients without reflux, p<0.05

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80 **USE OF IMPEDANCE-PH NORMAL VALUES TO ASSESS GASTROESOPHAGEAL REFLUX IN CHILDREN WITH CYSTIC FIBROSIS.** Hayat Mousa3, Rodrigo S. Machado1, Carlo Di Lorenzo3, Frederick W. Woodley2,3, 1Pediatric Gastroenterology, Federal University of Sao Paulo, Sao Paulo, Brazil; 2Gastroenterology, Nationwide Children's Hospital, Columbus, OH; 3Pediatrics, Ohio State University College of Medicine, Columbus, OH

**Background** We reported normal impedance-pH (IMP-pH) values for infants (birth-12 months) and children (>12 months-18 years) (Curr Gastroenterol Rep, 2014, 16:400). Shay and colleagues (Am J Gastroenterol, 2004, 99(6):1037) reported normal IMP-pH values for adults (>18 years). **Aim** To evaluate children and adults with cystic fibrosis (CF) using normal values for IMP-pH. **Methods** IMP-pH tracings from 16 CF children (median 8.2 yrs [range 3.0-17.7 yrs]) and 12 CF adults (median 24.2 yrs [range 18.2-48.9 yrs]) were manually analyzed to determine the number of acid gastroesophageal reflux episodes (#AGER), number of nonacid GER (#NAGER) episodes, #total GER episodes, percentage of total bolus contact time (%BCT), and median BCT. IMP-pH parameter values were compared to reported normal values. For children, reported normal values at the 95th percentile are 55, 34, 71, 2.4%, and 32 seconds (s), respectively. For adults, reported normal values at the 95th percentile are 55, 26, 73, 1.4%, and 44s, respectively. **Results** Among CF children, 5 (31%) had abnormal #AGER, 0 abnormal #NAGER, 4 (25%) abnormal #GER, 1 (6.3%) abnormal %BCT, and 0 abnormal BCT duration. For CF adults, 6 (50%) had abnormal #AGER, 0 abnormal #NAGER, 5 (41.7%) abnormal #GER, 7 (58.3%) abnormal %BCT, and 0 abnormal BCT duration. **Conclusions** The data show: 1) children and adult CF patients have normal #NAGER and overall bolus clearance; 2) 1/3 of CF children and 1/2 of CF adults have abnormal %BCT.

81 **SAFETY OF ANAL BOTULINUM TOXIN INFILTRATION IN CHILDREN WITH OUTLET OBSTRUCTION CHRONIC CONSTIPATION.** Claire Zar-Kessler1, Braden Kuo2, Jaime Belkind-Gerson1, 1Massachusetts General Hospital for Children, Boston, MA; 2Massachusetts General Hospital, Boston, MA

**Introduction:** Constipation is a common problem in pediatrics, specifically outlet obstruction constipation due to a non-relaxing or hypertonic sphincter. Previously, surgical anal sphincterotomy was frequently performed on these patients, but more recently Botulinum toxin (BT) injections have been found to be beneficial. Despite small studies reporting a positive response with this strategy, there remains concern regarding safety in the pediatric population. **Aims:** To investigate the safety of BT injection in the treatment of chronic constipation of pediatric patients. **Methods:** Retrospective review over 7 years (2006-2013) of 164 patients chronically constipated children (8mo-19 yrs) who underwent BT injection into the rectal sphincter. All patients had failed medication intervention or were medication dependent. Botulinum toxin injection dose was based on weight (6U/Kg total dose, with a maximum of 100U). This dose was divided into 4 quadrants of the internal anal sphincter, while the patients were under general anesthesia. Charts were reviewed for time course, symptoms and reports on patient's progress. Records were reviewed for each application of BT. For this analysis we included fecal incontinence as a side-effect, although it may also be considered a direct-effect of the medication.
Results: 22 patients were excluded due to lack of follow up visit, thus 142 were examined. Of these, 99 received BT injections one time, 25 received it twice and 14 received 3 or more times, with a total of 203 separate BT treatments analyzed. Twenty eight (16%) patients had an adverse response following botulinum injection: 21 experienced fecal incontinence, 3 with stool urgency, 3 urinary incontinence, 1 rectal prolapse and 1 pruritus ani. Of the 21 with fecal soiling following the procedure, 7 had had encopresis prior to treatment. In these, it was not possible to determine if BT was responsible for worsening encopresis. After injection, 13 (62%) had resolution of the fecal incontinence within a week, with only 2 lasting more than 1 month. Additionally, all the other side effects resolved within a week, except for one patient who continued to have urinary incontinence for 4 months and a patient with persistent pruritus ani lost to follow up.

Conclusions: Botulinum toxin infiltration into the anal sphincter is a safe intervention, without serious adverse reactions. It should be considered as a treatment before or instead of anal sphincterotomy, in pediatric patients with outlet obstruction constipation.

82 BASELINE ANAL CANAL PRESSURE DOES NOT PREDICT EFFICACY OF BOTULINUM TOXIN INJECTION FOR OUTLET OBSTRUCTION CONSTIPATION IN CHILDREN. Claire Zarin-Kessler1, Braden Kuo2, Jaime Belkind-Gerson1, 1Massachusetts General Hospital for Children, Boston, MA; 2Massachusetts General Hospital, Boston, MA

Introduction: Constipation is a common problem in pediatrics, particularly outlet obstruction constipation. Previously, surgical anal sphincterotomy was used for significantly elevated sphincter pressure on anorectal manometry (ARM). Botulinum toxin (BT) injections have recently been found to be beneficial, particularly as short term treatment. We have been using BT for several years, and report our experience in a large retrospective study.

Aims: To investigate the effect of BT injection, including length of response and association with rectal sphincter tone, in children with chronic constipation due to outlet obstruction

Methods: Retrospective review over 7 years (2006-2013) of 163 chronically constipated children (8 mo-19 yrs) who underwent BT injection. All patients had failed medication intervention or were medication dependent. BT dose was based on weight (6U/Kg total dose, with a maximum of 100U). This dose was divided into 4 quadrants into the internal anal sphincter, while the patients were under general anesthesia. Chart was reviewed for time course, symptoms and reports on patient's progress. Patients were separated into normal sphincter pressure (<50mmHg) or elevated sphincter pressure on ARM, while patient was under general anesthesia.

Results: 22 patients were excluded due to lack of follow up, thus 142 patients were analyzed. Ninety eight (70%) had a positive response. Thirty three (22%) had a response lasting greater than 6 mo, with 17 (17%) lasting greater than a year. Twenty two (17%) had a positive response, while 11 (31%) had no or minimal response. Of those with elevated pressure, 60 (68%) had a significant positive response, while 28 (32%) had no or minimal response. There was no statistical difference between the groups.

Conclusions: Botulinum toxin injections are an effective short-term treatment for patients with outlet obstruction constipation, and approximately half of cases lead to a prolonged beneficial response. This was seen even in patients who had failed medication intervention. Elevated sphincter pressure is not a good predictor of response to Botulinum toxin injection and therefore injection may be considered in all patients with outlet obstruction, regardless of anal canal baseline pressure.

83 CURRENT PRACTICES IN PEDIATRIC MOTILITY PROCEDURES. Rinarani Sanghavi1, Joseph Croffie2, 1UT Southwestern Medical Center, Dallas, TX; 2Section of Pediatric Gastroenterology, Hepatology and Nutrition, Indiana University School of Medicine, James W. Riley Hospital for Children, Indianapolis, IN

INTRODUCTION: Manometry is used to diagnose and tailor treatment for various motility disorders of the intestines. Over the past several years, many centers in North America have acquired the capability to perform these procedures in children; however, there are only a few programs that have a formal teaching curriculum for performing these procedures in pediatrics. We sought to look at the current providers of pediatric motility procedures, assess their procedural volumes, previous training of the providers and their familiarity with published standards. METHODS: A cross sectional survey was conducted via an email link to pediatric gastroenterologists who are users of the PEDGI message board and/or members of NASPghan. It consisted of 8 questions, with either yes/no responses and broad number categories. Responses were kept anonymous. RESULTS: 269 pediatric gastroenterologists participated in the survey. 29.37% did perform motility procedures. Of the respondents who completed the rest of the survey, that is, those that perform motility procedures, 48.84% said they interpreted 1-10 anorectal manometries annually, 58.2%, 64.15% and 62.96% personally interpreted 1-10 esophageal, colonic and antroduodenal manometries respectively annually.
66.34% said they personally interpreted studies during fellowship with oversight by an attending physician. Figure 1 shows volumes of procedures interpreted during fellowship. Out of 102 respondents, 66.67% said they were unaware of the minimum standards for procedures published in 2002.

CONCLUSIONS: Most pediatric neurogastroenterologists interpret between 1-50 procedures per year. The most common procedures interpreted are anorectal and esophageal manometry. A majority received training in the interpretation of motility studies during fellowship. Most pediatric gastroenterologists who perform motility studies are unaware of published minimum standards for performing these studies. This survey highlights an important defect which needs to be addressed. There is a need for better access to training programs and some form of certification to recognize appropriate training in neurogastroenterology and motility.

Table 1: Volumes of manometry procedures interpreted personally:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>% Interpret 1-10/yr</th>
<th>% Interpret 10-50/yr</th>
<th>% Interpret 50-100/yr</th>
</tr>
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<tbody>
<tr>
<td>Anorectal manometry</td>
<td>48.84</td>
<td>37.21</td>
<td>13.95</td>
</tr>
<tr>
<td>Esophageal manometry</td>
<td>58.02</td>
<td>39.51</td>
<td>2.47</td>
</tr>
<tr>
<td>Colonic manometry</td>
<td>64.15</td>
<td>22.64</td>
<td>13.21</td>
</tr>
<tr>
<td>Antroduodenal manometry</td>
<td>62.96</td>
<td>31.48</td>
<td>5.56</td>
</tr>
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</table>

Table 2: Procedures interpreted during fellowship

<table>
<thead>
<tr>
<th>NUMBER OF PROCEDURES INTERPRETED</th>
<th>% PHYSICIANS WHO INTERPRETED DURING TRAINING</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>17.28</td>
</tr>
<tr>
<td>10-50</td>
<td>34.57</td>
</tr>
<tr>
<td>50-100</td>
<td>29.63</td>
</tr>
</tbody>
</table>

84 GASTROESOPHAGEAL REFLUX DISEASE IN PEDIATRIC LUNG TRANSPLANT RECIPIENTS. Eric Chiou, Pediatrics, Baylor College of Medicine, Houston, TX

Background: Gastroesophageal reflux disease (GERD) has been linked to chronic rejection caused by bronchiolitis obliterans syndrome (BOS) in lung transplant recipients. The pathologic mechanism responsible for allograft dysfunction is not well understood, but is believed to involve microaspiration of gastric contents. The aim of this study was to characterize GERD and the association with allograft injury/dysfunction in pediatric patients in the immediate post-transplant period.

Methods: Patients who underwent lung transplantation at Texas Childrens Hospital, survived at least 6 months and had post-transplant 24-h esophageal impedance-pH studies were retrospectively reviewed. Antireflux medications were discontinued prior to the impedance-pH study. Demographic data, impedance-pH study results, bronchoalveolar lavage fluid (BALF) analysis and forced expiratory volume in one second (FEV₁) obtained at the time of impedance-pH study were collected.

Results: Twenty-eight patients met entry criteria, with median age of 13 years (range: 1-19 years). Studies were performed at a median time of 46 days post-transplant. Eight of 28 (28.6%) patients had evidence of abnormal acid exposure and subsequently underwent fundoplication surgery. Median acid exposure was 2.1% (range:0%-86%). Overall, there was a median of 29 reflux events (range: 5-222), with a median of 2 proximal reflux events (range: 0-87) per 24 hours. There was no significant correlation between acid exposure, total number of reflux events or proximal reflux events with BALF neutrophil levels or FEV₁ obtained at the time of studies.

Conclusions: GERD is prevalent among pediatric lung transplant patients. In the immediate post-transplant period, GERD was not associated with increased allograft injury or dysfunction. Future studies are needed to assess the role of fundoplication in prevention of BOS.
DOES PPI THERAPY INCREASE THE RISK OF MICROBIAL COLONIZATION OF THE DUODENUM?

Aim: There are controversial data regarding the association between PPI use and small intestinal microbial overgrowth. Our goal was to analyze the results of duodenal cultures obtained during upper gastrointestinal endoscopy.

Method: 243 children had duodenal cultures obtained during upper gastrointestinal endoscopy by using sterile brushes between April 2013 and May 2014. A CFU count over $10^4$/ml was considered abnormal for bacteria and $\geq 10^3$/ml for fungal species.

Results: Eighty six (35.4%) of 243 children were positive for microbial overgrowth noted within the duodenal cultures. Seventeen (19.8%) of the positive patients had fungal overgrowth and the rest of them had bacterial colonization. In the majority of the cases, the colonization consisted of aerobic upper respiratory flora. When comparing the positive and negative culture groups, the prevalence of prior PPI therapy was 40.7% in the positive group and 28.7% in the negative group. In the positive group neither the average age nor the colony count was different between those who had or did not have prior PPI therapy. There was no correlation between the age and colony count ($r=0.11$). The five highest CFU/ml (>500x$10^3$/ml) patients had celiac disease, Crohn's disease, hypoplastic left heart, chronic kidney disease and MEN-1.

Conclusion: It is easy to obtain a duodenal smear by brushing from the duodenal lining. Approximately one third of the patients had positive results. There was no statistical difference between the two groups regarding proton pump inhibitor use.

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VULNERABILITY AND CHRONIC ILLNESS MANAGEMENT IN PEDIATRIC KIDNEY AND LIVER TRANSPLANT RECIPIENTS. Alisha M. Mavis1, Allison Ertl2, Stacee Lerret1. 1Pediatric Gastroenterology, Hepatology, & Nutrition, Medical College of Wisconsin, Milwaukee, WI; 2Graduate School of Biomedical Sciences, Medical College of Wisconsin, Milwaukee, WI

Background: Solid organ transplant (SOT) is the treatment of choice for end stage organ failure and requires a transition from management of a life-threatening condition to a chronic illness. As pediatric SOT recipients live longer it is critical to not only manage medical complications, but also ensure supported and appropriate psychosocial adjustments. Despite research focusing on quality of life post-transplant, there is a gap addressing the role of managing a chronic illness focusing on vulnerability and impact on family. Identification of these issues may suggest opportunities for intervention to decrease overall family stress and improve adaptation to chronic illness management.

Objective: Identify patient and family patterns of adaptation among kidney and liver transplant recipients in regard to 1) vulnerability, 2) impact of illness on the family, 3) family functioning, and 4) quality of life (parent and child report).

Methods: Prospective cross-sectional study enrolling children 5-18 years of age and their parent at a single time point following kidney or liver transplant. Validated self-report tools were completed.

Results: 47 participants (24 kidney and 23 liver) were recruited. Average age at transplant was 4 (kidney) and 2.1 (liver) years. Average time post-transplant was 3.2 (kidney) and 3.6 (liver) years. Average age at report was 12.1 (kidney) and 7.1 (liver) years. Child vulnerability negatively correlated with 1) Family impact in the kidney (p<0.05) and liver transplant groups (p<0.05), 2) PedsQL™ subscales including Parent Emotional (p<0.05), Parent Social (p<0.01), Parent Psychosocial (p<0.01), Parent Physical (p<0.05), Parent School (p<0.05), and Child Social (p<0.001) in the kidney transplant group, 3) PedsQL™ Parent Emotional subscale (p<0.01) in the liver transplant group, and 4) Functional status (p<0.01) in the liver transplant group. Parent reported quality of life positively correlated with family impact for kidney (p<0.001) and liver (p<0.05) transplant recipients and functional status (p<0.05) for kidney recipients. Family impact subscale scores including parent health related quality of life and family functioning trended lower (NS) in the liver versus kidney transplant group. Age at report was significantly associated with child vulnerability (p<0.01),
family functioning (p<0.01), and impact of illness on family (p<0.05).

**Conclusions:** Child vulnerability provides insight into quality of life, impact of illness on the family and family functioning. A positive psychosocial adjustment is imperative for optimizing not only quality of life, but also overall patient and family functioning after pediatric SOT. Post-transplant care may benefit from routine assessment of not only quality of life and impact of illness on family but also vulnerability in order to provide specific support services and enhance chronic illness management.

98  **ELEVATED IRISIN EXPRESSION IN NASH LIVERS.** Colleen A. Nugent1, Susan S. Baker1, Wensheng Liu1, Lucy Mastrandrea2, Robert D. Baker3, Lixin Zhu1, 1Digestive Diseases and Nutrition Center at Women and Children's Hospital of Buffalo, State University at Buffalo, Buffalo, NY; 2Division of Endocrinology and Diabetes, Women & Children's Hospital of Buffalo, State University of New York at Buffalo, Buffalo, NY

**Background:** Data mining our microarray database suggested that irisin is one of the most highly elevated genes in the livers of non-alcoholic steatohepatitis (NASH). NASH, the severe form of non-alcoholic fatty liver disease (NAFLD), is characterized by hepatic steatosis, inflammation and fibrosis. Irisin is an adipomyokine produced by both adipose and muscle tissue. It induces a browning effect on white adipose tissue and may affect the metabolic status of NASH patients. We studied irisin expression in liver biopsies from patients with NASH and evaluated correlations with various components of NASH pathology and metabolic syndrome.

**Methods:** Biopsy-proven adolescent NASH patients were included in this study. Healthy livers from donors of similar age and gender were used as controls. Irisin gene expression was evaluated by microarray and quantitative real-time PCR. The correlations were sought between irisin expression and fasting glucose and insulin, IR-HOMA, fasting triglycerides, BMI, BMI z-score, LDL, HDL, fasting total cholesterol using Pearson's rank correlation coefficient analysis.

**Results:** Hepatic irisin gene expression is increased in NASH compared to controls. Microarray data showed, NASH/Normal = 30.49 (p = 0.0008) and qRT-PCR showed NASH/Normal = 152.04 (p < 0.05). Significant correlations were found between irisin message and fasting glucose (r = 0.7887, p= 0.012) but not between irisin and BMI, BMI Z-score, AST/ALT, total cholesterol, LDL, or HDL.

**Conclusions:** This study indicates that irisin gene expression is induced in NASH. The correlation between liver irisin expression with fasting glucose but not with lipids suggested a connection between carbohydrate metabolism and irisin expression. Irisin expression may be regulated in a response to aberrant carbohydrate metabolism in NASH livers.

99  **LIVER TRANSPLANTATION IN CHILDREN WITH WEIGHT UNDER 8KG IN A CENTER OF LATIN AMERICA.** D. D’Agostino, MC.Sanchez, V. Reynoso, G.Boldrini, V.Fernandez De Cuevas, M. Ciardullo, E. De Santibañez

**Gastroenterology-Hepatology Division And Liver -Intestinal Transplantation Center, Department Of Pediatrics-Hospital Italiano De Buenos Aires , Buenos Aires – Argentina, Daniel E. D’Agostino, Pediatrics, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina**

**Introduction:** The shortage of liver donor for small size and weight transplant recipients is a big trouble. The development of living related donor (LRD) and left lateral segment hypereduction technique permitted to alleviate this difficulty

**Objective:** To describe a series of liver-transplanted children under 8 kg in a center in Latin America.

**Material and Methods:** A descriptive, retrospective cross-sectional study of this population between 1992 and 2013 was performed.

**Results** The liver transplant program conducted to date has studied 320 pediatric transplant, of which 40 (12.2%) were under 8 kg and the hyper reduction technique was performed in 32 (80%). The series includes 22 women, with a mean age of 11.42 months (SD 4.57) and an average weight of 7.32 kg (SD 0.72). In 35 cases (87.5%) transplantation was carried out with LRD and on 5 cadaveric donors. Median operative time was 350 min (r 180-510 ), and an average of 21days remained in ICU (SD 14.87) Average inpatient days was 37 days (r 14-93) The morbidity was 70% complications were biliary disorders in 20% of cases and 30.5% were vascular complications. Survival to transplantation was 95%, year overall survival time was 93% and Hypereduce group was 92%

**Conclusion:** A very low weight group of patients could be transplanted using the LRD and Hypereduce technique. They had been delayed with high risk increase in the past. This is the first piece of information we have knowledge of about so small children to be treated in a Latin American Center.
INCIDENCE OF BLOODSTREAM INFECTIONS IN SMALL BOWEL TRANSPLANT RECIPIENTS RECEIVING SELECTIVE DECONTAMINATION OF THE DIGESTIVE TRACT: A SINGLE CENTER’S EXPERIENCE. David Galloway, Monique Goldschmidt, Trina Hemmelgarn, Lara Danziger-Isakov, Joshua Courter, Jamie Nathan, Maria Alonzo, Greg Tiao, Samuel Kocoshis, Gastroenterology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

Background: Pediatric patients undergoing small intestinal or liver/intestinal transplantation are at high risk for bloodstream infections (BSI), particularly from gram negative bacterial and fungal species, in the immediate post-transplant period. The use of selective digestive decontamination (SDD) is a strategy employed to reduce the incidence of these infections. In this study we hypothesized that the frequency of BSI will be reduced during the first 30 days following transplant in subjects taking a SDD directed against gram negative aerobes and fungal species compared to the subsequent 30 days following discontinuation of SDD. We also hypothesized that if patients became infected, organisms responsible for the BSI’s would differ depending on if patients were on or off SDD.

Materials and Methods: A retrospective chart review of 37 pediatric small bowel transplant recipients at the Pediatric Liver and Intestinal Care Center at Cincinnati Children's Hospital Medical Center from January 2003 to June 2011 was conducted. Demographics, SDD regimen and duration, incidence of BSI, number of other types of infection, organism identification from positive cultures, susceptibility profiles of positive cultures and antibiotics administered with duration were compared among transplant recipients during the immediate 30 day post-operative period and the subsequent 30 days following discontinuation of SDD. Comparative analyses were performed.

Results: The overall incidence of BSI did not differ among the two observed time periods (9.5 BSI per 1000 catheter days). Gram positive organisms predominated among BSI during the first 30 day post-operative period (7 of 8, 87%) while Gram negative organisms comprised the majority of BSI during the 30 day period following discontinuation of SDD (6 of 8, 75%). There was no difference in susceptibility patterns for the SDD drugs administered between both time periods as analyzed by mean inhibitory concentration (MIC) levels. These findings were significant.

Conclusion: Selective digestive decontamination does not alter the incidence of BSI in the immediate 30 day post small bowel transplantation period as compared to the 30 days following discontinuation of SDD in the pediatric population. However, SDD does exhibit a robust influence on BSI organism types, favoring gram positive organisms. Thirty days of SDD does not alter susceptibility patterns of organisms producing infections.

MS-275, A CLASS I SPECIFIC HISTONE DEACETYLASE INHIBITOR, DECREASES HEPATIC DE NOVO LIPOGENESIS GENE EXPRESSION IN MURINE MODELS OF OBESITY. Elizabeth L. Yu1, Michael Downes2, Ronald M. Evans1, 1The Salk Institute for Biological Studies, La Jolla, CA; 2Pediatric Gastroenterology, Hepatology and Nutrition, UCSD, La Jolla, CA

Background/Aims: Histone deacteylase inhibitors (HDACi), already used clinically in oncologic therapy, have previously been shown to improve metabolic markers and decrease hepatic steatosis in murine models of obesity. We hypothesize that the SREBP1c/FGF21 pathway may be a possible molecular explanation for decreased hepatic triglyceride accumulation after MS275 treatment. Methods: WT (wild type) mice were fed a high fat diet (HFD) where 60% of kcal came from fat for 14 weeks in order to induce obesity and NASH (non-alcoholic steato-hepatitis). WT mice fed regular chow (13% kcal from fat) were used as comparison. After histologic confirmation of NASH development in the HFD cohort, mice in both cohorts were treated with 4 weeks of daily intraperitoneal (IP) injections of either DMSO or MS275, a class I specific HDACi. Hepatic histology was evaluated at the end of the study period. qPCR from hepatic tissue and serum FGF21 levels were evaluated from both DIO (diet induced obesity) and control mice. Results: Hepatic histology from DIO (diet-induced obesity) mice treated with MS275 demonstrated decreased macrovesicular steatosis (p<0.05) compared to their vehicle treated counterparts. Hepatic gene expression demonstrated significant downregulation of SREBP1c, a gene responsible for regulation de novo lipogenesis, as well as SREBP1c downstream targets (GPAT, FAS, SCD-1) in MS275 treated mice. Additionally, MS275 treatment significantly upregulated both hepatic gene and serum concentrations of FGF21 - a suppressor of SREBP1c. Conclusions: MS275 decreased hepatic steatosis in murine models of obesity. MS275 treatment downregulates hepatic expression of genes involved in de novo lipogenesis. In conclusion, MS275 is a promising therapeutic candidate in NASH.
composition: fat mass (FM), fat free mass (FFM) and bone mineral density (BMD) measured by dual x-ray absorptiometry (DXA, Hologic Discovery W-series QDR). Reference patterns: Fomon's and Butte's. BMD was expressed a z-score. Statistics: Median, intercuartilar range (ICR), and Pearson correlation.

**Results:** Patients: Ten were females, median age was 14 months. Median liver damage cores were PELD 14 (ICR 15), Malatack 34 (ICR 28), Child 11 (ICR 5). Eighty percent had FFM and 66% FM below lower limits (median percentage). BMD z-score was below <-2SD in 80%. PELD, Child and Malatack scores had had significant correlations with FM (r = -0.75 p<0.001; r = -0.63, p=0.010; r = -0.61, p=0.016 respectively) and BMD (r = -0.89 p<0.001, r = -0.85 p<0.001, r = -0.72 p<0.001 respectively). No correlation was observed between FFM and liver damage scores.

**Conclusions:** The negative and significant correlation of PELD, Malatack and Child scores with FM and BMD, reflects the close relationship between body composition (loss of fat stores and impaired bone mineralization) and the severity of liver damage in infants and toddlers. Body composition may predict the degree of liver damage.

### 103 VACCINATION STATUS PRE-SOLID ORGAN TRANSPLANTATION: OPPORTUNITIES REVEALED!

**Katherine Twombley**, J. Antonio Quiros

**Background:** Vaccination history is typically reviewed prior to a solid organ transplant (SOT: heart, liver, kidney). Accelerated immunization schedules have been proposed, but are not allowed followed. A lot of chronically ill children do not routinely go to the primary care physician, and the primary care physician may not be familiar with the accelerated vaccine schedules. Utilizing an accelerated vaccine schedule could potentially benefit a large number of children receiving a SOT before they can be vaccinated at the recommended ages.

**Objective:** To determine the number of patients who would potentially benefit from an accelerated vaccination schedule by reviewing pre-transplant vaccination status for measles, mumps, rubella(MMR) and varicella (VAR) and surface antibody titers for hepatitis B (HepBsAb).

**Design/Methods:** A retrospective chart review was conducted of children who received a SOT between the year of 2008-2012. The review was limited to patients 1 year to 6 years of age at time of transplant since this is the time that children typically receive the recommended childhood vaccines and these are the children that would benefit the most from an accelerated schedule. Data were collected using the inpatient and outpatient medical records, pre-transplant records, as well as immunization records from primary care physicians when available. Treatment courses were also reviewed to identify periods of immunosuppressive therapy which would have prevented vaccination prior to transplant. Patients were excluded if they were on immunosuppressive therapy preventing live virus vaccination or if vaccine records or titers were not available.

**Results:** There were a total of 27 SOT recipients were eligible for review. 21 patients had vaccination records available for review, but 2 were excluded because they were immunosuppressed preventing live virus vaccination, leaving 19 pts. 24 pts had HepBsAb titers available for review. The majority of patients being evaluated for a SOT were incompletely vaccinated with live virus vaccines: 75% of heart recipients, 50% of kidney recipients, and 80% of liver recipients. 21% of patients had negative Hepatitis B antibodies (Ab) prior to transplant.

**Conclusions:** Sixty-three percent of our patients would have potentially benefited from an accelerated vaccine schedule of MMR and VAR and 37% would have benefited from a booster of HepB. Planning should occur as the patient awaits transplant to develop and complete a maximally effective immunization schedule. Our center will be starting a QI project based on this data to improve our pre-transplant vaccination rate.
104 CORRELATION OF CHANGES IN BMI Z-SCORE WITH ALT IN PEDIATRIC NAFLD. Jennifer Panganiban, Sandy Cope-yokoyama, Jon Oden, Jeffrey Browning, Charina Ramirez, Gastroenterology, UTSW, Dallas, TX; Pediatric Gastroenterology, UTSW, Dallas, TX; Pediatric Endocrinology, UTSW, Dallas, TX; Pathology, UTSW, Dallas, TX

Non-alcoholic fatty liver disease (NAFLD) has become the leading cause of chronic liver disease among children. The recommended treatment for NAFLD is weight loss by diet and exercise. Major outcome measures for multidisciplinary programs targeting NAFLD include weight loss with a subsequent decrease in aminotransferases, markers of fibrosis, intrahepatic triglyceride content and histologic improvement. Due to the difficulty in obtaining a liver biopsy in pediatric patients post intervention, a decrease in aminotransferases has become an accepted measure of presumed liver improvement in NAFLD.

Objective: To determine if a statistically significant decrease in BMI z-score will result in a reduction of alanine-transaminase (ALT) in patients with liver biopsy proven NAFLD.

Methodology: This is a retrospective chart analysis of patients 0-22 of age who underwent a liver biopsy at Children's Medical Center between January 2012 and January 2014. A total of 315 liver biopsies were performed and 32 patients (10%) had a histologic diagnosis of NAFLD. Other work up included serology to rule out autoimmune, viral and metabolic liver disease. The NAFLD subset was analyzed and baseline characteristics were established. Three patients were excluded from this data set due to a co-existing diagnosis of alpha 1 antitrypsin, ketogenic diet and steroid induced steatosis. ALT was correlated with BMI z-score. ALT decrease was defined as a reduction of ≤ 50% from baseline. A decrease in BMI z-score was defined as a decrease of >0.1 from baseline. Patients who had an elevation in ALT despite a decrease in BMI z-score were further characterized.

Results: Baseline NAFLD population was predominately male (59%), mean age of 12 (4-18 y/o) and of Hispanic ethnicity (81%). The baseline mean ALT was 180 IU/L and population was primarily obese (78%) with a BMI z-score >2. Correlation of changes in BMI z-score and ALT are seen in Table 1. Patients with an unexpected increase in ALT despite decrease in BMI z-score were characterized in Table 2.

Conclusion: There is an inconsistent correlation with a decrease in BMI z-score and ALT level. Thus ALT measurement alone would not be a reliable outcome measure to establish if weight loss intervention is effective in improving liver disease. Other modalities in conjunction with ALT should be employed to assess liver improvement in patients with NAFLD.
Changes in ALT and BMI z-score

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<td>5 (17)</td>
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Patient characteristics with a decrease in BMI z-score and increase in ALT

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<th>NAS score</th>
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105 CLINICAL CHARACTERISTICS OF NON-ALCOHOLIC FATTY LIVER DISEASE IN OUTPATIENT PEDIATRIC NATIVE AMERICAN PATIENTS. Justin C. Wheeler1, Chengcheng Hu2, Tamir A. Miloh1, 1GI/Hepatology, Phoenix Children's Hospital, Phoenix, AZ; 2Epidemiology and Biostatistics, University of Arizona College of Public Health, Phoenix, AZ

Background: Pediatric nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children. NAFLD is strongly associated with metabolic syndrome, which is more prevalent in Hispanics and Native Americans (NA). However, there are no studies examining NAFLD in the pediatric NA population. Phoenix Children's Hospital (PCH) has a substantial NA patient population, providing an ideal setting for the study.

Methods: This is a descriptive retrospective electronic medical record (EMR) chart review of NAFLD patients evaluated at the PCH GI clinic from 2/2009 through 11/2012. Patients were identified using ICD-9 codes for chronic hepatitis, obesity, and overweight. Patients were excluded if an alternative cause of chronic liver disease was identified. Clinical and laboratory data at initial presentation as well as biopsy results were compared between Hispanic, Caucasian, NA, and Other groups. Statistical analysis performed using Wilcoxon rank-sum test or Fisher's exact test, with linear regression models adjusting for age, gender and body mass index (BMI).

Results: 405 patients reviewed in study, 241 met inclusion criteria (59%). Patient distribution in study (vs all PCH patients in 2011) was 54.8% (39.2%) Hispanic, 23.6% (42.5%) Caucasian, 15.8% (2.4%) NA, and 5.8% (15.9%) Other. Ages ranged from 5-19 years. Results are summarized in Table 1. NA patients had significantly higher BMI, ALT, AST, and Hemoglobin A1C at initial presentation than all other patients when adjusted for age and gender (p<0.02). However, there was no statistical difference of AST, ALT or NAFLD Activity Score (NAS) from liver biopsy between NA patients and Hispanic patients or all other patients when additionally adjusted for BMI.

Conclusions: NA and Hispanic patients represented a larger proportion of NAFLD patients compared to the distribution of the general PCH patient population. NA patients presented with a higher BMI, ALT, AST, hemoglobin A1C and more fatigue than other ethnicities. However there was no statistical difference after correcting for BMI. Results could represent a referral bias. Further prospective studies are required to assess for additional clinical differences of NA patients with NAFLD.

Clinical Characteristics of NAFLD Patients by Ethnicity
THE PEDIATRIC NASH PREDICTIVE MODEL: A NOVEL ONLINE CALCULATOR TO AID IN THE DIAGNOSIS OF NASH IN CHILDREN WITH NAFLD. Katharine Eng, Vera Okwu, Rocio Lopez, DanielaLiccardo, Valerio Nobili, Naim Alkhouri. Department of Pediatric Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH; Department of Quantitative Health Sciences, Cleveland Clinic Foundation, Cleveland, OH; Liver Unit, Bambino Gesù Children’s Hospital and Research Institute, Rome, Italy; Digestive Disease Institute, Cleveland Clinic Foundation, Cleveland, OH.

Background: Nonalcoholic fatty liver disease (NAFLD) affects 10% of children in the United States and encompasses a spectrum of disease ranging from simple steatosis to the aggressive form of nonalcoholic steatohepatitis (NASH). We had previously developed a nomogram to non-invasively diagnose NASH in children with NAFLD. Utilizing this nomogram, we were able to create a simple online calculator predicting the risk of NASH using clinical and laboratory data. The aim of our current study was to test the performance of this calculator in predicting NASH.

Methods: Anthropometric, laboratory, and histologic data was obtained in a cohort of 302 children with biopsy-proven NAFLD. Multivariable logistic regression analysis was employed to create a nomogram predicting the risk of NASH, which includes waist circumference percentile, total cholesterol, and total bilirubin. An online prediction calculator termed the Pediatric NASH Predictive Model (PNPM) was constructed based on this nomogram. Sensitivity, specificity, negative predictive value, and positive predictive value were calculated at various nomogram prediction levels to ascertain the optimal cut-off values for the model.

Results: The PNPM was employed in all subjects. Forty-one subjects had PNPM-predicted values <40%. Of these patients, 29 did not have NASH on liver biopsy, resulting in a 94.1% sensitivity and 29.3% specificity for having NASH. One-hundred-and-twenty-two patients had PNPM-predicted values >75%. Of these patients, 103 had biopsy-proven NASH, resulting in a 50.7% sensitivity and 80.8% specificity for having NASH. When extrapolated to the subject population using these cutoff values, the PNPM would have prevented an unnecessary liver biopsy in a total of 163 of 302 subjects (54%).

Conclusions: We successfully created an online prediction calculator, termed the PNPM, based on our prior nomogram predicting the risk of NASH in children with NAFLD. Utilizing PNPM cutoff values of less than 40% to rule out NASH and values of greater than 75% to rule in NASH, this calculator can potentially prevent unnecessary liver biopsies in over 50% of children. This calculator is easily accessible to the public, and if validated externally, could serve as a ubiquitous tool for physicians evaluating children with NAFLD at risk for NASH.

TRENDS IN THE WAIT-LIST FOR INTESTINAL TRANSPLANTATION. Khalid Khan, Chirag Desai, Thomas Fishbein, Stuart Kaufman, MedStar Georgetown University Hospital, Washington, DC.

Background: We utilized intestinal transplant (ITx) wait-list data as a measure of changes in non-transplant care of patients with intestinal failure.

Method: United Network for Organ Sharing (UNOS) data were examined for trends in the ITx wait-list from 1993 to 2012, dividing patients in to those listed for an isolated ITx versus liver and intestine transplant (L-ITx).

Results: Registrants added to the wait-list increased from 59/year in 1993 to 317/year in 2006, then declined to 124/year...
year in 2012; Spline modeling showed a highly significant change in the trend in 2006, $p=< 0.001$. The largest group of registrants, <1yr of age, determined the trend for the entire population; other pediatric age groups remained stable while adult registrants increased until 2012. The largest proportion of new registrants were for L-ITx, compared to isolated ITx; the change in the trend in 2006 for L-ITx was highly significant, $p=< 0.001$, but not isolated ITx, $p=0.270$. New registrants for L-ITx, <1yr of age, had the greatest increase and decrease. New registrants for isolated ITx remained constant in all pediatric age groups. Wait-list mortality increased to a peak around 2002; it was highest for L-ITx, in patients <1yr of age and adults. Deaths amongst all pediatric age groups awaiting L-ITx have decreased; adult L-ITx deaths have dropped less dramatically.

Conclusion: Improved care of infants on parenteral nutrition has led to a dramatic decrease in the number referred for L-ITx. This demographic change will need a refocusing by ITx physicians and healthcare resources.

108 CORRELATION BETWEEN THE INDICATORS OF METABOLIC SYNDROME, LIVER TRANSAMINASES AND NON-ALCOHOLIC FATTY LIVER DISEASE IN OVERWEIGHT/OBESE CHILDREN AND ADOLESCENTS. Lina Diaz Calderon1, Adriana Herrera1, William Muinos2, Richard Arboleda2, Roberto Gomara2, Erick Hernandez2, Jesse Reeves-Garcia2, 1Medical Education, Miami Children’s Hospital, Miami, FL; 2Pediatric Gastroenterology, Miami Children’s Hospital, Miami, FL

Background: The prevalence of non-alcoholic liver disease (NAFLD) and metabolic syndrome (MS) are dramatically increasing along with the epidemic of childhood obesity. We studied the association of varying degrees of obesity with the features of the metabolic syndrome and its relation to elevated transaminases and NAFLD.

Patients and Methods: A descriptive, retrospective cross-sectional study was conducted in 197 overweight/obese children and adolescents. Age, sex, body mass index z-score, blood pressure, transaminases, serum lipid profile and serum blood glucose were assessed. Liver ultrasound was performed among 58.3% (n=115) of participants.

Results: A total of 197 patients, 107 females (54.3%) and 90 males (45.7%) with a mean age of 14.7 ± 3.8 years, were enrolled. All patients were overweight or obese, they were distributed among 3 groups based on body mass index standard deviation score distribution (BMI z-score) WHO growth charts as follows: +1SD (13.1% females vs 5.6% males), +2SD (51.4% females vs 52.2% males) and +3SD (53.5% females vs 42.2% males). When studying lipid risk, we observed that 36% had elevated triglyceride levels (>95th percentile for age), with higher prevalence in males than females (42.2% vs 30.8%, respectively). HDL levels were low (<5th percentile for age) in 18.3% of participants (20.6% female vs 15.5% male). Abnormal levels of HDL and triglycerides were significantly more common in obese patients with BMI z-scores of +2SD and +3SD.

Elevated transaminases levels were found in 42.2% of participants. Elevated alanine aminotransferase (ALT) levels were present in 23.8% of the total population, with a higher prevalence in boys than in girls (32.2% vs 16.8%, $P<0.01$). Aspartate aminotransferase (AST) levels were increased in 18.2% (12.1% female vs 25.5% male, $P<0.05$). NAFLD was detected in 54.7% (n=63) of the patients who had liver sonogram done. Children with NAFLD had significantly higher body mass index (BMI) and ALT compared to patients without fatty liver ($P<0.01$).

Conclusion: There is strong association between the degree of obesity, the presence of abnormal levels of ALT, HDL and triglyceride levels and the prevalence of NAFLD in the overweight and obese pediatric population.

109 ECG CHANGES AND SURVIVAL IN BILIARY ATRESIA PATIENTS LISTED FOR LIVER TRANSPLANT. Thaddaeus D. May1, Mansi Amin1, Charles Ho2, Megh Gore2, Pooja Yesentharao2, Yu Tong Zhang2, Sahar Noorani3, Moreshwar Desai3, Ross Shepherd1, 1Pediatric Gastroenterology, Hepatology, and Nutrition, Baylor College of Medicine, Houston, TX; 2Rice University, Houston, TX; 3Critical Care Medicine, Baylor College of Medicine, Houston, TX

Purpose: Optimal prioritization is critical to reduce the risk of acute on chronic liver failure (ACLF) and death in patients waiting for liver transplant (LT). Current prioritization approaches focus primarily on readily available biochemical parameters. There is however little knowledge regarding the relevance of the known tendency for patients with chronic liver disease to exhibit cardiac conduction abnormalities {e.g. prolonged corrected QT interval (QTc)} on 12 lead electrocardiogram (ECG). Proposed causes of these conduction abnormalities include electrolyte abnormalities, myocardial ischemia, sympathetic hyperactivity, and chronic cholestasis. Biliary atresia (BA), offers an opportunity to assess the relationship between chronic cholestasis and conduction abnormalities in a pediatric population. In this study we purposed to characterize ECG findings in children with BA who were listed for LT at a large volume pediatric LT center in order to examine the relationship between cardiac conduction abnormalities and acute on chronic liver failure and death.

Methods: Medical records were reviewed for 89 patients with BA listed for LT at Texas Children's Hospital between 2001 and 2013. Patients with congenital heart disease were excluded. Patients with ACLF met United Network for Organ Sharing criteria for status IB. Eighty patients (90%) had a listing ECG[HG1] available for review. All ECG parameters including QTc (calculated with Bazett's formula), were measured by a board certified pediatric cardiologist. Data analysis was performed using R (version 2.15.2 2012). Statistical significance was determined at $P \leq 0.05$. 
**Results:** Among the 80 BA patients reviewed 15 (19%) developed ACLF, of whom 9 (60%) died. Overall, 23 patients had a QTc > 440 msec (29%), 17 patients had a QTc > 445 msec (21%), 14 patients had a QTc > 450 msec (18%), [HG2] (normal range: <445 msec). Analysis of medians did not demonstrate significant difference between ACLF, non-ACLF, surviving, and non-surviving groups of patients (Table). Linear regression of ECG parameters did not demonstrate any significant correlations with calculated PELD scores at the time each ECG was obtained.

**Conclusion:** Our findings demonstrate an increased frequency of QTc prolongation in the setting of liver disease, (the average incidence of QTc > 445 msec in healthy pediatric populations has previously been estimated at <2%). However there was no correlation between these findings and ACLF or death before transplant. Although limited by a relatively small sample size and its retrospective approach this study is the largest study in children with BA to document cardiac conduction abnormalities. Future study should be directed towards examining the relationship of these findings with post transplant outcomes.

**Comparison of ACL, non-ACLF, Survivors, and non-Survivors**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ACLF Mean</th>
<th>Non-ACLF Mean</th>
<th>Wilcoxon P-Value (ACLF)</th>
<th>Surviving Mean</th>
<th>Non-Survivor Mean</th>
<th>Wilcoxon P-Value (Death)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR Interval</td>
<td>112.0 ± 15.4</td>
<td>113.5 ± 32.0</td>
<td>0.89</td>
<td>113.5 ± 30.7</td>
<td>110.6 ± 16.2</td>
<td>0.65</td>
</tr>
<tr>
<td>QTc</td>
<td>427.8 ± 29.8</td>
<td>431.0 ± 40.7</td>
<td>0.71</td>
<td>429.8 ± 39.4</td>
<td>434.2 ± 33.3</td>
<td>0.71</td>
</tr>
</tbody>
</table>

**110 THE HISTOLOGICAL SEVERITY OF NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) IS NOT ASSOCIATED WITH WORSENING RENAL FUNCTION IN CHILDREN.** Marwan Bakhach, Rocio Lopez, Naim Alkhouri, Valerio Nobili, Cleveland Clinic, Cleveland, OH

**BACKGROUND:** Nonalcoholic fatty liver disease (NAFLD) is a spectrum of progressive liver disease that includes simple steatosis, nonalcoholic steatohepatitis (NASH), fibrosis and ultimately, cirrhosis. Accumulating evidence suggests that NAFLD is associated not only with liver-related morbidity and mortality, but also with an increased risk of developing extrahepatic manifestation including chronic kidney disease. Recent adult data suggested that the severity of NAFLD (presence of NASH or fibrosis) is associated with pronounced renal dysfunction. The aim of this study was to assess the relationship between renal function and the histological severity of NAFLD in children. **METHODS:** Children with biopsy-proven NAFLD were included in this study and the histological features were scored using the NAFLD activity score (NAS). Fibrosis was staged from F0-F4. Renal function was assessed using creatinine clearance and urinary albumin excretion (UAE). A univariable and multivariable analyses were performed to assess the association of renal function with the presence of NASH. Spearman's correlation coefficients were computed to assess the correlation with histological features of NAFLD. A p value < 0.05 was considered statistically significant.

**RESULTS:** A total of 160 subjects with biopsy proven NAFLD were included in the analysis. Mean age was 11 ± 3 years and 38% were male. Sixty-nine percent of subjects had biopsy proven NASH and 68% fibrosis (stage 1-4). The mean creatinine clearance was 77.1 ± 22.8 mg/min and the median UAE was 8.0 [4.8, 11.9] mg/24 hr. After performing an automated stepwise variable selection method and adjusting for variables (hypertension, diabetes, bilirubin and GGT), there was no evidence to suggest that NASH is associated with UAE (odds ratio 1.04, 95% confidence intervals 0.97-1.1, p=0.26) or creatinine clearance (odds ratio 1.06, 95% confidence intervals 0.97-1.2, p=0.19). Moreover, there was no evidence of correlation between decreased renal function and any of the histological features of NAFLD or NAS as shown in the table. **CONCLUSION:** In contrast to previous adult studies, our study did not reveal a relationship between renal function (creatinine clearance and UAE) and the histological severity of NAFLD in children.
111 GENERATION OF A TALEN-MEDIATED STEM CELL MODEL TO STUDY NON-ALCOHOLIC FATTY LIVER DISEASE ASSOCIATED WITH A PNPLA3 POLYMORPHISM. Nidhi Goyal1, Maria P. Ordonez2, Lawrence S. Goldstein3, 4Pediatric Gastroenterology, University of CA, San Diego, San Diego, CA; 4Cellular and Molecular Medicine, University of CA, San Diego, San, CA

Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease in the adult and pediatric population and is a complex disease with both environmental and genetic components. Genome-wide association studies (GWAS) have identified a polymorphism in the gene PNPLA3 that has a strong association with risk and severity of NAFLD, with the variant allele of PNPLA3 being associated with more severe biochemical and histological abnormalities. The protein product of PNPLA3, or adiponutrin, is involved in lipid metabolism, but its exact function in humans remains unclear. The pattern of expression of adiponutrin is different in mice and humans, making it difficult to extrapolate findings from animal models. Using TAL effector nuclease (TALEN) technology, we have designed TALENs specific to the PNPLA3 SNP. Subsequently, we have generated isogenic lines of human induced pluripotent cells (hiPSCs) from a known genetic background with the variant and wild-type homozygous alleles of PNPLA3 using these site specific TALENs. We are able to induce differentiation of hiPSC to hepatocyte like cells (HLC) that have typical morphology and lineage specific markers. We will use hiPSC derived HLCs with the wild type and risk alleles of PNPLA3 to test the hypothesis that polymorphisms of PNPLA3 induce abnormal lipid processing as a potential early pathogenic event in NAFLD. To our knowledge, this is the first set of isogenic lines of hiPSCs designed specifically with the PNPLA3 wild type and variant alleles. These lines of cells are invaluable in studying the genetic contribution of this polymorphism, as it is a human model that can be analyzed in vitro to translate genetic variation into observable cellular phenotypes that may confer risk to develop a disease. We are comparing intracellular lipid accumulation by flow cytometry analysis of nile red staining of HLC and expression of genes involved in lipid metabolism including ChREBP, SREBP1, PNPLA2, and PPAR. The next aim is to translate this model to a clinical model by developing patient specific hepatocytes and provide the critical clinical link that is required in the study of human disease. Our approach translates a population-based GWAS into an in vitro human model to study the pathophysiology of NAFLD at a fundamental level. More broadly, our work is an example of how the combined use of hiPSC technology and targeted genome editing can serve as a strategy to model complex sporadic diseases.

112* DIFFERENCES IN EARLY VERSUS LATE LIVER TRANSPLANTATION FOR BILIARY ATRESIA. Sanjiv Harpavat1, John Hollier1, John A. Goss2, 1Pediatrics, Baylor College of Medicine, Houston, TX; 2Surgery, Baylor College of Medicine, Houston, TX

Background: Interventions for biliary atresia (BA) are often judged based on whether or not they prevent need for liver transplantation (LT). The underlying assumption of this criterion is that all LTs for BA are similar. However, LTs for BA can be very different, with varying complications rates and lengths of admissions. To better characterize these differences, in this study we divide LTs for BA into two groups: (i) early LTs (ELTs), which are performed in the first year of life and/or in patients diagnosed too late to receive the Kasai operation; and (ii) late LTs (LLTs), which are performed after the first year of life and in patients who had received the Kasai operation. We hypothesize that ELTs have significantly higher admission times and complication rates compared to LLTs.

Methods: All patients receiving a LT for BA at a single, large quaternary hospital from 2010 to 2013 were included. Deceased-donor LTs are performed at this hospital. Data on subjects were collected retrospectively by searching the electronic medical records. Parametric data were compared using the student t-test; nonparametric data were compared using the Mann-Whitney test.

Results: Forty-seven patients with BA received a deceased-donor LT during the study period, of which 25 received an ELT and 22 received a LLT. Subjects receiving ELTs and LLTs were similar in gender, race, and ethnicity. Patients...
receiving ELTs compared to those receiving LLTs required ICU care preoperatively (44% vs. 0.05%, p=0.002), remained intubated for greater than 24 hours after LT (48% vs. 0.05%, p=0.001), and required renal replacement therapy after transplant (28% vs. 0%, p=0.010). In addition, patients receiving ELTs compared to those receiving LLTs had a longer duration from admission to LT (median 12 vs. 0 days, p<0.001), from LT to discharge (median 28 vs. 9 days, p<0.001), and from admission to discharge (median 42 vs. 9 days, p=0.0001).

Conclusions: Outcomes for BA LTs can be further divided into two groups based on when they are performed. ELTs compared to LLTs are associated with significantly higher complication rates and longer hospital length-of-stays. Our findings suggest that delaying BA LTs to more than a year should be the clinical standard as this practice reduces peri- and postoperative complications and healthcare utilization.

113 SERUM SOLUBLE FAS LEVEL IS A USEFUL BIOMARKER FOR PEDIATRIC NONALCOHOLIC FATTY LIVER DISEASE. Vera Okwu1, Ammar Matloob1, Liping Tian2, David Grove3, Saha Partha4, Sara Lappe5, Ariel Feldstein5, Raed Dweik4, Naim Alkhouri1, 1Pediatric Gastroenterology, Cleveland Clinic Children's Hospital, Cleveland, OH; 2General Pediatrics, Cleveland Clinic, Cleveland, OH; 3Pathobiology, Cleveland Clinic, Cleveland, OH; 4Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH; 5Respiratory Institute, Cleveland Clinic, Cleveland, OH

Objectives: Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease in children. Nonalcoholic steatohepatitis (NASH) is the severe form of NAFLD. Recent adult data suggested that hepatocyte apoptosis may play a role in the development and progression of NAFLD. The aim of this study was to evaluate the use of serum soluble Fas (sFas) and Fas ligand levels, markers of hepatocyte apoptosis as noninvasive biomarkers for pediatric NAFLD.

Methods: Patients were recruited from our obesity clinic and the general pediatric clinic. NAFLD was diagnosed based on the presence of fatty infiltration on liver ultrasound. NASH was defined as the presence of fatty infiltration and ALT > 45 U/L. The obese control group included patients with no fatty liver on US and ALT < 22 U/L. The lean control group included normal-weight children seen for routine well-child visits. We measured serum sFas and Fas ligand levels using ELISA kits.

Results: 38 children were included in the analysis (11 lean controls, 12 obese controls without NAFLD, and 15 NAFLD patients). The mean age was 13.4 ± 4.4 years and 58% were male. sFas was significantly elevated in the children with NAFLD compared with obese and lean controls (1080.1 ± 208.1 pg/ml vs. 782.8 ± 201.9 respectively, p = 0.0015). Furthermore, those with NASH had the highest levels of sFas with a mean value of 1178.9 ± 330.2 pg/ml. There was no significant difference in Fas ligand levels between the NAFLD group and the control group (79.4 ± 46.8 pg/ml vs. 97 ± 33.5, respectively, p = 0.22).

Conclusions: sFas is elevated in children with suspected NAFLD and should be investigated further as a potential noninvasive biomarker for NAFLD and NASH.

114 VOLATILE ORGANIC COMPOUNDS IN THE EXHALED BREATH AS BIOMARKERS OF NONALCOHOLIC STEATOHEPATITIS IN CHILDREN. Vera Okwu1, Ammar Matloob1, David Grove2, Sara Lappe3, Rocio Lopez2, Raed Dweik4, Naim Alkhouri1, 1Pediatric Gastroenterology, Cleveland Clinic Children’s Hospital, Cleveland, OH; 2Pathobiology, Cleveland Clinic, Cleveland, OH; 3Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH; 4Respiratory Institute, Cleveland Clinic, Cleveland, OH

Objectives: Nonalcoholic steatohepatitis (NASH) is the most aggressive form of nonalcoholic fatty liver disease (NAFLD). Non-invasive children evaluated to identify children with NASH are urgently needed. The aim of this study was to evaluate the use of exhaled volatile organic compounds (VOCs) as noninvasive biomarkers for NASH in obese children.

Methods: Consecutive children evaluated at our childhood obesity program were included and breath samples were collected at the time of their clinic visit. All children underwent a liver ultrasonography (US) and ALT measurements to determine the presence of NAFLD. The diagnosis of NASH was based on the presence of fatty infiltration on US and ALT > 45 U/L. The "no NASH" group included obese children with ALT < 22 U/L for girls and < 25 U/L for boys with and without fatty infiltration on US (steatosis and obese control groups, respectively). Exhaled breath was collected and analyzed per protocol using selective ion flow tube (SIFT-MS) to identify new markers of NAFLD.

Results: A total of 96 subjects were included in the study. The mean age was 13.8 ± 2.8 years and 53% were male. NASH was diagnosed in 22 patients with a median ALT of 61.5 [56-92 U/L]. A comparison of the SIFT-MS results of patients with NASH to those with no NASH revealed differences in concentration of more 3 VOCs, namely ethanol (86.4 vs 60.6 ppb, p = 0.021), 3-methylhexane (15 vs 11.4, p = 0.022), and pentane (9.9 vs 8.2, p = 0.023). A combination of ethanol and 3-methylhexane showed good accuracy for diagnosing NASH with an area under the ROC curve of 0.73 (95% CI 0.62- 0.84) (Figure). We developed a predictive model for NASH using these two VOCs which provided a 90% negative predictive value (good screening tool to rule out NASH).

Conclusions: Exhaled ethanol and 3-methylhexane are promising noninvasive biomarkers for NASH in obese children. Future studies are needed to validate our findings in children with biopsy-proven NASH.
**115 ALTERED BILE FLOW DYNAMICS IN LIVER TRANSPLANT CHILDREN. A CAUSE OF LATER GRAFT INJURY?**

Virginia del Carmen Reynoso Lopez¹, Maria C. Sanchez¹, Isabel Hume Braun², Ana Mollerach², Daniel D'Agostino¹, ¹Gastroenterology, Hepatology Pediatric, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; ²Nuclear Medicine and Endocrinology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Biliary complications after liver transplantation (LT) in children are the "Achilles Heel" of pediatric transplantation. When severe complications of the bile duct anastomosis occur, re transplantation is the last treatment option.

**Aim:** to study the length of time of permanence of the radionuclide in the biliodigestive anastomosis in LT children using hepatobiliary scintigraphy.

**Methods:** LT children were prospectively included between July 2013-May 2014 in a single center. Patients with more than six months of LT were included and those who were hospitalized during the last month and had a history bile duct injury instrumented with good drainage were excluded.

Quantitative hepatobiliary scintigraphy with Tc 99-m was performed. Dynamic imaging with SPECT liver and sequential images were taken hourly until 6 hour or while the contrast observed. Maximum time 24 hs. They were divided in Group1 without and Group2 with biliary complications. The length of time of permanence between both groups were compared.

**Results:** 22 patients with x 150.5 months (IQR61.25-257.5), 54% female. Median time since LT 106.5 months (IQR37.75-205.75) the median length of time of permanence of the radionuclide in the biliary-enteric anastomosis was 135 min (IQR120-195). A statistical difference was found in the median time of the radionuclide in the anastomosis between G1 (N14) 120 min (IQR120-157.5) and G2 (n8) 300 min (IQR180-360) (p=0.00218).

**Conclusions:** Biliary complications showed an altered bile flow dynamic excretion, leading to a chronic stasis and could be possible later graft injury in the post transplant. This is the first study that evaluates it.

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**116 PHENOTYPIC DIFFERENCES OF PAS+ GLOBULE-CONTAINING AND GLOBULE-DEVOID HEPATOCYTES IN A PIZ MOUSE MODEL OF ALPHA-1 ANTITRYPSIN DEFICIENCY.**

Zahida Khan¹, Donna B. Stolz², David H. Perlmutter¹,², George K. Michalopoulos¹, ¹Gastroenterology, Hepatology, & Nutrition, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA; ²Cell Biology and Physiology, University of Pittsburgh School of Medicine, Pittsburgh, PA; ³Pathology, University of Pittsburgh School Of Medicine, Pittsburgh, PA

Alpha-1 antitrypsin deficiency (ATD) is the most common genetic cause of pediatric liver disease. Severely affected patients ultimately require liver transplantation. In classical ATD, the PIZZ mutation results in misfolded ATZ protein monomers that polymerize into insoluble aggregates, forming PAS+/diastase-resistant globules within hepatocytes. This toxic gain-of-function mechanism leads to chronic liver injury; however, for reasons unclear, the severity of liver disease varies among PiZZ homozygotes, suggesting the influence of other disease modifiers.

We hypothesize that differences in proteostasis, as reflected by globule-content among hepatocyte subsets, can influence the extent of liver injury vs. recovery in ATD. The PiZ transgenic mouse recapitulates the progression of human ATD, providing an ideal model to study hepatocyte globule biology both in vivo and in culture. Over time, livers from PiZ mice show spontaneous emergence of ATZ globule-devoid (GD) hepatocytes, which are known to have a proliferative and survival advantage over injured ATZ globule-containing (GC) hepatocytes. Since there are no published reports of studying these hepatocyte subsets in culture, we developed a method to isolate globule-enriched fractions of PiZ primary mouse hepatocytes using Percoll gradient fractionation. After standardization with density marker beads, a preformed 35% continuous Percoll gradient was used to isolate fractions enriched for GC and GD hepatocytes from PiZ mice, ages 2-4 months old. We consistently obtained 13 fractions based on Percoll density centrifugation using both male and female PiZ mice (n=6), and we were able to culture each fraction in serum-free conditions for up to 4 days +/- growth factors. PAS/d and A1AT staining was used to confirm globule phenotype, and globule ultrastructure was also characterized by electron microscopy. We are developing an imaging assay to quantitatively analyze globule morphometry and processing in response to specific cytokines and drugs. We are also analyzing expression of regeneration markers in GC vs. GD hepatocytes, and our preliminary results suggest the emergence of a progenitor cell phenotype that may be induced by chronic injury in ATD. Understanding the mechanisms of proteostasis and interactions among GD and GC hepatocytes can aid in development of novel therapeutic agents capable of reducing liver injury from toxic ATZ protein aggregates.
128 **EFFICACY OF A COGNITIVE BEHAVIORAL TREATMENT VERSUS A TRADITIONAL INTERVENTION TO REDUCE ADIPOSITY WITHIN A NUTRITIONAL INTERVENTION PROGRAM IN OBESE CHILDREN.** Leticia Salazar-Preciado, Alfredo Larrosa-Haro, Cecilia Colunga-Rodríguez, Enrique Romero-Velarde, Brenda Fernández-Castillo, Juan Ramón Vallarta-Robledo, 1 Unidad de Investigación Médica, Hospital de Pediatría, CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; 2 Departamento de Salud Pública, Doctorado en Ciencias de la Salud Pública, Universidad de Guadalajara, Guadalajara, Mexico; 3 Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

**AIM:** To compare the efficacy of a cognitive behavioral treatment (CBT) versus a traditional intervention (TI) trials to reduce the adiposity within a nutritional intervention program in obese children.

**SUBJECTS AND METHODS:** A clinical trial to reduce the adiposity and to modify the dietary and physical activity habits was conducted in 25 obese children attending an elementary school in Guadalajara Mexico. They were randomly assigned to TI or CBT intervention groups. The outcome variable of this report was the BMI z-score at times 4, 8 and 12 months of intervention.

**RESULTS:** Thirteen subjects (52%) were assigned to the TI and the remaining 12 to the CBT groups. The age median in the overall group was 10.9 years; 10 (40%) were girls. Age, gender and other demographic variables (parent's age, education, marital status, type of family and family income) had no differences between the study groups. In the TI group BMI z-score diminished at 4 and 8 months but increased at 12 months, without intra-group statistical difference. In the BCI group the BMI z-score diminished gradually from 2.8 to 2.5 SD with statistical difference (p=0.002).

**CONCLUSIONS:** Supporting a nutritional therapy to reduce adiposity in obese children with a CBT can lead to sustained medium and long-term results. This tool could increase its valuable if applicable to larger groups.

129 **WEEKEND CARBOHYDRATE INTake CORRELATES WITH ADIPOSITY IN PRESCHOOLERS: GENDER DIFFERENCE.** Elizabeth Lizarraga-Corona, Alfredo Larrosa-Haro, Juan Ramon Vallarta-Robledo, Larissa Velasco-Ruiz, Edgar M Vasquez-Garibay, Enrique Romero-Velarde, Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico

**BACKGROUND:** Current evidence has not made clear the association between a particular nutrient and increased adiposity. Environmental factors play an important role in the adipose phenotype that interacts with biological and genetic factors.

**AIM:** To evaluate the correlation of energy and macronutrient intake with adiposity in preschoolers.

**SUBJECTS AND METHODS:** A cross-sectional study was carried out in 89 children attending a kindergarten. Dependent variable: Adiposity. Independent variables: Energy and macronutrient intake. Adiposity was evaluated with the percentage of body fat (Slaughter's equation, PBF). Diet was estimated with two-day 24-hour recalls, and a food frequency questionnaire. Statistics: Pearson's correlations and Student's t test.

**RESULTS:** Mean age was 68.9 (SD 9.2) months, 54.0% were girls. The mean body fat percentage in girls was 18.0% (SD 3.8), in boys 15.3 (SD 5.4) (p=0.009); 12.4% had overweight and 10.2% obesity. In the overall group PBF had a positive correlation with carbohydrate intake (g/day) in the weekend (r=0.25, p=0.016) and in weekend plus weekday (r=0.23, p=0.033). This correlation remained significant in boys (r=0.31, p=0.048; (r=0.34, p=0.031), but was not significant in girls. Protein intake in weekday correlated significantly with adiposity in girls (r=0.29, p=0.047). Energy intake correlations were not significant by gender or by day of the week.

**CONCLUSION:** Carbohydrate seems to play an important role in development of adiposity in preschoolers. Nutritional intervention regarding the amount and type of carbohydrate ingestion during weekends may be useful in the regulation of adiposity in preschoolers.

130* **EFFECTS OF DIETARY INTERVENTIONS ON BREATH VOLATILE ORGANIC COMPOUNDS IN OBESE CHILDREN WITH HYPERCHOLESTEREMIA.** Ammar Matloob, Michael Macknin, Sara Lappe, David Grove, Frank Cikach, Vera Okwu, Sarah Worley, Raed Dweik, Naim Alkhouri, 1 Pediatric Gastroenterology, Cleveland Clinic Children’s Hospital, Cleveland, OH; 2 General Pediatrics, Cleveland Clinic, Cleveland, OH; 3 Pathobiology, Cleveland Clinic, Cleveland, OH; 4 Cleveland Clinic Lerner Medical School, Cleveland, OH; 5 Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH; 6 Respiratory Institute, Cleveland Clinic, Cleveland, OH

**Background:** Measuring the concentration of volatile organic compounds (VOCs) in the breath in different disease states has become a promising diagnostic tool due to its noninvasive nature. Although diet is considered an exogenous factor influencing composition of exhaled breath, research into the effect of different diets on VOC concentration is limited. In the present study, we followed excreted VOCs in obese hypercholesterolemic children and their parents over time while adhering to low fat vegan or AHA diet for 4 weeks.
Methods: Four-week pilot study of 28 families (each composed of one parent and one child) following the LFV (14 child-parent pairs) or AHA (14 pairs) diet for history of obesity and elevated cholesterol levels. Single exhaled breath was collected after an 8-hour fast and analyzed per protocol using selective ion flow tube (SIFT-MS) at baseline (day 1) and at the end of the study (day 28).

Results: The mean age of the children was 14.1 ± 3 and 36% were Caucasian. The mean total cholesterol was 213.8 ± 42 mg/dL with a mean LDL of 132.2 ± 29 mg/dL. After completing the 4 week diet, there was an improvement in BMI Z score and total cholesterol in both groups (to a greater extent in the LFV group). There were marked and significant changes in multiple VOCs in the breath of children from baseline to the end of the study (VOCs that decreased by more than 50% included acetonitrile, 1-decene, 1-octene, 1-heptene, 3-methylhexane). Similar changes were also noted in the parents. Interestingly, there were no significant differences in VOCs changes between the LFV and AHA groups for any of these compounds.

Conclusion: Dietary intervention can change the composition of VOCs in exhaled breath; however, it seems that this effect is mainly related to weight loss and favorable changes in the biochemical profile rather than the composition of the diet itself.

131 COLOMBIAN INFANTS WITH NUTRITIONAL EDEMA. Carlos A. Velasco, Yara Oñate, Pediatrics, University of Valle, Cali, Colombia

Introduction: The hospitalary undernutrition in Colombia, is around of 34%. In recent years has increased morbidity and mortality. Objective: To describe the clinical and paraclinical characteristics and morbidity and mortality of 11 infants with nutritional edema who consulted at Hospital Universitario del Valle (HUV) "Evaristo Garcia" from Cali, Colombia, during 2013. Methods: Descriptive observational study of medical record review conducted in 11 infants under 24 months who were hospitalized with a diagnosis of nutritional edema at the HUV. Results: We included 11 infants of 8.6±4.0 months, 63.6% male, 81.8% originating in Cali and Valle, with their parents at age 21.7±5.6 years. 63.6% were breastfeeding and complementary feeding before 6 months of age, respectively, and cow's milk during the first year of life in 27.3%. They presented weight = 5980.9±1852.8 grams and height = 63.5±8.6 cm, and according to WHO BMI = -0.1±0.9 SD, heigth/age = -1.2±2.0 SD, malnutrition = 20% and failure to thrive = 30%. In order of frequency, all had lower extremity edema with fovea positive sign, pallor 81.8%, pelagroide skin 63.7% and 54.5% diarrhea, vomiting and fever, respectively. Were paraclinical altered: leukocytes (16295.3±9034.8/mm3), neutrophils (46.7±17.8%), sodium (130.3±5.2 meq/l), hemoglobin (7.4±1.2 g/dl), arterial pH (7.3±0.0) and albumin (1.9±0.5 g/dl). They received parenteral (36.4%) and enteral (54.6%) nutrition. 83.3% were intolerant. There were complications such as anemia (63.4%), bacteremia (54.5%) and hydro electrolytic disorders (45.5%). They had a hospital stay of 25.0±13.9 days. 18.2% died. Conclusion: This group of infants with nutritional edema from HUV in Cali, Colombia, although within their background, apparently received an adequate and timely complete, balanced, adequate and proper food, their feedback was torpid in 83.3%, with 63.4% of morbidity and mortality of 18.2%.

132 CHARACTERIZATION OF NUTRITIONAL STATUS AND ITS RELATIONSHIP TO THE EATING PATTERN OF 300 CHILDREN 8-18 YEARS OF AN EDUCATIONAL INSTITUTION IN CALI, COLOMBIA. Carlos A. Velasco, Lina Valencia, Jorge L. Buitrago, Pediatrics, University of Valle, Cali, Colombia

Introduction: One of the main elements that determine the nutritional status of a population is its pattern of intake. Thus, a diet that does not provide food in sufficient quantity and variety to meet the needs of individuals or transferring an excess of these, causes malnutrition, which may be evidenced in anthropometric analysis of the population. Objective: To evaluate the relationship between food consumption patterns and the prevalence of risk of overweight, obesity, risk of thinness, severely underweight, stunting and severe stunting in 305 children between 6 and 18 years of school advertises in Cali, Colombia. Methods: Observational, descriptive, non-experimental study in 305 children between 6 and 18 years of school advertises in Cali-Colombia. Demographic variables (age and sex), anthropometric (weight, height, waist circumference and triceps skinfold) were taken and a nutritional survey-Reminder 24 hours each child was given. Anthropometric measurements were processed and classified using the WHO program Anthroplus stratification for risk of overweight, obesity, risk of thinness, severely underweight by BMI, and stunting, severe stunting as height/age. Analysis of the nutritional survey was conducted using the CERES program, which totally and macronutrient (protein, fat and carbohydrates) were determined caloric intake. The analysis of percent adequacy of nutritional requirements was performed by age group each child belonged. Results: A total of 318 students were analyzed ages 6 to 18 with a median age of 11.52±2.3 years, 56% male. Of the total population, 12.71% were diagnosed with overweight and obesity. The average consumption of kilocalories (Kcal) for all age groups was 1922.34±570.4. Average consumption kcal for the group of students with a diagnosis of obesity was higher (2117 kcal/day) compared with the other groups. Conclusions: Although a distribution of increased energy consumption in the population of students with a diagnosis of obesity was observed, there was no statistically significant difference in the consumption of kcal and macronutrients such as protein, fat and carbohydrates between groups (normal weight, thinness, risk of thinness, risk of overweight, overweight and obese).
133 NUTRITIONAL STATUS AND THERAPEUTIC RESPONSE TO MILTEFOSINE IN CHILDREN WITH CUTANEOUS LEISHMANIASIS. Carlos A. Velasco¹, Maria D. Castro¹, Alexandra Cossio², Maria A. Gomez², Nancy Gore³, Pediatrics, University of Valle, Cali, Colombia; ²CIDEM, Cali, Colombia

Background: Miltefosine is an effective therapeutic option for cutaneous leishmaniasis in pediatric populations. Nutritional status may modify the effect of this drug, either by changes in binding to proteins like albumin, or by alterations in the immune response. This exploratory study describes the nutritional status and therapeutic response to miltefosine in a cohort of pediatric patients with cutaneous leishmaniasis. Materials and methods: We followed a cohort of 20 children aged 2 to 12 years, participating in a Phase IV clinical trial of pharmacokinetics of miltefosine. Nutritional status was assessed by anthropometry using the growth standards of WHO (Z-score index of body mass / age, height / age and sex), hemoglobin and serum albumin. The therapeutic response was assessed at weeks 13 and 26 after initiation of treatment. Results: nineteen patients completed follow-up and three failed to treatment (15.8%). The proportion of low height/age was 15.8% and none child was classified in the category of stunting. Albumin values were normal for all children and the minimum value of hemoglobin was 11.6g/dl (mean 12.7 ± 0.81). Although the Z score of body mass index/age and sex in all patients was normal, the median of those with therapeutic failure was furthest from the zero point of the distribution compared to those who were cured at 26 weeks (-0.72 against -0.27). Additionally, the Z score of height/age and sex of all patients who cured was normal (median: -0.52), while two of the three that failed were found in the classification of low height/age (median: -2.4). Conclusions: findings of this exploratory study suggest that nutritional status may influence the therapeutic response to miltefosine and support the design and development of studies to discern this relationship.

134 RELATION BETWEEN PHYSICAL ACTIVITY-RELATED ENERGY EXPENDITURE AND BIOMARKERS OF METABOLIC SYNDROME AND OBESITY IN ADOLESCENTS. Jay Shah, Sari Acra, Vanderbilt University Medical Center, Nashville, TN

Objective: To determine the association between objectively measured physical activity-related energy expenditure (PAEE) in a free-living setting and biomarkers of metabolic syndrome (MetS) in African American and White American youth.

Methods: Free-living energy expenditure for a 10-day period using reference standard doubly-labeled water (DLW) and markers of metabolic risk, including blood pressure, BMI percentile, body fat percentage, truncal fat, truncal fat percentage, total cholesterol, HDL, LDL, triglyceride, insulin, leptin, and adiponectin were measured in African American (n=21, 13 males, 8 females) and White American (n=19, 9 males, 10 females) youth (10-17 years old) over a range of BMI percentiles (4th to 99th).

Results: Among females, there was a negative correlation between PAEE and serum triglyceride level (r=-0.705, p=0.0023). Among White Americans, PAEE was positively to HDL level (r=0.518, p=0.0231) and a negatively correlated with serum triglyceride level (r=-0.526, p=0.0207). There were no statistically significant correlations between PAEE and any MetS markers among males or African Americans.

Conclusions: In adolescent females, objectively measured PAEE in a free-living setting is negatively correlated with serum triglyceride level. In White American adolescents, PAEE is negatively correlated with serum triglyceride level and positively correlated with HDL level. There is no correlation between PAEE and markers of MetS in adolescent males or African Americans. Lack of correlation between physical activity and both BMI and body fat percentage points towards other factors, such as diet, having stronger associations with obesity in adolescence.

135 ASSESSING A MULTIPLE-PASS 24-HOUR DIETARY RECALL: WHAT IS THE ACCURACY IN NORMAL-WEIGHT AFRICAN AMERICAN CHILDREN? Jay Shah, Vanderbilt University Medical Center, Nashville, TN

INTRODUCTION: A multiple-pass 24-hour dietary recall is considered a reference standard for assessing energy and nutrient intake in free-living individuals. Since the intake data is often used in pediatric clinical practice, it is essential that the validity of the method be tested in various pediatric populations.

OBJECTIVE: The objective of this study is to evaluate the accuracy of the multiple-pass 24-hour food recall by comparing reported intake of food with measured intake measured during a 24-hour stay in the controlled environment of a whole-room indirect calorimeter.

METHODS: Fifty-two male and female African-American children (9-14 years old, BMI between 19.0 and 24.9 kg/m²) were recruited from the Nashville and Memphis areas in Tennessee, USA. The 24-hour recall was conducted in person using the multiple-pass recall methodology in the morning following a 24-hour monitored period in the room calorimeter, during which food intake was objectively measured.

RESULTS: There was a significant correlation between the number of items consumed and recalled at any meal or snack (r=0.2684, P<0.05). There was a significant correlation between measured and recalled energy (r=0.648), protein (r=0.523), fat (r=0.536) and carbohydrates (r=0.565; all P<0.001).
CONCLUSION: We conclude that the multiple-pass 24-hour recall accurately assessed objectively measured energy and macronutrient intake among normal-weight African-American children.

136 FOOD ADDICTION AND A DOPAMINE-RESISTANT (DRD2 A1) RECEPTOR POLYMORPHISM IN OBESE ADOLESCENTS AND COLLEGE STUDENTS: A PILOT STUDY. Joanna Yeh1, Amy Trang2, Susanne Henning2, David Heber2, Zhaoping Li3, 1Pediatric Gastroenterology, UCLA, Los Angeles, CA; 2Clinical Nutrition, UCLA, Los Angeles, CA

Background: Food addiction is increasingly being investigated as a potential contributor to obesity. The genetic polymorphism DRD2 A1 (rs1800497) has been implicated in food addiction. The reward deficient theory postulates that individuals with this polymorphism compensate for decreased dopamine receptor density by consuming more palatable food. There is a paucity of research looking at food addiction in adolescents and college students.

Objective: The aim of this study was to determine if there was a relationship between individuals with at least one DRD2 A1 allele (A1A1 or A1A2), food addiction questionnaires, and body measurements (body mass index and percent body fat) among two study populations: obese adolescents and college students. We also compared eating rate in obese adolescents for sugared versus non-sugared oatmeal to investigate the relationship between DRD2 genotype and eating behavior.

Methods: 12 obese adolescents and 132 college students were recruited. Participants underwent body composition measurement via bioelectrical impedance, blood draw for DRD2 genotyping, and answered subjective food craving (Food Craving Inventory) and food addiction (Power of Food Scale) questionnaires. Eating rate (grams/second) of sugared and non-sugared oatmeal was measured via the universal eating monitor on two separate occasions in the obese adolescent group.

Results: Among obese adolescents, despite reporting overall lower sugar cravings on questionnaire, those with at least one allele of A1 showed a tendency towards higher eating rate for both sugared and non-sugared oatmeal compared to those with A2A2. However, this did not reach statistical significance. In general, all obese adolescents ate sugared oatmeal at a faster rate. There is a positive linear trend between BMI z score and questionnaires for obese adolescents. Among college students, there was a higher percentage of A1 carriers among obese females compared to obese males. Differences in ethnic and gender groups are currently being explored.

Conclusions: This is the first pilot study to consider that the DRD2 A1 polymorphism may influence eating behavior, specifically, faster eating rate. Larger studies are needed to explore the relationship between eating behavior and genetic polymorphisms that may contribute to polygenic obesity, thereby allowing for the development of tailored obesity treatments, both behavioral and pharmacologic. In addition to age, both ethnic and gender differences should also be taken into consideration when researching food addiction.

137 INPATIENT DEMOGRAPHIC CHARACTERIZATION OF OVERWEIGHT AND OBESE PATIENTS AT PHOENIX CHILDREN'S HOSPITAL. Justin C. Wheeler1, Chengcheng Hu3, Vinay Vaidya2, Tamir A. Miloh1, 1Phoenix Children's Hospital, Phoenix, AZ; 2Phoenix Children's Hospital, Phoenix, AZ; 3Epidemiology and Biostatistics, University of Arizona College of Public Health, Tucson, AZ

Background: Pediatric patients of Hispanic, Native American (NA), and African American (AA) ethnicity, as well as patients of lower socioeconomic status, are at an increased risk of obesity. Understanding the demographic distribution of the obese inpatient population at our institution, Phoenix Children's Hospital, can provide insight for focusing diagnostic and preventative interventions.

Methods: This study is a descriptive retrospective chart review examining the relationship of BMI and multiple demographic markers, including ethnicity, gender, and insurance status of all patients hospitalized at Phoenix Children's Hospital (PCH) in 2011. Patients were excluded if no accurate weight or height was recorded or if the calculated BMI was non-physiologic. Patients were categorized by BMI <85th (normal weight), 85-95th (overweight), and >95th (obese) percentiles. Statistical significance of distribution was determined using Chi square test for gender, ethnicity, and insurance status and Kruskal-Wallis test for age.

Results: 11,431 patients were admitted to PCH in 2011, 7,384 met inclusion criteria (64.6%). Ethnicity distribution by BMI compared to all PCH 2011 admissions and general population of Phoenix based on 2010 US census is shown in Table 1. Demographic results outlined in Table 2. Obese patients tended to be older than normal weight patients (p<0.001). Distribution by gender was not statistically significant (p = 0.06). Hispanic, NA, and AA patients had higher proportion of obese patients than Caucasians (p<0.001). Obese patients were more likely to have Medicaid than private insurance (p<0.001).

Discussion: Hispanic, NA, AA, and Medicaid insurance inpatients were at increased risk of obesity. Inpatient admission may provide an opportunity for culturally sensitive obesity intervention programs.
### Ethnicity and BMI

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### Demographic Characterization at PCH by BMI

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<td>Other</td>
<td>70%</td>
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138 USE OF GEOGRAPHIC INFORMATION SYSTEMS AND ELECTRONIC HEALTH RECORDS TO INTEGRATE PRIMARY CARE WITH COMMUNITY ASSETS TO REDUCE CHILDHOOD OBESITY. Lauren G. Fiechtner1,3, Mona Sharifi2, Richard Marshall3, Daniel Slater4, Thomas Sequist5, Steve J. Melly1, Jeff Blossom6, Sarah N. Price2, Christine Horan2, Elsie M. Taveras1, 1Gastroenterology, Boston Children’s Hospital, Jamaica Plain, MA; 2General Pediatrics, Massachusetts General Hospital for Children, Boston, MA; 3General Pediatrics, Massachusetts General Hospital for Children, Boston, MA; 4Pediatrics, Harvard Vanguard Medical Associates, Boston, MA; 5Pediatrics, Harvard Vanguard Medical Associates, Boston, MA; 6Partners Health Care, Boston, MA; 7Environmental Health, Harvard School of Public Health, Boston, MA; 8Center for Geographic Analysis, Cambridge, MA

Background: Novel approaches to care delivery that leverage clinical and community resources and address socio-contextual factors could improve outcomes for high-risk, overweight and obese children.

Methods: We used geographic information systems (GIS) and BMI data of 49,770 children ages 4 to <19 who receive their care at 14 pediatric practices in Massachusetts to identify obesity "hotspots", defined as ZIP codes where >15% of children are obese. Using GIS we characterized the food and physical activity environment in all of the ZIP codes. Through interviews with parents, environmental health experts, and community partners, and with the use of GIS databases, we identified community assets that could support behavior change. These assets were then mapped on an interactive online map to be used in an obesity intervention that seeks to integrate primary care with community assets.

Results: Children lived in 198 ZIP codes, 66 were hotspots. Hotspots (v.non-hotspot) had a lower neighborhood median income ($63,655 v. $97,100; p<0.001). After adjustment, greater distance to a supermarket (OR:1.85 per km increase, 95%CI:1.24, 2.77)), fewer open spaces (OR:1.46 [1.20, 1.84]), and less sidewalk completeness (OR:4.57 [1.87, 11.16]) were associated with higher odds of being a hotspot. Based on these data and key informant interviews, we created a map with places to access healthful foods, spaces for recreation, social support and transportation.

Conclusion: Hotspots are characterized by lower median income, greater distances to supermarkets, fewer open spaces and sidewalk completeness. Connecting patients to community assets, including social support and transportation options to reach them, could help combat obesity in low-income neighborhoods.

139 PROTEIN SPARING MODIFIED FAST (PSMF) - AN EFFICACIOUS APPROACH TO WEIGHT LOSS IN SEVERELY OBESE ADOLESCENTS. Marwan Bakhach, Vaishal Shah, Tara Harwood, Sara Lappe, Natalie Bhexasia, Sana Mansoor, Na'im Alkhouri, Cleveland Clinic, Cleveland, OH

Background: The Protein sparing modified fast (PSMF) diet is a rigorous way of rapidly losing a large amount of body weight. It consists of elimination of all carbohydrates and added fats (which induces ketosis) in diet while obtaining nutrition from lean meat, poultry and seafood hence the term 'modified fast'. Although adult studies have shown PSMF to be an effective method for weight loss, data in adolescents are lacking. The aim of this study was to determine the efficacy and safety of PSMF in severely obese adolescents presenting to our outpatient obesity management program.

Methods: 10 patients who were seen in our obesity management program between 2011 -2014 were included in the study. They were initiated on PSMF after failing other conventional methods of weight loss for morbid obesity. Collected data included nutritional surveys, anthropometric measurements, side effects and laboratory values on initial and subsequent visits till 6 months of initial implementation. P-value < 0.05 was considered statistically significant.

Results: The mean age was 16±2.8 years with average BMI percentile of 98.36, out of which 90% were females and 90% subjects were Caucasians. A 3 month (8 patients) and 6 month (6 patients) follow up demonstrated an average weight loss of 7.8 kg (SD 4.4, 95% CI: 4 -11.5, p-value = 0.028 and mean 7.7% from baseline) and 9.8 kg from baseline (SD 5.4, 95% CI: 4.1-15.5, p-value = 0.028 and mean 8.4% from baseline) respectively (Table). 50% of subjects had >5 % weight loss and 20% had > 10% weight loss. Four patients were lost to the follow up (40%). An improvement was noted in total cholesterol and HDL (1 patient who had low HDL improved, 2 patients had reduction in total cholesterol with 1 decreasing to normal value) but sample size was very small for laboratory results to be possible to test for statistical significance. Side effects reported by patients were mild dehydration due to nausea (2 patients), decreased energy (1 patient) and transient labile mood (1 patient). No other side effects were reported.

Conclusion: Our results show that PSMF diet can be used as an effective and safe method in outpatient settings for
rapid weight loss in adolescents with severe obesity. While the initial weight loss was significant with few side effects, further continuation of weight loss and long-term compliance rate need to be determined.

Table - 1 - Wilcoxon signed rank test

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<td>4.00</td>
</tr>
<tr>
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<tr>
<td>Positive Ranks</td>
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</tr>
<tr>
<td>Total</td>
<td>9</td>
<td></td>
<td></td>
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<tr>
<td>Baseline Weight - Weight 6 Month</td>
<td>6</td>
<td>0.00</td>
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<td>Negative Ranks</td>
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<tr>
<td>Total</td>
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</tbody>
</table>

a. Baseline Weight < Weight 3 Month
b. Baseline Weight > Weight 3 Month
c. Baseline Weight = Weight 3 Month
d. Baseline Weight < Weight 6 Month
e. Baseline Weight > Weight 6 Month
f. Baseline Weight = Weight 6 Month

140 INTESTINAL METHANE PRODUCTION IS NOT ASSOCIATED WITH CHILDHOOD OBESITY. Sara Naramore1, Punit Jhaveri2, Ming Wang3, William J. Wenner2, 1Pediatrics, Penn State Hershey Medical Center, Hershey, PA; 2Pediatric Gastroenterology, Penn State Hershey Medical Center, Hershey, PA; 3Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA

Objectives: Childhood obesity is a significant health problem. It has been hypothesized that intestinal microflora contribute to the development of obesity. Studies in adults show a correlation between elevated breath methane and obesity. Our study evaluated for a similar association in children.

Methods: A retrospective review was conducted of the breath test results of all children less than 19 years old. Patients were classified as normal, overweight, or obese based on body mass index (BMI) for age. Substrates used were lactulose, lactose, fructose, or sucrose. Concentrations of methane were recorded per test protocol. Patients were divided into groups based on the rise in concentration of methane: negative, >3 ppm, or >10 ppm. An analysis using Fisher's exact and Pearson Chi-squared tests was conducted to compare the elevation in the concentration of methane and the BMI.

Results: 338 patients were included in the study. 60 were overweight and 50 were obese. Of the obese patients, 12% demonstrated a rise in methane production greater than 3 ppm and 20% had an elevation greater than 10 ppm. The group of patients with the highest elevation had an average BMI of 28.5. After Chi-square analysis, no statistically significant correlation was observed between higher levels of methane production and being overweight and/or obese.

Conclusion: This is the first study to examine methane production in obese children. No significant correlation was observed for either overweight or obese children. The presence of methanogenic bacteria may not be part of the etiology of obesity or weight gain.

141 PERINATAL DEPRESSION AND OBESITY AT 4 YEARS OF AGE IN AN URBAN LATINO COHORT.

Sofia G. Verstraete, Jacob Robson, Melvin B. Heyman, Janet Wojcicki, Pediatrics, UCSF, San Francisco, CA

Background: Maternal pre-and post-natal depression is associated with negative outcomes including preterm delivery, low birthweight, and attenuated growth in children under age 2. In contrast, postnatal depression in certain populations has been associated with overweight and obesity, as well as higher adiposity, in early childhood. Chronic depression has been associated with low weight in early childhood (age 2) in Latino children. We sought to analyze the association between depression and obesity in a slightly older (4yo) population of urban Latino children followed since birth.

Design/Methods: Latina women (n=201) were recruited during pregnancy at two hospitals in San Francisco for a prospective cohort study to evaluate the risk of childhood obesity (body mass index [BMI] >=95th percentile) at 4 years of age using perinatal depression categories as the primary predictor. Chi-square and t-tests were applied to evaluate associations between maternal and infant factors and perinatal depression. To adjust for possible confounders, the association between depression and obesity was assessed through multivariable logistic regression.

Results: Depression was categorized as no depressive symptoms at enrollment or postpartum (n=134, 66.7%), episodic
depression (n=46, 22.9%), or chronic depression (n=21, 10.4%) in 201 enrolled women. Of the 169 children available for follow up at 4 years of age 42 (25%) were obese. Perinatal depression was associated with obesity (p=0.045) in univariate analysis. After adjustment for infant's gender and gestational age, breastfeeding status at 1 year and rapid infant weight gain, as well as maternal marital status, years in the US, BMI and employment status, the statistically significant association was no longer identified (OR for obesity in children of episodically depressed mothers 2.39, 95% C.I. 0.88 to 6.49). Upon stratification by rapid infant weight gain (RIWG), defined as change in weight-for-age Z-score >0.67 standard deviations between birth and 6 months of age, we found an association in both univariate (p=0.013) and multivariate analysis (OR 6.6, 95% C.I. 1.03-43) between depressive symptoms and obesity in children with RIWG.

Conclusions: Urban Latino infants whose mothers suffered perinatal depression were at higher risk for obesity, although the association was weakened after adjustment for confounders with known associations to both obesity and depression. These findings suggest maternal perinatal depression may be a risk factor for childhood obesity in this population, indicating that efforts in screening and managing these symptoms may help mitigate early childhood obesity.

Supported in part by NIH grants K01 DK080825 and T32 Dk007762.

142 PERFORMANCE OF THE PEDIATRIC DIGITAL HOSPITAL MALNUTRITION SCREENING TOOL (PEDISMART) IN HOSPITALIZED INFANTS. Efstratia Daskalou1, Thomais Karagiozoglou-Lampoudi1, Charalampos Agakidis2, Nikoleta Printza2, Fotos Papachristou2, 1Nutrition-Dietetics, Alexander Technological Education Institute of Thessaloniki, Greece, Thessaloniki, Greece; 21st Pediatric Department, Aristotle University of Thessaloniki, Thessaloniki, Greece

Objectives and study: Hospital malnutrition in paediatric patients is associated with adverse outcomes, morbidity, length of hospital stay and mortality. The recently presented Pediatric Digital Scaled Malnutrition Risk screening Tool (PeDiSMART) was the first tool able to identify malnutrition risk in the full age range of patients hospitalized in pediatric departments. In the present study the performance of PeDiSMART was tested in a sample of hospitalized infants.

Methods: Two hundred and eighty eight infants (154 boys, 134 girls) age: 1-24 months (median age=6 months), consecutively admitted for hospitalization in a tertiary Greek hospital, were included. Upon admission, PeDiSMART was used to calculate malnutrition risk and anthropometry was performed. PeDiSMART’s association to the clinical outcome measures (weight loss/nutritional support and hospitalization duration) was assessed.

Results: According to PeDiSMART classification, 31 (10.8%) patients were at high risk for malnutrition, 108 (37.5%) at medium risk ("action required" groups) and 149 (51.7%) at low risk of malnutrition ("no action required" group). Statistically significant negative correlation was found between PeDiSMART score and WA, HA, WH, BMI, TSF, MUAC z-scores and their mean values differed significantly among the three PeDiSMART allocated risk groups (p<0.001 respectively). The outcome measures (weight loss/ nutritional support and LOS) differed significantly among the three PeDiSMART-allocated risk groups (<0.001). Logistic regression analysis with dependent variable the PeDiSMART-allocated malnutrition risk groups ("no action" and "action required") showed that the weight loss/nutritional support, and the LOS>7 days, was significantly independently associated with the malnutrition risk group allocation after controlling for anthropometric parameters and age.

Conclusions: Patient allocation according the PeDiSMART screening score on admission is associated to clinical outcome measures. Furthermore its use enhances efficacy and reproducibility in identifying pediatric patients at malnutrition-related risk for unfavourable outcome. PeDiSMART is applicable to the full age range of patients hospitalized in pediatric departments.

Logistic regression analysis in the PeDiSMART-allocated malnutrition risk groups (no action/action required)

<table>
<thead>
<tr>
<th>Outcome parameters</th>
<th>P</th>
<th>Exp(B)</th>
<th>95% CI for EXP(B)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>PeDiSMART</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>weight loss/nutritional support</td>
<td>0.001</td>
<td>0.313</td>
<td>0.160</td>
</tr>
<tr>
<td>Lenght of stay &gt; 7 days</td>
<td>0.001</td>
<td>2.243</td>
<td>1.375</td>
</tr>
</tbody>
</table>
143  ADMINISTRATION OF MCT/N-3 FA/A-TOCOPHEROL-ENRICHED PARENTERAL LIPID EMULSION IN PRETERM NEONATES IS ASSOCIATED WITH LIPID AND CYTOKINE PROFILES COMPATIBLE WITH ATTENUATED OXIDATIVE STRESS AND IMPROVED IMMUNE FUNCTION. Maria Skouroliakou1, Dimitris Konstantinou2, Charalampos Agakidis1, Paraskevi Massara1, Marina Antoniadi3, Themais Karagiogoglou-Lampoudi1, 1Nutrition-Dietetics, Alexander Technological Education Institute of Thessaloniki, Greece, Thessaloniki, Greece; 2Nutrition-Dietetics, Harokopeio University, Athens, Greece; 3Neonates Intensive Care Unit, IASO Maternity Hospital, Athens, Greece

Background-aim. Most preterm neonates need parenteral lipid emulsion (LE) administration, which can induce oxidative stress and inflammatory response associated with severe complications of prematurity. The aim of the study was to test the hypothesis that administration of aMCT/n-3 fatty acid (FA)/α-tocopherol-enriched IV LE in preterm neonates may be associated with a more favorable lipid profile and attenuated inflammatory response.

Patients-methods. In a double-blind, parallel-group study, 60 preterm neonates (gestational age =/<32 weeks were randomized to receive either a MCT/n-3 FA/α-tocopherol enriched LE (SMOF lipid group) or a soybean-based LE (INTRAlipid group). Serum lipids α, fatty acids, TNF-α, IL-6, IL-8 and α-tocopherol were assessed on days of life (DOL) 1, 15, and 30.

Results. Fifty one neonates (25 and 26 in SMOFlipid and INTRAlipid groups, respectively) were included in final analysis. The two groups had comparable α-tocopherol, cytokine, lipid, and FA levels at entry. On DOL15 and 30, the SMOF lipid group had significantly higher MUFAs and n-3 PUFAs (DHA, EPA) with lower n-6 FAs (LA, AA) and n-6/n-3 ratio. A-tocopherol increased significantly up the DOL30 in both groups, but the increase was significantly higher in the SMOF lipid group (p=0.004). SMOF lipid group had higher α-tocopherol (p=0.001) and α-tocopherol/total cholesterol ratio (p=0.003) on DOL30, indicating improved lipid profile. The IL-6 and IL-8 were lower in the SMOFlipid group on DOL30, with the difference being significant for the IL-8 (p<0.047).

Conclusions. Administration of MCT/n-3 FA/α-tocopherol-enriched parenteral LE in preterm neonates is associated with improved lipid, α-tocopherol, and cytokine profiles, compatible with attenuated both oxidative stress and pro-inflammatory response

144  THE ASSOCIATION OF METABOLIC/INFLAMMATORY BIOMARKERS AND INSULIN RESISTANCE IN OBESE CHILDREN FROM WEST VIRGINIA. Yoram Elitsur1, Deborah L. Preston1, Morghan S. Getty2, 1Pediatric, Gastroenterology, Marshall University School of Medicine, Huntington, WV; 2Internal Medicine, Marshall University, School of Medicine, Huntington, WV

Obesity is an increasing medical problem in children and little is known of the underlying mechanisms linking obesity to its metabolic and endocrine complications. Previous data in adults have shown that during adipose tissue expansion, there is an increased level of free fatty acids and various inflammatory markers that may influence the development of obesity related complications. The data in the pediatric population is very limited.

Aim: To investigate the association between metabolic/inflammatory serum markers and insulin resistance (IR) status in obese children compared to the control groups.

Materials: Obese and normal weight children who visited the gastroenterology clinic were prospectively recruited to the study. The children were divided in 3 groups: Group A (test) - obese children with IR; Group B (control-1) - obese children without IR, Group C (control-2) - Children with normal weight with no IR. Children who had any disease that might involve the immune system, systemic inflammation, or taking medications that affect the endocrine system were excluded. Fasting blood levels for liver aminotransferases, insulin, glucose, lipid profile (Cholesterol, TG, HDL, LDL), adiponectin, leptin, IL-6, and TNF-α were obtained in all children. Obesity was define according to the CDC BMI chart (BMI >95%) and IR was calculated according to the HOMA-2 equation (+ IR >2.0).

Results: A total of 37 children completed the study. Significant difference for lipid profile and inflammatory markers was noted between the groups (table). There were no statistical differences in the serum levels of AST, total cholesterol, LDL, adiponectin, and TNF-α between the Group A (test) and the controls (data not shown).

Conclusions: Insulin resistance is associated with metabolic/inflammatory markers in obese children. Those markers may participate in the complications associated with this condition. Assessing those markers early in the disease may improve the prognosis of these children.
### Metabolic and inflammatory markers in obese children

<table>
<thead>
<tr>
<th>Group</th>
<th>#pts</th>
<th>BMI-Z</th>
<th>IR (pos&lt;2)</th>
<th>Insulin (mg%)</th>
<th>ALT (±SEM)</th>
<th>HDL (MG%)</th>
<th>TG (mg%)</th>
<th>Leptin (±SEM)</th>
<th>IL-6 (±SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10</td>
<td>30.9</td>
<td>3.05</td>
<td>24.5</td>
<td>34.3</td>
<td>45</td>
<td>129</td>
<td>7812</td>
<td>2.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 3.4</td>
<td>± 0.28*</td>
<td>± 7.9*</td>
<td>± 5.6*</td>
<td>± 15.8*</td>
<td>± 67*</td>
<td>± 2421*</td>
<td>± 0.32*</td>
</tr>
<tr>
<td>B</td>
<td>10</td>
<td>30.1</td>
<td>1.35</td>
<td>10.7</td>
<td>23.8</td>
<td>46.3</td>
<td>118.8</td>
<td>8196</td>
<td>1.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 5.1</td>
<td>± 0.16</td>
<td>± 4.2</td>
<td>± 6.1</td>
<td>± 4.5</td>
<td>± 86</td>
<td>± 3950*</td>
<td>± 0.20*</td>
</tr>
<tr>
<td>C</td>
<td>17</td>
<td>21.3</td>
<td>1.17</td>
<td>9.13</td>
<td>16.1</td>
<td>50.9</td>
<td>62.5</td>
<td>825</td>
<td>1.58</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 3.2</td>
<td>± 0.10</td>
<td>± 3.3</td>
<td>± 0.8</td>
<td>± 8.2</td>
<td>± 19.2</td>
<td>± 195</td>
<td>± 0.60</td>
</tr>
</tbody>
</table>

*p-value vs. C 0.001 0.001 0.001 0.001 0.016 0.003 0.001 0.024

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**145 ETIOLOGICAL AND EPIDEMIOLOGICAL STUDY OF ACUTE PANCREATITIS: A SINGLE CENTER EXPERIENCE.** Chintan Gandhi, Tavleen Bhatia, Tiong The’, C S Pitchumoni, Saint Peter's University Hospital, New Brunswick, NJ

**INTRODUCTION:** The incidence of acute pancreatitis (AP) in children has increased significantly in the past two decades. Acute pancreatitis occurs in all age groups, even in infants. The aim of this study is to assess etiology and epidemiology of acute pancreatitis at a tertiary pediatric hospital.

**OBJECTIVE:** To analyze the cases of acute pancreatitis presented to a children's hospital in New Brunswick, New Jersey.

**MATERIAL AND METHODS:** All cases of AP and acute recurrent pancreatitis (ARP) admitted between January 2009 and December 2013 at Saint Peter's University Hospital, New Brunswick, New Jersey, were reviewed. Patients were identified by searching the hospital's electronic discharge records for the International Classification of Disease, Ninth Revision (ICD-9) code 577.0 (acute pancreatitis). ARP was considered as two or more episodes of AP per year or more than three episodes over a lifetime with intervening return to baseline. The following data were analyzed: demographic information, clinical, laboratory and imaging test results, etiology of pancreatitis, medical and surgical management, length of hospitalization (LOS), and outcome.

**RESULTS:** A total of 32 patients, 37 episodes of AP, were documented. Mean age in our patient population was 11.3 years (range, 2-17 years), male to female ratio was 1:1.3. There is an increased incidence of AP in adolescent females as compared to males. The most prevalent etiologies were idiopathic (40%) and biliary stones/sludge (27%). Male with AP due to idiopathic cause tend to be obese as compared to female (BMI of 32 vs 17.6; p=0.0000) and Female with AP due to gallstone disease tend to be obese as compared to male (BMI of 29.75 vs 20.8; p=0.0297). It proves that three Fs "Female, Fertile and Fat" of gall stone disease in adult population applies to pediatric population as well. Most common clinical feature was abdominal pain, present in 91% cases. Out of them, specifically epigastric pain reported in 31% cases vs diffuse abdominal pain in 69%. Vomiting was the second most reported symptoms (40%). 5 cases presented with Systemic Inflammatory Response Syndrome (SIRS) and had a higher incidence of left pleural effusion and fluid sequestration. Admission WBC count, hematocrit, calcium, albumin, amylase and lipase level did not correlate with severity of pancreatitis or presentation of SIRS. USG abdomen was done in 100% of cases vs CT scan was done in 45% of cases. MRI was done in 3 cases for recurrent pancreatitis. All the case were treated conservatively. Only 5 cases who presented with SIRS received antibiotics. Median length of stay (LOS) was 4 days (range, 2-32 days). Those who developed SIRS had a longer LOS (12.2 days vs 4.7 days; p=0.005). Recurrence rate is higher in our population (11/32; 34%). Underweight as compared to overweight (Chi square = 10.3; p=0.017) and males as compare to females (Chi square = 4.0631; p=0.045) had higher incidence of recurrence. Recurrence rate was not related to etiology, SIRS or antibiotic use during 1st episode.

**CONCLUSION:** This pediatric pancreatitis study highlights the multiple and complex etiology of this disease. Epidemiology of AP could be influenced by single center's characteristics. Better pediatric scoring systems and management algorithms are needed.
ACUTE PANCREATITIS IN THE PEDIATRIC INTENSIVE CARE UNIT. Praveen S. Goday1, Martin Wakeham1, Evelyn M. Kuhn2, Maureen Collins2, Steven L. Werlin1, 1Medical College of Wisconsin, Milwaukee, WI; 2Children's Hospital of Wisconsin, Milwaukee, WI

Background: Very little is known about acute severe pancreatitis in children.

Aim: To describe a population of children who were admitted with or developed acute pancreatitis (AP) in the pediatric intensive care unit (PICU).

Methods: This was a retrospective cohort study. Data were obtained from the VPSLLC database, a multi-site, clinical PICU database. PICU discharges with a primary or secondary diagnosis of AP between July 1, 2009 and June 30, 2013 from 113 centers collecting all the required data fields were included in the study. Due to the limitations of the database,
information about pancreatic enzymes and imaging studies was not available. We also obtained the Pediatric Index of Mortality 2 Risk of Mortality (PIM2ROM) which is an indicator of severity of illness and predicts the likelihood of the patient dying.

**Results:** Of a total of 360,162 PICU discharges, 2,026 had a diagnosis of AP (0.56%). 331 discharges had a primary diagnosis of AP while 1,695 discharges had a diagnosis of secondary AP. The racial distribution of the discharges with primary AP was Caucasian: 44.1%; African American: 14.7%; Hispanic: 31.3%; this race distribution was significantly different (p<0.001) from the race distribution of the overall PICU discharges during the same period (Caucasian: 52.1%; African American: 18.9%; Hispanic: 17.2%).

Among children with primary AP, 49.8% were male with a median age of 12 years (IQR 7.9-15.3). Among these children, 17.9% were underweight, 12.4% were overweight, 13.3% were obese and 7.9% were extremely obese. Median PIM2ROM was 1.0% (IQR 0.8-1.4%). 55 children with primary AP (16.6%) required mechanical ventilation for a median of 3.8 days (IQR 1.0-9.3). PICU length of stay was a median of 2.95 days (IQR 1.53-5.90). Only one of 331 patients died (mortality 0.3%).

Among children with secondary AP, 48.4% were male with a median age of 11.5 years (IQR 5.5-15.2). Among these children, 22.1% were underweight, 9.9% were overweight, 6.3% were obese and 5.3% were extremely obese. Median PIM2ROM was 1.1% (IQR 0.8%-4.0%). 711 children (42.0%) with secondary AP required mechanical ventilation for a median of 5.8 days (IQR 1.8-14.0). PICU length of stay was a median of 4.43 days (IQR 1.84-11.22). There were 115 deaths in this group (mortality 6.8%).

The overall weight distribution was significantly different between primary and secondary AP (p<0.001). Median PIM2ROM, PICU length of stay, mortality (all p<0.001) and length of mechanical ventilation (p=0.035) were all significantly greater in children with secondary AP than with primary AP.

**Conclusions:** 1. Unlike in adult series, children with AP requiring PICU treatment rarely die. 2. Patients with secondary AP are sicker at presentation and suffer more morbidity and mortality in the PICU than patients with primary AP. 3. The poorer outcomes in secondary AP may be related to the underlying primary diagnosis.

149 REGISTERED DIETITIANS’ PRACTICE PATTERNS IN ACUTE PANCREATITIS NUTRITION MANAGEMENT: A HOSPITAL WIDE SURVEY. Rebecca J. Wilhelm, Lin Fin, Maisam Abu-El-Haija., GI, Cincinnati Children’s Hospital Medical Center, Sunman, IN

**Background:** Acute pancreatitis (AP) is a common problem in pediatrics, with an incidence that is rising in the last two decades. Nutrition is an integral component in the management of AP. While early nutrition intervention is advised in adult patients based on available literature, there is no pediatric data on nutrition management in AP. There are limitations to applying adult data when managing pediatric patients. The aim of this survey was to determine current nutritional practices amongst Registered Dietitians (RD) in a hospital setting.

**Methods:** We surveyed 31 RDs at our pediatric tertiary care center. An internet-based survey instrument (Survey Monkey, Palo Alto, CA) was used for the survey enrollment and response collection.

**Results:** Out of 31 RDs surveyed 17 help in the management of patients with AP. Gastroenterology and Bone Marrow Transplant/Hematology-Oncology RDs see the majority of patients with AP. Sixty percent of RDs identified 24 to 72 hours as the length of NPO status for AP patients. Twenty-nine percent of the RDs surveyed chose enteral, naso-jejunal as their first mode of nutrition, 23% of the RDs recommended an oral, low-fat diet and 17% recommended either TPN or oral general diet for first mode of nutrition. Upon starting enteral feeding 47% of RDs would use an elemental, low fat formula as their optimal choice if nutrition in AP. 44% of RDs defined a low fat diet as less than 30% of total calories per day from fat where as 12% use either less than 5grams of fat per feeds 47% of RDs would use an elemental, low fat formula as their optimal choice if nutrition in AP. There was no agreement upon consensus on defining a low fat diet, amongst our RDs. Forty-four percent of RDs defined a low fat diet as less than 30% of total calories per day from fat where as 12% use either less than 5grams of fat per serving or 1 gram of fat/kilogram body weight. Only one of 331 patients died (mortality 0.3%).

There are no pediatric studies on optimal nutrition in AP. Optimal nutritional therapy in nutritional management in AP. We also show that there is a lack of consensus definitions of a “low fat diet” in pediatrics. There are no pediatric studies on optimal nutrition in AP. There is a lack of consensus definitions of a “low fat diet” in pediatrics. Gastroenterology and Bone Marrow Transplant/Hematology-Oncology RDs see the majority of patients with AP. Sixty percent of RDs identified 24 to 72 hours as the length of NPO status for AP patients. Twenty-nine percent of the RDs surveyed chose enteral, naso-jejunal as their first mode of nutrition, 23% of the RDs recommended an oral, low-fat diet and 17% recommended either TPN or oral general diet for first mode of nutrition. Upon starting enteral feeding 47% of RDs would use an elemental, low fat formula as their optimal choice if nutrition in AP. There was no agreement upon consensus on defining a low fat diet, amongst our RDs. Forty-four percent of RDs defined a low fat diet as less than 30% of total calories per day from fat where as 12% use either less than 5grams of fat per serving or 1 gram of fat/kilogram body weight. Only one of 331 patients died (mortality 0.3%).
The disease burden is substantial. Were performed in 30 (39%).

RADIOCONTRAST-INDUCED ACTIVATION OF ABERRANT CA\(^{2+}\) SIGNALS AND CALCINEURIN WITHIN THE PANCREAS. Abraham I. Orabi, Shunqian Jin, Tianming Le, John F. Eisses, Swati Sah, Sohail Z. Husain, Pediatric Gastroenterology, University of Pittsburgh, Pittsburgh, PA

Despite recent advances, the frequency of post-ERCP pancreatitis (PEP) in both children and adults is still approximately 4-8%, which makes PEP an important iatrogenic problem to tackle. Furthermore, the fundamental mechanisms by which radiocontrast induces pancreatic injury are unclear. We and others have previously demonstrated that pancreatitis insults which induce high amplitude, sustained CA\(^{2+}\) signals within the pancreas mediate injury through activation of the CA\(^{2+}\)-phosphatase calcineurin. In the current study, using several complementary in vitro and in vivo methods, we examined whether radiocontrast exposure causes pancreatitis through a CA\(^{2+}\)/calcineurin pathway. By live confocal microscopy, the perfusion of radiocontrast led to robust, high-amplitude CA\(^{2+}\) signals in both mouse and human acinar cells. Using an Ad-NFAT-luciferase reporter (a sensitive assay for calcineurin activation) in mouse acinar cells, radiocontrast caused a 4.5-fold increase in calcineurin activation above baseline (P<0.05), which was dependent on intracellular CA\(^{2+}\) release. Using Ad-NF-kB-luciferase infection of an acinar cell line, radiocontrast led to a 125-fold increase in NF-kB activation (P<0.05), which was mediated by phospholipase C, inositol 1,4,5 trisphosphate receptor CA\(^{2+}\) release and, importantly, calcineurin. In addition, radiocontrast induced a 6.4-fold increase in acinar cell injury, which was abrogated by pretreatment with the calcineurin inhibitors FK506 and cyclosporine A (P<0.05). In this study, we developed a novel in vivo model of PEP in mice by infusing radiocontrast into the pancreatic duct via a transduodenal surgical approach. Compared with the normal saline-infused sham conditions, radiocontrast infusion led to clinically relevant pancreatitis with increases in serum amylase and characteristic histological features in the pancreas. Experimental PEP was prevented by FK506 and cyclosporine A, and mice deficient in the calcineurin Aβ subunit were protected against PEP. In summary, this is the first demonstration in any organ that radiocontrast causes pathological CA\(^{2+}\) signals leading to injury. Further, this study is also the first to implicate calcineurin as a central CA\(^{2+}\) mediator of radiocontrast injury and pancreatitis. The findings point to a key role for using calcineurin inhibitors to prevent PEP.
agreement between EF and MF during PC at our institution. 

Methods: This was a retrospective review of all PC at UTSW from 1/1/13 - 12/31/13. Inclusion criteria: age<18, per-anal endoscopy beyond the splenic flexure, and at least one biopsy taken. Exclusion criteria: history of colonic resection or intestinal transplantation. EF was classified as normal or abnormal based on the operative report. MF was classified as normal, active inflammation, chronic inflammation, or other findings based on the pathology report. The primary endpoint was agreement between EF and MF. The secondary endpoint was identification of factors predictive of abnormal MF. A sub-analysis was performed to identify the agreement between EF and MF in specific patient populations (Group 1: abdominal pain, constipation, and/or diarrhea only indications and Group 2: those with a previous history of IBD).

Results: 724 PC were performed over the 1 year period, of which 638 met inclusion criteria and were analyzed. Of these, 612 (95%) were >2yrs old, 134 (21%) were Group 1, 97 (15%) were Group 2. Abnormal EF was seen in 237 (34%). Abnormal MF was seen in 331 (52%) and included 134 (21%) active inflammation, 137 (21%) chronic inflammation, and 221 (34%) other findings. Considering histology as the gold standard, endoscopy had a sensitivity=63%, specificity=91%, PPV=88% and NPV=69%. There was moderate agreement between any abnormal EF and any abnormal MF (76.2%, kappa=0.53). While Group 1 patients had only fair agreement (75%, kappa 0.28), no cases of chronic inflammation were missed by endoscopic assessment. Group 2 patients had poor agreement (82.5%, kappa=0.17) and ongoing chronic inflammation was identified in 60% of cases with normal EF. On multivariate analysis the following were predictive of any abnormal MF: any abnormal EF (OR 11.5, CI 6.8-19.6, pvalue<0.0001), known history of IBD (OR 10.3, CI 6.5-16.5, pvalue <0.0001), abnormal ESR/CRP/or albumin (OR 3.4, CI 1.5-7.5, pvalue <0.01) and GI blood loss (OR 1.8, CI 1.2-2.9, pvalue <0.05).

Conclusions: This review suggests that agreement between EF and MF in PC is moderate. In patients with a history of IBD, agreement is poor and endoscopy frequently misses ongoing chronic inflammation. In patients with abdominal pain, constipation and/or diarrhea as the only indications for PC, the agreement is only fair. Abnormal EF, a history of IBD, abnormal inflammatory markers and a history of GI blood loss prior to PC are predictors of abnormal MF. This data is inconsistent with recent single center reports and suggest that prospective, multicenter data is warranted before recommending biopsy sparing approaches in specific patient populations. These studies must also focus on the clinical significance of the discordance between EF and MF in specific patient populations.

NASPGHAN Capsule Endoscopy Prize

159  PEDIATRIC CAPSULE ENDOSCOPY: CLINICALLY IMPORTANT FINDINGS, MONITORING RESPONSE TO THERAPY IN CROHN’S DISEASE, ACHIEVING 0% CAPSULE RETENTION RATE AND ENDOSCOPIC PLACEMENT TECHNIQUE. Stephen Nanton, Joelle Roskens, Pediatrics, Avera McKennan Hospital, Sioux Falls, SD

OBJECTIVE: We evaluated the indications and clinical utility of video capsule endoscopy (VCE) in the diagnosis and management of gastrointestinal disorders in children.

SUBJECTS: We studied 426 consecutive children referred for VCE (age ranging from 2 to 21 years). The weight of the smallest child was 14.6 kg.

RESULTS: A total of 504 VCE procedures were performed. Indications for VCE included suspected Crohn's disease, anemia, abdominal pain, polyposis syndrome, celiac disease and GI bleeding. The majority of capsules were placed using a capsule delivery device. Ninety-one children ingested the video capsule in our office.

CAPSULE RETENTION RATE: There were no patients with capsule endoscope retention. Thus, our capsule retention rate was 0 percent. We achieved this ideal retention rate by performing a patency capsule examination on all patients with known Crohn's disease or vomiting, prior to placement of the capsule endoscope.

CELIAC DISEASE: A total of 51 children with elevated TTG levels were examined by VCE. A novel finding of proximal small bowel polyps were found in seven patients (14 percent of the celiac disease patients). One patient was subsequently diagnosed with Bannayan-Riley-Ruvalcaba syndrome. Other VCE findings included classic scalloping of duodenal mucosa, loss of villi and mosaic pattern.

INFLAMMATORY BOWEL DISEASE: VCE studies were performed on 57 patients with IBD. Two patients were found to have isolated small bowel disease.

MONITORING RESPONSE TO THERAPY IN CROHN’S DISEASE: Fifteen children with Crohn's disease underwent two or more VCE studies in order to monitor response to therapy. The VCE findings lead to changes in patient managements in 15 out of the 15 patients (100 percent). In six out of the 15 patients with Crohn's disease, who underwent multiple VCE to monitor therapy, step-up treatment from Mesalamine to 6-MP was initiated based on VCE findings. In eight out of 15 patients, biologic therapy was initiated based on VCE findings. In one patient, therapy with Budesonide was initiated for persistent small bowel Crohn's disease. Clinical improvement in response to step up therapy was noted in all 15 patients and endoscopic improvement was documented in eight of the 15 children by VCE.

POLYPS: Seventeen patients were found to have polyps in the small bowel. Two patients were known to have FAP. Three patients had IBD and eight patients had celiac disease.
DUODENAL WINDSOCK: A rare finding of duodenal windsock diverticulum was made by VCE when abdominal CT suggested intussusception.

ENDOSCOPIC PLACEMENT TECHNIQUE: In 25 (4.9 percent) patients, the capsule could not be placed using the standard technique, and a novel technique was developed using laryngoscopic assistance. By this method, 24 of these 25 patients had successful capsule placement. There were no complications.

CONCLUSION: The use of VCE in children is safe and has a significant impact on the diagnosis and management of pediatric gastrointestinal diseases.

160 GASTROINTESTINAL NEOPLASMS IN PATIENTS WITH BIALLELIC MISMATCH REPAIR GENE DEFICIENCY SYNDROME. Melissya Aronson1, Uri Tabori1, Jordan Lerner-Ellis2, Steven Gallinger3, Simon Ling1, Brittany Campbell1, David Malkin1, Harriet Drucker4, Hala Rimawi5, Roula Farah1, Musa Alharbi3, Shlomi Constantini6, Aaron Pollett1, Brandie Leach1, Matthew Kalady6, Shlomi Cohen6, Lynette Penney6, Moshin Rashid1, Douglas Riegert-Johnson12, Doua Bakry1, Carol Durno1,2, 1Hospital for Sick Children, Toronto, ON, Canada; 2Surgery, Mount Sinai Hospital, Toronto, ON, Canada; 3Jordan University, Irbid, Jordan; 4Saint George Hospital, Beirut, Lebanon; 5King Fahad City Center, Riyadh, Saudi Arabia; 6Dana Children’s Hospital, Tel-Aviv, Israel; 7Cleveland Clinic, Cleveland, OH; 8Cleveland Clinic, Cleveland, OH; 9Dana-Dweg Children’s Hospital, Tel Aviv, Israel; 10IWK Health Centre, Halifax, NS, Canada; 11IWK Health Centre, Halifax, NS, Canada; 12The Mayo Clinic, Jacksonville, FL

Background: Lynch syndrome is caused by heterozygous germline mutations in the DNA mismatch repair (MMR) genes MLH1, MSH2, MSH6, or PMS2. Individuals with biallelic MMR mutations (bMMRD) develop a novel syndrome including polyposis and early-onset gastrointestinal (GI) cancers, brain tumors, and hematological cancers. An international collaboration has been created to recruit and study individuals including a cancer surveillance program. Objectives include characterizing the GI phenotype: age of onset of polyposis, anatomical distribution of polyps and cancer, document adenoma to carcinoma sequence, molecular diagnosis and risk of GI cancer.

Methods: A central database was developed to prospectively collect clinical information and family history data on patients with bMMRD. Demographic, genetic and medical information was obtained and diagnoses were confirmed through pathology reports with blood and tissue stored in a central repository. GI screening data was requested on all participants with yearly updates from the time of recruitment.

Results: Thirty-five individuals from 19 kindreds were identified with bMMRD. Genes included MLH1 (n=4), MSH6 (n=11) and PMS2 (n=20). Forty percent of these mutations are novel mutations. Sixty-one malignant tumors were identified, the most prevalent being GI (n=22) and brain (n=21). GI screening data was available on 21 of 35 individuals totalling 62 screening years. Age at first endoscopy ranged from age 4 - 33 (mean: 13.38 SD= 6.9). Five individuals had no history of colorectal adenoma or cancer (age 4-14 years), although one of the individuals had a duodenal cancer. Sixteen patients had adenomas ranging from 1 - 100. Age at earliest diagnosis of colonic adenoma was 8 years old, and age of earliest colorectal cancer (CRC) was 9. High grade dysplasia was diagnosed at a mean age of 11.2 years (SD 2.1, range 8-13 years). Seven individuals had small bowel adenomas, the earliest adenoma and small bowel cancer diagnosed at age 11. Among the 22 GI cancers, there were 3 small bowel adenocarcinoma (mean age:19.6) and 19 colorectal tumors arising in eight patients (mean age: 16.7 ). Three of the eight patients had synchronous colorectal tumors with 3, 4, and 6 primaries. Colorectal malignant tumors were distributed throughout the colon. None of the patients under surveillance have died of a GI cancer. Consanguinity was reported in 2/3 of kindreds.

Conclusions: Patients with bMMRD develop small and large bowel polyps during the first decade of life. The prevalence of small bowel and CRC in this population, is extremely high. Synchronous colorectal cancer is frequent even among very young patients. In this largest bMMRD cohort reported, anatomic location of colorectal polyps and cancer is equally distributed. Adenoma to carcinoma progression is rapid. Surveillance is effective in identifying adenomas and early GI cancer that likely would have advanced if not screened. Consanguinity is prevalent among this syndrome and a clue to suspecting bMMRD. Recruitment of more patients with bMMRD will allow confirmation of these results and advance our understanding of this condition.

161 COMPLICATIONS OF PEDIATRIC ERCP. Matthew J. Giefer1, Richard Kozarek2, 1Seattle Children’s, Seattle, WA; 2Virginia Mason Medical Center, Seattle, WA

Background: Previous reports have suggested that endoscopic retrograde cholangiopancreatography (ERCP) in the pediatric population is a safe therapeutic option for pancreatobiliary diseases with a complication rate similar to that which has been observed in adults. Nevertheless, because the total number of pediatric ERCP cases reported in the literature remains small compared to the adult population, questions remain regarding appropriate utilization and safety of this procedure in children.

Methods: Pediatric patients who underwent ERCP between January 1994 and July 2011 were identified from a diagnostic and billing codes. Medical records were examined for age, gender, diagnosis codes, indication for ERCP, type of sedation, findings, interventions, and complications. Descriptive statistics were prepared for data including frequencies,
percentages for categorical variables and means and standard deviations for quantitative variables. Extensions of logistic regression were used to examine the relationship between demographic and clinical characteristics and post-ERCP pancreatitis.

Results: 425 ERCPs were performed on 276 pediatric patients. Patient age ranged from 72 days to 18 years and there was relatively equal gender distribution. The most common indications for ERCP were biliary obstruction (43.3%) and chronic pancreatitis (26.8%). Detailed medical records were available for 337 procedures including procedural and post-procedural complications. General anesthesia was used commonly (68.5%) and conscious sedation was associated with premature procedural discontinuation or conversion to general anesthesia (7.1%). The most common complication was post-ERCP pancreatitis which occurred in 26 cases (7.7%) and the majority were mild by consensus definition. Procedural characteristics significantly associated with post-ERCP pancreatitis included: pancreaticocigam (OR:1.09;95% CI:1.04,1.14;p<0.01), pancreatic sphincterotomy (OR:1.16;95% CI:1.04,1.30;p<0.01), pancreatic duct stenting (OR:1.08;95% CI:1.01,1.17;p<0.03) and pancreatic duct structure dilation (OR:1.22;95% CI:1.04,1.43;p<0.01). Other complications included technical inability to complete the intended intervention (4.7%) and post-procedure pain without evidence of pancreatitis (3.6%). Of the 176 patients who had an endoscopic sphincterotomy, immediate post-sphincterotomy bleeding occurred twice (1.1%) and both cases were successfully treated during the procedure. There was one instance of a possible delayed sphincterotomy bleed in a patient with an episode of melena one week after the ERCP. No mortality was observed.

Conclusions: This retrospective review is one of the larger ERCP series reported in the pediatric population and adds to the growing body of literature supporting that ERCP can be safely applied in younger patients. The complication rate found in this series closely parallels that observed in adults and the most common complication, post-ERCP pancreatitis, was found to occur in 7.7% of cases. All of the significant risk factors for post-ERCP pancreatitis involved pancreatic duct injection or manipulation. Prospective studies of pediatric ERCP are still required to more definitively define the safe and appropriate uses of this procedure in children.

Friday, October 24, 2014
10:30 – 12pm

Research Session II – Basic – Inflammatory Bowel Disease

162 EPICUTANEOUS TOLERANCE INDUCTION FOR THE TREATMENT OF COLITIS, David Dunkin1, Mansi Saxena2, Zaruhi Hovhannisyan2, Jean-Frederic Colombel3, Hugh Sampson2, Cecilia Berin2, Garabet Yeretsian2, 1Pediatric Gastroenterology and Hepatology, The Icahn School of Medicine at Mount Sinai, New York, NY; 2Immunology Institute, The Icahn School of Medicine at Mount Sinai, New York, NY; 3Gastroenterology, The Icahn School of Medicine at Mount Sinai, New York, NY

Introduction: Crohn's disease patients have an inherent defect in inducing T regulatory cells (Treg) via the gut. When Tregs are generated externally in response to food antigen and infused into patients, they suppress inflammation in Crohn's disease via bystander suppression.

Hypothesis: We hypothesized that Tregs could be induced by applying antigen to the skin, and after migration to the gut could block inflammation via bystander suppression.

Methods: Mice were exposed epicutaneously daily for 5 days to ovalbumin (OVA) 1mg. To determine if exposure blocked T-effector responses, mice were then immunized with OVA, and cytokine production by draining lymph nodes (LN) was assessed by ELISA. Treg development in the mesenteric LN, spleen and intestines were determined. To determine if epicutaneous tolerance induction could abrogate colitis, mice were epicutaneously exposed to OVA, mice were gavage fed OVA to induce Treg homing to the gut, and colitis was induced with dextran sodium sulfate (DSS) or S. typhimurium. Weight loss and inflammatory cytokine production by MLN and colon were assessed.

Results: Epicutaneous exposure to OVA induced tolerance as demonstrated by suppression of OVA-specific IFN-γ. OVA exposure induced proliferation of OVA-specific Tregs in the spleen, MLN, small intestine and colon. In the DSS colitis model, prior epicutaneous OVA exposure followed by oral feeding of OVA decreased inflammatory cytokine production (IFN-γ and TNF-α) from the MLN and colon (p<0.01). In the infectious model, inflammatory cytokine production (IFN-γ, TNF-α and IL-17) from the colon was decreased (p<0.05).

Conclusions: Epicutaneous exposure induces Tregs, which can migrate to the gut and suppress inflammation. Thus, epicutaneous tolerance induction has potential as a treatment for Crohn's disease and warrants further study.

163 CHARACTERIZING THE ROLE OF INTESTINAL STEM CELLS DURING REGENERATION IN A MOUSE MODEL OF COLITIS, Roy Nattiv, Department of Pediatrics, Division of Pediatric Gastroenterology, UCSF, San Francisco, CA

The intestinal epithelium is comprised of a single layer of cells that lines the gastrointestinal tract and is continuously replaced during homeostasis. The Lgr5-expressing crypt base columnar cells (CBCs) are the bona fide adult intestinal stem cells and are responsible for regeneration during homeostasis. The role of the intestinal stem cells and mixed
progenitors during regeneration following acute injury is not fully understood. METHODS: Lgr5-EGFP-IRES-CreERT2; Rosa26-RFP, Lgr5-DTR-EGFP and Bmi1-CreER; Rosa26-RFP mice were fed 3% dextran sodium sulfate (DSS) in drinking water for five days \textit{ad libitum}. Subsequently mice were fed regular drinking water. Mice expressing the CreERT2 allele were injected with tamoxifen at discrete time points to induce Cre activity and sacrificed at several time points to assess the presence of Lgr5- and Bmi1-expressing cells and to determine the ability of these cells to generate progeny. Ki67 and Edu staining was performed to monitor for proliferation. RESULTS: Following DSS-induced injury, mice displayed characteristic signs of colitis, including weight loss, diarrhea, and bloody stool. Histologic examination revealed ongoing proliferation in the colonic crypt throughout the recovery period. Interestingly, Lgr5-expressing CBCs were absent following injury and during early recovery (days 1-2). Lgr5-expressing CBCs gradually repopulated and cell counts returned to normal by day 4-6 of recovery. Similarly, Bmi1 expression was also absent during injury and early recovery. In contrast, we identified a relative increase in the number of proliferative absorptive progenitors marked by active Notch signaling (NICD). Flow cytometry confirms an enrichment for CD44+ Notch1+ cells in the absence of Lgr5+ CBCs during early recovery. FACS sorting of these absorptive progenitors followed by RNA analysis suggests possible mechanisms whereby these cells may evade injury and can proliferate during early regeneration in the absence of Lgr5+ CBCs. CONCLUSION: NICD expressing absorptive progenitors may evade DSS-induced intestinal injury and contribute to the early regenerative process. Future experiments will focus on the mechanisms that allow these absorptive progenitors to evade DSS-induced intestinal damage and on a possible role for reversion of these secretory progenitors through a dedifferentiation process during early recovery.

164 NOD2 DOWNREGULATES COLONIC INFLAMMATION THROUGH IRF-4 MEDIATED INHIBITION OF K63 DIRECTED POLYUBIQUITINATION OF NF-KB PATHWAY MOLECULES RICK AND TRAF6 MOLECULES. Tomohiro Watanabe, Naoki Asano, Tsushi Kitani, Ivan Fuss, Warren Strober, NIH/ Mucosal Imm. Section, Bethesda, MD; 2Department of Gastroenterology and Hepatology, Kyoto University Graduate School of Medicine, Kyoto, Japan; 3Division of Gastroenterology, Tohoku University Graduate School of Medicine, Sendai, Japan

Background: It has been demonstrated that polymorphisms of the caspase activation and recruitment domain 15 (CARD15), a major risk factor found in Crohn's disease (CD) patients, leads to loss of nucleotide-binding oligomerization domain 2 (NOD2) function. In a previous study exploring this question, we showed that activation of NOD2 in human dendritic cells by its ligand, muramyl dipeptide (MDP), a final breakdown product of bacterial cell wall coat, regulates and suppresses Toll-like receptor (TLR)-mediated inflammatory responses.

Aim: However, a molecular explanation of how this loss of function leads to increased susceptibility to CD has remained unproven. To discern the mechanisms involved in NOD2 suppression of TLR signaling we assessed the effects of MDP on the intracellular and nuclear molecules of activated antigen presenting cells.

Results: Herein we show that NOD2 activation results in increased interferon regulatory factor 4 (IRF4) expression and binding of IRF4 to intermediate NF-KB signaling molecules such as tumor necrosis factor receptor associated factor 6 (TRAF6) and RICK (receptor interacting serine-threonine kinase). We then found that such binding leads to IRF4-mediated inhibition of specific Lys63-linked polyubiquitination of TRAF6 and RICK and subsequent downregulation of nuclear factor (NF)-κB activation. Finally, we demonstrate that protection of mice from the development of experimental Trinitrobenzene sulfonic acid (TNBS) colitis by ip administration of either MDP or IRF4 administration is accompanied by similar IRF4-mediated effects on polyubiquitination of TRAF6 and RICK in colonic lamina propria mononuclear cells. These latter protective effects do not occur in vivo in NOD deficient animals nor in vitro in human CD patient LPMC.

Conclusion: These findings thus define a molecular mechanism of NOD2-mediated regulation of innate immune responses to intestinal microflora that could explain the relation of loss of function of CARD15 polymorphisms and resultant NOD2 dysfunction to CD pathogenesis.

Friday, October 24, 2014

12pm – 2pm

Poster Session II

*Poster of Distinction

Basic - Inflammatory Bowel Disease

165* LONG-TERM EFFICACY OF ADALIMUMAB IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE. William Faubion, Marla Dubinsky, Frank Rueemmele, Johana Escher, Joel Rosh, Andreas Lazar, Samantha Eichner, Yao Li, Nattanan Reilly, Roopal Thakkar, AbbVie Inc, North Chicago, IL; Cedars-Sinai Medical Center, Los Angeles, CA; Mayo Clinic, Rochester, MN; Hospital Necker-Enfants Malades, Universite Sorbonne Paris-Cite, Paris, France; Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands; Goryeb Children's
Hospital/Atlantic Health, Morristown, NJ; AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany

Introduction: The efficacy of adalimumab (ADA) in children with moderately to severely active Crohn's disease enrolled in the IMAgINE 1 trial has been reported up to week 52. Long-term efficacy of ADA in patients (pts) enrolled in the on-going open-label (OL) extension, IMAgINE 2, is presented.

Methods: Pts who completed IMAgINE 1 through week 52 were allowed to enroll in IMAgINE 2. Pts entering from blinded therapy received OL ADA according to body weight (≥40 kg: 40 mg ADA every other week [EOW]; <40 kg, 20 mg ADA EOW). At or after week 8, pts experiencing flares (increase in PCDAI ≥15 points compared to PCDAI at previous visit) could move to weekly (EW) dosing. Pts entering IMAgINE 2 from OL ADA (40 mg ADA EW or 20 mg ADA EW) continued to receive the same dose. Remission (PCDAI≤10) and response (PCDAI decrease ≥15 points from IMAgINE 1 baseline) over time were assessed in pts who entered IMAgINE 2. Missing data were handled using non-responder imputation (NRI) and last observation carried forward (LOCF). Endpoints are also reported as observed. A data cut-off of Jun 30, 2013 was used for this analysis.

Results: Of the 188 randomized pts in IMAgINE 1, a total of 100 pts enrolled in IMAgINE 2. As of Jun 30, 2013, a total of 54 pts are ongoing in the study. Approximately two-thirds of pts entered IMAgINE 2 in remission and almost all entered with response (67% and 95%, respectively). Observed remission and response rates remained stable over time during IMAgINE 2 (Table). Mean PCDAI scores decreased from 40.1 at IMAgINE 1 baseline to 8.6 at week 192 of IMAgINE 2 (Table). Adverse event rates up to week 260 from IMAgINE 1 baseline have been previously reported and no new safety signals were observed with prolonged ADA use.

Conclusion: Results of the on-going open-label study support clinically meaningful efficacy with long-term ADA therapy beyond four years of exposure in children with moderately to severely active CD.


Rates of remission and response and observed mean PCDAI scores during IMAgINE 2

<table>
<thead>
<tr>
<th>Week</th>
<th>0</th>
<th>24</th>
<th>48</th>
<th>72</th>
<th>96</th>
<th>120</th>
<th>144</th>
<th>168</th>
<th>192</th>
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<tbody>
<tr>
<td>Remission (%)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>NRI</td>
<td>67.0</td>
<td>59.0</td>
<td>55.0</td>
<td>50.0</td>
<td>54.0</td>
<td>51.0</td>
<td>51.0</td>
<td>42.0</td>
<td>26.0</td>
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<tr>
<td>LOCF</td>
<td>67.0</td>
<td>62.2</td>
<td>61.2</td>
<td>57.1</td>
<td>61.2</td>
<td>62.2</td>
<td>63.3</td>
<td>62.2</td>
<td>61.2</td>
</tr>
<tr>
<td>Observed</td>
<td>67.0</td>
<td>62.8</td>
<td>66.3</td>
<td>64.1</td>
<td>70.1</td>
<td>73.9</td>
<td>79.7</td>
<td>79.2</td>
<td>81.3</td>
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<tr>
<td>Response (%)</td>
<td></td>
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<tr>
<td>NRI</td>
<td>95.0</td>
<td>88.0</td>
<td>75.0</td>
<td>74.0</td>
<td>72.0</td>
<td>66.0</td>
<td>64.0</td>
<td>48.0</td>
<td>29.0</td>
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<tr>
<td>LOCF</td>
<td>95.0</td>
<td>91.8</td>
<td>85.7</td>
<td>87.8</td>
<td>85.7</td>
<td>85.7</td>
<td>87.8</td>
<td>82.7</td>
<td>81.6</td>
</tr>
<tr>
<td>Observed</td>
<td>95.0</td>
<td>93.6</td>
<td>90.4</td>
<td>94.9</td>
<td>93.5</td>
<td>95.7</td>
<td>100</td>
<td>90.6</td>
<td>90.6</td>
</tr>
<tr>
<td>Mean PCDAI</td>
<td>10.2</td>
<td>10.3</td>
<td>9.2</td>
<td>8.9</td>
<td>9.4</td>
<td>7.9</td>
<td>6.1</td>
<td>7.5</td>
<td>8.6</td>
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The number of pts declined over time due to discontinuations and because not all pts had reached later time points. Results after week 192 are not presented as only a few pts had reached longer study durations.

166 TRANSITIONING FROM ADOLESCENCE TO ADULTHOOD: DEVELOPMENT OF THE "IBD FINAL EXAM". Matthew Shields, Thomas Rossi, Lawrence Saubermann, Division of Pediatric Gastroenterology, University of Rochester Medical Center, Rochester, NY

Background: One of the biggest challenges that we face as pediatric gastroenterologists is the education of our adolescents with inflammatory bowel disease (IBD) about their illness and then transitioning them to an adult gastroenterologist. Many are in denial or just not interested in learning about their disease and, as a result, their transition into adulthood can be challenging. When these patients leave their pediatric gastroenterologist, their symptoms often worsen and their disease activity increases. This is often due to poor medication compliance and less healthy lifestyle choices. Adolescents need more effective means to educate themselves about their disease in order to decrease the likelihood that they will flare and have complications from their IBD.

Methods: We created a quality improvement educational instrument, entitled the "IBD Final Exam" that helped teach our adolescent patients about their disease before leaving our practice. The instrument was geared towards adolescents with either Crohn's disease or Ulcerative Colitis. It consisted of 5 True/False questions, 2 multiple choice questions, and 1 request to listen to a podcast on the gikids.org website. The questions asked about some basic principles regarding both Crohn's disease and Ulcerative Colitis, and it was administered to adolescents between the ages of 14 and 19 years old.
Results: Of the 12 patients who completed the "IBD Final Exam" exercise, 10 said that they either "agreed" or "strongly agreed" that the instrument helped them learn more about their IBD. Similarly, 10 out of 12 patients responded that they "agreed" or "strongly agreed" that they felt comfortable recognizing complications of their disease after they left the pediatric gastroenterology practice.

Conclusions: This pilot quality improvement project showed that a quick instrument which actively engages IBD patients about transitioning to an adult gastroenterology practice is feasible and well-received. Additionally, it may also be helpful to identify those patients who are at risk for having IBD complications while in college. Further investigation is necessary to compare transition outcomes using the "IBD Final Exam."

167 THE FOOD ADDITIVE POTASSIUM BROMATE INHIBITS CELL CYCLE PROGRESSION AND INDUCES CELL DEATH IN INTESTINAL EPITHELIAL CELLS. Michelle Edelman, Leahana Rowehl, Anupama Chawla, Grace Gathungu, Pediatric Gastroenterology, Stony Brook Long Island Children's Hospital, Stony Brook, NY

Background: Increased intestinal permeability is observed in both Crohn's disease patients and in their healthy, asymptomatic first-degree relatives. However, gut permeability can be increased physiologically in response to luminal nutrients or pathogens. Lipopolysaccharide (LPS), a bacterial endotoxin, induces an innate immune response and mucus hyperpermeability in vivo. It serves as a mediator of inflammation in IBD. Potassium bromate (KBrO₃), an oxidizing agent used to enhance food, cosmetic byproducts and disinfect water is neurotoxic, nephrotoxic and carcinogenic in animal studies. We explored KBrO₃ as a potential trigger of intestinal inflammation. We have shown (unpublished data) that KBrO₃ decreases transepithelial electrical resistance (TEER) on co-cultured intestinal epithelial cells (IECs) and increased the release of proinflammatory cytokines after 24 hours of treatment in a dose-dependent fashion. Cytokine release was enhanced with the addition of LPS. Interestingly, KBrO₃ at higher doses showed a marked decrease in cytokine protein expression. We therefore proposed that KBrO₃ induces IECs apoptosis. Objective: To examine the cytotoxic effect of KBrO₃ on intestinal epithelial cells. Methods: Co-cultured Human CaCo2-BBE and HT29 cell lines were grown to confluence for 14 days until the establishment of a polarized epithelial monolayer. Cells were treated with KBrO₃ 0.5, 1, 5 and 10mM for 24 hours. Proliferation and cellular viability was measured using alamarBlue Reagent and an MTT assay. RNA was extracted from the IECs. Primers were designed for the P21 gene and verified using Primer-BLAST. Gene expression of p21 was determined by real time Polymerase Chain Reaction. Statistical analysis was conducted using repeated measures analysis of variance on GraphPad Prism. Results: Percentage of cellular proliferation decreased and percentage of cell death increased following treatment with KBrO₃ in a dose dependent fashion. Expression of p21 increased and was significantly elevated following treatment with high doses of KBrO₃ (p= 0.0009). There was no synergistic effect on p21 expression with the addition of LPS. Discussion: This in vitro human IECs model demonstrates that KBrO₃ alters cellular proliferation, and increases cellular toxicity in a dose dependent fashion. Increased expression of p21 due to KBrO₃ treatment suggests that this food additive leads to arrest of cell cycle progression possibly through the mechanism of oxidative DNA damage. This process is not enhanced with the addition of LPS. We are examining the expression and distribution of tight junctions at the protein level to further understand the role of KBrO₃ in cell permeability and alteration of the intestinal epithelial barrier.

168 THE PROTECTIVE EFFECT OF ASTRAGALUS POLYSACCHARIDES ON TNBS-INDUCED ANIMAL MODEL OF COLITIS THROUGH CYTOKINE MODULATION. Min Yang¹, Huan-Bing Lin², Si-Tang Gong², Ding-You Li³, ¹Pediatric Gastroenterology, Children's Mercy Hospital, Kansas City, MO; ²Gastroenterology, Guangzhou Women and Children's Medical Center, Guangzhou, China; ³Center for Evaluation and Certification, Guangdong Food and Drug Administration, Guangzhou, China

Background: Astragalus membranaceus is a Chinese medicinal herb and has been shown to improve hapten-induced experimental colitis. One of its major components is polysaccharides.

Aim: To investigate the effect of Astragalus polysaccharides (APS) on body weight change, disease activity index (DAI), macroscopic and microscopic scores and expression of TNF-α, IL-1β and NFATc4 in a rat model of experimental colitis.

Methods: The experimental colitis model was induced by TNBS. Forty five rats were divided into five groups (n=9): Normal control group, receiving ethanol vehicle with no TNBS during induction and IP saline injection during treatment; TNBS colitis model group (TNBS+IP saline), receiving only IP saline vehicle treatment; APS low dose group (TNBS+L-APS), receiving APS 100 mg/kg; APS high dose group (TNBS+H-APS), receiving APS 200 mg/kg; and positive control group (TNBS+Dexm), receiving dexamethasone 0.3 mg/kg. The clinical features, macroscopic and microscopic scores were assessed. The expressions of TNF-α, IL-1β and NFATc4 were measured by real-time PCR and ELISA assays.

Results: Compared to normal control rats, TNBS+IP saline had significant weight loss, increased macroscopic and microscopic scores, higher DAI, up-regulation of TNF-α, IL-1β and NFATc4 mRNA expression and up-regulation of TNF-α and IL-1β protein expression. Compared to TNBS+IP saline, treatment with APS or dexamethasone significantly reduced DAI, partially but significantly prevented TNBS colitis-induced weight loss and improved both
macroscopic and microscopic scores; high dose APS or dexamethasone significantly down-regulated TNF-α and IL-1β expressions (both mRNA and protein) and up-regulated NFATc4 mRNA and protein expression. The effect of high dose APS and dexamethasone is comparable.

**Conclusions:** APS significantly improved experimental TNBS-induced colitis in rats through regulation of TNF-α, IL-1β and NFATc4 expression.

Celiac/EoE/Allergic Enteropathy

**172** ESOPHAGEAL MICROBIOME IN HEALTHY CHILDREN AND THOSE WITH EOSINOPHILIC ESOPHAGITIS: A PROSPECTIVE STUDY. Kalyan Ray Parashette1, Evelyn C. Toh2, Emily Contreras3, David E. Nelson4, Sandeep K. Gupta5, 1Riley Hospital for Children, Indiana University, Indianapolis, IN; 2Department of Microbiology & Immunology, Indiana University School of Medicine, Indianapolis, IN

**Introduction:** Gut microbiome plays a role in various diseases of gastrointestinal tract. However, there is limited knowledge about esophageal microbiome especially in pediatric population. Adult studies have shown that esophageal microbiome is altered in patients with reflux esophagitis, Barrett esophagus and esophageal adenocarcinoma.

**Aim:** Identify the esophageal microbiome in pediatric population.

**Methods:** In this prospective study, esophageal mucosal biopsies from seven subjects [3 normal subjects and 4 eosinophilic esophagitis (EoE) subjects] were analyzed for microbiome composition using 16S rRNA gene sequencing technique.

**Results:** The subject age range was 4 years to 16 years with mean age of 10 years. Four subjects (57%) were male. All subjects were on regular diet. None of the subjects were on systemic steroid or antibiotic for at least two months prior to esophagogastroduodenoscopy (EGD). Normal subjects were not on any acid blocker for at least two months prior to the EGD. EoE subjects were treated with high dose proton pump inhibitor (2mg/kg/day) for two months prior to the EGD. We defined common taxa as > 1% of relative abundance in any sample and rare taxa as <1% in any sample. The total microbiome reads in biopsy samples ranged from 42125 to 61909 with a mean of 48357 and SD of 7157. The number of taxa in samples ranged from 31 to 51 with a mean of 40.5 and standard deviation of 5.5.

The most relatively prevalent taxa (in descending order) were unclassified (30%), Streptococcus (25%), Prevotella (17%), Porphyromonas (8%), Fusobacterium (6%), Veillonella (6%), Neisseria (5%), Gemella (1%), Campylobacter (1%), and Granulicatella (1%).

Taxa were compared between normal subjects and EoE subjects. Prevotella (p=0.07) and Veillonella (p=0.08) taxa were relatively more abundant in normal subjects than EoE subjects. EoE subjects had higher proportions of unclassified taxa (p=0.07) and Fusobacterium (p=0.1) taxa compared to normal subjects.

**Conclusion:** Our pilot study suggests that esophageal mucosa in children is populated by microorganisms. Composition of microbiome is different in patients with EoE compared to healthy controls though result was not statistically significant. We are studying a larger cohort of samples to further explore relationship between EoE and esophageal microbiome. The findings could have significant clinical implications on pathogenesis, evaluation and treatment of patients with EoE.

**173** COMPARISON OF TWO COMMERCIAL TISSUE TRANSGLUTAMINASE ANTIBODY ASSAYS FOR THE DIAGNOSIS OF CELIAC DISEASE. Grace J. Lee1, Amy Leber2, Kathy Mack2, Brendan Boyle2, Tracy Ediger1, Ivor Hill1, 1Department of Gastroenterology, Hepatology, and Nutrition, Nationwide Children's Hospital, Columbus, OH; 2Department of Laboratory Medicine, Nationwide Children's Hospital, Columbus, OH

**Background:** The European Society of Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) guidelines recommend IgA anti-tissue transglutaminase antibody (TTG IgA) as the initial test for celiac disease (CD). These guidelines suggest that in patients with signs or symptoms consistent with CD, TTG IgA levels >10 times the upper limit of normal (ULN) with a positive anti-endomysial antibody and human leukocyte antigen-DQ2 and/or DQ8 heterodimer may be used to diagnose CD without intestinal biopsy. The guidelines also recommend that each assay be validated in pediatric CD patients and controls. Implementing the proposed non-biopsy diagnosis of CD is limited by variability and lack of standardization among available TTG IgA tests. The primary aim of this study was to compare two commercial TTG IgA assays among pediatric CD patients and controls. A secondary aim was to determine each assay's ability to identify patients with TTG IgA levels >10 times the ULN that could potentially have had a non-biopsy diagnosis of CD.

**Methods:** One hundred fifty patients who underwent endoscopy between September 2011 and April 2014 were retrospectively reviewed. Fifty children with confirmed CD as determined by TTG levels >75 utilizing the Quanta-Lite assay (Inova) and Marsh 3 histopathology were compared to 100 controls with Marsh 0 histopathology. The Quanta-Flash (QF) chemiluminescent assay (Inova) (ULN = 20, linear range 1.9-4965.5 chemiluminescence units) and EliA Celkey (EC) fluoroenzyme immunoassay (Phadia) (ULN = 10, linear range 0.1-128 U/mL) were used to measure TTG IgA levels from stored sera. Pearson correlation analysis was used to determine the correlation between the two assays.

The number of patients with a TTG IgA level >10 times the ULN was determined for each assay.

**Results:** Mean age of the CD group was 10.1 years (range 1.7-19.2 years) with 26 females (52%) and 11.5 years (range
TTG IgA levels for all CD patients were greater than the manufacturer's ULN as measured by the QF and EC assays. TTG IgA levels were within normal range in all control patients with both assays. The correlation between the two assays for all patients was $r = 0.938$ ($p < 0.0001$) and $r = 0.927$ ($p < 0.0001$) for CD patients alone. TTG IgA levels of CD patients ranged from 104-3740 (5.2-1870 times the ULN) with the QF assay and 21-7920 (2.1-792 times the ULN) with the EC assay. Significantly more CD patients had a TTG >10 times the ULN with the QF assay (45/50, 90%) than the EC assay (28/50, 56%) ($p=0.0001$).

Conclusions: In this cohort of CD patients with Marsh 3 histopathology and control patients with normal duodenal biopsies, the QF and EC assays accurately identified all CD patients and controls. The assays were well-correlated, although the QF assay provided a wider dynamic range. The QF assay identified a significantly larger proportion of patients with a TTG IgA level >10 times the ULN and would have potentially allowed for non-biopsy diagnosis of CD in more patients per the ESPGHAN guidelines. While TTG IgA assays may correlate well with one another, each assay should be individually validated prior to adopting a non-biopsy approach to the diagnosis of CD.

174 THE BENEFIT OF SEPARATE DUODENAL BULB BIOPSY IN CHILDREN UNDERGOING AN UPPER ENDOSCOPY. Rami Gebrail¹, Joseph A. Murray², Imad Absah¹, ¹Pediatric Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; ²Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN

Introduction: Upper endoscopy (EGD) is an essential diagnostic test in children with gastrointestinal diseases. Small bowel (SB) biopsies are collected from the distal duodenum, because Brunner glands in the proximal duodenum can interfere with the villous: crypt ratio and presumed risk of higher complications. A bulb biopsy is recommended in children with celiac disease (CD), because up to 8% have exclusive bulb injury. The aim is to determine the benefit of separate bulb biopsy in children undergoing EGD and if that is associated with higher endoscopic complications.

Methods: We reviewed the electronic records between 1996-2014. Children who had an EGD with separate bulb biopsy were included. Demographics, clinical and histopathological parameters were recorded. Results: A total of 211 children were identified, average age was 10 years (range 1-17) and 115 were males. 58 had CD and 153 were non celiac.

Indications for EGD are summarized in table 1. All patients with CD had positive TTG IgA, whereas in non-celiac 6 had positive serology (5 TTG IgG and 1 TTG IgA with normal biopsy). In patients with CD bulb biopsy was diagnostic in 2 (3%) with exclusive bulb injury and confirmatory in 3 (bulb Marsh 2 and Marsh 1 distally). In the non celiac group 7 patients (4.5%) had exclusive bulb injury (3 peptic duodenitis, 3 IEL's and 1 Crohn's disease). Conclusions: In children with CD separate bulb biopsy increased the diagnostic yield by 3% of, in the non celiac group. Isolated bulb injury was found in 4.5% with unclear clinical significance.

The indications for the upper endoscopy

<table>
<thead>
<tr>
<th>Indication for EGD (n=211)</th>
<th>Celiac group n=58 (%)</th>
<th>Non-celiac group n=153(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>37 (64%)</td>
<td>74 (48%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10 (17%)</td>
<td>30 (20%)</td>
</tr>
<tr>
<td>Poor weight gain</td>
<td>8 (14%)</td>
<td>20 (13%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (2%)</td>
<td>20 (13%)</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>2 (3%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Asymptomatic with positive celiac serology (TTG IgG/IgA)</td>
<td>0</td>
<td>6 (4%)</td>
</tr>
</tbody>
</table>

175 COLONIC EOSINOPHILIA: AN EVALUATION OF CLINICAL AND HISTOPATHOLOGICAL PRESENTATION. Jacob Mark¹, Shahan Fernando¹, Kelley E. Capocelli², Joanne Masterson¹, Glenn T. Furuta¹, Edwin F. deZoeten¹, ¹Pediatrics, Children's Hospital Colorado, Aurora, CO; ²Pathology, Children’s Hospital Colorado, Aurora, CO

Background: Colonic eosinophilia is a histological descriptor with a wide range of histological characterizations and clinical implications. While this finding can be observed in a number of conditions including inflammatory bowel diseases, eosinophilic colitis and food allergies, no clear consensus of a normal, much less a pathologic number of eosinophils has been described for colonic biopsies.

Objective: The aims of this study were to 1) categorize clinical features of children with histological evidence of colonic eosinophilia and 2) determine whether the level of colonic eosinophilia was associated with clinical symptoms.

Methods: We performed a 8 year retrospective chart review of clinical, histopathological and laboratory data recorded from children between the ages of 1 and 21 years whose colonic pathology reports included the key words of "eosinophilic colitis", "eosinophilia" or "elevated eosinophil counts". Histopathology and clinical records were reviewed independently by a board certified pediatric pathologist and members of the gastroenterology section. Eosinophil enumeration was completed in the mucosal surface and are reported as peak eosinophil counts/high power field.
Results: Seventy two pathology reports were identified from 72 unique subjects (58.3% male). The most common indication for colonoscopy was abdominal pain (52.8%). Duration of symptoms prior to endoscopy ranged from 0-24 months. Colonic eosinophilia ranged from 14-135 eos/hpf. Peak eosinophil counts were significantly higher in subjects with hematochezia (67.9 vs 49.7 eos/hpf, p<0.001). Peak eosinophil counts were significantly lower in three clinical findings, vomiting, (45.2 vs 60.7 eos/hpf, p=0.05), weight loss (46.2 vs 60.0 eos/hpf, p=0.05), and history of allergic diseases (52.4 vs 66.9 eos/hpf, allergies p<0.05). Pearson correlation revealed that peak eosinophil counts were positively correlated with anemia, elevated erythrocyte sedimentation rate, and low serum albumin.

Conclusion: The association of colonic eosinophilia with hematochezia, anemia and elevated ESR may indicate more significant inflammatory disease. In addition, the lack of correlation of elevated peak eosinophil count with allergic disease may further suggest that colonic eosinophilia is not related to an allergic disorder.

176 COMPARISON OF ESOPHAGEAL CLEARANCE TIMES OF ORAL BUDENSONIDE PREPARATIONS.
Jody N. Hefner1,2, Robin S. Howard3, Cade M. Nylund2,1, Matthew D. Goldman2,1, Steve B. Min1,2, 1Pediatric Gastroenterology, Walter Reed National Military Medical Center, Bethesda, MD; 2Pediatrics, Uniformed Services University of the Health Sciences, Bethesda, MD; 3Department of Research Programs, Walter Reed National Military Medical Center, Bethesda, MD

Objective: The purpose of this study was to compare the mucosal contact time of alternative oral viscous budesonide (OVB) slurries with conventional sucralose OVB and assess subject taste preference for each.

Patients and Methods: This was a blinded, randomized, cross-over trial investigating the esophageal clearance of three OVB slurry preparations: standard sucralose OVB, honey OVB, and xanthan gum OVB. Twenty-four healthy adult subjects ingested the standard sucralose OVB and either honey OVB slurry or xanthan gum OVB slurry. Within each patient the esophageal clearance of each OVB slurry was evaluated 1 hour apart. The order of ingestion was divided such that half of the subjects within each group ingested the standard sucralose OVB first, and the other half the honey or xanthan gum OVB first. Esophageal clearance as an area under the curve (AUC) was calculated via nuclear scintigraphy using 1 millicurie (mCi) of technetium-99m-Sulfur Colloid (Tc-99) co-administered in each OVB preparation. A validated taste scale was utilized to assess subject tolerance of the taste of each OVB.

Results: Honey OVB had a higher AUC relative to sucralose OVB in 7/12 subjects at 1 and 2 minutes, and 8/12 at 3 minutes (P=0.24). Median increase in esophageal contact time using honey OVB at 1, 2 and 3 minutes was 18%, 15% and 13%. Xanthan gum OVB had a higher AUC in 10/12 subjects at 1 and 2 minutes, and 12/12 at 3 minutes (P<0.002). Median increase in contact time of xanthan OVB at 1, 2 and 3 minutes was 24%, 40% and 47%. Taste scores for honey were significantly higher compared to sucralose (P=0.045). Taste scores for xanthan gum did not differ significantly from sucralose.

Conclusion: Honey based OVB slurry was not statistically different in AUC than sucralose based OVB slurry. Xanthan gum OVB showed statistically significant higher AUC in total esophageal mucosal exposure. Honey based OVB may be a suitable alternative for patients reluctant to use or intolerant of sucralose OVB. Xanthan gum based OVB may also be a suitable alternative to sucralose based slurry, and in addition with increased mucosal contact time may lead to improved outcomes vs sucralose with the added advantage of customizable taste.

177 ADHERENCE TO THE GLUTEN CONTAMINATION ELIMINATION DIET CAN RULE OUT REFRACTORY CELIAC DISEASE.
Mara Storto1, Stephanie Camhi2, Maureen M. Leonard2, Pamela Cureton1,2, Martha McInnis1, Alessio Fasano1, 1Pediatric Gastroenterology and Nutrition, Massachusetts General Hospital, Boston, MA; 2School of Medicine, University of Maryland, Baltimore, MD

Background: Celiac disease is an autoimmune enteropathy triggered by the ingestion of gluten, a protein contained in the cereals wheat, rye and barley. The method of treatment is adherence to a gluten free diet. Certain individuals, however, have persistent symptoms and/or intestinal damage despite following the suggested diet for more than 12 months. This subset of celiac patients is classified as having non-responsive celiac disease (NRCD). Rarely, patients within this group are found to have refractory celiac disease (RCD), a condition managed by immunosuppressants. In our tertiary center, we aimed to confirm the diagnosis of RCD by instructing patients to first follow a more restrictive diet: the gluten contamination elimination diet (GCED). In our experience, patients are unknowingly exposed and react to trace amounts of gluten in their already strict gluten free diet.

Method: In this retrospective study, we reviewed the longitudinal medical records of all pediatric and adult patients seen at our tertiary care center between February 2013 and May 2014. Particular focus was given to patients to whom the GCED was recommended. We made note of symptoms, biopsy pathology reports and serology results before and after adherence to the restrictive diet. Response to the GCED was defined as healing of the intestinal mucosa and improvement or resolution of symptoms. In ideal cases, an endoscopy would be performed prior to and following the GCED.
**Results:** Of the 278 (36%M) patients seen at our tertiary center, nearly half (42%) were pediatric cases with an age range of 15 months to 79 years. One hundred thirty-seven (49%) total patients and 65 (55%) pediatric patients had confirmed celiac disease, which included patients with a previous diagnosis as well as those diagnosed at our center. The remaining patients either had an unknown diagnosis (due to lack of follow-up, pending results or unwillingness to commit to a gluten challenge), suspected gluten sensitivity or celiac disease was ruled out entirely. Of the confirmed CD cases, 1 (0.7%) patient had confirmed RCD Type 1 and 18 (13%) patients, 9 (50%) being pediatric cases, came to our clinic with questionable RCD. All 18 individuals consulted with our dietitian and received formal instruction on the GCED. Twelve patients adhered to the diet for its entirety, a period of 3 to 6 months. Six (50%) patients had resolution of symptoms and intestinal healing, and 5 (83%) returned to a standard gluten free diet. Of those responding to the GCED, 3 (50%) were pediatric patients. Six (50%) patients did not respond to the GCED, evidenced by persistent enteropathy, and were prescribed immunosuppressants. Of the patients who did not respond to the restrictive diet, 2 (33%) did have a symptomatic response despite enteropathy.

**Conclusion:** The GCED is effective in assessing true refractory sprue cases. The restrictive diet reveals patients who react to minute amounts of gluten and thus must eliminate it entirely to ensure proper healing. Distinguishing this group of CD patients from true RCD cases is essential to proper disease management and to prevent unnecessary immunosuppressant use.

**178 THE GUT-BRAIN AXIS IN AUTISM AND SCHIZOPHRENIA: ANALYSIS OF TIGHT-JUNCTION PROTEINS AND MMPs.** Anna Sapone1, Stefania Senger2, Dario Siniscalco2, Nicola Cascella2, Deanna Kelly1, Nicola Antonucci1, Laura de Magistris2, Alessio Fasano3, Maria R. Fiorentino2, 3Harvard Medical School, Charlestown, MA; 2Department of Internal and Experimental Medicine Magrassi-Lanzara, Seconda Universita' degli Studi di Napoli, Naples, Italy; 3Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD; 4Mucosal Immunology and Biology Research Canter, Massachusetts General Hospital, Boston, MA

**Background and Aim:** Schizophrenia and Autism Spectrum Disorders (ASDs) are complex conditions stemming from the classic gene-environment interaction paradigm. There are no defined mechanisms explaining how environmental triggers can lead to these conditions. One hypothesis based on the gut-brain axis connection, suggests that inappropriate antigen trafficking through an impaired intestinal barrier followed by passage of these antigens through a permissive blood-brain barrier (BBB), can be part of the chain of events leading to these diseases. While evidence of a permeable gut barrier in ASDs and schizophrenia is increasingly reported, no information is available concerning a breach in the BBB. Dysfunction of the BBB has been associated with numerous inflammatory neurologic disorders. It has been shown that BBB disruption is accompanied by overexpression of Matrix Metalloproteinases (MMPs). MMP9 disrupts Claudin-5, highly expressed in brain endothelial cells. Our aim was to investigate changes in Tight Junction and MMPs gene expression in the frontal cortex (Brodman's area 45) and in the cerebellum (CBL) of ASD and Schizophrenic subjects to evaluate whether the "leaky" gut-BBB notion might be implicated in the pathogenesis of a subgroup of these two neuropsychiatric disorders. **Materials and Methods:** Post mortem human brain tissues from the cerebral frontal cortex and the CBL were obtained from 8 ASD, 10 Schizophrenic subjects and 14 healthy controls (HC). Venous blood was drawn from 22 HCs and 15 ASD patients. RNA was isolated, reverse transcribed into cDNA and subjected to real time RT-PCR to measure Claudins (CL)5-4 and MMP2-9 gene expression. **Results:** ASD patients showed significantly higher levels of CL5 in both the frontal cortex and CBL, compared to HCs (p=0.03; p=0.002, respectively). CL4 was higher in the cortex (p=0.004) but not in the CBL of ASD subjects. Increased expression of (CL)5-4 was paralleled by a significant enhancement of both MMP2 (p=0.04) and MMP9 (p=0.03) in ASD cortex area compared to HCs. No significant difference was observed in any of the evaluated genes between schizophrenics and HCs. MMP9 gene expression was significantly increased in PBMCs from ASD patients compared to HCs (p=0.005). **Conclusions:** We have shown that in the autistic brain there's an increased expression of CL5-4, paralleled by an abnormal expression of both MMP2-9. These results demonstrate that unlike schizophrenics, autistic subjects carry an alteration of the BBB, possibly associated to an inflammatory state. The increased expression of MMP9 in PBMCs from autistic patients leads us to speculate that the inflammatory insult might be started in the gut, via a breached intestinal barrier. In conclusion, our data suggest that increased gut-BBB permeability might be involved in the pathogenesis of ASDs, but not schizophrenia.

**179 INCREASED PREVALENCE OF AIRWAY REACTIVITY IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS.** Nadia Krupp, Sandeep K. Gupta, Robert S. Tepper, Sarita Sehra, Mark H. Kaplan, Indiana University School of Medicine, Indianapolis, IN

**Introduction:** Children with eosinophilic esophagitis (EoE) frequently have other atopic conditions. Asthma prevalence has previously been estimated at 24-42% in children with EoE versus 9% of general population, though all prior studies have solely used self-report. Pulmonary function testing including spirometry, methacholine bronchial challenge (to measure airway hyperresponsiveness, AHR) and exhaled nitric oxide (eNO) are often used to diagnose and assess asthma in children.
The study aim was to determine airway reactivity in EoE children compared to controls using baseline spirometry and methacholine bronchial challenge, and also assess serum biomarkers of atopy.

**Methods:** Healthy control (HC) and EoE patients, ages 7-18 years were enrolled in a cross-sectional prospective study. Methacholine bronchial challenge (AH)R defined as provocative concentration of methacholine <8mg/ml), and eNO were assessed. Serum biomarkers included levels of total IgE, specific IgE to foods and aeroallergens, eosinophil count, epidermal growth factor (EGF), fibroblastic growth factor 2 (FGF-2) and serum cytokines including eotaxin.

**Results:** 70 children were enrolled (33 with EoE; 37 HC; 76% male, mean 12.9 years, median age 12.6 years). Baseline spirometry was normal and similar between the groups. AHRR was present in 33% of children with EoE but only 10.8% HC (p=0.04). Overall, 69.7% of EoE subjects had either asthma (by report) or AHR (by testing) as compared to 10.8% HC. Within the EoE group, the large majority of subjects with AHR (72.7%) did not have a previous diagnosis of asthma. IgE and eNO were elevated in EoE subjects compared to HC, and AHR correlated strongly with serum IgE (p<0.0001) and eNO (p=0.0002). EGF and FGF-2 were elevated in subjects with EoE and asthma when compared to HC (p<0.05); however, these were similar between HC and EoE patients without asthma.

**Conclusions:** This prospective, randomized study shows that asthma and AHR may be more prevalent than previous estimates in children with EoE; this association has previously not been rigorously studied and dedicated evaluation for AHR should be considered in children with EoE due to risk of sub-clinical asthma. EGF and FGF-2 may be a marker of multifocal atopic disease as serum EGF and FGF-2 levels were elevated in EoE patients with asthma but not in those without asthma. Further study is needed to determine whether AHR, EGF and FGF-2 vary with EoE disease activity, and what effects dietary modification and corticosteroids have on these measurements.
weeks of PPI therapy prior to follow-up endoscopy in 2008-2012. Patients who received EoE therapy (i.e. oral topical or systemic steroid, diet therapy) were excluded. Using archived esophageal biopsies, eosinophils were quantified in H&E slides and eotaxin-3-positive epithelial cells were quantified in the proximal, mid, and distal esophagus of pre- and post-therapy biopsies by immunostaining. Results Among 264 children with esophageal eosinophilia, 10 met inclusion criteria. Five patients were classified as Responders (post-therapy biopsy with <15 eos/hpf). Five patients were classified as Non-Responders (post-therapy biopsy with >15 eos/hpf). The Responders had a higher frequency in poor weight gain and vomiting, and lower peak eosinophil count. The two groups exhibited similar demographics, co-existing allergies, symptoms, endoscopic findings, histopathology, and PPI dosing/duration. Collectively, the mean highest peak number of eotaxin-3-positive epithelial cells decreased significantly after PPI therapy (35 to 20 cells/hpf, P=0.01). Peak number of eotaxin-3-positive epithelial cells strongly correlated with peak eosinophil count (R=0.83, P<0.0001) in esophageal biopsies. There was a significant decrease in eotaxin-3-positive epithelial cells in the proximal esophagus (28 to 6 cells/hpf, P=0.0488) after PPI therapy, but not in the mid or distal esophagus. The number of eotaxin-3-positive epithelial cells correlated with eosinophil counts before and after PPI in the proximal esophagus (R=0.87, P<0.01; R=0.91, P<0.001, respectively). Conclusion In children with esophageal eosinophilia, PPI therapy significantly decreased eotaxin-3-positive epithelial cells in the proximal but not distal esophagus, which strongly correlated to a decrease in eosinophilia. This finding is surprising because the distal esophagus was expected to respond to PPI therapy since the benefit of PPI acid-inhibition would manifest in the distal esophagus where acid reflux is greatest. On the other hand, the proximal esophagus, where acid reflux is minimal, responded to PPI therapy suggesting that acid-independent mechanisms may play a role.

182** ULTRASTRUCTURAL FEATURES OF EOSINOPHILIC ESOPHAGITIS: IMPACT OF TREATMENT ON DESMOSOMES. Shahan Fernando1,3, Eric P. Wartchow2,3, Glenn T. Furuta1,3, Joanne C. Masterson1,3, Kelley E. Capocelli2,3, 1Digestive Health Institute, Children’s Hospital Colorado, Denver, CO; 2Pathology, Children’s Hospital Colorado, Aurora, CO; 3School of Medicine, University of Colorado, Aurora, CO

Background: A growing body of clinical and molecular evidence suggests a role for altered epithelial barrier function in the pathophysiology of eosinophilic esophagitis (EoE), but few have described the epithelial structure during inflammation. We hypothesized that the epithelial barrier ultrastructure would be abnormal in pediatric subjects with EoE. The purpose of this study was to define ultrastructural features of active, inactive, and control subject’s esophageal epithelium.

Methods: We prospectively enrolled patients who were undergoing diagnostic upper endoscopy for evaluation of EoE with symptoms that included abdominal pain, vomiting, diarrhea, and dysphagia. Mucosal pinch biopsies were obtained from the distal esophagus and processed for routine histology and electron microscopic assessment. Clinical features of enrolled subjects were analyzed and subjects were divided into 4 groups as follows: normal (symptoms necessitating endoscopy, no medications, normal biopsies), GERD (symptoms of esophageal dysfunction, <15 eos/HPF), inactive EoE (prior EoE diagnosis, on treatment, <15 eos/HPF), and active EoE (symptoms of esophageal dysfunction, ≥15 eos/HPF, other diseases ruled out). Representative photomicrographs were taken of the basal and superficial epithelia and reviewed by each investigator for abnormalities. Desmosomes, as defined by punctate structures spanning the intercellular space, were quantified on the surface of epithelia 3 to 4 prickle-cell layers above the basal layer.

Results: Twenty-nine pediatric subjects (ages 2-18 years) were enrolled in the study (7 normal, 4 GERD, 9 inactive EoE, 9 active EoE). We observed a significant decrease in the number of desmosomes per cell (DPC) of subjects with active EoE compared to inactive EoE (7.6 ± 0.6 DPC vs 13.2 ± 1.1 DPC, active EoE vs inactive EoE, p<0.001), GERD (7.6 ± 0.6 DPC vs 12.0 ± 1.1 DPC, active EoE vs GERD, p=0.05), and normal epithelia (7.6 ± 0.6 DPC vs 14.1 ± 0.9 DPC, active EoE vs normal, p<0.0001). With respect to DPC, no significant differences were found between inactive EoE compared to GERD or normal subjects. Additional ultrastructural features observed included epithelial micropliae and mast cell pseudopodia. Evidence of eosinophil transmigration, degranulation and sombrero formation was also identified.

Conclusion: Consistent with clinical and molecular findings, our ultrastructural data provide support for altered barrier in pediatric subjects with EoE. We speculate that this may be a secondary event that occurs as a result of eosinophilic inflammation since following treatment, the epithelia desmosome number returns to that observed in normal tissue.

183 A SINGLE-CENTER EVALUATION OF ADHERENCE TO UPPER ENDOSCOPY BIOPSY GUIDELINES. Sylvia Y. Ofei, Brendan Boyle, Tracey Ediger, Ivor Hill, Nationwide Children's, Columbus, OH

Background: Small intestinal histologic changes associated with celiac disease (CD) may initially be confined to the duodenal bulb with patchy distribution. To minimize the potential of missing the diagnosis of CD clinical guidelines from the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and American College of Gastroenterology recommend obtaining at least 1 duodenal bulb and 4 distal duodenal biopsy specimens during esophagogastroduodenoscopy (EGD). Guideline adherence among adult gastroenterologists is 37% for all EGD's and 39.5% when there is clinical suspicion for CD. Adherence to these recommendations among pediatric
gastroenterologists is unknown. Our aim was to determine whether pediatric gastroenterologists routinely take the recommended number of biopsies from both the duodenal bulb and distal duodenum.

**Methods:** A retrospective audit of medical records at our tertiary care children's hospital was performed. Endoscopies with CPT code 43239 (EGD with biopsy) between July 2012 and July 2013 were identified. The audit and analysis included all 22 attendings and 6 fellows within the department. All children with a confirmed diagnosis of CD and a random sample of age-matched controls undergoing routine EGD for non-specific gastrointestinal symptoms were selected. Endoscopy and pathology reports were reviewed and the site and number of biopsies obtained were recorded for each case. The Wilcoxon rank-sum test (nonparametric) was used to compare the number of biopsies obtained between the CD and control groups.

**Results:** Ninety-seven patients diagnosed with CD were compared to 104 non-CD controls. The CD group had 42 males (43.0%) with a mean age of 9.9 years (SD 4.1; range 2-19) and the non-CD group had 49 males (47.0%) with a mean age of 11.4 years (SD 5.3; range 2-20). The groups were similar in regards to gender and age. The mean number of duodenal biopsies was significantly higher in the CD group at 5.9 (SD 1.6; range 2-11) compared to the control group at 3.6 (SD 1.2; range 2-8) (p<0.0001). Only 13/104 (12.5%) of control patients had ≥ 5 biopsies compared to 78/97 (80.4%) of patients with CD (p<0.0001). In the non-CD group there was no documentation that biopsies were obtained from the duodenal bulb. Of the 97 CD patients, only 10 (10.3%) had documentation that biopsies were obtained from both the duodenal bulb and distal duodenum.

**Conclusions:** Our single center study demonstrated that when a diagnosis of CD is under consideration pediatric gastroenterologists are more likely to adhere to guideline recommendations for the number of biopsy samples obtained. This was significantly less likely to occur when the EGD was performed for indications other than CD. When CD was suspected, only 10.3% of patients had documentation that biopsies were obtained from the duodenal bulb while in all other cases this was never documented. Failure to obtain the recommended numbers of biopsies from both the duodenal bulb and more distal duodenum could potentially result in the underdiagnosis of CD. Adherence to the guideline recommendations should be considered in all patients undergoing an EGD as they present an opportunity to identify CD even if the diagnosis was not under consideration prior to the procedure.

184 CLINICAL CHARACTERISTICS OF EOSINOPHILIC ESOPHAGITIS WITH BULBAR DUODENITIS: A NOVEL DISEASE PHENOTYPE. Tony Ljuldjuraj, Emily Contreras, Cindy Sawyers, Sandeep K. Gupta, Pediatric Gastroenterology, Riley Hospital for Children - IU Health, Indianapolis, IN

**BACKGROUND:** Eosinophilic esophagitis (EoE) has been defined by its phenotype in the esophagus. Much focus has been placed on the esophageal phenotype of the disease but less attention on potential extra-esophageal manifestations of EoE. We have observed a sub-population of EoE patients who develop bulbar duodenitis (BD) as a part of their disease.

**AIM:** To define a population of patients with EoE who develop BD by exploring differences in demographics and clinical history.

**METHODS:** EoE cases, as defined per consensus guidelines, were identified from the EoE registry at our institution. Cases of BD (defined as predominately acute and/or chronic, non-eosinophilic inflammation of duodenal bulb) were identified from the hospital's pathology database; these patients did not have other obvious causes of BD such as *H. pylori*, IBD, or celiac disease. EoE patients with BD (Group 1) and EoE patients with endoscopically-normal duodenal bulb (Group 2) were individually reviewed and demographics, clinical findings, duration of symptoms, atopy history, endoscopic features, and histology data were collected. Study patients had no significant gastric or distal duodenal biopsy changes.

**RESULTS:** During the study period 2008-2014, there were 19 patients in Group 1 and we compared these to 74 patients from Group 2. All patients with BD had endoscopic abnormalities of the duodenal bulb such as erythema and erosions. Mean ages were similar between Group 1 and Group 2 (10.6 vs 10.9 years p>0.05) but BD tended to be more common in boys than girls (84% vs 16%). Group 1 and Group 2 patients were just as likely to have abdominal pain (47% vs 42% p>0.05), emesis (42% vs 45% p>0.05), and dysphagia (21% vs 36% p>0.05) though Group 1 patients were less likely to have food impactions (5% vs 27% p<0.05). Time from onset of symptoms to diagnosis of EoE was significantly shorter in Group 1 vs Group 2 (10.3 vs 19.3 months p<0.05). Group 1 patients also had significantly higher peak esophageal eosinophil load (65.4 vs 50.1 eos/HPF p<0.05) and were significantly more likely to have concomitant atopic disease (84% vs 62% p<0.05) compared to Group 2.

**CONCLUSIONS:** We have described a novel phenotype of EoE. EoE patients with BD were more likely to have atopic disease and higher esophageal eosinophil load. Symptoms between the groups were similar except those with BD (Group 1) were less likely to have food impactions compared to Group 2. These data suggest careful endoscopic and histological examination for BD in patients with EoE both at initial and at follow-up endoscopies. It is unclear why those with BD were evaluated sooner than Group 2; our ongoing research is studying a larger cohort of patients. We are also examining the clinical course of patients with BD and implications of BD on medical care and treatment.
IN PATIENTS WITH EOE WHO HAVE FURROWING, TREATMENT WITH PPI ALONE DOES NOT RESULT IN HISTOLOGICAL RESPONSE. Teena Sebastian, Vahe Badalyan, Seema Khan, Gastroenterology, Hepatology, and Nutrition, Childrens National Medical Center, Washington, DC

Background: Epidemiologic data show that the incidence of pediatric eosinophilic esophagitis (EoE) is rising. Endoscopic features are important for initial diagnosis of EoE, but it is unclear whether they can predict response to therapy.

Aim: To describe the demographic and clinical characteristics of pediatric EoE in the ethnically diverse referral population of the DC metro area. To determine if endoscopic features at initial evaluation predict response to subsequent PPI treatment.

Methods: We compiled epidemiologic and clinical data for children who were referred to the specialized EoE clinic between December 2011-May 2014 at Children's National Medical Center, Washington, DC.

Results: Records of 103 children were reviewed. Average age at presentation was 6.1 years (SD 5.1yrs). 80 children (77%) were male. 44% were white and 41% were African American. Abdominal pain was a common in children ≥3 yr (40%). While vomiting/regurgitation were commonly reported symptoms in children of all ages, abdominal pain was more common in children ≥3 yr (40%). Vomiting (73%), poor weight gain (24%) and feeding difficulties (22%) were the predominant presenting features in <3 yr. Dysphagia (43%) and abdominal pain (38%) were leading complaints in those ≥10 yr. 60 (58%) children had atopic conditions; allergic rhinitis (25/60), asthma (19/60), atopic dermatitis (17/60), and food allergies (15/60).

Dysphagia (43%) was more common in children ≥3 yr (40%). Vomiting (73%), poor weight gain (24%) and feeding difficulties (22%) were the predominant presenting features in <3 yr. Dysphagia (43%) and abdominal pain (38%) were leading complaints in those ≥10 yr. 60 (58%) children had atopic conditions; allergic rhinitis (25/60), asthma (19/60), atopic dermatitis (17/60), and food allergies (15/60).

Both first and second endoscopy records were available for 73 children. Median time between the 1st and 2nd endoscopy was 5.7 months. At the time of the first endoscopy, 15 (21%) were on PPI, 14 (19%) were on elimination diet, 14 (19%) were both on PPI and elimination diet, and 30 (41%) were on no therapy. 43 (59%) of the 73 children had abnormal findings at the first endoscopy, most commonly, furrows (44%), exudates (19%), and rings (10%). 44 out of 73 (60%) children were PPI naïve. In this subgroup, 22 (50%) had ≥1 endoscopic abnormality and 35 (80%) had a histologic abnormality. Of the 35 PPI naïve children with histologic findings, 7 (20%) were subsequently treated with PPI alone. In these 7 patients, furrowing was present in 5 and 4 patients at the 1st and 2nd endoscopy, respectively.

Of the 7 patients, 3 had a histological response, and 3/7 had symptom improvement. At the time of the second endoscopy, 13 (18%) were on PPI alone, 7 (10%) were on elimination diet alone, 39 (53%) were both on PPI and elimination diet, 7 (10%) were on no therapy, and the remaining 7 (10%) were on elemental diet or swallowed steroids, alone or in combination with PPI. 13 out of 73 (18%) children were PPI naïve.

Of the 27 patients who had furrows AND abnormal histology at first endoscopy, 13 (48%) were on PPI; this number increased to 20 (74%) at the time of the second endoscopy. Being on PPI alone at the time of 2nd endoscopy was associated with resolution of furrowing in 2 out of 6 patients, symptom improvement in 4 patients, and a histological response in none. Combination of PPI and elimination diet was associated with resolution of furrowing in 8/13 patients, symptom improvement in 7 patients, and a histological response in 4 patients.

Conclusions: In patients with EoE who have furrowing, treatment with PPI alone does not result in histological response.

Clinical/Translational Inflammatory Bowel Disease

EXPLORING NEEDS DURING TRANSITION FROM ADOLESCENCE TO ADULTHOOD IN YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE: A QUALITATIVE STUDY. Herbert Brill1, Romy Cho1, Natasha M. Wickert1, Anne F. Klassen1, Elena Tsangaris2, John K. Marshall3, Pediatrics, McMaster University, Hamilton, ON, Canada; 2Medicine, McMaster University, Hamilton, ON, Canada

Background: The period of transition from adolescence to adulthood is a vulnerable period for individuals with IBD. Current transition strategies are based on expert opinion and limited studies on the anticipated needs of adolescents and families. The aim of this study was to identify the needs of young adults with IBD at transition by examining the views of young adults who transitioned in the past and to see if those needs differed from IBD patients diagnosed as young adults.

Methods: A qualitative interpretive description approach was utilized. Participants aged 18-30 years recruited from the McMaster University Medical Centre IBD clinic between July 2012 and May 2013. Semi-structured interviews were conducted using an interview guide with questions probing participants to discuss their needs. Interviews were audiotaped, transcribed verbatim and coded using a constant comparative method. QSR NVivo10 was used to manage the data. Sample size was established when no new additional themes were encountered.

Results: Twenty-one young adults were interviewed: 15 subjects diagnosed < 18 years of age and 6 subjects diagnosed as young adults. Among those diagnosed < 18, transition needs were identified in the key areas of psychosocial, informational, self-management, and daily living needs. Psychosocial needs were most commonly reported with subjects citing needs for support networks, removing social barriers, and coping with anger, depression, sadness, and anxiety. Subjects detailed how IBD led to intentional self-isolation from social settings. A paucity of information was
reported on the impact of smoking, drugs, and alcohol use. Overcoming financial barriers and participation in decision-making were noted as the primary signs of achieving independence. Subjects diagnosed as adults more often sought peer support groups and experienced more difficulties with healthcare access, financial concerns, and social isolation. Participants with less severe disease sought more client-centered care and those with more severe disease were more likely to describe social isolation.

**Conclusions:** We report the first study in the transition literature of already transitioned individuals' needs during the transition process. Individuals with IBD who have undergone transition focus most on psychosocial and financial needs rather than self-management of their chronic illness. This finding is likely generalizable to most adolescents and young adults with chronic life-long diseases. Psychosocial and financial readiness are not presently assessed in existing transition and self-management tools, and may need to incorporate these areas to more effectively measure the success of transition interventions.

**191 MAGNETIC RESONANCE ENTEROGRAPHY ACCURATELY ASSESSES FOR MUCOSAL HEALING IN PEDIATRIC CROHN'S DISEASE.** Jess L. Kaplan1, Matthew P. Moy3, Christopher J. Moran2, Harland S. Winter2, Michael S. Gee3, Harvard Medical School, Boston, MA; 2Pediatric Gastroenterology, Massachusetts General Hospital for Children, Boston, MA; 3Department of Radiology, Massachusetts General Hospital, Boston, MA

**BACKGROUND:** Magnetic resonance enterography (MRE) has become a more popular imaging modality in the assessment of Crohn's disease (CD) and its lack of ionizing radiation has made it particularly desirable for children. The efficacy of MRE as a non-invasive marker of disease activity and progression is currently being evaluated. MRE has recently been shown to accurately assess response to treatment and mucosal healing in adults but similar data in children is lacking. In this study we evaluated qualitative and quantitative MRE findings in children with CD which best correlate with mucosal healing assessed by ileocolonoscopy as a reference standard.

**METHOD AND MATERIALS:** We retrospectively identified 30 patients diagnosed with CD prior to age 19 years who underwent MRE as well as ileocolonoscopy within 30 days of imaging with at least one prior endoscopy for comparison. A pediatric radiologist blinded to endoscopic findings evaluated 7 bowel segments (terminal ileum and six colonic segments) on MRE for several imaging features, including Magnetic Resonance Index of Activity (MaRIA). Two pediatric gastroenterologists blinded to MRE findings reviewed each endoscopy independently to identify bowel segments with mucosal healing or persistent inflammation. When there was disagreement, a third blinded pediatric gastroenterologist acted as the tiebreaker. Differences in imaging features between healed and persistently inflamed segments were evaluated.

**RESULTS:** The average patient age was 17.2 years (SD 3.2) with a mean time of 12.7 days (SD 7.9) between MRE and the more recent endoscopy. Of the 202 bowel segments evaluated on MRE, 44 had demonstrated endoscopic evidence of mucosal healing and 37 had demonstrated persistent inflammation on endoscopy. MaRIA score <8 was strongly associated with mucosal healing (accuracy 74%, sensitivity 84%, specificity 62%, p <0.0001). Several individual components of MaRIA were also associated with healing, including bowel wall thickness <4 mm (72%, 84%, 57%, p = 0.0002), lack of mucosal hyperenhancement (72%, 98%, 41%, p <0.0001), mesenteric hypervascularity (72%, 87%, 15%, p <0.0001) and relative contrast enhancement <130 (67%, 68%, 64%, p = 0.0038). Fibrofatty proliferation also correlated with mucosal healing (67%, 95%, 35%, p = 0.0005). The average bowel wall thickness in healing segments was 2.7 mm (SD 0.9) compared with 4.7 mm (3.1) in segments with persistent inflammation (P =0.0035).

**CONCLUSION:** MRE accurately assesses for mucosal healing in pediatric CD. While MaRIA, a multi-factorial MRE assessment, performed well, bowel wall thickness alone performed similarly and lack of mucosal hyperenhancement was the single MRE feature that correlated best with mucosal healing.

**192 EFFECT OF BUTANOL PURIFIED CHINESE HERBAL FORMULA FAHF-2 AND ITS INDIVIDUAL HERBS ON GM-CSF PRODUCTION BY PBMCs OF PEDIATRIC CROHN'S DISEASE SUBJECTS.** Joanne Lai1, Changda Liu2, Ying Song2, Clare Ceballos1, Nan Yan3, Keith Benkov4, Xiu-Min Li2, David Dunkin1, 1Division of Pediatric Gastroenterology, The Icahn School of Medicine at Mount Sinai, New York, NY; 2Division of Allergy and Immunology, The Icahn School of Medicine at Mount Sinai, New York, NY

**Background:** Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract that causes significant morbidity in children. Interest in complementary treatments for IBD is growing. Food Allergy Herbs Formula-2 (FAHF-2) is composed of nine herbal medications that have been used in traditional Chinese medicine to treat colitis. FAHF-2 and its compounds have been shown in prior studies to have immunoregulatory effects on human peripheral blood mononuclear cells (PBMCs) and lamina propria from children with IBD. Granulocyte-macrophage colony-stimulating factor (GM-CSF) plays an integral role in intestinal innate immunity and is thought to have a protective effect in human and mouse models of intestinal inflammation. The aim of this study was to investigate the effect of butanol purified FAHF-2 (B-FAHF-2) and its herbal components on the production of GM-CSF by PBMCs of pediatric IBD subjects.

**Methods:** Compounds ganoderic acid C1 and β1 (GA-C1 and GA-β) were isolated from ganoderma lucidum (GL) in
FAHF-2. PBMCs were isolated from pediatric subjects. PBMCs were cultured with B-FAHF-2, the 8 individual herbs comprising FAHF-2, GL fractions D and DR (GL-D and GL-DR), as well as compounds GA-C1 and GA-β. PBMCs were stimulated with lipopolysaccharide (LPS) or anti-CD3/CD28. GM-CSF production in culture supernatants was measured by ELISA.

**Results:** Stimulation with LPS or anti-CD3/CD28 did not cause an increase in GM-CSF. B-FAHF-2 increased GM-CSF (p< 0.01) production by PBMCs derived from pediatric IBD and control subjects. Of the nine herbal medicines that comprise B-FAHF-2, GL increased GM-CSF production most effectively (p<0.01). The fractions of GL, GL-D and GL-DR, and compounds GAC1 and GA-β, did not significantly increase GM-CSF production.

**Conclusions:** B-FAHF-2 and GL increased GM-CSF production by PBMCs of pediatric subjects. Increasing GM-CSF may have clinical benefit in a subset of Crohn's disease patients with GM-CSF deficiency. Current and future work involves testing the effects of B-FAHF-2 and specifically GL on blood and biopsy specimens from a larger sample size of pediatric IBD subjects as well as murine models that are deficient in GM-CSF, and determining their mechanism of action.

**A RANDOMIZED, CONTROLLED TRIAL OF YOGA IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: PRELIMINARY FINDINGS.** Alycia A. Leiby1, Annette Langseder2, Rami Bustami2, Madeline Marchell1, Madalena Ferrara1, Minal Vazirani1, Joel Rosh1, 1Pediatric Gastroenterology, Atlantic Health System/Goryeb Children's Hospital, Morristown, NJ; 2Atlantic Center for Research, Atlantic Health System, Morristown, NJ; 3Integrative Medicine, Atlantic Health System, Morristown, NJ; 4Siegener Center for Integrative Medicine, Barnabas Health, Livingston, NJ

**Background:** 25% of inflammatory bowel disease (IBD) is diagnosed in pediatrics with peak onset in the pre-adolescent years during a time of great psychosocial growth. IBD adds stressors of a chronic disease with unpredictable symptoms. Health Related Quality of Life (HRQOL) may be impaired by pain, school absences, and the chronic nature of IBD. Yoga may be well suited as an adjunct to conventional IBD therapy to decrease stress and improve HRQOL. There have not been any studies to date looking at the role of Yoga in IBD. The aim of this study is to determine if a structured Yoga program, in addition to standard medical therapy, improves HRQOL and self-efficacy in pediatric patients recently diagnosed with IBD.

**Methods:** Newly diagnosed patients 11-17 year old were randomized to either the yoga program or a wait-list control group. At three months from diagnosis the study group participated in 12 weeks of yoga in addition to standard medical therapy. The control group continued to receive standard medical therapy and at six months from diagnosis was offered yoga participation. At 3 and 6 months from diagnosis questionnaires were completed by both groups to measure HRQOL (PedsQL total score) and self-efficacy. Patients were required to complete at least 9 of 12 yoga classes. Demographic and disease-specific data included age, gender and disease type (Crohn's disease, Ulcerative Colitis). Descriptive statistics were performed for the study sample. Continuous variables were summarized using average and standard deviation and proportions were used for categorical variables. Total PEDSQL and self-efficacy scores were compared in the control group and yoga group using the Mann-Whitney U test. Positive differences in scores indicated improvement.

**Results:** A total of 12 patients were included: 6 in the yoga and 6 in the control group. Average age was 13 years (SD = 1.6), with 67% females. 67% had Crohn's disease. Overall median change was 25 for HRQOL and 1.5 for self-efficacy scores. Median change in total PEDSQL scores was 100.0 in the yoga group vs. only 12.5 in the waitlist group; despite the trend, this difference was not statistically significant (p = 0.52). The change in self-efficacy scores in the two groups also was not significantly different between groups (2.5 for yoga vs. 1.5 for waitlist; p = 0.37).

**Conclusion:** A formal yoga program in newly diagnosed pediatric patients with IBD showed trends toward improvement in HRQOL and self-efficacy, although not reaching statistical significance. Further study with a larger sample size will investigate if disease activity scores will change after yoga participation and determine if yoga will improve QOL in this population.

**NATURAL HISTORY OF PAEDIATRIC IBD INCLUDING SURGERY WITHIN THE AGE BANDS OF THE PARIS CLASSIFICATION.** Johan Van Limbergen1, Paul Henderson1, Hazel Drummond1, Richard Russell2, Jack Satsangi1, David C. Wilson2, 1Pediatric Gastroenterology & Nutrition, IWK Health Centre, Dalhousie University, Halifax, NS, Canada; 2Child Life and Health, University of Edinburgh, Edinburgh, United Kingdom; 3Gastrointestinal Unit, University of Edinburgh, Edinburgh, United Kingdom; 4Pediatric Gastroenterology & Nutrition, Yorkhill Hospital for Sick Children, Glasgow, United Kingdom

**Background:** Inflammatory bowel disease (IBD) genetic susceptibility loci are largely shared between adult and paediatric IBD. Compared with adult IBD, paediatric IBD has been shown to be more dynamic and extensive using the Montreal classification. An improved classification of paediatric IBD (Paris) has recently been proposed. Data on the natural history of paediatric IBD according to the Paris-classification are scarce.

**Aims:** Our aims were to characterise the phenotype and need for surgery of paediatric IBD in different age groups (A1a
OUTCOMES IN A YOUNG ADULT POPULATION.

Introduction of a 'L5' category of disease for oral +/- perianal CD in paediatric CD.

Discussion:

Conclusions: Using the new Paris classification of paediatric IBD, we have demonstrated that A1a CD is characterised by less ileal disease (L1+/−L4: 6/154 vs 32/313; p=0.01 OR 0.36 (0.15-0.87)) and more limited oral+-perianal CD (L5) at presentation (14/154 vs 3/313; p<0.0001 OR 10.33 (2.92-36.53)). These differences persist during follow-up of A1a and A1b (p=0.0007 and p=0.02 at 2y and 4y, respectively). By 4 years after diagnosis, A1a CD is characterised by less panenteric CD (L3+L4ab: 4/67 vs 18/103; p=0.03 OR 0.30 (0.10-0.93)). Within A1a, there is no difference in CD location between children diagnosed before 6 years of age and between 6 - 9 years of age, at diagnosis and at 2 years follow-up.

Whereas A1a CD remains largely inflammatory (B1) during follow-up, A1b CD behaviour progresses to intestinal penetrating complications (p<0.0001). By 2y after diagnosis, Paris location (of patients not L3+L4ab at diagnosis), changed in 20.8% (59/283). This change of location was due to ileal (from colonic to ileocolonic disease) in 24/59 (40.7%) vs colonic (from ileal to ileocolonic disease (n=8) or isolated colonic extension (n=5), 13/59 (22%) in the patients who extend (p=0.02 OR 2.43 (1.08-5.43)). 28/59 (47.4%) had extension into the upper gastrointestinal tract (L4a/b). 18/153 (11.8%) of A1a CD required surgical resection compared with 54/312 (17.3%) of A1b CD (p=0.12). UC presented as pancolitis (E4) in 60% of A1a (36/60) vs 74.8% of A1b (77/103), p=0.04 OR 0.51 (0.26-1.00). 4 years after diagnosis, E4 UC was less common in A1a compared with A1b (15/30 (50%) vs 20/26 (76.9%), p=0.03 OR 0.30 (0.09-0.96)). 14/61 A1a UC (23%) vs 21/108 (19.4%) of A1b UC required colectomy (p=0.58).

Conclusions: Using the new Paris classification of paediatric IBD, we have demonstrated that A1a CD is characterised by less ileal but more oral+-perianal disease compared with A1b CD. A1a CD behaviour remains largely inflammatory during follow-up but A1b CD behaviour progresses to penetrating disease. Childhood UC is extensive (E3/E4) at diagnosis but A1a UC is less often pancolitic than A1b UC. These differences persist during follow-up.

195 TRANSITION OF IBD CARE: ASSESSMENT OF TRANSITION READINESS FACTORS AND DISEASE OUTCOMES IN A YOUNG ADULT POPULATION. Danya Rosen1, Rachael Schneider1, Clare Ceballos1, Ruijun Bao1, Rachel Annunziato2, Jean-Frederic Colombel1, Keith Benkov1, 1Department of Pediatric Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, NY; 2Department of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, NY; 3Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY

Introduction: The incidence of Inflammatory Bowel Disease (IBD) in the pediatric age group is increasing. As there is a growing cohort of patients that will eventually move from pediatric to adult care, both pediatric and adult gastroenterologists need to be aware of issues specific to adolescents. The majority of studies on transition in IBD focus on descriptive data and expert opinions, but there is no data on what individual patient characteristics are most important in predicting a successful transition.

Methods: IBD patients ages 18 to 25 who are followed at the Mount Sinai Medical Center will be surveyed at the time of their outpatient visit with either a pediatric or adult gastroenterologist. The survey includes questions about the patient's own transition experience, as well as validated methods to assess transition readiness (Transition Readiness Assessment Questionnaire 3.0), socioeconomic status (Hollingshead criteria), and mental health (Mental Health Inventory-38). Blood work at the time of the visit will be recorded to look specifically at inflammatory markers. The patients will be followed prospectively over a 3 to 6 month period to assess disease activity as measured by ED visits, hospitalizations for IBD, changes in inflammatory markers, and compliance with follow up visits.

Results: In a preliminary analysis, 26 patients were surveyed. Average age at time of survey completion was 22 and average age at diagnosis was 13.7 (range 1 - 22.4 years). Nineteen (73%) had Crohn's disease and 7 (27%) had ulcerative colitis. Two patients were not included in transition analysis because they had never been followed by a pediatric gastroenterologist. Of the remaining 24 patients, 12 (50%) reported that their pediatric gastroenterologist had discussed transition with them, and 7 (29%) were given the name of an adult gastroenterologist to contact. Records were sent in 9 patients (37%), 10 patients (42%) reported that records were not sent from their pediatric gastroenterologist, and 5 (21%) were unsure. Eighteen (75%) identified themselves as "definitely ready" or "probably ready" to transition, and 6 (25%) identified themselves as "probably not" or "definitely not" ready. Average TRAQ 3.0 self-management score was 3.6 ± 0.18 (range 1-5) and average TRAQ self-advocacy score was 4.1 ± 0.11 (range 1-5).

Discussion: By identifying early predictors of transition success, we can work towards establishing a transition program that meets the needs of all IBD patients.
196 ARE STANDARD 30-DAY READMISSION RATES ADEQUATE FOR PATIENTS WITH IBD? Kelly C. Sandberg1,2, Jeremy Adler1,2, Katherine Auger3, Achamyeleh Gebremariam2, Matthew Davis2-4. 1Pediatric Gastroenterology, University of Michigan, Ann Arbor, MI; 2Child Health Evaluation and Research Unit, General Pediatrics, University of Michigan, Ann Arbor, MI; 3Hospital Medicine, Cincinnati Children's Hospital, Cincinnati, OH; 4General Medicine, University of Michigan, Ann Arbor, MI

**Background:** Hospitalization rates for children with inflammatory bowel disease (IBD) are increasing at a national level. It is unclear whether this increase is due to the hospitalization of more unique patients or to readmission of the same patients. Our aims were to determine longitudinal trends of readmission among children with IBD and to investigate potential associations of readmission.

**Methods:** Administrative data were supplemented with chart review in this retrospective analysis. We obtained discharge data for all children ages 1-18 with a diagnosis code for IBD (including Crohn disease and ulcerative colitis) on a GI or GI-related service from our tertiary care center from January 1, 2006 through December 31, 2012. We used Poisson regression to assess trends of 7, 30 and 90-day readmission over time. We used logistic regression to assess odds of readmission at the same intervals, adjusting for demographic factors, markers of disease severity, and nutritional therapies in our analysis.

**Results:** Overall, 291 children with IBD experienced 577 hospital admissions over the study period. Of the total number of hospitalizations, 122 patients experienced a majority (403, 69.8%) of hospitalizations. Baseline trend of IBD discharges across time was not statistically significant (P = 0.33). Trends in 7, 30, and 90-day readmissions across time were also not statistically significant (Ps = 0.52, 0.35, 0.98, respectively).

Adjusted odds of 7-day readmissions were significant for those patients undergoing an IBD-related surgery (2.10, 95% CI: 1.09 - 4.07; Table 1). There were no significant associations of 30-day readmissions. Adjusted odds of 90-day readmissions were significant for those patients who received total parenteral nutrition (OR 1.9, 95% CI: 1.1 - 3.1), or albumin or blood transfusions (OR 1.9, 95% CI: 1.1 - 3.1) during their index admission.

**Conclusions:** Trends in readmission across time are not significant at our tertiary center. Examination of only 30-day readmission rates may be missing an opportunity to understand and potentially prevent readmissions for pediatric patients with IBD. Understanding and planning for nutritional needs and interventions at discharge may help to prevent future readmissions.

Table 1: Associations of readmission by different time periods.

<table>
<thead>
<tr>
<th>Readmission time periods</th>
<th>7-day Adjusted OR</th>
<th>30-day Adjusted OR</th>
<th>90-day Adjusted OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 44</td>
<td>N = 121</td>
<td>N = 197</td>
</tr>
<tr>
<td>IBD Surgery</td>
<td>2.10 (1.09 - 4.07)</td>
<td>1.07 (0.65 - 1.77)</td>
<td>1.12 (0.73 - 1.74)</td>
</tr>
<tr>
<td>Nasogastric Nutrition</td>
<td>1.63 (0.33 - 8.09)</td>
<td>0.99 (0.27 - 3.68)</td>
<td>1.79 (0.61 - 5.24)</td>
</tr>
<tr>
<td>Total Parenteral Nutrition</td>
<td>0.68 (0.27 - 1.72)</td>
<td>1.26 (0.71 - 2.23)</td>
<td>1.87 (1.14 - 3.08)</td>
</tr>
<tr>
<td>Blood or Albumin Infusion</td>
<td>1.64 (0.73 - 3.72)</td>
<td>1.45 (0.83 - 2.55)</td>
<td>1.80 (1.10 - 2.97)</td>
</tr>
</tbody>
</table>

197 THE IMPACT OF PEDIATRIC CROHN'S DISEASE FROM PATIENTS' AND PHYSICIANS' PERSPECTIVES. Michelle Danby, Jamie Seabrook, Kevin Bax, Paediatrics, Western University, London, ON, Canada

**OBJECTIVES:** The normal study showed significant disparities between adult patients' and gastroenterologists' perceptions of the impact of ulcerative colitis on patients' quality of life (QOL). Our objective was to look at the possible differences in perspectives of pediatric patients and physicians on the impact of Crohn's disease (CD) on quality of life, and to see if this affects communication between pediatric CD patients and their doctors. We also looked at how compliance was viewed between the two groups.

**METHODS:** Patient surveys were developed using the IMPACT-III questionnaire, a validated tool to measure QOL in children with CD. Several questions were added to look specifically at compliance, in addition to the 6 QOL domains covered by the IMPACT-III. The physician survey was developed from this final survey to cover the same domains.

**RESULTS:** In total, 38 patients with Crohn's disease between 9 and 17 years of age completed the patient survey, and 13 Pediatric Gastroenterologists (not necessarily associated with the patients) completed the physician survey. There was no statistically significant difference when comparing each domain between patients and physicians. The average QOL overall for most domains was relatively high for patients, with a mean rating of 3.4±0.88, while the mean physician's rating of QOL of patients living with CD was 2.9±0.37, however, this difference was not statistically significant. The average individual domain scores for the physicians were fairly similar to those of the patients, being
only slightly lower overall. Compliance was rated as good by patients (4.05±0.65), and lower by physicians (2.66±0.43; p<0.001).

**CONCLUSIONS:** Pediatric inflammatory bowel disease has different physician and patient misperceptions than adult inflammatory bowel disease. Physician worries about medical adherence may be overdone. Patients and physicians generally have the same perception about quality of life measures when using the validated IMPACT III assessment tool.

Direct Question Comparison between Patients' and Physicians' Surveys: Compliance Domain

<table>
<thead>
<tr>
<th>Patient Response</th>
<th>Patients' Response (% Respondents)</th>
<th>Physician Response</th>
<th>Physicians' Response (% Respondents)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How afraid are you of medication side effects?</td>
<td>Many patients are not fully compliant with their medication regimen. How important do you think the following reasons are for this fact?</td>
<td>To avoid side effects</td>
<td></td>
</tr>
<tr>
<td>Very afraid</td>
<td>7.9</td>
<td>Very</td>
<td>0</td>
</tr>
<tr>
<td>Quite afraid</td>
<td>7.9</td>
<td>Quite</td>
<td>15.4</td>
</tr>
<tr>
<td>Somewhat afraid</td>
<td>28.9</td>
<td>Somewhat</td>
<td>53.8</td>
</tr>
<tr>
<td>Hardly afraid at all</td>
<td>31.6</td>
<td>Hardly</td>
<td>23.1</td>
</tr>
<tr>
<td>Not afraid at all</td>
<td>23.7</td>
<td>Not at all</td>
<td>7.7</td>
</tr>
<tr>
<td>How often do you forget to take your medication?</td>
<td>They forget</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very often</td>
<td>2.6</td>
<td>Very</td>
<td>46.2</td>
</tr>
<tr>
<td>Often</td>
<td>2.6</td>
<td>Quite</td>
<td>46.2</td>
</tr>
<tr>
<td>Sometimes</td>
<td>15.8</td>
<td>Somewhat</td>
<td>7.7</td>
</tr>
<tr>
<td>Rarely</td>
<td>34.2</td>
<td>Hardly</td>
<td>0</td>
</tr>
<tr>
<td>Never</td>
<td>44.7</td>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td>How well do you think your medication works?</td>
<td>They are not sure it really works</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does not work at all</td>
<td>2.6</td>
<td>Very</td>
<td>0</td>
</tr>
<tr>
<td>Hardly works at all</td>
<td>0</td>
<td>Quite</td>
<td>38.5</td>
</tr>
<tr>
<td>Somewhat works</td>
<td>34.2</td>
<td>Somewhat</td>
<td>46.2</td>
</tr>
<tr>
<td>Works well</td>
<td>36.8</td>
<td>Hardly</td>
<td>15.5</td>
</tr>
<tr>
<td>Works very well</td>
<td>26.3</td>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td>Do you worry about others noticing you taking</td>
<td>They don't want others to notice them taking</td>
<td></td>
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</tbody>
</table>
Pediatric inflammatory bowel disease (IBD)—consisting of Crohn's disease (CD) and ulcerative colitis (UC) varieties—can result in significant morbidity requiring frequent healthcare utilization. While it is known that the overall financial impact of pediatric IBD is significant, the direct impact on pediatric patients and their families has not been adequately explored. Traditional studies have largely relied on claims, medical records, and other large data sets. Furthermore, family and patient-specific attributes that might correlate with increased pediatric IBD cost burden have not been explored from the direct perspective of patients and families themselves. We hypothesized that children with moderate-to-severe pediatric IBD, and those in families of lower socioeconomic strata, disparately absorb substantial financial stress. To test that hypothesis, we completed a cross-sectional, survey-based study that encompasses the development of an online HIPAA-secure Qualtrics survey, collection of results from pediatric IBD patients and their families, and analysis of results using multivariate analysis. To participate, patients had to be <18 years of age at time of study, carry a diagnosis of pediatric Crohn's disease or ulcerative colitis, reside in and receive medical care in California, and not have any other complex, chronic disease requiring on-going medical care.

We recruited patients using CCFA e-newsletters, social media announcements, and point of contact flyers. Preliminary results from >100 participants demonstrate that for pediatric IBD patients across a spectrum of ages, the financial impact of IBD is variable. In our study, 64.7% of patients were Caucasian, 89.9% were privately insured, and 80% of patients had at least one parent with a Bachelor's, graduate, or doctorate degree. While 46.5% of families fell into the $50,001 - $100,000 annual income bracket, and 29.3% fell into the > $100,000 bracket, there were 15.2% in the $0 to $50,000 range, and 9.1% did not disclose. 27.3% of patients studied had total OOP costs over the past year greater than $500, including 5.1% who had costs > $5,000. While the total OOP cost difference between CD and UC patients was not statistically significant, it was driven in part by the higher procedure and test cost incurred by CD patients. We found that with spending of >$500 on procedures and tests, there is approximately 5.5 times increased odds of a high total OOP cost burden > $500 (OR 5.49, 95% CI 2.27 - 13.3). Additionally, with 4+ lifetime hospitalizations, there is nearly four times increased odds of a high total OOP cost burden > $500 (OR 3.93, 95% CI 1.43 - 10.8). The odds of high total OOP cost burden > $500 is increased by nearly 3.5 times with two or more annual pediatrician clinic visits (OR 3.45, 95% CI 1.48 - 8.07). The results of this study have the potential to influence the health policies around the financing and medical care of pediatric IBD.

199 BODY MINERAL DENSITY GROWTH AND NUTRITIONAL STATUS IN CHILDREN AND ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE. Marisol Ballinas-Zapata¹, Rocio Macias-Rosales¹, Alfredo Larrosa-Haro², ¹Pediatric Gastroenterology and Nutrition, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; ²Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Guadalajara, Mexico

Aim: Evaluate the correlation between bone mineral density, with the involvement of growth and nutritional status in children and adolescents with inflammatory bowel disease.


Results: We performed lumbar spine bone densitometry in 13 patients with a diagnosis of inflammatory bowel disease in which about 30% were abnormal. The median age in months at the time was bone mineral density (BMD) in relation to duration of disease was 31 months, there was no statistical difference. When comparing gender BMD statistical difference was not found and the age group most affected was teenagers. Statistical difference was found when comparing the height-for-age females. When correlations of BMD z-score anthropometric indicators with different statistical difference was found only with the z score of mid-arm circumference, total area and arm fat area.
Conclusions: Documented a significant proportion of involvement in bone mineral density, to make the correlation with anthropometric indicators statistical difference was observed only with indicators of body composition. It follows that there is a probable involvement of fatty tissue deficiency in the mineral and energy reserves by different mechanisms related malnutrition present in these patients.

200  **AN ASSESSMENT OF EXERCISE IN CHILDREN WITH CROHN'S DISEASE.** Matthew Shields2, Marilyn Brown2, Deborah Fowell1, Thomas Rossi2, Mary Caserta1, Hong Yue Wang2, Karen Mustian1, Lawrence Saubermann2, 1Division of Pediatric Infectious Diseases, University of Rochester Medical Center, Rochester, NY; 2Division of Pediatric Gastroenterology, University of Rochester Medical Center, Rochester, Rochester, NY; 2Director, PEAK (Physical Exercise Activity and Kinesiology) Clinical Research laboratory, University of Rochester Medical Center, Rochester, Rochester, NY; 4Department of Microbiology and Immunology, University of Rochester Medical Center, Rochester, Rochester, NY; 5Department of Biostatistics and Computational Biology, University of Rochester Medical Center, Rochester, NY

**Objective:** Physical activity has been shown to be important in treating chronic gastrointestinal diseases including gastroesophageal reflux disease, cholelithiasis and irritable bowel syndrome; however, the data looking at effects of physical activity on inflammatory bowel disease (IBD) has been inconsistent. There is also little data that looks at the relationship between physical activity and IBD activity in children. The purpose of this study was to compare physical activity levels in children with Crohn's disease vs. controls, as well as to evaluate the associations between physical activity, disease activity and quality of life (QOL) in children with Crohn's Disease. We hypothesized that a greater level of physical activity would correlate with decreased levels of disease activity and improvement in QOL.

**Methods:** Fifty-one subjects with Crohn's Disease and 30 control subjects completed the Physical Activity Questionnaire - Adolescents (PAQ-A) to assess levels of physical activity and were divided into three groups based on their activity level. Crohn's Disease subjects then completed the Pediatric Crohn's Disease Activity Index (PCDAI) to assess disease activity and the IMPACT-III questionnaire to assess quality of life.

**Results:** There was no significant difference in physical activity levels between Crohn's Disease subjects and control subjects. Different levels of physical activity were not found to be significantly correlated with disease activity in children with Crohn's Disease. However, there was a statistically significant difference in quality of life between the low physical activity group and the high physical activity group (p < 0.02). There was also a statistically significant difference in three QOL subdomains when comparing the low physical activity group to the high physical activity group. These subdomains included bowel symptoms (p < 0.02), social functioning (0.02) and systemic symptoms (p < 0.0001).

**Conclusion:** There is a statistically significant correlation between increased physical activity and improved QOL, as well as three subdomains in children with Crohn's disease, but no statistically significant correlation between increased physical activity and disease activity. Further interventional studies will better examine this link between physical activity and quality of life.

201  **LONG-TERM EFFECTS OF TOP-DOWN THERAPY IN PEDIATRIC CROHN'S DISEASE.** Melissa Rose1, Rachel Reed2, Aliza Solomon1, 1Pediatric Gastroenterology, New York-Presbyterian Hospital/Weill Cornell, New York, NY; 2Pediatrics, New York-Presbyterian Hospital/Weill Cornell, New York, NY

**Objective:** Treatment of pediatric patients with Crohn's disease has traditionally entailed a step-up approach, with gradual intensification of therapy. A newer treatment paradigm involves a top-down method with the introduction of immunomodulators or biologic agents early in the disease course. Our aim is to show that pediatric patients with Crohn's disease have a faster and more sustained remission with less morbidity with top-down therapy in comparison to patients using a step-up approach to treatment.

**Patients and Methods:** A retrospective analysis was conducted of 83 pediatric patients with Crohn's disease ages 4.5-19.8 seen at New York-Presbyterian Hospital/Weill Cornell between 7/2005 and 2/2012. Patient demographics, treatment course and outcomes were reviewed. These patients were classified as either receiving step-up or top-down therapy based on a time period of 3 months from diagnosis to initiation of biologic or immunomodulator therapy. Outcomes including hospitalizations, surgery, and time to remission were measured over 3 years from the start of immunomodulators or biologics.

**Results:** Among the 83 patients, 40 patients (48%) were treated in a top-down manner, with 24 (29%) receiving immunomodulators and 16 (19%) receiving biologics within 3 months of diagnosis. Of the top-down patients, 19 (47.5%) were hospitalized and 8 (20%) required surgery including bowel resection or stricturoplasty. Of the step-up patients, 16 (37.2%) were hospitalized and 5 (11.6%) required surgery. The step-up group was hospitalized an average of 8.4 months (range 1-29 months) and had surgery an average of 27 months (range 24-31 months) after starting immunomodulators or biologics. The top-down group was hospitalized an average of 11.3 months (range 1-33 months) and had surgery an average of 9.6 months (range 2-25 months) after starting immunomodulators or biologics. At the time of starting therapy, the top-down group had a mean PCDAI of 23.9 and the step-up group had a mean PCDAI of 16.5. The top-down group on average reached remission (PCDAI <10) by 3 months, while the step-up group on average...
reached remission by 6 months. The top-down group had an average PCDAI decrease of 17.32 over the first 3 months of treatment with 18/30 (60%) having a PCDAI decrease greater than or equal to 12.5. The step-up group had an average PCDAI decrease of 13.85 over the first 3 months of treatment with 14/31 (45%) having a PCDAI decrease greater than or equal to 12.5. 32.5% of the step-up group was on biologics or immunomodulators at one year, 43% at two years and 51% at three years after diagnosis.

Conclusions: The top-down group was found to have a faster rate of remission with a more substantial decrease in PCDAI, though this was not statistically significant. The top-down group had similar rates of adverse outcomes to the step-up group even though they were more ill at presentation. Over fifty percent of the step-up patients required immunomodulator or biologic therapy during their disease course, with data suggesting that these patients may benefit from earlier initiation of this treatment.

202 PRACTICAL USE OF INFlixIMAB CONCENTRATION MONITORING IN A LARGE PEDIATRIC IBD CENTER. Phillip Minar, Shehzad Saeed, Lee A. Denson, Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: Drug concentration testing that guides infliximab (IFX) intensification strategies has been shown to improve IFX efficacy. The aims of this study was to evaluate the clinical impact of testing for IFX concentrations and determine the incidence and risk factors associated with inadequate (below the reference value) IFX levels and antibody to IFX (ATI) in pediatric Crohn's disease (CD) and ulcerative colitis (UC) patients who had IFX testing performed.

Methods: In 2007, a formal guideline to monitor IFX serum levels was developed to standardize practice at Cincinnati Children's for inflammatory bowel disease (IBD) patients receiving IFX. We performed a single center retrospective chart review of IBD patients receiving recurring IFX infusions who had either the Prometheus® ELISA or Prometheus® ANSER® test sent from 12/2009-9/2013. The ELISA and ANSER® reference values for IFX concentrations are 1.4 μg/ml and 1 μg/ml respectively.

Results: 233 IFX tests were sent on 87 IBD subjects (73 CD, 14 UC). 206/233 were ELISA assays and 27 were ANSER®. We found the mean IFX dose at time of testing was 7.9 (SD 2.7) mg/kg with a mean dosing frequency of 6.5 (SD 2) weeks. 19/87 subjects were receiving concurrent immunomodulators (IM; methotrexate or 6-mercaptopurine). The majority of the tests were trough samples (161/233) with an ATI incidence of 23% (20/87 subjects). In addition, we found 19% (28/149) of the trough tests without ATI had inadequate IFX levels. We also found that subjects with inadequate IFX levels or ATI had a significant elevation in ESR (p<0.01) at the time of the IFX test was sent compared to subjects with adequate IFX levels without ATI. ESR >20 mm/hr. was 55% sensitive and 75% specific for inadequate IFX levels or ATI. ANSER® obtained either prior to IFX induction or during therapy are effective in alerting clinicians of high-risk patients who may benefit from more frequent IFX concentration monitoring or empiric dose adjustments.

Conclusions: IFX serum concentration testing is valuable in guiding medication adjustments. Routine laboratory tests obtained either prior to IFX induction or during therapy are effective in alerting clinicians of high-risk patients who may benefit from more frequent IFX concentration monitoring or empiric dose adjustments.

203 PREVALENCE AND RISK FACTORS OF NEPHROLITHIASIS IN PEDIATRIC INFLAMMATORY BOWEL DISEASE. Ramya Ramraj1,2, Yasemen Eroglu1, Amy Garcia1, David Mosen1, 1Kaiser NW Permanente, Portland, OR; 2Pediatric Gastroenterology, Hepatology and Nutrition, Oregon Health and Science University, Portland, OR; 3Center for Health Research NW, Portland, OR

Background: Nephrolithiasis is one of the extra intestinal manifestations of Inflammatory Bowel Disease (IBD). Its prevalence in adult patients has been reported between 10-18%. Some of the previously identified risk factors in adult IBD patients include a diagnosis of Crohn's disease, presence of small intestinal disease and need for surgery. In children, limited data is available regarding the prevalence and risk factors for nephrolithiasis in IBD.

Methods: Patients between ages 0-20 with a diagnosis of IBD and those with IBD and nephrolithiasis were identified using ICD9 codes from the electronic database at Kaiser NW Permanente between 2001-2012. Patients' demographic and clinical characteristics including age at diagnosis, date of diagnosis, sex, race and exact subtype of IBD (Crohn's disease vs. Ulcerative Colitis) were identified via electronic pull. The patient charts were then individually reviewed to confirm the diagnosis of IBD and obtain additional pertinent clinical information including the type of medications used.
to induce and maintain remission and treat disease flares. Chi-square test or Fisher's exact test was utilized to analyze categorical variables. Multivariate logistic regression analysis was done for all variables associated with the presence of renal calculi.

Results: A total of 283 patients were identified with a confirmed diagnosis of IBD. There were 17 patients who were diagnosed with nephrolithiasis before age 20. Among the baseline characteristics between the IBD patients with and without nephrolithiasis, significant differences were observed with the use of the systemic steroids (at any time in the disease course vs. no systemic steroid use) and history of surgery. There were no significant differences with age of diagnoses, gender, race, type of IBD or use of salicylates, immunomodulators or TNFα inhibitors. On multivariate analysis, the use of steroids (OR 4.69 CI 1.05-20.95, p = 0.04) and history of intestinal surgery (OR 4.6 CI 1.643-12.875, p = 0.004) were found to be risk factors for nephrolithiasis in pediatric IBD.

Conclusion: The prevalence of nephrolithiasis in this cohort of pediatric IBD patients is 6%, which is slightly lower than that reported in adults. Use of systemic steroids and history of intestinal surgery are found to be significant risk factors for presence of nephrolithiasis.

204 THE OUTCOME OF MEDICAL MANAGEMENT WITH IV ANTIBIOTICS OF INTRA-ABDOMINAL ABSCESSES IN CHILDREN WITH CROHN'S DISEASE. Razan H. Alkhouri1, Gracielle Bahia1, Wael N. Sayej2, 1Digestive Disease and Nutrition Center, University at Buffalo, Buffalo, NY; 2Connecticut Children's Medical Center, Connecticut, CT

Introduction: Crohn's disease (CD) is a chronic inflammatory condition of the gastrointestinal tract. Intra-abdominal abscesses develop in 10-30% of patients with CD. To avoid surgical resection of their bowel, antibiotic therapy, with or without interventional radiology drainage (IR) is first undertaken. Our objective in this study is to examine the outcome of IV antibiotics alone and compare it to IR plus IV antibiotics.

Methods: Retrospective chart review of all CD patients diagnosed with an intra-abdominal abscess between 2004-2014. 24 patients were identified ages 11-21 years (mean 15 years; 48% male). Parameters examined at presentation included the pediatric Crohn's disease activity index (PCDAI), Montreal classification, demographics, inflammatory markers, imaging, management outcome, and time to abscess resolution.

Results: All 24 patients received IV antibiotics (16 had one intra-abdominal abscess and 8 had two at the same time). 11 patients underwent drainage and catheter placement by IR, 10 (91%) of which eventually required surgery for drain failure. Of the 13 who did not have IR drainage due to non-drainable size or unreachable location, 7 (54%) needed surgery and 6 (46%) resolved with IV antibiotics alone. A total of 17 patients (75%) failed medical therapy with or without IR and required surgery. Organisms isolated from drained abscesses included E. coli, Enterococcus, Staphylococcus aureus, Klebsiella pneumonia, Clostridium, and Streptococcus viridans. No correlation was found between medical failure and size of abscess, age of patient, PCDAI, ESR, CRP, IBD serology panel or choice of antibiotics.

Conclusion: Our results show that the majority of our patients required surgical intervention for abscess treatment and resolution of associated findings. Although, only 25% of patients responded to medical therapy, we do recommend a trial of IV antibiotics for at least 2 weeks before proceeding to surgery.

205 MUCOSAL DISEASE ACTIVITY MAY PREDICT THERAPEUTIC RESPONSE TO FECAL MICROBIOME TRANSPLANTATION IN PEDIATRIC ULCERATIVE COLITIS. Richard Kellermayer1,2, Dorottya Nagy-Szakal1,2, Faith Ihikweazu1,2, Ruth Ann Luna1,2, Deborah A. Schady3,2, Peera Hemarajata3,2, James Versalovic1,2, 1Section of Pediatric Gastroenterology, Baylor College of Medicine, Houston, TX; 2Texas Children's Hospital, Houston, TX; 3Department of Pathology, Baylor College of Medicine, Houston, TX

BACKGROUND: Fecal bacteriotherapy (FB) or fecal microbiome transplantation (FMT) is an emerging unconventional treatment for ulcerative colitis (UC). The disruption of healthy microbiota composition (dysbiosis) may be an important element of the disease and the restoration of normal microbiota structure may be therapeutic for this condition. In spite of encouraging outcomes in small cohorts, including children, recent FB trials incorporating metagenomic (bacterial DNA) analyses provided discouraging results. However, none of the published trials utilized more than 5 consecutive treatments thus far. The most recent negative adult studies treated patients with moderate to severe UC indicating that patients with milder disease, or who are in medically induced remission may be better candidates for this unconventional treatment modality. In the meantime, there is limited information towards patient selection and the number of treatments required to promote the therapeutic success of FB in UC.

METHODS: We studied 7 patients with immunotherapy (steroid, immunomodulator, or biologic agent) dependent pediatric UC. The patients enrolled into an FB trial with a weaning course of rectally (colonoscopy and retention enemas, 37 treatments over a year) administered FMTs during the withdrawal of their immunotherapy. The trial is FDA approved (IND#15734) and listed on clinicaltrials.gov (NCT01947101). Two patients enrolled twice (a year apart) into the trial. Therefore, we evaluated 7 patients during 9 treatment courses. Eight treatment courses utilized the same single donor, one a second donor. Clinical (as defined by the pediatric ulcerative colitis activity index [PUCAI]) and

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endoscopic disease severity was recorded at the initiation of the trial. The subjects were required to have mild clinical (PUCAI< 35) disease, or remission within 4 weeks of starting the treatments.

RESULTS: Patients who had endoscopic remission or mild disease (5 patients, Mayo endoscopic score 0-1) tolerated the treatments and the withdrawal of their immunotherapy while maintaining clinical remission. However, subjects with moderate to severe endoscopic disease (4 patients, Mayo 2-3) developed moderate to severe symptoms within 2-10 days (2-10 daily treatments received) and were withdrawn from the study according to protocol. Therefore, patients with mild to no mucosal disease were significantly (Fischer's exact test, p=0.0079) more likely to tolerate immunotherapy withdrawal during FB treatments, compared to those with moderate to severe mucosal disease activity.

CONCLUSION: Our findings support the prediction that FB may be a potential treatment modality for UC patients with medically induced colonic mucosal remission or mild endoscopic disease.

Endoscopy/Potpourri

216 FEASIBILITY OF AN ADVANCED ENDOSCOPY TRAINING TRACK FOR PEDIATRIC GASTROENTEROLOGY FELLOWS AT A LARGE PEDIATRIC CENTER. Brad Barth1,2, Tami Turribiarte2, David Troendle1,2 1University of Texas Southwestern, Dallas, TX; 2Children's Medical Center Dallas, Dallas, TX

Background: Despite a need for additional skilled advanced endoscopists in the field of Pediatric Gastroenterology, there are currently no fellowship programs offering formal training of this type in North America. This project was undertaken to investigate the feasibility of training advanced endoscopists over a two year period during a Pediatric Gastroenterology fellowship.

Methods: Hospital and divisional databases were retrospectively queried to determine the number of specific types of advanced endoscopic cases performed over a two year period by an entire Pediatric GI division, and a fellow without a planned curriculum, but focusing on advanced endoscopy. These numbers were then compared to recommended procedural volume targets published by NASPGHAN1.

Results: Table 1 lists various advanced procedures performed between July 1, 2012 and May 28, 2014 (22 months). NASPGHAN targets were reached by the division as a whole for all procedures except ERCP and EUS. Targets were reached by the fellow for stricture dilation, PEG placement, transpyloric catheter placement, and endoscopic deployment of video capsule. Targets were not reached by the fellow for control of bleeding, antegrade single balloon enteroscopy, ERCP, EUS, small bowel capsule endoscopy interpretation, BRAVO capsule placement or pneumatic dilation of achalasia.

Conclusion: Procedure volume is adequate to train advanced endoscopic fellows at this, and likely other large pediatric centers. Outside training will likely be required for ERCP and EUS. A planned, well designed curriculum for advanced therapeutic endoscopy fellows is necessary to ensure that target goals are reached.

### PROCEDURES PERFORMED OVER 22 MONTHS AT A LARGE PEDIATRIC CENTER

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Total Performed</th>
<th>Fellow Performed</th>
<th>NASPGHAN Target for competency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variceal band ligation</td>
<td>22</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Variceal sclerotherapy</td>
<td>7</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Control of bleeding</td>
<td>15</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>13</td>
<td>15*</td>
</tr>
<tr>
<td>Colonic manometry catheter placement using SB colonoscopy</td>
<td>40</td>
<td>2</td>
<td>N/A</td>
</tr>
<tr>
<td>Single balloon enteroscopy antegrade</td>
<td>11</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Esophageal stricture dilation</td>
<td>163</td>
<td>38</td>
<td>10</td>
</tr>
<tr>
<td>Percutaneous endoscopic gastrostomy</td>
<td>111</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>Endoscopic gastrojejunostomy placement and AD manometry catheter placement</td>
<td>9</td>
<td>5</td>
<td>5**</td>
</tr>
<tr>
<td>ERCP</td>
<td>117</td>
<td>91</td>
<td>200</td>
</tr>
<tr>
<td>EUS</td>
<td>12*</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Small bowel capsule endoscopy</td>
<td>51</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>BRAVO capsule placement</td>
<td>14</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Endoscopic deployment of wireless video capsule</td>
<td>14</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Pneumatic dilation for achalasia</td>
<td>5</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>

*NASPGHAN target refers to "EGD and/or colonoscopy with control of bleeding variceal or nonvariceal-various methods"

**NASPGHAN target refers to "endoscopic placement of transpyloric feeding tubes or catheters, including motility catheters"

#EUS cases NOT hands-on, but observed and managed pre and post-operatively

217  **HISTOPATHOLOGY IN COLOMBIAN CHILDREN WITH FAILURE TO THRIVE.** Carlos A. Velasco¹, Otto Calderon¹, Rommel Segura², ¹Pediatrics, University of Valle, Cali, Colombia; ²Universidad Libre, Cali, Colombia

**Introduction:** Within the diagnostic orientation of children with failure to thrive (FT), defined as greater than height for age (HA) - 3 standard deviations from the tables of the WHO, performing an endoscopy of upper gastrointestinal tract (EUGT) is required to determine the possible etiology of gastrointestinal origin. **Objective:** To describe the main histopathological findings at the endoscopy in children with FT of Pediatric Endoscopy Unit of Cali, Colombia.

**Methodology:** Prevalence study in 15 children with FT who underwent upper endoscopy with biopsy. Were considered socio-demographic, clinical and histopathological variables. Statistical analysis included estimation %, mean, and other descriptive measures with their corresponding standard deviations and ranges. **Results:** We included 15 children aged 7.1±4.9 years (range=2 to 16), 53.3% of the female gender; with symptoms such as abdominal pain 53.3%, no weight gain at 46.7%, anorexia in 26.7%, 13.3% vomiting and bloating in the 6.7 %, respectively, with the presence of *H. pylori* in the 6.7%. Means ± standard deviations were for weight=16.4±9.3 kg (range=7.8 to 39.9), height=100.9±25.2 cm (range=74 to 152), according to WHO BMI=-0.8±1.2 SD (range=-3.1 and 1.3) and HA=-3.8±1.5 SD (range=-6.4 and -1.3). The main histopathological findings of the EUGT included esophagitis in 73.3%, 46.7% in gastritis and duodenitis in 40.0%, with the presence of Giardiasis in 13.3%. **Conclusion:** In more than 40% of the children studied with FT alterations occurred in the histopathological findings of the upper digestive tract at the endoscopy, the main gastrointestinal symptoms abdominal pain, no weight gain, loss of appetite and vomiting

218  **NON-ATTENDANCE AT OUTPATIENT PEDIATRIC ENDOSCOPY UNIT OF A TERTIARY CENTER.** Deboral Kogan-Liberman, Yolanda Rivas, John Thompson, Gitit Tomer, Pediatric Gastroenterology and Nutrition, Children's Hospital at Montefiore, Albert Einstein Medical College, Bronx, NY

**Background:** Failure to attend pediatric endoscopic procedures leads to inefficient use of resources, financial waste, longer wait-times and delay in diagnoses. Since there is an increase demand for pediatric endoscopic procedures, non-attendance should be kept to minimum. The causes for pediatric endoscopy non-attendance are not well studied.
Aim: To identify factors associated with failure to attend endoscopic procedures and to assess the value of interventions implemented to improve pediatric endoscopy attendance.

Methods: We collected non-attendance data from November 2011 to November 2013. Non-attendance was defined as a no show or cancellation within 24 hours of scheduled endoscopic appointment. Information collected included: procedure type, age, gender, time on the waiting list, history of previous procedures and reason for non-attendance. The following interventions were implemented sequentially: an appointment reminder letter, a scheduler telephone call 1 week prior to procedure, and creation of an electronic medical note dedicated to endoscopy appointment documenting communication with caregiver/patient. Pareto chart and statistical process control chart were used for analysis.

Results: During the 2-year study period, a total of 1103 pediatric patients were scheduled for outpatient endoscopic procedures. Of those, 55% of patients were scheduled for esophagastroduodenoscopy (EGD), 26% for combined EGD/colonoscopy, 5% for colonoscopy, 7% for percutaneous endoscopic gastrostomy (PEG)/PEG change and 7% had other procedures (liver biopsies, rectal suction biopsies). A total of 160 non-attendees (14.5%) were identified. Of the missed appointments 52% were for EGD, 29% for combined EGD/colonoscopy, and 7% for colonoscopy. EGD/colonoscopy and colonoscopy had a trend for non-attendance compared to all other procedures (p=0.07). There was no significant difference between attendees and non-attendees in relation to gender, age or having a previous procedure. The average waiting time in patients who kept their appointment was 26 days and 33 days for those who did not keep their appointment. Longer waiting time was associated with increased risk for non-attendance (p=0.0007). The most common causes for not attending a procedure were: illness (31.5%) on the day prior to procedure or on the day of the procedure, followed by caregiver/patients who no longer wanted the procedure (17.7%) and patients who improved and did not need the procedure anymore (12.9%). From November 2011 to December 2012, during the pre intervention period, 591 patients had scheduled procedures appointments and the average of nonattendance was 17%. From January 2013 to November 2013, during the post intervention period, 512 patients had scheduled procedures and nonattendance was reduced to 11% (p=0.005). No show rate was reduced from 5% to 0.9% (p=0.00001).

Conclusions: Longer waiting time for endoscopic procedure is associated with non-attendance. Appointment reminder letters sent prior to procedure, and telephone reminders, summarized in electronic medical record phone notes improve pediatric endoscopy unit attendance. Given the increased pediatric endoscopy demand, strategies should be implemented to reduce wait time for pediatric endoscopy.

219 SAFETY AND OUTCOMES OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE PLACEMENT IN INFANTS LESS THAN FIVE KILOGRAMS WITH CONGENITAL HEART DEFECTS. Christina Baldwin1, Kejal Patel2, Ernest K. Amankwah1, Anthony Sochet2, Jeffrey Jacobs1, Gul Dadlani1, Michael Wilsey1,2, 1All Children’s Hospital, St. Petersburg, FL; 2University of South Florida, Tampa, FL

Background: Feeding difficulties and growth failure are commonly seen in infants with congenital heart defects (CHD). Growth failure in infancy is associated with adverse post-operative outcomes as well as long term nutritional and neurodevelopmental deficits. Many infants with congenital heart defects require enteral nutritional support. Percutaneous endoscopic gastrostomy (PEG) and gastro-jejunostomy (PEG-J) tubes are well-established means to provide nutritional support for infants with growth failure. However, limited data exist regarding safety and efficacy of PEG and PEG-J placement in infants with congenital heart defects. The aim of this study is to evaluate the safety and outcomes of PEG and PEG-J placement in infants with CHD undergoing cardiac surgery within sixty days of life.

Methods: After IRB approval, a retrospective chart analysis of 245 infants who underwent cardiac surgery at less than 60 days of age from January 2007 to December 2013 was performed. Patients were categorized by type and severity of CHD and surgical repair; other morbidities including chromosomal abnormalities, seizures, renal dysfunction, vocal cord paralysis, and gastro-esophageal reflux were also compared. Safety of PEGs and PEG-Js were evaluated by reviewing intra-operative and post-operative data, including operative times, post-operative complications, and incidence of mortality after tube placement. Efficacy was determined by reviewing growth velocity post-tube placement, time to initiation of enteral feeding, time to discharge after tube placement, and duration of tube use.

Results: Of the 96 identified with gastrostomy tubes, 77 were placed via endoscopy: 59 PEGs and 18 PEG-Js. The remaining 19 were placed surgically. Birth weight for patients with gastrostomy tubes ranged from 1.41 kilograms (kg) to 4.17 kg. Procedure weight ranged from 2.33 kg to 6.15 kg with a mean age of 67.1 days at time of procedure. Mean weight gain before (0.61 kg) and after (0.48 kg) gastrostomy placement were not statistically different (p= 0.24), with the average weight at time of study completion (12/31/2013) or of tube removal of 9.57 kg. Mean operative time of PEG procedure was 6.18 minutes and 17.2 min for PEG-Js. Minor post-operative complications included cellulitis requiring topical antibiotics (2.6%), and benign pneuomoperitoneum (5.1%). One infant (1.3%) was treated for peritonitis with IV antibiotics; no other major post-operative complications were noted. Of the 77 infants who received PEGs or PEG-Js, 74 survived to hospital discharge (96.1%), and 67 survived to study completion (87%). Of those that died, the causes of death were unrelated to gastro-intestinal complications. Of the 149 infants who did not undergo gastrostomy placement, 121 survived to study completion (81.2%) when compared to the 87% of living infants who had a PEG or PEG-J (p= 0.30). Average time to enteral feeds after tube placement was 1.5 days.
Conclusions: PEGs and PEG-Js can be safely placed in infants < 5 kg with congenital heart defects who have undergone cardiac repair, and post-operative complications after tube placement are rare.

220 IMPACT OF PRE-PROCEDURE PHONE CALL ON NO-SHOW RATE IN PEDIATRIC ENDOSCOPY UNIT. Jyoti Mani, Linda Franklin, Harpreet Pall, Gastroenterology, Hepatology, and Nutrition, St. Christopher's Hospital for Children, Philadelphia, PA

INTRODUCTION: Endoscopy is an integral tool in the diagnosis and management of gastrointestinal diseases in children. However, there is limited literature focusing on quality improvement initiatives in pediatric endoscopy. The primary goal of this project was to reduce the no-show rate in the Endoscopy Unit at St. Christopher's Hospital for Children. Also, we aimed to improve patient and family satisfaction with the procedure by identifying opportunities for improvement in the current system. METHODS: In March 2013, a pediatric endoscopy quality improvement initiative was formed at St. Christopher's Hospital for Children. We identified risk factors for no-show to the scheduled endoscopy procedure. A checklist was designed based on these potential causes to identify patients at risk. The endoscopy nurse coordinator made a pre-procedure phone call 48-72 hours before the procedure as a reminder and to address any of these risks for non-compliance. A patient satisfaction survey covering various aspects of care was used during the intervention period to identify other areas of potential improvement. RESULTS: The no-show rate decreased from an average of 7% (22 out of 298 scheduled procedures) in the pre-intervention phase (January 2013-June 2013) to 2% (5 out of 223 scheduled procedures) in the post-intervention phase (July 2013-November 2013), p value=0.009. The survey provided insight into present quality of care. We analyzed the survey results from 33 patients who underwent a procedure from September 2013-October 2013. 91% of the patients/family recorded an overall satisfaction of 4 or 5 on the survey. CONCLUSIONS: The pre-procedure phone call substantially decreased the no-show rate and enhanced efficiency. A patient satisfaction survey helped in identifying areas for potential improvement.

221 ASSESSMENT OF ENTRUSTABLE PROFESSIONAL ACTIVITIES IN PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION FELLOWSHIP--A PILOT PROJECT. Jacob Robson1, Toba Weinstein2, Cary Sauer3, 1Pediatric Gastroenterology, Benioff Children's Hospital, University of California San Francisco, San Francisco, CA; 2Pediatric Gastroenterology, Cohen Children's Medical Center, Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY; 3Pediatric Gastroenterology, Emory University, Atlanta, GA

Background: Entrustable Professional Activities (EPAs) are an innovative construct that may be leveraged to provide competency-based assessment of trainees in a meaningful clinical context. EPAs specific to a subspecialty can be used to define the essential work of that field. A trainee's successful accomplishment of these observable, work-based, EPAs implies achievement of linked milestones and competency domains. In conjunction with the American Board of Pediatrics, the NASPGHAN EPA Task Force developed 10 EPAs specific to Pediatric Gastroenterology, Hepatology and Nutrition. Herein we discuss a pilot project reviewing the first attempts at assessment of these newly developed EPAs.

Design/Methods: 6 Pediatric Gastroenterology, Hepatology and Nutrition program directors submitted data for this cross-sectional, pilot study. Program directors were asked to fill out EPA assessment tables for each of their trainees, using descriptive behavioral anchors to choose an "entrustment level" on a 1-5 scale, with level 4 signifying the trainee was "entrustable" for unsupervised practice. Additionally, program directors rated trainees on a more traditional 1-9 scale of "expertise level," ranging from 1=novice to 9=expert. Summary statistics were calculated by fellowship training year and variation between training levels was assessed using linear regression.

Results: We received anonymized data on 22 trainees (6 first year, 8 second year and 8 third year fellows) from the participating programs. Mean expertise and entrustment level scores improved with each training year (see table) and differences between training levels (eg first year versus second year) were statistically significant for both scales (p<0.01). There was a wide range on entrustment level scores across EPAs, with 3rd year trainees averaging >=4.0 on only one EPA (mucosal disease) and as low as 2.85 (liver transplant). We noted that mean entrustment scores for GI/Nutrition EPAs (mean: 2.87) were significantly higher (P<0.01) than those for Liver/Biliary/Pancreas EPAs (mean: 2.44). Further, only two fellows on whom we received data scored at the level of ready for unsupervised practice on all 10 EPAs.

Conclusions: In this pilot study, we report the use of EPA Assessment Tables in competency-based assessment of trainees. As opposed to assessments on the domains of competence, which struggle to discriminate between fellows at different training levels, we showed that EPA assessment ratings had a clear, stepwise progression as fellows advanced in training. The entrustment level score may be particularly useful to clinical competency committees, who will be charged with making decisions regarding a trainee's readiness for independent practice. As EPAs allow faculty to make judgments about trainees in the clinical context in which they practice and can be mapped to milestones and domains of competence, EPA assessment may supplant other forms of competency-based assessment in the near future.

Analysis of Fellow's Entrustment and Expertise Level Scores, Across 10 EPAs for Pediatric Gastroenterology, Hepatology and Nutrition, May 2014
### Table 1: Entrustment Level Scores

<table>
<thead>
<tr>
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<th>1st Year Fellows</th>
<th>2nd Year Fellows</th>
<th>3rd Year Fellows</th>
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<tbody>
<tr>
<td>Mean (SD)</td>
<td>1.54 (0.41)</td>
<td>2.53 (0.55)</td>
<td>3.74 (0.46)</td>
</tr>
<tr>
<td>95% Confidence Intervals</td>
<td>1.10-1.97</td>
<td>2.07-2.98</td>
<td>3.35-4.12</td>
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### Table 2: Expertise Level Scores

<table>
<thead>
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<th>1st Year Fellows</th>
<th>2nd Year Fellows</th>
<th>3rd Year Fellows</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>3.47 (0.62)</td>
<td>4.89 (0.82)</td>
<td>6.56 (0.78)</td>
</tr>
<tr>
<td>95% Confidence Intervals</td>
<td>2.82-4.11</td>
<td>4.20-5.57</td>
<td>5.91-7.21</td>
</tr>
</tbody>
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222  **IMPROVING ACCESS TO OUTPATIENT FOLLOW-UP AFTER DISCHARGE FROM AN ACUTE CARE PEDIATRIC ACADEMIC HOSPITAL.** Jacqueline E. Crawford, Jonathan A. Flick, Sara Kunzman, Maryann Chilkatowsky, April Taylor, Alison Marx, Children's Hospital of Philadelphia, Philadelphia, PA  
**Team:** Jackie Crawford, Sara Kunzman, Maryann Chilkatowsky, April Taylor, Alison Marx, Jonathan Flick  
**Background:** Lack of timely outpatient follow-up after hospital discharge has been cited as a factor driving hospital readmissions and an impediment to continuity of care.  
**Purpose:** To identify GI inpatients needing an outpatient follow up visit and schedule the appointment within 2-3 days but ideally before the patient is discharged from the hospital. All identified inpatients will be seen in GI clinic within 2-3 weeks from date of hospital discharge.  
**Methods:** GI clinical nurse specialist (CNS) position created in January 2013 and inpatient scheduling clinic coordinator created in March 2013. The CNS and inpatient scheduling clinic coordinator worked in collaboration with the GI Quality Improvement and Patient Safety Subcommittee to create an inpatient follow up appointment process.  
**Inpatient follow-up appointment process:**  
- CNS reviews GI inpatient list daily  
- Potential discharges within the next 24-72 identified and emailed to inpatient scheduling clinic coordinator daily  
- Scheduling coordinator calls family at the bedside to schedule appointment  
- Inpatient follow-up appointments are automatically populated and printed on each patient's discharge summary  
- Monthly EPIC (electronic medical record) report beginning in July, 2013 identifying all patients discharged from GI service and follow-up appointment status  
- CNS reviews report and works with scheduling coordinator for those patients requiring outpatient follow-up not scheduled at time of discharge  
**Results:** The percent of patients discharged with appropriate follow-up scheduled exceeded the target of 91%. The GI inpatient service readmission rates remain unchanged. The no show rate for inpatient follow-up appointments are 0.3%.  
**Conclusions:** The development of a formal inpatient follow-up appointment process directed by a clinical nurse specialist and with data support from EPIC allowed us to exceed our target of 91% of patients having outpatient follow-up appointments in place within 2-3 days after discharge from inpatient GI service. By having a dedicated inpatient scheduling clinic coordinator work directly with families prior to or immediately after discharge, the no-show rate for follow-up outpatient visits was very low (< 3%, vs. 10 % average GI clinic no-show rate). Our failure to observe any changes in readmission rates highlights the complexity of factors that drive hospital readmissions.  
**Next Steps:** An automated referral process in EPIC to generate requests for outpatient follow-up appointments will be piloted on GI service in June 2014. The inpatient front line ordering clinician will enter referral for GI follow-up appointment in EPIC upon discharge. The referrals will be routed to inpatient scheduling coordinator. The CNS will monitor results using the EPIC report.

223*  **EFFECTS OF PANETH CELL DISRUPTION ON INTESTINAL MICROBIOME COMPOSITION IN IMMATURE SMALL INTESTINE.** Jessica Stumphy¹, Mark Underwood², Karen Kalanetra³, David Mills³, Huiyu Gong⁴, Steven McElroy⁴, Pediatrics, University of Iowa, Iowa City, IA; ²Pediatrics, UC Davis, Sacramento, CA; ³Viticulture and Enology, UC Davis, Sacramento, CA  
**Background:** Necrotizing enterocolitis (NEC) remains a significant cause of morbidity and mortality in premature infants. While the pathophysiology of NEC is incompletely understood, loss of antimicrobial peptide-secreting Paneth cells has been associated with development of gastrointestinal diseases, including NEC. Paneth cells contribute to
regulation of the intestinal microbiome. Therefore, the depletion of Paneth cells associated with NEC may explain why infants experience a shift in microbiome diversity prior to development of the disease. However, the relationship between Paneth cell disruption, the microbiome and NEC remains unclear. Our hypothesis is that disruption of Paneth cells will result in decreased diversity of the immature intestinal microbiome.

Aim: The aim of this proposal is to establish the acute and chronic effects of Paneth cell disruption on the composition and function of the intestinal microbiome.

Methods: Fourteen-day old mice received intraperitoneal dithizone (induces Paneth cell-specific loss), or dithizone followed by an oral gavage of Klebsiella pneumonia (combination induces NEC), and were compared to sham controls. Mice injected with dithizone were harvested at 1, 6 or 24 hours following injection. Mice receiving NEC treatment were gavaged with Klebsiella 6 hours after dithizone injection and then sacrificed 10 hours later. Cecal tissue was harvested and sent to the University of California at Davis for DNA extraction, 16s ribosomal sequencing, and sequence analysis by QIIME. To determine the transit time of Klebsiella, mice were gavaged with GFP-labeled Klebsiella and sacrificed at 30 minute intervals. Small intestinal tissue was harvested and quantified for fluorescence compared to controls.

Results: Dithizone-induced Paneth cell disruption causes time-dependent changes in the prevalence of multiple bacterial families. Additional compositional changes were observed in the NEC cohort. Enterobacteriaceae sp. were absent in control and dithizone treated mice, but were significantly increased in the NEC treated animals. GFP-labeled Klebsiella peak in the small intestine at 1.5 hours following gavage and are cleared by 5 hours after administration.

Conclusions: Paneth cell disruption and NEC induce time-dependent changes in the intestinal microbiome. The sharp increase in Enterobacteriaceae seen only in the NEC group is particularly interesting because it consists of different Enterobacteriaceae sp. than the gavaged Klebsiella used in our model. This finding is significant because a similar increase in this bacterial family was observed in human infants who developed NEC, suggesting that this model can be used to study the microbiome changes seen in human NEC.

224 A NEW ENDOSCOPIC METHOD FOR GASTROJEJUNAL TUBE PLACEMENT IN PEDIATRICS. Joseph Picoraro, Anne Pierog, Norelle Rizkalla Reilly, Ali A. Mencin, Pediatric Gastroenterology, Hepatology and Nutrition, Columbia University Medical Center, New York, NY

BACKGROUND: By providing both post pyloric feeding and gastric decompression, gastrojejunal feeding tubes (GJT) are used in the treatment of pediatric patients with gastroparesis, gastroesophageal reflux and aspiration. Though GJTs can be placed endoscopically either by using hemoclips to secure the GJT to the small bowel or by dragging the GJT into place with forceps, these methods can be difficult and are not utilized in most gastroenterological practices. Instead, interventional radiology has largely appropriated the business of GJT placement by employing a fluoroscopic guidewire technique. In this case series, a new and relatively easy method of endoscopic GJT placement via an established gastric stoma was described which minimizes fluoroscopy time, can be performed without sedation, and which permits the gastroenterologist to place GJTs independently. This case series reviewed the success rate, complications, and technical issues associated with endoscopic GJT placement.

METHODS: All endoscopic GJT placements between June 14, 2013 and May 23, 2014 were reviewed. Data collected included indication for GJT placement, patient demographics and medical history, use of sedation, fluoroscopy time, as well as procedural and post-procedural complications. The method of placement was as follows: A neonatal endoscope was inserted through the gastrostomy stoma and advanced to the distal duodenum or jejunum. A guidewire was then placed through the endoscope into the small bowel, the scope was withdrawn, and a GJT was advanced over the guidewire. Proper position was confirmed by fluoroscopy with contrast injection. If the GJT later dislodged or was clogged, the GJT was replaced using the same technique.

RESULTS: A total of 30 GJT placements were performed, all of which resulted in successful tube placement in the distal duodenum or jejunum. Ten patients underwent conversion of gastrostomy tube to GJT by the endoscopic approach. This technique was further used in 20 replacements. Patient age ranged from 1-19 years. Indications included aspiration (5), gastroesophageal reflux (2), dysmotility with refractory vomiting (2), pancreatitis (1), and malfunctioned GJT (7). Fluoroscopy time ranged from 2 to 34 seconds with a mean time of 11.5 seconds. The average fluoroscopy time of 10 patients who had previously undergone IR based placement was 5 minutes and 52 seconds. In four patients, more than one attempt was required due to coiling in the stomach. Pyloric obstruction caused by the GJT balloon developed in one patient necessitating replacement with a smaller GJT. Sedation was used in 9 placements. Tube lifespan after GJT placement ranged from 4 days to 40 weeks with a mean duration of 13.5 weeks.

DISCUSSION: In this case series, endoscopic GJT placement utilizing a guidewire technique through the gastrostomy site was a safe, reliable and effective method for post-pyloric feeding that could be performed without sedation and with minimal fluoroscopy. This technique can be performed independently by pediatric gastroenterologists and provides a new option for GJT placement in pediatric patients. Larger and longer term prospective studies comparing different GJT placement methods would be required to properly determine the optimal placement method.
GERD/Motility/Functional Disorders

240 FUNCTIONAL GASTROINTESTINAL DISORDERS IN SALVADORANS SCHOOL CHILDREN. Carlos A. Velasco1, Roberto Zablalah2, Miguel Saps3, 1Pediatrics, University of Valle, Cali, Colombia; 2Hospital Nacional de Niños, San Salvador, El Salvador; 3Children's Hospital of Chicago, Chicago, IL

Introduction: The prevalence of functional gastrointestinal disorders (FGDs) in Panama, Ecuador and Colombia is between 22.8% and 31.4%. Objective: To determine the prevalence of FGDs in school children in San Salvador, El Salvador in 2014. Methodology: Prevalence study in 223 school children. Sociodemographic variables were considered. Statistical analysis included estimation of the proportion of children with FGDs and corresponding 95% estimate, %, percentiles, means, medians and other descriptive measures with their corresponding standard deviations and ranges. Results: There was a prevalence of 19.28% FGDs, with an average age of 10.21±1.46 years. The FGDs were functional constipation (FC) in 53.49%, irritable bowel syndrome (IBS) in 18.6%, functional abdominal pain (FAP) in 9.3% and in 4.65%, respectively, functional dyspepsia (FD), abdominal migraine (AM), functional abdominal pain syndrome (FAPS) and cyclic vomiting syndrome (CVS). Predominated in girls (56.36%). Conclusion: The prevalence of FGDs in Salvadorans school children between 8 and 14 years in San Salvador, El Salvador, was 19.28%, with the most frequent FC and IBS in girls.

241 KNOWLEDGE, ATTITUDES AND PRACTICES OF COLOMBIAN PEDIATRICIANS ABOUT GASTROESOPHAGEAL REFLUX DISEASE. Carlos A. Velasco, Carlos Echandia, Jairo Alarcon, Pediatrics, University of Valle, Cali, Colombia

Introduction: Gastroesophageal reflux disease (GERD) is a common cause of digestive diseases in children. Objective: To determine the knowledge, attitudes and practices in Colombian pediatricians about GERD. Methodology: In June 2011, an anonymous survey was conducted to 215 pediatricians who attended the XXVII Colombian Congress of Pediatrics on the diagnosis and management of GERD in children. Results: 50.2% were male, mean age 42.6±8.5 years (range 28 to 73 years), predominantly male (50.2%); be a graduate of Colombian public university (44.2%); have graduated in the last decade (47.4%); come from Bogota, Colombia (28.4%), and perform outpatient (65.1 %). The 32.6% asking some paraclinical: 21.4% upper gastrointestinal tract, 12.1% scintigraphy digestive tract, 7.9% pHmeter/impedance and 1.9% endoscopy of the upper gastrointestinal tract with biopsy; 25.6% after empirical treatment (ET) for 2 months. In the ET is 83.8% with 74% prokinetic (domperidone in 42.4%) and proton pump inhibitor (PPI) in 65.6% (45.6% omeprazole). IBP indicated in 34.5% in infants (0-24 months), especially 1 time per day (48.4%) and 49.9% from 4 to 8 weeks. Other therapeutic measures in the 37.3% are nutritional (fractionation and thickening) and 45.6% position changes. The primary cause of GERD surgery in the 16.7% was the anti-therapeutic failure. Conclusions: One third of Colombian pediatricians asking paraclinical to diagnose GERD; three quarters starting ET with prokinetic and IBP, about half for 1-2 months, and the third between 0 and 2 years of age, being the main cause of anti-GERD surgery, the treatment failure.

242 FUNCTIONAL GASTROINTESTINAL DISORDERS IN COLOMBIAN SCHOOL OF DIGESTIVE ENDOSCOPY UNIT. Carlos A. Velasco, Otto Calderon, Pediatrics, University of Valle, Cali, Colombia

Introduction: The prevalence of abdominal pain (AP) associated with functional gastrointestinal disorders (FGDs ) in Colombian school is 11.1%. The upper gastrointestinal tract endoscopy (UDTE) is indicated in the study of children with AP to study. Objective: To determine the prevalence and possible risk factors of FGDs in school from a Pediatric Unit of Digestive Endoscopy (PUDE) of Cali, Colombia by the Rome III criteria in Spanish. Methodology: Prevalence study in 37 schools were considered sociodemographic, family and clinical variables. Statistical analysis included estimation of the proportion of children with FGDs and corresponding 95% CI; estimate of %, percentiles, means, medians and other descriptive measures with their corresponding standard deviations and ranges; univariate analysis; possible occurrence of association between the variables; Fisher exact test with a p value < 0.05 , two-tailed , significant, and multiple logistic regression analysis. Results: The prevalence for FGDs was 73%, with 11.3±2.1 years old. There was a predominance in females, be malnourished by BMI, eutrophic by height/age, as not being an only child, have separated or divorced parents and have no intra-family FGDs. There were no significant FGDs to present to the variables studied predominance, and none explained the presence of FGDs. Conclusion: The prevalence of FGDs in school between 8 and 15 years of PUDE from Cali, Colombia was 73%, with the main FGDs: functional abdominal pain in 37.0% and irritable bowel syndrome in 33.3%.

243 AUTONOMIC GASTROINTESTINAL DYSFUNCTION IS ASSOCIATED WITH A HIGH RISK FOR MALNUTRITION IN CHILDREN WITH RETT SYNDROME. Siddharth Gupta1, Anil Darbari2, Nga Hong Brereton1, Abanti Sanyal3, Sakkubai Naidu3, Carmen Cuffari1, 1Pediatrics, The Johns Hopkins University, Lutherville, MD; 2Neurology, The Johns Hopkins University, Baltimore, MD; 3Johns Hopkins Biostatistics Center, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; 4Pediatrics, Children’s National Hospital, Washington, DC

Introduction: Rett syndrome is associated with feeding impairment and constipation. These two characteristic clinical
phenotypes are believed to reflect some as yet undefined abnormality within the autonomic nervous system. Although these gastrointestinal disorders are relatively common, there is tremendous variability in disease severity and often complicated by severe malnutrition. Our aim is to assess autonomic gastrointestinal function in children with Rett syndrome, and correlate disease severity with MeCP2 mutations.

**Methods:** Prospective clinical study to assess esophageal motor function, as measured through esophageal manometry and impedance pH probe testing. Constipation was assessed on clinical grounds, as measured by stool frequency. All patients underwent a formal evaluation by a nutritionist experienced in the assessment and management of children with Rett syndrome.

**Results:** 44 of 69 girls with a median (range) age of 4.1 yrs. (2.5-8.6) underwent esophageal manometry. 17 out of the 69 patients had impedance pH probe testing. 45% had dysmotility as determined by lower esophageal sphincter dysfunction, hypertonic esophageal tone or signs of poor esophageal clearance. 47% of patient had impedance pH probe criteria for GERD. 62% had clinical criteria for severe constipation requiring medical intervention, 27% had failure to thrive based on a BMI z-score of less than -1. Among these patients 11.6% had either a gastrostomy tube, nasogastric tube or modified diet to improve the patients overall caloric intake. Regression analysis showed that the combination of esophageal motor dysfunction with constipation was associated with an increased risk of malnutrition (OR:1.5); and among these patients early aggressive nutritional intervention was protective (OR:0.5). There was no correlation between these clinical phenotypes with MeCP2 mutations.

**Conclusion:** A multidisciplinary approach to assess autonomic gastrointestinal function through impedance pH probe, and esophageal manometry testing may allow clinicians to identify clinical phenotypes predisposed to dysphagia. Among these patients, early and aggressive nutritional intervention may avoid complications of long-standing malnutrition. Future studies are needed to determine if these manifestations of autonomic gastrointestinal function are centrally mediated.

**244 CHARACTERIZATION OF PSYCHOTHERAPEUTIC TREATMENT OF FUNCTIONAL GASTROINTESTINAL PAIN DISORDERS IN PEDIATRIC GASTROENTEROLOGY PATIENTS.** Claire Zar-Kessler1, Jaime Belkind-Gerson1, Suzanne Bender1, Braden Kuo2, 1Massachusetts General Hospital for Children, Boston, MA; 2Massachusetts General Hospital, Boston, MA

**Introduction:** Functional abdominal pain and irritable bowel syndrome are often treated with antidepressants including tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRI) but much remains unknown about the efficacy, specifically with SSRIs. Although SSRIs are known to cause diarrhea and TCA's are known to produce constipation, physicians will frequently prescribe these medications without significant consideration to the patients' medical etiology who have been treated with SSRIs or TCAs. IBS was classified using the clinician's notes as patients with chronic abdominal pain with a negative workup and alterations of bowel habits, while FAP were patients with abdominal pain not meeting criteria for IBS. 961 patient charts reviewed, 531 met criteria as having functional pain and 244 of 69 girls with a median (range) age of 4.1 yrs. (2.5-8.6) underwent esophageal manometry. 17 out of the 69 patients had impedance pH probe testing. 45% had dysmotility as determined by lower esophageal sphincter dysfunction, hypertonic esophageal tone or signs of poor esophageal clearance. 47% of patient had impedance pH probe criteria for GERD. 62% had clinical criteria for severe constipation requiring medical intervention, 27% had failure to thrive based on a BMI z-score of less than -1. Among these patients 11.6% had either a gastrostomy tube, nasogastric tube or modified diet to improve the patients overall caloric intake. Regression analysis showed that the combination of esophageal motor dysfunction with constipation was associated with an increased risk of malnutrition (OR:1.5); and among these patients early aggressive nutritional intervention was protective (OR:0.5). There was no correlation between these clinical phenotypes with MeCP2 mutations.

**Conclusion:** A multidisciplinary approach to assess autonomic gastrointestinal function through impedance pH probe, and esophageal manometry testing may allow clinicians to identify clinical phenotypes predisposed to dysphagia. Among these patients, early and aggressive nutritional intervention may avoid complications of long-standing malnutrition. Future studies are needed to determine if these manifestations of autonomic gastrointestinal function are centrally mediated.

**Aims:** To investigate the use of SSRI and TCA treatment in pediatric patients with functional abdominal pain (FAP) and irritable bowel syndrome (IBS), including examining the efficacy and medication selection based on GI symptom profile.

**Methods:** Retrospective review over 8 years (2005-2013) of children (5-21yo) with abdominal pain with no underlying medical etiology who have been treated with SSRIs or TCAs. IBS was classified using the clinician's notes as patients with chronic abdominal pain with a negative workup and alterations of bowel habits, while FAP were patients with abdominal pain not meeting criteria for IBS. 961 patient charts reviewed, 531 met criteria as having functional pain and 197 of these had SSRI or TCA therapy initiated while being followed by gastroenterology. Total follow up time ranged from 4 weeks to 5 years. Charts were reviewed to assess patient's symptoms, treatment length and response to therapy.

**Results:** A total of 91 patients met criteria with SSRI therapy. 7 were excluded due to lack of documented follow up resulting in 84 patients analyzed. 63 (75%) reported improvement with 20 (24%) of these reporting persistence of milder symptoms. 21 reported no response (25%) with 5 (6%) of these having initial response that disappeared within 6 months. A total of 106 patients met criteria with TCA therapy. 14 were excluded as they had no follow up documented and 92 patients were analyzed. 56 (61%) reported improvement, with 13 (14%) of these reporting persistence of milder symptoms. 36 (39%) reported no response with 8 (9%) reporting an initial response that disappeared. The response to SSRIs was significantly greater than response to TCA's (P=0.04). Of the 67 patients with presenting symptoms of constipation, 32 (48%) received TCAs and of the 45 patients with associated diarrhea, 26 (58%) received SSRI treatment. 2 SSRI patients reported GI side effects, both with IBS-D and 2 TCA patients reported GI side effects leading to discontinuation, both with IBS-C.

**Conclusion:** Patients had positive response to SSRI therapy, significantly greater response than to TCA, supporting the increased utilization of SSRIs for treatment of functional gastrointestinal pain disorders. Minimal consideration was given to patient's associated gastrointestinal symptoms when determining the use of specific psychotherapeutic medications.
CONCLUSIONS confirm our previous report showing that patients with CF have prolonged CC. Increases while CC duration decreases. Significant differences in PSPW Index between CF and non-CF controls.

Aim To compare the two methodologies. Methods IMP-pH tracings from 16 CF children (3-18 years) and 16 symptomatic age-matched non-CF controls were analyzed in two ways: 1) CC duration and CC rate was calculated for both groups and 2) PSPW Index was calculated for both groups. PSPW Index was calculated by counting seconds following the episode, and then dividing by the number of total IDG episodes. Correlation between CC rate was F=27.43, p=.0000145 and F=17.7, p=.00024, respectively. Pearson's correlation was r= -0.69, p=.00001, 95% CI [-0.84,-0.45] for PSPW and CC duration, and r=0.59, p=.0004, 95% CI [(0.78),(0.31)] for PSPW and CC rate.

Results CC duration comparisons revealed that 9 of the 16 CF children (56.3%) had CC durations that were above the upper end of normal (i.e. >116.2 seconds) while only 2 age-matched non-CF children (12.5%) had abnormal CC durations (McNemar's Test - c2 = 5.14, p=.02). Also, odds ratio analysis showed that CF patients were 8.3-times [95% CI 1.3-99.9] more likely to have abnormally prolonged CC by comparison to non-CF children. Conclusions These data are consistent with our previous report showing that CC in patients with CF is significantly prolonged. However, these data also show that not all CF patients have abnormal CC; 7 of 16 CF patients (44%) had CC durations that fell within the normal range. Since prolonged CC has been linked to complications associated with GERD (Neuropsychiatric Motil 25:399), CF patients might benefit from a CC assessment upon clinical examination.

Background: Constipation is a common problem in children. What was thought a problem of developed countries, turned to be a worldwide problem. Patients and methods: All patients with constipation followed at our Pediatric gastrointestinal clinic between Sept. 2009 and December 2012 were included. Their medical hospital files were reviewed. Data was presented as averages and percentages. Results: During the study period our pediatric gastroenterology clinic managed 528 patients. 137 patients (25.9%) had constipation. All patients excluded due to insufficient data. 69 (54.8%) were males. The average duration of constipation before consultation was 14.9 months (1-126 months), which was noticed to increase with age. The most common symptom was painful, hard and dry stool (92%) followed by infrequent defecation (52%). Fecal mass in the rectum was the most common physical finding. It was seen in half of the patients. Functional constipation was the most common cause of constipation in our cohort; it affects 82% of the patients. Surgical causes comprises one third of the organic causes. Conclusion: Childhood constipation is a significant cause of pediatric gastroenterology consults in our part of the world. Still functional constipation is the single most common cause of childhood constipation in our cohort. Further studies needed to determine the size of the problem in our community.

USE OF NORMAL VALUES FOR CHEMICAL CLEARANCE (CC) SHOWS THAT THE MAJORITY OF CHILDREN WITH CYSTIC FIBROSIS (CF) ARE SIGNIFICANTLY MORE LIKELY TO HAVE ABNORMAL CC WHEN COMPARED TO AGE-MATCHED NON-CF CONTROLS. Frederick W. Woodley1,2, Rodrigo S. Machado3, Carlo Di Lorenzo1,2, Hayat Mousa1,2, Gastroenterology, Nationwide Children's Hospital, Columbus, OH; Pediatrics, Ohio State University College of Medicine, Columbus, OH; Pediatric Gastroenterology, Federal University Sao Paulo, Sao Paulo, Brazil

BACKGROUND We recently reported normal values for chemical clearance (CC) of acid gastroesophageal reflux (GER) for children and infants (JPGN, 57:E130). We also reported that CC is significantly prolonged in children with CF when compared to age-matched non-CF controls (Dig Dis Sci 59:623). Aim The purpose of this investigation was to use the normal CC values to determine how many CF children and non-CF control children had "abnormal" CC. Methods Normal values (90th percentile) for CC duration were compared to CC duration values calculated for 16 CF children (ages 3-18 yrs) and for 16 age-matched non-CF controls. Results CC duration comparisons revealed that 9 of the 16 CF children (56.3%) had CC durations that were above the upper end of normal (i.e. >116.2 seconds) while only 2 age-matched non-CF children (12.5%) had abnormal CC durations (McNemar's Test - c2 = 5.14, p=.02). Also, odds ratio analysis showed that CF patients were 8.3-times [95% CI 1.3-99.9] more likely to have abnormally prolonged CC by comparison to non-CF children. Conclusions These data are consistent with our previous report showing that CC in patients with CF is significantly prolonged. However, these data also show that not all CF patients have abnormal CC; 7 of 16 CF patients (44%) had CC durations that fell within the normal range. Since prolonged CC has been linked to complications associated with GERD (Neuropsychiatric Motil 25:399), CF patients might benefit from a CC assessment upon clinical examination.

POST-REFLUX SWALLOWING-INDUCED PERISTALTIC WAVE (PSPW) INDEX CONFIRMS A PREVIOUS STUDY THAT CHILDREN WITH CYSTIC FIBROSIS (CF) HAVE PROLONGED CHEMICAL CLEARANCE (CC) OF ACID GASTROESOPHAGEAL REFLUX (AGER). Frederick W. Woodley1,2, Rodrigo S. Machado3,4, Carlo Di Lorenzo1,2, Hayat Mousa1,2, Gastroenterology, Nationwide Children's Hospital, Columbus, OH; Pediatrics, Ohio State University College of Medicine, Columbus, OH; Pediatric Gastroenterology, Federal University Sao Paulo, Sao Paulo, Brazil; Pediatrics, University of Cincinnati, Cincinnati, OH

BACKGROUND We recently reported normal values for chemical clearance (CC) of acid gastroesophageal reflux (GER) for children and infants (JPGN, 57:E130). We also reported that CC is significantly prolonged in children with CF when compared to age-matched non-CF controls (Dig Dis Sci 59:623). Frazzoni and colleagues recently reported their use of IMP-pH and the PSPW Index to assess CC in patients with GERD (Neurogastroenterol Motil 25:399). Aim To compare the two methodologies. Methods IMP-pH tracings from 16 CF children (3-18 years) and 16 symptomatic age-matched non-CF controls were analyzed in two ways: 1) CC duration and CC rate was calculated for both groups and 2) PSPW Index was calculated for both groups. PSPW Index was calculated by counting seconds following the episode, and then dividing by the number of total IDG episodes. Correlation between CC durations and PSPW and between CC rate and PSPW, was tested. Results PSPW Index (median) was 41.8% [29.7-53.2] for CF patients and 55.1% [48.2-71.8] for controls, (p=.007). Association of PSPW with CC duration and with CC rate was F=27.43, p=.0000145 and F=17.7, p=.00024, respectively. Pearson's correlation was r= -0.69, p=.00001, 95% CI [-0.84,-0.45] for PSPW and CC duration, and r=0.59, p=.0004, 95% CI [(0.78),(0.31)] for PSPW and CC rate. Conclusions PSPW Index is strongly correlated with CC duration and CC rate; as the PSPW increases, the CC rate also increases while CC duration decreases. Significant differences in PSPW Index between CF and non-CF controls confirm our previous report showing that patients with CF have prolonged CC.
Background: History and physical exam are the cornerstones of diagnosing constipation with fecal impaction. Studies fail to demonstrate a correlation between the findings on abdominal radiographs (AXR) and a diagnosis of constipation. While established guidelines do not include AXR as a diagnostic criterion, many children presenting to the Emergency Department (ED) with a history consistent with fecal impaction continue to receive an AXR. In addition, it's been our impression that many of these patients do not have a digital rectal exam (DRE) performed as part of the evaluation. We hypothesize that an educational intervention (EI) for ED providers informing them of established guidelines for the diagnosis of constipation and fecal impaction will decrease the use of AXR.

Aims: The aim of this study is to determine the use of AXR and frequency of DRE in children presenting to the ED with suspected constipation and fecal impaction, and determine the impact of an EI on the use of AXR and DRE as part of the evaluation.

Methods: Healthy patients ages 4 to 18 years presenting to Ann & Robert H. Lurie Children's Hospital of Chicago ED with the chief complaint of abdominal pain and discharged with a diagnosis of constipation were included. Exclusion criteria were chronic medical problems or previous abdominal surgeries. Records were reviewed for demographics, radiographic studies, medical history, and physical exam. We reviewed records two months prior and two months after an EI consisting of presentation of pre-intervention data and established guidelines for diagnosis of constipation to all ED providers by both an in-person and a PowerPoint presentation. Pre and post intervention analysis was performed using the Chi Square test. The Institutional Review Board at Lurie Children's approved this study.

Results: In the pre-EI period, 365 children presented to the ED with the chief complaint of abdominal pain, 145 were discharged with a diagnosis of constipation, and 106 met the inclusion criteria. After the EI, of 342 children with abdominal pain, 136 were discharged with a diagnosis of constipation, and 94 met the inclusion criteria. After the EI, there was a significant decrease in the number of AXRs performed from 69.8% to 26.6% (p ≤.001) and a significant increase in the number of patients who had a DRE performed from 22.6% to 47.9% (p ≤.001). There were no differences in age, sex, race, or insurance status of patients who had an AXR or who had a DRE.

Conclusion: Our findings demonstrate that an education intervention presenting a practical, guideline based approach for diagnosing constipation with fecal impaction results in a decrease in the usage of AXR in the ED. The implications are that this will decrease cost, radiation exposure, and time spent in the ED for this patient population.

EFFECT OF OCTREOTIDE ON THE COLONIC MOTILITY IN PEDIATRIC PATIENTS WITH CHRONIC RECALCITRANT CONSTIPATION.

Kalyan Ray Parashette, Debra Horn, Ali M. Shah, Shamaila Waseem, Joseph Croffie, Riley Hospital for Children, Indiana University, Indianapolis, IN

BACKGROUND: Constipation is commonly encountered in pediatrics. Bongers et al reported that nearly 30% of constipated patients were symptomatic despite aggressive medical and behavioral therapy. These subsets of patients with intractable constipation often need a colonic motility study to determine if their symptoms are due to a colonic dysmotility. There is a need to identify newer medical therapies to treat patients with intractable constipation and colonic dysmotility.

Octreotide is a synthetic octapeptide analog of somatostatin. Von der Ohe et al reported improvement in the colonic motility index and statistically significant pressure phasic activity in the octreotide group compared to placebo. Cullen et al showed that octreotide has a dose dependent action on colonic motility; used in low doses it acted as a prokinetic agent. We have used octreotide during a colonic motility study in seven patients who had no response to a standard dose of bisacodyl. All patients had HAPC's after administration of octreotide.

SPECIFIC AIM: We aimed to study the effect of octreotide on colonic motility in pediatric patients with recalcitrant chronic constipation/encopresis and other suspected colonic motility disorders.

RESEARCH DESIGN AND METHODS: This was a non-randomized, single center, open label, and prospective study. Fasting motility was recorded for one hour, then octreotide 1mcg/kg (max of 50mcg) was administered SQ, and colonic motility was monitored. Manometry was then continued per routine. The motility index (MI) of pressure tracings at each pressure transducer was calculated for each patient for a period of 15, 30 and 45 minutes before and after octreotide injection. Change in MI was compared by Wilcoxon signed rank test.

RESULTS: Thirteen patients (5 male) were enrolled in the study. The age range was 4.6-16.2 years. Eleven patients (84%) had normal colonic manometry and two patients (16%) had colonic neuropathy. Of the 11 healthy patients, none had fasting HAPCs, one had post-octreotide HAPCs, two had postprandial HAPCs, and all had post bisacodyl HAPCs. MI (mm Hg) for the 15 minutes before and after octreotide infusion was 6.03 ± 1.26 (95% CI, 5.35-6.72), and 5.32 ±
were performed using propensity scores to match patients by comorbidities. Modeling was performed to determine predictors of hospitalization after a diagnosis of aspiration. Additional analyses were included if they were trialed and maintained on oral thickening for the duration of follow up. Logistic regression reviewed. Patients in the gastrostomy group were included if they underwent a primary percutaneous endoscopic gastrostomy tube placement; discharge diagnoses from subsequent hospital admissions (total and urgent) were included. All patients had 1 year of follow up after their initial abnormal swallow or primary gastrostomy tube placement; discharge diagnoses from subsequent hospital admissions (total and urgent) were included.

CONCLUSION: Our study shows that administration of octreotide resulted in no significant changes in colonic motility index in pediatric patients with chronic recalcitrant constipation. We previously have shown that octreotide induced HAPC's in patients who had no response to a standard dose of bisacodyl. This observation suggest that octreotide likely enhances effect of bisacodyl. However further research is needed to confirm this hypothesis.

250 ADHD AND DEFECTION DISORDERS: IMPACT ON FAMILY. Katja Kovacic1, Alan H. Silverman2, Carlo Di Lorenzo3, Suzanne Mugie1, Samuel Nurko1, Nicole Heinz1, Christina Gorges1, Ananthasekar Ponnambalam2, Rinarani Sanghavi1, Manu R. Sood1, 1Center for Motility and Functional Gastrointestinal Disorders, Boston Children's Hospital, Boston, MA; 2Division of Pediatric Gastroenterology, University of South Alabama Children's and Women's Hospital, Mobile, AL; 3Division of Pediatric Gastroenterology, UT Southwestern Medical College, Dallas, TX; 4Division of Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI; 5Division of Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH

Background: The relationship between ADHD and defecation disorders is incompletely described. Studies indicate that children with fecal incontinence (FI) have more attention and hyperactivity problems than the 3-5% reported ADHD prevalence in healthy children. Retrospective data from our institution indicate that children with constipation have a higher incidence of ADHD (13%) and are more prone to retentive FI despite medical treatment. We hypothesized: 1) ADHD is more prevalent in children with defecation disorders, especially in children with constipation-related fecal incontinence (C-FI); 2) families of children with ADHD and defecation disorders have lower quality of life; and 3) older children with ADHD and defecation disorders have lower quality of life than their younger counterparts.

Methods: A prospective, multi-center study of 389 children seen at five large regional children's hospitals across the U.S. Children who met Rome III criteria for functional constipation were included and divided into two groups: 1) constipation and 2) C-FI. Parents completed five measures of psychosocial functioning: the PedsQL, the PedsQL-Family Impact Module (FIM), the Functional Disability Inventory (FDI), the Pediatric Inventory for Parents (PIP) and the Pediatric Symptom Checklist (PSC).

Results: 362 children ages 2-18 years (mean=7.8 years; SD±3.5 years) met inclusion criteria. 163 (45%) children had constipation and 199 (55%) children had C-FI. Of those with constipation, 24 (15%) had ADHD while 41 (21%) of those with C-FI had ADHD. Children with ADHD and defecation disorders overall had lower family functioning (FIM;F=3.1). Older children with ADHD and FI had poorer psychosocial functioning (PSC;F=9.9) although this was not explained by the combination of ADHD and type of defecation disorder. A trend of increased parental stress level was observed in caregivers of children with ADHD. There was no association between physical functioning (FDI) and ADHD.

Conclusions: The prevalence of ADHD in children with defecation disorders, especially those with FI, is significantly higher (4x) than reported in the general population. These children have worse family functioning, and the older ones have more psychosocial problems. Fortunately, physical functioning does not appear to be affected. Children with ADHD may have decreased sensory awareness of bowel movements due to traits of distractibility and impulsivity, placing them at higher risk of severe defecation disorders. As such, early identification of ADHD in constipated children is clinically relevant. Aggressive treatment including psychological interventions for both child and the whole family may also be suitable, as the family at large appears affected.

251 GASTROSTOMY TUBES INCREASE HOSPITALIZATION RATES IN ASPIRATING CHILDREN. Maireade McSweeney, Jessica Kerr, Janine Amirault, Heather J. Litman, Rachel L. Rosen, Boston Children's Hospital, Boston, MA

Background: Gastrostomy tubes are often placed in aspirating children at risk for respiratory complications. There is no pediatric data to support this practice despite its widespread use. The aim of this study was to determine differences in hospitalization rates of aspirating children with and without gastrostomy tubes.

Methods: Patients with a documented abnormal modified barium swallow study at Boston Children's Hospital between 2006-2013 were included. All patients had 1 year of follow up after their initial abnormal swallow or primary gastrostomy tube placement; discharge diagnoses from subsequent hospital admissions (total and urgent) were reviewed. Patients in the gastrostomy group were included if they underwent a primary percutaneous endoscopic gastrostomy (PEG) placement without any preceding oral thickening trial. Patients without a gastrostomy (No PEG) were included if they were trialed and maintained on oral thickening for the duration of follow up. Logistic regression modeling was performed to determine predictors of hospitalization after a diagnosis of aspiration. Additional analyses were performed using propensity scores to match patients by comorbidities.

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**Results:** One hundred and forty nine patients (99 PEG, 50 No PEG) were included in the primary analysis. The median (IQR) age in the PEG and No PEG group were similar, 12 (5, 41) and 14 (8,20) months, respectively. The median (IQR) weight in the PEG and No PEG group was 8.1 kg (4.7, 14.3) and 10.4 kg (8.4, 12.2) respectively. Logistic regression results are shown in the table below. Patients with PEGs had higher ICU admissions (p=0.001) and urgent gastrointestinal admissions (p<0.001) than No PEG patients. There were no significant differences in urgent respiratory admissions between groups (p=0.73). After propensity score matching, an analysis of 50 patients (25 PEG, 25 No PEG) revealed that PEG patients continued to have more total admissions than orally fed patients, with a median (IQR) of 2 (1,3) admissions versus 1 (0,1) in the No PEG group (p<0.001).

**Conclusions:** After adjusting for various comorbidities, children who aspirate and are orally fed had decreased hospitalizations compared with patients who underwent gastrostomy placement. Additional prospective studies of gastrostomy tube placement versus oral feeding in aspirating children are needed. Results of logistic regression models to predict odds of hospitalization for aspirating patients with PEGs compared to those without PEGs

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**252** VISCERAL HYPERSENSITIVITY IN ADOLESCENTS WITH IRRITABLE BOWEL SYNDROME IS ASSOCIATED WITH ABNORMAL SALIENCE DETECTION AND COUPLING OF THE SALIENCE NETWORK. XiaoLin Liu1, Alan H. Silverman2, Mark Kern3, Douglas Ward4, Shi-Jiang Li5, Reza Shaker5, Manu R. Sood6, 1Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI; 2Division of Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI; 3Division of Gastroenterology, Medical College of Wisconsin, Milwaukee, WI; 4Division of Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI

**Introduction:** Functional magnetic resonance imaging (fMRI) studies of irritable bowel syndrome (IBS) in adults have produced conflicting results. Single region-of-interest analysis showed profound differences in brain activation patterns to experimentally controlled rectal distension stimuli across various sensation levels. Recent advances in cognitive neuroscience suggest that the determination of brain network interactions underlying cognitive processing, particularly those among the default mode network (DMN), executive control network (ECN) and salience network, may be better suited for understanding the neural basis of cognition in healthy and disease brain conditions. Of these, the salience network, one of the recently identified intrinsic brain networks, anchored in anterior insular (AI) and anterior cingulate cortices (ACC), was suggested to play a pivotal role in mediating attentional and cognitive processing and behavioral responses, particularly those related with visceral, somatic, gastrointestinal and motor systems. Using fMRI, this study seeks to determine, in pediatric IBS patients, regional brain activity in response to subliminal, liminal and non-painful supraliminal rectal distensions, and test the hypothesis that rectal stimuli-related salience network functional connectivity has abnormal coupling patterns with the DMN and ECN in IBS patients compared with those in healthy controls.

**Methods:** Nine pediatric IBS patients (4 males; 12-17 y/o) and eight age-matched controls (5 males; 12-16 y/o) underwent brain fMRI (3T; TR, 2s; RES, 3.75x3.75x4 mm³) under subliminal (two runs), liminal (two runs), and non-painful supraliminal (one run) stimulation with rectal distension set at 15±5, 25±4, and 31±5 mmHg, respectively. Each run contains four repeat cycles each consisting of a 15-second pressure and a 25-second rest. Rectal distension-induced brain activations were evaluated at each of the three sensation states, and stimuli-related salience network connectivities were determined by a novel fMRI-guided connectivity analysis.

**Results:** IBS patients demonstrated greater activation in neuronal structures of the salience network and the limbic system (e.g., ACC and anterior insula) as well as deactivation in areas involved in sensory and motor functions. Seed regions for determining rectal stimuli-related salience network were identified in the cingulate cortex during liminal sensation state, specifically, the anterior mid-cingulate cortex (aMCC) for controls and perigenual ACC (pACC) for patients. Compared with healthy controls, stimuli-related salience network in IBS patients revealed a significant overlapping with the DMN and ECN in posterior cingulate and dorsal medial prefrontal cortices.

**Conclusion:** Our study supports that visceral hypersensitivity in pediatric IBS patients is characterized by pathologically enhanced salience detection and mapping. Excessive coupling of the salience network with other intrinsic...
networks (e.g., DMN and ECN) can naturally invoke more extensive and aberrant attentional, affective and regulatory processing of visceral sensory stimuli in IBS. Our findings together suggest an explanatory central neural mechanism for the long-observed visceral hypersensitivity in IBS.

**253 AGE RELATED DIFFERENCES IN BASELINE ESOPHAGEAL INTRALUMINAL IMPEDANCE PARAMETERS.** Maria G. Donato Bertoldi, Judith Cohen Sabban, Laura S. Villafane, Federico Ussher, Marina Orsi, Pediatric Gastroenterology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Multichannel Intraluminal Impedance (MII) is a valuable tool to study gastroesophageal reflux (GER). Changes in baseline impedance (BI), bolus clearance (BCT), and acid exposure time (AE) may be indicative of esophageal damage. Recent reports suggest that age can be an additional factor to be considered.

**Aim:** To compare BI, BCT, Acid clearance time (ACT) and AE at different ages in children suspected GER.

**Materials and methods:** Tracings between January 2012- January 2014 were evaluated, including those in which both, pHmetry score and impedance were either normal or abnormal, dividing into 4 groups: Infants (<1yr) abnormal (n=19), normal (n=21); Children (>1yr) abnormal (n=14), normal (n=14). Mean IB was automatically calculated in all MII channels in 24 hr tracings. T-test was used and P<0.05 was considered as statistically significant.

**Results:** We analyzed 180 studies, 68 of which met the inclusion criteria. Compared with children > 1 yr, infants had a significantly lower mean IB, while AE, BCT and ACT were more prolonged. Comparison of pathologic vs normal tests among infants indicated that EA, ACT were statically significant (205 ± 75 vs. 86 ± 36 , t-6,7, p=0.000) but mean BI and BCT were not((15.2± 5.3 vs. 5±3 , t-6,7, p=0.000). Comparison of pathologic vs. normal tests among older children in distal channels showed mean BI (Ch5 1981 ± 632 vs. 2588± 880 , t2, p=0.046) (Ch6 1970 ± 623 vs. 2489± 913 , t3, p=0.004), AE (34.7 ± 20vs. 8.3± 4 , t-19, p=0.000) and ACT (219± 130 vs. 33 ± 20 , t-5, p=0.000) but not BCT (16.4± 5.5 vs. 14 ± 4 , t-1.16, p=0.25)

**Conclusions:** Age related differences were seen in all the evaluated parameters. These findings may be due to mechanical and/or functional changes as the child grows up or the variable impact of a more longstanding disease

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<th>Channel</th>
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<td>110</td>
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Baseline EA BCT and ACT Infant (n:40) vs Children (n:28)

**254 JOINT BEHAVIORAL HEALTH/GASTROENTEROLOGY CLINIC FOR FUNCTIONAL DISORDERS INCREASES FOLLOW-UP TO BEHAVIORAL HEALTH.** Cheyenne Hughes-Reid, Kelly Rodriguez, Maia Noeder, Matthew D. Di Guglielmo, Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE

**Background:** Functional gastrointestinal disorders (FGIDs) are common in the pediatric population. By Rome III criteria the prevalence of irritable bowel syndrome, functional abdominal pain, or functional constipation is estimated at 10%. Behavioral health interventions such as cognitive behavioral therapy, relaxation techniques, and biofeedback are paramount to the successful FGID treatment. Previous research has demonstrated significant, medium-sized treatment effects of these techniques on FGID symptoms. As a result of these empirical findings, an integrative approach to medical and behavioral health treatment has become a greater focus in the current health care environment. Given that attrition from behavioral health services is a common problem in child and adolescent outpatient mental health clinics, early engagement in behavioral health services may be critical in ensuring appropriate follow-up care for patients with FGIDs.

**Objective:** We explored a novel method for integrating services of Gastroenterology (GI) and Behavioral Health (BH) using a joint visit with a consultative pediatrician (who previously evaluated the patient) and a pediatric psychologist.
The goal was to improve access to follow up behavioral health care, decrease attrition, and reduce the behavioral health burden on GI and Emergency Department (ED) resources related to FGIDs by facilitating acceptance and use of BH services through the joint clinic.

Hypotheses: Participants in a joint GI/ BH clinic are more likely to follow-up with BH compared to patients seen by a GI subspecialist and referred to BH. Patients with FGIDs who see BH utilize the (ED) less than those who do not see BH.

Methods: A joint office visit, lasting 1 hour, was built into the template of a consultative pediatrician working in GI and a pediatric psychologist from BH with GI expertise. A total of 4 joint sessions per month were held. Using our shared electronic medical record, we determined the number of patients with FGIDs seen by GI from September 2012 through April 2014 that were referred to Behavioral Health. We then determined how many of these patients went on to see BH for at least one visit; a rate of follow-up was calculated. We completed the same analysis for patients with FGIDs seen in the joint clinic as a comparison. We analyzed ED use after BH visits as a secondary outcome.

Results: In the period studied, GI subspecialists saw 279 patients with FGIDs. 140 were referred to BH; 65 went on to follow-up with BH (46.4%). The joint GI/BH clinic team saw 35 patients with FGIDs and referred 33 patients to BH; 19 went on to follow-up (57.6%). In both groups, the use of the ED after BH visits was low (0% joint, 4.6% GI, p=0.55). Patients referred to BH who did not follow-up used the ED at a similar rate, (5.3%, NS).

Conclusions: We observed that for patients with FGIDs, there was a relative increase in follow-up with BH after seeing the joint pediatrician/psychologist team rather than the GI subspecialists (+11.2%, p=0.51), but it was not statistically significant. For both groups of patients, there was less utilization of the ED if seen by BH. Where access and time are limited, management of FGIDs may be better served by implementing a joint clinic with a medical provider and a BH provider.

255 THE ROLE OF INFLAMMATION IN CELIAC DISEASE (CD). ARE HLA DQ2/DQ8 ASSOCIATED WITH CHRONIC ABDOMINAL PAIN (CAP)? Sona Young2, Stefano Guandalini2, Chandani Patel2, Jacob B. Lissoos6, Cenk K. Pusatcioglu1, Stijn Mintjens3, Miguel Saps1, 1Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 2University of Chicago, Chicago, IL; 3Academic Medical Center, Amsterdam, Netherlands; 4Northwestern University, Chicago, IL

Background- CAP and abdominal pain (AP) predominant-functional gastrointestinal disorders (AP-FGIDs) are common in children. Pediatric studies found that infectious and non-infectious GI-inflammation increases the risk of developing CAP after the inflammation resolves. Children with AP-FGIDs with infection that resolves with gluten-free diet (GFD). If CD behaves similarly to other GI inflammations, children with CD should be more likely to develop CAP despite being on GFD. Studies found that DQ2/DQ8 genetic subtypes are associated with GI dysmotility in non-CD subjects. DQ2/DQ8 is more prevalent in CD siblings than general population. No adult or pediatric studies have assessed the prevalence of CAP in non-CD DQ2/DQ8 subjects. Aims: Compare the prevalence of CAP in CD patients on GFD, healthy siblings (HS) and healthy controls (HC). Hypothesis: 1- CAP is more common in children with CD on GFD than non-related HC. 2- CAP is more common in HS than HC. Methods- Three groups of children (CD-GFD for >6 months, HS, HC) completed the Questionnaire Pediatric Gastrointestinal Symptoms-Rome III (QPGS-RIII) to diagnose AP-FGIDs. Sample-size: Based previous studies, prevalence of CAP (CD-GFD 24.5%, HC 7%), 53 children in each arm, power=0.80, alpha=0.05. Results- 53 children in each group. CD (11.4±3.3 years, 32 females), HS (10.5±3.2 years, 30 females), HC (11.2±3.1 years, 30 females). Prevalence CAP: CD-19%, HS-17%, HC-11%. CD vs. HS (p=1.00), CD vs. HC (p=0.42), HS vs. HC (p=0.58). Prevalence AP-FGIDs: CD (4%), HS (8%), HC (0%) (NS). NS difference in pain location, stool characteristics and interference with daily activities between 3 groups. Conclusions- Prevalence of CAP in CD-GFD and HS is similar. Children with CD-GFD and HS have higher prevalence of CAP than HC but difference NS. Sample size estimate may explain NS. If larger studies find significant difference in CAP prevalence between the groups of CD-GFD and HS compared to HC, it would suggest that DQ2/DQ8 and not post-inflammatory changes can explain symptoms.

256 A NEW COMBINED CLINICAL ENDPOINT FOR CLINICAL TRIALS IN ABDOMINAL PAIN FUNCTIONAL GASTROINTESTINAL DISORDERS (AP-FGIDs) IN CHILDREN. Miguel Saps, Cenk K. Pusatcioglu, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

Background- There are no validated primary clinical endpoints for clinical trials in FGIDs. The Food and Drug Administration (FDA) and European Medical Agency (EMA) proposed 30% improvement in intensity in abdominal pain (AP) for adults with IBS. There are no endpoints for clinical trials in children. The use of the FDA and EMA endpoints in children has been criticized as 30% improvement does not reflect changes in disability (an important outcome in children with AP-FGIDs) and not all children meeting the EMA-FDA proposed criteria reported feeling better when asked to summarize their progress. These problems suggest that alternative endpoints should be used. We propose a combined endpoint. We analyzed changes in disability and somatization in children who met 30% improvement in AP but also reported feeling better at the end of the study using a global satisfactory relief question that
was previously validated in studies in adult patients with IBS. **Methods**- This is a secondary analysis of a database of children that participated in a randomized placebo controlled parallel clinical trial on amitriptyline for AP-FGIDs. Children completed daily questionnaires that included questions on disability and a visual analog scale (VAS) daily during run-in period and intervention. At the end of the study children completed questionnaires that included a question on satisfactory relief (worse, same, better). Answers to this question were analyzed in a binary fashion. Subjects also completed a set of validated questionnaires that included disability at entry and end of study (Functional Disability Inventory, FDI) and somatization (Children Somatization Inventory, CSI). Results of children who reported feeling better and had an improvement greater than 30% from run-in period to last week of study were compared with those of children who did not meet both criteria. **Results**- 67 children completed the study and had complete information for the analysis. 26 (39%) children met both criteria while the rest did not. There was no statistical difference in age or gender between both groups: met criteria 12.5 ± 3.1 years, 73% females, did not meet criteria 12.5 ± 2.7 years, 63% females. 18 out 26 (69%) children met a minimal clinical difference (MCID) proven to be reliably calculated based on RCI for this sample and measure (95% confidence interval for change scores based on the test-retest reliability of VAS measure). Children meeting both endpoints had >30% improvement in FDI in 19 (73%) cases vs. 20 (48%) in children who did not meet both endpoints (p<0.05) and a decrease in somatic complaints scores based on validated questionnaire (CSI) 9.1 ± 10.6 vs. 4.6 ± 6.9 (p<0.05). **Conclusions**- The study suggests that the combination of 30% improvement in AP with a positive response to a question of satisfactory relief could be used as primary efficacy endpoints in trials. Larger studies are needed to confirm our findings.

**257 COPING PREDICTS PSYCHOSOCIAL OUTCOMES IN BOTH IBD AND FAP PATIENTS.** Miranda A. van Tilburg1, Robyn Claar1, Joan Romano3, Shelby Langer5, William E. Whitehead1, Bisher Abdullah2, Dennis Christie4, Rona Levy5, 1Department of Gastroenterology and Hepatology, University of North Carolina, Chapel Hill, NC; 2Prime Health Clinic Tacoma, Puyallup, WA; 3Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA; 4Division of Gastroenterology, Seattle Children's Hospital, Seattle, WA; 5School of Social Work, University of Washington, Seattle, WA

**Background:** Two common gastrointestinal disorders (GI) in children are Inflammatory Bowel Disease (IBD) and Functional Abdominal Pain (FAP). Both carry a high risk for depression, and disability. It is not yet known what factors influence development of these negative psychosocial outcomes and if these factors vary by disorder. We hypothesized that both symptom severity and how children cope with symptoms are important factors in determining outcomes. The aim of the current study was to examine if children with FAP and IBD differ in coping and if coping predicts depression and disability independent of symptom severity. **Methods:** Subjects were N=200 children with FAP (72% girls; 86% Caucasian; Mean age 11.2) and N=189 children with IBD (49% girls; 79% Caucasian; Mean age 13.8). Given age and gender differences between samples, all analyses were controlled for age and gender. Children completed the Pain Response Inventory (PRI), the Children's Depression Inventory, the Functional Disability Inventory, and a measure of IBD or FAP symptom severity. The PRI measures three forms of coping: active coping which aims to directly change the situation, accommodative coping which focuses on adjusting to the situation and passive coping which is characterized by withdrawal and dependence. **Results:** Compared to IBD patients, FAP patients scored higher on passive coping (Mean= 1.2 vs 0.8; p <.001) and active coping (Mean=2.2 and 1.9, p<.05); no differences were found for accommodative coping. Regression analyses revealed that passive coping significantly predicted disability while both passive and active coping predicted depression when controlling for GI symptoms (see Table) explaining 36-51% of the variance across outcomes. Separate analyses including all passive and active subscales indicated that passive coping (most importantly catastrophizing and social isolation) was associated with depression and disability. Only one active subscale (seeking social support) was negatively associated with depression in IBD. **Conclusion:** FAP patients are more likely to use passive and active coping than IBD patients. Passive coping, in particular catastrophizing and social isolation, was associated with poor outcomes independent of symptom severity. In fact, symptoms were not a significant predictor of depression in IBD, but coping was. Clinicians should monitor patients' catastrophizing (expecting the worst) and social isolation, which may be risk factors for poor psychosocial and functional outcomes in both patient groups.
Table: Regression analyses: Passive coping and symptoms predicting outcomes.

<table>
<thead>
<tr>
<th>Symptom or Coping Strategy</th>
<th>Depression</th>
<th>Functional Disability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F = 26.3 p &lt; 0.001</td>
<td>F = 33.9 p &lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>R² = 0.45</td>
<td>R² = 0.51</td>
</tr>
<tr>
<td>IBD or FAP symptoms</td>
<td>β = 0.07</td>
<td>β = 0.44***</td>
</tr>
<tr>
<td>Passive Coping</td>
<td>β = 0.65***</td>
<td>β = 0.38***</td>
</tr>
<tr>
<td>Active Coping</td>
<td>β = -0.13*</td>
<td>β = 0.02</td>
</tr>
<tr>
<td>Accommodative Coping</td>
<td>β = -0.02</td>
<td>β = -0.04</td>
</tr>
</tbody>
</table>

*p < .05; **p < .01; ***p < .001

258* LIQUID GASTRIC EMPTYING AND PLASMA GHRELIN IN CHILDREN WITH FUNCTIONAL DYSPEPSIA, POST-PRANDIAL SUBTYPE. Nadia Hijaz1, Robin E. Pearce2, Susan M. Abdel-Rahman2, Jennifer Schurman1, Craig A. Friesen1, Gastroenterology, Children’s Mercy Hospital, Kansas City, MO; 2Division of Clinical Pharmacology and Therapeutic Innovation, Children’s Mercy Hospital, Kansas City, MO; 3Division of Developmental & Behavioral Sciences, Children’s Mercy Hospital, Kansas City, MO

Introduction: Post-prandial distress syndrome (PDS) is a functional dyspepsia (FD) subtype described in adults that has been associated with low basal ghrelin, altered post-prandial ghrelin responses, and delayed liquid gastric emptying (GE). Some evidence exists to suggest that the PDS subtype also may be meaningful in children, but plasma ghrelin and its relation to liquid emptying have not yet been investigated in children fulfilling PDS criteria.

Methods: Ten pediatric patients (M age = 12.9 ± 3.8 yr, mean BMI 19.3 ± 3.2 kg/m²) diagnosed with FD who also fulfilled PDS criteria and 17 healthy controls (M age = 12.2 ± 2.9 yr, mean BMI 20.2 ± 2.6 kg/m²) were evaluated. Plasma acyl ghrelin (AG) and desacyl ghrelin (DG) were measured at baseline and at 20, 40, and 60 minutes after intake of a liquid meal. All participants underwent measurement of liquid gastric emptying utilizing 13C-sodium acetate breath tests (ABT). Breath samples were collected for 13CO2 concentration measurements at baseline and up to 13 time points over 240 min. PK modeling was performed to determine: 1) the cumulative area under the curve of delta over baseline (AUC 60), 2) cumulative percent of dose recovered (PDR) at 20, 40, and 60 minutes, and, 3) the time to maximum DOB concentration (Tmax).

Results: Baseline AG was significantly lower in FD patients compared to controls (14.2 ± 9.5 vs. 26.9 ± 14.0 fmol/mL, p < 0.01) as was the baseline AG/DG ratio (0.05 ± 0.32 vs. 0.32 ± 0.25, p = 0.035). In controls, AG was significantly decreased from baseline (26.9) at 20 (17.2; p < 0.01), 40 (13.39; p < 0.01), and 60 (16.69; p < 0.05) minutes; in contrast, no significant decrease was observed from baseline in FD patients at any time point measured. In controls, the AUC 60 was significantly correlated with baseline DG (r = 0.75, p < 0.001), as well as DG at 20 (r = 0.64; p < 0.01), 40 (r = 0.71; p < 0.01), and 60 (r = 0.7; p < 0.01) minutes, respectively. AUC 60 was negatively correlated with the AG/DG ratio (r = -0.49; p < 0.05). No significant relationships between AUC 60 and ghrelin were found in FD patients. In controls, PDR at 40 minutes correlated with DG at baseline (r = 0.66; p < 0.01), as well as at 20 (r = 0.54; p < 0.05), 40 (r = 0.63; p < 0.05), and 60 (r = 0.61; p < 0.05) minutes. PDR at 40 minutes also correlated negatively with the AG/DG ratio (r = -0.58; p < 0.05). In FD patients, PDR had no relationship to DG concentration at any time point measured. However, AG at 20 minutes correlated with PDR at 20 (r = 0.76; p < 0.05), 40 (r = 0.85; p < 0.01), and 60 (r = 0.79; p < 0.05) minutes for FD patients. Tmax was significantly longer in FD patients (48.89 ± 18.84 compared to controls (35.76 ± 11.77; p < 0.05). AG/DG was positively correlated with Tmax in controls (r = 0.58; p < 0.05) and negatively correlated with Tmax in FD patients (r = -0.68; p < 0.05).

Conclusions: FD-PDS subtype in pediatric patients is associated with lower baseline AG and AG/DG ratio compared to controls, as well as a loss of the normal post-prandial decrease in AG observed in controls. Relationships between GE and ghrelin differ significantly between children with FD-PDS and controls. These data suggest a role for altered ghrelin physiology in the pathogenesis of FD.

259* PH IMPEDANCE FINDINGS IN THE AERODIGESTIVE PATIENT. Rayna Grothe1, Ahmad Alsafadi1, Paul Boesch1, Shelagh Cofer2, Laura Orvidas3, Erin Knoebel3, Isabelle Krisch3,1Pediatric Gastroenterology, Mayo Clinic, Rochester, MN; 2Otorhinolaryngology, Mayo Clinic, hester, MN; 3Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN Objective: The Pediatric Aerodigestive Clinic is a multi-specialty and patient-centered 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),

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microlaryngobronchoscopy (MLB) and flexible bronchoscopy as well as a pH impedance study to evaluate the possible causes of symptoms and disease. Esophageal biopsies and bronchoalveolar lavage with cultures are done to assess for inflammation. The objective of the study was to determine association of acid and nonacid impedance events with 1) upper airway findings of laryngeal edema (LE), vocal cord edema (VCE) and upper airway cobblestoning (UAC) 2) bronchoscopy findings of visual bronchitis and positive bronchial cultures 3) visual esophageal inflammation on EGD.

Methods: We retrospectively reviewed the charts of 80 aerodigestive patients who received a triple scope and pH impedance study on the same day of their evaluation occurring between September 2012 and March 2014. pH impedance results were analyzed using Sandhill software for total reflux events, total acid and nonacid events, proximal acid and nonacid events, and Boix-Ochoa score. Wilcoxon nonparametric tests were used to determine the association of impedance events and Boix-Ochoa score to airway and esophageal findings.

Results: Total reflux events and acid reflux events were positively associated with visual esophageal inflammation (p.002 and p.004). Total reflux events, acid reflux events, and nonacid reflux events were not associated with upper or lower airway findings. The Boix-Ochoa score was associated with esophageal visual inflammation (p.008) and with VCE (p.037), but not with LE, UAC, visual bronchitis or positive bronchial culture. Proximal acid reflux events were not associated with upper or lower airway findings. Proximal nonacid reflux events were associated with VCE but not LE, UAC, bronchitis or positive cultures.

Conclusions: Proximal nonacid reflux events were associated with VCE only, suggesting a role of nonacid reflux in upper airway inflammation. Proximal acid and distal acid and nonacid impedance events were not associated with evidence of lower or upper airway inflammation. The Boix-Ochoa score which reflects length of acid exposure as well as number of acid reflux events was associated with upper airway inflammation (VCE only). Gastroesophageal reflux (GER) is more likely to be associated with upper airway inflammation rather than lower airway disease. This suggests that GER alone is not sufficient to cause lower respiratory tract inflammatory disease. Future studies may elucidate in which situations GER may cause or exacerbate lower airway disease.

RELATIONSHIP BETWEEN ADHD SYMPTOMS AND PROBLEMATIC TOILETING BEHAVIOR IN CHILDREN WITH FECAL INCONTINENCE. Rose L. Schroedl1, Anthony Alioto1, Anita Fouch2, Carlo Di Lorenzo2, 1Psychology, Nationwide Children's Hospital, Columbus, OH; 2Gastroenterology, Hepatology and Nutrition, Nationwide Children's Hospital, Columbus, OH

Pediatric defecation disorders are a chronic condition which account for 25% of gastroenterology clinic visits and occur in 1%-8% of children. The association between Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms and fecal incontinence is well established. Studies have found that 37% of children with fecal incontinence exhibit attention/hyperactivity symptoms and 9% carry the diagnosis of ADHD. Moreover, there is evidence that children with comorbid ADHD and fecal incontinence have a poorer response to medical/behavioral treatment. However, little is known about how the presence of ADHD symptoms may impact problematic toileting behaviors which are commonly the target of fecal incontinence treatment. The current study evaluated the relationship between ADHD symptoms and problematic toileting behaviors in children with fecal incontinence.

A chart review was conducted on 77 patients seen from May 2009-May 2010, in a specialized gastroenterology clinic for children with fecal incontinence. The Eyberg Children's Behavior Inventory (ECBI), a screening measure of externalizing behavior problems, was completed by caregivers to assess the presence of ADHD symptoms. Patients were classified into two groups (symptomatic group and non-symptomatic group) based on clinical cut-off scores on the ECBI attention problems subscale. Caregivers completed a clinic developed toileting behaviors questionnaire, which assesses the presence of problematic toileting behaviors which are clinically relevant for treatment. Questions selected for analysis included: 1) frequency of fecal incontinence episodes per day, 2) if the child argues when completing sit times, 3) if the child has difficulty taking medication, 4) if the child senses urgency for stool and 5) if child notices if underwear is soiled.

Participants were 75% male with a mean age of 7.9 years (SD= 2.9). Thirty-six percent of participants had scores above the clinical cut-off for ADHD symptoms. The symptomatic group did not differ significantly from the non-symptomatic group across all toileting behaviors (Table 1). The prevalence rate for ADHD symptoms found in this clinical sample of children with fecal incontinence is similar to previously reported prevalence rates. The presence of ADHD symptoms was not related to the presence of problematic toileting behaviors, suggesting that children with ADHD symptoms and fecal incontinence exhibit similar problematic toileting behavior as children without ADHD symptoms. Further investigation into the ADHD-specific behavioral factors, such as attending to bodily sensations and stopping tasks to use the toilet, is needed to better understand the link between ADHD, fecal incontinence and treatment outcomes.
Comparison of Symptomatic and Non-Symptomatic Groups

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic</th>
<th>Non-Symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of Accidents/day (M, SD)</td>
<td>2.3(5.4)</td>
<td>3.5(.85)</td>
</tr>
<tr>
<td>Senses urgency for stool</td>
<td>46%</td>
<td>58%</td>
</tr>
<tr>
<td>Notices when underwear are soiled</td>
<td>68%</td>
<td>65%</td>
</tr>
<tr>
<td>Arguing during sit times</td>
<td>79%</td>
<td>86%</td>
</tr>
<tr>
<td>Difficulty taking medication</td>
<td>22%</td>
<td>26%</td>
</tr>
</tbody>
</table>

261 ROLE OF BIOFEEDBACK IN PEDIATRIC PATIENTS WITH FUNCTIONAL CONSTIPATION. Rupinder K. Gill1, Brenda Mapes2, Grace Walker2, Anupama Chawla1,1 Pediatric GI, Stony Brook University, Stony Brook, NY; 2Motility, Stony Brook University, Stony Brook, NY

Constipation affects up to almost 30% of children and over 90% of the cases are secondary to functional constipation (FC). Standard of medical care consists of stool softeners, laxative therapy, fiber supplements and increased intake of dietary fiber along with behavioral therapy. However, over 50% of the patients remain symptomatic despite aggressive medical and behavioral therapy. Over half of the patients with FC suffer from dyssynergic defecation. Pelvic floor retraining/biofeedback involves training the right use of the pelvic floor muscles in patients with dyssynergic defecation. We present a case series of 7 patients (6 males and 1 female) who all presented with FC with a duration ranging from 2-7 years. All patients underwent high-resolution anorectal manometry (HRAM) and were noted to have dyssynergic defecation and referred for biofeedback (BF) therapy. The time to referral to BF from initial presentation to a pediatric gastroenterologist ranged from 1-17 months. Each patient was on miralax in addition to either laxative or fiber supplements. 3 of the 7 patients were also followed by a behavioral psychologist specializing in functional constipation. Each patient underwent 3-5 sessions of BF. Only 3 of the 7 patients had follow-up visits after finishing the BF sessions and reported an improvement in their symptoms. The remaining 4 patients reported symptomatic improvement during their biofeedback sessions but had no follow-up in the clinic. We conclude that BF therapy in conjunction with standard medical therapy is likely more effective than standard medical and behavioral therapy alone in pediatric patients with FC.

262 DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EXAMINE THE EFFECTS OF DIETARY FIBER IN TREATING CHILDHOOD CONSTIPATION. Sabeen A. Syed, Warren Bishop, Fariha Ilyas, Riad Rahhal, Pediatrics, USA Children's and Women Hospital, Mobile, AL

Background: Constipation accounts for 3% of general pediatrics visits and 25% of gastroenterology visits. Few randomized control trials have been done to study the effect of different types of fiber on stool consistency and frequency in children with constipation.

Hypotheses: The addition of fiber can be beneficial in the treatment of functional constipation in children by allowing children to have more normal stool consistency and frequency.

Methods: This was a prospective double-blind, placebo-controlled 4-week long study. 35 children between ages 2-16 years who meet Rome III criteria for functional constipation were enrolled. All subjects received a rice-based snack bar once daily for four weeks. Children were randomized in a 1:1:1 ratio to placebo bars, or bars containing soluble corn fiber or another soluble fiber, inulin. Snack bars were indistinguishable in taste and texture between groups, and labeling did not reveal fiber content. All participants were asked to take low-dose Miralax (0.3g/kg/day) to avoid worsening of constipation in all groups. Adjustment of Miralax dosing was allowed after week 2 as required to soften stools. During the prestudy period, baseline characteristics, quality of life scores and a 3-day diet diary were obtained. During the study period, families completed a weekly online diary via internet link on RedCap. At the end of the study, all characteristics of interest were reassessed, and analysis was performed.

Results: At baseline, groups were comparable in age, weight and quality of life scores. All groups had an increase in weekly stool frequency and improvement in stool consistency. Subjects in both fiber groups required lower daily Miralax doses compared to the placebo group to achieve these results. There was no significant increase in bloating, belching or excessive gassiness in subjects receiving either fiber type.

Conclusion: The addition of dietary fiber can assist in the treatment of functional constipation in children leading to more frequent and softer stools and less reliance on osmotic laxative therapy.
263 HOW USEFUL IS AN UPPER GASTROINTESTINAL SERIES (UGI) IN DIAGNOSING GASTROESOPHAGEAL REFLUX DISEASE WHEN COMPARED TO THE GOLD STANDARDS? Sarah Kinder, Jeremy Prager, Jason Soden, Emily Deboer, Robin Deterding, Ben Corbett, Sparrow Helland, Amanda Ruiz, Emily Jensen, Joel Friedlander, 1Breathing Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO; 2Department of Pediatric Otolaryngology, University of Colorado School of Medicine, Children's Hospital Colorado, Aurora, CO; 3Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO; 4Aero-Digestive Program, Children's Hospital Colorado, Aurora, CO; 5Department of Pediatric Radiology, Children's Hospital Colorado, Aurora, CO

**Background:** The upper gastrointestinal series (UGI) is a commonly ordered radiographic study. Although numerous studies have revealed its poor accuracy in diagnosing gastroesophageal reflux (GERD), many pediatric providers still order the UGI for suspected GERD. Inaccurately diagnosing a patient with GERD by UGI may expose a patient to increased costs of care, unnecessary antacid use, additional radiation and potentially anti-reflux procedures. Although GERD can be diagnosed clinically, the gold standard remains the pH probe and more recently the pH Impedance probe (pHI). Previous research demonstrates the superiority of pH evaluations as compared to UGI. However, these studies have not evaluated the pH and UGI in a designated time frame for increased accuracy and reliability, nor have they utilized endoscopic biopsy results.

**Purpose:** To identify the sensitivity and specificity of the UGI study in predicting GERD as compared to pHI results and esophageal biopsies within a narrow time frame of 30 days in all patients referred to the Aero-Digestive Clinic (a multi-disciplinary clinic that includes ENT, GI and Pulmonary physicians).

**Methods:** Retrospective chart review of 331 patients that have participated in the Aero-Digestive Clinic at the Children’s Hospital Colorado from 2010-2013. Eligible patients needed to have an UGI and pHI completed within 30 days of each other. Data was also collected from esophagogastroduodenoscopy (EGD) if available within the same time. A pH was interpreted as abnormal if there was pathologic esophageal acid exposure (percent time with pH below 4), a reflux symptom correlation of over 50%, or an increased number of bolus reflux events (greater than 100 events/24 hours if less than 1 year of age or greater than 50 events/24 hours in patients over 1 year). Biopsy results from EGD were abnormal if esophageal inflammation was present and not otherwise attributable to active infection or eosinophilic esophagitis.

**Results:** 53 patients had both an UGI completed and a pHI completed within 30 days. 51 of 53 (96%) also had an EGD completed within the same time frame. 15 of the UGI studies were reported as positive for “reflux.” Of the patients that had an abnormal UGI, 7 of 15 showed GERD based on either abnormal pH result and/or abnormal biopsies. This demonstrates the sensitivity of the UGI to be 37% with a specificity of 76%. Of the 53 patients undergoing UGI, 34/53 (64%) were on acid suppression medication (either PPI or H2RA). The UGI was normal in 38 patients, 12 of whom had pathologic GERD based on either biopsy results or an abnormal pH. Of those 38 patients with normal UGIs, the remaining 26 patients had a normal EGD / pH results which led to a negative predictive value of 68%. The PPV of the UGI was 47%.

**Conclusions:** As previous studies have shown, the sensitivity of the UGI for the accurate prediction of GERD is poor, but its specificity is tolerable. In our experience with this patient population the use of an upper GI series should be limited to evaluate for anatomic abnormalities and should not be used to determine whether a patient has GERD.

<table>
<thead>
<tr>
<th>Test Result</th>
<th>EGD (esophageal biopsy) or pH Impedance Probe Positive</th>
<th>EGD (esophageal biopsy) or pH Impedance Probe Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>UGI study positive</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UGI study negative</td>
<td>12</td>
<td>26</td>
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</table>

264* ANALYSIS OF EXHALED VOLATILE ORGANIC COMPOUNDS REVEALS NEW BIOMARKERS FOR IRRITABLE BOWEL SYNDROME. Sophia A. Patel, Nishaben Patel, Vera Okwu, Ammar Matloob, David Grove, Ellen Rome, Raed Dweik, Naim Alkhoury, Pediatric GI, Cleveland Clinic Children’s, Cleveland, OH; Cleveland Clinic, Respiratory Institute, Cleveland, OH; Pediatrics, Cleveland Clinic Children’s, Cleveland, OH

**Objectives:** Irritable bowel syndrome (IBS) is a common problem encountered in pediatric gastroenterology. Patients with IBS often undergo extensive testing including costly and invasive endoscopic, radiographic, histologic and laboratory workup. The aim of this study was to analyze exhaled volatile organic compounds (VOCs) in patients with IBS vs those of healthy controls as a noninvasive screening tool.

**Methods:** An IRB approved prospective study was conducted at a tertiary center. Patients (age range, 6-21 years) with IBS were identified through an electronic medical record search and were recruited in the Pediatric Gastroenterology Clinic. Controls were recruited through the hospital’s healthy volunteer registry, and were matched to patients by age and sex. Exhaled breath samples were collected using a customized device and analyzed using gas chromatography-mass spectrometry (GC-MS) for VOCs.

**Results:** A total of 38 patients with IBS and 38 healthy controls were enrolled in the study. The most common VOCs identified in patients with IBS were 2-butanone, 3-methyl-1-butanol, and 3-butanol. These VOCs were significantly increased in patients with IBS compared to controls. Additionally, a classifier model was developed to predict the presence of IBS with an accuracy of 76%.

**Conclusions:** The analysis of exhaled volatile organic compounds reveals new biomarkers for irritable bowel syndrome. These findings suggest that exhaled VOCs may serve as a noninvasive screening tool for IBS.
documented IBS according to the Rome III criteria were recruited from the Pediatric Gastroenterology Clinic. Healthy controls were recruited during well-child visit from the General Pediatric Clinic. Exhaled breath was collected and analyzed using a selective ion flow tube (SIFT-MS) to identify new markers or patterns of IBS.

**Results:** 77 total patients were evaluated (22 with IBS and 55 healthy controls), 52% were female and the majority were Caucasian. The control group was significantly more likely to be male (p=0.04), and the IBS group was significantly more likely to have a higher BMI percentile, 67.8 percentile vs 55.7 percentile (p=0.03). Analysis of VOCs by SIFT-MS showed significant increases in IBS patients compared to healthy controls in the following compounds: benzene (2.9ppb vs 1.9ppb, p=0.02), dimethyl sulfide (3.2ppb vs 1.3ppb, p=0.01), 1-octene (10.3ppb vs 5.9 ppb, p=0.026), and 3-methylhexane (33.3 ppb vs 16.4 ppb, p=0.015). Discriminant analysis via stepwise variable selection of mass scanning ion peak data showed 3 misclassified patients (4.2%) with a likelihood ratio of 17.5. The analyzed VOCs showed good accuracy for diagnosing IBS with an area under the ROC curve of 0.99.

**Conclusions:** Children with IBS have a unique pattern of breath VOCs that distinguishes them from healthy controls. Exhaled benzene, dimethyl sulfide, 1-octene, and 3-methylhexane are significantly elevated in patients with IBS. Analysis of exhaled VOCs may be a promising noninvasive screening tool in diagnosis of IBS in pediatric patients.

**265 BOTULISM TOXIN INJECTION TO THE INTERNAL ANAL SPHINCTER IS EFFECTIVE IN TREATING INTRACTABLE CONSTIPATION IN CHILDREN WITH DYSSYNERGIC DEFECATION.** Yamen Smadi, Shaista Safder, Jeffrey A. Bornstein, Devendra Mehta, Center For Pediatric Digestive Health and Nutrition, Orlando Health, Orlando, FL

**INTRODUCTION:** Dyssynergic defecation [DD] defined as failure to relax pelvic floor during defecation is a common cause of intractable constipation in children. Biofeedback helps in improving the symptoms. Patients who fail BF treatment might benefit from botulism toxin [BoTox] injection to the internal anal sphincter. **OBJECTIVES:** To study the long-term effect of internal anal sphincter injection with [BoTox] on intractable constipation in children with dyssynergic defecation disorders who failed behavioral biofeedback therapy. **METHODS:** We conducted a retrospective review of children who received anal sphincter [BoTox] at a tertiary medical center. Children with DD were included and they were classified into two long-term clinical outcome groups (Improvement and failure). Children who received [BoTox] were compared with children who failed biofeedback treatment and did not receive [BoTox]. **RESULTS:** A total of 15 children [10 males] [Mean age 9.5 years, range 6-16 years] received anal sphincter [BoTox] injections. Four children with Hirschsprung's disease were excluded and 11 children with DD were included. Two children out of 11 have anal achalasia. Two children received two sessions of [BoTox] injection and the rest received only one session. Mean follow-up was 13 months [range 7-30 months]. Improvement was seen in 8 out of 11 children (72 %) after the injection. Two children out of three in the failure group required surgical intervention [one colectomy and one antegrade continent enema (ACE)]. No long-term side effects were reported. None of the children who failed biofeedback and did not receive [BoTox] [n=15] has improved. **CONCLUSIONS:** Anal sphincter [BoTox] may be an effective and safe long-term therapy for children with dyssynergic defecation who failed biofeedback therapy.

**Liver**

**276 ARGINASE 2 DEFICIENCY RESULTS IN SPONTANEOUS STEATOHEPATITIS: A NOVEL LINK BETWEEN INNATE IMMUNE ACTIVATION AND HEPATIC DE NOVO LIPOGENESIS.** Laura A. Navarro, Alexander Wree, Davide Povero, Michael P. Berk, Sudakshina Ghosh, Bettina G. Papouchado, Serpil C. Erzurum, Ariel Feldstein, Department of Pediatrics, UCSD, La Jolla, CA; 2Department of Cellular and Molecular Medicine, Lerner Research Institute Cleveland Clinic, Cleveland, OH; 3Department of Pediatrics, University of Pittsburgh Medical Center, Pittsburgh, PA; 4Department of Pathobiology, Lerner Research Institute Cleveland Clinic, Cleveland, OH; 5Department of Pathology, UCSD, La Jolla, CA

**BACKGROUND & AIMS:** Innate immune activation has been postulated as a central mechanism for disease progression from hepatic steatosis to steatohepatitis in obesity-related fatty liver disease. Arginase 2 competes with inducible nitric oxide synthase (iNOS) for its substrate and the balance between these two enzymes plays a crucial role in regulating immune responses and macrophage activation. Our aim was to test the hypothesis that arginase 2 deficiency in mice favours progression from isolated hepatic steatosis, induced by high fat feeding to steatohepatitis. **METHODS:** Arginase 2-knockout (Arg2−/−) mice were studied for changes in liver histology and metabolic phenotype at baseline and after a short term course (7 week) feeding with a high fat (HFAT) diet. In additional experiments, Arg2−/− mice received tail vein injections of liposome-encapsulated clodronate (CLOD) over a three-week period to selectively deplete liver macrophages. **RESULTS:** Unexpectedly, Arg2−/− mice showed profound changes in their livers at baseline characterized by significant steatosis as demonstrated with histological and biochemical analysis. These changes were independent of systemic metabolic parameters and associated with marked increase mRNA levels of genes involved in hepatic de novo lipogenesis. Liver injury and inflammation were present with elevated serum ALT, marked infiltration of F4/80 positive cells, and increased mRNA levels of inflammatory genes. HFAT feeding exacerbated these changes. Macrophage depletion after CLOD injection significantly attenuated lipid deposition and normalized lipogenic mRNA profile of livers from Arg2−/− mice. **CONCLUSIONS:** This study identifies arginase 2 as novel link between innate
immune responses, hepatic lipid deposition, and liver injury.

277 REAL-LIFE MANAGEMENT OF CHRONIC VIRAL HEPATITIS IN CHILDREN. Ana Catalina Arce-
Clachar, Vera Hupeertz, Kadakkal Radhakrishnan, Naim Alkhouri, Cleveland Clinic, Shaker Heights, OH

BACKGROUND: The management of chronic hepatitis B and C in adults has been revolutionized by the development of direct-acting antivirals. Children with chronic viral hepatitis differ from adults in the mode of transmission, progression to chronic disease and its complications, but mainly differ in the management due to the limited drugs available for children. The aim of our study is to assess the clinical characteristics and management of children with chronic hepatitis B and C in the real-life settings outside of clinical trials.

METHODS: This is a retrospective study, that included all children with chronic hepatitis B or hepatitis C followed at our institution. Demographic, clinical, laboratory and pathologic data were collected, and management strategies were obtained.

RESULTS: Of a total of 29 patients, 12 were diagnosed with chronic hepatitis B and 17 with chronic hepatitis C. Hepatitis B patients had a mean age at diagnosis of 2.57 years, with main mode of transmission being vertical (91%). At diagnosis, the mean viral load was 268,523 IU/ml, 42% were immune active, 33% inactive carrier and 25% immune tolerant. Nine had a liver biopsy, 4 showed mild fibrosis, 1 bridging fibrosis, 4 mild inflammation and 4 moderate inflammation. None had steatosis or cirrhosis. Eight patients were treated, 50% received lamivudine monotherapy, 25% had a combination with lamivudine and interferon, 12.5% had interferon monotherapy and 12.5% had lamivudine plus adefovir. Main side effects were fever, fatigue and weight loss. Four patients (50%) achieved HBeAg seroconversion and of these, 1 achieved HBsAg seroconversion. Virologic and biochemical response was achieved in 75% of the patients treated and 25% developed resistance. Of the 17 hepatitis C patients, the mean age at diagnosis was 7.4 years. The mode of transmission was vertical in 76.47%, blood transfusion in 5.88% and IVDU in 17.64%. At diagnosis, mean viral load was 1,785,725 IU/ml. Thirteen patients were genotype 1 (4 subtype a, 4 subtype b and 5 did not have a subtype available), 2 were genotype 3a, 1 was genotype 6 and 1 patient did not have a genotype available. Liver biopsies were performed in 12 patients, 7 with periportal fibrosis, 1 with few septae, 9 with mild inflammation and 1 with moderate inflammation. None had steatosis or cirrhosis. Only 6 patients were treated, of which 4 received peg-interferon plus ribavirin, 1 had peg-Interferon, ribavirin and boceprevir and 1 had peg-interferon, ribavirin and amantadine. Mean duration of treatment was 36 weeks and main side effects were fever, fatigue and neutropenia. Two patients achieved RVR, EVR and SVR. Two patients relapsed and 2 had null response.

CONCLUSIONS: Children with hepatitis B and C are challenging to manage. Most of the current available therapies are directed to the adult population and only few medications have been approved in children. New emerging antiviral therapies can bring new options for these children.

278 ASSOCIATION BETWEEN HEPATITIS C VIRUS INFECTION AND BIOMARKERS OF VASCULAR
DYSFUNCTION IN CHILDREN AND YOUTH. Andrea Barreto1, Michelle K. Godbee1, Roshan Raza1, Elsa Yumar1, Betania Negre1, David A. Ludwig1, Maureen M. Jonas2, Raymond T. Chung2, Aymin Delgado-Borrego1,2,1 University of Miami Miller School of Medicine, Miami, FL; 2Harvard Medical School, Boston, MA

Background and Aims: Hepatitis C virus (HCV) infection is associated with a pro-inflammatory state. Inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) have been shown to be elevated in HCV infected adults. In addition, HCV has been noted to increase the levels of certain biomarkers of vascular dysfunction including soluble intracellular cell adhesion molecules (sICAM) and soluble vascular cell adhesion molecules (sVCAM). These adhesion molecules are associated with the development of atherosclerotic lesions at an early age, suggesting a risk for cardiovascular disease. We performed a cross sectional study to compare biomarkers of vascular dysfunction and other inflammatory cytokines between HCV infected (+) children and uninfected (-) controls.

Methods: A total of 105 children and young adults (mean age=16.0, SD=6.1) from Boston Children's Hospital and the University of Miami were included. Of these, there were 56 HCV infected subjects and 49 uninfected controls matched by age and body mass index (BMI) category. Forty-seven percent of the HCV+ subjects and 33% of the HCV- controls were male. Subjects were excluded if they were undergoing antiviral therapy or if they had other chronic illnesses. HCV viremia was confirmed by HCV ribonucleic acid testing. Logistic regression analysis was used to discriminate between HCV+ and HCV- subjects. Independent effects included gender, IL-6, TNF-α, sICAM, sVCAM, sP-Selectin and sE-Selectin, MCP-1, and HOMA2 IR. Logarithmic transformations were performed to correct for normality.

Results: In nominal logistic analysis, after univariate adjustment for gender, HCV status was independently associated with loge sVCAM (χ2(1) = 5.72, p = 0.0167) and loge sICAM (χ2(1) = 11.25, p = 0.0008). Five percent of the variance was unique to loge sVCAM and 10% to loge sICAM. HCV+ prediction tended to be sensitive (.84) and specific (.76). Total area under the curve was 86% and the full model generalized R² explained 27% of the HCV between group variance. None of the other independent variables demonstrated statistically significant associations with HCV status.

Conclusions: HCV infection creates an inflammatory environment capable of causing an increase in inflammatory cytokines and certain biomarkers of vascular dysfunction. We found a strong correlation between HCV status and
sICAM as well as sVCAM, with higher levels of these vascular dysfunction markers in the HCV+ group. These results suggest that HCV infection may represent a risk for cardiovascular disease even in the young. Further studies are warranted to address this possibility.

279 TRIGLYCERIDE AND GLUCOSE LEVELS AS POSSIBLE INDICATORS OF HOMA2-IR IN HEPATITIS C VIRUS INFECTED AND UNINFECTED CHILDREN AND YOUTH. Amanda Fifi1, Michelle K. Godbee1, Andrea Barreto1, Roshan Raza2, Elsa Yumar3, Betania Negre1, David A. Ludwig1, Maureen M. Jonas2, Raymond T. Chung3, Aymin Delgado-Borrego1,2, 1University of Miami Miller School of Medicine, Miami, FL; 2Harvard Medical School, Boston, MA

Background: Hepatitis C virus (HCV) infection is known to be associated with insulin resistance (IR), which in turn can lead to significant morbidity and worsened progression of liver disease. Currently, the homeostasis model of assessment (HOMA2-IR) is used for evaluation of IR. This test requires measurement of insulin which is costly and not always readily available. The combined use of other markers including triglycerides and glucose has been reported to correlate with HOMA2-IR in some adult cohorts (S. Petta et al. Journal of Viral Hep, 2011, 18, e372-380). We performed a cross-sectional study to evaluate the roles of triglyceride and glucose levels as predictors of HOMA2-IR among HCV infected (+) children and uninfected (-) controls.

Methods: A total of 90 children and young adults (median age: 17, SD =5.6) from Boston Children's Hospital and University of Miami Miller School of Medicine were included. Of these, there were 47 HCV infected subjects and 43 uninfected controls matched by age and body mass index (BMI) category. Forty-seven percent of the HCV+ subjects and 33% of the HCV- controls were male. Subjects were excluded if they were undergoing antiviral therapy or if they had other chronic illnesses. Fasting laboratory studies including glucose, lipid panel, and insulin were obtained. HCV positivity was confirmed by ribonucleic acid testing. Classification and Regression Trees (CART) analysis of HOMA2-IR using triglycerides, glucose, and HCV status was performed.

Results: The CART analysis indicated that the most discriminating variable was triglycerides ($R^2 = .144$). Subjects with high triglycerides ($\geq 73$ mg/dl) had a corresponding mean HOMA2-IR of 1.75 ($n = 50$) compared to 1.02 for subjects below the 73 mg/dl cut-point ($n = 40$). Within the high triglycerides group, positive HCV status ($n = 30$) had an associated mean HOMA2-IR of 1.96 compared to 1.43 for HCV- subjects ($n = 20$). The HCV status split increased the model $R^2$ value to .184. Those subjects with high triglycerides and HCV negative status were further subdivided at a glucose cut-point of 91 mg/dl (full model $R^2 = .242$). Mean HOMA2-IR for the low ($n = 13$) versus high ($n = 7$) glucose groups were 1.08 and 2.10, respectively.

Conclusions: Children and young adults with the highest risk of having a HOMA2-IR greater than the often-referenced 1.5 cutoff point fall into two groups: those with triglycerides levels greater than 73 mg/dl and with a positive HCV status, and those with triglycerides higher than 73 mg/dl, negative HCV status and glucose greater than or equal to 91 mg/dl. Children and young adults at low risk of having a HOMA2-IR below the 1.5 cutoff point also fall into two groups: those with triglycerides lower than 73 mg/dl, and those with triglycerides higher than 73 mg/dl, negative HCV status, and glucose lower than 91 mg/dl. In conclusion, triglyceride levels with or without glucose levels can be used to identify subjects at risk for IR in the HCV- and HCV+ youths respectively.

280 CHRONIC HEPATITIS B EPIDEMIOLOGY, GENETICS AND PHENOTYPES IN AN URBAN CHINESE IMMIGRANT PEDIATRIC POPULATION. Fernando J. Windemuller, Sadaf Saghier, Simon S. Rabinowitz, Hanh Vo, Steven Schwarz, Jiliu Xu, Pediatric Gastroenterology, SUNY Downstate, Brooklyn, NY

Background and aim: In adults with chronic hepatitis B virus (HBV) infection, viral factors including HBV e antigen (eAg) status, viral load, genotype, and specific mutations influence disease progression. Of 10 known HBV genotypes, genotypes A, the most prevalent in the US, and type B have higher rates of spontaneous eAg seroconversion, whereas types C and D are associated with higher risks for cirrhosis and progression to hepatocellular carcinoma (HCC). With the recent influx of Chinese immigrants into the urban US, the prevalence of non-A genotypes, particularly types B and C have been increasing. The aim of this study was to determine HBV genotypes, precore and basal core promoter (BCP) mutations, and their association with eAg serology, immune tolerance status and HCC among a cohort of children who recently immigrated to New York from China.

Methods: Thirty-one Chinese children with chronic HBV infection were followed at Children's Hospital at Downstate from July 2010 to May 2014. HBV serology, DNA levels, genotype, precore and BCP mutations were determined. Results: In all 31 patients (mean age: 12.2 years), only genotypes B (11/31, 35.5%) and C (16/31, 51.6%) were identified. In 4/31 (12.9%) the genotype was unknown. 3/11 (25.0%) genotype C and 0/10 in genotype B subjects exhibited precore mutation G1896A. 5/14 (37.6%) genotype B and 10/11 (90.9%) genotype C children were eAg positive. 1/6 (62.5%) in genotype C and 4/6 (66.7%) in genotype B were positive for persistent hypertransaminasemia. 1/6 (62.5%) in genotype B and 1/11 (9.1%) in genotype C developed HCC.

Conclusions: 1. HBV genotypes B and C are prevalent in patients of Chinese origin; 2. Similar to findings in adults, determining both HBV genotype and viral mutations in children with chronic HBV infections is important, to identify
those at risk for HCC; 3. The presence of precore or BCP mutations in genotype B or C demands close monitoring and consideration of early antiviral treatment; 4. AASLD guidelines which are based on HBV genotype A behavior, should be applied with caution to other HBV patients; 5. Considering increased Chinese immigration to the US, a multicenter study evaluating a larger patient cohort is warranted, to confirm our preliminary findings.

281  **EFFECTS OF PARENTERAL NUTRITION (PN) SOLUTIONS ON HEPATOCYTE VIABILITY AND LIPID METABOLISM.** Fernando J. Windemuller, Jiliu Xu, Simon S. Rabinowitz, Steven Schwarz, Pediatric Gastroenterology, SUNY Downstate, Brooklyn, NY

Introduction: The influence of intravenous lipid on development of PN-associated liver disease (PNALD) is well described. We recently reported, in an in vivo murine model, that lipid-free (i.e. high dextrose-containing) PN solutions increase hepatic steatosis, when compared with solutions containing carbohydrate + lipid (JPEN, in press). In the present study, we sought to examine the effects of lipid-free PN solutions on intracellular lipid metabolism, using an established, in vitro hepatocyte culture model.

Methods: Huh7 cells (an immortal hepatocellular carcinoma cell line) were cultured in standard media until achieving ~80% confluence. Cells were then incubated in media combined with different volumes of lipid-free PN solutions containing 0-4.5% dextrose, along with standard amounts of electrolytes, micronutrients and protein. Triplicates of incubates ranging from 5-20% PN solution by volume were incubated for 10 hours under iso-osmolar conditions (310-330 mOsm/L). Cells were assessed for viability and lysates collected for measurement of protein, triglyceride, and cholesterol. Experiments were then conducted under the same conditions, with dextrose added to reach 6% dextrose (400 mOsm/L).

Results: Huh7 cells incubated in iso-osmolar media with and without PN solution showed no statistical differences in cell viability, in production of triglycerides or cholesterol. Huh7 cells incubated in dextrose-supplemented hyperosmolar media, with and without PN solution, also showed no statistical differences in these measurements.

Conclusions: In an in vitro hepatocyte culture model, neither cell viability nor lipid production is influenced by exposure to up to 6% dextrose in the culture medium. These findings suggest that dextrose, per se, may not be primarily responsible for hepatic steatosis in PNALD. Further studies with prolonged incubation times and a transition to an animal model are needed to further elucidate these findings.

282  **TENOFOVIR DISOPROXIL FUMARATE TREATMENT FOR PEDIATRIC PATIENTS WITH PERINATALLY ACQUIRED CHRONIC HEPATITIS B: A RETROSPECTIVE STUDY.** Ricardo A. Arbiza, Susan S. Baker, Rafal Kozielski, Robert D. Baker, Pediatric Gastroenterology, State University of New York at Buffalo, Buffalo, NY; Pathology, Women & Children's Hospital of Buffalo, Buffalo, NY

Background and Methods: after exposure to hepatitis B virus (HBV), perinatally infected infants have an approximate 90% risk of developing chronic hepatitis B (CHB). The result is progressive, asymptomatic liver damage related to viral replication. CHB patients are at increased risk of developing cirrhosis, liver failure and hepatocellular carcinoma. Therapeutic interventions that reduce HBV replication are expected to limit liver damage progression. Tenofovir Disoproxil Fumarate (TDF) was approved for use in patients with CHB and has been proven to be efficacious and well tolerated in adults and adolescents, but it has not been studied in pediatric patients with history of perinatally acquired CHB. Therefore the aim of this study was to examine the effects of TDF on HBV replication, alanine aminotransferase (ALT) normalization, hepatitis envelope antigen (HBeAg) clearance, and hepatitis envelope antibody (anti-HBe) seroconversion on pediatric patients with perinatally acquired CHB who completed at least 72 weeks of treatment.

Results: 55 cases were analyzed of which 26 were treated with TDF. The majority were immigrants or international adoptees from Southeast Asia and Africa. Most were infected with HBV genotype C. All treated patients were HBeAg positive and anti-HBe negative at baseline, 14 (54%) had immune active hepatitis and 12 (46%) were in the immune tolerant phase. In both groups, no difference in inflammation or fibrosis scores was found on liver biopsy prior to starting therapy. The mean HBV DNA level at baseline was 9 log_{10} copies/mL. HBV DNA levels declined to 5.9 log_{10} copies/mL at 40 weeks of therapy and were undetectable in 19/26 (73%) of the patients by week 72. Baseline ALT levels normalized by 32 weeks in the immune active hepatitis group and no breakthrough elevations were seen in the two groups. Overall, 11 (42%) and 9 (35%) of the patients had HBeAg clearance and anti-HBe seroconversion respectively by 72 weeks of treatment with TDF.

Conclusion: TDF is an effective therapy in pediatric patients with perinatally acquired CHB in decreasing HBV DNA levels, normalizing ALT and promoting HBeAg clearance and anti-HBe seroconversion in both immune active hepatitis and immune tolerant phase patients. In this study, baseline ALT levels and liver histopathology findings did not seem to affect the response to TDF.
AN EMR-BASED APPROACH TO THE IDENTIFICATION OF DRUG-INDUCED LIVER INJURY IN CHILDREN. Clayton Habiger, Tracy Sandritter, Jennifer Goldman, Jennifer Lowry, J.S. Leeder, Ryan Fischer, 1Clinical Pharmacology and Therapeutic Innovation, Children's Mercy Hospital, Kansas City, MO; 2University of Kansas Medical Center, Kansas City, KS; 3Gastroenterology, Children's Mercy Hospital, Kansas City, MO

Background: Drug-induced liver injury (DILI) is the leading cause of liver failure in the United States and accounts for nearly 10 percent of acute hepatitis cases in adults. Limited data exists for pediatric populations on the incidence of DILI, and its natural history and pathophysiology are poorly understood. We sought to explore DILI in our single-center pediatric population using a novel electronic medical records (EMR)-based approach to identify probable and possible DILI patients.

Methods: The Individualized Pediatric Therapeutics Drug Safety Service (DSS) was established at our hospital in 2010 to improve detection of Adverse Drug Reactions (ADR). This is accomplished via multiple mechanisms including voluntary reporting and automated trigger tools. In the case of DILI, an EMR-based program was implemented to automatically report all patients with clinical chemistry criteria concerning for DILI defined as 1. Serum ALT > 5xULN, 2. Serum bilirubin > 1.5x ULN with an ALT > 3x ULN, and 3. Serum bilirubin > 1.5x ULN. Once notified, the DSS staff physician or pharmacologist reviews the medical history of all patients meeting DILI criteria. Causality is assessed based on exposure, clinical response to drug timing and withdrawal, and physician or pharmacologist review. The injury relationship is further defined by application of the RUCAM and/or Naranjo probability assessment scales.

Results: Between January of 2012 and July of 2013, 10 patients were positively identified as having possible or probable DILI by our ADR reporting mechanisms. Out of the identified patients, there were 4 males, and the group's average age was 9.9 years. Hepatocellular damage (7) was more commonly reported than cholestatic (1) and mixed (2) injury. Implicated agents included 7 antibiotics, 2 psychotropic agents, and 1 immunosuppressant. Minocycline and trimethoprim-sulfamethoxazole were implicated twice. RUCAM scores included 3 "possible" cases (score of 3-5), 6 "probable" cases (score of 6-8) and 1 "highly probable" case.

Conclusions: DILI is an important cause of acute hepatitis and/or liver failure, but under-recognized and poorly understood in pediatrics. Our ADR program successfully identified 10 probable/possible DILI cases over the course of 18 months, demonstrating high rates of detection at a single pediatric center. Improved awareness and more vigilant vigilance in our single-center population has been achieved.
programming can generate better data on DILI in children and improve our understanding of the condition.

Characteristic of DILI patients

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<th>Sex</th>
<th>Type</th>
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<th>Bili</th>
<th>RUCAM</th>
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285* ANALYSIS OF TRENDS IN INCIDENCE, MANAGEMENT, ETIOLOGY AND DEATH [TIMED] DUE TO PEDIATRIC ACUTE LIVER FAILURE [ALF]; RESULTS OF ANALYSIS OF THE PEDIATRIC HEALTH INFORMATION SYSTEM [PHIS], 2008 – 2013. Sakil Kulkarni2, Carla Perez2, Caren Pichardo1, Lina Castillo2, Michael Gagnon3, Consuelo Beck-Sague1, Erick Hernandez4, Rani Gereige2, 1Health Promotion and Disease Prevention, Florida International University, Miami, FL; 2Medical Education, Miami Children's Hospital, Miami, FL; 3Quality and Safety, Miami Children's Hospital, Miami, FL; 4Pediatric Gastroenterology, Miami Children's Hospital, Miami, FL

Background: ALF is a rare but frequently fatal pediatric condition. Using the PHIS database, we studied TIMED due to pediatric ALF in children admitted from 2008 to 2013 to 16 US pediatric liver transplant centers contributing to the PHIS database.

Methods To validate the case-finding strategy for ALF, we reviewed medical records of patients admitted to Miami Children's Hospital with the principal ICD 9 diagnosis "Acute Necrosis of the Liver" (570.00). The specificity of the search criterion in identifying patients who met the ALF case definition was 90 %. After validation we selected patients with the principal diagnosis code 570.00 from 16 PHIS transplant centers. Data collected included hospital identifier and region, admission and discharge dates, age, sex, pharmacy and procedure information, disposition and >21 other diagnoses. Patients with diagnoses suggesting chronic liver disease among other diagnoses were excluded.

Results A total of 583 patients met ALF diagnostic criteria; each center averaged 9.1 ALF cases per year. The mean (median) ages at presentation were 9.4 (10.0) years (range=1-18, SD=5.6); 46.7% were male. In over half (52.5%) the etiology was not determined. Acetaminophen toxicity (APAP) [18.7%] was the most commonly determined etiology. The most common complication was hepatic encephalopathy (HE) [38.6%]. Length of stay ranged from 1-175 (median=8) days; 95.4% survived, 73.4% without a liver transplant. Malignant infiltration of liver causing ALF (odds ratio [OR]=4.0, p=0.02), acute respiratory failure (OR=3.4, p=0.035), acute kidney injury (AKI) (OR=3.6 p=0.003) (Figure 1) and cerebral edema (CE) (OR 3.6, p =0.02) (Figure 2) were significantly associated with increased risk of mortality after controlling for other factors in logistic regression. Most (53%) mortality occurred within the first 7 days of hospital stay. Spontaneous survival with native liver was significantly more likely in patients whose ALF was related to APAP (OR=4.0, p<0.001) and was less likely in the presence of acute respiratory failure [OR=0.5, p=0.03], HE [OR=0.3, < 0.001] and cardiovascular compromise [OR=0.1, p<0.001] when controlled for other factors in logistic regression. The most common type of liver transplant performed was cadaveric [70.7%]. Use of N-acetyl cysteine in non-APAP-induced liver failure, sepsis, and use of intracranial pressure monitoring decreased during the study period.

Conclusion: TIMED analysis suggests that ALF remains a rare but a condition with high morbidity and mortality. The high proportion of idiopathic cases represents an important research need.
### Complications and Incidence

<table>
<thead>
<tr>
<th>Complication</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic Encephalopathy</td>
<td>38.6%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>30%</td>
</tr>
<tr>
<td>Acute Respiratory Failure</td>
<td>23.5%</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td>17.5%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>12.9%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>10.2%</td>
</tr>
<tr>
<td>Cerebral Edema</td>
<td>8.6%</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>6%</td>
</tr>
<tr>
<td>DIC</td>
<td>3.6%</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>4.8%</td>
</tr>
<tr>
<td>Intracranial Bleed</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

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**286** HEPATIC STIFFNESS IN THE GLENN CIRCULATION: CONSEQUENCES OF VENOUS DRAINAGE INTO A SYSTEMIC ARTERIAL ATRIUM. Shaija Kutty¹, Ming Zhang², David Danford², Scott Fletcher², John Kugler², James M. Hammel², Ruben E. Quiros-Tejeira¹, Shelby Kutty², ¹Pediatric Gastroenterology, University of Nebraska Medical Center, Omaha, NE; ²Pediatric Cardiology, University of Nebraska Medical Center, Omaha, NE

Background: Hepatic dysfunction is a well-recognized phenomenon in the total cavopulmonary (Fontan) circulation, and assumes great significance in the care of single ventricle heart disease. It influences surgical choices including Fontan revision and heart transplantation. Despite these observations, very little is known about the origin and progression of liver fibrosis in this population. We hypothesized that hepatic injury in single ventricle patients has origins earlier than the Fontan operation, and sought to quantitatively measure hepatic stiffness using ultrasound (US) and shear wave elastography (SWE) in a bidirectional cavopulmonary circulation (Glenn) cohort. We also compared results with controls and a historical cohort of Fontan subjects.

Methods: Glenn subjects and controls were prospectively recruited for echocardiography and real-time hepatic duplex US with SWE for hepatic stiffness (kPa). The SWE ultrasound system (SuperSonic Imagine Aixplorer®) and selected broad bandwidth curved and linear transducers (SC6-1 and SL15-4) enabled generation of transient shear waves simultaneously with real-time B-mode imaging for analysis. Measurements of hepatic stiffness were expressed in terms of Young's Modulus (kPa). Doppler peak velocities, velocity time integral (VTI), resistive, pulsatility, acceleration indices (RI, PI, AI), and flow volume were measured in the celiac artery, superior mesenteric artery (SMA) and main portal vein. Comparisons were made between groups using Student t tests.

Results: In all, 35 subjects were studied including 15 patients with Glenn physiology and 20 controls. The hepatic stiffness in patients with Glenn physiology elevated significantly compared to controls (7.5 versus 5.3 kPa, P = 0.04). Glenn patients had significantly higher celiac artery RI (0.85 versus 0.77, P=0.001), PI (2.16 versus 1.68, P=0.001), and systolic-diastolic flow ratio (8.6 versus 5.2, P=0.005). Celiac artery VTI (32.3 versus 47.8 mL/min in controls, P=0.04) and SMA VTI (23.2 versus 36.6, P=0.01) were lower in Glenn patients. Comparison of hepatic stiffness with previously evaluated Fontan subjects showed Glenn patients to have lower hepatic stiffness (7.5 vs. 15.6 kPa, P< 0.001).

Conclusions: Hepatic venous drainage at the Glenn stage of single ventricle palliation faces lower resistance than in the normal circulation. Consistent with a working theory that resistance to venous drainage is the primary cause for hepatic stiffness in the single ventricle, our preliminary results indicate hepatic stiffness at the Glenn stage to be intermediate between normal and Fontan findings. Longitudinal assessments of hepatic stiffness in this cohort in conjunction with serum fibrosis markers and search for gene mutations that may predispose to liver disease are ongoing.

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**287** IMPACT OF SEBELIPASE ALFA ON SURVIVAL AND LIVER FUNCTION IN INFANTS WITH RAPIDLY PROGRESSIVE LYSOSOMAL ACID LIPASE DEFICIENCY. Simon A. Jones¹, Dominique Plantaz², Roshni Vara¹, John J. Gargus¹, Joanne Hughes³, Stephen Ecker⁴, Sandra Rojas-Caro⁵, Anthony G. Quinn⁶, Vassili Valayannopoulos⁷, ¹University of Manchester, Manchester, United Kingdom; ²Hopital Couple Enfant CHU Grenoble, Grenoble, France; ³Evelina Children's Hospital, London, United Kingdom; ⁴University of California Irvine Medical Center, Irvine, CA; ⁵The Children's University Hospital, Dublin, Ireland; ⁶Synageva BioPharma Corp., Lexington, MA; ⁷Hôpital Necker-Enfants Malades, Paris, France

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. Prominent clinical manifestations include marked failure to thrive, severe hepatic disease with massive hepatomegaly, liver failure and cytopenias.

To investigate the effects of any therapy in affected infants, a historical cohort is required. In a natural history study, failure to thrive, liver complications 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 (n=21), the K-M estimate (95% CI) of survival past 1 year of age was 0.00 (0.00, 0.00). Those treated with HSCT or liver transplant survived slightly longer but still died before 1 year of age (median age 8.6 months).

In the absence of any safe or effective therapies, a phase 2/3 trial (LAL-CL03) assesses the safety and efficacy of sebelipase alfa (SA) in 9 LAL deficient infants with growth failure in the first 6 months of life from Europe, USA and Middle East. The median baseline liver function tests reveal significant underlying liver dysfunction with a median ALT and AST of 145 IU/L and 125 IU/L respectively. At symptom onset, subjects had diarrhea/vomiting (n=6), hepatomegaly (n=9), splenomegaly (n=8), or adrenal calcification (n=6). In the infants with available data, the median baseline ferritin was 586 ug/L.

As of June 9, 2014, six subjects have met the primary endpoint of survival at 12 months of age with a mean age of 22 months and continue to receive SA. Three subjects died after receiving four or fewer doses. All deaths were unrelated to SA and were deemed to be either related to underlying disease or, in one subject, due to complications of an abdominal paracentesis. In addition to improved survival relative to the historical cohort, all subjects demonstrated an encouraging response with improved weight gain, improvement of GI symptoms, and reductions in hepatosplenomegaly. In addition to these clinical effects, rapid improvements in biochemical and hematological markers including ALT, AST, hemoglobin, and bilirubin have been observed. Majority of the SAEs were unrelated. One SA-related SAE occurred: an infusion reaction of malaise with tachycardia and fever. The majority of the infusion associated reactions were reported as fever, diarrhea, or vomiting. To date, four subjects tested positive to anti-SA antibodies and all four continue weekly infusions of SA.

Analysis from this ongoing clinical trial suggests that SA 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 carefully matched historical control group.

**288 RELATIONSHIP BETWEEN ANOMALOUS PANCREATICOBILIARY DUCTAL UNION AND PATHOLOGIC INFLAMMATION OF BILE DUCT IN CHOLEDOCHAL CYST.** Sowon Park¹, Hong Koh¹, Jung-Tak Oh², Seok Joo Han², Seung Kim², ¹Pediatrics, Severance Children's Hospital, Seoul, Republic of Korea; ²Pediatric Surgery, Severance Children's Hospital, Seoul, Republic of Korea

**Aim:** Choledochal cyst is a cystic dilatation of common bile duct. Although the etiology is uncertain yet, anomalous pancreaticobiliary ductal union (APBDU) is thought to be a major etiology of choledochal cyst. In this study, we analyzed the clinical and anatomical characteristics and pathologies of patients with choledochal cyst in a single institute for 25 years. **Methods:** Total of 113 patients, diagnosed with choledochal cyst and received an operation in Severance Children's Hospital from January 1988 to May 2013, were included. Medical records, including clinical and demographic data, surgical procedures, Todani's classification, and relationship between anomalous union of pancreaticobiliary duct (APBDU) and surgical pathology were reviewed. **Results:** Among 113 patients, 77 (68.1%) patients presented symptoms such as hepatitis, pancreatitis and/or cholecystitis. Eighty three patients (73.4%) had APBDU and 94 patients (83.2%) showed inflammatory pathologic changes. APBDU, pathologic inflammation and presence of symptoms showed a statistically significant correlation to one another. **Conclusion:** APBDU is thought to be one of etiologic factors of choledochal cyst. It is related to the inflammatory changes of bile duct which can lead to the cystic dilatation.
Patients Characteristics Analyzed by Pathology

<table>
<thead>
<tr>
<th></th>
<th>Inflammation (N = 94)</th>
<th>No inflammation (N = 19)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>33 (35.1)</td>
<td>4 (21.1)</td>
<td>0.234</td>
</tr>
<tr>
<td>Age (months)</td>
<td>23.5 (0 - 182)</td>
<td>10.0 (0 - 204)</td>
<td>0.675</td>
</tr>
<tr>
<td>Symptomatic patients (%)</td>
<td>68 (72.3)</td>
<td>9 (47.4)</td>
<td>0.033</td>
</tr>
<tr>
<td>Duration until lab normalizes (days)</td>
<td>8.0 (5 - 30)</td>
<td>8.0 (7 - 30)</td>
<td>0.430</td>
</tr>
<tr>
<td>APBDU (%)</td>
<td>73 (77.7)</td>
<td>10 (52.6)</td>
<td>0.024</td>
</tr>
</tbody>
</table>

Data are presented as median. APBDU, Anomalous pancreaticobiliary ductal union.

Patients Characteristics Analyzed by Presence of APBDU

<table>
<thead>
<tr>
<th></th>
<th>APBDU(N = 83)</th>
<th>Non-APBDU(N = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>26 (31.3)</td>
<td>11 (36.7)</td>
<td>0.593</td>
</tr>
<tr>
<td>Age (months)</td>
<td>26.0 (0 - 204)</td>
<td>2.50 (0 - 166)</td>
<td>0.039</td>
</tr>
<tr>
<td>Symptomatic patients (%)</td>
<td>62 (74.7)</td>
<td>15 (50.0)</td>
<td>0.013</td>
</tr>
<tr>
<td>Pathologic inflammation (%)</td>
<td>73 (88.0)</td>
<td>21 (70.0)</td>
<td>0.024</td>
</tr>
<tr>
<td>Duration until lab normalizes (days)</td>
<td>8.0 (5 - 30)</td>
<td>7.0 (5 - 30)</td>
<td>0.137</td>
</tr>
</tbody>
</table>

Data are presented as median. APBDU, Anomalous pancreaticobiliary ductal union.

289 EVALUATION OF KNOWLEDGE AND ATTITUDES ABOUT INFANT STOOL COLOR AMONG MOTHERS OF NEWBORN BABIES. Stefany B. Honighbaum1, Anna Schuettge1, Grace Felix2, Christopher Golden3, Douglas Mogul1. 1Pediatric Gastroenterology and Nutrition, Johns Hopkins Hospital, Baltimore, MD; 2Pediatrics, Johns Hopkins Hospital, Baltimore, MD; 3Neonatology, Johns Hopkins Hospital, Baltimore, MD

INTRODUCTION: Biliary atresia (BA) is a congenital disease characterized by fibrosis, obstruction and obliteration of the biliary system and is universally fatal without surgical intervention. Early diagnosis and intervention with a hepatoportoenterostomy is associated with better outcomes. One tool to diagnose BA earlier is stool color education, and a nationwide stool color card program in Taiwan has led to improved survival and decreased rates of liver transplantation for children with BA. As part of a randomized control trial to evaluate the effects of stool color education in a US cohort of healthy babies, we evaluated baseline knowledge and attitudes about infant stool color among mothers of healthy newborns.

METHODS: Only healthy mothers of babies admitted to the well-baby nursery at Johns Hopkins Hospital were included. They were required to be English-speaking and 18 years or older. They were given a 25-question survey testing attitudes and knowledge about infant stool color. Questions regarding attitude about stool color were developed using a 7-point Likert scale (i.e., absolutely agree, strongly agree, somewhat agree, neutral, somewhat disagree, strongly disagree, absolutely disagree). Mothers were also provided with 10 photographs to test their baseline knowledge about normal/abnormal stool color. Frequencies were calculated for all variables, and mean/SD/range was calculated for continuous variables. A chi-square test was used to evaluate the association between maternal experience raising previous children, and attitudes/knowledge about infant stool color. Frequencies were calculated for all variables, and mean/SD/range was calculated for continuous variables. A chi-square test was used to evaluate the association between maternal experience raising previous children, and attitudes/knowledge about infant stool color.

RESULTS: 80 mothers, mean age 28.7 years (range 18-42 years; SD 6.9), were enrolled. Fifty-four (67.5%) stated they had experience caring for other infants as compared to 26 (32.5%) with no prior experience. When asked to respond to the statement: "stool color may be useful in providing information about the health of my baby," 77 (97.5%) agreed with this statement and the remainders were ‘neutral.’ When asked: "I am confident I know what is a normal stool color," 64 (81%) agreed, 10 (12.7%) were neutral, and 5 (6.4%) disagreed; there was no association between experience and confidence in recognizing normal/abnormal stool color (P = 0.28). When asked "I feel comfortable discussing concerning stool with my pediatrician," 100% of participants agreed. Mothers were provided 10 photographs of infant stool including normal, acholic and bloody stools. Results were normally distributed with a mean score of 7.8/10 (range 5-10%; SD 1.26). Only 28/80 (35%) correctly identified all three acholic stools and the ability to recognize acholic stools was independent of experience (P = 0.28).

CONCLUSION: While mothers recognize the importance of stool color as reflecting the health of their infant and many
are confident in their ability to recognize normal stools, they are unable to correctly identify abnormal stool color with even greater difficulty in identifying acholic stools. Stool color card education programs in the US may be a valuable tool in educating parents about stool color in order to improve outcomes for children with BA.

290  ZINC MONOTHERAPY IN YOUNG PEDIATRIC PATIENTS WITH PRESYMPTOMATIC WILSON DISEASE: LONG-TERM EFFICACY AND SAFETY. Takahito Takeuchi1, Keisuke Eda1, Tadahiro Yanagi1, Yoshitaka Seki1, Tatsuki Mizuochi1,2,1Pediatrics and Child Health, Kurume University School of Medicine, Kurume, Japan; 2Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: AASLD and EASL guidelines recommend zinc monotherapy as a treatment for presymptomatic patients with Wilson disease (WD). However, there have been few reports of zinc monotherapy for young pediatric patients with WD and measures of successful treatment are ill defined. We previously reported that a reasonable goal in treating young pediatric patients with WD using zinc to be maintaining 24-hour urinary copper excretion between 1 and 3 μg/kg/day for the first 1-2 years (Mizuochi, et al. JPGN 2011;53:365).

Aims: To evaluate long-term efficacy and safety of zinc monotherapy in young pediatric patients with WD and to establish appropriate benchmarks of maintenance therapy.

Methods: We performed a retro- and prospective study to examine 4 girls (mean age 5.5 years, range 5-7) who satisfied diagnostic criteria for WD and were treated solely with zinc acetate prior to symptom onset. WD was diagnosed in all patients after increased serum AST and ALT concentrations were appreciated. No additional WD sequelae, such as jaundice, hepatomegaly, or neurologic abnormalities were noted. We monitored serum AST and ALT, nonceruloplasmin serum copper, and 24-hour urinary copper for 5 years after initiation of zinc monotherapy. Additional monitoring included white blood cell count, hemoglobin, platelet count, serum total bilirubin, albumin, iron, amylase, lipase, and prothrombin time, as well as 24-hour urinary zinc excretion. We performed abdominal ultrasonography and evaluated clinical WD manifestations, drug compliance, and adverse effects of zinc. The prescribed dosage of zinc acetate for patients 5 years was 25 mg twice daily; for those children 6 years or older, the dose was 25 mg 3 times daily. We increased the dosage of zinc if the patients had AST/ALT ≥ 50 U/L, and decreased it if they had adverse effects of zinc such as iron-deficiency anemia or pancytopenia.

Results: At the time of diagnosis, AST/ALT and 24-hour urinary copper were 306±186/419±168 U/L and 136±50 μg/day (7.7±3.9 μg/kg/day), respectively. All patients continued to take zinc for 5 years without any evidence of zinc toxicity. None of our 4 patients became clinically symptomatic. AST/ALT sharply decreased to 36±1/42±15 U/L at 1 year after treatment and was mostly maintained less than 50U/L for the remainder of the study (AST/ALT: 31±9/34±8 U/L at 5 years after treatment). Twenty four-hour urinary copper decreased to 54±10 μg/day (2.6±0.7 μg/kg/day) at 1 year after treatment and was mostly maintained between 1 and 3μg/kg/day for the remainder of the study (1.5±0.7 μg/kg/day at 5 years after treatment).

Conclusions: Long-term zinc monotherapy in young pediatric patients with presymptomatic WD proved highly effective and safe. A reasonable goal in treating young children with WD using zinc appears to be maintaining both AST/ALT under 50 U/L and 24-hour urinary copper excretion between 1 and 3 μg/kg/day.

291  HEPATIC MITOGENIC EFFECTS OF T3-RECEPTOR β AGONISTS. Tamara Feliciano1, Sucha Singh2, Minakshi Poddar2, Satdarshan P. Monga2, Pediatric Gastroenterology, Children's Hospital Pittsburgh of UPMC, Pittsburgh, PA; 2Pathology, Pittsburgh University, Pittsburgh, PA

Background: T3 hormone is known to be a strong inducer of hepatocyte proliferation in rats and mice. Its actions are mediated via interaction with thyroid hormone nuclear receptors. Recent work has shown that the molecular mechanism for T3's mitogenic effect may be Protein Kinase A (PKA)-dependent activation of the β-Catenin signaling pathway. This finding has shed light on the potential therapeutic use of thyroid hormone in liver insufficiency. However, systemic side effects of T3 may preclude its clinical use. GC-1 and KB2115 are T3 hormone analogs that bind selectively to the T3 hormone β-receptor (THRβ). Activation of THRβ does not seem to produce the undesirable cardiovascular effects that are typically associated with THRα activation in the heart.

Aim: Since hepatocytes are known to predominantly express THRβ, we investigate whether selective THRβ activation by T3 analogs GC-1 and KB2115 induces hepatocyte proliferation in mice.

Methods: C57BL/6 male mice (2-3 months old) received 8 daily intra-peritoneal injections of GC-1 or KB2115 at 0.3mg/kg body weight or DMSO (control). BrdU was added to drinking water, which was available ad libitum for the duration of the experiment to measure cell proliferation. Mice were sacrificed, serum was obtained for liver biochemistry analysis and livers were harvested for Western Blot and immunohistochemistry analysis for b-Catenin, cyclin-D1 and other markers of cell proliferation.

Results: Livers from mice injected with GC-1 and KB2115 showed increased levels of P-β-Catenin (Ser675) and Cyclin D-1 on Western Blot, compared to the controls. We also saw an increase in β-Catenin, Cyclin D-1, Ki-67, and BrdU by immunohistochemistry. No aberrations in serum biochemistry were observed in any group.

Conclusion: Selective thyromimetics that bind to THRβ can activate β-Catenin signaling, which in turn induces Cyclin-
D1 expression to induce hepatocyte proliferation in healthy mice. With further studies, these drugs may prove useful as an adjunct therapeutic option in select cases of liver failure.

292* USING HUMAN INDUCED PLURIPOTENT STEM CELLS TO MODEL LIVER DISEASE ASSOCIATED WITH CLASSIC MUTATIONS OF ALPHA-1 ANTITRYPSIN. Tamara N. Taketani1,2, Maria P. Ordonez1,2, Lawrence S. Goldstein1, Cellular and Molecular Medicine, UC San Diego, La Jolla, CA; 2Pediatric Gastroenterology, Rady Children's Hospital San Diego, San Diego, CA

A major obstacle to the development of new therapies is the poor understanding of how genetic modifiers alter the onset and outcome of various diseases. A classic example is AAT deficiency, a metabolic liver disease in which the mutant gene and its product are known, but where clinical progression and outcome are extremely variable and thought to be influenced by genetic modifiers.

Despite being the leading genetic cause of liver disease in children, mutations of AAT occur infrequently when compared to sporadic liver diseases. The relatively low incidence of AAT deficiency makes it impossible to obtain insight into the genetic factors that may affect progression of disease from genome-wide association studies (GWAS). The study of hepatocytes derived from AAT mutant human induced pluripotent stem cells (hiPSC) may overcome this limitation by identifying cellular phenotypes that correlate with clinical severity of disease in existing AAT patients. For this purpose, we have generated hiPSC lines from existing AAT patients (ZZ) with variable degrees of liver disease, including those without evidence of liver damage and those who have suffered a more aggressive course leading to end stage liver disease. We are using control and AAT hiPSC-derived hepatocyte like cells (HLCs) to probe the hypothesis that the significant heterogeneity seen in disease progression due to AAT ZZ mutations is related to genetically determined variability of fundamental biological hepatocyte processes involved in cellular disposal, stress response, and cell survival pathways, including proteasomal degradation, ER stress, autophagy, and apoptosis.

Prior data obtained in mouse and cell line models has shown that autophagy may act as a primary route of intracellular degradation of mutant AAT protein. Although traditionally regarded as a cellular adaptive process triggered by nutrient deprivation, autophagy in hepatocytes may also provide an important hepatoprotective mechanism. Our preliminary results show that HLCs derived from AAT mutant patients with no evidence of liver disease (AAT NLD) have increased activation of autophagy at baseline compared to AAT mutants with severe liver disease (AAT LD). Furthermore, AAT hepatocytes from patients with severe liver disease show a weaker autophagy induction response upon serum deprivation. Our data supports a role for autophagy as a potential modifier in the pathobiology of AAT related liver disease, and opens the way for mechanistic studies involving this and other basic biological pathways that may modulate hepatic injury in AAT.

Our studies can impact the way we approach AAT deficiency: 1) by developing predictive diagnostics through discovery of biomarkers that identify patients at risk for severe liver disease, and 2) by promoting therapeutic candidate discovery through validation of new or existing therapeutic targets in live human hepatocytes.

Nutrition

304 CORRELATION ADIPOSITY OF INFANTS WITH THE ADIPOSITY OF THEIR PARENTS AND SIBLINGS. Jagguit X Fregoso-Bailon1, Alfredo Larrosa-Haro1, MC Rocio Macias-Rosales2, Elizabeth Lizarraga-Corona1, Alejandro Gonzalez-Ojeda1, Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2Servicio de Gastroenterología y Nutrición Centro Medico Nacional de Occidente, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; 3Unidad de Investigacion en Epidemiologia Clinica, Centro Medico Nacional de Occidente, Instituto Mexicano del Seguro Social, Guadalajara, Mexico

AIM: Our aim was to correlate the adiposity of infants attending day-time nurseries with the adiposity of their parents and siblings.

SUBJECTS AND METHODS: This cross sectional study was performed in families of 100 infants from 3 day-care nurseries in Guadalajara Mexico. Anthropometric measurements: weight, length/height, skin-folds and arm circumference. Anthropometric indicators: BMI; weight/height; arm circumferences, skin-folds and areas. Z-scores were calculated from these measurements with WHO-2006, Frisancho and Sann reference patterns. Adiposity percentage was calculated with Slaughter's formulas. Statistical analysis: Pearson correlation, ANOVA, chi square and Student's t.

RESULTS: Mean age of infants was 12.4 months (DE 4.6), 54% were females. Z-scores of adiposity indicators were between -2 and +2 SD in >95% of the infants under study. The proportion of anthropometrical indicators of adiposity > +2SD increased twice in the siblings and 10 times in the parents (p=0.021). The adiposity trend was a progressive increase related to age. Overweight plus obesity was identified in 17.3% of siblings, in 54.4% in parents 10-30 years old and in 76.9% of parents 30-50 years old (p=0.006). With a few exceptions, no significant correlations of the adiposity indicators were demonstrated between the infants and their siblings or parents.

CONCLUSIONS: Although this was a cross-sectional study, our observations showed that adiposity indicators >2SD were almost absent in infants and that the proportion of adiposity excess increased progressively with age. The changes
in the phenotype with age probably reflect the continuous exposure of an obesogenic environment.

305 CORRELATION OF ADIPOSITY ANTHROPOMETRIC INDICATORS WITH THE NUMBER OF STEPS PER MINUTE DURING THE SCHOOL RECESS IN PRESCHOOLERS: GENDER DIFFERENCES. Elizabeth Lizarraga-Corona1, Alfredo Larrosa-Haro2,3, Juan Ramon Vallarta-Robledo2, Larissa Velasco-Ruiz2, Enrique Romero-Velarde1, Edgar M Vasquez-Garibay2, 1Unidad de Estudios de Nutrición Infantil, Hospital Civil de Guadalajara Dr. Juan I Menchaca, Guadalajara, Mexico; 2Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 3Departamento de Salud Pública, Doctorado en Ciencias de la Salud Pública, Universidad de Guadalajara, Guadalajara, Mexico

BACKGROUND: Adiposity may be associated to spontaneous physical activity (SPA). SPA may be estimated by step-count in a specific period of time.

AIM: To correlate the number of steps/minute (NSM) with anthropometrical indicators of adiposity in preschoolers.

SUBJECTS AND METHODS: One-hundred and thirty-four preschoolers attending a kindergarten were evaluated. The number of steps was estimated by a pedometer measurement (Tanita PD-637®) during the school recess. Total step count was adjusted to the time the pedometer was used. Anthropometric indicators of adiposity were calculated from weigh, height, arm circumference; triceps and calf skinfolds. The percentage of body fat was estimated by Slaughter's equation. Z-scores were calculated with Frisancho's reference pattern. Statistics: Pearson's correlations.

RESULTS: Mean age was 61.2 (SD 9.0) months, 50.7% were girls. The overall mean time of pedometer use was 35.1 (SD 6.9) minutes, without gender differences. Boys mean NSM was 52.7; in girls it was 37.7, with statistical difference (p<0.001). In the overall group, the percentage of body fat had a negative correlation with the NSM (r=0.3, p=0.016); overall group correlations with the other indicators of adiposity were not significant. In boys significant negative correlations were found for body fat percentage (r=0.26, p=0.033), triceps skinfold (r=0.25, p=0.041) and arm fat area (r=0.25, p=0.042). Girls did not show not significant correlations.

CONCLUSIONS: Boys had higher spontaneous physical activity and it correlated significantly with most adiposity indicators. Gender differences in NSM may be cultural or constitutional. Short time step-count pedometry may be a useful tool to estimate spontaneous physical activity.

306 HOW PAIN AND COST ARE AFFECTED BY MOVING FROM TUBE TO ORAL FEEDING: FINDINGS FROM A RANDOMIZED CONTROLLED TRIAL. Ann M. Davis1, Kelsey Dean2, Amanda Bruce4, Sarah Edwards5, Hayat Mousa1, JOSE T. COCJIN2, Paul Hyman5, 1Pediatrics, University of Kansas Medical Center, Kansas City, KS; 2Pediatrics, Children's Mercy Hospitals & Clinics, Kansas City, MO; 3Gastroenterology, Nationwide Columbus Children's Hospital, Columbus, OH; 4Psychology, University of Missouri Kansas City, Kansas City, MO; 5Gastroenterology, New Orleans Children's Hospital, New Orleans, LA

Infants with neonatal intensive care hospitalizations or serious medical problems may miss opportunities for learning to eat, or associate eating with pain or discomfort. Although the causes for hospitalizations may resolve, a tube feeding requirement may persist. There are several methods for teaching non-verbal toddlers to eat, but no optimal solution. Our long term goal is find the best method for moving children from tube feeding to oral eating. In the current randomized controlled trial our team is assessing amitriptyline as part of a multidisciplinary outpatient protocol for moving medically complicated children ages 9 mo to 8 yr of age from tube feeding to oral eating. The protocol includes behavioral and oral motor guidance, along with amitriptyline 1 mg/kg/d or placebo (randomly assigned), and continuous drip gastro-jejunal tube feedings 12-20 h/d for 8 weeks. Next, subjects receive the appetite stimulant megesterol 3 mg/k BID. After 5 d of megesterol tube feedings are reduced by 1 h/d. To date, 14 subjects have enrolled, and 13 have completed across three sites. The Non-communicating Children's Pain Checklist (NCCPC) and Cost of Care (COC) standardized measures were collected to determine the effects of moving from tube to oral feeding on both pain and cost. Because the study is ongoing, subjects and researchers remain blind to group assignment (amitriptyline vs. placebo). At baseline data indicate relatively high levels of pain on the NCCPC (M = 12.94, SD = 11.29) which decreased significantly after being in the study for 10 weeks (M = 8.9, SD = 10.10; t = 2.15, P >.05). Data on cost indicate families were spending $747.07 (SD = 1796.67) at baseline in medical care for their child, and after moving from tube to oral feeding, this amount per week decreased to $121.06 (SD = 176.66; t = 1.08, p >.05). These data suggest that regardless of the use of amitriptyline or placebo, moving children from tube to oral feeding significantly improves their pain and decreases the medical costs to the family.

307 SAFE TRANSITION TO HOME PN: A QUALITY IMPROVEMENT INITIATIVE TO TRACK EARLY DISCHARGE COMPLICATIONS. Abayomi Ajala1, T. S. Fernando2, Glendalis Grullon1, Mary Gallotto1, Meghan K. Dalton1, Brittany Tellier1, Christopher Duggan1, Bram P. Raphael1, 1Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; 2Department of Medicine, Boston Children's Hospital, Boston, MA

BACKGROUND: Children with intestinal failure are increasingly discharged on home parenteral nutrition (HPN), as it can lead to improved quality of life, reduced medical expenses, and good safety profile. Unfortunately, HPN is also
associated with preventable complications, such as infection and readmission.

**AIM:** To measure the incidence of first central line associated blood stream infection (CLABSI) and first unscheduled readmission following discharge in a cohort of children receiving HPN.

**METHODS:** Retrospective review of 52 children (ages 0-21 years) managed at the Boston Children's Hospital HPN Program during a 27-month period. HPN duration less than 60 days were excluded. CLABSI was defined using the CDC definition. Data analyzed using STATA 11.2 edition and Chart Runner Lean 3.0.

**RESULTS:** The median (IQR) age at HPN initiation was 26.6 (11.9) months. The most common indications for HPN were short bowel syndrome 32 (62%), motility disorders 8 (15%), and inflammatory bowel disease 6 (12%). First CLABSI occurred in 5 (10%) of patients within 30 days of discharge. 24 (46%) of first unscheduled readmissions occurred within 30 days of discharge. Of all initial unscheduled readmissions, 37 (76%) were HPN-related, including infection 26 (53%), fluid/electrolyte imbalances 8 (16%), catheter events 2 (4%), and hypoalbuninemia 1 (2%). Over the 27-month period, we did not detect a significant change in rates of CLABSI or HPN-related unscheduled readmissions within 30 days of discharge.

**CONCLUSIONS:** We observed a high rate of first CLABSI and unscheduled readmissions in this cohort of high-risk patients, likely due to the steep learning curve required upon leaving the hospital during the first weeks on HPN. Based on these findings, our program is moving forward with developing innovative learning modules to better equip caregivers prior to discharge. HPN quality benchmarks are needed to identify best practices across specialized programs.

**308 WEIGHT GAIN AFTER NUTRITIONAL SUPPORT IN A NEONATAL INTENSIVE CARE UNIT.** Carlos A. Velasco, Guillermo Farfan, Pediatrics, University of Valle, Cali, Colombia

**Introduction:** Fasting causes in the newborn (NB), deterioration of their nutritional status and growth in the short and long term. **Objective:** To determine the weight gain in critically ill NB (CINB) after parenteral nutrition (PN).

**Methodology:** In this cross-sectional observational in 110 CINB of both gender, at term (AT) and preterm (PreT) from Social Security of Bucaramanga, Colombia, who received central or peripheral PN. Data were obtained as sex, gestational age, weight, grams/kg/day of carbohydrate, protein and fat, kcal/kg/day baseline and final days of PN and underlying pathology. Statistical analysis included measures of central tendency and position, frequencies, univariate and bivariate tests, comparing means and medians, Chi Square and Fisher, with level of significance of 0.05. **Results:** We included 63 ATNB and 47 PreTNB with principal diagnosis necrotizing enterocolitis in 40 (36.4%). The average at the end of the PN of protein and fat was 1.3 g/kg/day and 2.5 g/kg/day, respectively. Had increased basal and final weight of 14.2 g/day, and significant differences in the progression from baseline to the final weight in the ATNB (p=0.015) and PreTNB (p=0.000), even with weight < 1500 g (p=0.000) and between 1500 to 2500 g (p=0.004).

**Conclusions:** All CINB receiving PN from the first day of life, at lower doses than those currently recommended, improved nutritional status presented with daily weight variation.

**309 BODY MASS INDEX, HEIGHT FOR AGE AND DENTAL CARIES IN COLOMBIAN CHILDREN WITH HIV/AIDS.** Carlos A. Velasco, Maria C. Arango, Pediatrics, University of Valle, Cali, Colombia

**Introduction:** Dental caries in children infected with HIV through vertical transmission, could compromise their nutritional status. **Objective:** To determine the nutritional status using body mass index (BMI) and height for age (HA) according to WHO, in Colombian children infected by vertical transmission HIV/AIDS and dental caries, and identify possible associations. **Methodology:** Prevalence study to assess the nutritional status of children 51 children with HIV/AIDS through vertical transmission and dental caries. Sociodemographic, clinical and paraclinical variables were considered. Statistical analysis included: estimation of measures of central tendency; univariate analysis; possible association between the variables (OR with their respective confidence intervals of 95%); Fisher exact test with a p value < 0.05, two-tailed, significant; and multiple logistic regression analysis. **Results:** There was altered the BMI from 31.3% and 64.7% of the HA, and dental caries prevalence of 78.4%, with an mean age of 124.2±34.8 months, 58.8% of the female gender. Predominated variables: male gender, school (5-12), eutrophic by BMI and altered HA, Icdas 2 and viral load < 400 copies load. BMI was greater altered in male gender, stage C and viral load >30,000<-100,000 copies. There was greater involvement of HA in male gender, stage C and viral load >400<-30,000 copies. The only possible factor associated to HA was stage (OR=4.0, 95% CI 1.5-10.3 (p=0.004). **Conclusion:** There was altered nutrition >31.3% by BMI and HA (WHO) infected children to HIV/AIDS and dental caries, with only one possible risk factor for HA nutritional status.

**310 SERUM LEVELS OF VITAMIN D IN SCHOOLCHILDREN WITH NORMAL NUTRITIONAL STATUS, OVERWEIGHT AND OBESITY.** Carmen A. Sánchez-Ramírez, Mario Del Toro-Equihua, Monica Cruz-Marquez, Yunue Flores-Ruelas, Facultad de Medicina, Universidad de Colima, Colima, Mexico

**Aim.** To compare the serum levels of vitamin D between schoolchildren with overweight, obesity and normal nutrition status.
**Patients and Methods.** Design: cross sectional. Data were collected from 43 schoolchildren randomly selected in a local primary school in the city of Colima, Mexico. The mean age was 9.4 years (1.9, SD); twenty-six (60.5%) children were girls. The nutritional status was determined with body mass index; the classification was based on the age-specific body mass index Z score established by the World Health Organization. Serum levels of vitamin D were determined with enzyme-linked immunosorbance assay. The association between the nutritional status and the serum levels of vitamin D was assessed with U-Mann Whitney and Kruskall-Wallis test. The data was described as medians and interquartile range.

**Results.** Twenty children (46.5%) were classified with normal nutritional status, 6/43 (14%) with overweight and 17/43 (39.5%) with obesity. The median serum levels of vitamin D in the group of children with normal nutrition status was 51.9 nmol/L (23.4-73.2) and in the group of children with overweight plus obesity was 36.5 nmol/L (2.8-73.7) with statistical significance (p=0.014). Only 20/43 (46.5%) of the children presented desired values of vitamin D. Pearson correlation coefficient analysis showed significant inverse relationship between vitamin D and body mass index (r=-0.32, p=0.034).

**Conclusions.** The prevalence of vitamin D deficiency was presented in more than half of the schoolchildren studied and the serum levels of vitamin D were significantly decreased in schoolchildren with overweight and obesity compared to children with normal nutrition status.

<table>
<thead>
<tr>
<th>Nutritional Status</th>
<th>Median</th>
<th>Interquartile Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>51.9</td>
<td>(35.8-64.9)</td>
</tr>
<tr>
<td>Overweight</td>
<td>27.6</td>
<td>(3.9-41.6)</td>
</tr>
<tr>
<td>Obesity</td>
<td>39.3</td>
<td>(2.8-73.7)</td>
</tr>
</tbody>
</table>

*p=0.002 (Kruskall-Wallis test)

311 **VALIDATION OF A NOVEL SEMI-OBJECTIVE FAILURE TO THRIVE DIAGNOSIS TOOL.** Catherine Larson-Nath1, Alisha Mavis1, Lori Duesing1, Catherine Karls2, Praveen S. Goday1, 1Medical College of Wisconsin, Wauwatosa, WI; 2Children's Hospital of Wisconsin, Milwaukee, WI

**Background:** Currently there are seven published definitions of failure to thrive (FTT), each with poor sensitivity and specificity. Subjective tools using a structured approach accurately identify malnourished children, but data in FTT are lacking. A quick and reliable method to assess patients for FTT is needed. The semi-objective failure to thrive diagnosis tool (SOFTT) consists of objective and subjective measures that can be applied quickly in the clinical setting. We aimed to demonstrate concurrent validity of the SOFTT diagnosis tool with standard anthropometric measurements. To test predictive validity we assessed improvements in growth when families were compliant with nutritional interventions. We hypothesized that the SOFTT diagnosis tool can quickly and accurately diagnose FTT in young children.

**Methods:** Patients <5 years of age seen in our pediatric gastroenterology clinic who met one of the seven accepted definitions for FTT were enrolled. Children who were non-FTT were used as controls. The SOFTT tool was used by one of two physicians to diagnose each child as normal, mild FTT, or severe FTT. A scoring system based on tool results was not used because of the semi-objective nature of the tool. Twenty patients were assessed by two raters to determine inter-rater reliability. An independent assessor obtained anthropometric measurements for weight, length, occipital frontal circumference (OFC), mid-upper arm circumference (MUAC), and triceps skinfold thickness (TSF). Z-scores were generated for the measurements and for weight-for-length/BMI. For children with non-organic FTT who were compliant with prescribed interventions and controls, repeat anthropometric measurements were recorded at the next two follow-up visits.

**Results:** Seventy patients met the criteria and were enrolled. The mean age of enrollees was 1.05 years (SD 1.1) and 57.1% were male. SOFTT tool results revealed 24 normal, 40 mild FTT, and 6 severe FTT patients. Spearman's rank correlation demonstrated concurrent validity between the assigned FTT group (normal, mild FTT and severe FTT) and anthropometric measurements associated with FTT including weight, weight-for-length, BMI, MUAC, and TSF z-scores (*p*<0.05). As expected, length and OFC were not significantly correlated with FTT designation. Pairwise comparisons showed a significant difference between all FTT designations and weight, weight-for-length, TSF, and BMI z-scores (*p*<0.05).

There was 100% inter-rater agreement in the 20 patients examined (3 normal, 16 mild FTT, 1 severe FTT, *k*=1.0). Seventeen children had follow-up data available. Children with FTT showed a trend towards improvement in the change in weight z-score when compared with controls (0.9 vs 0.36, *p*=0.07).

**Conclusion:** The SOFTT tool accurately diagnoses FTT in young children. The tool shows concurrent validity and...
excellent inter-rater reliability. More numbers are needed to confirm predictive validity. When validated, the tool will serve as a new way to quickly and accurately diagnose FTT.

312 PHYSICIAN PERCEPTIONS ON PROBIOTICS: RESULTS OF A MULTINATIONAL SURVEY. Christian G. Boggio Marzet1, Andras Arato2, Roberto Berni-Canani3, Serhat Bor4, Ener Cagri Dinleyici5, Uday Chand Ghoshal6, Francisco Guarner7, Aldo Maruy8, Annalisa Passariello9, Ettair Said10, Sohail Thobani11, Lin Zhang12, 1Pediatric Gastroenterology & Nutrition Section, Hospital Gral. Agudos “Dr. I.Pirovano”, Buenos Aires, Argentina; 2First Department of Paediatrics, Semmelweis University, Budapest, Hungary; 3University of Naples Federico II, Naples, Italy; 4Tıp Fakültesi Gastroenteroloji Kliniği, Ege Üniversitesi, İzmir, Turkey; 5Department of Pediatrics, Eskisehir Osmangazi University, Eskisehir, Turkey; 6Department of Gastroenterology, S.G.P.G.I, Lucknow, India; 7Department of Translational Medical Science, University of Naples Federico II, Naples, Italy; 8Digestive System Research Unit, Vall d’Hebron Research Institute, Barcelona, Spain; 9Pediatric Gastroenterology, Hospital Nacional Cayetano Heredia, Lima, Peru; 10Pediatric Gastroenterology, Department of Pediatrics, Rabat, Morocco; 11Pediatric Gastroenterology, Aga Khan University, Karachi, Pakistan; 12Department of Pediatrics, 3rd Hospital of Hebei Medical University, Hebei, China

Introduction: Despite the scientific evidence accumulated during the last decade and the vast number of publications on the medical uses of probiotics, it is not clear whether this information reaches the how well clinicians and has an impact on their practice.

Aim: To evaluate the knowledge, attitudes and current practices of physicians with regards to probiotics in 10 countries.

Methods: A closed-ended structured questionnaire was implemented in 10 different countries (Argentina, Peru, Spain, Italy, Hungary, Morocco, Turkey, Pakistan, India and China). Target and Sample Size: 90 to 190 physicians interviewed per country (General Practitioners-GP-, Pediatricians-Peds-, Gastroenterologists-Gastrots-). Total sample: 1670.

Representativeness: adapted criteria according to each country’s reality (quota method).

Results: All doctors in 10 countries feel that they were adequately informed about probiotics, with the highest prevalence among Gastro in China (100%) and GP in (India 91%). However 39% Moroccan physicians expressed a lack of information. Concerning probiotic definition 94% of Turkish doctors responded according to FAO/WHO criteria while in Pakistan only 39% of doctors did. Saccharomyces boulardii and Lactobacillus rhamnosus GG have been scientifically proven to work in acute infectious diarrhea & antibiotic associated diarrhea (46% and 30%) showing very different scores with no parallel with global guidelines. GPs are less aware of proofs on these strains in these indications whereas Peds remain the most aware target in the sample (36% boulardii/20% GG in GPs vs 51%/35% in Peds population). Similar significant GPs differences recorded in local samples in India, Turkey and Spain. There is an international consensus on safety (84%) with no differences per target. Doctors do recommend probiotics to their family (82%) or themselves (68%). Pediatricians recommend more frequently probiotics in acute diarrhea (66%). Feeling informed and feeling comfortable are correlated at 0,594 and feeling informed and feeling confident are correlated at 0,533 (Linear correlation). Prescribe/ recommend and feeling confident are correlated at 0,390, prescribe/ recommend and feeling comfortable are correlated at 0,376, prescribe/ recommend and feeling informed are correlated at 0,327. There were no correlation between knowledge scoring/prescription (0.036) and between prescription and exposure to scientific paper (0.288) (Pearson Correlation Test)

Conclusions: Most doctors feel well informed about probiotics. The more informed are, the more comfortable and confident they are. Moreover, the more comfortable and confident they are, the more doctors prescribe or recommend probiotics. This is the first multinational survey on probiotics awareness.

313 OUTCOMES OF A MEDICAL MULTIDISCIPLINARY OUTPATIENT INTENSIVE FEEDING THERAPY PROGRAM COMPARED TO TRADITIONAL WEEKLY FEEDING THERAPY IN CHILDREN WITH ENTERAL FEEDING TUBE DEPENDENCE. Caitlin Williams, Kelly VanDahm, Janet Iurilli, Elizabeth Linos, Dana I. Ursea, Phoenix Childrens Hospital, Phoenix, AZ

Purpose: We compared outcomes of our 5-week multidisciplinary intensive feeding therapy (IFT) program with age matched children undergoing traditional once weekly feeding therapy (TT) to determine reduction of enteral tube nutrition (ETN) dependence and increase in age appropriate feeding in medically complex children with dysphagia.

Methods: This was a retrospective cohort design. Statistical analysis was performed using the Mann Whitney test to compare ETN reduction of the two groups. Measured variables were: ETN energy intake as a percentage of daily energy goal, percentage ideal body weight (IBW) and number and variety of oral foods.

Results: 23 IFT and 22 TT patients were analyzed. Patients were primarily between ages 1-3Y, medically complex, but in stable health, with ETN dependence of greater than 1year. IFT patients experienced a median reduction of ETN of 49% (35%, 59%) compared with a reduction of 0% (0%, 25%) for TT patients (p>0.0001). This reduction occurred over 5 weeks for IFT patients versus 25+ weeks for TT. Half of IFT patients no longer required ETN by the end of the 5 weeks compared with no TT patients. IFT patients demonstrated an increase in number and variety of foods (average 10 new foods and 4 new varieties). IFT patients with little or no reduction in ETN either had active oral aspiration (n=2) or
significant behavioral problems (n=2). Predicted timeframe for complete ETN wean is 10 weeks for IFT (with 2 rounds of IFT) versus 3 years for TT, resulting in significant reductions of ETN associated co-morbidities and healthcare costs. **Conclusion:** The IFT program resulted in significant reduction of ETN in children with complex medical conditions over a 5-week period as compared with children in TT. Treatment of dysphagia and feeding disturbances in ETN dependent young children by a multidisciplinary team has superior outcomes to the traditional model of feeding therapy alone.

<table>
<thead>
<tr>
<th>Patients</th>
<th>IFT</th>
<th>TT</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 23 (11 male, 12 female)</td>
<td>n = 22 (11 male, 11 female)</td>
<td></td>
</tr>
<tr>
<td>Age at therapy visit #1</td>
<td>30 mo (13-82 mo)</td>
<td>27 mo (11-64 mo)</td>
</tr>
<tr>
<td>Primary co-morbidity</td>
<td>Congenital heart = 7</td>
<td>= 3</td>
</tr>
<tr>
<td></td>
<td>Prematurity = 5</td>
<td>= 5</td>
</tr>
<tr>
<td></td>
<td>Aerodigestive Abn = 3</td>
<td>= 2</td>
</tr>
<tr>
<td></td>
<td>GI (GERD, EoE, motility) = 2</td>
<td>= 7</td>
</tr>
<tr>
<td></td>
<td>Heart Transplant = 2</td>
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<tr>
<td></td>
<td>Liver Transplant = 1</td>
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<td></td>
<td>Diaphragmatic hernia = 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Renal = 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IU/GR/SGA = 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Genetic Syndrome = 1</td>
<td></td>
</tr>
<tr>
<td>Dysphagia with active oral aspiration</td>
<td>N = 5</td>
<td>N = 5</td>
</tr>
<tr>
<td>Duration of ETN</td>
<td>25 mo (10-82 mo)</td>
<td>18 mo (3-64 mo)</td>
</tr>
<tr>
<td>%ETN at therapy visit #1</td>
<td>76% (17% - 100%)</td>
<td>80% (26% - 100%)</td>
</tr>
<tr>
<td>%IBW at therapy visit #1</td>
<td>80% - 89%</td>
<td>80% - 89%</td>
</tr>
<tr>
<td></td>
<td>90% - 99%</td>
<td>90% - 99%</td>
</tr>
<tr>
<td></td>
<td>≥ 100%</td>
<td>≥ 100%</td>
</tr>
</tbody>
</table>

**BODY COMPOSITION ESTIMATION IN CHILDREN WITH ALTERED GROWTH PATTERNS.** Danielle Wendel¹, Sheela Magge¹,², Andrea Kelly¹,², Virginia Stallings¹,², Mary Phipan¹,², Mary Leonard¹,², Nicolas Stettler³, Babette Zemel¹,², ¹Children's Hospital of Philadelphia, Philadelphia, PA; ²The University of Pennsylvania, Philadelphia, PA; ³The Lewin Group, Falls Church, VA

**Background:** Previously published skinfold prediction equations to estimate body composition have not been validated for children with altered growth patterns.

**Objective:** To evaluate published and newly developed skinfold prediction equations across several pediatric samples.

**Design:** Anthropometric and dual-energy x-ray absorptiometry (DXA) body composition measures were obtained from children with Down syndrome (DS) and typically developing (TD) controls. Published equations were used to estimate body composition. Factors associated with differences between anthropometric and DXA body composition measures were identified. New equations that included sex, height and Tanner stage were developed using data on 828 TD controls. They were validated in the DS cohort as well as in children with Crohn disease and nephrotic syndrome.

**Results:** Body composition measures from published equations and DXA were highly correlated (r=0.98, 0.99, and 0.81 for fat mass (FM), fat free mass (FFM) and percent body fat (%BF)), but with poor agreement (mean difference [limits of agreement]) between measures (2.2kg [-2.1, 6.4], -1.8kg [-6.4, 2.7], 5.6% [-3.8, 15] for FM, FFM and %BF) for children with DS. Newly developed equations produced similar correlation results (r=0.98, 0.99, and 0.84 for FM, FFM and %BF) but the bias was eliminated and improvements made in measures of agreement (-0.2kg [-3.7, 3.4], 0.5kg [-
315  **NUTRITIONAL STATUS, ENERGY INTAKE, MACRONUTRIENTS, VITAMINS AND INORGANIC NUTRIENTS IN PATIENTS WITH IBD.** Elizabeth Arce-Mojica¹, Rocío Macías-Rosales², Alfredo Larrosa-Haro², ¹Gastroenterología y Nutrición, UMAE Hospital de Pediatria CMNO IMSS, Guadalajara, Mexico; ²Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Guadalajara, Mexico

**Aim:** Association of energy intake, macronutrients, vitamins, inorganic nutrients and nutritional status in patients with IBD.

**Methods:** 10 patients with UC and 2 with CD were included in this cross-sectional study. Nutritional status was assessed using anthropometry and energy intake; macronutrients, vitamins and inorganic nutrients using 24-hour recall and food habits throughout food consumption frequency. Median and interquartile range were used for statistical analysis. Association of variables was established with $X < 2 < +$, Fisher's exact, Mann-Whitney U and linear bivariate correlations.

**Results:** The overall energy intake was lower than the value reported by the National Academy of Sciences while the overall carbohydrate and protein intake was higher. Overall polyunsaturated fat ingestion was found to be lower than daily recommendation. Energy input percentage in a protein, carbohydrate and lipid diet was lower as well. Vitamin E and folic acid RDA was lower than recommended. Calcium, zinc, selenium, iron and magnesium intake was less than recommended. Food consumed most was: whole milk, chicken, beef, beans, peanuts, carrots, apples, tortillas, canola oil, natural water, chips and beef tacos. 17.5% of patients had a z-score below -2 SD for height-for-age and one patient (8.3%) for mid-arm circumference. Correlations with statistically significant difference were triceps skin fold z-score value and total protein grams as well as triceps skinfold z-score value and both vitamin B12 and folic acid micrograms.

**Conclusions:** Even though patients were in remission they still had nutritional deficiencies.

316  **A HUMAN MILK CARBOHYDRATE IMPROVES THE LONG-TERM ADAPTIVE RESPONSE TO INTESTINAL RESECTION.** Ethan A. Mezoff, Jennifer Hawkins, Nambi Sundaram, Ardythe L. Morrow, Michael Helmrecht, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

**Abstract:** Supplements designed to improve the adaptive response to small bowel resection possess the potential to dramatically reduce costs and disease in patients suffering from short bowel syndrome. An improved clinical adaptive response has been observed in breastfed infants compared to infants fed formula. 2-fucosyllactose (2’FL), a common human milk oligosaccharide, is a non-caloric prebiotic, which supports the growth of beneficial microbial communities and protects against pathogens. We sought to describe the impact of 2FL supplementation on the adaptive response to ileo-cecal resection (ICR).

**Methods:** Two groups of C57Bl/6 mice underwent ileocecal resection (ICR) as previously described by our lab. The experimental group was provided water containing 2.5 mg/mL 2’FL. The control group received standard, sterile water. Both groups were weighed periodically and taken to 56 days after resection, at which time histologic markers were assessed. Weight change in relation to pre-operative weight was analyzed using a generalized estimating equation.

**Results:** Weight recovery following resection occurred in both groups, with no difference between groups up to day 21. However, mice fed 2’FL underwent significantly ($p<0.001$) greater weight gain after 21 days after ICR. The experimental group displayed a significant increase in crypt depth ($p<0.05$) and increased villus height. The intestinal length to body weight ratio was smaller in animals fed 2’FL, however, bowel circumference increased.

**Conclusion:** 2’FL supplementation improves the long-term adaptive response to intestinal resection. Further study may yield insights into the feasibility of microbial modulation for improving adaptation as well as provide a potential therapeutic formula additive for children who undergo bowel resection.

317  **ETHANOL LOCK EFFICACY AND COMPLICATIONS IN PEDIATRIC INTESTINAL FAILURE.** Ethan A. Mezoff, Misty Troutt, Monir Hossain, Kim Klotz, Samuel Kocoshis, Conrad Cole, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

**Introduction:** The use of ethanol lock therapy (ELT) has been shown to reduce central line-associated blood stream infections (CLA-BSI’s) in children with intestinal failure (IF). However there are concerns regarding the risk for associated central line complications, specifically line occlusions. Our goal was to describe our experience with ethanol locks in a cohort of patients with IF.

**Methods:** Our ELT protocol utilizes a 70% ethanol solution with dwell time greater than or equal to two hours. Indications for ELT include two or more previous CLA-BSI. Patients on ELT from 2010 to 2013 were identified by review of our intestinal rehabilitation registry. Patient demographics, CLA-BSI events, and line complications were extracted. Infection and complication rates were calculated and comparisons made between time on and off ELT by
pairwise T-test.

**Results:** During the study period, 30 patients were started on ELT. CLA-BSI's when on and off ELT were 3.1 and 5.5 per 1,000 catheter days respectively (p=0.33). Line occlusion rates were halved on ELT, from 0.6 to 0.3 per 1,000 catheter days. Breakage rates remained the same at 1.5 to 1.8 per 1,000 catheter days on and off ELT. Infecting organisms were similar on and off ELT and both experienced a similar number of polymicrobial infections. *Klebsiella pneumoniae* was the most common infecting organism in both groups.

**Conclusion:** Ethanol locks improve rates of CSA-BSI's without increasing complication rates in children with IF. A failure to show significance may be related to an overall low BSI rate in our cohort.

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**318 13C-STARCH BREATH TESTS REVEAL THAT α-AMYLASE INSUFFICIENT TODDLERS OF MALI HAVE ADEQUATE MUCOsal α-GLUCOSIDASE ACTIVITIES FOR SORGHUM PORRIDGE DIGESTION TO GLUCOSE.**  Fatimata Cisse1,2, Atossa Rahmanifar2, Mariam Sylla2, Hawa G. Diâ2, Roberto Quezada-Calvillo6,5, Anotoke Opeku2, Michael A. Grusak6, Amy H. Liu2, Buford L. Nichols6,1, Bruno P. Chumpitazi1, Bruce R. Hamaker2, 1Pediatrics, Baylor College of Medicine, Houston, TX; 2Department of Food Science, Purdue University, West Lafayette, IN; 3Institut d’Economie Rurale du Mali (IER), Bamako, Mali; 4Département de Pédiatrie, Centre Hospitalier et Universitaire Gabriel Toure, Bamako, Mali; 5CIEP-Facultad de Ciencias Quimicas, Universidad Autonoma de San Luis Potosi, San Luis Potosi, Mexico; 6USDA ARS Children’s Nutrition Research Center, Houston, TX

**Background:** Starches are dominant sources of dietary energy in complimentary feeding of growing toddlers. Glucose is the only carbohydrate oxidized by the brain. In toddlers, 40% of the glucose needed for brain metabolism comes from the diet with the remainder produced by endogenous gluconeogenesis from amino acids. After weaning, dietary glucose is digested from starch which is the main component of most complimentary foods. Young infants lack secreted α-amylase until weaning and after this period malnourished toddlers have reduced α-amylase activity. **Hypothesis:** Malnourished (stunted) weaned toddlers have impaired ability to digest starch due to developmental and/or nutritional pancreatic α-amylase insufficiency which impedes normal growth when fed with the sorghum porridges used at home.

**Methods:** Non-invasive modified 13C-breath tests (BT) were used to assess α-amylase activity and the ability to digest sorghum starch in healthy (n=16) and moderately stunted toddlers (n=32) from 18 - 30 months of age in Bamako, Mali. Three different 13C substrates (uniformly labeled [UL]-algal starch, UL-algal limit dextrins, and partially enriched sorghum) were fed on separate days. Serial breath samples (every 15 min for 3 hours) were collected and analyzed using a 13C-IRMS infrared spectrophotometer. **Results:** α-Amylase insufficiency was present in both healthy and stunted toddlers. Toddlers with α-amylase deficiency digested, absorbed, and oxidized the released glucose well from the normal sorghum porridge. **Conclusions:** 1. α-Amylase sufficiency can be tested by non-invasive 13C-starch substrate BTs. 2. The digestion of sorghum porridge starch to glucose was unrelated to α-amylase sufficiency. 3. Sorghum porridge is a starch containing complimentary food that is well digested because of sufficient Sucrase-isomaltase and Maltase-glucoamylase glucosidase activities in Malian weaned toddlers. 4. The stunting of Malian toddlers was unrelated to sorghum feeding and starch digestion to glucose. 5. The hypothesis that stunted toddlers mal-digest sorghum porridge is disproven.

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**319 PROSPECTIVE STUDY OF HOSPITALIZATION FOR FAILURE TO THRIVE.** Catherine Larson-Nath, Praveen S. Goday, Medical College of Wisconsin, Milwaukee, WI

**Aims:** We aimed to prospectively characterize children admitted to a tertiary children's hospital with the diagnosis of failure to thrive (FTT) and the outcomes from admission.

**Methods:** All children < 18 years of age admitted to the Children's Hospital of Wisconsin with a diagnosis of FTT were prospectively enrolled. Descriptive statistics were used to analyze the data.

**Results:** A total of 59 patients were enrolled in the study over a 10-month period. Thirty-three were male (55.9%) with an average age of 1.13 years. Fifty-three (90%) underwent laboratory testing, 35 (59%) underwent radiologic imaging, and 9 (15%) had endoscopic evaluation. A prior medical diagnosis was felt to be the primary etiology for FTT in nine (31%) patients. Seven (12%) children had a new diagnosis made during their hospitalization. Laboratory, imaging, or endoscopic evaluation led to the primary cause of FTT in three of these children. The positive tests included one child with a positive genetic work-up, one with a positive imaging study for malrotation, and one with a positive colonoscopy for allergic colitis. These findings were all suspected based on clinical history and/or exam. In addition, two children were clinically diagnosed with laryngomalacia and two others were diagnosed with allergic colitis based on clinical response to interventions. Non-organic FTT was the final diagnosis in the remaining 43 patients (73%).

Weight gain defined as average grams per day weight gain during hospitalization was significantly higher in children with non-organic FTT compared to those with organic FTT (median 58 g/d vs 34 g/d, p=0.001). The change in weight z-score over the same time span was also significantly different between these two groups (0.29 vs 0.035, p=0.036). For children with non-organic FTT the most common hospital interventions were structured meals and snacks (83.7%).
and increased calories (67.4%). Child protective services were involved in 9 (21%) cases of children with non-organic FTT.

**Conclusions:** The majority of patients admitted to the hospital for FTT were found to have primary non-organic etiologies of FTT. Laboratory, imaging, and endoscopic evaluation rarely provided a diagnosis for the etiology of FTT. While all children in this study gained weight during hospitalization, children with non-organic FTT gained weight better than those with organic FTT.

### 320 ADHERENCE IMPROVES WEIGHT GAIN IN PEDIATRIC FAILURE TO THRIVE.

**Catherine Larson-Nath, Praveen S. Goday, Medical College of Wisconsin, Milwaukee, WI**

**Aims:** We aimed to describe patients referred to a pediatric gastroenterology clinic with the diagnosis of failure to thrive (FTT) and the impact of adherence to provider recommendations on growth.

**Methods:** All English speaking children <18 years of age seen for the first time in the outpatient pediatric gastroenterology clinic with a diagnosis of FTT were prospectively enrolled in the study. General data regarding history, growth parameters, evaluation, and intervention were recorded. Adherence to provider recommendations was determined based on provider assessment at follow-up visits. Descriptive statistics were used to analyze the data.

**Results:** A total of 83 patients were enrolled in this study over a 10-month period. Fifty-one (61.4%) were male with a mean age of 2.4 years. At the time of enrollment there was no significant difference in anthropometric measures between children with organic and non-organic FTT. Of the enrolled children, 44 (53%) had laboratory evaluation, 24 (30%) had imaging performed, and 9 (11%) underwent endoscopy. Labs aided in the diagnosis for one patient who has cystic fibrosis. Endoscopy was diagnostic in two children diagnosed with eosinophilic esophagitis and one child diagnosed with allergic colitis. Of the 73 patients who had a final diagnosis, 64 (87.7%) had non-organic failure to thrive.

At follow-up of the children with non-organic FTT 30 (70%) patients were adherent with provider recommendations and 13 (30%) were not. There was no difference between children who were adherent to provider recommendations and those who were not in regards to gender, age, race, insurance type, presence of both parents or other children in the home, presence of other children in the home, or the nutritional and behavioral recommendations given. Post-intervention, children who were non-adherent with recommended interventions had significantly lower z-scores for weight compared to those who were adherent (-2.3 vs -2.8, p=0.02), weight-for-length (-2.3 vs -2.07, p=0.47), and BMI (-2.34 vs -2.19, p=0.001). They also had significantly lower change in z-score for weight (0.03 vs 0.36, p=0.002) and weight-for-length/BMI (0.00 vs 0.44, p=0.026).

**Conclusion:** The majority of children referred to our pediatric gastroenterology clinic with FTT have non-organic FTT. Slightly more than half of the children seen with concerns for FTT undergo laboratory evaluation. Children who are adherent to provider recommendations show improved growth. This study demonstrates that methods to improve patient adherence are needed to improve clinical outcomes.

**Friday, October 24, 2014**

**2:30 – 4pm**

**Research Session III – Clinical/Translational – Inflammatory Bowel Disease**

### 321 THE MUCOSA-ASSOCIATED MICROBIOME IN PEDIATRIC CROHN’S DISEASE: INCREASING TAXA IDENTIFICATION WITH A NOVEL ANALYTIC METHOD.

**Jess L. Kaplan1,2, Feng Wang1, Manoj Bhasin2, Naomi L. Ward2, Christopher J. Moran3, Scott E. Dowd2, Stephen B. Cox1, Tovia A. Libermann4, Leonid A. Mirny8, Kirill S. Korelev5, Harland S. Winter2,3, 1Graduate Program in Bioinformatics, Boston University, Boston, MA; 2MassGeneral Hospital for Children, Boston, MA; 3Harvard Medical School, Boston, MA; 4Bioinformatics & Systems Biology Core, Beth Israel Deaconess Medical Center, Boston, MA; 5Department of Botany, University of Wyoming, Laramie, WY; 6MR DNA Molecular Research LP, Shallowater, TX; 7Research and Testing Laboratory, LLC, Lubbock, TX; 8Institute for Medical Engineering and Sciences, MIT, Cambridge, MA; 9Department of Physics, Boston University, Boston, MA**

**Background:** Variations in mucosa-associated microbiota have been well demonstrated in pediatric Crohn's disease (CD) and such differences may hold clues to disease pathogenesis and improved treatment and outcomes. Prior analyses of gut microbiota have relied on mean taxa abundance with typically broad distributions across individuals, posing challenges in association studies. Here we apply new analytic techniques to both a new pediatric CD cohort and to a large, previously published, pediatric CD cohort.

**Methods:** Ileal mucosal biopsies were obtained from 87 children (ages 2-17) undergoing ileocolonoscopy for evaluation of possible IBD. Of these, 24 were diagnosed with CD and 63 with non-IBD. Bacterial community structure was determined by 454 Pyrosequencing of 16S ribosomal RNA genes. Associations between the diagnosis and bacterial taxonomic units were identified using novel methods based on log-transforms and mutual-information measures with permutation tests to assess statistical significance.

**Results:** We found signs of bimodal distribution of log-abundance in several taxa with one of the modes more common.
in controls and the other in CD patients. Corrected for multiple hypothesis testing, we found differences in 5 orders (Enterobacteriales, Coriobacteriales, Clostridiales, Bacteroidales, Bacillales) and 4 genera (Roseburia, Blautia, Salmonella, and unknown Lachnospiraceae) in CD subjects versus controls. The most significant differences were seen in the genera Roseburia (decrease in CD, p < 10^{-3}), Blautia (decrease in CD, p < 4 \times 10^{-5}) and Salmonella (increase in CD, p < 3 \times 10^{-6}). Three of the orders (Enterobacteriales, Clostridiales, Bacteroidales) and three of the genera (all except Salmonella) detected in this study were also identified in a similar study of the RISK cohort. Our methods were able to detect a similar number of associations as in the RISK cohort despite 10 times fewer patients and 10 times fewer reads per patient. Importantly, the application of our analysis methods to the RISK cohort data more than doubled the number of identified taxa leading to 18 genera significantly associated with CD.

Conclusions: Novel analytic methods allow for increased taxon identification and improved description of gut mucosal microbial community structure.

Supported in part by The Pediatric IBD Foundation and the NIH.

322 ANTI-TNFα THERAPY IS ASSOCIATED WITH EPSTEIN BARR VIRUS LYTIC ACTIVATION. Sameer Lapsia1, Siva Koganti2, Anupama Chawla1, Jing Ming Wang3, Sumita Bhaduri-McIntosh2, 1Pediatric Gastroenterology, Stony Brook Children's Hospital, Stony Brook, NY; 2Stony Brook Children's Hospital, Stony Brook, NY; 3Stony Brook University, Stony Brook, NY

Background: Anti-tumor necrosis factor-alpha (anti-TNFα) therapy such as infliximab, which is known to suppress T cell immunity, is gaining popularity for treatment of autoimmune conditions including inflammatory bowel disease (IBD). T cell suppression increases the risk for development of Epstein Barr Virus (EBV)-lymphomas/lymphoproliferative diseases (LPD). There are increasing reports of lymphomas and primary intestinal lymphoproliferative disorders in patients with IBD exposed to immunosuppressants including anti-TNFα therapy, with many of these reported incidences EBV-related.

Hypothesis: Since EBV lytic (re)activation is essential for the development of EBV-LPD, we hypothesized that patients treated with anti-TNFα demonstrate greater EBV lytic activity in blood.

Design/Methods: In this pilot study, 10 IBD patients solely on anti-TNFα antibodies for at least 6 months were recruited and compared to 3 control groups (10 IBD patients not on immunosuppressive therapy, 10 patients with abdominal pain but without IBD, and 10 healthy subjects). Whole blood was taken and peripheral blood mononuclear cells (PBMC) were isolated. We used flow cytometry to ascertain T cell frequencies in the study population compared to controls. We tested our hypothesis by measuring 1) total EBV load in PBMC using quantitative PCR to amplify the viral genome (range 116-1341 genomes) per 10^6 PBMC as compared to the other three groups which collectively had on average 161 genomes (range 5-430 genomes) per 10^6 PBMC (p ≤ 0.05). This corresponds to a > 3.5 fold increase in viral load in the TNFα blocker group. This group also had increased levels of transcripts from EBV lytic genes (p≤0.04) of all kinetic classes compared to the 3 control groups. Finally, we found that exposure of EBV-infected B cell lines to therapeutic concentrations of anti-TNFα resulted in EBV lytic gene expression.

Results: Consistent with the finding that anti-TNFα antibodies suppress T cell activity, patients on anti-TNFα therapy had 16% fewer T cells (p<0.05) compared to the other 3 control groups. IBD patients on anti-TNFα had on average 578 genomes (range 116-1341 genomes) per 10^6 PBMC as compared to the other three groups which collectively had on average 161 genomes (range 5-430 genomes) per 10^6 PBMC (p ≤ 0.05). This corresponds to a >3.5 fold increase in viral load in the TNFα blocker group. This group also had increased levels of transcripts from EBV lytic genes (p≤0.04) of all kinetic classes compared to the 3 control groups. Finally, we found that exposure of EBV-infected B cell lines to therapeutic concentrations of anti-TNFα resulted in EBV lytic gene expression.

Discussion: Supporting our hypothesis, IBD patients on TNFα blockers had a greater EBV load as well as increased lytic gene expression. In addressing potential mechanisms, we found that anti-TNFα antibodies have a direct effect on inducing EBV lytic gene expression; a likely additional mechanism is anti-TNFα antibody-mediated suppression of T cell immune-surveillance towards EBV. Although this is a pilot study using a small number of subjects this is the only study evaluating patients solely on anti-TNFα therapy without concomitant immunomodulator therapy. Prospective studies looking at larger groups of subjects at different time-points and for longer durations will be essential to make conclusive statements about the effect of TNFα blockers.

323 DURABILITY OF ADALIMUMAB THERAPY IN CHILDREN WITH CROHN'S DISEASE. Rose Lee1,2, Trudy Lerer1, Anne Griffiths1, Marian Pfefferkorn1, Anthony Otley1, James Rick1, David Mack1, Jose Cabrera1, Joel Rosh1, Athos Bousvaros1, Marsha Kay1, Maria Oliva-Hemker1, Shehzad Saeed1, Neal LeLeiko1, Andrew Grossman1, David Keljo1, Michael Kappelman1, William Faubion1, Colette Deslandres1, Brendan Boyle1, James Markowitz1, Jeffrey Hyams1, 1Pediatric IBD Collaborative Res Grp, Hartford, CT; 2University of CT School Med, Farmington, CT

Background: Anti-TNFα therapy is now commonly used in children with Crohn's disease (CD). While most children are initially treated with infliximab (IFX), many lose response and/or develop immunogenicity and are changed to adalimumab (ADA). ADA has demonstrated efficacy in both IFX experienced as well as IFX naïve patients. To date there are little data on the durability of ADA therapy in children with CD.

Aims: To evaluate durability of ADA and identify predictive factors associated with longer durability in a large inception cohort of children with CD.

Methods: Data were obtained from the pediatric IBD Collaborative Research Group Registry, a prospective North American
OBSERVATIONAL STUDY OF NEWLY DIAGNOSED CHILDREN ≤ 16 YEARS OF AGE STARTED IN 2002. AGE, GENDER, PHYSICIAN GLOBAL ASSESSMENT (PGA), DISEASE EXTENT AT DIAGNOSIS, PREVIOUS USE OF INFliximAB (IFX) OR OTHER IMMUNOMODULATORS (IM) (6-MERCAPTOPURINE (6MP), AZATHIOPRINE (AZA), METHOTREXATE (MTX)) WERE ASSESSED. PRESERVATION OF DURABILITY (LIKELIHOOD OF REMAINING ON ADA) UP TO A 5-YEAR FOLLOW-UP PERIOD WAS ESTIMATED BY KAPLAN-MEIER ANALYSIS AND ANY DIFFERENCES BETWEEN SURVIVAL CURVES WERE CALCULATED WITH THE LOG-RANK TEST. RESULTS: OF 1406 PATIENTS WITH CD IN THE REGISTRY, 150 RECEIVED ADA (52% FEMALE). ADA WAS USED IN 109 PATIENTS WHO WERE IFX EXPERIENCED AND AS PRIMARY ANTI-TNFα THERAPY IN 32 PATIENTS (IFX NAÏVE). 9 RECEIVED IFX ONLY AFTER ADA AND ARE NOT PART OF THIS ANALYSIS. MEAN AGE AT DIAGNOSIS WAS 11.7±2.5 YR WHILE MEAN AGE AT FIRST ADA THERAPY WAS 14.8±2.7 YR. 17/150 SUBJECTS HAD PREVIOUSLY UNDERGONE RESECTONAL THERAPY. THE DURABILITY OF ADA AT 1, 2, 3, 4, AND 5 YRS WAS 77±0.4, 71±0.4, 69±0.4, 69±0.4, AND 64±0.6, RESPECTIVELY. PREVIOUS USE OF IFX ADVERSELY Affected ADA DURABILITY. AT 1, 3 AND 5 YEARS THE LIKELIHOOD OF REMAINING ON ADA WAS 93±0.5, 93±0.5, AND 93±0.5 IN THOSE WHO WERE IFX NAÏVE VersUS 77±0.4, 68±0.5, AND 60±0.8 IN THOSE WHO WERE IFX EXPERIENCED (P=0.008). CONCOMITANT TREATMENT WITH IM AT ADA START HAD NO SIGNIFICANT EFFECT ON ADA DURABILITY IN EITHER IFX EXPERIENCED OR IFX NAÏVE TREATED PATIENTS. CONCLUSION: PREVIOUS IFX USE HAD A SIGNIFICANT NEGATIVE EFFECT ON ADA DURABILITY. ADA DURABILITY WAS ALSO SIGNIFICANTLY BETTER IN MALES COMPARED TO FEMALES. IN OUR ADA COHORT, CONCURRENT IM USE DID NOT APPEAR TO IMPROVE ADA DURABILITY.
Background: A subset of children with acute pancreatitis develop repeat episodes or acute recurrent pancreatitis (ARP). The factors and etiologies that predispose children to ARP are poorly understood, as is the burden of disease. The aim of this study is to address this knowledge gap.

Methods: A multicenter pediatric study group, INSPIRE (International Study Group of Pediatric Pancreatitis; In search for a cure), was developed to collect clinical data of well-phenotyped children with ARP and chronic pancreatitis (CP) using physician and patient questionnaires. We report the preliminary findings on ARP from the INSPIRE database.

Results: Of the 174 patients who were enrolled, 98 patients had ARP and 76 had CP. Of the patients with ARP, 54 (54%) were females; 66 (66%) were Caucasian and 13 (13%) were Hispanic. The mean (SD) age at recruitment was 11.5 (4.7) years and the mean (SD) age at the initial episode of acute pancreatitis was 8.6 (4.9) years. The mean (SD; range) number of recurrent attacks was 6.7 (6.1; 2-31). Complications were reported in 17%, with pseudocysts being the most common (n=9 [9%]). Family history of acute or chronic pancreatitis was documented in 30 patients (31%). The most common etiologies were genetic and obstructive diseases. Among those who had genetic testing, genetic risk factors were found in 34/55 (62%) with some overlap: PRSS1 9/53 (17%), CFTR 20/58 (34%), SPINK1 12/48 (25%) and CTRC 2/27 (7%). Obstructive factors were found in 34/95 (36%) including pancreatic divisum 12/95 (13%), lithiasis 7/95 (7%) and choledochal cyst 4/95 (4%). 5/12 (42%) subjects with pancreatic divisum also had mutation(s) associated with pancreatitis including CFTR in 3 and CFTR plus SPINK1 in 2. 11/30 (37%) patients with a family history of acute or chronic pancreatitis had positive genetic testing including PRSS1 in 7, CFTR in 3 and SPINK1 in 1. Toxins (i.e. alcohol and smoking), medications, autoimmune and metabolic factors were uncommon etiologies. Medical treatment was attempted in 27 (28%): pancreatic enzymes in 22 (22%), octreotide in 2 (2%), vitamins in 9 (9%) and corticosteroids in 1 (1%). Surgical therapy was attempted in 15/96 (16%), with cholecystectomy being the most common intervention in 11 patients. 79/95 (81%) patients reported pain from pancreatitis in the past year. Patients reported a mean (SD) number of 4.9 (4.8) ED visits, 4.3 (4.9) hospitalizations, and, in the month preceding completion of the questionnaire, 4.1 (7.1) missed school days.

Conclusions: Based on the largest cohort of pediatric patients with ARP, we can conclude that pediatric ARP frequently begins in early childhood and is most often associated with genetic and/or obstructive factors. A family history of pancreatitis is common and often signals hereditary disease. ARP is associated with significant disease burden with many children requiring medical and surgical therapies and experiencing repeated hospitalizations, ED visits and missed school days.

Methods: Review of 75 children who received TP-IAT for chronic pancreatitis between 1989-2012 at a single center.

Results: Etiology was hereditary or genetic in 60%. All patients were on narcotics before the operation and had failed medical therapy, endoscopic therapy or failed surgical treatment or had progressive hereditary disease. Median follow up was 3.86 Years (Range - 0.6 years to 23.49 years; Interquartile Range = 6.09 years). Surgical complications occurred in 15 (20%). No patient developed portal vein thrombosis. There was one in-hospital mortality due to sepsis(1.3%). The Complication rate was significantly lower in younger children (p=0.041). Pain relief: Pancreatitis pain and the severity of pain improved in 90% of patients after TP-IAT (p <=0.001). Narcotic use was statistically reduced after TP-IAT. Much of this decline occurred in the first year and remains relatively constant at between 10 % and 20 % from the first year after TPIAT forward. The relief from narcotics was sustained. Beta cell function: 31 (41.3%) achieved insulin independence. 28 of the 31 patients achieved insulin independence within 12 months after TPIAT. Insulin independence has been observed for as long as 10years after TP-IAT. Younger age (p=0.032), lack of prior Puestow (p=0.018), lower
body surface area (p=0.048), Islet cell equivalents (IEQ) per Kg Body Weight (p=0.001) and total IEQ (100,000) (0.004) were associated with insulin independence. By multivariate analysis, 3 factors were associated with insulin independence after TP-IAT: (1) male gender, (2) lower body surface area and the (3) higher total IEQ per kilogram body weight. Total IEQ (100,000) was the single factor most strongly associated with insulin independence (OR = 2.62; p value < 0.001). Quality of life evaluated by SF-36 health survey among those >12 yrs of age showed a statistical improvement in physical and mental health following TP-IAT (p=0.007). Significant improvements were seen in all 8 subscales, with the most dramatic improvements in raw score for role-physical (14 ±7 at baseline vs. 83 ±10 at 1 year, p<0.001) and bodily pain (25 ±5 at baseline vs. 70 ±7 at 1 year, p=0.001). The percent of parents reporting lost days at school declined from 80% to 20% after TP-IAT (p < 0.001).

**Conclusions:** TP-IAT provides sustained pain relief and improved quality of life. Islet auto transplant is safe in children. Beta cell function is dependent on islet yield. TP-IAT is an effective therapy for children with chronic painful pancreatitis that fail medical and or endoscopic management.

### 327 VALPROIC ACID PREDISPOSES PATIENTS TO PANCREATITIS BY INHIBITING THE EPIGENETIC FACTORS THE HISTONE DEACETYLASES AND PROVOKING AN IMBALANCE IN PANCREATIC RECOVERY.

**John F. Eisses**, **Zachary R. Dionise**, **Swati Sah**, **Sheharyar Sarwar**, **Angela Criscimana**, **Abraham I. Orabi**, **Farzad Esni**, **Sohail Z. Husain**, **Pediatrics, University of Pittsburgh and the Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA; **Surgery, University of Pittsburgh and the Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA**

There is currently a black box surrounding the mechanisms by which certain drugs induce pancreatitis. A definite cause of acute pancreatitis seen in children is due to the ingestion of the anti-epileptic drug valproic acid (VPA). Based on three crucial observations—(1) that VPA is an inhibitor of an important class of epigenetic factors the histone deacetylases (HDACs); (2) that HDACs mediate embryonic development of the pancreas; (3) and that several aspects of pancreas development are recapitulated during recovery of the pancreas from injury—we hypothesized that VPA predisposes patients to pancreatitis by inhibiting HDACs and provoking an imbalance in pancreatic recovery. In two complementary mouse models of pancreatic ablation and subsequent recovery—(1) caerulein hyperstimulation and (2) selective pancreatic diphtheria toxin receptor (DTR)-expression (Pdx1-Cre-DTR-transgenic)—we found that by qPCR, Western blot, and nuclear acetylation activity assays, that pancreatic expression of class I HDACs (which are the primary VPA targets) rose at least 4-fold above adult baseline levels during the middle phase of pancreatic recovery (p<0.05) for each assay. Systemic administration of VPA to mice (at doses and serum levels approximating human intake) inhibited pancreatic HDACs by 15-fold (p<0.05). The same amount of VPA administration delayed recovery of the pancreas and, in the late phase of recovery, led to the persistence of acinar-to-ductal metaplastic complexes, which predisposes patients to pancreatitis by inhibiting HDACs and provoking an imbalance in pancreatic recovery. The work also elucidates a new paradigm for therapies that could exploit epigenetics to enhance pancreatic recovery and thus therapeutically impact pancreatitis.

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**Saturday, October 25, 2014**

**8:15 – 10am**

**Plenary Session II**

**NASPGHAN Fellow Research Award**

### 328 BILE ACID SIGNATURES IN CHILDREN CONFER PROTECTION FROM CLOSTRIDIUM DIFFICILE INFECTION.


**Pediatric Gastroenterology, Baylor College of Medicine/ Texas Children's Hospital, Houston, TX; Pathology, Baylor College of Medicine/ Texas Children's Hospital, Houston, TX; Pediatric-Gastroenterology, University of Houston, Houston, TX; Internal Medicine, Infectious Disease, UTMB, Galveston, TX; Clinical Sciences and Administration, University of Houston, Houston, TX**

Clostridium difficile infection is one of the most common causes of bacterial diarrhea in the developed world. Although children are less susceptible to infection than adults and tend to have milder disease, pediatric cases are rising dramatically and can require fecal microbiota transplantation for cure in refractory cases. The gut-liver axis is emerging as an important pathogenesis mechanism in C. difficile infection (CDI), and altered bile acid production in this axis may promote C. difficile spore germination. This view is supported by epidemiological reports that patients with liver disease or transplantation are especially susceptible to CDI.
In this study, we profiled stool bile acid profiles in healthy children (n=44) and adults (n=24) using unbiased global metabolomics, and compared these to patients with symptomatic CDI (n=31) and antibiotic-associated diarrhea (n=24). We additionally profiled bile acid composition in an experimental mouse model of CDI, and in patients following liver transplantation (n=4). Antibiotic-associated shifts in primary bile acid composition favoring *C. difficile* spore germination were recorded in both patients and experimental disease models (significant increases in spore germinants taurocholate (140-fold) and taurochenodeoxycholate (36-fold), and a significant reduction in spore inhibitor chenodeoxycholate (5-fold)). Analysis of bile acid composition in children (7-12 years of age) demonstrated unique profiles that potentially confer additional CDI resistance e.g. significantly elevated chenodeoxycholate levels compared with adults. By contrast, in patients following liver transplantation, a bile acid profile favoring spore germination was identified. Ingenuity Pathway Analysis of these bile acid-metabolite networks implicated the FXR-FGF19 pathway in the regulation of bile acid synthesis in CDI patients. This was supported by measurement of serum FGF19 levels in a larger cohort of CDI patients (n=131) and by quantification of serum C4 levels - a marker of CYP7A1 activity, a rate limiting enzyme in bile acid synthesis. Promoter analysis and in vitro cell culture studies using HT29 colonocytes identified *C. difficile* virulence factors toxins A and B as potent regulators of FGF19 production, via FXR-independent activation of the FGF19 promoter.

In conclusion, significant developmental shifts in microbiome composition and bile acid profiles from childhood to adulthood appear to account for increased CDI susceptibility in adulthood. Enterohepatic hormones have therefore evolved as autocrine regulatory signals in *C. difficile* pathogenesis, and may serve as novel serum biomarkers of active disease in infected patients.

**NASPGHAN Young Investigator Award**

329 **ANALYSIS OF CANDIDATE GENES BY WHOLE EXOME SEQUENCING IN VERY EARLY-ONSET IBD,**

Judith Kelsen1, Christopher Moran2, Ariella Sasson3, Helen Pauly-Hubbard4, Eric Rappaport4, Petar Mamula1, David Piccoli5, David Artis5, Gregory Sonnenberg5, Harland Winter2, Robert Baldassano1, Marcella Devoto6, 1Center for Biomedical Informatics, The Children's Hospital of Philadelphia, Philadelphia, PA; 2Pediatrics, MassGeneral Hospital for Children, Boston, MA; 3Center for Biomedical Informatics, The Children's Hospital of Philadelphia, Philadelphia, PA; 4Nucleic Acid/PCR Core, The Children's Hospital of Philadelphia, Philadelphia, PA; 5Department of Microbiology and Institute of Immunology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA; 6Division of Genetics, Department of Biostatistics and Epidemiology, The Children's Hospital of Philadelphia, Philadelphia, PA

**Background:** Very early onset IBD (VEO-IBD) is frequently considered a different disease process than IBD that presents in older children and adults. The severe phenotype and young age suggest a more pronounced genetic susceptibility and dysregulated immune response. We hypothesized that rare or novel variants in genes associated with primary immunodeficiencies (PI), including pathways involved in both B and T cell development and activation, were enriched in patients with severe VEO-IBD.

**Methods:** IBD patients 5 years and younger, and parents were recruited. DNA was isolated from whole blood. Exome capture was performed by Agilent SureSelect V4, and sequencing was done using the Illumina HiSeq platform at an average coverage depth of 100X. Alignment to human genome GRCh37 was performed followed by post processing and variant calling. Following functional annotation, only variants likely to alter protein function, such as missense and loss of function mutations, were kept for subsequent analysis. Further filtering included only those with minor allele frequency less than 0.1% in data from the 1000 Genomes Project and Exome Variant Server (EVS) and less than 1% in The Children's Hospital of Philadelphia's internal whole exome cohort (>400 samples). Primary focus of the analysis was on genes associated with PI and related pathways (>400 genes).

**Results:** 138 samples were included, comprising 59 probands with VEO-IBD and 79 parents. Patients' age ranged from 4 weeks to 4 years. The genes associated with PI contain 6,500 coding exons totaling more than 1 Mbp. In these regions, 86.9% of coding exons were fully covered at more than 20X. Analysis revealed novel and rare putative causative variants within these genes in multiple families that are currently being further evaluated. In a patient with severe VEO-IBD who presented at 6 months of age and in whom a rare *IL-10RA* non-synonymous variant was detected, a novel non-synonymous coding variant was found in the *IL-21R* gene. Additionally, a rare *RAG2* non-synonymous coding variant (VAI→Ile) was detected in heterozygosity in a 2 year old female with severe colonic VEO-IBD. Laboratory evaluation demonstrated low NK cell population, and reduced FoxP3 expression in regulatory T cells. Among other immunological functions, IL-21 and IL-10 are critical for B cell class switching (both memory and naïve cells), and similarly, RAG2, associated with SCID, is important in both B and T cell development, including B cell class switching.

**Conclusions:** Candidate causative mutations in VEO-IBD can be identified by exome sequencing, and it is likely that some patients harbor mutations in both B and T cell pathways. Thus, the heterozygous variants detected may have contributed to the phenotype of VEO-IBD. Ongoing analysis is being performed, including evaluation of parental transmission; however, we anticipate that additional causative variants may occur in genes not previously associated with IBD.
William Balistreri Prize
330 A PROSPECTIVE NEWBORN SCREENING STUDY FOR BILIARY ATRESIA. Sanjiv Harpavat, Joseph A. Garcia-Pruts, Milton J. Finegold, Pediatrics, Baylor College of Medicine, Houston, TX

Background: Infants with biliary atresia (BA) benefit from a timely diagnosis, with those identified and treated earlier (i.e., before 30 days of life in some studies) having better outcomes (1). Unfortunately, in the US, the diagnosis of BA is often delayed because infants are not systematically screened for the disease. One screening method used successfully in other countries is the stool color card program. However, the program has a sensitivity of only 82.9% for identifying infants before 45 days of life (2). In this study, we prospectively test another screening method: newborn serum direct or conjugated bilirubin (DB or CB) measurements.

Methods: Two populations of infants born between July 2013-June 2014 had newborn DB or CB concentrations measured within the first 60 hours of life, and, if elevated, re-measured at the two-week well-child visit. Infants in the first group were born in a quaternary care children's hospital (hospital A), which measures CB concentrations in newborns using a derived reference interval of 0.0-0.2 mg/dL. Infants in the second group were born in a publically funded general hospital (hospital B), which measures DB concentrations in newborns using a derived reference interval of 0.0-0.3 mg/dL. Infants were considered positive if they had elevated concentrations initially that increased with repeat testing.

Results: In hospital A, 5100 infants were born and two were eventually diagnosed with BA. Of these, 4520 had newborn CB measurements, 13 had high concentrations initially, and three (including the two subjects with BA) were positive with persistently high concentrations at the two-week repeat test. In hospital B, 3387 infants were born and none was diagnosed with BA. Of these, 3326 had newborn DB measurements, 65 had high concentrations initially, and three were positive with persistently high concentrations at the two-week repeat test. Combining infants from both hospitals, the screening program has a sensitivity of 100% (95%CI 19.9-100), specificity of 99.9% (95%CI 99.9-100), and positive predictive value of 33.3% (95%CI 6.0-75.9) for identifying BA in the first weeks of life.

Discussion: Our initial results demonstrate that newborn DB or CB measurements are an effective way to screen a diverse population of infants for BA. The test has a high sensitivity and specificity for identifying the disease early, and its positive predictive value is comparable to newborn screening tests for other diseases. In addition, in the US, the test is widely available and easy to interpret. Future work will (i) continue screening more infants to validate the findings, and (ii) analyze screening from a cost-effectiveness perspective.

References

NASPGHAN Clinical Young Investigator Award
331 POOP-MD, A MOBILE HEALTH APPLICATION, ACCURATELY IDENTIFIES ACHOLIC STOOLS. Amy Franciscovich1, Dhananjay Vaidya1, Joe Doyle2, Josh Bolinger2, Montserrat Capdevila1, Marcus Rice2, Leslie Hancock2, Douglas Mogul1, 1Johns Hopkins, Baltimore, MD; 2HCB Health, Austin, TX

Background: Biliary atresia (BA) is the leading cause of pediatric end-stage liver disease in the United States. Education of parents in the perinatal period with stool cards depicting acholic and normal stools has been associated with improved time-to-diagnosis and survival in BA. PoopMD is a mobile application that educates parents about normal/abnormal stool color. PoopMD utilizes a smartphone's camera and color recognition software to analyze an infant's stool and determine if additional follow-up is indicated.

Methods: PoopMD was developed using custom HTML5/CSS3 and wrapped to work on iOS and Android platforms. Images from the Taiwan stool card were converted to RGB hexcodes. In order to define the gold standard, seven pediatricians were asked to review 45 photographs of infant stool rate them as acholic, normal, or indeterminate. The gold standard was defined as samples for which 6+ pediatricians demonstrated agreement and only these samples were included in the analysis. Accuracy of PoopMD was assessed using an iPhone 5s with incandescent lighting. Variability in analysis of stool photographs was compared among three laypeople (Kuser) with the images imported into the iPhone photo stream. Variability in output was also assessed between an iPhone 5s and a Samsung Galaxy S4 (Kphone), as well as between incandescent lighting and compact fluorescent lighting (Klight).

Results: 6+ pediatricians agreed on 27 normal and 7 acholic photographs; no photographs were defined as indeterminate. The sensitivity was 7/7 (100%). The specificity was 24/27 (89%) and there were no false positives (Table). Kuser was 0.69, Kphone was 0.88, and Klight was 0.81.

Conclusion: PoopMD accurately differentiates acholic from normal color with minimal variability across two popular smartphones, ambient lighting, or user. PoopMD may be a valuable tool to help parents identify acholic stools in the perinatal period, and provide guidance as to whether additional evaluation with their pediatrician is indicated.
Ultimately, PoopMD may improve outcomes for children with BA.

### Table: Gold Standard Accuracy of PoopMD to Differentiate Acholic and Normal Infant Stool Photographs

<table>
<thead>
<tr>
<th></th>
<th>Gold Standard</th>
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<tbody>
<tr>
<td></td>
<td>Acholic</td>
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<tr>
<td>PoopMD</td>
<td>7</td>
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<tr>
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<tr>
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Saturday, October 25, 2014
10:30am – 12pm
Research Session V – Celiac/EoE/Allergic Enteropathy

332 **ROLE OF MICROBIAL DERIVED METABOLITES AND PRO-INFLAMMATORY CYTOKINE IFNγ IN MODULATING FOXP3 ISOFORMS EXPRESSION IN CELIAC PATIENTS.**

**Gloria Serena**¹ ², Stephanie S. Camhi¹, Shu Yan¹, Karen M. Lammers¹, Alessio Fasano¹, ¹MGH, Boston, MA; ²University of Maryland, Baltimore, MD

**Background:** Celiac disease (CD) is an autoimmune enteropathy triggered by gluten in genetically predisposed individuals. FOXP3 plays a major role in regulatory T cells (Treg) development and function. Unlike other autoimmune diseases, CD is associated with an increased number of Treg cells, therefore suggesting that functional defects of the Treg cells rather than quantitative ones may be associated to the onset of the disease. Two main isoforms of FOXP3 have been described: the full length (FL) is entirely functional, while the so called FOXP3 Delta 2 (Δ2) is thought to have a reduced suppressive function due to the missing RORγt binding site that plays an important role in regulating differentiation between Th17 and Treg cells. We have previously observed that active CD patients are characterized by an increased intestinal expression of the less functional FOXP3Δ2 isoform compared to healthy subjects (HC). Interestingly we didn't find the same difference in the peripheral blood. These data suggest that factors characteristic of the intestinal microenvironment such as bacterial derived metabolites and/or pro-inflammatory cytokines may play a role in modulating the expression of FOXP3 isoforms in CD patients.

**Aim:** To evaluate the role that bacterial derived metabolites and pro-inflammatory cytokine IFNγ may have in modulating FOXP3 isoforms expression.

**Methods:** We isolated peripheral blood mononuclear cells (PBMC) from whole blood samples of CD patients in remission and HC subjects. We cultured the PBMC in medium alone, in presence of increasing concentrations of bacterial derived metabolites lactate and butyrate or 100 mg/ml of IFNγ. RNA from the cells was extracted with Trizol and RT-PCR was run to detect gene expression of FOXP3 isoforms and RORγT. Statistical significance was determined using the two-tailed non parametric Mann-Whitney test and p values < 0.05 were deemed significant.

**Results:** Our data show that in CD patients IFNγ triggers an increased expression of FOXP3 Δ2 (p=0.03), and RORγT (p=0.02), while no differences were found in the expression of FOXP3 FL. Furthermore in CD patients, stimulation with butyrate led to a dose dependent increase of both FOXP3 isoforms (p=0.004 (FL) and p=0.008 (Δ2)) when compared to HC subjects, while high concentration of lactate triggered an increase of FOXP3 Δ2 (p=0.02).

**Conclusions:** Our data show for the first time that components of the intestinal microenvironment have the capability of modulating the expression of FOXP3 isoforms in celiac patients. We hypothesize that the metabolomic profile of subjects predisposed to celiac disease may lead to the altered expression of FOXP3 Δ2. Furthermore we suggest that the pro-inflammatory environment characteristic of active CD patients may play a role in sustaining FOXP3 Δ2 over-expression therefore impeding a proper regulation of the immune response.

**NASPGHAN/APFED Award for Eosinophilic Disorders**

333 **DIGITAL MRNA PROFILING OF ESOPHAGEAL TISSUE BIOPSIES AS A NOVEL DIAGNOSTIC APPROACH TO EOSINOPHILIC ESOPHAGITIS (EoE).**

Willem S. Lexmond¹, Lan Hu², Michael Pardo¹, Nicole Heinz¹, Katharine P. Rooney¹, Jessica LaRosa¹, Eleonora Dehlink¹ ², Edda Fiebiger¹, Samuel Nurko¹, ¹GI/Nutrition, Boston Children's Hospital, Boston, MA; ²Center for Cancer Computational Biology, Department of Biostatistics and Computational Biology, Dana-Farber Cancer Institute, Boston, MA; ³Division of Paediatric Pulmonology, Allergy and Endocrinology, Medical University of Vienna, Vienna, Austria

**Introduction:** Quantification of tissue eosinophils in combination with appraisal of clinical symptomatology remains the golden standard in identifying patients with eosinophilic esophagitis (EoE). Unfortunately, this diagnostic approach suffers from poor specificity, and in daily practice the distinction between reflux-associated eosinophil infiltration and EoE often proves particularly difficult. It has been recognized that the histopathological changes that occur in esophageal tissue of patients with EoE are associated with a disease-specific gene transcriptome. We hypothesized that...
high-throughput digital mRNA profiling targeted at a set of EoE-specific and Th2 inflammatory genes could help differentiate patients with EoE from those with reflux esophagitis (RE) or normal tissue histology.

**Methods:** The digital mRNA expression profile of 79 target genes was analyzed in both proximal and distal biopsies of 156 patients by nCounter® Nanostring technology. According to clinicopathological diagnosis, these patients were grouped in a training set (35 EoE, 30 RE, 30 normal) for model building, and a blinded predictive set (N=47) for model validation. From genes that were differentially expressed between all three disease conditions, a three-class (EoE, RE, normal) predictor model was built using the random forest method.

**Results:** Expression analysis of our target gene panel revealed ten genes in distal biopsies that were differentially expressed between all three conditions. The three-class prediction model built using the ten distal genes was able to differentiate with 100% sensitivity and specificity between conditions in the training set. When applied to the predictive set for validation, our model was able to correctly predict EoE in 14 out of 18 patients with EoE (sensitivity 78%, 95% CI 52%-93%), while no false positive diagnosis of EoE was made in any of the RE or normal control patients (specificity 100%, 95% CI 85%-100%). When a cut-off of >50% EoE probability in either the proximal or distal biopsy was used to identify patients with EoE, sensitivity was increased further to 94% (95% CI 71%-100%) without compromising specificity, which remained at 100%. Furthermore, when applied to 14 cases with an equivocal diagnosis after first diagnostic endoscopy, our model was able to correctly predict the long-term clinical course of these patients.

**Conclusion:** Our results show that mRNA expression analysis of a small subset of EoE-specific target genes identified EoE cases amongst a heterogeneous group of inflammatory and normal control patients with high sensitivity and specificity. We conclude that mRNA profiling is an auxiliary diagnostic strategy in detecting EoE, which could potentially help distinguish true underlying EoE from secondary causes of tissue eosinophilia and lead to faster installment of appropriate therapy.

### 334 AN ENTEROID MODEL OF CONGENITAL TUFTING ENTEROPATHY SHOWS ALTERATIONS IN EPITHELIAL ARCHITECTURE AND ACTIN DISORGANIZATION.

**Mamata Sivagnanam, Ronald Marchelletta, Carla Pena, Matthew Mcgeough, Pediatrics, University of California, San Diego, San Diego, CA**

Congenital Tufting Enteropathy is a severe diarrheal disease of infancy. We previously identified mutations in Epithelial Cell Adhesion Molecule as the cause of CTE. We developed an inducible in vivo mouse model of CTE based on EpCAM mutations found in patients (Δ4). In order to establish enteroids, intestinal crypts were isolated from ind. Epcam<sup>WT/WT</sup> and ind. Epcam<sup>Δ4/Δ4</sup> mice using cold chelation buffer (5mM EDTA/ HEPES buffer) and cultured in matrigel with DMEM/F12 supplemented with N-acetylcysteine, vitamin B12, and Glutamax. After incubation in specialized culture media supplemented with the required growth factors (priority reagents: Noggin, EGF and R-spondin) for 7 days, the organoids were isolated from matrigel and placed in standard culture media. Enteroids have now been successfully established in our lab. Like mice, enteroids are able to be induced by tamoxifen exposure. Post induction we recognized striking alterations in the structure of ind. Epcam<sup>Δ4/Δ4</sup> enteroids vs. ind. Epcam<sup>WT/WT</sup>/TAM enteroids, with disorganization, lack of clear luminal compartment and central heaping of cells. The intracellular domain of EpCAM has 2 binding sites for alpha actinin. Additionally, a recent Xenopus model showed PKC inhibition was shown to be caused by a short segment of the EpCAM cytoplasmic tail. Thus actin and PKC-epsilon staining were undertaken using Alexaflor 647 phalloidin and PKC. Murine enteroids with EpCAM mutation show actin disorganization and increases in PKC-e as compared with ind. Epcam<sup>WT/WT</sup>/TAM. These findings suggest EpCAM mutations may alter cytoskeleton components in the intestinal epithelium, which may serve as a mechanism of enterocyte disorganization and "tufting" seen in congenital tufting enteropathy. We also establish the first enteroid model of congenital tufting enteropathy which will allow for enhanced understanding of the pathophysiology of this disease and testing of therapeutic options.

**Saturday, October 25, 2014**

**Poster Session III**

*Poster of Distinction*

**Basic - Inflammatory Bowel Disease**

### 335 IMPACT OF DISEASE DURATION ON CLINICAL OUTCOMES WITH ADALIMUMAB TREATMENT IN PATIENTS FROM IMAGINE 1.

**Marla Dubinsky<sup>1</sup>, Jeffrey Hyams<sup>1</sup>, Joel Rosh<sup>2</sup>, James Markowitz<sup>3</sup>, Frank Ruemmele<sup>4</sup>, Samantha Eichner<sup>1</sup>, Andreas Lazar<sup>5</sup>, Yao Li<sup>6</sup>, Brandee Pappalardo<sup>7</sup>, Roopal Thakkar<sup>7</sup>, AbbVie Inc, North Chicago, IL; Cedars-Sinai Medical Center, Los Angeles, CA; Connecticut Children's Medical Center, Hartford, MA; Goryeb Children's Hospital/Atlantic Health, Morristown, NJ; Cohen Children's Medical Center of NY, New Hyde Park, NY; Hospital Necker-Enfants Malades, Universite Sorbonne Paris-Cite, Paris, France; AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany**

*Introduction:* Adalimumab (ADA) was shown to be an effective treatment in inducing and maintaining remission in
children with moderately to severely active Crohn's disease (CD) in the IMAGINE 1 trial. The impact of baseline disease duration on the safety and efficacy of ADA is evaluated in patients from IMAGINE 1.

Methods: In IMAGINE 1, patients aged 6-17 years with baseline PCDAI >30 received open-label (OL) induction of ADA at weeks 0/2 according to body weight (≥40kg, 160/80mg; <40kg, 80/40mg). At week 4, patients were randomized according to body weight to double-blind higher-dose (HD) ADA (≥40kg, 40mg every other week [EOW]; <40kg, 20mg EOW) or lower-dose (LD) ADA (≥40kg, 20mg EOW; <40kg, 10mg EOW) to week 52. Patients experiencing disease flare or non-response could move to blinded weekly dosing after week 12, then to OL weekly HD ADA for continued flare/non-response. Patients with loss of response or intolerance to infliximab (IFX) could enroll in IMAGINE 1. Remission (PCDAI≤10) and response (PCDAI decrease ≥ 15 points from baseline) were assessed in the disease duration subgroups. Data were analyzed using non-responder imputation (NRI), whereby patients with missing data or that obtained after moving to weekly dosing were considered not to have efficacy, and a modified NRI (mNRI) whereby only patients with missing data were considered as non-responders.

Results: Greater rates of remission and response were observed across the three disease duration subgroups ≤ 3yrs at both weeks 26 and 52 relative to those with disease duration > 3 yrs (Table). IFX naive patients had numerically higher rates of remission relative to IFX exposed patients regardless of disease duration subgroup. Rates of serious adverse events (AEs) and AEs leading to discontinuation were lower in patients with shorter duration of CD (≤ 3yrs).

Conclusion: Higher efficacy rates and lower incidence of serious adverse events in patients with a shorter duration of CD suggests early treatment with ADA may be beneficial for patients.


<table>
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<th>Disease Duration Subgroup</th>
<th>Week 26</th>
<th>Week 52</th>
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<tbody>
<tr>
<td>≤1.0 yr</td>
<td>13 (30.2)</td>
<td>7 (16.3)</td>
</tr>
<tr>
<td>&gt;1.0-≤2.0 yrs</td>
<td>15 (50.0)*</td>
<td>14 (46.7)*</td>
</tr>
<tr>
<td>&gt;2.0-≤3.0 yrs</td>
<td>15 (50.0)*</td>
<td>12 (27.9)</td>
</tr>
<tr>
<td>&gt;3.0 yrs</td>
<td>18 (39.5)</td>
<td>20 (27.8)</td>
</tr>
</tbody>
</table>

*p<0.05 disease duration >1.0-≤2.0yrs vs >3yrs (Chi-squared test); †p<0.01 disease duration ≤1yr vs >1-≤2 yrs (Chi-squared test)

336 PREVALENCE OF OVERWEIGHT AND OBESITY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE IN SAUDI ARABIA. Mohammad El Mouzan1, Omar Saadah5, Mohammad Al Mofarreh3, Khalid Al Saleem2, Mohammed Hasosah4, Ali Al Mehadib2, Khalid Alquaer6, 1Pediatrics, King Saud University, Riyadh, Saudi Arabia; 2Pediatrics, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; 3Mofarreh PolyClinics, Riyadh, Saudi Arabia; 4National Guard Hospital, Jeddah, Saudi Arabia; 5Pediatrics, King Abdul Aziz University Hospital, Riyadh, Saudi Arabia; 6Pediatrics, North West Military Hospital, Tabuk, Saudi Arabia

Background and aim: Excess weight in inflammatory bowel disease (IBD) represents an additional morbidity, and yet the prevalence has been rarely reported. The aim of this report is to establish the prevalence of overweight and obesity in children with IBD in the Kingdom of Saudi Arabia (KSA). Methods: Data from a cohort of children in the KSA diagnosed with IBD were analyzed retrospectively. Growth parameters were recorded at diagnosis and body mass index (BMI) was calculated using the formula (weight/height²). The KSA growth charts were used as reference. Excess weight categories were defined as overweight (BMI-for age ≥ 85th to < 95th), obesity ≥ 95th to <97th), and severe obesity ≥ 97th percentile. Chi-square test was used and p-value of <0.05 was considered significant. Results: There were 417 children from birth to 18 years of age, including 133 ulcerative colitis (UC) (32%), and 284 Crohn disease (CD) (68%). The prevalence of excess weight was 12/133 (9%) in UC and 23/284 (8.1%) in CD (p=0.063) much lower than in

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Western reports. However, the more common prevalence of excess weight in UC than CD, although not significant (p=0.063), was similar to patterns from other population. The commonest form of excess weight was overweight 20/35 (57%), followed by obesity 9/35 (26%), and severe obesity 6/35 (17%). Conclusion: The pattern of excess weight in KSA children with IBD is similar to Western literature. However, a much lower prevalence is demonstrated.

Identification of factors associated with overweight and obesity in IBD needed for preventive purposes.

337 FASCIOILA HEPATICA INFECTION EXACERBATES MURINE COLITIS. Shahan Fernando1,2, Eoin N. McNamee2,6, Lindsay Hosford3,6, Paul Jedlicka5,2, James J. Lee4, Alan W. Baird7, Glenn T. Furuta3,5, Joanne C. Masterson3,5, 1Biochemistry and Molecular Biology, Mayo Clinic Arizona, Scottsdale, AZ; 2Anesthesiology, University of Colorado, Aurora, CO; 3Digestive Health Institute, Children's Hospital Colorado, Denver, CO; 4Pathology, Children's Hospital Colorado, Aurora, CO; 5School of Medicine, University of Colorado, Aurora, CO; 6Mucosal Inflammation Program, University of Colorado, Aurora, CO; 7School of Veterinary Medicine, University College Dublin, Dublin, Ireland

Background: Epidemiologic studies implicate the eradication of helminths as a potential cause of the rising incidence of autoimmunity. Current literature suggests a protective role of some helminthic infections against autoimmune and inflammatory conditions such as inflammatory bowel disease (IBD). Fasciola hepatica has previously been reported to suppress experimental autoimmune encephalitis by suppressing Th1/Th17 inflammation. Here we seek to study the role of Fasciola hepatica on a subsequent Th1/Th17-associated acute experimental murine model of colitis.

Methods: F. hepatica (10 metacercariae) was gavaged to 7 week old male/female C57BL/6J mice. Twenty-one days later, colitis was induced by orally administering 3.5% (w/v) Dextran Sodium Sulfate (DSS) in drinking water for up to 7 days, while control mice received water alone. Disease activity indices (DAI) were monitored daily. Colonic tissues were harvested and processed for histologic assessment of inflammation on H&E stained sections, cellular profiling by immunohistochemistry, and molecular profiling of inflammatory cytokines by Taqman based RT-PCR.

Immuno-histochrometric profiling of colonic leukocyte populations was performed using associated markers MBP (eosinophils), MPO (neutrophils), and F4/80 (macrophage).

Results: Mice pre-infected with F. hepatica (DSS-FH) developed 1. significantly higher DAI compared to uninfected controls (8 vs 6.1, DSS-FH vs DSS control, day 6, p<0.05; 11 vs. 9.3, DSS-FH vs DSS control, day 7, p<0.0001) and 2. higher histologically assessed inflammatory index (15.2 vs 11.2, DSS-FH vs DSS control, p<0.05). Molecular analysis revealed significantly greater expression of TNF-α (11.7 fold increase vs 3.6 fold increase, DSS-FH vs DSS control, p<0.05), but no differences in Th2 cytokines (TGF-β, IL-5, IL-10, IL-13). DSS-FH mice also had increased numbers of tissue neutrophils (286.3 vs 116.2 per hpf, DSS-FH vs DSS control, p<0.01), decreased quantity of infiltrating eosinophils (114.7 vs 168.2 per hpf, DSS-FH vs DSS control, p<0.01), and no difference observed in the number of macrophages (61.3 vs 68.4, DSS-FH vs DSS control, n.s.).

Conclusion: Prior infection with Fasciola hepatica further increases traditional markers associated with DSS-induced experimental colitis.

338 ADHERENCE TO NASPGHAN GUIDELINES FOR BONE MINERAL DENSITY SCREENING AT AN IBD CENTER. Sussi Vivar2, Francisco Sylvester1, 1Connecticut Childrens Medical Center, Hartford, CT; 2Connecticut Childrens Medical Center Hartford, CT

Background: Children with inflammatory bowel disease (IBD) are at increased risk for significant bone mineral density (BMD) deficits and vertebral fractures due to disease and treatment factors. NASPGHAN guidelines concerning bone mineral density (BMD) screening in children with IBD were published in 2011. However, adherence to these guidelines in clinical practice is not known.

Aim: We planned a quality improvement initiative to improve adherence to NASPGHAN BMD guidelines in our practice. As a first step, we investigated baseline adherence to NASPGHAN recommendations for performing dual X-ray absorptiometry (DXA).

Methods: A chart review was conducted to examine the number of completed DXA screening in patients with Crohn disease (CD), ulcerative colitis (UC) or IBD-undefined (IBD-U) diagnosed between January 2012 and March 2014.

Results: 165 consecutive charts were reviewed: 104 CD; 55 UC; 6 IBD-U. Mean age at time of diagnosis was 13 ± 3 years (range 7 - 20 years, 68 females), 7 patients (4.2 %) had a DXA prescribed at the time of diagnosis; 5 of these patients completed their DXA shortly after starting treatment, while one patient started treatment after DXA. Of the 6 patients that had DXA, 5 had a normal BMD Z-score > -1.0 at the lumbar spine and total body less head (TBLH) and 1 had a BMD Z score spine Z score -1.9 and TBLH = -1.5 of TBLH and a history of amenorrhoea; 1 did not pursue the screening test despite the physician's recommendation. All patients received age-appropriate recommendations for adequate calcium and vitamin D intake by a registered dietitian.

Conclusions: In our practice, adherence to NASPGHAN BMD screening recommendations is less than ideal. Our next step will be an intervention to improve BMD screening in patients with IBD that are at highest risk for low bone mass.
DIAGNOSTIC PERFORMANCE AND APPLICATION OF TTG IN PEDIATRIC CELIAC DISEASE: A POPULATION BASED ANALYSIS. Anna K. Petersen1, Raza Patel1, Matthew Bryce2, M. K. Jensen1, 1Pediatric Gastroenterology, University of Utah, Salt Lake City, UT; 2Data Analysis, Intermountain Health Care, Salt Lake City, UT

BACKGROUND: The current guidelines for celiac disease diagnosis include screening patients with serum antibodies and gold-standard confirmation with duodenal biopsies. European gastroenterology guidelines currently offer a less-invasive diagnostic algorithm using elevated tTG immunoglobulin and endomysial antibodies, coupled with HLA testing. In North America this diagnostic approach has not been uniformly adopted. With the changing face of health care reform, the rising costs of endoscopy procedures, and families now faced with "high deductible" health care plans, there is a significant negative socio-economic impact of GFD on children with CD & their families. Physicians should be aware of such impacts and should be trained well to handle them; this can be achieved through proper dietary education & psychological counselling training programs.

RESULTS: Three thousand four hundred patients met inclusion criteria. The overall specificity for tTG IgA was 99%. A tTG value >5x ULN (n = 374) had a PPV of 97.3%, with only 3 (2.7%) false positives. The NPV of tTG tests under 5x ULN was 94.5%.

CONCLUSION: Compliance to GFD among children with CD is a major concern in Saudi population; this is could be related primarily to the limited availability of trusted GFD products and their expensive price. There is a significant negative socio-economic impact of GFD on children with CD & their families. Physicians should be aware of such impacts and should be trained well to handle them; this can be achieved through proper dietary education & psychological counselling training programs.
high positive predictive value, as well as high accuracy of a tTG-IgA for diagnosing celiac disease. Because endoscopy is costly and has unavoidable risks, our results identify patients in whom endoscopy may not be required. For patients with intermediate tTG less than 5x ULN, gold standard endoscopy should still be utilized.

344 PREDICTIVE SEROLOGIC MODEL REPLACES HISTOPATHOLOGIC DIAGNOSIS IN A SUBSET OF CHILDREN WITH CELIAC DISEASE. Dascha C. Weir, Allison McKeown, Adie Kalansky, Mary Warlaumont, Jeffrey Goldsmith, Heather Litman, Hongyu Jiang, Alan M. Leichtner, GI & Nutrition, Boston Children’s Hospital, Somerville, MA

Objectives: Duodenal biopsy is the "gold standard" in the diagnosis of celiac disease (CD). However, some literature suggests that, in children, very high tissue transglutaminase IgA (TTG IgA) levels are strongly predictive of CD and may eliminate the need for biopsy. ESPGHAN guidelines suggest that symptomatic children with both TTG IgA levels > 10 times the upper limit of normal and positive endomysial IgA (EMA IgA) antibodies can be diagnosed with CD without biopsy. The aim of this prospective study was to determine if using altered test cutoff levels of celiac serologic tests, alone or in combination, could predict the presence of CD in a North American pediatric population. Methods: Between November 2007 and October 2008, 179 eligible subjects undergoing esophagogastroduodenoscopy for signs and symptoms consistent with possible CD were enrolled. Multiple duodenal biopsies were obtained and reviewed using modified Marsh criteria. All cases of Marsh II or greater were considered consistent with CD. TTG IgA, deamidated gliadin peptide IgA (DGP IgA) and IgG (DGP IgG) levels were assayed by ELISA (positive>25 U/ml). EMA IgA levels were assayed by immunofluorescence (positive>1:2.5). Test performance was assessed at predetermined cutoffs. Tree analysis was run to assess test performance of serologic markers in combination with patient characteristics to determine a predictive model for diagnosis of pediatric CD. Sensitivity and specificity of the predictive logistic regression model generated were calculated on a separate cohort of all patients that had a positive TTG IgA and EMA IgA obtained between December 2008 and December 2010 at our institution. Results: 78/179 (44%) of enrolled subjects had duodenal biopsies with Marsh II-III lesions. The predictive model of a TTG IgA of > 125 and a positive EMA IgA showed 100% specificity for diagnosis. Addition of clinical characteristics did not improve the model. Our retrospective analysis identified 150 subjects with positive TTG IgA and EMA IgA. Of the 130 cases with biopsies, 119 (91.5%) had confirmed CD. 14/150 (9.3%) subjects had a TTG IgA >125 and 10/14 had available biopsies to review. In these cases, serology predicted CD with a specificity of 100% and a sensitivity of 8.4%. Conclusion: In a small subset of pediatric patients, small bowel biopsy confirmation of CD is unnecessary if TTG IgA > 125 and EMA IgA is >1:2.5. This study supports ESPGHAN guidelines for the diagnosis of CD and is the first to demonstrate it in a North American cohort.

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<tr>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
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<td>TTG IgA</td>
<td>&gt;25 U/ml</td>
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<tr>
<td>&gt;75 U/ml</td>
<td>&gt;125 U/ml</td>
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<tr>
<td>79%</td>
<td>65%</td>
</tr>
<tr>
<td>61%</td>
<td>97%</td>
</tr>
<tr>
<td>97%</td>
<td>99%</td>
</tr>
<tr>
<td>DGP IgA</td>
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</tr>
<tr>
<td>63%</td>
<td>&gt;1:250</td>
</tr>
<tr>
<td>28%</td>
<td>&gt;1:25</td>
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<tr>
<td>94%</td>
<td>95%</td>
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<tr>
<td>97%</td>
<td>100%</td>
</tr>
<tr>
<td>DGP IgG</td>
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<td>78%</td>
<td>&gt;1:500</td>
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<tr>
<td>1%</td>
<td>&gt;1:25</td>
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<tr>
<td>93%</td>
<td>98%</td>
</tr>
<tr>
<td>99%</td>
<td>100%</td>
</tr>
<tr>
<td>EMA IgA</td>
<td>&gt;1:2.5</td>
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<tr>
<td>&gt;25 U/ml</td>
<td>&gt;1:2.5</td>
</tr>
<tr>
<td>82%</td>
<td>82%</td>
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<tr>
<td>43%</td>
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<td>34%</td>
<td>98%</td>
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345 QUALITY OF LIFE IN CHILDREN AND ADOLESCENTS WITH CELIAC DISEASE ON GLUTEN FREE DIET. Abeer Alzaben1, Seema Rajani2, Leanne Shirton1, Rabin Persad1,2, Justine M. Turner1,2, Diana Mager1,3, 1Division of Pediatric Gastroenterology, Stollery Children's Hospital, Edmonton, AB, Canada; 2Department of Pediatrics, University of Alberta, Edmonton, AB, Canada; 3Department of Agricultural, Food & Nutritional Science, University of Alberta, Edmonton, AB, Canada

Background: Celiac disease (CD) is a life long autoimmune disease. Little is known regarding parental and child perceptions of quality of life in children with CD and other gastrointestinal disorders (GI) in Canada. The study objective was to compare parent and child perceptions of quality of life in children with CD and chronic GI disorders. Methods: A prospective study was conducted in children and adolescents with biopsy proven CD (n=40; 9.6 ± 3.2 yrs; 11M, 29F) and in children with chronic GI diseases (GI-controls; n=20; 9.9 ± 4.5 yrs; 11 M, 9F). QoL was measured using the parent-proxy and child-reports for PEDSQL 4.0 and the CDDUX. Parent-child differences (d) in perceptions of QoL were determined by dividing the absolute differences by the standard deviation of each QoL domain (psychosocial, school, emotion, physical functioning, average) reported by the child. Weight and height-z scores were calculated using CDC Epi Info Software. A positive value > 0.2 indicates a parent ranked the child QoL lower than the child; -0.2 the parent ranked the QoL higher than the child.

Results: Weight-for-age z-scores were significantly different between CD-children (-0.43± 1.27) and GI-control (0.50 ±
0.94; p=0.01). CD-children had higher average QoL (81 ± 10 vs 73 ± 9; p<0.01); and higher physical functioning scores (91± 9 vs 81 ± 11; p<0.01) than GI-control. Parents of children with CD perceived the child to have a lower QoL than the CD child when compared to parents of children with other GI disorders (1.3 1.3 ± 3.1 (CD) vs -2.2 ± 6.7 (GI controls); p=0.02). Higher QoL scores were reported by CD-children without GI symptoms for school functioning (86 ± 9 (-) vs 71 ± 17 (+); p<0.01), psychosocial (88 ± 7 (-) vs 75 ± 15 (+); p<0.01), and average QoL score (86 ± 5 (-) vs 77 ± 11 (+); p=0.01) than those CD children without GI symptoms.

**Conclusion:** In general, CD-children report better QoL than children with undifferentiated gastrointestinal complaints. Parents of CD-children perceived their child's QoL more adversely than the child's perception, even in the absence of GI symptoms.

**346 GASTROINTESTINAL ULCERS IN CELIAC DISEASE.** Hasan A. Yuksekaya¹, Meltem Gümüş¹, Aylin Y. Yucel¹, Hasan Esen². ¹Pediatric Gastroenterology, Necmettin Erbakan University, Meram Medicine of Faculty, Konya, Turkey; ²Pathology, Necmettin Erbakan University, Meram Medicine of Faculty, Konya, Turkey

**Background:** Celiac disease (CD) is essentially a systemic disease which has also intestinal and extraintestinal manifestations. However, gastrointestinal bleeding or ulcer is not a feature of CD. On the other hand, the results of recent studies have suggested that peptic ulcer disease is not uncommon in patients with CD. It has been recommended that CD included in the differential diagnosis of patients with unexplained peptic ulcer disease.

**Methods:** Between February-2009 and June-2014, we examined 216 children (122-female, 94-male, median age: 6 (1-17year) with celiac disease. The upper gastrointestinal endoscopy, colonoscopy and/or capsule endoscopy were performed at time of diagnosis of celiac disease.

**Results:** The gastrointestinal ulcers were found in 15 of 216 patients with celiac disease. Nobody active GI bleeding due to the ulcers except for one with jejunoileal ulcers who has abundant bleeding in which blood transfusion was required. Histories revealed that eleven patients used NSAIDs, except four patients. Endoscopic evaluation indicated multiple ulcers of the duodenal bulb and second part of the duodenum in teen children, the pre-pyloric region in two, the gastric corpus and antrum in two and the jejunoileal region in another. Histopathological examination revealed helicobacter pylori infection in four of those fifteen cases. The characteristics of patients are shown in Table-1.

**Conclusion:** The ulceration of the duodenal bulb was described in association with celiac disease in children although these ulcerations are due to the use of nonsteroidal anti-inflammatory drugs rather than being related to celiac disease. Gastric and jejunoileal ulcers can be seen in celiac disease as well as duodenal ulcers. Since abdominal pain usually occurs in celiac disease, it needs to be established whether these patients use NSAIDs.
Table-1: The characteristics of patients with gastrointestinal ulcers in celiac disease

<table>
<thead>
<tr>
<th>No</th>
<th>Age (year)</th>
<th>Sex</th>
<th>TTG-IgA EMA-IgA</th>
<th>Marsh stage</th>
<th>H. pylori</th>
<th>Use of NSAIDs</th>
<th>Region of ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>M</td>
<td>&gt;200 (++)</td>
<td>3</td>
<td>(-)</td>
<td>No</td>
<td>Duodenal Bulb</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>M</td>
<td>&gt;200 (++)</td>
<td>2</td>
<td>(+)</td>
<td>Yes (ibuprofen)</td>
<td>Prepyloric</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>M</td>
<td>&gt;200 (+++)</td>
<td>3</td>
<td>(-)</td>
<td>Yes (ibuprofen)</td>
<td>Duodenal Bulb, second part of duodenum</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>F</td>
<td>&gt;200 (+++)</td>
<td>3</td>
<td>(-)</td>
<td>Yes (ibuprofen)</td>
<td>Duodenal Bulb</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>M</td>
<td>&gt;200 (+)</td>
<td>3</td>
<td>(-)</td>
<td>Yes (ibuprofen)</td>
<td>Duodenal Bulb</td>
</tr>
<tr>
<td>6</td>
<td>15</td>
<td>F</td>
<td>&gt;200 (+++)</td>
<td>3</td>
<td>(+)</td>
<td>Yes (ibuprofen)</td>
<td>Gastric corpus</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>M</td>
<td>&gt;200 (+++)</td>
<td>3</td>
<td>(-)</td>
<td>Yes (naproxen)</td>
<td>Jejunoileal region</td>
</tr>
<tr>
<td>8</td>
<td>12</td>
<td>M</td>
<td>&gt;200 (+++)</td>
<td>4</td>
<td>(-)</td>
<td>No</td>
<td>Duodenal bulb, second part of duodenum</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>F</td>
<td>&gt;200 (+++)</td>
<td>3</td>
<td>(-)</td>
<td>Yes (ibuprofen)</td>
<td>Duodenal bulb</td>
</tr>
<tr>
<td>10</td>
<td>17</td>
<td>F</td>
<td>&gt;200 (+++)</td>
<td>3</td>
<td>(-)</td>
<td>Yes (naproxen)</td>
<td>Duodenal bulb</td>
</tr>
<tr>
<td>11</td>
<td>15</td>
<td>M</td>
<td>&gt;200 (+++)</td>
<td>4</td>
<td>(+)</td>
<td>No</td>
<td>Duodenal bulb, second part of duodenum</td>
</tr>
<tr>
<td>12</td>
<td>8</td>
<td>E</td>
<td>&gt;200 (+)</td>
<td>3</td>
<td>(+)</td>
<td>Yes (ibuprofen)</td>
<td>Duodenal bulb</td>
</tr>
<tr>
<td>13</td>
<td>9</td>
<td>F</td>
<td>&gt;200 (+++)</td>
<td>4</td>
<td>(-)</td>
<td>Yes (salicylic-acid)</td>
<td>Prepyloric, duodenal bulb, second part of duodenum</td>
</tr>
<tr>
<td>14</td>
<td>1</td>
<td>F</td>
<td>&gt;200 (++)</td>
<td>4</td>
<td>(-)</td>
<td>No</td>
<td>Duodenal bulb</td>
</tr>
<tr>
<td>15</td>
<td>4</td>
<td>F</td>
<td>&gt;200 (++)</td>
<td>4</td>
<td>(-)</td>
<td>Yes (ibuprofen)</td>
<td>Gastric corpus, antrum</td>
</tr>
</tbody>
</table>

347 THE GLUTEN FREE DIET: ASSESSING ADHERENCE IN A PEDIATRIC CELIAC DISEASE POPULATION. Jenna K. Dowhaniuk1, Heather Mileski2, Perri Tutelman2, Ji Cheng1, Joanne Saab2, Herbert Brill2.

1Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada; 2Department of Pediatrics, McMaster University, Hamilton, ON, Canada

Background: Celiac Disease (CD) is one of the most common chronic diseases in childhood. A strict, lifelong gluten-free diet (GFD) remains the sole treatment for CD. The assessment of adherence to the GFD in pediatric studies is often based on self-report and visual analogue scales which lack proven validity. We sought to compare parental self-report of GFD adherence to expert Registered Dietitian (RD) assessments, the accepted best available standard.

Methods: Parents of children with biopsy-proven CD followed at McMaster Children's Hospital scored their adherence to the GFD on a 5-point Likert scale similar to that used in previous pediatric CD studies. Each family was then evaluated by a RD expert in CD management who conducted a comprehensive and standardized assessment and scored the family's adherence; a second dietitian also scored the family based on clinic notes. The agreement between parents and the RD was assessed using paired t-test and intraclass correlation coefficient (ICC) based on their scores. Inter-rater reliability was used to compare RD assessments.

Results: One hundred and twenty-two children and their families participated in the study with a median of 32 months on a GFD. Excellent adherence (score 5/5) was attributed to 60.5% of the sample by the RD. The parents scored adherence higher than the RD by an average difference of 0.41 scale points (95% CI:0.28,0.54; p<0.001). The agreement between parents and the Registered Dietitian was poor (ICC = 0.21).

Conclusion: Reliance on self-report through Likert scales for GFD adherence overestimates adherence and misses opportunities for patient and family education. Future studies will attempt to develop an effective tool for assessing adherence to the GFD. In the interim, regular assessment by a RD in a dedicated CD clinic remains the most reliable way to assess adherence.

TABLE 2: Agreements of Likert scales between groups for the evaluation of GFD adherence

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Method</th>
<th>Parent vs RD1(n=108)</th>
<th>Parent vs Child(n=122)</th>
<th>Child vs RD1(n=108)</th>
<th>RD1 vs RD2(n=122)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreement based on Likert score</td>
<td>ICC</td>
<td>0.21</td>
<td>0.64</td>
<td>0.34</td>
<td>0.71</td>
</tr>
<tr>
<td>Difference (95% CI), p-value</td>
<td></td>
<td>0.41 (0.28, 0.54),&lt;0.001</td>
<td>0.13 (0.05, 0.20),&lt;0.001</td>
<td>0.28 (0.16, 0.39),&lt;0.001</td>
<td>-0.004 (-0.08, 0.07), 0.912</td>
</tr>
</tbody>
</table>

Abbreviations: GFD, Gluten-free diet; RD1, Registered Dietitan assessing primary outcome; RD2, Registered Dietitian reviewing documentation; ICC, intraclass correlation coefficient; CI, confidence interval. Intraclass correlation coefficient and Kappa reference values; κ <0.2: Poor, κ 0.21 - 0.40: Fair, κ 0.41 - 0.60 Moderate, κ 0.61 - 0.80: Substantial, κ 0.81 - 1.00: Almost Perfect (45)

348 FOOD ALLERGY AFTER INTESTINAL TRANSPLANTATION. Khalid Khan, Chirag Desai, Thomas Fishbein, Stuart Kaufman, MedStar Georgetown University Hospital, Washington, DC

Background: Atopic disorders are conjectured to be increased after organ transplantation as a result of the immune modulating effect of calcineurin inhibitors in particular tacrolimus. Reports have been most common in children after liver transplantation. We postulate that the liver and intestine are involved in antigen handling and the intestine may have a greater impact on the development of food allergy given that absorption of antigenic macromolecules from food proteins is determined by intestinal dysfunction.

Method: This was a single center retrospective analysis of the prevalence of food allergy in children after intestinal transplantation. We examined data from the MedStar Georgetown University Hospital transplant institute using standard statistic al methods and compared patients that developed food allergy and those that did not.

Results: Data was reviewed on 66 pediatric patients transplanted between 2004 and 2012. Symptoms of food allergy supported by radioallergosorbent tests (RAST) to specific allergens were reported in 10/66 (15.2%). The most common positive RASTs were cow milk protein (5/10) and eggs (7/10). In another 11/66 (16.7%) there was evidence of eosinophilic inflammation in the gastrointestinal tract but no history of food allergic symptoms, and 45/66 (68%) had no clinical evidence of food allergic problems. Findings included combined liver-bowel transplants being more common in the allergy group, 8/10 (80%) versus 20/45 (44%), p=0.042. Therefore isolated small bowel transplant was less common in the allergy group 1/10 (10%) versus 18/45 (40%), p=0.072. Acute cellular rejection was less common in the allergy group, but not statistically significant, 1/10 (10%) versus 12/45 (26.7%), p=0.262. The donor (but not recipient)
nucleotide-binding oligomerization domain-containing protein 2 (NOD2) was more common in the allergy group 2/10 (20%) versus 0/45 (0%), p=0.02. Conclusion: Food allergy is common after intestinal transplantation and more likely with a liver inclusive graft. A comparison to other organ transplants is necessary to understand the additional burden of the liver graft on developing food allergy after solid organ transplantation.

349 PREVALENCE OF COAGULOPATHY IN CHILDREN WITH CELIAC DISEASE. Lalit Bharadia, Shyam Sunder Sharma, Deepak Shivpuri, Fortis Escorts Hospital, Jaipur, India

**Background:** Celiac disease may induce malabsorption of many nutrients including vitamin K which in turn can cause coagulopathy. Diagnosis of Celiac disease involves endoscopy and multiple duodenal biopsies. Risk of bleeding with endoscopy and biopsy is more if there is underlying coagulopathy.

**Aim:** To assess the prevalence of coagulopathy in children with Celiac disease.

**Method:** Children (< 18 years) suspected to have Celiac disease referred for duodenal biopsies were recruited after informed consent and approval by Hospital Ethics committee. A complete blood count, prothrombin time (PT) and activated partial thromboplastin time (APTT) was tested and endoscopy performed under IV sedation.

**Results:** Study recruited 152 subjects of which 114 (75%) children (M:F= 1:1.5) were confirmed to have histology suggestive of celiac disease. Abnormal PT (INR > 1.4) was noted in 29 (26%) subjects (INR range 1.4-9.6). PT derangement was mild in 83% (INR 1.4 to 2.49), moderate in 10% (INR 2.5 to 4.99) and severe in 7% (INR 5 and above). Abnormal aPTT (value more than 8 seconds of control) was seen in 28 (25%) subjects. APTT derangement was mild in 57% (8-16 sec of control), moderate in 3% (17-24 sec of control) and severe in 40% (more than 24 sec of control). Subjects with moderate and severe coagulopathy received one dose parenteral Vit K. None had any overt bleeding.

**Conclusion:** This study shows a significant prevalence of coagulopathy (25%) in celiac disease children at the time of diagnosis. We propose screening for coagulopathy in children with Celiac disease.

350 EOSINOPHILIC ESOPHAGITIS IN CHILDREN WITH CELIAC DISEASE. Laura S. Villafane1, Veronica B. Busoni2, Federico Ussher1, Claudia Paris3, Juan P. Santino4, Daniel D'Agostino1, Marina Orsi1, 1Pediatric Gastroenterology and Hepatology Division, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 2Immunology Division, Hospital Italiano, Buenos Aires, Argentina; 3Pathology Anatomy Division, Hospital Italiano, Buenos Aires, Argentina

Celiac disease (CD) and eosinophilic esophagitis (EoE) are immunoallergic diseases of the digestive tract with specific clinico-pathological features. Despite the increase of both in the last decade, reports of this association are still scarce.

**Aim:** To describe the association of EoE and CD in children.

**Material and Methods:** Retrospective analysis of pediatric patients diagnosed with CD and/or EoE, evaluated by endoscopy with biopsies of the esophagus, stomach, and duodenum regardless of the appearance of the mucosa. The histological CD diagnosis was carried out according to Marsh classification (II-III), and EoE whenever 15 or more eosinophils per high power field (HPF) were seen only in esophageal mucosa.

**Results:** Between May 2008 and 2014, 243 patients were diagnosed with CD and 13 with EoE. 4/243 with CD also presented with EoE as an incidental finding (1.6%). The average age at diagnosis of CD and EoE was 6.6 years (r:4.9-8.9), 3/4 patients were male and all referred history of atopy. The EoE diagnosis was an incidental finding with normal endoscopic appearance in 2 and longitudinal furrows in the rest with complete eosinophilic infiltration (average 33 Eo/HPF) in all cases. The histological examination of the duodenum showed 2 cases with Marsh III A and 2 with III B. In 2/4 HLA studies showed DQ2 and DQ2/DQ8 respectively. The 4 patients with EoE required topical corticosteroids as additional treatment.

**Conclusions:** The coexistence of EoE and CD although infrequent in our series, should be considered. Biopsies of an endoscopically normal esophagus in celiac children will allow an earlier diagnosis of this association.

351 CHANGE IN THE PRESENTING PATTERN OF PEDIATRIC CELIAC DISEASE. Maan Khatib, Robert D. Baker, Rafal Kozielski, Susan S. Baker, Division of Pediatric Gastroenterology and Nutrition, Women and Children’s Hospital of Buffalo, SUNY at Buffalo, Buffalo, NY

Celiac disease (CD), an autoimmune condition that classically presented with diarrhea and malnutrition in young children. With the development of sensitive serologic tests, safe endoscopy, and a serious effort to educate pediatricians, the disease presentation appears to have changed. The primary aim of this study is to evaluate the pattern of presentation of CD in pediatric patients. Secondary aim is to evaluate correlation between serum TTG IgA level, Marsh score (MS) and disaccharidase assay (DA) in newly diagnosed CD.

We carried out a retrospective chart review of 175 pediatric patients with biopsy proven diagnosis of CD. Patients' age, gender, race, presenting complaint, serum albumin, vitamin D level, TTG IgA level, MS, tissue DA and DEXA scan z-score were collected. Data was analyzed by a certified biostatistician.
One Hundred and Sixty-five children between ages of 2 and 18 years from 2003-2013 were diagnosed with CD. The mean age at presentation was 10.68± 4.3, 43.4% male. Presenting complaints were: abdominal pain(87) 52.7%, constipation(65) 38.9%, diarrhea(52) 31.1%, family history(47) 28.1%, Diabetes mellitus type1(37) 22.2%, failure to thrive(36) 21.8%, reflux (25)15.1%, vomiting(24)14.5%, fatigue(15) 9%, short stature(9)5.4%, thyroid disease(9) 5.4%, Down's syndrome(8) 4.8%.

We found no correlation between MS and serum TTG IgA level at the time of diagnosis using Spearman correlation analysis. Similarly we found no correlation between presenting complaint and TTG IgA level, presenting complaint and MS, TTG IgA and DA. There was no correlation between the age and the presenting complaint, except that there was a negative correlation [95%(CI -56.85 to -18.96)],(p=0.0002) between age at diagnosis and reflux as a presenting complaint. MS correlated with Sucrase,Maltase and Palatinase levels, but not Lactase.

We conclude that children newly diagnosed with CD have less severe symptoms than the classical presentation of CD. Further, we show that abdominal pain and constipation were the most common presenting symptoms for children who were diagnosed with CD.

Table 1: Demographics and nutritional status of 175 patients

<table>
<thead>
<tr>
<th></th>
<th>10.68 ± 4.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>2 - 18.3</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>76:99</td>
</tr>
<tr>
<td>Ethnicity n(%)</td>
<td>White: 167(95.4%), Black: 2 (1%), Others: 6 (3%)</td>
</tr>
<tr>
<td>BMI z-score</td>
<td>0.2 ± 1.15</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.1 ± 0.63</td>
</tr>
<tr>
<td>Vitamin D (nmol/mL)</td>
<td>31.9 ± 10.1</td>
</tr>
<tr>
<td>Percent deficient</td>
<td>44%</td>
</tr>
<tr>
<td>DEXA SP z-score</td>
<td>-0.38 ± 1.09* Median: -0.3</td>
</tr>
<tr>
<td>DEXA WB z-score</td>
<td>-0.37 ± 1.1* Median: -0.55</td>
</tr>
</tbody>
</table>

Mean ± SD, SD: Standard deviation.
Normal range for albumin (3.5-5) g/dL, vitamin D (30-74) nmol/L.
DEXA: dual energy x-ray absorptiometry, obtained within 6 months from diagnosing celiac disease. z-score is standardized to age and gender.
SP: Bone density of the spine, WB: Whole body bone density.
* z-score was 2 SD below mean for 2 patients' SP and for 1 patient's WB DEXA scan.

Table 2: Disaccharidase assay in 175 celiac disease patients:

<table>
<thead>
<tr>
<th>Disaccharidase (normal level, ug/min/g-protein)</th>
<th>Duodenal tissue enzyme level Mean ± SD</th>
<th>Percent Deficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactase (&gt;15)</td>
<td>6.11 ± 10.76</td>
<td>92.5</td>
</tr>
<tr>
<td>Sucrase (&gt;25)</td>
<td>21.01 ± 19.54</td>
<td>71.4</td>
</tr>
<tr>
<td>Maltase (&gt;100)</td>
<td>73.25 ± 55.33</td>
<td>73.7</td>
</tr>
<tr>
<td>Palatinase (&gt;5)</td>
<td>4.23 ± 4.01</td>
<td>71.4</td>
</tr>
</tbody>
</table>

Patients with pan-disaccharidase deficiency n(%) 124(70.8)

352 PREVALENCE OF CELIAC DISEASE IN CHILDREN: A SINGLE CENTER EXPERIENCE. Maureen M. Leonard¹, Alexander Asch², Rhonda Fogle³, Aubrey Katz⁴, ¹Pediatric Gastroenterology and Nutrition, Massachusetts General Hospital, Boston, MA; ²Pediatrics, Massachusetts General Hospital, Boston, MA
Background: The prevalence of celiac disease (CD) in the U.S. has increased 5-fold over the last thirty years. Despite increased awareness by physicians and accurate diagnostic serum studies, the majority of individuals remain undiagnosed. The presentation of CD has diversified with half of individuals diagnosed now asymptomatic and many others presenting with non-specific complaints. Although case finding has been shown to be the most economical choice to identify patients, the changing presentation and possibility of developing CD at any age makes potential patients a moving target. For that reason, a private pediatric practice has been screening their patients for CD. The aim of this study was to determine the prevalence of CD in at-risk and not at-risk pediatric patients in this primary care
practice.

Methods: The records of 2755 (51%M) patients ranging in age from 10 months to 29 years (mean age 14.65) who received care at a practice in Middlesex County, MA and who were screened with serum IgA tissue transglutaminase (tTG) between January 2009 and May 2014 were reviewed. This practice is located in the greater Boston area in a predominantly Caucasian, middle class community and cares for 4067 patients. Thirteen children had been previously diagnosed with CD and thus were not included in the study. All patients were classified as at risk or not-at risk based on available clinical data. At risk individuals were defined as those individuals with a first-degree family member with CD, those who presented with celiac associated symptoms such as abdominal pain, diarrhea, constipation, or poor growth. Additionally, subjects with celiac associated disorders such as anemia, osteoporosis, alopecia, and autoimmune thyroid disease were included in the at-risk group. Patients classified as not-at risk were asymptomatic at diagnosis, did not have any celiac associated signs or symptoms, or had no records at MGH and thus no referrals to specialists here. Patients found to have an elevated IgA tTG were referred to Massachusetts General Hospital Pediatric Gastroenterology Unit and encouraged to undergo intestinal biopsy.

Results: A total of 41 patients were found to have elevated IgA tTG in this practice over a 5 year period. An additional three patients with normal IgA tTG were anti-endomysial positive and were also recommended to undergo further evaluation and duodenal biopsy. Of these 44 patients, two were evaluated at an outside institution, two patients had elevated IgA tTG with normal duodenal biopsies, one patient has not yet undergone biopsy, and one parent refused duodenal biopsy. In at risk patients the prevalence of CD was 4.7%. The prevalence of CD in not-at-risk patients was 1%.

Conclusions: The prevalence of CD in healthy adolescents undergoing routine screening in this practice is much higher (>3 times) than previous reports which placed prevalence in a similar not-at-risk group at 1:320. Additionally, the prevalence in at risk patients is nearly 5 times higher than previous reports. Although this practice is not truly generalizable to the population at large given the over-represented Caucasian population, this study suggests that primary practitioners should consider their population and keep CD high on their differential diagnosis.

353 THE RELIABILITY IN PEDIATRIC CLINICAL PRACTICE OF DEAMINATED GLIADIN ANTIBODIES (DGA) AND TISSUE TRANSGLUTAMINSE IGA (TTG-IGA) IN THE DIAGNOSIS OF CELIAC DISEASE (CD).

Michael J. Pettei, Matthew D. Haller, Toni Webster, Pediatrics, Cohen Childrens Medical Center, NSLIJ Health System, New Hyde Park, NY

The reportedly high sensitivity and specificity of the newer and easily obtained celiac antibodies TTG and DGA has lead to their widespread use. This combined with increased awareness of the prevalence of CD in various populations has resulted in the diagnosis of CD with increased frequency over recent years. Most of the sensitivity and specificity data for CD serologic tests have been obtained from studies conducted in a research setting. Observations of variation in results from different clinical laboratories suggest that these tests may not perform as well in the clinical setting. The purpose of this study was to ascertain the performance of the DGA-IgG , DGA-IgA, and TTG-IgA antibodies in a clinical pediatric gastroenterology practice. Methods: The records of patients who underwent upper endoscopy in our pediatric GI practice for the year 2013 were reviewed. Those with previously diagnosed CD, Inflammatory Bowel Disease, Eosinophilic Esophagitis, and IgA deficiency were excluded. Those remaining who had CD serologies, an IgA level, and a small bowel biopsy were included. Results: 321 pts (1-20y, mean 10.5y; 155 female, 162 male) met the inclusion criteria of which 60 (18.7%) had the initial diagnosis of CD. The antibody results for these 321 pts were analyzed and the results presented in Table 1. In addition to the parameters for the individual antibodies, we combined the results for DGA-IgA and TTG-IgA. In this analysis, only those who had both DGA-IgA and TTG-IgA positive were considered a positive test, and both DGA-IgA and TTG-IgA negative were considered a negative test. Conclusion: In clinical practice these celiac antibodies do not have the reliability expected from prior reports. While the tests in general were good at detecting the absence of disease (specificity) they all had some degree of difficulty in correctly identifying those with disease (sensitivity). The high PPV of the combined assays is promising but is mitigated by the high prevalence of CD in this population which influences the PPV. Overall, these results generally tend to support the need to confirm the presence of CD with biopsy.
**Table 1: Results**

<table>
<thead>
<tr>
<th>Testing Positive</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Pos Pred Value (PPV)</th>
<th>Neg Pred Value (NPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGA-G</td>
<td>53.3</td>
<td>98.5</td>
<td>89</td>
<td>90</td>
</tr>
<tr>
<td>DGA-A</td>
<td>41.6</td>
<td>95.0</td>
<td>66</td>
<td>88</td>
</tr>
<tr>
<td>TTG-A</td>
<td>83.3</td>
<td>98.7</td>
<td>89</td>
<td>96</td>
</tr>
<tr>
<td>DGA-A/TTG-A</td>
<td>40</td>
<td>100</td>
<td>100</td>
<td>88</td>
</tr>
</tbody>
</table>

**354* SEROLOGICAL DIAGNOSIS OF CELIAC DISEASE:A PILOT STUDY TOWARD CHANGING LOCAL PRACTICE IN CANADA.** Seema Rajani1, Leanne Shirton2, Cheryl Kluthe2, Hien Q. Huynh3, Rabin Persad4, Justine M. Turner1,2, 1Pediatrics, University of Alberta, Edmonton, AB, Canada; 2Gastroenterology, Stollery Children's Hospital, Edmonton, AB, Canada

**Introduction:** Celiac disease (CD) is the most common autoimmune disorder of the gastrointestinal tract. Traditional diagnosis of CD includes an initial serological screen, usually IgA-antitissue Transglutaminase (aTTG), followed by endoscopy and intestinal biopsy. In 2012, the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) changed their guidelines for diagnosis: children with >10x normal aTTG on two occasions and with positive celiac HLA haplotypes, can be diagnosed by serology. The purpose of this study is to apply ESPGHAN-like diagnostic criteria in a prospective manner; using non-invasive monitoring of intestinal dysfunction and inflammation, to determine if outcome on the gluten free diet (GFD) is impacted by diagnostic strategy.

**Methods:** Children ages 3-18 referred for a diagnosis of CD were recruited from the Stollery Children's Hospital Multidisciplinary Celiac Clinic. Patients with aTTG ≥200 U/ml (28x upper limit) were eligible for serologic diagnosis, provided confirmatory repeat aTTG and HLA haplotypes. Patients with aTTG <200 U/ml were recruited as controls, given biopsy diagnosis. In both groups, intestinal permeability and inflammation, as a non-invasive marker of mucosal disease, was assessed using standard urine testing (following lactulose, mannitol and sucrose loading) and measurement of fecal calprotectin. Age appropriate controls for intestinal permeability were used for comparison; a laboratory normal value of ≤50μg/g was used for fecal calprotectin. Statistical analysis used kruskal-wallis one-way analysis of variance (significance≤0.05). Data is presented as medians and range (Table 1); only baseline data is presented as the study is ongoing.

**Results:** From January 2013 to June 2014, 117 patients from 170 eligible patients referred for diagnosis of CD were recruited (69%), 25 were excluded. 42 subjects consented to serologic diagnosis (group 1); 50 subjects consented to biopsy diagnosis (group 2). As expected aTTG was significantly different between groups (p<0.001).

<table>
<thead>
<tr>
<th></th>
<th>Serological Diagnosis</th>
<th>Biopsy Diagnosis</th>
<th>Control</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>aTTG (U/ml)</td>
<td>590 (200-4000)</td>
<td>46 (7.1-170)</td>
<td>≤7.0</td>
<td>0.000</td>
</tr>
<tr>
<td>Lactulose:Mannitol</td>
<td>0.047 (0.0220-0.2920)</td>
<td>0.033 (0.0110-0.1550)</td>
<td>0.022 (0.0100-0.0720)</td>
<td>0.000</td>
</tr>
<tr>
<td>Sucrose (mg/ml)</td>
<td>0.31 (0.0683-2.7902)</td>
<td>0.28 (0.0506-0.8724)</td>
<td>0.099 (0.0298-1.7244)</td>
<td>0.000</td>
</tr>
<tr>
<td>FC Calprotectin (μg)</td>
<td>95.2 (6.9-3068.1)</td>
<td>50.1 (4.9-1755.4)</td>
<td>≤50</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Data is presented as median (range). 1- Values refer to laboratory normal values.

**355 PRESENCE OF CELIAC DISEASE ASSOCIATED AUTOANTIBODIES AND HUMAN LEUKOCYTE ANTIGENS DQ2/DQ8 IN THE TYPE-I DIABETIC POPULATION AND THEIR RELATIVES.** Stephanie S. Camhi1,2, Craig Sturgeon1,2, Maureen M. Leonard3,4, Eliese A. Addonizio1, Alessio Fasano1,2, 1Mucosal Immunology and Biology Research Center, Massachusetts General Hospital, Boston, MA; 2Center for Celiac Research and Treatment, Mass General Hospital for Children, Boston, MA

**Background:** Celiac disease (CD) is an autoimmune enteropathy triggered by the ingestion of gluten in genetically
susceptible individuals. Though the prevalence of CD is approximately 1% worldwide, the prevalence of CD in individuals with type-1 diabetes mellitus (T1DM) is estimated at between 4 and 5%. Human leukocyte antigens (HLA) DQ2 and DQ8 constitute a genetic profile compatible with disease development and similarly underlie the commonest autoimmune diseases (AD) including CD, T1DM, systemic lupus erythematosus, rheumatoid arthritis and autoimmune thyroid conditions. Historically, presence of a DQ2 allele (DQA1*05 or DQB1*02) is shown to be strongly associated with CD, while DQ8 (DQA1*03 or DQB1*0302), though still associated with CD but to a lesser extent than DQ2, is described for its association with T1DM.

**Objective:** To assess the prevalence of celiac disease in the type-1 diabetic population and their first and second-degree relatives; to understand the genetic risk factors that may differentially predispose individuals within these subgroups to the development of CD.

**Method:** We conducted a large-scale screening for presence of tissue transglutaminase 2 (IgA) antibodies at an educational conference targeted toward families of children with T1DM. All participants underwent venipuncture and were typed for HLA DQ2/DQ8 and subsequently informed of their CD status (elevated or normal (Tg IgA) and genetic compatibility. Participants also completed a screening intake form assessing their past and current symptoms and medical history.

**Results:** Two hundred and forty participants, consisting of 76 individuals with T1DM (31%) and 164 of their relatives (69%), were screened. Twelve (5%) participants (4 with T1DM and 8 relatives) were found to have elevated Tg IgA; an additional 5 participants (3 with T1DM and 2 relatives) reported a previously confirmed diagnosis of CD. Overall, the incidence of CD was 9% in individuals with T1DM and 6% in their relatives. Preliminary genetic analysis revealed DQ8-DR4 to be the most commonly detected allele within the sample (56% of patients screened), irrespective of DQ2 absence or presence. Analysis by odds ratio indicated that carrying both DQ2 and DQ8 significantly increased the odds of developing an AD (CD, T1DM, or both conditions) by four-fold (OR 4.13, 95% CI 1.76-9.69, \(p=0.001\)).

**Conclusions:** Consistent with previous screening studies, we observed an increased incidence of CD in individuals with T1DM (9%) and in relatives of individuals with T1DM (6%) as compared to that known to be observed in the general population (1%). Our data suggest that individuals who carry heterodimers coding for both DQ2 and DQ8 alleles are at increased risk of AD development. Though a substantial percentage of patients within the sample carried DQ8-DR4, these patients were not significantly more prone to develop AD unless coupled with a DQ2 heterodimer. Standardized screening practice for CD has been fervently debated for its utility and cost-effectiveness in high-risk populations; these data suggest that our scope of "high-risk" should soon shift, not only to encompass individuals with AD and their relatives, but also to account for genetic markers of the disease.

### 356 THE RATE OF CELIAC DISEASE IN WV CHILDREN- THE VIEW FROM THE ENDOSCOPY SUITE.

**Yoram Elitsur, Deborah L. Preston, Pediatric, Gastroenterology, Marshall University School of Medicine, Huntington, WV**

The rate of celiac disease in the United States in the general population has been estimated at about 1%. In a large epidemiological study, the rate of celiac disease in children was reported in 1:320 subjects (Fasano A et al. 2003). Those data were usually confirmed following positive serology. The rate of celiac disease suspected by histology first compared to serology first has never been investigated.

**Aim:** 1. To investigate the overall rate of celiac disease in a cohort of West Virginian children who undergo upper endoscopy for various gastrointestinal symptoms. 2. To investigate the rate of celiac disease diagnosed in children who had positive histology first compared to children who had positive serology first.

**Methods:** Charts of all diagnostic upper endoscopy procedures from 2009 - 2013 were reviewed. Histological data of the small intestine and duodenal bulb biopsies were reviewed. In all procedures, at least 2 biopsies were available from both locations, irrespective of the mucosal appearance. Patients were then divided according to the following groups: Patients who had positive histology followed by positive serology (group A), patients with positive serology followed by positive histology (Group B), patients with positive histology with negative serology (group C), and patients with negative histology followed by positive serology (Group D).

**Results:** A total of 761 upper endoscopic charts were reviewed (Jan. 2009 - July 2013). Fifteen children were confirmed with celiac disease (1.97%). No significant difference in the rate of celiac disease was observed between histology- led vs. serology- led celiac diagnosis (1.18% vs. 0.79%, \(p = 0.273\)) (Table).

**Conclusion:** 1. The rate of celiac disease in the cohort of children from WV was higher than expected (1.97%). 2. A similar rate of celiac disease was found in symptomatic children whom the diagnosis was led by positive histology compared to those who were led by positive serology (1.18% vs. 0.79%, respectively). 3. Celiac disease should be suspected in each diagnostic upper endoscopic procedure thus, appropriate number of biopsies is recommended.
Endoscopy-led vs. Serology-led celiac diagnosis

<table>
<thead>
<tr>
<th>Total</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac Dis</td>
<td>(+)EGD/</td>
<td>(+)Serology/</td>
<td>(+)EGD/</td>
<td>(+)Serology/</td>
</tr>
<tr>
<td></td>
<td>(+)Serology</td>
<td>(+)EGD</td>
<td>(-)Serology</td>
<td>(-)EGD</td>
</tr>
<tr>
<td>15 (1.97%)</td>
<td>9 (1.18%)</td>
<td>6 (0.79%)</td>
<td>1 (0.13%)</td>
<td>2 (0.26%)</td>
</tr>
<tr>
<td>Marsh grade</td>
<td>M1/M2/M3</td>
<td>2/0/7</td>
<td>1/0/5</td>
<td>0/0/1</td>
</tr>
</tbody>
</table>

p value = 0.273 between group A and group B (Two tailed, Chi-square analysis)

Clinical/Translational – Inflammatory Bowel Disease

361 TICKIT® - AN I-PAD ENABLED HEADSS ADOLESCENT RISK AND RESILIENCE ASSESSMENT - USE IN A PEDIATRIC IBD CLINIC. Robert Issenman1,2, Sufian Odeh1,2, Pei Yoong Lam2, Mariana Deevska1, Sandy Whitehouse2, 1Pediatrics, McMaster Children's Hospital, Hamilton, ON, Canada; 2BC Children's Hospital, Vancouver, BC, Canada; 3Pediatrics, McMaster University, Hamilton, ON, Canada; 4UBC, Vancouver, BC, Canada

Introduction: The IBF care team struggles to consistently assess the emotional and social issues in adolescents with chronic disease. We studied the use of TickiT® (www.shifthealth.ca). This application, presents the widely used HEADSS interview which surveys home, education, employment, activities, drugs, sexuality, suicide and depression in a graphical interactive questionnaire presented on an iPad.

Study Design: After obtaining informed consent, a research assistant presented this iPad enabled TickiT questionnaire to consecutive adolescent patients attending the McMaster Children's Hospital Pediatric IBD Clinic from January to June 2014 as part of a larger study on acceptability and ease of use by patients, physicians and staff at McMaster and BC Children's Hospitals. iPads were presented and retrieved at registration. Responses were automatically uploaded upon participant submission to a secure password protected website. Tabulated results highlighting areas of concern and "protective factors" were subsequently presented to the patient's attending physicians. We report preliminary results.

Acceptability: In the larger study (n=80, age 14-18 years) 99% of patients agreed to participate with 99% completion rate. 94% of subjects were comfortable with the questions, 94% found the platform easy to use and 92% found the questions easy to understand. All of the youth completed TickiT within 15 minutes. (50% took less than 10 minutes)*

McMaster IBD Population: 53 patients with ulcerative colitis and Crohn's disease participated; 31 males and 22 females between ages of 8-17 years old (mean age 14.9 years old). TickiT was easily incorporated into the clinic visit. Neither parents nor physicians were involved in administering the HEADSS questionnaire allowing teens a greater degree of confidentiality around sensitive topics such as gender identity issues, drug and alcohol use, thoughts of self-harm or running away. Concerning results were presented to the attending physician in a tabular format highlighting areas of concern maximizing physician time while allowing comprehensive screening. Issues of concern were identified in 10 patients (19%). Positive and proactive behavior was present in 30 (57%).

Conclusion: Use of the iPad enabled TickiT HEADSS questionnaire is a practical and efficient way to consistently secure confidential adolescent risk and resilience screening in a busy pediatric IBD clinic.

Reference: * S. Whitehouse, P.Lam, M Daveeska, R. Issenman. Evaluating a technological innovation TickiT™ using the IHI Triple Aim Framework in 2 Canadian Pediatric Hospitals, CAPHC, Toronto 2013

362 TICKIT®: I-PAD ENABLED QUESTIONNAIRE HELPING CLINICIANS UNDERSTAND THE INTERPLAY BETWEEN LIFESTYLE AND INFLAMMATORY BOWEL DISEASE. Robert Issenman1,2, Sufian Odeh1, Stephanie Rosinski4, Sandy Whitehouse3, 1Pediatrics, McMaster Children's Hospital, Hamilton, ON, Canada; 2McMaster University, Hamilton, ON, Canada; 3BC Children's Hospital, Vancouver, ON, Canada; 4Shift Health Paradisms Ltd, Vancouver, BC, Canada

Introduction: Lifestyle and health powerfully influence quality of life among children/teens with chronic disease. We studied the use of TickiT® (www.shifthealth.ca), an iPad enabled HEADSS interview in pediatric Inflammatory Bowel Disease (IBD) patients.

Study Design: Fifty-three patients, (31 male and 22 female, age 8 to 17 years, average 14.9 years) attending the McMaster's Children Hospital Pediatric IBD Clinic agreed to participate in this pilot study. Participants were approached at registration and given an iPad questionnaire prior to seeing the attending clinician.

Acceptability: One hundred per cent agreed to participate, 96.2% were comfortable with the questions and found them easy to understand, 98.1% found the electronic platform easy to use and 100% completed the questionnaire. Upon
randomized in this pilot study by block design to either 10,000 (n=18) or 5,000 IU (n=14) of vitamin D3 per 10 kg body weight is both safe and effective at normalizing vitamin D nutriture in pediatric IBD patients. Repletion therapy for hypovitaminosis D with once-weekly dosing for 6 weeks of either 5,000 or 10,000 IU of vitamin D3 per 10 kg body weight per week orally for six weeks. Serum 25(OH)D, calcium, and parathyroid hormone (PTH) levels were measured at baseline, week 8 and week 12. Fitzpatrick skin types were also assessed at enrollment for comparison of subjects with varying skin color. RESULTS: In the higher dosing group, serum 25(OH)D concentrations increased from 23.7 ± 8.5 ng/mL at baseline to 49.2 ± 13.6 ng/mL at 8 weeks; P<0.001. In the lower dosing group, serum 25(OH)D levels increased from 24.0 ± 7.0 ng/mL at baseline to 41.5 ± 9.6 ng/mL at 8 weeks; P<0.001. Although not statistically significant, the higher dosing group achieved superior serum 25(OH)D levels at week 8 compared to the lower dosing group (p = 0.10). At 12 weeks (6 weeks after discontinuation of vitamin D treatment), serum 25(OH)D levels were 35.1 ± 8.4 ng/mL and 30.8 ± 4.2 ng/mL for the higher dose regimen and for the lower dose regimen, respectively. No differences in blood measures were observed at week 8 or 12 when subjects were stratified by Fitzpatrick skin type. Mean serum calcium and PTH levels remained within their respective reference ranges of 8.9-12.0 mg/dL and 14.5-81.1 pg/mL, respectively; no patient exhibited hypercalcemia and no serious adverse events occurred. CONCLUSIONS: Repletion therapy for hypovitaminosis D with once-weekly dosing for 6 weeks of either 5,000 or 10,000 IU of vitamin D3 per 10 kg body weight is both safe and effective at normalizing vitamin D nutriture in pediatric IBD patients. However, 6 weeks after the last vitamin D dose, serum 25(OH)D concentrations were trending toward baseline values, suggesting that six weeks of therapy alone with either dose of vitamin D3 is insufficient to sustain therapeutic vitamin D status. We conclude that either 5,000 or 10,000 IU per 10 kg per week repletion therapy with vitamin D3 for 6-weeks is therapeutic, but effect may wane after a period of weeks in pediatric IBD. Maintenance vitamin D therapy after the initial 6 weeks of repletion is likely required to keep serum 25(OH)D in the optimal range. Skin pigmentation does not appear to play a significant role in the dosing of these short-term repletion regimens for hypovitaminosis D.
Serum 25(OH)D3 concentrations at weeks 0, 8, and 12

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Mean [25(OH)D3] ± SD (ng/mL)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 8</td>
</tr>
<tr>
<td>5,000 IU/10 kg/wk</td>
<td>24.0 ± 7.0</td>
<td>41.5 ± 9.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10,000 IU/10 kg/wk</td>
<td>23.7 ± 8.5</td>
<td>49.2 ± 13.6</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
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</tbody>
</table>

P-values indicate pairwise comparison adjusted for multiple testing.

364 THE ASSOCIATION BETWEEN DRUG LEVELS, ANTI-DRUG ANTIBODIES, AND THERAPEUTIC RESPONSE DURING INFliximab THERAPY IN PEDIATRIC CROHN DISEASE. Ronen E. Stein1, Dale Y. Lee1, Mary B. Leonard1,2, Meena Thayu1, Rita M. Herskovitz1, Theresa A. Kerbowski1, Emil Chuang1, Robert N. Baldassano1,2,1, The Children's Hospital of Philadelphia, Philadelphia, PA; 2Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA; 3Nestle Institute of Health Sciences, Vevey, Switzerland

INTRODUCTION: Inflimimab (IFX) can effectively induce and maintain remission in children with Crohn Disease (CD), but the role of serum IFX levels and antibodies to IFX (ATI) in predicting clinical outcomes in pediatric CD is unclear.

AIM: To determine the association between serum IFX levels, inflammatory markers, and Pediatric Crohn Disease Activity Index (PCDAI) in pediatric CD.

METHODS: In 82 children with active CD starting IFX, serum IFX levels, ATI, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and PCDAI were prospectively measured at baseline, 10 weeks, 6 months, and 12 months. Serum was sent to Prometheus Laboratories Inc. for evaluation of IFX and ATI levels. T-tests and chi-square tests were used to evaluate continuous and categorical covariates.

RESULTS: At 12 months, 10/69 patients (15%) had detectable ATI levels. Patients with detectable ATI had lower mean (+SD) serum IFX troughs at 6 months (0.9±0.2 vs. 7.6±9.3 ug/mL; p < 0.009) and 12 months (2.5±3.4 vs. 9.5±10.3 ug/mL; p < 0.036). Serum IFX levels were not associated with PCDAI scores at any time point. Patients with CRP >=1 had lower mean IFX levels at 10 weeks (7.5±11.1 vs. 20.6±12.3 ug/mL; p < 0.001) and 12 months (3.5±5.0 vs. 9.8±10.5 ug/ml; p < 0.026). ESR >=20 was associated with lower IFX levels only at 10 weeks (p <0.006).

CONCLUSION: Low serum IFX levels are associated with the development of ATI and with markers of ongoing inflammation, but are not associated with clinical disease activity as measured by PCDAI.

365 ASSOCIATION OF BEING OVERWEIGHT OR OBESE ON HOSPITALIZATIONS, SURGERIES, AND ESCALATION OF MEDICAL THERAPY IN INFLAMMATORY BOWEL DISEASE. Jeffrey Morganstern1, Sameer Lapsia1, Trudy Lerner2, James Markowitz1, Anne Griffiths1, Jose Cabrera2, David Mack2, James R. Rick2, Anthony Otley2, Marian Pfefferkorn3, Joel Rosh10, Marsha Kay1, Maria Oliva-Hemko12, Shehzad Saeed13, Neal LeLeiko14, Ryan Carvalho15, Andrew Grossman16, David Keljo17, Boris Sudeith18, Michael Kappelman19, Subra Kugathasan21, Paul Schaefer22, Gitit Tomer23, Collette Deslandres24, 1Pediatric Gastroenterology, Stony Brook Children's Hospital, Stony Brook, NY; 2Connecticut Children's Medical Center, Hartford, CT; 3Cohen Children's Medical Center, Lake Success, NY; 4Hospital for Sick Children, Toronto, ON, Canada; 5Medical College of Wisconsin, Milwaukee, WI; 6Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 7Dayton Children's Medical Center, Dayton, OH; 8WK Health Centre, Halifax, NS, Canada; 9James Whitcomb Riley Hospital for Children, Indianapolis, IN; 10Morristown Memorial Hospital, Morristown, NJ; 11The Cleveland Clinic Foundation, Cleveland, OH; 12The Johns Hopkins University School of Medicine, Baltimore, MD; 13Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 14Rhode Island Hospital, Providence, RI; 15Nationwide Children's Hospital, Columbus, OH; 16Children's Hospital of Philadelphia, Philadelphia, PA; 17Children's Hospital of Pittsburgh, Pittsburgh, PA; 18University of Minnesota, Minneapolis, MN; 19UNC Chapel Hill, Chapel Hill, NC; 20Mayo Clinic, Rochester, MN; 21Emory University, Atlanta, GA; 22Hershey Medical Center, Hershey, PA; 23Children's Hospital At Montefiore, Bronx, NY; 24CHU Sainte-Justine Hospital, Montreal, QC, Canada

Background: The prevalence of childhood obesity has dramatically increased over the past decade. Even in pediatric
patients (pts) with inflammatory bowel disease (IBD), approximately 20% with Crohn's disease (CD) and 33% with ulcerative colitis (UC) are overweight or obese. Adult reports indicate that obese pts with CD have a more severe course with more anoperineal involvement than their nonobese counterparts; however, they do not differ in number of surgeries or escalation of therapy.

Aim: To determine if overweight and obese children with IBD require more hospitalizations and surgeries as well as more rapid escalation of medical therapy compared to their non-overweight counterparts.

Methods: Data were obtained from the Pediatric IBD Collaborative Research Group Registry, a prospective observational study of newly diagnosed children ≤ 16 years. A total of 173 pts (69 with UC, 104 with CD) who were overweight or obese (Body Mass Index, BMI ≥ 90%) were identified and frequency matched by disease-type (either CD or UC) with 519 controls (207 with UC, 312 with CD). Demographic characteristics and outcomes, including time to first immunomodulator (thiopurine, methotrexate, cyclosporine, or tacrolimus) and first biologic (anti-TNFα medications) were documented. All hospitalizations and surgeries were also recorded. Statistical analysis was conducted using χ² and multiple logistic regression models.

Results: Mean BMI percentile for the overweight and obese group was 95.1 ± 3.0%. Mean control group BMI percentile was 32.4 ± 27.5%. Patients were 57% male and 43% female with a mean age of 12 ± 3 years in both groups. There was no significant difference in gender, (p=0.72) age distribution (p=0.14), or disease severity at baseline between the two groups. Overweight/obese pts with IBD had similar rates of initiation of immunomodulator therapy compared to non-overweight pts by 2, 3, and 5 years post-IBD diagnosis (~63%, 65%, and 67%, respectively). The 2 groups did not differ in rates of initiation of biologic therapy at these time points (~28%, 32%, and 35%, respectively). Number of hospitalizations and surgical procedures when controlled for gender and age at diagnosis were alike. However, when these pts were additionally controlled for full range of disease severity scores at baseline, overweight and obese pts were more likely to be hospitalized compared to non-overweight pts, OR=1.47 (95% CI= 1.02-2.11) p=0.04. Furthermore, these same pts were more likely to undergo a surgical procedure compared to non-overweight pts, OR=1.67 (95% CI= 1.00-2.79) p=0.048. These differences were not detectable when separately evaluating CD patients from UC patients.

Discussion/Conclusion: Being overweight or obese with childhood IBD is associated with increased hospitalizations and surgical procedures, but only when taking disease activity at baseline into account. This suggests that disease activity may be acting as a moderator of the effect between weight and hospitalization or surgery. Future prospective studies with greater number of patients may be more likely to reveal detectable differences in hospitalizations and surgeries in the separate CD and UC populations, as well as differences in escalation of therapy and overall IBD mortality.

366 RELATIONSHIP BETWEEN DIET, INTESTINAL MICROBIOME AND DISEASE ACTIVITY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE. Sarah Kinder1, Tom Flass2, Edward J. Hoffenberg1, Janine Higgins3, Daniel Frank4, Edwin de Zoeten1, 1Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO; 2Pediatric Gastroenterology, St. Vincent Healthcare, Billings, MT; 3Section of Pediatrics, Department of Nutrition, Children's Hospital Colorado, Aurora, CO; 4Microbiome Research Consortium Colorado (MiRC), University of Colorado School of Medicine, Division of Infectious Disease, Aurora, CO

Background: 25% of all patients with inflammatory bowel disease (IBD) are diagnosed during adolescence. Although treatment strategies for IBD rely on immunosuppression and anti-inflammatory medications, there is increasing interest in the role played by diet and the intestinal microbiome on disease activity. Studies have shown that the incidence of IBD is higher in countries with a "westernized" diet including increased intake of sugars and fats. Studies of the intestinal microbiome have shown significant differences in population diversity and bacteria species in patients with IBD versus healthy controls. Our pilot study was designed to determine if there are differences in both the dietary intake and the intestinal microbiome in pediatric patients with poorly controlled IBD versus those with well controlled IBD.

Methods: Fifty-four patients age 9-18 were recruited from the Children's Hospital Colorado Pediatric IBD Center from Nov 2012 through Nov 2013. Patients with IBD (either Crohn's disease or Ulcerative Colitis) must have been diagnosed at least six months prior. Each subject completed a validated youth/adolescent food frequency questionnaire (FFQ) and submitted a stool sample for microbiome analysis. Using either the PCDAI for Crohn's disease (scale 0-90) or the partial Mayo score for UC (scale 0-9) each subject was characterized as either well-controlled (PCDAI < 15 or UC score ≤ 2) or poorly controlled (PCDAI ≥ 15 or UC score > 2) based on physician assessment at the time of enrollment. Data from each individual's FFQ was calculated and compiled using software from Harvard School of Public Health Department of Nutrition and was then analyzed using SAS. The stool was processed and fecal DNA extracted, amplified, and sequenced using the Illumina Miseq sequencing platform. Analysis of the microbiome data was completed using Explicet.

Results: Forty-eight patients completed the FFQ and 28 of these patients submitted stool samples. 52% of participants were male and 58% had Crohn's disease. 32 patients were classified as well controlled (18 submitted stool samples) and were 16 poorly controlled (10 submitted stool samples). Analysis of the microbiome revealed no statistically significant
difference in the relative microbial diversity between well-controlled IBD and those with poorly controlled IBD. However, there were significant differences in the relative abundance of bacterial types between the two groups. Patients with well controlled IBD had statistically significant increased abundance of the phylum Firmicutes, specifically within the Clostridia family. Analysis of the dietary intake revealed that a significantly lower average intake of dairy based fats and animal based fats was correlated with patients who had well controlled IBD.

**Conclusions:** This data mimics patterns seen in studies of adult patients with our well-controlled patients having microbiome profiles similar to healthy adult controls while our pediatric patients with poorly controlled or active IBD have microbiome profiles similar to adult IBD patients. Although the data does not imply causation, there are statistically significant differences in both the diet and the microbiome which implicate both as potential future targets for therapy.

367* **WHOLE EXOME SEQUENCING IDENTIFIES ATG16L2 VARIANT AS SUSCEPTIBILITY GENE FOR CROHN'S DISEASE IN KOREAN CHILDREN WITH SEVERE PHENOTYPE.** Seak Hee Oh1, Jinmin Cho1, Kyung Mo Kim2, Kyuyoung Song2, 1Pediatrics, Seoul Asan Medical Center Children's Hospital, Seoul, Republic of Korea; 2Biochemistry and Molecular Biology, University of Ulsan College of Medicine, Seoul, Republic of Korea

**INTRODUCTION:** The differences in genetic susceptibility of Crohn's disease (CD) between Asian and Western populations have been noted. Among well-established CD candidate genes, NOD2/CARD15, ATG16L1, and PTPN2 failed to be replicated in Asians. A recent GWAS study of approximately 2000 Korean patients with CD introduced ATG16L2 as a novel susceptibility gene for CD (Yang et al. *Gut* 2014; 63: 80-7), instead of variants in ATG16L1, which regulates autophagy and Paneth cell secretion containing antimicrobial peptides. We applied whole exome sequencing (WES) to 22 pediatric patients with CD and 18 controls with the aim of identifying risk loci for CD with severe phenotypes.

**METHODS:** Twenty-two CD cases with severe phenotypes and early-onset were diagnosed at the Inflammatory Bowel Disease (IBD) Clinic of the Seoul Asan Medical Center. The WES analysis pipeline involved quality checks, alignments, and annotation to identify nucleotides that differed between the patient and reference sequences. The captured, purified and amplified exome-targeting library from each patient was sequenced on an Illumina HiSeq2000. Variants were subsequently annotated by another program, ANNOVAR (ver. November 2011), from file conversion to its input format, filtering with dbSNP for the version of 135, and SNPs from the 1000 genome project (http://genome.ucsc.edu/cgi-bin/hgLiftOver). For additional filtering, 263 genes were selected based on recent public data for IBD (Jostins et al. Nature 2012; 491: 119-24, Christodoulou, *Gut* 2013; 62: 977-84) and additional four new loci from Korean population were used (Yang et al. *Gut* 2014; 63: 80-7).

**RESULTS:** Following a series of quality-control steps (SNP quality > 50, total read depth > 10, alternative read depth > 3), 72 variants in 53 IBD-associated genes were identified across the 22 CD probands. All probands carried a wide spectrum of heterozygous/homozygous variants of IBD-related genes. Among these variants, 19 variants in 17 IBD-related genes (ADAD1, ATG16L2, CREB5, FAM55A, GALC, HLA-DQA1, ITIH4, LRRK2, MST1, PLC1L1, PTPN22, RFTN2, SLC11A1, SULT1A1, SULT1A2, TRAF3IP2, and ZMIZ1) were noted to be deleterious at least in SIFT and PolyPhen2 and evolutionarily conserved (PhyloP score >1.0). Thirteen variants in 12 IBD-related genes (ATG16L2, HLA-DRB5, IFIH1, IL10RA, IL17REL, IL31RA, MANBA, MLH3, MST1, NOS2, SLC11A1, and TBC1D1) were noted to be carried by at more than two probands. Nine (40.9%) of the 22 probands carried variant of ATG16L2 (rs11235604, R220W). This variant was deleterious in SIFT and PolyPhen2 and evolutionarily conserved. The second common variant was IL17REL (rs142430606, P262L) carried by four probands (21.1%).

**CONCLUSION:** Genetic susceptibility factors for CD in Korean pediatric patients with early-onset and severe phenotype overlapped substantially with those in Western populations. Nearly half of the probands carried a deleterious variant of ATG16L2, suggesting a hypothesis that ATG16L2 may play a role in the development of severe CD in Korean Children. Functional validation must be done to determine the biological effect of Atg16l1 in CD.

368 **VITAMIN D LEVELS AT DIAGNOSIS ARE ASSOCIATED WITH COMPLICATED CROHN'S DISEASE.** Sheetal Wadera*, Namita Singh1, Myung S. Sim1, Marla C. Dubinsky1, 1Department of Pediatrics, Pediatric IBD Center, Cedars-Sinai Medical Center, Los Angeles, CA; 2Pediatric Gastroenterology, Hepatology, and Nutrition, UCLA, Los Angeles, CA

**Background:** Studies suggest that Vitamin D deficiency is associated with an increased risk of surgery and hospitalization in Crohn's disease (CD). It is unknown if Vitamin D 25 OH levels at time of diagnosis is associated with risk of developing a CD-related stricture or fistulizing complication, often leading to surgery. We hypothesize that low vitamin D 25 OH levels at time of diagnosis is associated with rapid progression to disease related complications in pediatric patients with CD. We aimed to determine if vitamin D 25 OH levels at time of diagnosis are associated with CD complication and/or surgery.

**Methods:** CD patients ages 2-26 were identified by chart review. Patient demographics, age at diagnosis, disease
photon, complication date and type, surgery date and type, and date of last follow-up were recorded for each subject. Vitamin D 25 OH levels were collected at diagnosis (+/- 3 months). Univariate and multivariate analyses tested associations of vitamin D 25 OH levels at diagnosis and clinical and demographic data with CD related complications (stricture, or penetrating disease behavior or surgery).

**Results:** Of the 84 phenotyped CD patients (median age: 11 [2-26] yrs) who had Vitamin D 25 OH levels available at time of diagnosis, 22 (26%) patients developed a complication. Median vitamin D levels were 28 (range 17-55) ng/mL in 62 patients who remained uncomplicated as of last follow up, compared to 20.7 (17-26.6) ng/ml in those who developed a complication, p = 0.02. In multivariate analysis, Vitamin D levels at diagnosis remained significant, p = 0.04. Age at diagnosis, PANCA and ASCA status, and small bowel disease location were not significant. For every 1 ng/mL increase in vitamin D level, the odds of developing complication by 24 months is reduced by 9.5% (OR 0.905 [0.867, 0.944], p <.0001).

**Conclusion:** Vitamin D 25 OH levels at diagnosis are associated with complicating Crohn's disease. Vitamin D levels should be checked at diagnosis and supplementation is warranted. The impact on Vitamin D normalization on preventing complication merits further exploration.

369 **IDENTIFICATION OF INFLAMMATORY BOWEL DISEASE PATIENTS WITH STEROID-INDUCED DIABETES MELLITUS USING AN ELECTRONIC HEALTH RECORD.** Sivan Kinberg1,2, Lyudmila Ena2, Herbert Chase2, Carol Friedman1, 1Division of Pediatric Gastroenterology, Hepatology and Nutrition, Columbia University, New York, NY; 2Department of Biomedical Informatics, Columbia University, New York, NY

**Introduction:** Glucocorticoids are commonly used to treat patients with inflammatory bowel disease (IBD), often for prolonged periods of time. Although glucocorticoids have potent anti-inflammatory effects, they have been implicated in the development of steroid-induced diabetes mellitus (S-DM) in patients with various conditions. Hyperglycemia, even transient, has been associated with adverse events. Conversely, control of hyperglycemia during acute illness has been associated with improved outcomes. Despite this, S-DM and steroid-induced hyperglycemia (i.e. prediabetes) are often under-diagnosed and under-treated. In patients with IBD, the current knowledge of S-DM and steroid-induced prediabetes is limited.

**Aim:** Using automated extraction of data in the electronic health record (EHR), we aimed to determine the prevalence of and risk factors for S-DM and steroid-induced prediabetes in patients with IBD.

**Methods:** This was a retrospective cohort study that examined pediatric and adult patients with IBD who were treated with glucocorticoids between 2004 and 2012, excluding patients with pre-existing diabetes mellitus. Notes from the EHR were parsed using a natural language processing system to structure and encode the information in the notes, and the coded output was stored in a structured patient database where the relevant data were queried. We identified patients with IBD based on the intersection of ICD-9 codes and coded information from the clinical notes. The diagnoses of S-DM and prediabetes were based on ICD-9 codes and on the American Diabetes Association diagnostic criteria. Patients with IBD treated with glucocorticoids were compared with IBD patients who never received glucocorticoids.

**Results:** A total of 1,719 patients with IBD were identified based on the intersection of ICD-9 codes and coded information in the notes. We found that 140 (20.1%) of 698 patients with IBD treated with glucocorticoids developed S-DM compared with 21 (5.8%) of 363 patients not treated with glucocorticoids (OR=7.42, 95% CI: 4.41-12.48). Prediabetes was identified in 192 (27.5%) IBD patients treated with glucocorticoids and in 67 (18.5%) patients not treated with glucocorticoids (OR=2.25, 95% CI: 1.59-3.17). Multivariable analysis determined increasing age and parenteral nutrition as risk factors for S-DM, and male sex and parenteral nutrition as risk factors for prediabetes.

**Conclusion:** To our knowledge, this is the first study to determine the prevalence of and risk factors for S-DM and prediabetes in patients with IBD. Gastroenterologists should be aware of the high prevalence of S-DM and prediabetes in patients with IBD and should screen those treated with glucocorticoids for hyperglycemia. Using the EHR for automated detection of high-risk patients is possible and could result in earlier diagnosis, timelier treatment, and possibly improved outcomes.

370 **DEVELOPMENT OF LYMPHOPENIA IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS ON THIOPURINE THERAPY.** Sophia A. Patel1, Vera Okwu1, Matthew J. Wyneski2, Jonathan Moses1, 1Pediatric GI, Cleveland Clinic Children's, Cleveland, OH; 2Akron Children's Hospital, Akron, OH

**Objectives:** Thiopurines (TP) such as 6-mercaptopurine (6MP) and azathioprine (AZA) are indicated in the treatment of moderate-severe pediatric ulcerative colitis (UC) and Crohn's disease (CD). They are primarily used for maintenance of remission and as a steroid-sparing medication. These immunosuppressants begin as either 6MP, or AZA, a prodrug of 6MP, and undergo a complex metabolism to their active metabolites, 6-thioguanine (6TG) and 6-methylmercaptopurine (6MMP). TP have been shown to cause lymphopenia on average, in about 15-35% of adult IBD patients. Lymphopenia puts patients at high risk of opportunistic infections. In pediatric patients, there has been no determination of unsafe levels of lymphopenia, and few studies in the adult literature describe the natural course of lymphopenia in patients with IBD on TP. The aim of this study was to elaborate the natural history of lymphopenia in pediatric IBD patients on TP
therapy. The secondary aim was to identify risk factors for development of lymphopenia and the occurrence of opportunistic infections in this patient population. **Methods:** Charts of 110 patients seen at the Pediatric Gastroenterology Department at the Cleveland Clinic in Cleveland, OH with diagnosis of UC or CD who were maintained on AZA or 6MP therapy were retrospectively reviewed. Data collected were patient demographics, current medications, laboratory findings, concurrent office visits for infections, and distribution of disease. Lymphopenia was defined as an absolute lymphocyte count (ALC) < 1.0 k/uL. Labwork was evaluated up to 1 year after initiation of AZA or 6MP. **Results:** A total of 111 patients were studied. There were 71 (65%) male patients and 38 (35%) female patients. 90% were Caucasian, 5% were African American, 6% were other. 11 patients had UC and 100 had CD. The majority of the CD patients disease location was in the terminal ileum. 101 patients were on AZA and 10 patients were on 6MP. Of 111 patients, 40 patients (36%) developed lymphopenia. Of these 40 patients, development of lymphopenia occurred in 61 days (range of 0-427 days). The mean ALC was 0.8 k/uL. The mean time to resolution of lymphopenia was 48.5 days (range of 6-265 days), with resolution ALC on average of 1.5 k/uL. 5 patients developed opportunistic infections, in the form of respiratory viral illnesses. The incidence of opportunistic infections in lymphopenic vs non-lymphopenic patients did not differ significantly between groups (3 patients vs 2 patients). Patients with lymphopenia had lower albumin at follow-up 4.2 g/dl vs 4.0 g/dl (P=0.026) than those without. Lymphopenic patients were more likely to be female, have marginally higher PCDAI scores (11.3 vs 8.4), slightly lower AST at follow-up (19.5g/dl vs 29.9 g/dl) and slightly lower ALT at follow-up (15.2 g/dl vs 26.5 g/dl) with P-values between 0.05 and 0.10. **Conclusions:** Patients on AZA and 6-MP developed lymphopenia at a mean of 61 days and resolution of lymphopenia was within 48.5 days. The incidence of opportunistic infections in patients with lymphopenia and those without did not differ significantly between groups, but interpretation is limited by small sample size. Further prospective studies should be completed for evaluation of lymphopenia in patients with IBD on TP therapy.

**371 FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE RESULTS IN SUSTAINED ERADICATION OF CLOSTRIDIUM DIFFICILE.** Suchitra Hourigan2,1, Greggory Laroche2, Cindy Sears3, Maria Oliva-Hemker2, 1Pediatric Gastroenterology and Nutrition, Pediatric Specialists of Virginia, Fairfax, VA; 2Pediatric Gastroenterology and Nutrition, Johns Hopkins School of Medicine, Baltimore, MD; 3Infectious Disease, Johns Hopkins School of Medicine, Baltimore, MD

**Background:** There is an increased rate of recurrent *Clostridium difficile* (*C. difficile*) disease and colonization in children with inflammatory bowel disease (IBD) compared to the general pediatric population. It is unknown whether Fecal Microbiota Transplantation (FMT) eradicates *C. difficile* from patients with IBD suffering from recurrent infection.

**Aims:** To investigate whether there is eradication of *C. difficile* after FMT for recurrent *C. difficile* infection in children with IBD.

**Methods:** Patients with IBD and a history of recurrent *C. difficile* infection manifested by ≥ 3 recurrences refractory to standard antibiotic therapy including vancomycin taper, underwent FMT via colonoscopy. Donor stool was obtained from identified relatives who underwent extensive evaluation and screening of blood and stool for acute and chronic infections. Stool samples were collected at least 12 weeks after the FMT and analyzed with polymerase chain reaction (PCR) of the *C. difficile* toxin B gene. Clinical effectiveness and adverse reactions of FMT in these patients was evaluated.

**Results:** 4 patients with Crohn's disease and 1 with ulcerative colitis underwent FMT for recurrent *C. difficile* (Table). All had eradication of *C. difficile* at 12 -20 weeks after FMT. Three patients provided samples 6 months after the procedure and these were also negative for *C. difficile*. All patients had resolution of symptoms associated with their *C. difficile* infection after 1 FMT and no patient required repeat FMT. Transient mild abdominal pain was reported in 2 patients immediately after the procedure, with no other immediate or delayed side effects reported. 3 out of the 5 patients were being treated with systemic corticosteroids and/or TNF antagonists at the time of FMT without adverse effects reported. No exacerbation of IBD symptoms were reported and no escalation in IBD therapies were required in the 12 weeks post FMT.

**Conclusions:** FMT gives sustained *C. difficile* eradication in children with IBD who have had recurrent *C. difficile* infection. In this series, FMT was well tolerated.
Patient and Donor characteristics, and C. difficile status after FMT

<table>
<thead>
<tr>
<th>Patient</th>
<th>Donor</th>
<th>C. difficile toxin B gene</th>
<th>PCR of Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age Relationship 12-20 weeks 6 months</td>
</tr>
<tr>
<td>No</td>
<td>Age (years)</td>
<td>IBD Type</td>
<td>IBD location</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>Crohn's Disease</td>
<td>Pancolitis</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>Crohn's Disease</td>
<td>Ileocolonic</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>Crohn's Disease</td>
<td>Ileocecal</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>Ulcerative Colitis</td>
<td>Pancolitis</td>
</tr>
<tr>
<td>5</td>
<td>13</td>
<td>Crohn's Disease</td>
<td>Ileocolonic</td>
</tr>
</tbody>
</table>

372 TEXT MESSAGES IMPROVES ADHERENCE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE. Tamir A. Miloh, Mitchell Shub, Gary Silber, Dana I. Ursea, Kristy Ingebo, Jackie Schenkein, Ramon Montes, Brad Pasternak, Phoenix Children's Hospital, Phoenix, AZ

Successful treatment of patients with inflammatory bowel disease (IBD) requires regular intake of medication. Non-adherence is associated with increased relapses, morbidity and cost. The aim of this study was to investigate whether text messaging (TM) medication reminders in children (<18y) with IBD affects medication adherence and clinical outcome over 1 year. A prospective study, sending medication reminders to the primary medication administrator (patient or caregiver) of pediatric IBD recipients at specific times set by the medication administrator was conducted. The patient was required to confirm intake by TM. Failure to confirm resulted in a TM alert to caregiver. Weekly compliance reports with motivational messages were sent to patients, caregivers and healthcare providers. Inclusion criteria; pediatric IBD patients taking oral medication followed at Phoenix Children's Hospital who had TM services. Children were randomized by age, gender, medication administration responsibility (self vs parent) and disease activity (PCDAI or PUCCDAI) into either TM intervention or standard of care. The study was approved by the IRB. Patients' medical records were reviewed and an adherence Morisky questionnaire was completed at recruitment, 6 and 12 months. Results: 51 children randomized (21 TM and 30 control). Dropout rates were 26.7% in the control and 28.6% in the TM group.

Patient population summarized in table 1 and results in table 2. There was no statistical significance in clinical flares, admissions, surgery and ER visits between both groups after 1 year.

Conclusion: TM may be effective in promoting adherence in children with IBD. The effect is greater at the first 6 months. Larger and longer multicenter studies are required to assess the clinical effect.
Table 1: Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Text Messages</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td># of subjects</td>
<td>30</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Age in years (median)</td>
<td>15 (10-20)</td>
<td>16 (12-21)</td>
<td>0.1</td>
</tr>
<tr>
<td>Median age at diagnosis years</td>
<td>11.5 (3-16)</td>
<td>13 (5-17)</td>
<td>0.25</td>
</tr>
<tr>
<td>Diagnosis; Crohn's</td>
<td>15</td>
<td>10</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>15</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Male # (%)</td>
<td>12 (40%)</td>
<td>11 (52%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Caucasian # (%)</td>
<td>25 (83%)</td>
<td>19 (90%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Patient medication responsibility</td>
<td>28 (93%)</td>
<td>21 (100%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Median BMI</td>
<td>20.4 (15.9-39)</td>
<td>21.4 (15.7-45)</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Table 2: Results

<table>
<thead>
<tr>
<th>Morisky score in median</th>
<th>Control</th>
<th>Text Messages</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.8 (2.5-8)</td>
<td>5 (1-8)</td>
<td>0.3</td>
</tr>
<tr>
<td>Change in 6 months</td>
<td>0</td>
<td>1 (-1.2-4.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Change in 12 months</td>
<td>0</td>
<td>0.8 (-2-4.8)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

373 STOOL POLYMERASE CHAIN REACTION-BASED ASSAYS AND PROCALCITONIN IN THE DETECTION OF CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE (IBD). Toni Webster, Toba Weinstein, Michael J. Pettei, James Markowitz, Cohen Children’s Medical Center, Lake Success, NY

Background: In children with IBD, acute onset of abdominal pain and bloody diarrhea can indicate disease activity or an enteric infection such as C difficile (C diff). Recently, highly sensitive stool polymerase chain-reaction (PCR) assays for C diff toxin B gene have replaced direct toxin identification as the gold standard for diagnosis of C diff infections (CDI). However, there are sizeable numbers of asymptomatic carriers of toxigenic C diff in the pediatric population and PCR does not distinguish between toxigenic strains that are or are not actually producing toxin. While detection of C diff toxin gene may be adequate in diagnosis of CDI in the general population with acute diarrhea, in symptomatic children with IBD, PCR+ may only represent C diff colonization.

Aims: 1. To estimate the prevalence of C diff colonization in asymptomatic and symptomatic children with IBD. 2. To evaluate whether serum procalcitonin (PCT), a possible marker of infectious enterocolitis, might differentiate IBD from CDI.

Methods: Fecal and serum samples were prospectively collected from asymptomatic IBD children without diarrhea and in remission and symptomatic IBD children with both diarrhea and elevated disease activity as classified by PUCAI or abbrPCDAI. Risk factors for CDI were recorded for all subjects. PCR (GeneXpert, Cepheid, California) was performed on all samples. Cytotoxicity assay (CTA) (Bartels, Trinity Biotech, Ireland) was performed on all PCR+ stools from symptomatic subjects. Serum PCT (VIDAS, bioMérieux, North Carolina) was measured from all subjects (undetectable <0.05ng/mL). Asymptomatic PCR+ subjects were considered colonized, as were symptomatic PCR+/CTA- subjects. These latter subjects were considered to have active IBD. Symptomatic PCR+/CTA+ subjects were defined as CDI. All subjects who were PCR- were not considered colonized.

Results: 53 children (33 Crohns, 19 UC, 1 IBD-U, mean age = 14 yrs) were recruited. Stool samples from 5/25 (20%) asymptomatic subjects were PCR+ and thus colonized with C diff. All PCR+ subjects had Crohn's disease, 1/5 was taking probiotics, and only 1/5 had a single risk factor for CDI (antibiotic use). PCT was >0.05ng/mL in 2/5 colonized asymptomatic subjects. Stool samples from 5/28 symptomatic subjects were PCR+, but only 1/5 was CTA+. Colonization rate was 14.3% and CDI rate 3.6%. The CDI subject had 4 risk factors (antibiotic use, steroid use, PPI therapy, surgery) while 3 colonized subjects had 1 or 2 risk factors (PPI [2], antibiotics [2]). There was a significant association between IBD activity and PCT (p<0.0008). PCT ≥0.05ng/mL was found in 2/25 (8.7%) IBD remission subjects, 2/11 (18.2%) with mild disease, 4/11 (36.4%) with moderate disease, and 5/5 (100%) with severe disease. The highest PCT (1.41ng/mL) occurred in a PCR- subject with severe IBD. There was a significant association between CRP and PCT (p<0.0165) and between ESR and PCT (p<0.0039).

Conclusions: As up to 20% of children with IBD are colonized, diagnosing CDI solely by PCR+ appears problematic.
Direct toxin identification should be used to confirm CDI in this population. Preliminarily PCT does not distinguish CDI from active IBD; however, PCT may be considered a marker of IBD severity.

374 ANTI-SACCHAROMYCES CEREVISEAE ANTIBODY TITERS CORRELATE WITH DISEASE ACTIVITY IN CHILDREN WITH CROHN'S DISEASE. Wael El-Matary, Karine Dupuis, AbdulRazaq Sokoro, 1Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada; 2Manitoba Institute of Child Health, Winnipeg, MB, Canada; 3Internal Medicine and Pathology, Faculty of Medicine, University of Manitoba, Winnipeg, MB, Canada

Objectives: There has been continuous search for biological markers of Crohn's disease (CD) activity. The aim of this study was to assess an association between clinical disease activity and quantitative anti-saccharomyces cerevisiae antibody (ASCA) titers in children with CD. Methods: ASCA IgA and IgG titres, pediatric Crohn's disease activity index (PCDAI), serum albumin and C-reactive protein (CRP) were repeatedly measured simultaneously in children with CD. ASCA IgA and IgG were considered positive if titers > 20 RU/mL. A possible association between ASCA IgA and IgG titers and changes in PCDAI was examined. Results: 136 measurements of ASCA IgA and IgG titres in 57 children with CD (36 boys, mean age at diagnosis 11.9 ± 2.2) over a mean duration of 3.1 ± 2.1 years. The mean ASCA IgA antibody level (91.1 ± 84.6 RU/mL) was higher than that of IgG (63.9 ± 69.4 RU/mL) (p=0.06). In a univariate linear regression model, there were significant correlations between ASCA IgA titers and PCDAI (P<0.001, 95% CI 0.36-0.61), CRP (P<0.01, 95% CI 0.10-0.41) and low serum albumin (P<0.001, 95% CI -0.27- -0.55) respectively. Similarly ASCA IgG titers correlated with PCDAI (P<0.001, 95% CI 0.21-0.50), CRP (P<0.05, 95% CI 0.04-0.36) and low serum albumin (P<0.001, 95% CI -0.19- -0.49) respectively. These associations seemed to be independent of presence or absence of immunosuppressive medications. Conclusion: In children with Crohn's disease, both ASCA IgA and IgG quantitative titers seem to correlate with clinical Crohn’s disease activity, CRP and low serum albumin. Measuring these antibodies should be considered during routine clinical care for those patients. Large prospective well-designed studies are needed to confirm our conclusions.

Endoscopy/Potpourri

385 FAMILY-CENTERED ROUNDS WITH CARE-COORDINATION TEAM LEADER FOR INPATIENT GASTROENTEROLOGY SERVICES: A NOVEL QUALITY IMPROVEMENT INITIATIVE. K. T. Park, Karen Wayman, Lisa Kohn, Ivette Becerra-Ortiz, Susan Herman, Christy Sandborg, Joe Kim, Stanford University, Palo Alto, CA

Background: Optimizing clinical flow of hospitalized patients remains a top priority for clinicians, administrators, and patients. Specifically, quality improvement (QI) measures to increase inpatient discharge accuracy have been an ongoing focus among hospital policy makers at the national level, as average discharge accuracy is consistently near 40% among tertiary pediatric care centers. In particular, improving care-coordination for pediatric gastroenterology patients with complex chronic diseases represents a unique QI opportunity in acute care services.

Methods: We hypothesized that a novel Family Centered Rounds (FCR) initiative at Lucile Packard Children's Hospital will enhance accuracy of estimated discharge dates. We prospectively implemented a system-wide 1-year pilot intervention for all hospitalized patients primarily managed by the Pediatric Gastroenterology and Liver Transplant service teams using the standardized FCR care map and checklist. Our unique FCR care map and checklist leverage a designated Care-Coordination Team Leader who maintains a standardized point-of-care assessment for each patient, including daily calibrations of the estimated target discharge date during inpatient rounds.

Results: Analysis of available data come from 2 fiscal quarters before and after implementing FCR with Care-Coordination Team Leaders for GI services. A pre-FCR discharge accuracy of 29.7% (n=106) improved to 55.2% (n=128) (P<0.01) in the post-FCR quarter. This represents an incremental treatment effect of nearly 93% improved accuracy.

Conclusion: Standardized implementation of a novel FCR with Care-Coordination Team Leader for gastroenterology inpatient services significantly improves discharge accuracy. Adoption of this QI intervention may represent a promising system-wide initiative to improve discharge accuracy rates among inpatient services at pediatric tertiary care centers.

386 CLINICAL CHARACTERISTICS OF PEDIATRIC MICROSCOPIC COLITIS IN A TERTIARY CARE FACILITY. Luis Sifuentes-Dominguez, Jason Park, 1Pediatric Gastroenterology, UT Southwestern Medical Center, Dallas, TX; 2Pathology, UT Southwestern Medical Center, Dallas, TX; 3Pathology, Children's Medical Center, Dallas, TX

Background: Microscopic colitis (MC) is a term used to describe two chronic gastrointestinal disorders, lymphocytic colitis (LC) and collagenous colitis (CC). MC is characterized by watery diarrhea, normal endoscopic findings and abnormal histology. It is rare in pediatric populations. We report a single pediatric center experience with this condition.

Methods: The pathology database at Children's Medical Center Dallas was searched from 2003 through 2013 for colonic biopsies that were consistent with MC. Patients were included if they presented with diarrhea lasting for at least
2 weeks in the absence of enteric infections. In addition, the patients all had normal or only mild changes by colonoscopy. We collected demographic information, clinical patient characteristics (symptoms at presentation, prior medication use and autoimmune diseases), family history of autoimmune diseases and management response when available.

**Results:** Thirty-one distinct patients were identified. Seventeen of these patients had not presented with diarrhea and were excluded from analysis. The remaining 14 patients (median age of 8.5 years, 71.5% female) met inclusion criteria and were included in the study (2 CC and 12 LC).

Symptoms other than diarrhea included abdominal pain (64%), weight loss (50%), nausea (28.5%), vomiting (7%), blood in stool (21%), and oral ulcers (7%). Three patients had positive antinuclear antibodies. One patient had a prior history of eosinophilic colitis. At the time of diagnosis five patients were taking medications associated with MC, including PPI (n=1), SSRI (n=3) and NSAID's (n=1); additionally one patient was taking a combination of carbamazepine and aripiprazole. Three patients had a family history of autoimmune diseases.

Eleven patients had clinical follow-up. Of these eleven patients, only one had self resolving symptoms and did not receive any therapy. The remaining 10 patients received either budesonide (60%), mesalamine (20%), metronidazole (10%) or loperamide (10%). Only patients who received budesonide achieved clinical response (4 of 6 patients).

Follow-up endoscopy was performed on 6 of the treated patients and all those who received budesonide (n=4) had histological improvement.

**Conclusion:** Microscopic colitis is a rare childhood condition that leads to chronic diarrhea. We report associations of pediatric MC to known adult risk factors, such as medication use and autoimmune diseases. The use of budesonide for the treatment of pediatric MC is associated with clinical and histological response.

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**387**  
**Fecal Microbial Transplant for the Eradication of Recurrent Clostridium Difficile Infections in Children.** Mark G. Bartlett, Sahil Khanna, Darrell Pardi, Pediatric Gastroenterology, Mayo Clinic, Rochester, MN; Gastroenterology, Mayo Clinic, Rochester, MN

Clostridium difficile infection (CDI) has grown to epidemic proportions in the United States over the last two decades and the incidence among children has been increasing rapidly. Despite the efforts to develop new therapies, the standard treatment of CDI with antibiotics has a relapse rate of over 25%. Fecal microbiota transplantation (FMT), the transfer of stool from a healthy individual to the individual with recurrent CDI, is emerging as the most effective way to eradicate recurrent infections. While a number of centers are offering this for adults, there are still limited data for outcomes of FMT in children. At Mayo Clinic Children's Center we initiated a protocolized FMT program in March of 2013. Twenty children aged 1-17 years underwent FMT during the initial 12 months with 19 of 20 (95%) resulting in successful eradication of the Clostridium difficile toxin and 17 of 20 (85%) having resolution of symptoms.

20 Children with at least two documented toxin-positive recurrences of symptomatic CDI after Vancomycin therapy were evaluated and found to be suitable for FMT. The patients ranged in age from 1 to 18 with a mean age of 8.25 years. 7 were male and 13 were female. Gastrointestinal co-morbidities included Ulcerative Colitis (2), and IBS (2). Other co-morbidities included congenital heart disease, T-cell dysfunction, and Velo-Cardio-Facial defect. Three had undergone solid organ transplantation (2 kidney and 1 heart). Of the 20 patients, 19 (95%) had been on antibiotics before the initial CDI diagnosis. 2 (10%) had been on PPIs. 5 of 20 (25%) were on immunosuppressive medications. Symptoms at time of presentation included diarrhea, abdominal pain, blood in stool, and weight loss. The dominant symptom was diarrhea in 15 patients (75%) and abdominal pain in 5 (25%). The mean duration of symptoms prior to FMT was 9.3 months with a mean number of relapses of 2.5

FMT was conducted using donor stool from screened family members. Donors included parents (14), siblings (3), other relatives (1), and friends (2). Fresh samples were processed just prior to the procedure and instilled via colonoscopy. There were no side effects or bad outcomes resulting from any of the transplants.

Patients were surveyed by telephone 3 months after the FMT to assess for symptom resolution. Of the 17 who had diarrhea as the dominant symptom, 16 had resolution. Of the 5 with abdominal pain, 3 had complete resolution and 2 (those with prior diagnosis of IBS) had pain that persisted even with eradication of the CDI and toxin. Two patients had documented toxin-positive recurrences of CDI after FMT. These children underwent repeat transplants, with one patient's CDI resolving after the second FMT, and one child not responding even after 3 tries.

Overall, the initial year of FMT at our center was successful with the process being well tolerated by all participants. With 95% of recipients remaining free from CDI for three months post FMT, we are increasingly confident that this treatment should be available to children with recurrent Clostridium difficile that is resistant to antibiotic treatment.

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**388**  
**Assessing Independence and Health Responsibility: Bridge to Adult Cystic Fibrosis Care.** Michelle Edelman, Anupama Chawla, Deborah Salvatore, Theresa Carney, Catherine Kier, Pediatric Gastroenterology, Stony Brook Long Island Children's Hospital, Stony Brook, NY

Introduction: With significant advances in cystic fibrosis (CF) clinical care, median predicted age of survival is 37.8 years and 49% of CF patients in the US are adults (2012 CF registry). With changing demographics, transition to adult care for CF patients is an emerging challenge for cystic fibrosis centers.
CF Care Centers are encouraged. Identification of problems unique to CF adults have been identified including diabetes, bone disease and psychosocial issues including depression. There has been a great interest to probe into these emerging issues that may dictate treatment approaches and affect quality of life. Recent studies have been performed to assess the safety of this process and even the readiness of adult CF patients to these changes.

Objective: The aim of our study is to assess the level of independence and personal health responsibility in CF teens and adults.

Method: We developed a questionnaire that focused on 4 domains: psychosocial, nutrition, sleep, exercise. During CF outpatient visits, patients 12 years and older were asked to complete the questionnaire to identify lifestyle and needs and to determine level of independence. Independence markers were examined including current residence, means of transportation, ability to shop/prepare own meals, education and employment status. Personal health responsibility were examined including nutrition, exercise, sleep hygiene, and enzyme administration.

Results: To date, 22 surveys are completed - age range 12 to 52 years, median age of 19 years, 55% male, 73% Caucasian and 82% at least reached high school.

For independence markers, 91% continue to live with their parents, 71% have parents still shop for and prepare their meals, although 81% of those age appropriate patients drive and 68% have a current or prior history of employment. For personal health responsibility, 80% always take their enzymes with meals, however, 40% often skip meals because of no appetite and/or busy schedule. All patients eat at least 1 snack per day and eat vegetables daily, 71% patients eat at least one fruit daily although 43% drink sweetened beverages, soda or juice multiple times per day. Thirty-five percent engage in regular physical exercise and 82% of the patients are well rested with no sleep complaints.

Conclusion: Preliminary data reveal that our CF patients aged 12 to 52 years have a delay in independence. Majority has parents still shop and prepare for their own food, and majority are still living with their parents.

389 COLONIC POLYPS, ADENOCARCINOMA AND BRAIN TUMOR IN TWO SIBLINGS WITH CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY DUE TO HOMOZYGOUS BI-ALLELIC MSH6 MUTATION. Mohsin Rashid, Lynette Penney, Samina Afzal, Department of Paediatrics, Dalhousie University, IWK Health Centre, Halifax, NS, Canada

Background: The mismatch repair machinery is important for genomic integrity and the MLH1, MSH2, MSH6 and PMS2 genes play an important role in this process. Constitutional Mismatch Repair-Deficiency (CMMR-D) is a rare cancer predisposition syndrome in patients with bi-allelic mutations in one of these genes. Heterozygous mutations cause the adult onset Lynch syndrome-associated tumors. However, CMMR-D can lead to childhood onset cancers, particularly gastrointestinal, hematological and brain malignancies.

Cases: A 14-year-old boy was referred with rectal bleeding, anemia and marked hypoalbuminemia. He had café au lait macules, axillary and inguinal freckling and bilateral, multifocal congenital hypertrophy of the retinal pigment epithelium (CHRPE). There was a past history of kaposiform hemangioendothelioma. Colonoscopy revealed numerous large multilobulated polyps scattered all over the colon in which 6 invasive adenocarcinomas were identified. The colon cancers were MSI-H and by immunohistochemistry the tumour cells and adjacent normal mucosa were negative for MSH6 and positive for MLH1, MSH2 and PMS2. A homozygous pathogenic MSH6 mutation was identified. Testing of the APC and MUTYH genes was normal. This is also a unique case of CMMR-D with CHRPE that fits the clinical criteria for both neurofibromatosis -1 and familial adenomatous polyposis but where the testing for APC and MUTYH genes was normal.

The patient was treated with total colectomy followed by radiation and chemotherapy. There was no known family history of colonic polyps/cancer. Both parents were found to be heterozygous for the mutation.

The patient's 12-year-old sister was also discovered to be homozygous for MSH6 mutation. She had history of headaches and investigations revealed a large frontal lobe glioblastoma multiforme. This required surgical excision followed by radiation and chemotherapy. A colonoscopy showed numerous large polyps with adenomatous changes. Conclusions: Colon cancer is very rare in children and its presence should raise the suspicion of an underlying genetic abnormality even with a negative family history. Appropriate genetic testing should include mutations for constitutional mismatch repair deficiency. This should be done for all family members for early detection of malignancies in various organs.

390 THE USE OF THE OBJECTIVE STRUCTURED CLINICAL EXAM IN PEDIATRIC GASTROENTEROLOGY FELLOWSHIP EDUCATION. Rachel Reed1, Lisa Malter2, Elizabeth Weinsheil2, Aliza Solomon1, 1Pediatrics, New York Presbyterian Hospital - Weill Cornell, New York, NY; 2New York University Langone Medical Center, New York, NY

Background: The Accreditation Council for Graduate Medical Education (ACGME) has described six core competencies with which a Pediatric Gastroenterology (GI) fellow should demonstrate proficiency. Using the Objective Structured Clinical Exam (OSCE), a well-validated tool, we aimed to assess these competencies among Pediatric GI
fellows (PG). **Methods**: Eight first-year PG's from six medical centers in the tri-state area participated in a four-station OSCE with trained standardized patient actors (SP). The first case ("ED Consult") involved an "emergency room resident" consulting the GI fellow via telephone regarding lower GI bleeding; the goal was to effectively communicate with a colleague and show strong medical judgment. In the second case ("Breaking Bad News"), the fellow was to discuss a new diagnosis of cystic fibrosis (CF) with a mother, focusing on its nutritional implications and complications. A third case ("Second Opinion") involved a concerned mother who was seeking a second opinion for chronic abdominal pain; the objective was to explain functional abdominal pain and demystify ancillary medical therapies. In the final case ("Transition of Care"), the fellow was to meet with a teenage patient with inflammatory bowel disease who was transitioning to adult care, with the goal to educate and empower her about her disease. At each station, an attending faculty Pediatric Gastroenterologist (FO) observed the encounters behind a one-way mirror. This FO provided immediate feedback to the PG after each case. Previously validated OSCE checklists were used to assess the PG's performance by the SP. After the fellows completed all four OSCEs, they attended a debriefing session where they completed surveys about the educational value of the program. **Results**: Overall, the SP's rated the PG completely or mostly professional in 91% cases. SP's reported they would recommend the PG to a friend without reservations 69% of the time. 67% of PGs made statements of partnership to enable a shared decision environment. FO's rated a median score of 3 for the published Pediatric Subspecialty Milestones Guidelines (PC1, PC2, PC3, PC4, MK1), and they rated case specific skills and knowledge as a median of 2.75 (1=inadequate and 5 = exemplary). Fellows training at smaller programs found the "Breaking Bad News" OSCE to be the most challenging, citing little experience with CF patients. Overall, the fellows rated the educational value of the program highly, reporting that the OSCEs felt realistic and that the cases were well selected. **Conclusions**: To our knowledge, while the OSCE has been validated in other medical fields, this is the first OSCE program developed for Pediatric GI fellows. These OSCEs have touched upon all six ACGME competencies, serving to assess fellows' skills in these areas while exposing them to challenging medical and psychosocial cases that they may not frequently encounter.

**391 COST-EFFECTIVENESS ANALYSIS OF TREATMENT STRATEGIES FOR INITIAL CLOSTRIDIUM DIFFICILE INFECTION.** Raghu U. Varier2,1, Eman Biltaji2, Kenneth J. Smith1, Mark S. Roberts3, M. K. Jensen2, Joanne LaFleur2, Richard E. Nelson2, 1Northwest Pediatric Gastroenterology, LLC, Portland, OR; 2University of Utah, Salt Lake City, UT; 3University of Pittsburgh, Pittsburgh, PA

**BACKGROUND**: **C. difficile infection (CDI)** is costly. Current guidelines recommend metronidazole as 1st-line therapy, though vancomycin is recommended as an alternative. Recurrence is common. Fecal microbiota transplantation (FMT) is an effective therapeutic option for recurrent CDI (RCDI). There are no studies exploring its use in initial CDI (iCDI). This study explores cost-effectiveness of FMT and vancomycin vs. metronidazole for iCDI.

**METHODS**: We constructed a decision-analytic computer simulation using inputs from the published literature to compare a 10-14 day course of oral metronidazole or vancomycin to FMT for iCDI. Parameters included cure rates for metronidazole [80%(65-85%)], vancomycin [90%(88-92%)] and FMT [91%(83-100%)]. Direct costs of metronidazole, vancomycin and FMT, adjusted to 2011 dollars, were $57($43-72), $1347($1195-1499) and $1086($815-1358), respectively (Table 1). Our effectiveness measure was quality-adjusted life years (QALYs). One-way and probabilistic sensitivity analyses were conducted from the 3rd-party payer perspective.

**RESULTS**: Base case analysis showed that FMT ($1669, 0.242 QALYs) was more costly and more effective than metronidazole ($1167, 0.238 QALYs), yielding an ICER of $124,964/QALY. FMT was dominant (less expensive and more effective) compared to vancomycin (Table 2). Tornado analysis showed that the probabilities of primary cure for metronidazole and FMT impacted the model the most. One-way sensitivity analyses showed that metronidazole dominated both strategies if its probability of cure was >90%; FMT dominated if its cost <$584. In a probabilistic sensitivity analysis at a willingness-to-pay threshold of $100,000/QALY, metronidazole was favored in 55% of model iterations; FMT was favored in 38%.

**CONCLUSIONS**: Our results suggest that metronidazole, as the 1st-line treatment for CDIs, may be less costly, but FMT and vancomycin are more effective. However, FMT is less likely to be economically favorable, and vancomycin is unlikely to be favorable as first line therapy when compared to FMT, due to higher cost and less effectiveness.
Model Parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Case (Range)</th>
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</thead>
<tbody>
<tr>
<td>Probabilities</td>
<td></td>
</tr>
<tr>
<td>Primary Cure: Metro</td>
<td>80% (65-85%)</td>
</tr>
<tr>
<td>Primary Cure: Vanco</td>
<td>90% (88-92%)</td>
</tr>
<tr>
<td>Primary Cure: FMT</td>
<td>91% (83-100%)</td>
</tr>
<tr>
<td>Fulminant Colitis</td>
<td>16% (6-27%)</td>
</tr>
<tr>
<td>Adverse Events of FMT</td>
<td>0.28% (0.17-0.58%)</td>
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<tr>
<td>Death</td>
<td>0.03% (0.00-0.09%)</td>
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</table>

<table>
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<tr>
<th>Direct costs (2011 USD)</th>
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<tbody>
<tr>
<td>Metro</td>
<td>$57 ($43-72)</td>
</tr>
<tr>
<td>Vanco</td>
<td>$1,347 ($1,195-1,499)</td>
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<tr>
<td>FMT</td>
<td>$1,086 ($815-1,358)</td>
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<tr>
<td>Adverse Events of FMT</td>
<td>$30,009 ($16,255-43,762)</td>
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<tr>
<td>Fulminant Colitis</td>
<td>$23,717 ($17,888-29,646)</td>
</tr>
<tr>
<td>RCDI</td>
<td>$2,136 ($1,602-2,670)</td>
</tr>
</tbody>
</table>

Utilities

| Adverse Events of FMT | 15% (0-65%) |
| Fulminant Colitis | 57% (32-82%) |
| RCDI | 88% (80-100%) |

Base-case results

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost ($)</th>
<th>IC ($)</th>
<th>Effectiveness (QALY)</th>
<th>IE (QALY)</th>
<th>ICER ($/QALY)</th>
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<tbody>
<tr>
<td>Metro</td>
<td>1,167</td>
<td>-</td>
<td>0.238</td>
<td>-</td>
<td>-</td>
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<tr>
<td>FMT</td>
<td>1,669</td>
<td>503</td>
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<td>Vanco</td>
<td>1,890</td>
<td>305</td>
<td>0.241</td>
<td>-0.0002</td>
<td>Dominated</td>
</tr>
</tbody>
</table>

**392 SAFETY AND EFFICACY OF BEDSIDE PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT IN THE NEONATAL INTENSIVE CARE UNIT.** Annie Gao1, Rebecca Levine2, Kelly Driver3, Ernest Amankwah4, Fauzia Shaked5, Michael Wilsey6, 1Children’s Research Institute, Johns Hopkins All Children’s Hospital, St. Petersburg, FL; 2Neonatology, Johns Hopkins Medicine All Children's Hospital, St. Petersburg, FL; 3Pediatrics, University of South Florida College of Medicine, Tampa, FL; 4Gastroenterology, Johns Hopkins All Children's Hospital, St. Petersburg, FL

**Introduction:** The neonatal intensive care unit (NICU) is an environment where providing nutrition is often a challenge. Infants admitted to the NICU present with various pathologies that may make oral feeds difficult or even impossible. In these situations, percutaneous endoscopic gastrostomy tube (PEG) placement can be a life-saving procedure. The PEG procedure began in 1979. Numerous studies have concluded that PEG placement is a safe and effective procedure that can have a significant impact on the nutritional status, growth, and development of medically complex patients. Few studies, however, have looked at outcomes and safety of bedside PEG placement in the NICU population prior to hospital discharge. **Aim:** To describe the safety and efficacy of bedside PEG placement in a large level 3 NICU. **Methods:** An IRB approved single institution retrospective chart review was performed on all neonates < 6kg who received a bedside PEG placement in the NICU at All Children's Hospital between 2007 and 2013. Neonates were identified via a query of neonatal R-base data source. Patient demographics including gestational age, weight, and sex were recorded. Perioperative, operative and post-operative outcomes data were recorded including total anesthesia time, respiratory status prior to procedure, ventilator support after the procedure, size of PEG placed, and medications used. Short-term outcomes included any complication post procedure, length of times spent on the ventilator, and time to initiate feeds. All major and minor complications were noted. Long-term outcomes included time to full feeds, length of stay, necessary revisions to the original procedure, and growth velocity pre and post PEG placement, and z-scores. **Results:** 115 PEGS were placed at the bedside in neonates < 6kg hospitalized in the NICU at All Children's hospital.
between 2007 and 2013. 98% were successfully placed on first attempt. The median gestational age was 35 weeks (ranging between 21 and 41 weeks), with PEG placement at a mean of 45 weeks corrected gestation. The median weight at birth was 2.4 kg (ranging between 0.33 kg and 5.82 kg), and there was a mean weight of 4.1 kg at the time of PEG placement. Prematurity and primary CNS or genetic abnormalities accounted for the majority of underlying diagnosis, with 20% of primary diagnosis of a GI origin. 88% percent of infants were extubated within 24 hours of the procedure. The median length of time to first feed was 1 day, and the median time to full feeds was 2 days. The average length of time between PEG placement and discharge from the NICU was 10 days. We found a total complication rate of 7.8% with only 1 major complication diagnosed with buried bumper syndrome. There were 8 minor complications including localized cellulitis, erythema, and stomal leakage. Conclusion: There is a low complication rate with bedside PEG placement. Bedside PEGs allows for early reinitiation of feeds, early success at reaching goal feedings, and very little need for ventilator support. Placement at the bedside in the NICU in neonates less than 6 kg is a safe and effective procedure for providing nutritional support for a variety of diagnosis.

393 PATTERN RECOGNITION RECEPTORS (PRR) MODULATE INTESTINAL SECRETION TRIGGERED BY SHIGELLA FLEXNERI, SHIGELLA DYSENTERIAE AND EPEC. Stefania Senger1,2, Maria R. Fiorentino1,2, Jill Harper3, Shu Yan1, Jinggang Lan1, Alessio Fasano1,2, 1Mucosal Immunology and Biology, MGH, Charlestown, MA; 2Pediatrics, Harvard School of Medicine, Boston, MA; 3School of Nursing, University of Maryland, Baltimore, MD

Background: Diarrheal diseases are cause of roughly 4% of all deaths worldwide, including 1.0 million of children per year. Diarrhea occurs when the regulation of ion transporters in the intestinal epithelium are altered by pathogens colonization causing increase of intestinal secretion.

Aims: With this study we aimed to address the implication of Pattern recognition receptors (PRR) signaling in small intestine secretion after exposure to conditioned media of S. flexneri, S. dysenteriae and Enteropathogenic Escherichia Coli (EPEC).

Methods: We evaluated the secretion response of mice small intestine treated with bacteria conditioned media by measuring short circuit current (DIscc) change in USSING chambers.

Results: In WT mice, EPEC induced significantly high intestinal secretion, compared to either PBS alone or commensal bacteria E. coli strain (HS). Interestingly S. dysenteriae did not elicit any secretory response. However changing culture conditions by adding Congo red, dramatically increased the activity of both Shigella serogroups conditional media. Evaluation of DIscc in PAR2 and TLR4 KO mice revealed a reduced responsiveness to both Shigella serogroups conditioned media compared to the response obtained in WT mice. Whereas EPEC conditional medium elicited a similar secretory response when added to WT and TLR4 KO, but it caused a lower response in PAR2 KO mice intestine.

Conclusions: Our study revealed that both PAR2 and TLR4 are required to promote intestinal secretion after treatment with Shigella serogroups conditioned media. Conversely, PAR2 but not TLR4 contributes to EPEC secretion stimulation. Activation by Congo red of virulence plasmid (Inv), containing ShET-2 gene, was able to greatly increase the pro-secretory activity of both S. dysenteriae and S. flexneri conditioned media, supporting the notion that ShET-2 is among the virulence factors in Shigella that can promote secretion in small intestine.

394 IMPROVING COMMUNICATION, EDUCATION, AND DISCHARGE TIME WITH MULTIDISCIPLINARY FAMILY CENTERED PEDIATRIC GASTROENTEROLOGY ROUNDS: A QUALITY IMPROVEMENT INITIATIVE. Victoria J. Martin, Kathryn Wynne, Samantha Baras, Nina Gluchowski, Catherine Chapin, Anne Fonseca, Esther Israel, Ann Kao, Inbar Spefford, Massachusetts General Hospital for Children, Boston, MA

INTRODUCTION: The literature supports family centered rounds in the pediatric inpatient setting to improve team communication, patient care, and the patient and family experience. There is little reported on the utility of involving sub-specialists in multidisciplinary rounds. We report our experience with a quality improvement initiative at an academic pediatric referral center incorporating the pediatric gastroenterology (GI) team into multidisciplinary family centered rounds.

SPECIFIC AIMS:
(1) To improve communication between the pediatric GI inpatient team, pediatric housestaff, and nursing.
(2) To improve pediatric GI education for pediatric housestaff.
(3) To improve the timeliness of discharges.

METHODS: We designed and implemented a 5 month intervention with multidisciplinary family centered rounds including the pediatric GI team to address communication challenges, lack of housestaff GI education, and delayed discharges. Residents and nurses were surveyed pre- and post- intervention using a 5-point Likert scale (Never, Rarely, Sometimes, Most of the time, Always). Discharge time for GI patients is currently being analyzed.

RESULTS: Sixty-seven pediatric housestaff and 60 staff nurses were surveyed with a 57% and 47% response rate, respectively. Here we report the top two answers chosen. Pre-intervention, pediatric housestaff reported that they
Contemporary methods of treatment for constipation in pediatric patients may include physical therapy.

**Aims:** To investigate the effects of pelvic floor physical therapy (PT) and external biofeedback (BF) in pediatric patients with dyssynergic defecation.

**Methods:** Retrospective review over 15 mo (Sept 2012-Dec 2013) of 82 constipated children (4-19 yrs) with 3D-ARM studies consistent with dyssynergic defecation. Pelvic floor dysynergia was diagnosed based on 3D-ARM results demonstrating poor relaxation of the anal canal, insufficient increase in rectal pressure or paradoxical puborectal contraction during simulated defecation. Patients were referred to PTBF for chronic constipation, including medication dependence and who had findings of dysynergic defecation on 3D-ARM. Physical therapy sessions included abdominal muscle strengthening, pelvic muscle relaxation and external biofeedback. Chart reviewed for time course, symptoms and reports on patient's progress.

**Results:** 18 patients were excluded for completing less than 3 sessions of PTBF. 64 children were analyzed: 48 had complete 3D ARMs with pelvic floor dysynergia and an additional 2 had water perfusion ARMs. Of these 48 patients, 41 had poor relaxation of the anal canal, an additional 4 only had insufficient rectal pressure and 3 were only unable to pass the balloon. The average number of sessions was 5.6 (range 3-17). Of the patients with pelvic floor dysynergia who underwent physical therapy, 38 (78%) responded. 7 patients had autism spectrum disorder, with 4 (57%) reporting progress.

13 of the 38 improved patients had follow up appointments with an average of 11 weeks after treatment (range 1-32 weeks). All continued to have overall improved symptoms, but 3 had symptom worsening since completion of treatment. Additionally, 5 patients had diastasis rectus abdominis (separation of the rectus abdominis muscle) of 2cm or greater noted on physical therapy exam and all had improvement with treatment.

**Conclusions:** Pelvic physical therapy and external biofeedback can be beneficial for patients with constipation, specifically pelvic floor dysynergia and weak abdominal muscles. Patients may benefit from refresher physical therapy sessions to maintain improvement. Further prospective studies need to be done to continue evaluating this form of intervention and long-term outcomes.
having functional pain and 197 of these had SSRI or TCA therapy initiated while being followed by gastroenterology. Total follow up time ranged from 4 weeks to 5 years. Charts were reviewed to assess prescribers and patient side effects.

**Results:** A total of 91 patients met criteria with SSRI therapy. 7 were excluded due to lack of documented follow up resulting in 84 patients analyzed. A total of 106 patients met criteria with TCA therapy. 14 were excluded as they had no follow up documented and 92 patients were analyzed.

Both TCA and SSRI had a similar number of side effects. Of the patients on SSRIs, 21 (25%) reported side effects, with 3 (4%) reporting GI issues and 5 (6%) reporting mood disturbances. Of the patients on TCAs, 20 (22%) reported side effects, with 2 (2%) reporting GI symptoms and 13 (14%) reporting mood disturbances (p=.07). Of the patients on SSRIs, three (4%) discontinued within two weeks of initiation due to side effects while six (7%) TCA patients reported early discontinuation due to side effects (p=.37). Overall, 23 (27%) SSRI patients discontinued the medication, 12 (14%) of them due to side effects while 31 (34%) of the TCA patients discontinued with 16 (17%) due to side effects. IBS-D patients reported more side effects, with 13 (29%) discontinuing due to a side effect, while only 7 (8%) in the IBS-C groups discontinued due to side effects (p<.01)

Gastroenterologists more frequently prescribed TCAs as compared to psychiatrists with 81 (87%) completed by almost half of the SSRI prescriptions for GI issues are by psychiatrists. Patients were more likely to discontinue TCA's due to side effects both in the early and late stages. IBS-D patients were more sensitive to side effects. Although the majority of prescriptions for TCA's are written by gastroenterologists, almost half of the SSRI prescriptions for GI issues are by psychiatrists.

**Conclusions:** SSRI and TCA therapy have similar number of side effects with TCA's having more mood side effects. Patients were more likely to discontinue TCA's due to side effects both in the early and late stages. IBS-D patients were more sensitive to side effects. Although the majority of prescriptions for TCA's are written by gastroenterologists, almost half of the SSRI prescriptions for GI issues are by psychiatrists.

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**413 ROLE OF STEM CELL FOR LUNG HYPOPLASIA IN EXPERIMENTAL MODEL OF NITROFEN INDUCED CONGENITAL DIAPHRAGMATIC HERNIA.** Fatima S. Alatas1,2, Kouji Nagata2, Ratih Yuniartha2, Takayoshi Yamaza2, Yoshiaki Kinoshita2, Tomoaki Taguchi2, 1Department of Child Health, Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia; 2Department of Pediatric Surgery, Reproductive and Developmental Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan, Fukuoka, Japan; 1Department of Molecular Cell and Oral Anatomy, Faculty of Dental Science, Kyushu University, Fukuoka, Japan, Fukuoka, Japan

**Introduction** Lung hypoplasia is still a major problem in children with congenital diaphragmatic hernia (CDH). In this study we aim to know the role of stem cell for lung hypoplasia in an experimental model of nitrofen-induced CDH.

**Methods** Pregnant wistar rats were divided into 3 groups; pregnant rats given nitrofen via gavage at day 9-10th of gestational age (PN group); control group consist of pregnant rats, no intervention (PC group); pregnant rats given nitrofen and MSCs transplanted via uterine vein at day 12-13th of gestational age (PN+MSC group). MSC from wistar rat lung were isolated and expanded before transplantation, additionally transgenic rats expressing enhanced green fluorescent protein (eGFP) were used to detect the homing of transplanted cells. At birth, rat babies were sacrificed and their lung were harvested for evaluation.

**Results** Stem cell transplantation via uterine vein showed good engraftment. MSCs expressing eGFP identified by anti-GFP were detected in lung babies of PN+MSC group. Babies' lung from PN+MSC group as well as control float in phosphate buffer solution (PBS), while PN group babies' lung drowned in PBS. Hypoplasia showed by lung density, number of alveolar, and air spaces were significantly improved in PN+MSC group compared to PN group. PCNA positive cell, SPC expression, Podoplanin expression were significantly higher in the PN+MSC group, compared to PN group.

**Conclusion** Stem cell transplantation improved lung hypoplasia in experimental model of CDH. Stem cell therapy might give promising results to improve lung development in CDH babies with lung hypoplasia.

**Keywords:** Stem cell, transplantation, Congenital Diaphragmatic Hernia, lung hypoplasia

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**414 ARE WE THERE YET? RESULTS OF THE NASPGHAN TASK FORCE SURVEY ON PERCEPTIONS OF GENDER EQUALITY.** Giti Tomer1, Stavra A. Xanthocos2, Sandra C. Kim3, Meenakshi Rao2, Heather J. Litman2, Linda Book6, Laurie N. Fishman1, 1Pediatric Gastroenterology and Nutrition, Children's Hospital at Montefiore, Albert Einstein Medical College, Bronx, NY; 2Pediatric Gastroenterology, Childrens Hospital Boston; Harvard Medical School, Boston, MA; 3Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 4Division of Gastroenterology, The Ohio State University College of Medicine, Nationwide Children's, Columbus, OH; 5Division of Pediatric Gastroenterology Hepatology, & Nutrition, Columbia University Medical Center, New York, NY; 6Pediatric Gastroenterology, Hepatology and Nutrition, University of Utah College of Medicine, Salt Lake City, UT

Background: Gender equality has become an area of increased interest, in business as well as medicine. However, there is little published data in pediatric gastroenterology. Therefore, North American Society of Pediatric Gastroenterology
Hepatology and Nutrition (NASPGHAN) leadership appointed a task force to address gender-specific issues. Methods: The task force created a 32-question survey exploring three main domains (career parity, work-life balance; harassment). All NASPGHAN members were invited to take the electronic survey. Responses were anonymous.

Results: Responses were obtained from 303 members (21%) with geographic region and age distributed evenly. Men and women participated equally (52% male). Most respondents (93%) are employed full-time, while 6% are officially part-time. Academic practice comprised 70%.

Most respondents (92%) live with a spouse or significant other. Males are significantly more likely to have spouses with "more flexible" jobs (p<0.001), with 35% of males reporting spouses having "very flexible" jobs (vs. 14% of females). However, neither males nor females show an association between satisfaction with work-life balance and having a spouse with a "flexible job". Having preschool or school aged children did not affect satisfaction with work-life balance for either gender. Overall, females are more likely to be dissatisfied with work-life balance than males (p=0.046).

Regarding career parity, 46% of men, but only 9% of women, feel that "women earn the same as men" (p<0.001). Respondents in academia are most likely to respond that men earn slightly more (40%) while those outside of academia are most likely to respond that men and women earn the same (37%).

With regards to promotion, 48% of men responded that "women rise at the same rate as men" vs. 12% of women (p<0.001). There was no difference in perception by age, but those in academia were more likely to perceive men's promotion as faster (p=0.008). Women had higher dissatisfaction with mentoring than males (29% vs. 13%; p=0.03). Significantly more women report feeling more uncomfortable with words/actions of a peer, colleague, or supervisor with regards to gender/sex than men (p<0.001); however, these situations were overall considered rare.

Conclusions: Work satisfaction levels are significantly lower amongst female versus male pediatric gastroenterologists. Family factors, such as the flexibility of the spouse's job or the age of children, were not related to job satisfaction. There is a strong perception amongst female pediatric gastroenterologists that parity of promotion and compensation is lacking for women compared to men. Whether this perception reflects significant promotion and compensation disparities is not known and requires further investigation. Dissatisfaction with mentoring among women suggests one potential risk factor for such disparities.

**415 COMPARISON OF STANDARD AND STANDARD PLUS VITAMIN E THERAPY FOR HELICOBACTER PYLORI ERADICATIONS IN CHILDREN.** Gokhan Tumgor1, Masallah Baran2, Murat Cakir3, Hasan A. Yuksekkaya4, Sema Aydogdu5, 1Ped. Gastroenterology, Cukurova University Medical Faculty, Adana, Turkey; 2Dept of Pediatric Gastroenterology, Tepecik Training and Research Hospital,, Izmir, Turkey; 3Dept of Pediatric Gastroenterology, Karadeniz Technical University Medical Faculty, Trabzon, Turkey; 4Dept of Pediatric Gastroenterology, Necmettin Erbakan University Medical Faculty, Konya, Turkey; 5Dept of Pediatric Gastroenterology, Ege University Medical Faculty,, Izmir, Turkey

**Aim:** Although various drugs can be used for *H. pylori* eradication in adults, treatment options are limited in children. The aim of this study is to compare the effect of classical lansoprazole, amoxicillin, clarithromycin (LAC) protocol and LAC + Vitamin E (LACE) combination for *H. pylori* eradication.

**Materials and Methods:** The study included 90 children, aged between 10 and 17 years old, who were admitted to four pediatric gastroenterology centers between March 2011 and November 2012 with dyspeptic symptoms and had positive 13C urea breath test. Patients were randomized into two groups. LAC Group (45 pts) was administered standard regimen consisting of lansoprazole 1mg/kg/day, amoxicillin 50mg/kg/day and clarithromycin 14mg/kg/day, each given in equally divided two doses every 12 hours, for 14 days and LACE Group (45 pts) was administered standard regimen and vitamin E 200 IU/day for 14 days. *H. pylori* eradication was assessed by 14C urea breath test on the 6th weeks after cessation of treatment.

**Results:** *H. pylori* was eradicated in 21 (46.6%) patients in LAC Group, while in 29 (64.4%) patients in LACE Group. There was no statistical difference between two groups (p=0.13).

**Conclusions:** The eradication rate of *H. pylori* in childhood with LAC regimen is decreased in the last years. LACE regimen is associated with increased eradication rate but can reach to statistically significance. Further studies with larger cohorts are needed in order to examine the success of LACE regimen for *H. pylori* eradication.

**416** COLONIC INFLAMMATION INDUCES NEUROGENESIS VIA A 5-HT4-DEPENDENT PATHWAY. Jaime Belkind-Gerson1, Ryo Hotta2, Alyssa R. Thomas2, Weihua Pan2, Allan M. Goldstein2, 1Pediatric GI/Neurogastroenterology, Massachusetts General Hospital, Newton, MA; 2Pediatric Surgery, Massachusetts General Hospital, Boston, MA

**Introduction:** Human inflammatory bowel disease is associated with hyperganglionosis with increased numbers of enteric neurons and glial cells, suggesting that inflammation may contribute to neurogenesis and gliogenesis in the gut. However, while enteric neurogenesis has been observed in vitro, its demonstration in adult animals in vivo has been limited to specific injury models and not observed consistently. The goal of this study is to understand the mechanisms...
that lead to inflammation-induced neurogenesis in the gut, and to determine the role of serotonin signaling in this process.

**Methods:** Dissociated neurospheres prepared from postnatal mouse colon were cultured for 7 days in the presence or absence a 5-HT4 receptor agonist (RS67506). Neuronal and glial differentiation were determined by immunofluorescence and cell proliferation determined by EdU incorporation. **In vivo** neurogenesis was tested in adult mice treated with dextran sodium sulfate (DSS) to induce colitis, with or without supplementation with the 5-HT4 receptor antagonist GR125487. EdU was injected intraperitoneally on alternate days and mice were sacrificed 48 hrs after completing DSS. The effect of DSS on neuronal and glial density and proliferation was compared to untreated controls and to mice treated with DSS and a 5-HT4 antagonist. Enteric neurogenesis was also examined following naïve T cell transfer into RAG -/- mice, an alternate model of colitis. Finally, glial cells were isolated by flow cytometry using anti-CD49b+ antibody and the effect of 5-HT4 agonism analyzed.

**Results:** In cultured cells, 5-HT4 agonism increased neuronal and glial cell proliferation, but only led to an increase in neuronal, not glial, cell numbers. Glial cell apoptosis was not increased by 5-HT4 agonism. Similarly, mice with DSS colitis had a 68% increase in the number of mypereneic neurons in the distal colon as compared to controls (p<0.005), with no increase in glial cell numbers. Only 1.2% of neurons and 5.6% of glial cells incorporated EdU. This neurogenic response was abrogated in the presence of a 5-HT4 antagonist. We observed a similar neurogenic response in the immunologically-mediated T cell transfer model of colitis, where neuron number increased by 83% after colitis compared to control. The correlation coefficient between colitis score and number of neurons was 0.74. In vitro, CD49b-immunoselected enteric glial cells gave rise to enteric neurons, and this effect was blocked by 5-HT4 antagonism.

**Conclusions:** Colonic inflammation is associated with postnatal enteric neurogenesis. The observed increase in neuronal numbers is independent of extensive cell division. Our in vitro data suggest that new neurons may arise from transdifferentiation of enteric glial cells via 5-HT4-mediated signaling.

**417 TREATMENT VARIABILITY IN CHILDREN WITH IRRITABLE BOWEL SYNDROME.** Javier Monagas1,2, Eric Lee3,9, Miguel Saps8, Mark A. Beningha6, Carlo Di Lorenzo7, Samuel Nurko5, Jeffrey Hyams4, Paul Hyman3,9, 1Pediatric, Baylor College of Medicine, San Antonio, TX; 2Pediatric, Children's Hospital of San Antonio, San Antonio, TX; 3Pediatric, LSU Health Sciences Center, New Orleans, LA; 4Pediatric, Connecticut Children's, Hartford, CT; 5Pediatric, Boston Children's Hospital, Boston, MA; 6Pediatric, Emma Children's Hospital, Amsterdam, Netherlands; 7Pediatric Gastroenterology, Hepatology and Nutrition, Nationwide Children's Hospital, Columbus, OH; 8Pediatric, Children's Hospital of Chicago, Chicago, IL; 9Pediatric Gastroenterology, Children's Hospital of New Orleans, New Orleans, LA

**Background:** Irritable bowel syndrome (IBS) is a common diagnosis in pediatric gastroenterology clinic. The purpose of this study was to prospectively gather information on treatment and outcomes of children with IBS.

**Methods:** Data was obtain from the Digestive Health Alliance Children's Research Network. At the time of enrollment IBS was confirmed with the Rome III Diagnostic Questionnaire for the Pediatric Functional GI Disorders.Treatment was determined by the attending physician.

**Results:** We enrolled 144 subjects (97 female) aged 4-17 years. We found Diarrhea-predominant IBS (d-IBS) in 60, constipation-predominant IBS (c-IBS) in 43, alternating IBS (a-IBS) in 31, and no subtype in 10. Of the 144 IBS subjects, 71 (49%) subjects also met criteria for functional dyspepsia, and 39 (27%) for abdominal migraine. Other co-morbid disorders included aerophagia in 19, cyclic vomiting syndrome in 9, rumination syndrome in 5 and non-retentive fecal incontinence in 1. At the first visit 64% of subjects had missed school within the past month because of symptoms. Therapies prescribed included drugs 90% (laxatives in 42%, gastric acid suppressants in 27%), cognitive behavioral therapy 18%, and 9% chose no medical or psychological intervention (Table 1). Laxative was used in 25% of subjects who met criteria for d-IBS (Table 2). Follow-up visits varied from one to 9 visits in the first year following diagnosis. Five subjects (3%) withdrew because their diagnosis changed: 2 Crohn's disease, 2 celiac disease and 1 neutropenia. Forty-four subjects were lost to follow-up. One year after the first visit, we interviewed 95 subjects (69%). Twenty-one subjects (22%) were asymptomatic, 37 (39%) were improved, 26 (27%) were unchanged, and 6 (7%) were worse. Age, sex (regardless of the onset of puberty), IBS subtype, BMI, and co-morbid functional disorders did not predict outcome. Treatment changed over the year of follow-up.

**Conclusion:** Children presenting with IBS symptoms frequently have other FGIDs. There is little consensus on therapy. The common use of acid inhibitors may reflect attempts to treat co-morbid dyspepsia or IBS with a safe placebo. A majority of children presenting with IBS miss school because of symptoms.
List of treatments at the baseline, and 1 year.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>First Visit Number (%)</th>
<th>One year visit Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laxative</td>
<td>60 (42.0)</td>
<td>19 (20.9)</td>
</tr>
<tr>
<td>Acid suppressant</td>
<td>38 (26.6)</td>
<td>14 (15.4)</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>32 (22.4)</td>
<td>9 (9.9)</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>27 (18.9)</td>
<td>17 (18.7)</td>
</tr>
<tr>
<td>Cognitive therapy</td>
<td>26 (18.2)</td>
<td>8 (8.8)</td>
</tr>
<tr>
<td>Fiber</td>
<td>13 (9.1)</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>Dietary supplements</td>
<td>10 (7.0)</td>
<td>7 (7.7)</td>
</tr>
<tr>
<td>CAM</td>
<td>8 (5.6)</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td>Appetite Stimulants</td>
<td>3 (2.1)</td>
<td>3 (3.3)</td>
</tr>
<tr>
<td>Prokinetics</td>
<td>1 (0.7)</td>
<td>2 (2.2)</td>
</tr>
<tr>
<td>No treatment</td>
<td>13 (9.1)</td>
<td>33 (36.3)</td>
</tr>
</tbody>
</table>

Common treatment at the baseline visit by subtypes.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>a-IBS Number (%)</th>
<th>c-IBS Number (%)</th>
<th>d-IBS Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laxative</td>
<td>13 (41)</td>
<td>30(70)</td>
<td>15(25)</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>7 (23)</td>
<td>4(9)</td>
<td>13(22)</td>
</tr>
<tr>
<td>Cognitive therapy</td>
<td>8 (26)</td>
<td>4(9)</td>
<td>12(20)</td>
</tr>
<tr>
<td>Acid suppressants</td>
<td>8 (26)</td>
<td>13(30)</td>
<td>13(22)</td>
</tr>
<tr>
<td>Fiber</td>
<td>1(3)</td>
<td>3(7)</td>
<td>9(15)</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>6(19)</td>
<td>7(16)</td>
<td>18(30)</td>
</tr>
</tbody>
</table>

418 VALIDATION OF THE ROME III CRITERIA FOR FUNCTIONAL GASTROINTESTINAL DISORDERS ASSOCIATED WITH PAIN IN CHILDREN. Jennifer V. Schurman1,2, Bryan T. Karazsia3, Craig A. Friesen4, 1Division of Developmental & Behavioral Sciences, Children's Mercy, Kansas City, MO; 2Division of Gastroenterology, Hepatology, & Nutrition, Children's Mercy, Kansas City, MO; 3Department of Psychology, The College of Wooster, Wooster, OH

Objectives: In 1999, Rome II criteria for functional gastrointestinal disorders (FGIDs) were established. For disorders related to pain, the pediatric working group essentially adopted the adult criteria and established four FGIDs related to pain: irritable bowel syndrome (IBS), functional dyspepsia (FD), functional abdominal pain syndrome and abdominal migraine. For the FD diagnosis, two subtypes were created and named ulcer-like dyspepsia and motility-like dyspepsia. In 2006, the revised Rome III criteria for adults eliminated the original subtypes in favor of two new subtypes: post-prandial distress syndrome (post-prandial fullness and/or early satiety) and epigastric pain syndrome (intermittent pain and/or burning localized only to the epigastrium). The pediatric committee also eliminated original FD subtypes, but did not adopt the new adult subtypes due to a lack of data. To date, no statistical validation has occurred to determine whether current Rome III diagnoses adequately represent naturally occurring symptom clusters in children. The purpose of this study was to offer the first empirical evaluation of these diagnoses using a pediatric, clinical sample. Methods: Clinical data were collected from the electronic medical record of 255 consecutive patients ages 8-17 years (inclusive) seen for initial evaluation of chronic functional abdominal pain within a subspecialty GI clinic. Data included a large number of gastrointestinal symptoms, as well as frequently reported non-GI symptoms (e.g., headache, dizziness, joint pain). Factor analysis was employed to examine whether symptoms occur in a pattern consistent with Rome III pediatric and/or adult criteria for FD and IBS, the two most prevalent FGIDs associated with pain. Preliminary Results: Confirmatory factor analyses indicated that both the pediatric and adult (including the two FD subtypes) theoretical models based on Rome III diagnostic criteria replicate well in a pediatric patient sample. Extending previous research, non-GI-specific symptoms correlated significantly and strongly (according to Cohen's conventions) with proprandial and epigastric symptom clusters, but not IBS symptoms. Conclusions: GI symptoms in children presenting for initial evaluation of chronic functional abdominal pain occur in a pattern consistent with current Rome III criteria. Given that
the adult model, with FD subtypes, fits equally well in this pediatric sample, further investigation is warranted to determine if this subtyping is clinically meaningful and may predict differential response to treatment.

419 PEDIATRIC AERODIGESTIVE PROGRAMS, WHAT DO ALL THE TESTS TELL US? Sarah Kinder2, Jeremy Prager2, Jason Soden2, Emily Deboer3, Robin Deterding4, Ben Corbett4, Jacklyn Deck5, Jennifer Maybee5, Megan Koons6, Jessica Youngberg6, Sparrow Helland6, Amanda Ruiz7, Emily Jensen7, Bethany Thomas7, Maria Rojas8, John Fortunato9, Joel Friedlander2,1, Pediatric Otolaryngology, University of Colorado School of Medicine, Aurora, CO; 2Digestive Health Institute, Children's Hospital of Colorado, Aurora, CO; 3Aerodigestive Program, Children's Hospital Colorado, Aurora, CO; 4Breathing Institute, Children's Hospital of Colorado, Aurora, CO

Background and Aims: Multi-disciplinary pediatric aerodigestive programs are proliferating as an essential resource in the diagnosis and management of medically complex children with combined gastrointestinal and airway disorders. Such care necessitates the services of a gastroenterologist, pulmonologist, otolaryngologist, with associated feeding and nutrition support services. Historically these services were provided in sequence on as needed approach rather than simultaneously. There is a paucity of research on the aerodigestive program's utilization of earlier broad procedural testing as compared to standard sequential testing. The objective of this study was to evaluate the procedural results and the impact routine gastrointestinal diagnostic testing used in the aerodigestive clinic has on the patient's clinical management.

Methods: A Retrospective Chart Review of 331 patients in the aerodigestive program at Children's Hospital of Colorado from 2010-2013 was performed. The number of esophagogastroduodenoscopies (EGD), Upper Gastrointestinal Fluoroscopy Studies (UGI) and Ph Impedance probes (PhI) done within 30 days of the clinic evaluation were evaluated with result data tabulated and compared to clinical management change pre and post diagnosis as a result of the studies.

Results: A total of 302 of EGD, 188 PhI, and 53 UGI were performed within 30 days of the aerodigestive clinic visit. 193/302 (64%) of EGDs were normal. 145/188 (77%) of PhI were normal. 46/53 (87%) UGI were anatomically normal. 159/188 patients who had both an EGD and PhI were labeled as previously having gastroesophageal reflux disease (GERD) prior to the studies. 296/302 patients who underwent an EGD were labeled as having GERD. 105/188 (55.9 %) who underwent both PhI and EGD were on a form of acid blockade during studies. 196/302 (64.9%) patients who underwent an EGD were taking an acid blocking medication. Of the patients who underwent PhI and EGD, 76.6% (144/188) of all subjects utilizing both PhI and EGD underwent an acid suppression dose change. 14 new diagnoses of Eosinophilic Esophagitis were made.

Discussion: Procedural testing on children with complex airway disorders by a gastroenterologist in an aerodigestive clinic has positive findings similar to the general population. Several medication dose adjustments were made suggesting there is utility to performing such testing. Although significant cost savings and decreased risk of anesthesia can be found by combining anesthesia events, an algorithm could be developed to improve positive yield. Further cost/risk/benefit analysis would be needed to evaluate whether the possible prolonged, delayed, or misdiagnosis of GERD, Esophagitis, or EoE justified earlier or changed diagnosis of GERD.


420 EFFECTIVENESS OF ACUPUNCTURE IN PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN PEDIATRIC PATIENTS UNDERGOING EGD WITH WIRELESS PH PROBE PLACEMENT.

Malik Nouri1, Chris Heine1, Brian Schmutzler2, Chansamone Saysana2, Joseph Croffie3, Angie Plummer2, 1Pediatrics, Indiana University School of Medicine, Riley Children's Hospital, Indianapolis, IN; 2Anesthesia, Indiana University School of Medicine, Riley Children's Hospital, Indianapolis, IN

BACKGROUND: Pediatric patients undergoing EGD under general anesthesia for wireless pH probe placement are at high risk for post operative nausea and vomiting (PONV) and retching that could cause probe dislodgment. This risk is enhanced by the need to avoid prophylactic use of antiemetics for fear of altering pH data. It has been reported that acupuncture may be a safe and effective way to treat nausea and vomiting during pregnancy or in patients suffering from motion sickness or undergoing chemotherapy. The objective of this study was to determine if acupuncture would prevent PONV in children undergoing EGD for wireless pH probe placement.

METHODS: 23 patients with symptoms suggestive of GERD undergoing EGD and pH probe placement were randomized to two groups, the acupuncture treatment group and control group (no acupuncture).

Both groups received a standardized general anesthetic consisting of premedication with 0.5 mg/kg PO Midazolam, mask induction with Sevoflurane, Lidocaine 2mg/kg IV for ETT placement, maintenance with oxygen in Sevoflurane, and IV fluids with LR as a 10cc/kg bolus followed by a maintenance rate of 4-2-1 cc/kg/hr. The trachea was extubated deep after probe placement.

The treatment group received electro-acupuncture at PC6, ST36, LI4, CV12 for twenty minutes at 50 Hz. The needles were placed by a trained physician acupuncturist. Both treatment and control patients had band-aids placed at the S183
acupoint sites to blind the recovery room nurses who recorded incidences of nausea and vomiting (FLACC or VAS) at 15, 45, and 90 minutes and patient satisfaction (scale of 0-2) at 90 minutes. The Reflux Index (RI) and the Johnson and Demeeester Score (JDS) were calculated from the pH probe data. Wilcoxon rank sum test was used to compare age, incidence of nausea and/or vomiting and patient satisfaction as well as RI and JDS between the two groups. Chi-square test was used to determine differences between the sexes.

RESULTS: Two patients were excluded from analysis due to protocol violation. There was no difference between the two groups with respect to scores for nausea and/or vomiting and overall satisfaction at 90 minutes (Table 1). There were, however, statistically significant differences in both RI and JDS between the two groups in favor of the treatment group (Table 2).

CONCLUSION: Acupuncture did not prevent immediate PONV. Acupuncture, however, may have prevented or treated GERD during the period of study.

### Results of Post-OP Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Treatment (N=12)</th>
<th>Control N=9</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male N (%)</td>
<td>5(42)</td>
<td>7(78)</td>
<td>0.10</td>
</tr>
<tr>
<td>Age, Mean(SE)</td>
<td>11(1.24)</td>
<td>9.6(1.51)</td>
<td>0.50</td>
</tr>
<tr>
<td>Nausea/Vomiting 15min,N (%)</td>
<td>2(17)</td>
<td>1(11%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Nausea/Vomiting 45min,N (%)</td>
<td>4(33)</td>
<td>1(11)</td>
<td>0.24</td>
</tr>
<tr>
<td>Nausea/Vomiting 90min,N (%)</td>
<td>4(33)</td>
<td>1(11)</td>
<td>0.24</td>
</tr>
<tr>
<td>Patient Satisfaction at 90min, Mean (SE)</td>
<td>1.75(0.13)</td>
<td>1.67(0.17)</td>
<td>0.72</td>
</tr>
</tbody>
</table>

### Results of pH probe

<table>
<thead>
<tr>
<th>pH Probe Results</th>
<th>Treatment</th>
<th>Control</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Av. RI</td>
<td>2.15</td>
<td>5.56</td>
<td>0.027</td>
</tr>
<tr>
<td>Av. JDS</td>
<td>8.75</td>
<td>28.36</td>
<td>0.0098</td>
</tr>
<tr>
<td>Abnormal RI or JDS(%)</td>
<td>0(0)</td>
<td>5(56)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

### 421 Risk of Small Intestinal Bacterial Overgrowth in Children Taking Proton Pump Inhibitors

**Background:** It has been suggested that prolonged use of proton pump inhibitors is a risk factor for small intestinal bacterial overgrowth due to alteration of gastric acid barrier and thus leading to a change in intestinal bacterial flora. Several studies measured the risk of SIBO in adults taking proton pump inhibitors and obtained mixed results; however, this risk has not been measured in children. **Aim:** The aim of this study is to evaluate the risk of SIBO in children taking proton pump inhibitors versus those without through breath hydrogen testing. **Methods:** Evaluation of SIBO was obtained by glucose breath hydrogen test. Patients younger than 18 years of age taking a proton pump inhibitor longer than six months were compared to healthy control subjects. Subjects were excluded from the study if diagnosed with other conditions that could promote intestinal bacterial overgrowth; e.g., motility disorder or abdominal surgery. Subjects were also excluded if they received antibiotics or probiotics within one month of their scheduled breath hydrogen test. After a night of fasting, 50gm of glucose was administered to all subjects, and breath samples were obtained every 15 minutes for two hours. A rise in breath hydrogen or methane above 12ppm was considered diagnostic of SIBO. **Results:** A total of 69 subjects were tested, 38 (55%) were males and 32 (46%) were females. Age ranged from 3 to 17 years with an average of 10.5 ± 3.4 years. Out of the 69 subjects, 49 were on long term treatment of a proton pump inhibitor. Breath hydrogen testing was abnormal in 10% (5/49) of patients taking a proton pump inhibitor versus 5% (1/20) in the control group, p=0.49. **Conclusion:** To our knowledge, this is the first study measuring the risk of SIBO in chronic proton pump inhibitors in children. From our study, chronic proton pump inhibitor users were not found to have a statistically significant associated risk of SIBO when compared to control subjects. This is an important finding, as proton pump inhibitors are readily prescribed for children.

### 423 Antroduodenal Manometry in Children: Correlation with Gastrointestinal Symptoms and Utility in Predicting Treatment Outcome

**Introduction:** The antroduodenal manometry (ADM) is often performed in children with upper gastrointestinal
Conclusions: Treatment response to therapy (present in 59% of responders compared to 32% in those who failed to respond, p=0.009). We found an association between the presence of a normal small bowel MMC (spontaneous or octreotide-induced) and vomiting as the main symptom compared to other symptoms (61.5% vs. 81%, p=0.008). In regards to treatment outcome, we observed a lower proportion of normal octreotide response in those with vomiting phenotype relationships and the need to consider genetic sucrase deficiency as a potential cause for nonspecific chronic idiopathic symptoms. One of the 4 common CSID variants as a potential pathophysiology for chronic, idiopathic nonspecific GI symptoms. 1. Each subject had gone through a progression of various GI diagnoses before consideration was given to genetic SI inheritance. The 13C-S/G BT revealed that the CSID case had a 6.4% coefficient of glucose oxidation for sucrose (CGO - 73.5% vs 85%, p=0.041) and octreotide-induced phase III of the MMC (62.7% vs. 89%, p=0.001) and higher frequency of antral post-prandial hypomotility (75.8% vs. 64%, p=0.049) and small bowel post-prandial hypomotility (29.2% vs. 25.6%, p=0.005). We also observed a lower proportion of normal octreotide response in those with vomiting as the main symptom compared to other symptoms (61.5% vs. 81%, p=0.008). In regards to treatment outcome, we found an association between the presence of a normal small bowel MMC (spontaneous or octreotide-induced) and response to therapy (present in 59% of responders compared to 32% in those who failed to respond, p=0.009).

Results: A total of 257 ADM studies performed in same number of patients between 2006 and 2013 were included; outcome information was available in 124 patients. The median age of patients was 6.5 years (range 0.2 - 24 years) and 133 (51.8%) were female. The presenting symptom was vomiting in 128 (49.8%), abdominal pain in 60 (23.3%), abdominal distention in 39 (15.2%) and nausea in 30 (11.7%). In regards to groups of symptoms, we observed that those with obstructive symptoms compared to those with functional symptoms had a lower frequency of spontaneous (73.5% vs 85%, p=0.041) and octreotide-induced phase III of the MMC (62.7% vs. 89%, p=0.001) and higher frequency of antral post-prandial hypomotility (75.8% vs. 64%, p=0.049) and small bowel post-prandial hypomotility (29.2% vs. 25.6%, p=0.005). We also observed a lower proportion of normal octreotide response in those with vomiting as the main symptom compared to other symptoms (61.5% vs. 81%, p=0.008). In regards to treatment outcome, we found an association between the presence of a normal small bowel MMC (spontaneous or octreotide-induced) and response to therapy (present in 59% of responders compared to 32% in those who failed to respond, p=0.009).

Conclusions: ADM is a useful study in children with UGI symptoms refractory to medical therapy. Obstructive symptoms are associated with abnormal ADM findings and the presence of normal MMC correlates with successful response to therapy.

422 SUCRASE-ISOMALTASE GENETIC VARIANT CARRIERS CAN BE SYMPTOMATIC. Aileen De Jonge2, Kristofer S. Norris1, Heather Elser1, Antone Opekun3, 1Clinical Operations, QOL Medical, LLC, Raleigh, NC; 2CSID Communities, Patient Liaison Contact, Hudsonville, MI; 3Medicine and Pediatrics, Baylor College of Medicine, Houston, TX

BACKGROUND: Congenital Sucrase Isomaltase Deficiency (CSID) is an autosomal-recessive condition causing oligosaccharide maldigestion. Pathogenic variants of the sucrase-isomaltase (SI) gene prevent synthesis or apical transport of SI (a heterodimer pro-enzyme) that causes dysfunctional enzyme activity resulting in sucrose and starch maldigestion. Maldigested substrates can lead to symptoms that include diarrhea and abdominal pain which resemble an irritable bowel-like syndrome. Heterozygous "carriers" with common SI-genetic variants have been found to most commonly resemble typical IBS. Heterozygous carriers are estimated to occur in 2% to 9% of Americans of European decent and suggests that SI insufficiency may be under-recognized. OBJECTIVE: The purpose of this familial case study was to illustrate the relationship between nonspecific GI IBS-like symptoms and haploinsufficiency for the Chr. 3 q25-26.2 SI-gene product. Such illustration provides further understanding and appreciation of familial phenotype-to-phenotype relationships and the need to consider genetic sucrase deficiency as a potential cause for nonspecific chronic idiopathic symptoms. METHODS: A child of northern European descent with the compound heterozygous CSID condition and subsequent family members were clinically assessed for SI-genetic variants by SI-exon sequencing, endoscopic biopsy assay for sucrase activity (range 54.4+/25.4; ABNML<25.0 uM/min), and the 13C-Sucrose/Glucose Breath Test (13C S/G BT). All subjects were consented. RESULTS: The mother, father, grandmother, and siblings of the CSID case reported lifelong IBS-like symptoms including postprandial diarrhea, abdominal pain, and bloating (Table 1). Each subject had gone through a progression of various GI diagnoses before consideration was given to genetic SI variants as a potential pathophysiology for chronic, idiopathic nonspecific GI symptoms. One of the 4 common CSID mutations, c.5234T>G p.Phe1745Cys (sucrose domain), was found in each of the four family members. The CSID-affected case was found to have an additional mutation in the isomaltase domain, C.2222T>C p.Leu741Pro, of paternal inheritance. The 13C-S/G BT revealed that the CSID case had a 6.4% coefficient of glucose oxidation for sucrose (CGO-S, Normal >87.5%), and each of the three carriers had diminished CGO-S distribution between 71%-79%. DISCUSSION: Nonspecific GI symptoms including chronic diarrhea, abdominal pain, and/or bloating are common phenotypic presentations of CSID. Carriers of the SI-genetic variants exhibited symptoms similar to IBS, and low functional sucrase activity by the new 13C S/G BT. Therefore, a greater consideration for the testing of genetic sucrase deficiency and/or functional sucrase activity during the diagnostic workup for IBS is reasonable. It is unclear what percentage of patients diagnosed with IBS also have SI insufficiency.
## Familial Inheritance of SI Variants

<table>
<thead>
<tr>
<th>Family Member</th>
<th>GI Symptoms</th>
<th>Progression of Diagnoses</th>
<th>Disaccharidases (µM/min/gram)</th>
<th>Genetics (Method and Variant(s))</th>
<th>13C-S/GBT (CGO-s)</th>
</tr>
</thead>
</table>
| **Index Case (F) (CSID)** | Chronic diarrhea, gas, bloating, abdominal pain, growth retardation, rash, reflux, hyperhidrosis, polyuria, hypotonicity. | 1. Viral & Bacterial Gastroenteritis  
2. Food Allergies & hypersensitivities  
3. Celiac  
4. Cystic fibrosis  
5. IBS  
6. Lactose intolerance  
7. Pancreatic insufficiency  
8. CSID | Sucrase 0.0, Maltase 33.4, Palatinase 0.0, Lactase 41.2 | Compound Heterozygous p.Phe1745Cys (sucrase domain), p.Leu741Pro (isomaltase domain) | 6.4%, Abnormal |
| **Mother (Carrier)** | Lifelong intestinal symptoms of abdominal pain, belching, gas and chronic diarrhea, abdominal pain, belching, gas and chronic and intermittent diarrhea. | 1. IBS  
2. Non-specific Colitis  
3. Spastic bowel  
4. Celiac disease  
5. Intermittent hypoglycemia  
6. Duodenitis  
7. Heterozygous | Sucrase 25.5, Maltase 95, Palatinase 5.9, Lactase 17.7 | p.Phe1745Cys (sucrase domain) | 71.6%, Abnormal |
| **Father** | Toddler's diarrhea as child, intermittent gas and diarrhea into adulthood, persists | 1. Hypercholesterolemia  
2. Prediabetic | Not tested | Carrier p.Leu741Pro (isomaltase domain) | 90.0%, Normal |
| **Maternal Grandmother (Carrier)** | Lifelong IBS (mixed) with constipation and occasional diarrhea that progressed with age. Symptoms improved significantly with low carbohydrate diet. | 1. IBS  
2. GERD  
3. Benign Colon Polyps  
4. Sm Intestinal Bacterial Overgrowth 5. Suspect Pancreatic Insufficiency  
6. Breast Cancer  
7. Heterozygous | Not tested | p.Phe1745Cys (sucrase domain) | 79.4%, Abnormal |
Sibling 1 (F)(Carrier)
Chronic diarrhea, bloating, severe reflux and dysmotility, hypotonicity, growth retardation, hyperhidrosis  1. Fructose Malabsorption, 2. GERD, 3. Rapid gastric emptying, 4. Heterozygous  
Carrier  p.Phe1745Cys (sucrase domain)  71.7 %, Abnormal

Sibling 2 (M)
Alternating constipation and diarrhea, abdominal pain, bloating  1. Toddler's Diarrhea  
Not tested  
Carrier  P.Leu741Pro (isomaltase domain)  73.7 %, Abnormal

424 RELATIONSHIP BETWEEN COMPASS 31 AND NAUSEA PROFILE AND GASTROINTESTINAL SYMPTOMS DURING HEAD-UP TILT TABLE TESTING IN PEDIATRIC PATIENTS. Mary K. Boruta1, Richard J. Boruta2, Sally E. Tarbell2, Kathryn K. Collins3, John E. Fortunato1, 1Pediatric Gastroenterology, Hepatology and Nutrition, University of Colorado School of Medicine, Aurora, CO; 2Pediatric Cardiology, University of Colorado School of Medicine, Aurora, CO; 3Pediatric Psychology, University of Colorado School of Medicine, Aurora, CO

Background: Chronic nausea and dizziness are common in children. Previous work has demonstrated an association between functional gastrointestinal symptoms and autonomic disorders.

Objective: We aimed to assess the relationship between symptoms measured by the Composite Autonomic Symptom Score (COMPASS-31) and Nausea Profile (NP) before head-up tilt testing (HUT) with symptoms and heart rate changes during HUT.

Methods: Pediatric patients referred to gastroenterology for nausea and abdominal pain were retrospectively reviewed if they completed the COMPASS-31, NP, and 70-degree HUT for 45 minutes. Vital signs were recorded every minute. Symptoms of nausea, dizziness, abdominal pain, and headache were assessed every 5 minutes using a 10-point Likert scale. Total and subscale scores from questionnaires were compared to cardiovascular changes and symptom scores during HUT.

Results: Of the 34 subjects (mean age 14.7 [10-19] years), 65% were female. COMPASS-31 total score correlated with abdominal pain (r=0.410, p=0.03), headache (r=0.514, p=0.005), and dizziness (r=0.422, p=0.02) during HUT. COMPASS-31 orthostatic intolerance subsection also correlated with nausea (r=0.402, p=0.028). NP total score correlated significantly with abdominal pain (r=0.416, p=0.028) and dizziness (r=0.440, p=0.015) during HUT. COMPASS-31 and NP total scores correlated with each other (r=0.387, p=0.024). There was no association between heart rate changes during HUT and either questionnaire scores or HUT symptoms. The highest heart rate was observed in the last 15 minutes of HUT in the majority of subjects (mean 31 minutes). HUT was terminated in 3 subjects due to syncope.

Conclusion: COMPASS-31 and NP scores accurately predict GI and orthostatic symptoms during HUT in children. The absence of an association between symptoms and heart rate raises the question as to the timing of biochemical factors leading to GI symptoms relative to cardiovascular changes. This underscores the need to reevaluate the frequency and duration of recording cardiovascular measures and GI symptoms during HUT.

425 WHEN IS PAIN IMPROVEMENT CONSIDERED CLINICALLY MEANINGFUL? - FIRST STUDY ON MINIMUM CLINICALLY IMPORTANT DIFFERENCE (MCID) IN CHILDREN WITH ABDOMINAL PAIN (AP)-PREDOMINANT FUNCTIONAL GASTROINTESTINAL DISORDERS (AP-FGIDs). John Lavigne, Miguel Saps, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

Background- Clinical trials in irritable bowel syndrome (IBS) rely on patient reported outcomes (PROs) as primary endpoints. The Food and Drug Administration (FDA) and European Medical Agency (EMA) established guidelines for the clinical evaluation of drugs for adults with IBS. These agencies established 30% improvement of pain as primary efficacy endpoint in clinical trials for IBS. Despite the importance of establishing efficacy endpoints in children, both agencies have not established PROs for children. The MCID is defined as the smallest improvement considered meaningful by the child. There have been no studies on MCIDs in children's AP rating in children with AP-FGIDs; because MCIDs in adults and children may differ, this is an important step in establishing meaningful pediatric PROs. We compared three alternative approaches to determining the MCID in children with AP-FGIDs. Methods- participants were 80 children enrolled in a published, multi-site drug study with AP-FGIDs. The 3 approaches to calculating the MCID from a VAS-Likert scale (0-100 mm) were: (a) anchor-based approach based on responses to a global satisfactory relief question at the end of trial (e.g., "feeling better"); (b) FDA and EMA-recommended percentage-based approach (cutoffs for improvement of 30% improvement in AP intensity); (c) a distribution-based approach, in which the MCID

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was based on the reliable change index (RCI), i.e., the smallest change score that indicates the 95% confidence interval for change scores based on the test-retest reliability of VAS measure. Calculation of the amount of change was based on the changes in VAS score from baseline to week 4 (endpoint) of the clinical trial. Results- For the anchor-based approach, 48 (57.1%) children reported overall improvement ("better") of pain. MCID for those reporting being "better" from baseline to week 4 was -20.00 mm in the VAS-Likert scale. 39 (48.8%) children had ≥30% improvement in AP. MCID for >30% pain improvement was -27.76 mm in the VAS-Likert scale. For the distribution-based approach, the mean test-retest reliability was 0.81. For there to be a reliable change at the 95% CI, the decline in MCID had to exceed -21.23 to be considered reliable. The anchor-based MCID for global satisfactory relief is lower than the reliability of the score based on the RCI; therefore, scores considered improved on either the anchor-based ("better") or FDA's and EMA's 30% change criteria will frequently not reflect reliable changes. To increase the likelihood that the child's rating of VAS change in a clinical trial will be reliable, and if the PRO wants to be exclusively based on AP changes, the RCI is preferable to either the anchor-based ("better") or percent change criterion. Conclusions- We have defined the MCID in children. A reliable MCID in children varies between 20 mm and 27.76 mm depending on the methods used for its calculation.

426 COMPARISON OF PRIMARY EFFICACY ENDPOINTS RECOMMENDED BY REGULATORY AGENCIES IN CHILDREN WITH FUNCTIONAL GASTROINTESTINAL DISORDERS. Saeed Mohammad, Cenk K. Pusaticioglu, Miguel Saps, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

Objectives- Irritable bowel syndrome (IBS) is a multi-symptom construct with abdominal pain (AP) acting as the driving symptom of patient reported severity. There is controversy regarding which are the optimal primary end points to establish efficacy of IBS treatment in adults and children. The FDA recommended ≥30% improvement in AP from baseline as primary efficacy endpoint in adults. There is no pediatric data. It is unclear whether studies in children should use this cutoff or the 50% improvement suggested by the European Medical Agency (EMA) for children. We investigated the relation between ≥30% and ≥50% improvement in AP intensity with children's report of satisfactory relief and disability. Methods- Secondary analysis of data from 72 children who completed a randomized clinical trial for abdominal pain-associated functional gastrointestinal disorders. Children completed: 1- daily assessment of AP intensity, 2-Functional Disability Inventory (FDI), 3-questions regarding pain's interference with activities and 4- two global assessment questions (satisfactory relief and satisfaction with treatment). Results- Changes in intensity of AP: ≥30% and ≥50% changes in AP intensity correlated with satisfactory relief and satisfaction with treatment (p<0.01). Sensitivity to detect satisfactory relief and satisfaction with treatment: ≥30% AP improvement=65%; ≥50% AP improvement =40%. Specificity: ≥30% AP improvement =71%; ≥50% AP improvement=94%. ≥30% AP improvement was not significantly associated with interference with daily activities, while ≥50% improvement was (p=0.017). Neither of the AP pain intensity measures was significantly associated with 30% change in FDI. Global outcomes: Satisfaction with treatment was inversely related to the child's report of interference with activities (p<0.01) and symptom relief was positively associated with ≥30% improvement in FDI scores (p<0.009). Conclusions- Changes in AP intensity are significantly associated with global relief. 30% improvement in AP is more sensitive but less specific than 50% improvement in AP in detecting global relief. Sensitivity of >50% is low. The use of >50% as primary efficacy endpoint in clinical trials would result in a large proportion of children that considered themselves relieved having negative results in clinical trials. Alternative primary efficacy endpoints should be considered.

427 CONCORDANT PARENT-CHILD REPORTS OF ANXIETY PREDICT IMPAIRMENT IN YOUTH WITH FUNCTIONAL ABDOMINAL PAIN. Natoshia R. Cunningham, James Squires, Michael Farrell, Mitchell Cohen, Adam Mezoff, Anne Lynch-Jordan, Susmita Kashikar-Zuck, Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Functional abdominal pain (FAP) is a common pediatric disorder associated with persistent pain and significant impairment in functioning. Anxiety is common in youth with FAP, and is associated with increased disability. Current literature examining anxiety characteristics in youth with FAP has found the most common anxiety disorders in youth with FAP are: generalized anxiety, separation anxiety, and social anxiety; however, these findings are limited by small sample sizes , are often based on child report alone, and use lengthy diagnostic tools that are impractical in medical settings. It is unknown 1) if a brief (i.e., 5 minute) screening tool is feasible to examine anxiety characteristics in youth with FAP, 2) whether parent and child reports of anxiety are congruent, and 3) whether parent and child agreement of child anxiety symptoms corresponds to increased impairment. The purpose of this investigation was to examine the rates and subtypes of anxiety in a larger sample (N = 100) using parent and child reports. Additionally, the congruence of parent and child anxiety was explored, and agreement/disagreement was examined in relation to pain and disability. Participants were patients with FAP between the ages of 8 and 18 who presented to a pediatric gastroenterology clinic and their primary caregiver; they completed measures of pain intensity, pain-related disability, and anxiety (Screen for
Anxiety and Related Disorders; SCARED). Clinically significant anxiety symptoms were highly prevalent and more commonly reported by youth (54%) than their parents (30%). Panic/somatic symptoms (44%), generalized anxiety (43%), and separation anxiety (42%) were the most commonly endorsed anxiety characteristics based on patient-reports whereas generalized anxiety (34%), separation anxiety (26%), and school avoidance (22%) were most commonly reported by parents. The majority (65%) of parents and children agreed on (26%) presence or (39%) absence of child anxiety symptoms. Among the discordant reports, 27% of patients reported high anxiety whereas their caregiver did not and only 4% of patients reported low anxiety with parents reporting high child anxiety. Multivariate analysis of variance revealed that parent-child agreement of elevated child anxiety was significantly related to increased pain and disability via patient reports (F (2, 89) = 2.05, p <0.05). These findings suggest a brief anxiety screening instrument can be easily used and interpreted by GI physicians/nurses to identify patients with anxiety. The results of this screening instrument may open the door to discussion with the family about sources of anxiety (school, peer or home issues) and appropriate referrals could be initiated.

428 OUTCOMES FOR FEEDING TUBE DEPENDENT CHILDREN WITH SEVERE ORAL AVersion IN AN INTENSIVE DAY TREATMENT PROGRAM, Parker L. Huston1,2, Nancy Bandstra1,2, Kate Zvonek1, Carly Heinz1, Lynn Fagerman1, Emily Piccione1, 1Helen DeVos Children's Hospital, Grand Rapids, MI; 2Pediatrics & Human Development and Psychiatry, Michigan State University, East Lansing, MI

INTRODUCTION: Feeding problems are common in the pediatric population with incidence rates between 25-45% (Linscheid et al., 2003). There is a wide variety of conditions which preclude or limit children's ability to develop typical feeding behaviors (e.g., prolonged intubation, GI disease). There are specific negative health outcomes associated with feeding disorders in children, including placement of feeding tubes or other invasive procedures. Although feeding tubes are beneficial for physical development, they may negatively impact the development of oral feeding behaviors by limiting hunger drive and opportunities for exposure to stimulation associated with eating (Byars et al., 2003). A significant barrier to returning tube dependent children to more typical oral eating is the presence of oral defensiveness. Children with oral defensiveness demonstrate extreme intolerance for stimuli in or around the face and mouth, as evidenced by hyper-reactive behavioral responses to oral sensory input (Arvedson & Brodsky, 2002). In many cases, oral defensiveness leads to absolute food refusal and feeding tube dependency. In order to progress in feeding tube weaning for these children, treatment typically involves an interdisciplinary team approach, with medical, oral-motor, and behavioral approaches. At this time, there is a paucity of research regarding outcomes for children with feeding difficulties and severe oral defensiveness. The current study seeks to fill this gap by providing clinical outcomes for a sample of such children treated using an intensive multidisciplinary approach.

METHODS: A group of 22 patients who have completed an admission to our intensive feeding program (IFP) were selected based on criteria for demonstrating significant oral aversion and feeding tube dependency at admission (mean age=44 months; range 24-89 months). Medical diagnoses included dysphagia (N=22), GERD (13), and GI dysmotility (4). Mean percentage of tube dependency at admission was 99% of daily calories. Average intake at baseline meals was 8 grams. During their admission to IFP, children have 3 treatment meals per day, 5 days per week, across a 6- to 8-week time frame. A behavioral protocol is used in the meals as well as oral-motor exercises designed to help with desensitization and improving oral-motor strength/coordination.

RESULTS: Preliminary analyses indicate significant improvement of these patients at time of discharge. Paired sample t-tests indicate significant improvement in all measured outcomes (see table). Further analyses and graphs will be available tracking patient progress throughout the treatment process.

CONCLUSIONS: Results demonstrate the effectiveness of the multidisciplinary IFP model for treatment of feeding disorders by increasing acceptance of oral intake, decreasing behavioral problems at mealtimes, and decreasing Gtube reliance, even in a population of patients typically identified as difficult to treat due to severe oral aversion.

Paired Samples t-test Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Discharge</th>
<th>Mean Change</th>
<th>t-value</th>
<th>df</th>
<th>sig (2-tail)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tube dependence</td>
<td>98.75%</td>
<td>34.14%</td>
<td>-64.61%</td>
<td>-9.67</td>
<td>21</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Oral calories/day</td>
<td>11.05</td>
<td>820.55</td>
<td>809.50</td>
<td>8.14</td>
<td>21</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Behavior problems</td>
<td>63.45%</td>
<td>11.14%</td>
<td>-52.32%</td>
<td>-9.89</td>
<td>21</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Bite/drink acceptance</td>
<td>40.68%</td>
<td>96.86%</td>
<td>56.18%</td>
<td>10.88</td>
<td>21</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

N=22 for all analyses
HIGH RESOLUTION MANOMETRY WITH IMPEDANCE: A NOVEL TOOL TO DIAGNOSE RUMINATION SYNDROME AND ITS SUBTYPES. Rachel L. Rosen, Leonel Rodriguez, Samuel Nurko, Center for Motility and Functional Gastrointestinal Disorders, Boston Children’s Hospital, Boston, MA

Background: Differentiating reflux from rumination is a difficult and equivocal cases often require invasive testing, including antrroduodenal manometry testing to confirm the presence of R waves. However, this test is invasive and not available at all institutions. We propose that prolonged high resolution esophageal manometry with impedance (HRM-MII) is a novel, superior test to diagnose rumination that not only identifies R waves but more importantly shows retrograde esophageal fluid movement which allows for differentiation of true rumination from other causes of increased abdominal pressure.

Methods: We performed prolonged HRM-MII in 18 patients referred for possible rumination. We performed an initial stationary manometry followed by a meal with the HRM-MII catheter in place. The HRM-MII catheter was placed such that there was a minimum of 6 pressure sensors in the stomach. The remaining sensors were distributed throughout the esophagus with both the lower esophageal sphincter (LES) and upper esophageal sphincter (UES) visualized simultaneously. Rumination was defined as the presence of R waves and evidence of associated retrograde esophageal bolus movement.

Results: We studies 18 patients (5M:11 F), with a mean age of 15 ±0.5 years. 17 patients had normal manometry by Chicago classification and 1 patient had EGJ outflow tract obstruction s/p fundoplication but had symptoms of rumination despite the fundoplication. Rumination was demonstrated in 15/18 patients. We also disproved a diagnosis in 2 patients in whom R waves were visualized but there was no bolus movement into the esophagus, and 1 patient in whom there were LES relaxations and reflux episodes without the presence of R waves. In the remaining 15 patients, we detected 59 rumination episodes with 3 subtypes of rumination: (1) episodes where LES relaxations preceded R waves (N=42, 71%), (2) episodes where there was no LES relaxation (n=12, 20%), and (3) episodes in which the LES relaxations occurred after R waves (N=5, 9%). Of the ruminations associated with LES relaxation, 64% of LES relaxations were TLESRS versus 36% which were swallow-associated. In 49% of ruminations, the bolus entered simultaneously with R waves, in 37% bolus entry preceded R waves, and in 14% bolus entry followed R waves. The UES opened in 86% of episodes, and the bolus reached the UES in 63% of episodes. Rumination episode characteristics are shown in the table.

Conclusions: HRM-MII is a novel tool to diagnose rumination syndrome that not only detects R waves but also retrograde bolus flow. We also identified three unique patterns of rumination in children defined by the presence of R waves relative to LES relaxation and retrograde flow. The most common type being LES relaxation preceding R waves. Identifying subtypes of types of rumination raises the possibility of different therapies depending on the subtype identified.

Liver

SERUM ALPHA 1-ANTITRYPSIN LEVELS DO NOT PREDICT LIVER INFLAMMATION IN CHILDREN WITH NASH. Adrian Chapa-Rodriguez, Razan H. Alkhour, Sarita Singhal, Robert D. Baker, Lixin Zhu, Susan S. Baker, Digestive Disease and Nutrition Center, Women and Children Hospital at Buffalo, Buffalo, NY

Introduction: Non-Alcoholic Fatty Liver disease (NAFLD) is characterized by steatosis of the liver. The histologic spectrum of NAFLD ranges from simple steatosis to non-alcoholic steatohepatitis (NASH), in which there is inflammation and fibrosis, in addition to steatosis. Erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP) can be elevated in children with NASH, but do not correlate with inflammatory changes on liver biopsy. Ferritin which is a marker for iron storage, also behaves as acute face reactant in presence of inflammation. Alpha 1-antitrypsin (A1AT) is a protein produced by the hepatocytes and behaves as an acute phase reactant. The role of A1AT as a marker for inflammation in liver disease has not been studied in children. We hypothesize that serum A1AT level correlates with the degree of liver injury.

Methods: Retrospective chart review of all percutaneous liver biopsies performed from 2010 to 2013; in patient between 1 month and 21 years with persistent elevation of liver enzymes and/or abnormal ultrasound finding. Demographic characteristics, liver enzymes, ESR, CRP, Ferritin and A1AT were recorded. We included patients with histologic evidence of NASH who also documentation of inflammatory markers.

Results: A total of 218 biopsies were performed; Ninety-one were from NASH patients. Only 40 charts had all documentation of all ESR, CRP, Ferritin and A1AT. ESR and CRP were mildly elevated, A1AT was within normal limit. There was no correlation between ESR, CRP and A1AT and degree of inflammation on biopsy. ESR had positive correlation with the degree of fibrosis (r=0.49; p=0.001), and ferritin correlated with steatosis (r=0.33; p=0.03)

Conclusion: Serum A1AT does not correlate with the degree of hepatic inflammation, fibrosis or steatosis in pediatric patients with NASH and cannot be used to predict histological findings on biopsy.
Correlation between inflammatory markers and histologic changes

<table>
<thead>
<tr>
<th>Variables</th>
<th>r value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade of Inflammation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR</td>
<td>0.17</td>
<td>0.28</td>
</tr>
<tr>
<td>CRP</td>
<td>0.33</td>
<td>0.16</td>
</tr>
<tr>
<td>A1AT</td>
<td>-0.02</td>
<td>0.89</td>
</tr>
<tr>
<td>Ferritin</td>
<td>0.09</td>
<td>0.58</td>
</tr>
<tr>
<td><strong>Stage of Fibrosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR</td>
<td>0.49</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP</td>
<td>0.31</td>
<td>0.18</td>
</tr>
<tr>
<td>A1AT</td>
<td>0.14</td>
<td>0.38</td>
</tr>
<tr>
<td>Ferritin</td>
<td>-0.025</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Grade of Steatosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR</td>
<td>-0.06</td>
<td>0.7</td>
</tr>
<tr>
<td>CRP</td>
<td>0.41</td>
<td>0.07</td>
</tr>
<tr>
<td>A1AT</td>
<td>-0.21</td>
<td>0.18</td>
</tr>
<tr>
<td>Ferritin</td>
<td>0.33</td>
<td>0.03</td>
</tr>
</tbody>
</table>

431* IMPROVEMENTS IN BIOCHEMICAL MARKERS OF DISEASE ACTIVITY WITH SEBELIPASE ALFA TREATMENT ARE ACCOMPANIED BY REDUCED STEATOSIS AND FIBROSIS IN PATIENTS WITH LYSOSOMAL ACID LIPASE DEFICIENCY. Anthony G. Quinn1, Chester B. Whitley2, Vassili Valayannopoulos3, Véra Malinová4, Reena Sharma5, Chris Bourdon6, Simeon B. Boyd7, Bruce Kessler8, Christoph Twelves9, Stephen Eckert1, Sandra Rojas-Caro1, Synageva BioPharma Corp., Lexington, MA; 2University of Minnesota, Minneapolis, MN; 3Hôpital Necker-Enfants Malades, Paris, France; 4First Faculty of Medicine Charles University, Praha, Czech Republic; 5Salford Royal NHS Foundation Trust, Salford, United Kingdom; 6Health Sciences North, Sudbury, ON, Canada; 7University of California-Davis, Sacramento, CA; 8Eureka Internal Medicine, Eureka, CA; 9St. James's University Hospital, Leeds, United Kingdom

In patients with Lysosomal Acid Lipase Deficiency (LAL D), pathologic accumulation of cholesteryl esters and triglycerides results in dyslipidemia, hepatomegaly, liver injury with elevated transaminases, hepatic steatosis, and fibrosis with frequent progression to cirrhosis. Data on the safety and efficacy of enzyme replacement therapy with sebelipase alfa were obtained from LAL D patients (N=8) who enrolled into an extension study where patients continued long term dosing with 1 mg/kg or 3 mg/kg every-other-week infusions.

Six patients with available data who had received two-years of treatment with sebelipase alfa demonstrated sustained improvements in serum transaminases (ALT/AST) and serum lipids (Table). At baseline in the extension study, 5/8 (63%) and 4/8 (50%) patients had ALT and AST levels greater than the upper limit of normal. In all patients ALT levels normalized after 25 weeks and in 5 of the 6 patients, AST levels normalized by 2 years.

Historical pretreatment and post-sebelipase alfa treatment liver biopsy results were obtained for 2 patients. Patient 1 had a historical pretreatment biopsy at age 17 which showed notable “microversicular and macrovesicular steatosis of hepatocytes,” “secondary macrophage lipid overloading,” and “fibrous retention associated with extensive fibrosis, with numerous fibrous bridges and incipient nodulations.” A subsequent liver biopsy conducted after 1.5 years of treatment with sebelipase alfa at age 22 showed steatosis with mild microvesicular predominance associated with foamy macrophage masses, and perportal fibrosis associated with some septa. Comparison of the biopsies indicated a substantial reduction of steatosis and fibrosis. Patient 2 had a historical liver biopsy at age 37 which showed extreme fat content with microvesicular steatosis and fibrosis. Biopsy results after ~2 years of treatment with sebelipase alfa at age 44 showed mild microvesicular steatosis with no significant fibrosis.

Related adverse events (AEs) across all patients to date have been generally mild or moderate in severity. While uncommon, infusion-associated reactions were noted, most of which were mild and gastro-intestinally related. No serious AEs related to sebelipase alfa have been observed, and other than one low titer result that was reported at a single time point in one subject, there was no evidence of anti-drug antibody formation in the subjects studied. Improvements in LAL D related dyslipidemia and reductions in markers of liver injury are maintained with long-term
treatment with sebelipase alfa. These biochemical changes are accompanied by concordant improvements in hepatic steatosis and fibrosis. An ongoing phase 3 clinical trial will provide further data on the impact of sebelipase alfa on the liver histology of children and adults with LAL D.

Mean Percent Change From Baseline in Serum Lipids and Hepatic Transaminases in 6 LAL D Patients Treated With Sebelipase Alfa for 2 Years

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase</td>
<td>-58%</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td>-28%</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol</td>
<td>-54%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-31%</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol</td>
<td>+18%</td>
</tr>
</tbody>
</table>

432. SHORT TERM OUTCOMES AND COMPLICATIONS OF ACETAMINOPHEN INDUCED PEDIATRIC ACUTE LIVER FAILURE [APAP ALF] FROM 2008 TO 2013 USING THE PEDIATRIC HEALTH INFORMATION SYSTEM [PHIS] DATABASE. Caren Pichardo1, Sakil S. Kulkarni1, Lina Castillo1, Carla Perez1, Michael Gagnon2, Consuelo Beck-Sague1, Rani Geiger1, Erick Hernandez1, 1Department of Medical Education, Miami Children's Hospital, Miami, FL; 2Department of Health Promotion and Disease Prevention, Stempel College of Public Health and Social Work, Florida International University, Miami, FL; 1Department of Pediatric Gastroenterology, Miami Children's Hospital, Miami, FL

Using the PHIS database, we attempted to study recent trends, regional variations and short-term outcomes of children admitted with APAP ALF to 16 liver transplant centers, who are also members of PHIS, from 2008 to 2013. We selected patients with the diagnosis of "Acute Liver Necrosis" or ICD 9 code "570.00" associated to diagnosis of "Poisoning by Aromatic Analgesics" or ICD 9 code "965.4" from 16 transplant centers. A total of 109 patients were obtained that met both criteria. Data was analyzed regarding the hospital identifier, admission dates, discharge dates, age, sex, pharmacy information, procedure information, disposition of the patient and up to 21 diagnoses using Epi Info version 7.

The mean (median) age at presentation was 14.03 (10.0) years (SD=5.6); 71.56 % were female. The median inpatient length of stay was 6 days. The most common complication was hepatic encephalopathy [HE] [22.02%] and spontaneous survival without a liver transplant was 94.5%, 2 patients required liver transplant [1.83%], total mortality was 2.75%. On binomial analysis the following complications were associated with increased risk of mortality: Cardiovascular compromise (odds ratio [OR] =0.02, p=0.000177), acute respiratory failure (OR=0.0957, p=0.017), acute kidney injury [AKI] (OR=0.0852 p=0.008), cerebral edema (OR 0.0365, p =0.00079) and hepatic encephalopathy (OR=0.12, p=0.0205). Only cardiovascular compromise was associated to worse prognosis when controlled for other factors in logistic regression analysis. (OR=33.34, p=0.01).

We determined the most common outcomes, complications, age group, sex and length of stay of acetaminophen induced liver failure in 16 liver transplant centers in the United States.

In this study acetaminophen induced acute liver failure had an excellent outcome. The survival outcomes of our study are similar to previous acute liver failure studies by Squires et al.

433. HEPATOCYTE-DERIVED MICROPARTICLES WITH A SPECIFIC ANTIGENIC COMPOSITION ARE RELEASED IN BLOOD DURING NASH DEVELOPMENT: IMPLICATIONS FOR BIOMARKERS DEVELOPMENT. Davide Povero, Akiko Eguchi, Casey D. Johnson, Alexander Wree, Milos Lazic, Ariel Feldstein, Department of Pediatrics, UC San Diego, La Jolla, CA

BACKGROUND & AIMS. Nonalcoholic steatohepatitis (NASH) is a serious public health problem. There is currently a lack of effective treatments and noninvasive diagnostic markers. We have recently demonstrated that hepatocyte-derived microparticles (MPs) are critical signals that contribute to angiogenesis and liver damage in NASH (Presidential Plenary AASLD 2012). Here we tested the hypothesis that circulating hepatocyte-MPs are novel targets for noninvasive monitoring of NASH. METHODS. Male C57BL/6 mice were placed on Choline Deficient L-Amino Acid (CDAQ) diet, Choline Supplemented L-Amino Acid (CSAA) or regular Chow diet for 4 and 20 weeks. These time points were chosen as they have been shown to be associated with early stage and established NASH, respectively. Circulating MPs were isolated from platelet-free plasma (PFP), detected by flow cytometry and extensively characterized by electron microscopy in liver tissue and circulation, dynamic light scattering and by LC MS/MS proteomic analysis. Liver specimens were collected and used for histological, biochemical, and molecular analysis of steatosis, inflammation, angiogenesis, fibrosis and cell death. RESULTS. A marked increased in circulating levels of MPs were detected in mice with established NASH (20wks CDAQ diet: 304,400 MPs/mL vs. 20 wks CSAA 34,300 MPs/mL vs. Chow 2,000
Patients received a median initiation dose of 1.89 mg/kg body weight (IQR 1.01-2.04) with a target of 25% pressure by reaching a significant reduction in heart rate or showing no signs of EV on endoscopy examination. We determined the dosage of propranolol which presumably decrease the portal pressure to control EV bleeding in children. Though DILI is a clinical diagnosis, in rare cases liver biopsy may be indicated if the cause of hepatitis cannot be elucidated. Management of DILI includes early recognition of drug toxicity and withdrawal of the offending agent. When stopping any drug suspected of causing DILI, patients should be followed with serial laboratory monitoring until laboratory parameters normalize. Consideration should be taken for hepatology consultation if concern for acute liver failure arises. Though DILI is a clinical diagnosis, in rare cases liver biopsy may be indicated if the cause of hepatitis cannot be elucidated.

Conclusion: Clinicians should be aware of this rare but potentially serious adverse reaction. With an estimated 24.4 million fluoxetine prescriptions in 2011, this adverse effect should be considered in patients with similar symptoms who were recently started on fluoxetine.

435 EFFECTIVE PROPRANOLOL DOSE FOR PREVENTION OF HEMORRHAGE IN PEDIATRIC ESOPHAGEAL VARICES PATIENTS. 

Fatima S. Alatas, Cut N. Hafifah, Hanifah Oswari, Department of Child Health, Universitas Indonesia, Jakarta, Indonesia

Background: Hemorrhage is often lethal in esophageal varices (EV) patients. Beta-blockers are the mainstay of treatment for preventing variceal bleeding. However, there are only few reports regarding effective dose and duration of beta-blockers to control EV bleeding in children.

Objective: To evaluate the use of propranolol to prevent variceal bleeding in pediatric EV patients.

Methods: We retrospectively studied data from 22 patients with hematemesis melena who underwent endoscopy examination in the last 7 years. We determined the dosage of propranolol which presumably decrease the portal pressure by reaching a significant reduction in heart rate or showing no signs of EV on endoscopy examination.

Results: Propranolol treatment was introduced immediately after diagnosis was confirmed from endoscopy in almost all patients. Patients received a median initiation dose of 1.89 mg/kg body weight (IQR 1.01-2.04) with a target of 25%

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reduction from baseline heart rate. Five patients maintain the same dose of propranolol, while others had an adjustment in dosing. At the last visit, these patients have an adjusted dose of 1.89-3.21 mg/kg body weight. Median total time of propranolol use was 15.1 months (IQR 5.6-42.6). Two patients had no EV after 60-108 days, one patient had failure of propranolol treatment, and others had no further episode of hemorrhage. Median duration of free banding are 4 months (IQR 0.9-5.5). There are no adverse effect found in these patients.

**Conclusion:** Propranolol with a dose of 1.89-3.21 mg/kg body weight may reduce risk of hemorrhage in pediatric EV patients.

**Keywords:** esophageal varices, propranolol, variceal bleeding

**436 HISTOLOGIC SCORING AND CHARACTERISTICS OF CONGENITAL HEPATIC FIBROSIS.** Gihan Naguib, Theo Heller, David Kleiner, Meral Gunay-Aygun, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD; National Cancer Institute: Lab of Pathology, National Institutes of Health, Bethesda, MD; Pediatric Gastroenterology, University of Maryland, Baltimore, MD; NIDDK: Liver Disease Branch, National Institutes of Health, Bethesda, MD

**Introduction:** Autosomal recessive polycystic kidney disease (ARPKD), the most common ciliopathy of childhood, is characterized by congenital hepatic fibrosis (CHF) and cystic degeneration of the kidneys. We aim to describe hepatic histologic features including histologic scoring of the hepatic pathologic changes seen in CHF and correlate these features with each other.

**Methods:** A cohort of 16 patients with CHF were evaluated using a novel set of histologic features derived from the liver biopsy. Histologic parameters included scores for lobular inflammation (0-2), inflammation at the ductal plate (0 - 2), inflammation in the bile ducts (0 - 1), portal venopathy (0 - 2), bile inspissation (0 - 1), duct dilatation (0 - 2), ductular reaction (0 - 2), central vein fibrosis (0-1), and fibrosis (0 - 3).

**Results:** The ages ranged from 4-75 years with a median age of 11 years. Seven patients were male and 9 were females. Lobular inflammatory scores were in general low, only one patient had a score of 2, 8 patients had no lobular inflammation receiving a score of 0, and 7 had mild lobular inflammation (score of 1). Lymphocytic infiltration was also not pronounced with only one patient scoring a 2 and 4 patients scoring a 1, 11 patients scored 0. Acute inflammation in the ducts was rare with only one patient scoring 1, the remainder being 0. Portal venopathy was common with 14 patients scoring 2 and no patients scoring 0. Nine patients had inspissation of bile and most patients had some duct dilatation (1) and only 3 with either a score of 0 or 2. Eight patients had no ductular reaction, and 4 patients had either a 1 or a 2. Six patients had central vein fibrosis and overall fibrosis was common with only 1 patient scoring 0, 3 scoring 1, 6 scoring 2, and 5 scoring 3. Portal venopathy correlated negatively with lobular inflammation (r=-0.50, p=0.02), however correlated positively with bile inspissation (r=0.42, p=0.04) and fibrosis (r=0.56, p=0.01). The presence of fibrosis also showed a positive correlation with central vein fibrosis (r=0.8, p=0.00), lymphocytic infiltration (r=0.67, p=0.002), and bile inspissation (r=0.56, p=0.01).

**Conclusion:** Inflammatory scores were in general low in contrast to fibrosis with the majority of patients exhibiting significant fibrosis despite the relatively young median age of the cohort. Acute ductular inflammation was rare. The majority of the cohort had portal venopathy, which correlated positively with fibrosis and bile inspissation, and negatively with lobular inflammation. The association between fibrosis and lymphocytic inflammation at the ductal plate is the only feature suggesting a direct link between fibrosis and inflammation. This suggests that inflammation may not be the primary cause of fibrosis in congenital hepatic fibrosis and that mechanisms other than inflammation may play a role in the development of fibrosis and disease progression in congenital hepatic fibrosis.

**437 PREVALENCE AND PREDICTORS OF TRANSAMINITIS AMONG HOSPITALIZED ADOLESCENTS WITH ANOREXIA NERVOSA.** Jason M. Nagata, KT Park, Kelley Colditz, Neville H. Golden, Pediatrics, Stanford University, Palo Alto, CA

**Background and Objectives:** The time course, evolution, and physiopathology of transaminitis during hospitalization for anorexia nervosa (AN) remains unclear. The objective of this study was to analyze the prevalence, predictors, and evolution of transaminitis in a large sample of adolescents hospitalized with AN.

**Methods:** Electronic medical records of all subjects 10-22 years of age with AN, first admitted to a tertiary children's hospital from January 2007 to December 2012, were retrospectively reviewed. Demographic factors, anthropometric factors, duration of illness, initial prescribed calories, and alanine aminotransferase levels (ALT) were recorded. Multivariate analysis was performed to assess the effect of patient-level variables, including degree of malnutrition and initial calories prescribed, on transaminitis (ALT ≥ 40 IU/L).

**Results:** A total of 356 subjects met eligibility criteria (age 16.1 ± 2.4; 89.0% female; admission BMI 15.9 ± 1.9; admission percentage median BMI (%mBMI) 78.2 ± 8.5), with transaminitis present in 37.0% on admission and in 41.1% at any point during the hospitalization. Lower %mBMI was significantly associated with odds of transaminitis on admission (adjusted odds ratio [aOR] 0.96; 95% confidence interval [CI] 0.93-0.99). Higher initial prescribed calories was associated with odds of transaminitis after admission (aOR 1.003; 95% CI 1.000-1.006).
Conclusions: In this largest study of AN and transaminitis to date, degree of malnutrition predicted transaminitis on admission but initial prescribed calories may also be associated with transaminitis after admission in a small proportion of patients. Future research should better characterize the evolution of elevated transaminases in patients hospitalized with AN undergoing refeeding.

Odds ratios for determinants of transaminitis (ALT ≥ 40) at admission among patients hospitalized for anorexia nervosa

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<th>Variable</th>
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<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tr>
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<td>Odds ratio (95% CI)</td>
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<td>Initial prescribed calories</td>
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<tr>
<td>Rate of weight loss</td>
<td>347</td>
<td>1.03 (0.89-1.19)</td>
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</table>

Abbreviations: CI, Confidence interval

Odds ratios for determinants of transaminitis (ALT ≥ 40) after admission among patients hospitalized for anorexia nervosa

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<th>Variable</th>
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<td>Age</td>
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<td>Initial prescribed calories</td>
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<td>Rate of weight loss</td>
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</table>

Abbreviations: CI, Confidence interval

438 CLINICAL FEATURES, MUTATION ANALYSIS AND OUTCOMES OF ALAGILLE SYNDROME IN KOREAN CHILDREN: A SINGLE CENTER EXPERIENCE. Jinmin Cho, Kyung Mo Kim, Seak Hee Oh, Hyun Jin Kim, Pediatrics, Asan Medical Center, Seoul, Democratic People's Republic of Korea

Background: Alagille syndrome (AGS) is a multisystem autosomal dominant disorder that affects the liver, heart, eyes, face, bone and other organs. AGS is caused by mutations in one of two genes, in the Notch signaling pathway that functions in cell fate determination, Jagged1 (JAG1) or NOTCH2. The aim of the study is to evaluate the clinical features, JAG1 and NOTCH2 mutation analysis and outcomes of AGS in Korean Children.

Methods: Between January 1997 and December 2013, 19 children were diagnosed as AGS in our center. We retrospectively analyzed the clinical features, JAG 1 and NOTCH2 mutation analysis and outcomes of children with AGS.

Results: Of the 19 patients, the prevalence of the clinical features is as follows; Dysmorphic face 100% (n=19/19), liver 89% (n=17/19), heart 95% (n=18/19), eye 67% (n=10/15), skeleton 47% (n=9/19), and kidney 21% (n=4/19). Growth retardation was present in 11 of 19 (58%) patients. Moyamoya disease was seen in one patient. JAG1 mutations were identified in 14 patients. No NOTCH2 mutations were identified. Six of fourteen JAG1 mutations were novel. The fourteen JAG1 mutations include five deletions, 2 insertions, 1 duplication, three missense, and three nonsense mutations. Two patients who received liver transplantation are still alive. Two patients died of comorbidities related to AGS; one with cardiac failure at age of 4 years 11 months and one with hepatic failure at age of 2 years 9 months.

Conclusion: Genetic studies have demonstrated 14 different JAG1 mutations and no NOTCH2 mutations in Korean AGS children. AGS shows multisystem abnormalities with variable expressivity from subclinical to severely affected individuals. Complex heart anomaly and progressive liver dysfunctions have resulted in significant morbidity and mortality in AGS.
A1AT deficiency is a genetic disease affecting both lung and liver, but in the pediatric population, liver disease typically predominates. Only about 10% of patients with ZZ genotype will develop neonatal jaundice, and only 2-3% will have progressive disease during infancy which will require liver transplant. The association between tetralogy of Fallot and A1AT deficiency has not been reported in the literature. A1AT deficiency should be considered in the differential diagnosis of the child presenting with both neonatal cholestasis and complex congenital heart disease.

CHOLESTASIS IN AN INFANT WITH CONGENITAL HEART DISEASE: IT'S NOT WHAT YOU THINK!
Kinanah Yaseen, Elizabeth Collyer, Skyler Kalady, Alex Golden, Naim Alkhouri, Cleveland Clinic Children's Hospital, Cleveland, OH
Neonatal cholestasis is a serious problem that indicates hepatobiliary dysfunction and requires a systematic approach to define the underlying etiology and ensure the best outcome. 20% of biliary atresia cases are associated with extrahepatic complex congenital cardiac malformations, and about 90% cases of Alagille syndrome have associated cardiac anomalies. The association of A1AT deficiency with other congenital anomalies is not well reported.

We report a case of a two-month old female with tetralogy of Fallot presenting with a two week history of jaundice. Laboratory evaluation revealed total bilirubin of 5.6 mg/dL and direct bilirubin of 4.5 mg/dL as well as elevation of AST to 241 U/L and ALT to 243 U/L. The patient underwent evaluation for biliary atresia with HIDA scan that showed normal excretion of tracer. She underwent evaluation for features of Alagille Syndrome including CXR with normal vertebrae. A liver biopsy was scheduled to further evaluate the etiology of her cholestasis; however, her A1AT level came back low at 30 mg/dL (normal 100-220 mg/dL). Phenotype testing demonstrated that she was ZZ phenotype for A1AT consistent with a diagnosis of A1AT Deficiency. Due to worsening jaundice and failure to thrive, the patient was started on ursodeoxycholic acid 15 mg/kg/day and liver enzymes and bilirubin have improved since its initiation. She underwent surgical repair for her tetralogy of Fallot at the age of 5 months without developing any liver-related morbidity. A1AT deficiency is a genetic disease affecting both lung and liver, but in the pediatric population, liver disease typically predominates. Only about 10% of patients with ZZ genotype will develop neonatal jaundice, and only 2-3% will have progressive disease during infancy which will require liver transplant. The association between tetralogy of Fallot and A1AT deficiency has not been reported in the literature. A1AT deficiency should be considered in the differential diagnosis of the child presenting with both neonatal cholestasis and complex congenital heart disease.
441 PON1 GENE EXPRESSION CORRELATES WITH THE DEGREE OF FIBROSIS IN NON-ALCOHOLIC STEATOHEPATITIS. Maan Khattib, Susan S. Baker, Sonal Desai, Wensheng Liu, Robert D. Baker, Lixin Zhu, Department of Pediatric Gastroenterology and Nutrition, University at Buffalo, New York; Women and Children's Hospital, Buffalo, NY

**Background:** Non-alcoholic steatohepatitis (NASH), the severe form of non-alcoholic fatty liver disease (NAFLD), is characterized by steatosis, inflammation and fibrosis. Oxidative stress (OS) plays a key role in the pathophysiology of NASH. We have identified several peroxidases that counteract OS. The purpose of this study is to assess paraoxonase 1 (PON1) expression level in pediatric NASH livers, and to evaluate correlation between PON1 expression and degree of steatosis, inflammation and fibrosis in pediatric NASH livers.

**Methods:** We evaluated the mRNA expression of PON1 by microarray and qRT-PCR. The PON1 protein level was evaluated in liver and serum by Western blot analyses. Liver tissue biopsies obtained by BARD true-cut gun were evaluated by a certified pathologist. Each biopsy was given a score for steatosis, inflammation and fibrosis according to the pathology committee of the NASH clinical research network scoring system.

**Results:** NASH livers exhibited elevated mRNA and protein expression of PON1 compared to normal control. Serum PON1 protein and activity were not elevated. There was a significant correlation between PON1 expression and the degree of liver fibrosis using the Spearman correlation analysis ($r = 0.49$ and $p = 0.01$), but not with the severity of steatosis or inflammation.

**Conclusion:** The end result of OS is liver fibrosis the advanced disease stage in NASH. PON1 expression in NASH livers correlated strongly with fibrosis. This suggests that PON1 enzyme could be used to monitor disease progression.

442 PRIMARY THROMBOPHILIA IN CHILDREN WITH EXTRHEPATIC PORTAL HYPERTENSION. Marcela L. Ramírez, Yolanda Alicia C. de Leon, Ana Rebeca J. Cruz, Roberto Francisco G. Covarrubias, Maria C. Bojorquez-Ramos, Maria del Carmen Rocio M. Rosales, Gastroenterologia Pediátrica, UMAE Hospital Pediatría CMNO, Guadalajara, Mexico

**Objective:** Know the frequency of primary thrombophilia in extrahepatic portal hypertension.

**Material and methods:** From January 2012 to February 2013 a prospective, transversal and descriptive study was conducted on patients from 1 month to 16 years of age with extrahepatic portal hypertension. Two samples were collected. The first of which is collected in 2.7 ml with trisodium citrate buffer for determining clotting inhibitors, the second one of 5 ml in a sterile tube with DTA for DNA extraction and determination of genetic mutations. Statistical analysis was performed on the 21st version spps program.

**Results:** A total of 27 patients were included. The frequency of primary thrombophilia was (40.6%). The deficit of protein C (PC) in 1 (3.7%), protein S deficiency (PS) in 2 (7.4%), no patient had antithrombin deficiency. Genetic mutations correspond to (29.6%) in 8 patients. The primary mutation was methylenetetrahydrofolate reductase (MTHFR) in 7 (25.9%) patients. Prothrombin mutation G2010A 1 (3.7%). Factor V Leiden (FV) was not found present.

**Conclusions:** Primary thrombophilia is present in children with extrahepatic portal hypertension in a comparable manner to previous studies in pediatric literature. Because of the association with local factors that may favor thrombosis, further studies should be conducted.

443 ACUTE ON CHRONIC LIVER FAILURE IN PEDIATRICS. Mounif El-Youssef1, Ruba Azzam1, Uzma Shah1, Jody A. Weckwerth2, Laura Holmes1, Pamela Boone1, 1University of Chicago, Chicago, IL; 2Mayo Clinic, Rochester, MN; 3Mayo Clinic, Rochester, MN; 4MGH, Harvard Medical School, Boston, MA

**Aims:** To review the characteristics, and outcome of acute on chronic liver failure in three pediatric tertiary care centers. Methods: With IRB approval of each institution, the charts of patients aged between 0-21 years diagnosed with acute liver disease were reviewed. Inclusion criteria were ALF alone or with other organ failure as defined by the PALF study group. Exclusion criteria were absence of pre-existing liver disease. Age, demographics, cause of chronic liver disease, precipitating event, and multiorgan involvement were identified. The PELD/MELD, SIRS, and SOFA scores were obtained. Outcomes were survival without a transplant, transplant, or death. Results: Of patients with acute liver disease 9/185 (2006-13); 2/189 (2009-13); 10/206 (2006-13) met the definition of ACLF at the MC, MGH, and U of C respectively. The table identifies the characteristics of the patients with ACLF from these cohorts.

**Conclusion:** ACLF is a separate entity that occurs in Pediatric patients. At our centers, 3.2% of patients with acute liver disease had ACLF. Previous liver disease was identified as intrinsic or due to other causes such as cardiac cirrhosis or previous chemotherapy with intense iron overload. Precipitating events can lead to multiorgan failure. This initial study identifies a group of patients that require close attention to multiorgan failure due to pre-existing liver disease. In contrast to viral hepatitis leading the cause of ACLF in the Far East, our patients have different etiological backgrounds. GI bleeding and infection are the main precipitating events. Overall survival was 63% in this small series. Transplant-free survival was only 26%. A separate study group within the PALF with much wider participation is needed for further investigations.
Methods: This was a retrospective cross-sectional study in patients who had undergone clinically indicated liver biopsy and experimental TE between 1/25/12 and 5/27/14 at Boston Children's Hospital. Eligible patients, with a variety of liver diseases and thoracic perimeter >75 cm, had liver biopsy within 1 year prior to CAP measurement (76% within 75 days). Patients with BMI>40 kg/m² were excluded. Histologic steatosis was reported as none (<5%), mild (5 -30%), moderate (31-60%), or marked (>60%). The reported CAP was the median of 10 measurements using the M (medium) probe, and is compared across steatosis grades using rank-sums.

Results: 49 patients (mean age 15.7±3.3 yrs, 67% male, 14%≥18 yrs) were included. Subjects had a variety of liver diseases (29% autoimmune hepatitis, 25% viral hepatitis, 14% NAFLD, 6% metabolic disease, 2% cholestasis, 2% allograft rejection, and 22% other). 13/49 subjects had steatosis on liver biopsy (4 mild, 9 marked). Median CAP value

444 DOES CONTROLLED ATTENUATION PARAMETER CORRELATE WITH LIVER BIOPSY ASSESSMENT OF HEPATIC STEATOSIS IN PEDIATRIC PATIENTS? Nirav K. Desai1, Sarah Harney1, Roshan Raza1, Paul D. Mitchell2, Maureen M. Jonas1, 1Division of Gastroenterology, Hepatology, and Nutrition, Boston Children's Hospital, Boston, MA; 2Clinical Research Center, Boston Children's Hospital, Boston, MA

Background: Liver biopsy remains the standard for assessing steatosis but is limited by invasiveness, cost, and the potential for sampling error. FibroScan® (Echosens, Paris, France) is an ultrasound-based technology used to assess fibrosis using transient elastography (TE). Recently, a FibroScan® measurement called "controlled attenuation parameter" (CAP) has been developed to detect and quantify steatosis. CAP represents the ultrasonic attenuation coefficient during TE, expressed as dB/m. There are no reported data regarding use of CAP in the pediatric population.

Objective: To assess whether CAP measurements predict the degree of steatosis as determined by liver biopsy correlates with in a pediatric cohort.

Methods: This was a retrospective cross-sectional study in patients who had undergone clinically indicated liver biopsy and experimental TE between 1/25/12 and 5/27/14 at Boston Children's Hospital. Eligible patients, with a variety of liver diseases and thoracic perimeter >75 cm, had liver biopsy within 1 year prior to CAP measurement (76% within 75 days). Patients with BMI>40 kg/m² were excluded. Histologic steatosis was reported as none (<5%), mild (5 -30%), moderate (31-60%), or marked (>60%). The reported CAP was the median of 10 measurements using the M (medium) probe, and is compared across steatosis grades using rank-sums.

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Barath Jagadisan, Anshu Srivastava, Surender Kumar et al Acute On Chronic Liver Failure from the Developing World. JPGN _ Volume 54, Number 1, January 2012 77-81
Objective: To compare MRI determination of steatosis with CAP value in a pilot pediatric cohort.

Methods: Pediatric patients followed in a Preventive Cardiology Clinic with LDL≥160 mg/dL or TG≥150mg/dl and BMI≥85th %-tile were participating in an intervention study that included MRI and CAP assessments. Demographic, anthropometric, and biochemical data were recorded on the day of enrollment. Patients underwent FibroScan® and MRI within one month of enrollment. The MRI was a 3T system, and spectroscopy was used to assess percent fat. Steatosis on MRI was reported using the steatosis grade of the NAFLD activity score (S0: <5%, S1: 5-33%, S2: 34-66%, S3: >67%). CAP value was compared to steatosis grade using the Wilcoxon rank-sum test.

Results: 9 patients (median age 12.7 years, range: 8.3-19.7) with median (range) BMI percentile 97.2 (90.8-99.1), total cholesterol 230 (168-299) mg/dL, LDL 160 (72-244) mg/dL, triglycerides 253 (42-625) mg/dL, and ALT 16 (10-102) U/L underwent both MRI and CAP measurements. One subject had two sets of studies 6 months apart, after a dietary intervention. 7 MRI studies demonstrated S0 and 3 demonstrated S1 steatosis. Median CAP (IQR) measurement for the S0 group was 218 (196, 277) dB/m and for the S1 group 332 (304, 358) dB/m, P=0.048.

Conclusion: In this small pilot study, a significant difference in CAP was seen between S0 and S1 as distinguished by MR spectroscopy. These findings are consistent with those from studies in adults. A larger group will be required to assess whether CAP can be useful to distinguish between greater degrees of hepatic steatosis in children.

445 A PILOT STUDY COMPARING CONTROLLED ATTENUATION PARAMETER AND MRI SPECTROSCOPY TO ASSESS HEPATIC STEATOSIS IN PEDIATRIC PATIENTS. Nirav K. Desai1, Sarah Harney1, Roshan Raza1, Paul D. Mitchell2, Stephan Voss1, Sarah D. de Ferranti3, Maureen M. Jonas1, 1Division of Gastroenterology, Hepatology, and Nutrition, Boston Children's Hospital, Boston, MA; 2Clinical Research Center, Boston Children's Hospital, Boston, MA; 3Department of Cardiology, Boston Children's Hospital, Boston, MA

Background: Based on autopsy studies, one in 10 children in the United States has NAFLD. Liver biopsy remains the standard for assessment of the degree of steatosis and the severity of fibrosis but is limited by invasiveness, cost, and the potential for sampling error, and rarely can result in complications. FibroScan® (Echosens, Paris, France) is an ultrasound-based technology used to assess fibrosis using transient elastography (TE). Since fat can affect ultrasound propagation, a FibroScan® measurement called "controlled attenuation parameter" (CAP) has been developed to detect and quantify steatosis. CAP represents the ultrasonic attenuation coefficient during TE, expressed as dB/m. There are no reported data regarding use of CAP in the pediatric population.

Objective: To compare MRI determination of steatosis with CAP value in a pilot pediatric cohort.

Methods: Pediatric patients followed in a Preventive Cardiology Clinic with LDL≥160 mg/dL or TG≥150mg/dl and BMI≥85th %-tile were participating in an intervention study that included MRI and CAP assessments. Demographic, anthropometric, and biochemical data were recorded on the day of enrollment. Patients underwent FibroScan® and MRI within one month of enrollment. The MRI was a 3T system, and spectroscopy was used to assess percent fat. Steatosis on MRI was reported using the steatosis grade of the NAFLD activity score (S0: <5%, S1: 5-33%, S2: 34-66%, S3: >67%). CAP value was compared to steatosis grade using the Wilcoxon rank-sum test.

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Conclusion: In this small pilot study, a significant difference in CAP was seen between S0 and S1 as distinguished by MR spectroscopy. These findings are consistent with those from studies in adults. A larger group will be required to assess whether CAP can be useful to distinguish between greater degrees of hepatic steatosis in children.

446 SPLENIC RUPTURE IN CHILDREN WITH SPLENOMEGALY DUE TO PORTAL HYPERTENSION. Orith Waisbourd-Zinman1, Henry C. Lin1, Elizabeth B. Rand1,2, 1Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 2Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

Introduction: There is varying clinical assessment and practice among Pediatric Gastroenterologists regarding the potential for splenic rupture in children with splenomegaly resulting from portal hypertension. There is no good data in the medical literature regarding the incidence of splenic rupture in this population. The available literature describes splenic rupture related to infectious mononucleosis, hematological diseases, or severe blunt trauma; however splenic rupture in these circumstances would be expected to be quite different from that hypothesized to occur in the setting of portal hypertension. There is also controversy among practicing Pediatric Gastroenterologists regarding the necessity of physical activity restrictions as well as the usefulness of wearing a spleen guard. Anecdotally recommendations from Gastroenterologists range from restriction of nearly all organized sports and use of spleen guard starting in toddlerhood to restrictions only from contact sports and no use of spleen guard. Our aim is to describe the experience with splenic rupture and the practice for restrictions of physical activity / spleen guards among pediatric Hepatologists in North America.

Methods: We designed a 10-question survey to be completed by clinical Pediatric Hepatologists working in tertiary academic centers in North America with at least 10 years experience managing children with portal hypertension. The email list was generated form the ChiLDREN and PALF contact lists and the NASPGHAN directory. The survey will be emailed to the hepatologists in July 2014. We have conducted a preliminary survey that was sent to seven senior
hepatologists practicing at different tertiary pediatric centers with a 100% response rate.

**Results:** Amongst the seven hepatologists included in the preliminary survey, there were two reported cases of splenic rupture, both associated with significant trauma (one child hit by a motor vehicle, one with a fall down cement stairs). All surveyed recommended restrictions on activities ranging from avoiding only contact sports (like varsity football) to avoiding a wide range of sports and recreational activities. Three out of the seven surveyed recommended restriction only if platelet count is low, variously defined as 20,000 to 75,000. None of the surveyed recommended a spleen guard for toddlers. Five recommended a spleen guard to be used only when participating in an identified restricted activity. We will report the data from the larger survey.

**Conclusion:** Our preliminary survey suggests that splenic rupture in patients with portal hypertension and splenomegaly is very rare. The practice amongst surveyed senior Pediatric Hepatologists is to restrict contact sports (restrictions vary) or activities with a risk of blunt abdominal trauma.

447 **BISPHENOL A EXPOSURE AND NON-ALCOHOLIC FATTY LIVER DISEASE: IS THERE AN ASSOCIATION IN PEDIATRIC POPULATION?** Prasanna K. Kapavarapu1,5, Jimmy Duong2, Maida Galvez3, Ali A. Mencin4, 1Pediatrics, Harlem Hospital Center, New York, NY; 2Biostatistics, Maliman School of Public Health, Columbia University, New York, NY; 3Pediatrics-Preventive Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; 4Pediatric Gastroenterology, Hepatology and Nutrition, Columbia University, New York, NY; 5Pediatrics, Columbia University, New York, NY

Background: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of liver disease in children and is strongly associated with obesity and the metabolic syndrome. Studies of adults have demonstrated associations between bisphenol A (BPA), a chemical with endocrine disrupting properties found in food packaging and consumer products with obesity, diabetes and altered liver enzymes. There have been no data in children examining the associations of BPA with alanine aminotransferase (ALT), the liver enzyme most commonly used to screen for NAFLD.

Objective: To examine whether BPA is associated with elevated ALT.

Methods: NHANES data collected from 2003-2010 were analyzed for an association between BPA and elevated ALT. Both BPA (ng/ml) and ALT (U/L) were available in 2,293 subjects aged 12-21 years. Urinary BPA concentrations were adjusted for creatinine.

Results: In this cohort, 37% of the subjects were overweight or obese. The sample was comprised of a roughly equal proportion of girls (48%) and boys (52%). The ethnic breakdown of the sample was as follows: Mexican American (28.3%), Other Hispanic (7.0%), Non-Hispanic White (29%), Non-Hispanic Black (30%) and Other (5%). Mean and median BPA levels were 4.80 ng/ml and 2.70 ng/ml respectively. Only 4% of patients had no detectable level of BPA. 9.7% of the subjects had an ALT greater than 30(U/L). Although BMIZ score was significantly associated with increasing ALT (p <0.001), no association was seen between BPA and ALT in the data set (p = 0.77). Furthermore, in a multiple regression analysis controlling for age, sex, race and body mass index (BMI), there was no association between BPA and elevated ALT (p = 0.65). In addition, in models where BPA levels were categorized into quartiles no association was apparent.

Conclusion: Preliminary data from NHANES (2003-2010) suggest no association between BPA and elevated ALT. Further analyses will evaluate whether associations between BPA and ALT differ by weight status. The role of environmental chemical exposures in NAFLD is an emerging area of research.

448* **OUTPATIENT ULTRASOUND GUIDED PERCUTANEOUS LIVER BIOPSY IN CHILDREN: COST AND PATIENT CHARACTERISTICS A SINGLE CENTER REVIEW.** Razan Bader1, Jennifer Panganiban1, Niviann Blondet1, Neil Fernandes2, Meghana Sathe1, 1Pediatric Gastroenterology, UT Southwestern, Dallas, TX; 2Radiology, UT Southwestern, Dallas, TX

**Background:** Outpatient pediatric percutaneous liver biopsy (PLB) is increasingly being performed by interventional radiologists (IR) rather than pediatric gastroenterologists (GI) based on national survey data. PLB practices vary from center to center but based on a NASPGHAN Medical Statement in 1996 they recommend observing patients at a medical facility for at least 6 hours post-PLB with a repeat hematocrit to assess for occult bleeding. Recent data in adults including the AASLD position paper in 2009 has recommended reducing post-PLB time between 2 to 4 hours. The reduction in post-PLB observation has been evaluated to be cost effective in adult studies through reduction in facility costs.

**Objective:** Is to compare and contrast patient characteristics, post-operative practices and cost effectiveness of outpatient PLB performed by interventional radiologists (IRLB) versus gastroenterologist (GILB) in a single center.

**Methodology:** Retrospective chart analysis was done evaluating 100 children who underwent an outpatient ultrasound-guided PLB at Childrens Medical Center from January 2011 to January 2014; 50 PLB performed by GI and 50 performed by IR. Cases were evaluated for PACU cost, postoperative care, perioperative laboratory monitoring and success of obtaining adequate tissue sampling.

**Results:**
We divided our results to 4 categories:

1. **Patient characteristics:** there was no significant difference in the weight%, age, gender or the type of insurance between the 2 groups.

2. **Biopsy related characteristics:** the number of biopsy fragments and the size of the longest biopsy were significantly larger and longer in the IR group.

3. **Perioperative laboratory monitoring:** there was no difference in the post-operative hemoglobin drop between the two groups. No patient required a blood transfusion.

4. **PACU cost:** IRLB was significantly less expensive than GILB. Cost difference was due to the length of stay in PACU and higher operative PACU costs compared to the radiology suit PACU. PACU stay charges, (average ± SD) in $ for GILB was 3396 ± 854, for IRLB was 1381 ± 1001 (2.45x) with a P. 0.0001. The PACU charge as a % of the total charge was 33% ± 8.4 for GILB and 27.3% ±14 for IRLB.

**CONCLUSIONS:** In our center, the characteristics of patients referred to interventional radiology for liver biopsy seemed to be no different than those done by pediatric gastroenterologists. The cost of the IRLB was significantly lower and hemoglobin drop in children post PLB was not seen in our sample. Using the lower cutoff of post-operative PACU observation time of 2 hours will result in cost cut ~13-16 % without jeopardizing patient safety. Obtaining either hemoglobin or a hematocrit instead of both serologic tests to detect occult bleeding PLB was also found to be cost effective.

**Nutrition**

462 ORAL SUPPLEMENTATION WITH β-HYDROXY-β-METHYLBUTYRATE ENHANCES PROTEIN SYNTHESIS IN SKELETAL MUSCLE OF NEONATES. Michelle Kao1,2, Daniel Columbus1,2, Suryawan Agus1,2, Julia Steinhoff-Wagner1,2, Adriana Hernandez-Garcia1,2, Hanh V. Nguyen1,2, Steven R. Davis3, Marta L. Fiorotto1,2, Teresa A. Davis3,4, USDA/ARS Children's Nutrition Research Center, Houston, TX; 2Pediatrics, Baylor College of Medicine, Houston, TX; 3Abbott Nutrition, Columbus, OH

**BACKGROUND:** Premature infants are at risk of poor growth due to their inability to achieve adequate protein intake. Parenteral and enteral administration of leucine, a branched-chain amino acid, stimulates protein synthesis in skeletal muscle of neonates. Recently, we showed that acute parenteral administration of the leucine metabolite, β-hydroxy-β-methylbutyrate (HMB), enhances protein synthesis in skeletal muscle of neonates by stimulating the mammalian target of rapamycin complex 1 (mTORC1) - dependent pathway that regulates translation initiation. **OBJECTIVE:** The purpose of this study was to determine the effects of enteral administration of HMB on protein synthesis in skeletal muscle of the neonate and to identify the mechanisms involved. **METHODS:** Overnight fasted, neonatal piglets were either studied immediately (Fasted) or fed for 24 h by intermittent bolus 1 of 5 diets: Low Protein diet (LP; 8.3 g protein•kg•day-1), High Protein diet (HP; 18 g protein•kg•day-1), or LP diet supplemented with 4 (HMB-4), 40 (HMB-40), or 80 (HMB-80) µmol•kg•day-1 of HMB. **RESULTS:** Protein synthesis in LD and gastrocnemius muscles increased with HMB-80 supplementation compared to LP, HMB-4, and Fasted (P < 0.05), and increased further with HP (P < 0.05). Phosphorylation of both p70 ribosomal S6 kinase 1 (S6K1) and eukaryotic initiation factor (eIF) 4E binding protein 1 (4EBP1), and formation of the active eIF4G -eIF4E complex increased (P < 0.05) with HMB-80 supplementation compared to LP feeding. eIF2α phosphorylation in muscle seemed to be no different than those done by pediatric gastroenterologists. The cost of the IRLB was significantly lower and hemoglobin drop in children post PLB was not seen in our sample. Using the lower cutoff of post-operative PACU observation time of 2 hours will result in cost cut ~13-16 % without jeopardizing patient safety. Obtaining either hemoglobin or a hematocrit instead of both serologic tests to detect occult bleeding PLB was also found to be cost effective.

463 VARIABLES PREDICTIVE OF INTESTINAL TRANSPLANTATION IN PEDIATRIC INTESTINAL FAILURE: A SECONDARY ANALYSIS FROM THE PEDIATRIC INTESTINAL FAILURE CONSORTIUM. Monique Goldschmidt1, Christopher Duggan1, Heather Litman1, Jane Balint2, Beth Carter3, Simon Horslen5, Tom 463 was unaffected by treatment. **CONCLUSIONS:** Our results suggest that enteral HMB supplementation increases protein synthesis in skeletal muscle of neonates when protein intake is limiting. The increase in protein synthesis with HMB supplementation was achieved through enhanced activation of translation initiation. (Supported by Abbott Nutrition)

**Introduction:** Improvements in the management of pediatric intestinal failure at specialized centers have led to fewer complications. The need for intestinal transplantation as a therapeutic option has increased. The purpose of this study was to determine the variables predictive of intestinal transplantation in pediatric intestinal failure. **Objective:** To identify variables that were predictive of intestinal transplantation in the Pediatric Intestinal Failure Consortium. **Methods:** The consortium included 27 centers that referred patients for intestinal transplantation between 2000 and 2015. A total of 1083 patients were included in the study. Multivariable logistic regression analysis was used to identify variables predictive of intestinal transplantation. The results were compared to a previous study that included patients referred to the Pediatric Intestinal Failure Consortium and a third study that included patients referred to interventional radiology for liver biopsy. **Results:** The variables that were predictive of intestinal transplantation were age, gender, weight, type of insurance, and type of transplant. The results were compared to a previous study that included patients referred to the Pediatric Intestinal Failure Consortium and a third study that included patients referred to interventional radiology for liver biopsy. **Conclusions:** The variables that were predictive of intestinal transplantation were age, gender, weight, type of insurance, and type of transplant. The results were compared to a previous study that included patients referred to the Pediatric Intestinal Failure Consortium and a third study that included patients referred to interventional radiology for liver biopsy.
children requiring intestinal transplantation (ITx), which warrants evaluation of the predictors of ITx in an ongoing attempt to identify candidates in a safe and timely manner.

**Methods:** IRB approval was obtained for retrospective analysis of children with intestinal failure enrolled in PIFCon centers. Data on 272 infants were collected over ≥2-year time interval amongst 14 sites. Infants who died without transplantation were excluded (n=58). Bivariate analyses were performed to identify variables associated with transplantation.

**Results:** 214 infants with median (IQR) gestational age of 34 weeks (31, 37) were followed for 30.4 months (17.6, 47.3). Children with volvulus were more likely to require ITx than have success with rehabilitation (31.7% vs 17.5% respectively, p = 0.02). Variables positively associated with ITx included Caucasian race (OR 2.37 (95% CI: 1.13, 4.97)), gestational age (weeks) (OR 1.12 (95% CI: 1.03, 1.22)), birth weight (kg) (OR 1.44 (95% CI: 1.01, 2.06)), and direct bilirubin (mg/dL) (OR 1.34 (95% CI: 1.05, 1.72)). Residual intestinal length (cm) (OR 0.96 (95% CI: 0.94, 0.98)) and use of breast milk (OR 0.19 (95% CI: 0.04, 0.82)), anti-motility medications (OR 0.19 (95% CI: 0.04, 0.82)), or iron supplementation (OR 0.21 (95% CI: 0.05, 0.91)) were associated with a decrease in the odds of ITx.

**Conclusions:** Specific variables predict the need for ITx in pediatric intestinal failure. While the presence of cholestasis has been historically associated with intestinal transplantation, bowel length and using breast milk, anti-motility medications, or iron supplementation decreased the likelihood for ITx.

**COW’S MILK PROTEIN INTOLERANCE STUDY; THE NASPGHAN INTERNET RESEARCH INITIATIVE: PRELIMINARY REPORT.** Sudipta Misra, Sari Acra, Elizabeth Gleghorn, Justin Turner, James Rick, Yvonne McFarlane-Ferreira, Zarella Molle-Rios, Matthew DiGuglielmo, Stephanie Page, Rana Ammoury,

1Pediatrics, Brody School of Medicine, ECU, Greenville, NC; 2Pediatrics, Vanderbilt University Medical School, Nashville, TN; 3Pediatrics, University of Alberta, Alberta, AB, Canada; 4Gastroenterology, The Children’s Medical Center of Dayton, Dayton, OH; 5Pediatrics, New York Methodist Hospital, New York, NY; 6Gastroenterology, Nemours/Alfred I. duPont Hospital for Children, Wilmington, DE; 7Gastroenterology, Children's Mercy Hospital, Kansas City, MO; 8Pediatric Gastroenterology, University of Arizona, Tuscon, AZ; 9Gastroenterology, Children's Hospital of Oakland, Oakland, CA

Cow’s Milk Protein Intolerance (CMPI) is a common clinical problem. This study has been designed to define the presentation, treatment and follow up of CMPI in the actual practice setting. Material and Methods: In this prospective observational study CMPI was defined as bleeding per rectum in an otherwise healthy baby with age of onset below 6 months; diagnosed to be due to CMPI by the treating gastroenterologist. The clinical data at initial and follow up visits, tests and interventions ordered were recorded on a structured data collection form in the internet based REDCap data base. Informed consent was obtained from parents. Results: Forty infants (31 male; 30 Caucasian, 4 Hispanic; 24 full term, 9 premature; 3 with failure to thrive) were enrolled in 8 centers (4 academic and 4 private practice). The mean ages of onset of symptoms was 39 days and at initial evaluation was 95 days. At presentation at Primary Care Provider (PCP) 26 children were exclusively breast fed, 5 were on supplemental formula and 8 were on exclusive formula feeds (6 cow’s milk based and 2 Soy) (Table). Interventions at PCP’s office included elimination of milk from maternal diet (20) and change of formula in 22, no intervention was done in 4. At presentation to Gastroenterologist, 23 were on breast milk, 17 mothers had eliminated milk from their diet and 21 were on formula (Table). There was family history of food allergy in 5 and environmental allergy in 8. At the specialist office 37 had normal examination, one had malnutrition and 3 had skin rashes. Tests were done in 24 (60%), common being occult blood test (13).Flexible sigmoidoscopy was performed in 1. No intervention was done 15, exclusion of milk from maternal diet was continued in 14, formula was changed in 16 (10 to semi elemental, 3 to elemental) (Table) and I patient was also put on probiotic. 22 infants returned for follow up, all but 4 were reported to be free of symptoms. Among those 4, elemental formula was started in 2, breast feed was re started in 1 and restricted diet was advised in 1. There was no significance difference between all the parameters among academic and private practices. However, elemental formula was exclusively prescribed by academic practices. Conclusion: Most of the CMPI patients referred to GI specialist were breast fed (65%). These children were seen about 60 days after onset of symptoms. Restriction of maternal diet was commonly recommended (50%) and majority of mothers (85%) followed it. Active intervention like change of formula was done at GI office in only 40% of patients, most commonly to semi elemental formulas (40%). Use of elemental formula was less common (23%). Probiotics were rarely used. No significant difference was found in practice patterns among private and academic practices. Further analysis of prognosis with different treatment regimens and confounding factors such as allergy, prematurity will be done with further enrollment.
Breast feeding provides optimal nutrition for infants. Infant formula is patterned after human milk and evidence suggests that human milk oligosaccharides (HMOs) may play a significant role in the protective properties of human milk. In addition, recent research has demonstrated that the energy density of human milk is lower than previously reported. A prospective, randomized, controlled, growth and tolerance study was conducted with three infant formulas at a caloric density of 643 kcal/L (19 kcal/fl oz). The control formula contained galactooligosaccharides (GOS), while the two experimental formulas contained varying levels of human milk oligosaccharides plus GOS. The three formula groups were compared with a human milk reference group. Healthy, singleton infants age 0-5 days and birth weight > 2490 g were enrolled and either exclusively fed formula (n=189) or human milk (n=65) from birth to 4 months of age. No significant differences between the four groups were observed for weight, length or head circumference growth over the 14-119 day study period. The formulas were well tolerated in all groups and were comparable for mean rank stool consistency, average number of stools per day, or percent of feedings associated with spit-up or vomit during the four-month study period. This is the first study to demonstrate growth and tolerance in infants fed unique formulas with a caloric density closer to breast milk containing an HMO that is abundant in human milk. This study was sponsored by Abbott Nutrition.
Unfortunately, there are often symptoms associated with formula feedings via gastrostomy tube, including constipation, reflux, and irritability. The pureed diet has been identified as an adequate nutritional alternative to commercialized formulas. However, there are very limited data on the effects of the pureed diet. In this pilot study, we aimed to identify our pediatric population’s tolerance of a pureed diet via gastrostomy tube.

Methods: First, a retrospective review was performed on pediatric patients (ages 8 months to 18 years) who had been trialed on a pureed diet via gastrostomy tube at our institution. Nutritional markers, weight, and reports of symptomatology were assessed. Next, the parents participated in a prospective telephone survey detailing overall tolerance, gagging/retching, oral tolerance, reflux, stooling patterns, and general logistics of the pureed diet. The variables were compared before and during pureed diets.

Results: Six pediatric patients (mean age, 4 years 10 months) participated in the study. Average duration on the pureed diet was 21 months. Increase in weight velocity was noted in 83 percent. All of the families reported overall superior tolerance to the pureed diet compared to the previous commercialized formulas. All participants reported a reduction in gagging and retching. Eighty-three percent stated increase oral tolerance. Average time to prepare pureed meal was 5 minutes. No child had worsened symptoms on the pureed diet.

Conclusions: The pureed diet via gastrostomy tube is an alternative diet that can improve gagging/retching, oral tolerance, weight gain, and stooling habits. This is a pilot study that warrants a full study with a larger sample size.

COW'S MILK PROTEIN INTOLERANCE MANIFESTED AS FEEDING INTOLERANCE IN THE NICU SETTING. Jonathan Cordova, Hilary Jericho, Stacy Kahn, Ranjana Gokhale, Stefano Guandalini, Timothy Sentongo, Pediatric Gastroenterology, Hepatology and Nutrition, The University of Chicago, Chicago, IL

Introduction: Cow's milk protein intolerance (CMPI) affects approximately 7% of healthy infants; however, the condition is poorly recognized or described in preterm and critically-ill newborn infants. This study examined the clinical events preceding a positive diagnosis of CMPI in infants receiving parenteral nutrition (PN) support.

Methods: This was a retrospective study of all infants admitted during a 12-month period to a level III neonatal intensive care unit (NICU) who received PN therapy. Study data was collected and managed using REDCap electronic data capture tools. Clinical parameters assessed included gestational age, birth weight, clinical diagnosis, duration and number of course of PN therapy, age at initiation of enteral feeds and type of enteral feed at full enteral autonomy. CMPI was diagnosed on the basis of persistent feeding intolerance symptoms that resolved after change of enteral feeds to a protein hydrolysate (PH) or crystalline amino acid (CAA) formula. Weight for age z-scores were computed using Olsen and WHO reference data.

Results: Three hundred forty-eight infants received PN therapy during the period of interest. The median birth weight and weight z-scores were 1618g (range 425 to 5110) and -0.22 (range -3.25 to 4.83), respectively. The median age at starting PN was day 1 of life (range 0 to 158) and 51/348 (14%) infants required multiple courses of PN therapy. Nineteen infants (5%) presented with persistent feeding intolerance symptoms that resolved after change of feeds to a PH or CAA formula. The median birth weight and weight z-scores for these 19 infants were 1065g (range 500 to 3800) and -0.28 (range -3.24 to 2.01), respectively. There was a higher proportion of infants subsequently diagnosed with CMPI in the group that received multiple courses of PN (14/51) compared to the group that only required a single course of PN therapy (5/297); 27% vs. 2%, p<0.001. Among the group requiring multiple courses of PN therapy and diagnosed with CMPI (N=14), 11 (79%) presented with necrotizing enterocolitis (NEC) during the first 4 weeks of life. However, on resumption of enteral feeding with standard infant formula, there was recurrence of feeding intolerance symptoms including NEC-like illness in 4 infants at a mean age of 65 days that persisted until change of enteral feeds to a PH or CAA formula.

Conclusion: Requirement for multiple courses of PN therapy in preterm and critically-ill newborn infants is a predictor of cow's milk protein intolerance. Similarly, late onset or recurrence of NEC-like illness in preterm infants should be considered a manifestation of CMPI and prompt a dietary change to a PH or CAA formula.

DETERMINANTS OF ANEMIA AMONG SCHOOL-AGED CHILDREN IN COLOMBIA AND THE UNITED STATES. Sana Syed1, O.Yaw Addo2, Thomas R. Ziegler1, Parminder R. Suchdev1,2, 1School of Medicine, Emory University, Atlanta, GA; 2Rollins School of Public Health, Emory University, Atlanta, GA

Anemia globally affects a quarter of all school-aged children (SAC) and is frequently ascribed to iron deficiency (ID). Other nutritional, demographic and socio-economic factors are often unmeasured. We obtained data from two national cross-sectional surveys - 2010 Encuesta Nacional de Nutrición Situación Colombia and the 2003 to 2006 US National Health and Nutrition Examination Survey. We analyzed data for 8055 Colombian and 1043 US children aged 5 to 14.9 years. Associations were studied using survey regression methods with adjustment for inflammation, potential confounders and complex survey design effects.

Colombian data showed 58% females, 11% black, 11% stunted, 4% wasted, 4% overweight, 0.5% obese. Prevalence of anemia was 0.9%; ID was 9%. US data showed 81% females, 16% black, 5% stunted, 5% wasted, 18% overweight, 4% obese. Prevalence of anemia was 2%; ID was 13%. In Colombia, anemia was associated with age >= 13.5y (OR 7.0,
being in the poorest quintile (OR 2.0, p=0.02) and with ID (OR 4.6, p<0.0001). In the US, there was no anemia in males, modelling showed that anemia was associated with age >= 13.5y (OR 2.6, p=0.03), being black (OR 12.4, p<0.0001), being in the poorest quintile (OR 2.0, p=0.04) and with ID (OR 8.0, p<0.0001). In conclusion, there was extremely low prevalence of anemia in both countries. In general, ID was associated with anemia with inconsistent associations with socioeconomic factors. Additional countries (Mexico and Malawi) are planned for future analyses. Research support: Bill & Melinda Gates Foundation, CDC, GAIN, NICHD, NIH ACTSI. Anthropometric and biochemical characteristics of all SAC 5 - 14.99 y in the USA and Colombia

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>USA/N=1043</th>
<th>Colombia/N=8055</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n*</td>
<td>% or mean (SE)</td>
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<tr>
<td>Age in years</td>
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<tr>
<td>&lt; 13.5y</td>
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<td>13.5y-14.99y</td>
<td>382/1043</td>
<td>36.3 (1.7)%</td>
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<tr>
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<td>Ethnicity</td>
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<tr>
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<tr>
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<tr>
<td>Poorest</td>
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<td>15.2 (1.6)%</td>
</tr>
<tr>
<td>All Other</td>
<td>770/1007</td>
<td>84.8 (1.6)%</td>
</tr>
<tr>
<td>1 Iron Deficiency %</td>
<td>157/961</td>
<td>12.7 (1.5)%</td>
</tr>
<tr>
<td>2 Low Ferritin%</td>
<td>..</td>
<td>..</td>
</tr>
<tr>
<td>3 High sTFR%</td>
<td>178/1043</td>
<td>13.2 (1.5)%</td>
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<tr>
<td>4 Elevated CRP (ng/mL) %</td>
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<tr>
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<td>Anemia %</td>
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<td>2.4 (0.5)%</td>
</tr>
<tr>
<td>Iron Deficiency Anemia %</td>
<td>22/961</td>
<td>1.2 (0.4)%</td>
</tr>
</tbody>
</table>

* Reported n is of actual sampled population. Reported % are weighted per the survey design

1 Iron Deficiency assessed using serum ferritin (SF) in Mexico & Colombia, corrected for inflammation excluding CRP >5.0 ng/mL; Age>=5y, SF <15 µg/L and using soluble Transferrin Receptor (sTFR) in the USA, corrected for inflammation excluding CRP >5.0 ng/mL, Males sTFR> 5.0 mg/dL, Females >4.4 mg/dL

2 Low Ferritin% and High sTFR% uncorrected for inflammation

3 Vitamin A Deficiency assessed using serum retinol <0.70 µmol/L

4 Elevated CRP >5.0 ng/mL

5 Anemia definition: Age <11.99y, Hb(g/dL) <11.5; Age>=12y, Hb(g/dL) <12.0
**470 THE EFFECTS OF LACTOFERRIN SUPPLEMENTATION ON THE INTESTINAL MICROBIOTA OF PREMATURE INFANTS RECEIVING PROBIOTICS.** Kelly Grzywacz$^{1,3}$, James Butcher$^4$, Ibrahim Mohamed$^4$, Keith Barrington$^4$, David Mack$^{2,4}$, Alain Stintzi$^{1,4}$, Ottawa Institute of Systems Biology, Department of Biochemistry Microbiology and Immunology, University of Ottawa, Ottawa, ON, Canada; $^3$Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; $^4$Pediatric Gastroenterology Hepatology and Nutrition, CHU Sainte Justine, Montreal, QC, Canada; $^5$Neonatology, CHU Sainte Justine, Montreal, QC, Canada

**Background:** Lactoferrin is the major whey protein in mammalian milk and an important exogenous neonatal protective component. It exhibits anti-inflammatory properties, antibacterial activity, and influences the composition of the intestinal microbiome.

**Objective:** To compare the stability and diversity of the intestinal microbiota of premature infants receiving probiotics with and without lactoferrin supplementation.

**Design/Methods:** We performed a prospective randomized controlled trial. Infants less than 31 weeks gestation were randomized to receive a daily dose of 500 mg of FloraBABY$^\text{TM}$ a probiotic mixture of Bifidobacterium and Lactobacillus (control group), or this probiotic with 100 mg of bovine lactoferrin (treatment group). The initial meconium and one stool sample was collected each week for the first month of life. DNA was extracted from stool samples, and the bacterial 16S ribosomal RNA V6 region was amplified by polymerase chain reaction (PCR), purified and deep sequenced using the HiSeq 2000 Illumina system. Microbial analyses were performed using DNA analysis tools like QIIME.

**Results:** A total of 70 infants were recruited for the study. Following stringent quality filtering criteria, 88 stool samples representing the intestinal microbiota of 47 babies were analyzed. No differences in the diversity (Shannon Index, Chao 1) of the intestinal microbiota of the two groups were determined. Overall the Enterobacteriaceae Family had the highest relative abundance (32.2%, +/- 16%) in all samples. No difference in the relative abundance of the strains in Florababy$^\text{TM}$, namely Lactobacillus species unidentified (0.7% +/- 0.61%), Bifidobacterium species unidentified (0.1% +/- 0.27%), B. breve (0.2% +/- 0.26%), B. bifidum (0%), or B. longum (0.3% +/- 0.4%) was determined between the 2 groups (p>0.05).

**Conclusions:** Enterobacteriaceae predominance was observed in premature infant intestinal microbiota in the present study, and this is consistent with the current literature. Futhermore this family of bacteria consists of pathogenic genera such as the Klebsiella and Escherichia. A similar diversity of the intestinal microbiota was determined in infants receiving either probiotic with lactoferrin supplementation compared to probiotic alone. Bifidobacteria and Lactobacillus despite being in the orally administered probiotic displayed very low relative abundance in both groups.

### Relative Abundance of Probiotic Strains

<table>
<thead>
<tr>
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<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
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<tbody>
<tr>
<td></td>
<td>Lactoferrin</td>
<td>Control</td>
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<tr>
<td>Lactobacillus s</td>
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<td>0.01028</td>
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<tr>
<td>Bifido s</td>
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<td>Bifido breve</td>
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<tr>
<td>Bifido longum</td>
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</tbody>
</table>

**471 INFECTIOUS ETOLOGY OF DIARRHEA IN TANZANIAN INFANTS AND YOUNG CHILDREN USING A NOVEL PCR-BASED TAQMAN ARRAY METHOD.** Kerri Gosselin$^4$, Said Aboud$^4$, Christine McDonald$^4$, Sabrina Mayo$^4$, Nasim Khavari$^4$, Karim Manji$^4$, Rodrick Kisenge$^4$, Wafaie Fawzi$^5$, Gibson Kibiki$^5$, Jean Gratz$^6$, Jie Liu$^6$, Eric Houpt$^6$, Christopher Duggan$^4$, 1Division of Gastroenterology and Nutrition, Boston Children's Hospital, Boston, MA; 2Muhimbili University of Health and Allied Sciences, Dar es Salaam, United Republic of Tanzania; 3Lucile Packard Children's Hospital at Stanford, Palo Alto, CA; 4Harvard School of Public Health, Boston, MA; 5Kilimanjaro Clinical Research Institute, Moshi, United Republic of Tanzania; 6Division of Infectious Diseases and International Health, University of Virginia, Charlottesville, VA

**Background:** Diarrheal diseases are a leading cause of morbidity and mortality in children worldwide, but the etiology of diarrhea in resource-limited settings is poorly defined.

**Methods:** We sought to determine the etiology of community-acquired diarrhea in Tanzanian infants and young children, and assess the association with anthropometric measures. A convenience sample of infants enrolled at 6 weeks of age in a prospective trial of zinc and/or multivitamin supplementation in Dar es Salaam, Tanzania was selected. Subjects were followed for 18 months. Stool samples were obtained from children with diarrhea, defined as three or more watery stools in a 24 hour period. Morbidity and anthropometric data were collected at monthly, outpatient
follow-up visits. A novel, PCR-based TaqMan array method was used to screen stool samples for 19 diarrhea-causing enteropathogens. Pathogen-specific quantification cycle cutoffs were used to assess pathogen burden.

Results: 123 subjects with diarrhea were enrolled. The mean ± SD age at sample collection was 12.4 ± 3.9 months, and 50.4% of the subjects were female. 30 pathogens were identified in 28 (22.8%) subjects: 11 rotavirus, 9 diarrheagenic *Escherichia coli* (including 6 enteropathogenic *E. coli* and 3 enterotoxigenic *E. coli*), 7 *Shigella spp*, and 3 *Cryptosporidium spp*. At the last clinic visit, subjects with any identified enteropathogen had significantly lower weight-for-length and weight-for-age z-scores, compared to those without an identified pathogen (Table 1). There was no difference in pathogen detection in those children receiving zinc supplementation.

Conclusions: This novel, PCR method allows for the identification of enteropathogens that place children at higher risk for poor growth. Targeted interventions may reduce the burden of diarrhea and optimize nutritional outcomes in this population.

<table>
<thead>
<tr>
<th><strong>Anthropometric outcome (mean +/- SD)</strong></th>
<th>Positive for ≥1 pathogen</th>
<th>Negative for all pathogens</th>
<th>P^1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length-for-age z score</td>
<td>-1.22 ± 0.96</td>
<td>-1.11 ± 1.28</td>
<td>0.61</td>
</tr>
<tr>
<td>Weight-for-length z score</td>
<td>-0.63 ± 1.17</td>
<td>0.01 ± 1.27</td>
<td>0.02</td>
</tr>
<tr>
<td>Weight-for-age z score</td>
<td>-0.97 ± 1.02</td>
<td>-0.48 ± 1.23</td>
<td>0.04</td>
</tr>
</tbody>
</table>

^1 Obtained from a t-test

472  **EFFECT OF FISH OIL LIPID EMULSION ON CATHETER-RELATED THROMBOSES IN PATIENTS WITH INTESTINAL FAILURE.** M M. Jami, Russell J. Merritt, Intestinal Rehabilitation Program, Pediatric Gastroenterology, Children's Hospital Los Angeles, Keck School of Medicine, University of Southern California, Los Angeles, CA

**Purpose:** Central Venous Catheters (CVCs) are used to deliver parenteral nutrition (PN) in patients with intestinal failure. Catheter-related thrombosis (CRT) is a recognized complication of such devices. In patients with intestinal failure associated cholestatic liver disease (IFALD), fish oil lipid emulsion (FOLE) is used as an investigational or compassionate use drug to reverse IFALD. We postulated that the anti-inflammatory and anti-thrombogenic effects of fish oil may reduce the risk of CRT. Our aim was to compare the occurrence of CRT in intestinal failure patients who received FOLE with those who received conventional soy based lipid emulsion (SOLE) as their lipid source.

**Methods:** Seventy patients were identified from our electronic medical records who received PN for intestinal failure through our intestinal rehabilitation service. 35 patients received FOLE for IFALD; these subjects were compared to 35 with intestinal failure during the same period who received only SOLE. CRT was identified by clinical or ultrasound evidence of thrombosis associated with CVC used for parenteral nutrition. Patients received 10% FOLE at a dose of 1 gm/kg/day or 20% SOLE at 1-3 gm/kg/day.

**Results/Conclusions:** We found a strikingly decreased risk of CRT in patients with intestinal failure receiving FOLE compared to those receiving SOLE (See Table). Due to the complexity of the underlying medical conditions and the potential for cholestatic liver disease to affect hemostasis, additional clinical and mechanistic studies to confirm and further assess this observation are warranted.

**Results:** Thrombosis occurrence with FOLE and SOLE

<table>
<thead>
<tr>
<th></th>
<th>Received FOLE</th>
<th>Received SOLE</th>
<th>Chi^2 p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>35</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Age range</td>
<td>2 months-18 years</td>
<td>3 months-19 years</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>M=18, F=17</td>
<td>M=16, F=19</td>
<td></td>
</tr>
<tr>
<td>Estimated days of lipid infusion</td>
<td>6000</td>
<td>16,000</td>
<td></td>
</tr>
<tr>
<td>Patients with one or more CRT</td>
<td>0</td>
<td>11</td>
<td>&lt;.0003</td>
</tr>
</tbody>
</table>

473  **LOW PROFILE NON-BALLOON GASTROSTOMY TUBES IN CHILDREN; COMPLICATIONS, OUTCOMES AND SURVIVAL IN A RETROSPECTIVE COHORT.** Temara Hajjat, Riad Rahhal, Pediatric Gastroenterology, University of Iowa, Iowa City, IA

**PURPOSE:** Non-balloon low profile gastrostomy tubes are used for enteral nutritional support in the small subset of pediatric patients with feeding difficulties when oral intake is inadequate and use of other tube types is problematic. Different brands of non-balloon low profile gastrostomy tubes are available in the US but comparative studies are lacking.
METHODS: This was a retrospective study comparing complications and survival between the BARD button (BARD Access Systems) and the Capsule Non-Ballon Mini-ONE button (Applied Medical Technology) in a cohort of pediatric patients followed in the Pediatric Gastroenterology Division over 10 years between November 15, 2003 to November 15, 2013.

RESULTS: 45 subjects were identified that underwent a total of 150 tube placement procedures. Demographics were similar between groups. Subjects in the BARD group had significantly longer duration of follow-up. Placement of BARD buttons was significantly associated with mild bleeding at insertion (41% vs 4%, P<0.0001). More subjects in the BARD group reported leakage problems (48% vs 11%, P<0.0001) while more subjects in the MINI-ONE group reported accidental dislodgement (1% vs 33%, p<0.0001). BARD buttons remained in place significantly longer than MINI-One buttons with a reported duration of use at 310 vs 171.8 days respectively (P=0.0004).

CONCLUSION: BARD buttons were more likely to be associated with mild bleeding at placement and with leakage with ongoing use while MINI-One buttons were at higher risk for dislodgement and earlier replacement.

474 PEDIATRIC FEEDING DISORDERS: MULTIDISCIPLINARY INPATIENT TREATMENT EFFECTS.
Laura Nathans1,2, Sonya L. Cornwell1, Laura Austin1, Christine Murphy1, 1Feeding Program, Baylor, Dallas, Dallas, TX; 2University of North Texas, Denton, TX
Multidisciplinary inpatient treatment of pediatric feeding disorders has effectively reduced dependence on gastrostomy tube feedings with combined nutritional management and behavioral therapy while addressing oral-motor, and sensory processing difficulties (Cornwell, Kelly, Austin 2010). To further support the combined treatment as evidence based practice, a follow-up review was completed on patients admitted for gastrostomy tube weaning between 2006 and 2013 (N = 93). Inpatient treatment averaged 28 days (SD = 4). Ages ranged from 16 to 155 months (M = 49.77, SD = 31.18). 53.8% of patients were male, and 46.2% were female. Treatment resulted in a significant reduction in G-tube caloric intake from admission (first three days average) G-tube caloric intake (M = 985.85 kcal, SD = 518.82 kcal) and discharge (last 5 days average) G-tube caloric intake (M = 429.41 kcal, SD = 356.39 kcal), with t(92) = 9.08, p < .001. This difference reflected a large effect size of d = 1.25. Oral caloric intake showed a significant increase between admission (M = 502.65 kcal, SD = 395.11 kcal) and discharge (M = 772.02 kcal, SD = 485.53 kcal), with t(92) = -8.02, p < .001. This difference reflected a medium effect size of d = 6.1. Twenty-one patients (23%) completely weaned from tube feedings. These results provide additional support of Cornwell et al. (2010)’s findings with a more recent sample of inpatients. Results also indicate that most children will continue to require further dietary and therapeutic intervention on an outpatient basis.

475 DEFINING THE SPECIFIC AND SYNERGISTIC EFFECTS OF PROBIOTIC AND/OR LACTOFERRIN SUPPLEMENTATION ON THE GUT MICROBIOTA COMPOSITION OF NEWBORN PIGLETS. Kelly Grzywacz1,2, James Butcher2, Guillaume Romain2, Ibrahim Mohamed3, Keith Barrington2, David Mack4, Alain Stintzi2, 1Pediatric Gastroenterology Hepatology and Nutrition, CHU Sainte Justine, Montreal, QC, Canada; 2Ottawa Institute of Systems Biology, Department of Biochemistry Microbiology and Immunology, University of Ottawa, Ottawa, ON, Canada; 3Neonatology, CHU Sainte Justine, Montreal, QC, Canada; 4Pediatric Gastroenterology Hepatology and Nutrition, Children’s Hospital of Eastern Ontario, Ottawa, ON, Canada
Background: Probiotic supplementation has become common practice in many neonatal intensive care units as a strategy to reduce necrotizing enterocolitis. Lactoferrin, a whey protein with antibacterial properties naturally found in breast milk, has been added to infant formula in clinical trials in an attempt to reduce neonatal infections. Piglets are an excellent model for the neonatal gastrointestinal tract, and therefore facilitate microbiome studies in this vulnerable population.

Objective: To determine the effect of probiotic and/or lactoferrin supplementation on the development of the gut microbiota in vivo using a newborn piglet model.

Design/Methods: Fourteen newborn piglets were divided into 4 groups; controls, probiotics, lactoferrin, and probiotics with lactoferrin and fed every 5 hours with a milk replacer. We administered 500 mg of FloraBABY, a probiotic mixture of Bifidobacterium and Lactobacillus and/or 100 mg of bovine lactoferrin once daily via syringe to the piglets in each respective group. Fresh stool samples were collected daily and the piglets were sacrificed after seven days of probiotic and/or lactoferrin supplementation. Both luminal and mucosal samples were taken from each section of the small and large bowel. DNA was subsequently extracted from the samples and the microbiota composition was characterized by high-throughput sequencing of the V6 hyper-variable region of the 16S rRNA gene. The resulting reads were analyzed using QIIME to determine significant alterations in the microbiota over time (stools) and across the intestinal tract (luminal/mucosal samples) in the different groups.

Results: A total of 105 stool samples and 153 intestinal samples were analyzed. Alpha Diversity, an indicator of the richness and complexity of the microbiome did not statistically differ over time in the stool samples, nor did it differ across the different segments of the intestine. However, there was a trend towards decreased diversity of the microbiota on day 2, which coincides, with the introduction of both the probiotics and the lactoferrin supplements. No difference in
beta diversity was seen across intestinal segments. Differences were apparent in the relative abundance of bacterial taxa in the small bowel versus large bowel. The former showed higher levels of Firmicutes of the Bacilli class (23%/+-16%) and Proteobacteria (31%/+-19%) while the latter displayed higher levels of Bacteroidetes (25%/+-6.8%), and Firmicutes of the Clostridia class (37%/+-12%). In contrast the bacterial composition of the stool samples remained fairly constant over time and did not differ between piglet groups. Lactobacillus showed the highest relative abundance amongst the probiotics present in FloraBABY1TM (4.7%/+-5.8%).

**Conclusion:** A similar diversity of the intestinal microbiota was seen in piglets receiving milk replacement, probiotics, and/or lactoferrin. In addition, the relative abundance of Lactobacillus was much more predominant than Bifidobacterium in all groups.

**476 DISACCHARIDASE ACTIVITY IN CHILDREN UNDERGOING ESOPHAGOGASTRODUODENOSCOPY: A SYSTEMATIC REVIEW.** Taylor Daileda1, Morgan E. Sutter2, Grace Yang3, Peter Baek2, Kalpesh Thakkar4, 1Baylor College of Medicine, Houston, TX; 2Rice University, Houston, TX

**Background:** We performed a systematic review to examine the intestinal disaccharidase activity reported in duodenal biopsy specimens in pediatric patients. We also examined the effect of ethnicity, underlying conditions, histological findings, and region of origin on disaccharidase activities in children.

**Methods:** All full-length articles published in English during 1966-2013 were included if: (i) participants had small intestinal biopsy evaluation of disaccharidase activity, (ii) levels of lactase, sucrase, maltase or palatinase were reported, (iii) age under 18 years.

**Results:** Eighteen articles examining 2,544 patients fulfilled the inclusion and exclusion criteria. All were observational and most (13) were retrospective. Nine studies were performed in the United States and of those two were prospective. The largest study examined 399 procedures and 13 studies examined less than 100 procedures. Five studies examined patients with celiac disease and 2 studies examined patients with autism. None of the studies analyzed the association of clinical symptoms or signs to disaccharidase activities.

**Conclusions:** Our findings suggest that a large study examining patient characteristics and histologic features associated with disaccharidase deficiency and comparing disaccharidase levels across patient groups based on clinical morphology is needed.

**477 SACCHAROMYCES CEREVISIAE FUNGEMIA: AN ASSOCIATION WITH SACCHAROMYCES BOULARDII ADMINISTRATION?** John-Paul Berauer, Pediatrics, Advocate Lutheran General Children's Hospital, Giltz, IL

**Background.** Saccharomyces boulardii (Florastor®) is widely used as a probiotic compound for the prevention and treatment of various diarrheal disorders. Although traditionally regarded as a safe and nonpathogenic agent, its use has been associated with several reports of invasive *Saccharomyces cerevisiae* fungemia. Recent molecular studies definitively recognized *S. boulardii* as an asporogenous strain of *S. cerevisiae*, not a separate species; however, accurate strain identification using DNA microsatellite typing to confirm clonality between isolated strains of *S. cerevisiae* from patients and the *S. boulardii* capsule has been performed in only a few published cases. In addition, data regarding the relative risk associated with *S. boulardii* administration has not been previously reported.

**Aims.** Our goal is to establish evidence-based guidelines for the administration of *S. boulardii* within the Advocate Health Care system as well as other hospitals by determining the relative risk of fungemia due to *S. boulardii* exposure and identifying subsets of patients at increased risk for infection with *S. cerevisiae*.

**Methods.** We retrospectively reviewed the medical records of 38 patients with positive *S. cerevisiae* cultures who were hospitalized at an Advocate Health Care hospital between January 2006 and August 2013, performed microsatellite DNA typing on available isolates, and collected data from the Advocate Central Microbiology Laboratory Database to capture information related to our aims. Categorical variables were compared between groups using Fisher's exacts tests.

**Results.** *S. cerevisiae* was isolated in 38 patients. *S. boulardii* administration was documented in 45% of those patients (n=17; 71% children and 39% adults, p =0.2). The most common sites of isolation were blood (n=19) and abdominal abscesses or peritoneal fluid (n=6). DNA microsatellite typing revealed clonality between the *S. boulardii* capsule and isolated strains of *S. cerevisiae* from patients in 5 of 7 isolates tested. The risk of *S. cerevisiae* fungemia in patients receiving *S. boulardii* was 0.09% (7/7676) compared to 0.0014% (7/500338) in those who had not received *S. boulardii* [p = 0.00; RRR -64, CI: -205 to -20; NNT: 1114, CI: 725-2396]. Children receiving *S. boulardii* (2/490) were more likely to have a positive blood culture than adults (2/490 vs.5/7186) [p=0.069, OR: 5.9 (0.8-34.0), RR: 5.9 (0.8-33.7)]. Only 45% of patients were receiving Florastor® at the time of *S. cerevisiae* isolation, indicating potential for indirect transmission.

**Conclusions.** Despite increasing reports of invasive fungal infections due to *S. cerevisiae*, *S. boulardii* remains a remarkably safe drug. However, the risk of *S. cerevisiae* isolation from blood in patients receiving *S. boulardii* is significantly higher. Consideration of the risk-benefit ratio of this agent, particularly for critically ill or
immunocompromised patients receiving broad-spectrum antibiotics and those with indwelling catheters, must be emphasized. In addition, proper contact precautions must be implemented when handling S. boulardii preparations.

478  **HOMA, PHYSICAL ACTIVITY, LIPID PROFILE AND HEIGHT/AGE ACCORDING TO WHO IN COLOMBIAN SCHOOL OVERWEIGHT.** Carlos A. Velasco, Lina Valencia, Ofelia Florez, Oscar Jimenez, Pediatrics, University of Valle, Cali, Colombia

**Introduction:** One of the objectives of the Monitoring Program of Obesity and Overweight SOS Colombia, involves identifying the nutritional status of students in public and private schools. **Objective:** To determine the HOMA (index of insulin resistance), the PA physical activity (test strength endurance and aerobic capacity), lipid profile (LP) and anthropometry (BMI, and H/A according to WHO) overweight in schoolchildren of a public school from Cali, Colombia. **Methodology:** A descriptive non-experimental observational study type prevalence in school was made in a public school of Cali, Colombia to were taken, age, sex, weight, height, blood glucose, insulin, LP and PA. **Results:** There were 40 school 65% female, mean age 13.9±2.5 years (range 8-19), weight = 62.4±13.8 kg (range 29.8 and 86.5) and height = 1.55±0.12 mt (range 1.2-1.79). 51.2% had risk of overweight and 48.8% overweight. The PA was poor in 55.0%. All were normoglycemic; hypercholesterolemia showed 25.0% and 32.5% hypertriglyceridaemia; showed altered blood 42.5% rate, HOMA 52.5% and H/A 28.2%. **Conclusion:** More than a quarter of school overweight Public Educational Institution of Cali, Colombia showed altered to their nutritional status: 28.2% in the H/A, 52.5% in HOMA, 55.0% in PA and 80.0% in one or more of paraclinical LP (cholesterol, triglycerides, HDL-c, VLDL-c, LDL-c, arterial index).

479  **DIETARY FIBER CONSUMPTION IN COLOMBIAN INFANTS UNDER 2 YEARS AND FUNCTIONAL CONSTIPATION.** Carlos A. Velasco, Sandra Giraldo, Pediatrics, University of Valle, Cali, Colombia

**Introduction:** The inclusion of dietary fiber (DF), has multiple benefits on human health, but in pediatrics, wide gaps concerning the relationship of fiber and constipation. **Objective:** To describe bowel habit in infants <2 years of age and your fiber intake. **Methodology:** Descriptive observational not experimental in infants between 3-24 months of age with acute diagnoses first time without exclusive breastfeeding for 6 months who visited a University Hospital Level of care. This study was approved by the Institutional Ethics Committee. A nutritional survey was conducted by 24-hour recall before becoming ill. According bowel habit, were divided in infants with and without EF, and by age group in < and > infants. Consideration was given to breast-feeding, the start time of supplementary feeding and history of mother or caregiver with EF. The results are expressed as X ± SD. Statistical analysis included X2 and Spearman or Fischer test. **Results:** We studied 125 infants of 13±7 months, 86 male. There were no significant differences in age, sex, consumption of grams of fiber/d, or with breastfeeding, the start time of supplementary feeding and history of mother or caregiver with EF. **Conclusion:** We found no association between bowel habit and grams of fiber consumed, or breastfeeding, complementary feeding starting early and EF history of the mother or caretaker.

480  **PREVALENCE AND PREDICTORS OF OVERWEIGHT AND OBESE DIAGNOSIS IN A PEDIATRIC TRAINING PROGRAM.** Alaina K. Hersch, Marcelo Rains, Khiet Ngo, Megan Schwartz, Jessica Claridge, Belinda Dao, Yushi Lin, Nicole Choi, Pediatrics, Loma Linda University Children's Hospital, Irvine, CA

The rate of overweight (OW) and obese (OB) documentation in pediatric practices has been shown to be poor. Given that long-term practice habits often begin during training, it is important to better understand documentation practices during these formative years. **Objectives:**
1) Determine the prevalence of OW/OB documentation in a pediatric residency practice.
2) Understand the clinical factors associated with appropriate diagnosis of OW/OB.

**Methods:**
IRB-approved retrospective analysis of patients 2-21 years seen at Loma Linda University Children's Resident Clinic from June 1, 2011 to June 1, 2012. Medical records of patients meeting criteria for OW/OB status (BMI 85th-94th and > 95th %, respectively) were reviewed. Descriptive and bivariate analyses were conducted using SPSS v18. P-value < 0.05 was considered statistically significant. **Results:**
Of 4,359 patient records screened, 1,363 patients met criteria for OW/OB (a total of 662 females and 701 males). Prevalence of OW/OB was 35.6%. Less than half (46%) of OW/OB patients were appropriately diagnosed. Documentation of the following clinical variables was associated with appropriate OW/OB diagnosis: weight discussion, diet, exercise, screen time, previous diagnosis, co-morbidities, family risk factors, and/or physical exam (Table 1). Correct documentation of OW/OB status was associated with the following interventions: counseling (diet, exercise, and/or screen time), handouts, referrals (labs and/or sub-specialty), and follow up visits. **Conclusion:**
1) The prevalence of documentation of OW/OB status in a pediatric resident clinic is poor.
2) The prevalence of OB diagnosis was higher than OW diagnosis, suggesting practice preferences among trainees and their facilitators.
3) Documentation of physical exam findings on OW/OB patients was most strongly associated with a subsequent diagnosis.
4) Establishing a diagnosis of OW/OB effects subsequent intervention.
5) Results of this study support the development of programs to improve the rate of trainee recognition and diagnosis of OW/OB status in children.

Association between making the diagnosis of OW/OB with documented history items.

<table>
<thead>
<tr>
<th>Variable (History Item)</th>
<th>Documentation status of variable</th>
<th>Diagnosis of OW or OB Documented During Index Visit</th>
<th>p-value</th>
<th>Phi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual Weight Classification</td>
<td>Overweight</td>
<td>OW/OB Not Documented 435 (77.7%)</td>
<td>OW/OB Documented 125 (22.3%)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>OW/OB Not Documented 289 (36.5%)</td>
<td>OW/OB Documented 502 (63.5%)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>OW/OB Not Documented 372 (51.7%)</td>
<td>OW/OB Documented 347 (48.3%)</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>OW/OB Not Documented 353 (55.1%)</td>
<td>OW/OB Documented 288 (44.9%)</td>
<td></td>
</tr>
<tr>
<td>Asked about weight</td>
<td>Documented</td>
<td>OW/OB Not Documented 65 (31.9%)</td>
<td>OW/OB Documented 139 (68.1%)</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>Not Documented</td>
<td>OW/OB Not Documented 659 (57.1%)</td>
<td>OW/OB Documented 495 (42.9%)</td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>Documented</td>
<td>OW/OB Not Documented 687 (52.4%)</td>
<td>OW/OB Documented 625 (47.6%)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Not Documented</td>
<td>OW/OB Not Documented 38 (74.5%)</td>
<td>OW/OB Documented 13 (25.5%)</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>Documented</td>
<td>OW/OB Not Documented 293 (42.6%)</td>
<td>OW/OB Documented 394 (57.4%)</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>Not Documented</td>
<td>OW/OB Not Documented 432 (63.9%)</td>
<td>OW/OB Documented 244 (36.1%)</td>
<td></td>
</tr>
<tr>
<td>Sleep</td>
<td>Documented</td>
<td>OW/OB Not Documented 342</td>
<td>OW/OB Documented 299</td>
<td>0.71</td>
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<tr>
<td></td>
<td>Not Documented</td>
<td>OW/OB Not Documented 381</td>
<td>OW/OB Documented 337</td>
<td></td>
</tr>
<tr>
<td>Previous Dx</td>
<td>Documented</td>
<td>OW/OB Not Documented 7 (9.7%)</td>
<td>OW/OB Documented 65 (90.3%)</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>Not Documented</td>
<td>OW/OB Not Documented 716 (55.6%)</td>
<td>OW/OB Documented 572 (44.4%)</td>
<td></td>
</tr>
<tr>
<td>Family risk factors</td>
<td>Documented</td>
<td>OW/OB Not Documented 461 (49.2%)</td>
<td>OW/OB Documented 476 (50.8%)</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>Not Documented</td>
<td>OW/OB Not Documented 264 (62%)</td>
<td>OW/OB Documented 162 (38%)</td>
<td></td>
</tr>
<tr>
<td>Physical exam</td>
<td>Documented</td>
<td>OW/OB Not Documented 32 (9.6%)</td>
<td>OW/OB Documented 303 (90.4%)</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>Not Documented</td>
<td>OW/OB Not Documented 693 (67.4%)</td>
<td>OW/OB Documented 335 (32.6%)</td>
<td></td>
</tr>
</tbody>
</table>

**481 FREQUENCY OF STOOLS IS RELATED WITH DIETARY INTAKE IN CHILDREN WITH NIEMANN-PICK DISEASE TYPE C.** Liliana Ladino², Erika Ochoa¹, Natalia Sepulveda Valbuena³, ¹Departamento Nutrición y Bienestar Integral. Escuela de Ciencias para la Vida. Instituto Tecnológico y de Estudios Superiores de Monterrey., México D.F., Mexico; ²Universidad El Bosque. Facultad de Medicina. Instituto de Nutrición, Genética y Metabolismo IIINGM., Bogotá, Colombia; ³Departamento Nutrición y Bioquímica. Facultad de Ciencias. Pontificia Universidad Javeriana., Bogota, Colombia

**Background:** The intake of some nutrients has been related with the stool frequency, mainly with constipation and diarrhea. The patients NPC should control the carbohydrates intake in order to decrease the gastrointestinal disturbance caused by medical treatment. The relationship between nutrients intake and stool frequency in children with Niemann-Pick type C (NPC) has not been related so far.

**Aim:** The aim of this study was to identify if macronutrients intake and the percentage of total energy value (%TEV) is related with stool frequency in NPC patients in Colombia.

**Methodology:** Pediatric patients were recruited in a nutrition private practice in different cities of Colombia. Twenty-four hour dietary recalls in nine appointments was recorded and analyzed, considering as normal intake DRIs of the Food and Nutrition Board. Frequency stool was inquired in each appointment and was classified in four groups: Group 1: less than one stool per day, Group 2: one stool per day, Group 3: between 2 and 3 stools per day, and Group 4: more than three stool per day. ANOVA test with Bonferroni adjusted was used for the analysis in SPSS 21.0.

**Results:** Fourteen pediatric patients between 1 and 18 years of life were recruited. Stool frequency was related with
RESULTS

The HSCs was studied by immunofluorescence. HSC activation was determined by quantitation of the expression of pro-fibrogenic markers. Internalization of MPs into primary human HSC) for 6 and 24hrs. Migration was assessed by Boyden’s chamber and wound healing response (MPs vs. MP-free supernatant, p<0.001) and wound healing response (MPs vs. MP-free supernatant, p<0.002) mainly after 24hrs of incubation. MPs internalization by HSC was crucial for the MP effects and the HSC’s migration (MPs vs. MP-free supernatant, p<0.001) and wound healing response (MPs vs. MP-free supernatant, p<0.001) were increased. Exposure of primary HSC and LX2 cells to MPs released by hepatocyte during lipotoxicity resulted in a significant phenotypic change characteristic of their activation, with increased proliferation (MPs vs. MP-free supernatant, p<0.04) and wound healing response (MPs vs. MP-free supernatant, p<0.001). Wound healing response (MPs vs. MP-free supernatant, p<0.002) was mediated at least in part through a Vanin-1-dependent mechanism. Indeed, activation and migration of HSC were increased with hepatocytes-derived MPs and MP-free supernatant (VNN1 nAb) and controls were used to treat HSC (LX2 and human hepatoma cells (HepG2) were treated with a saturated free fatty acids (FFA) including palmitic acid (PA), and released MPs were characterized via flow cytometry. The activation of inflammatory cells by MPs was assessed in vitro using primary monocytes and macrophages in or in vivo using mouse peritoneal injection. In obese mouse model, the circulating MPs (cMPs) were characterized and the macrophage activation by cMPs was assessed via flow cytometry. To investigate the effect of MPs on liver inflammation, cMPs from obese mice were transplanted into lean mice by IV injection and monocyte activation was analyzed in the blood and liver via flow cytometry. The exposure of 3T3-L1 adipocytes to PA results in marked increase of MPs (p<0.01), with around 200 nm size. MPs activated primary monocytes (p<0.001) and macrophages (p<0.01), and recruited monocytes and macrophages in the mouse peritoneal cavity. The number of cMPs was dramatically increased in obese mice (p<0.001) and cMPs activated primary macrophages. Transplantation of cMPs from obese mice into lean mice resulted in significant activation of monocytes and macrophages and infiltration of activated macrophages in the liver. Conclusion: This study demonstrates for the first time that hypertrophied adipocytes release MPs that are novel contributors to liver inflammation through monocytes/macrophages activation.

492 HEPATOCYTES-DERIVED MICROPARTICLES RELEASED DURING LIPOTOXICITY INDUCE HEPATIC STELLATE CELLS ACTIVATION AND MIGRATION. Davide Povero1, Nadia Panera2, Akiko Eguchi1, Anna Alisi1, Valerio Nobili2, Ariel Feldstein1, 1Department of Pediatrics, UC San Diego, La Jolla, CA; 2Cleveland Clinic, Cleveland, OH; 3UCSD, La Jolla, CA

Background & Aim. Hepatic fibrosis represents the most worrisome histopathologic feature in non-alcoholic steatohepatitis (NASH) and it suggests a more severe and progressive liver damage. Understanding the mechanisms linking NASH to fibrogenesis is essential for defining potential novel therapeutic strategies. We have demonstrated that hepatocyte-derived microparticles (MPs) are released in the bloodstream during experimental NASH and their levels strongly correlate with severity of liver fibrosis. Here we tested the hypothesis that MPs released by hepatocytes during lipotoxicity alters hepatic stellate cells (HSC) biology resulting in its activation. Methods. For induction of lipotoxicity, the human hepatoma cells (HepG2) were treated with a saturated free fatty acids (FFA) including palmitic acid, or stearic acid, for up to 24hrs with various concentrations (0.25 to 0.50 mM). MPs and MP-free supernatant were isolated from cell-free supernatants by ultracentrifugation and quantitated by FACS analysis. Hepatocytes-derived MPs, MP-free supernatants, MP+Vanin-1 neutralizing antibody (VNN1 nAb) and controls were used to treat HSC (LX2 and primary human HSC) for 6 and 24hrs. Migration was assessed by Boyden's chamber and wound healing response while HSC activation was determined by quantitation of the expression of pro-fibrogenic markers. Internalization of MPs into the HSCs was studied by immunofluorescence. Results. Exposure of HSC with hepatocytes-derived MPs resulted in significant increase expression of key pro-fibrogenic genes, including α-SMA, TIMP1 and Collagen-I (p<0.01) and proliferation (MPs vs. MP-free supernatant, p<0.04). Exposure of primary HSC and LX2 cells to MPs released by hepatocyte during lipotoxicity resulted in a significant phenotypic change characteristic of their activation, with increased migration (MPs vs. MP-free supernatant, p<0.001) and wound healing response (MPs vs. MP-free supernatant, p<0.002) mainly after 24hrs of incubation. MPs internalization by HSC was crucial for the MP effects and was mediated at least in part through a Vanin-1-dependent mechanism. Indeed activation and migration of HSC were...
significantly abrogated by neutralizing Vanin-1 on the MPs by a specific neutralizing antibody (MP vs. MP+VNN1 nAb, p<0.04). Conclusion. Our study demonstrates that MPs released from dying hepatocytes during lipotoxicity are critical signals that contribute to HSC activation in a process dependent on Vanin-1 expression. These results provide a mechanistic link between MPs and liver fibrosis and has important implications for development of novel diagnostic and therapeutic strategies for patients with this condition.

493 PELD AS A PREDICTOR OF CHANGE TO SECOND-LINE THERAPY IN CHILDREN WITH AUTOIMMUNE HEPATITIS: A NATIONAL MULTI-CENTRE RETROSPECTIVE COHORT STUDY. Andreeanne N. Benidir1,2, Carolina Jimenez-Rivera3,4, Simon C. Ling1,2, Vicky L. Ng1,2, Binita M. Kamath1,2, The Canadian Pediatric Hepatology Research Group (CPHRG)5, 1Department of Pediatrics, University of Ottawa, Ottawa, ON, Canada; 2Department of Pediatrics, University of Toronto, Toronto, ON, Canada; 3Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 4Division of Gastroenterology, Hepatology & Nutrition, Children’s Hospital of Eastern Ontario, Ottawa, ON, Canada; 5Division of Gastroenterology, Hepatology & Nutrition, The Hospital for Sick Children, Toronto, ON, Canada

Background: Currently, there are no defined predictors of disease severity and treatment response in children with autoimmune hepatitis (AIH). Adult studies of AIH have shown a possible association between model of end-stage liver disease (MELD) score and resistance to first-line treatment, requiring escalation to second-line therapy. We sought to determine if the pediatric end-stage liver disease (PELD) score would similarly predict treatment-resistant disease in pediatric AIH at presentation.

Methods: A national multi-centre retrospective cohort database of children diagnosed with AIH between 2001 and 2009 was used to test the hypothesis that PELD is associated with change to second-line therapy. Children <18 years from 13 participating academic Canadian centres that fulfilled the IAIHRG criteria for AIH were included. Those with clear evidence of overlap with primary sclerosing cholangitis (PSC) at presentation, missing data on at least one PELD variable (albumin, INR, total bilirubin, age or history of growth failure), or whose initial treatment was other than prednisone ± azathioprine were excluded. PELD score was calculated for all patients regardless of age in order to have a comparable continuous variable for the entire cohort. Univariate analysis was performed to test the unadjusted association between PELD score and change to second-line therapy. To explore the contribution of potential predictors, we performed a change in parameter estimate to select one of four additional variables (conjugated bilirubin, ALT, age, IgG) for the final model. Based on sample size, only one additional non-collinear variable could be included. INR was excluded as it was collinear with PELD. A multivariable logistic regression model was then constructed and verification of assumptions was performed.

Results: Of the 172 children in the original cohort, 107 (61% female) were included in the analysis after exclusion criteria were applied. Median age was 11 years (range 2-17y). Mean PELD score was -3.70±8.07. Length of follow-up was 123 months (62-178 mos). Second-line therapy was used within 24 months of diagnosis in 14/107 (13%) patients. Univariate analysis revealed that a change to first-line therapy within the first 2 years was associated with a higher PELD score (p=0.04) and INR (Χ²=7.05, p=0.008). Change in parameter estimate was largest for conjugated bilirubin. In the multivariate model which adjusted for conjugated bilirubin, the odds of PELD being associated with a change to second-line therapy within 24 months of diagnosis was 1.12 (95% CI 1.02-1.23) (p=0.02).

Conclusion: This analysis of a multi-centre cohort of children with AIH demonstrates that a higher PELD score at presentation predicts subsequent change to second-line therapy in the first 2 years of follow-up. Future studies should explore the predictive value of INR alone as these data would suggest it is the most contributory variable to the association of PELD with second-line therapy.

Saturday, October 25, 2014
2 – 3:30pm

Research Session VII – Motility and Functional Disorders

NASPGHAN Neurogastroenterology and Motility Prize - Basic

494 THE INTERPLAY BETWEEN OROPHARYNGEAL, LUNG AND GASTRIC MICROFLORA IN PATIENTS TAKING ACID SUPPRESSION. Rachel L. Rosen1, Janine Amirault1, Lan Hu2, Doyle Ward3, Melanie Baskind1, Samuel Nurko1, 1Boston Children’s Hospital, Boston, MA; 2Dana Farber Cancer Institute, Boston, MA; 3The Broad Institute, Boston, MA

Background: We have previously shown that full column, non-acid reflux burden is highly associated with a positive bronchoalveolar lavage culture in children with respiratory symptoms. We have further shown that, when non-acid reflux burden is increased even further with acid suppression, additional changes in gastric and lung bacterial abundance and diversity ensue. However, what is not known is whether lung microflora changes result from direct aspiration of gastric fluid or of oropharyngeal contents that have been altered by full column, non-acid reflux.

Methods: We performed 16S deep sequencing on secretions from oropharyngeal swabs from 116 children, 57 off
proton pump inhibitors (PPIs) and 59 patients on PPIs. 16S sequencing results from oropharyngeal swabs were compared to 16S sequencing results from gastric and lung samples from the same patients. A subset 50 patients underwent pH-MII testing at the time of endoscopy. We compared differences in prevalence and relative abundance between oropharyngeal gastric and lung sites by creating prevalence ratios and performing Metastats analyses. We created correlation matrices between continuous reflux variables and bacterial abundance. Principal component analysis was performed to determine the uniqueness microflora populations.

**Results:** Ten different bacterial genera, including *Streptococcus*, were more abundant in the oropharynx of children taking PPIs, a finding of clinical importance as *Streptococcus* was also more abundant in the gastric fluid of PPI patients, suggesting a mechanism to explain the increased risk of pharyngitis in PPI treated patients. We also found that there was an increased prevalence of oropharyngeal *Butyrivibrion* (OR: 8.0, p=0.02), a bacteria more abundant in the lungs of PPI patients. Abnormal pH-MII testing was associated with increased concentrations of oropharyngeal *Chryseobacterium* (p=0.01), *Cloacibacterium* (p=0.004), *Fusobacterium* (p=0.03) and *Neisseria* (p=0.02), the latter two of which are known to cause pharyngitis and upper respiratory tract infections, respectively. There were significant correlations between the percentage of full column reflux episodes and oropharyngeal concentrations of *Fusobacterium* (p=0.02), *Neisseria* (p=0.009), and *Porphyromonas* (p=0.03). Full column, non-acid reflux was specifically correlated with concentrations oropharyngeal *Neisseria* (p=0.04). When comparing oropharyngeal to gastric and lung microflora, we found that, while there was significant overlap in bacterial genera in both the oropharynx and stomach, eight genera were found uniquely in the stomach. Of these eight, seven genera including classically enteric bacteria (*Proteus, Bacillus, Lactococcus, Leuconostoc, Lactobacillus, Bacteroidetes, and Pseudomonas*) were also abundant in the lungs suggesting direct exchange between sites independently of the oropharynx. Principal component analysis revealed that oropharyngeal microflora were distinct from both lung and gastric microflora.

**Conclusions:** We have proven that while some bacteria may enter the lungs through aspiration of oropharyngeal contents, some of the most abundant bacteria in the lungs originate from direct aspiration from the gastrointestinal tract independently of the oropharynx.

**NASPGHAN Neurogastroenterology and Motility Prize - Clinical**

495 **ALTERED AMYGDALA FUNCTIONAL CONNECTIVITY REFLECTS ABNORMAL EMOTIONAL PROCESSING IN PATIENTS WITH IRRITABLE BOWEL SYNDROME.** Xiaolin Liu1, Alan H. Silverman1, Mark Kern1, Douglas Ward1, Shi-Jiang Li2, Reza Shaker3, Manu R. Sood1, 1Division of Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI; 2Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI; 3Division of Gastroenterology, Medical College of Wisconsin, Milwaukee, WI

**Introduction:** Abnormal neurocognitive and emotional processing to visceral sensory signal have been implicated in visceral hypersensitivity in irritable bowel syndrome (IBS). However, the neural processes specifically involved in emotional expression and modulation of emotional responses in IBS patients are poorly understood. Amygdala, a key neuronal structure in the limbic system, plays a primary role in mediating emotional experience and regulating the generation of emotion-related behavioral responses. Here we seek to identify altered patterns of amygdala functional connectivity in pediatric IBS patients using functional magnetic resonance imaging (fMRI) techniques. Most reported fMRI studies of IBS in adults have focused on identifying brain activation to experimentally controlled visceral stimulation. Recent advances in neuroscience suggest that cognitive and affective processing requires the participation of large-scale distributed brain networks. Functional connectivity analysis that measures the temporal correlation among spatially distinct brain regions is an effective approach for identifying network function/dysfunction in a specific cognitive and mental state. We hypothesize that, compared with healthy controls, amygdala functional connectivity network in IBS patients will exhibit distinct patterns that reflect an elevated level of fear and anxiety to anticipatory rectal distension stimuli but a weak regulation of emotion-related behavioral responses.

**Methods:** Nine pediatric IBS patients (4 males; 12-17 y/o) and eight age-matched controls (5 males; 12-16) underwent two fMRI runs (3T; TR, 2s; RES, 3.75x3.75x4 mm3) under subliminal (below perception threshold) and liminal rectal distension stimulation set at 15±5 and 25±4 mmHg, respectively. Each run contains four repeat cycles of a 15-second pressure and a 25-second rest. Emotional responses of IBS patients in experimental runs were determined by functional connectivity of Amygdala seed (including left and right) manually drawn for each participant.

**Results:** Widespread but significantly different amygdala functional connectivities were observed in the two groups across the two rectal sensation settings. In the subliminal state, IBS patients exhibited prominently more amygdala-prefrontal connections than controls; frontal connections were significantly reduced in both groups in the liminal state. In contrast, controls showed substantial amygdala connections in the thalamus, insular and anterior cingulate cortices, caudate, putamen, and precuneus in both states; however, IBS patients did not.

**Conclusion:** The unique prominent amygdala-prefrontal connectivity in IBS patients during subliminal stimulation indicates the involvement of the prefrontal cortex in top-down modulation of the amygdala to contain fear and anxiety to anticipatory aversive rectal stimuli in IBS patients. The distinctive substantial amygdala connections in controls with a set of cortical and subcortical areas involved in autonomic regulation of visceral states suggest that normal regulation
of emotion-related behavioral responses is compromised in IBS patients. Our study provides for the first time neuroimaging evidence of altered amygdala connectivity reflecting abnormal emotional processing in IBS patients.

**496 DIETARY PROBIOTICS AND PREBIOTICS PREVENT THE DEVELOPMENT OF VISCERAL HYPERALGESIA IN A RAT MODEL OF NEONATAL COLONIC IRRITATION.** Pradeep Kamamapathi, Adrian Miranda, Soumya Pochiraju, Maciej Chichlowski, Brian M. Berg, Colin Rudolph, Mitchell Bruckert, Jyoti N. Sengupta; Global Discovery R&D, Mead Johnson Pediatric Nutrition Institute, Evansville, IN; Pediatrics, Medical College of Wisconsin, Milwaukee, WI; Gastroenterology, Medical College of Wisconsin, Milwaukee, WI

**Objectives:** To determine if prebiotic or probiotic treatment can alter colonic sensitivity in a neonatal rat model of chronic visceral hyperalgesia and to investigate the effect on the neurotransmitter levels in brain regions involved in pain modulation. **Methods:** Chronic visceral hyperalgesia was induced in rats by administration of intracolonic zymosan for three days during postnatal day 14-16 (P14-P16). Controls received intracolonic normal saline. On postnatal day 21 (P21), rats were fed control (AIN-93G) or prebiotic diet (polydextrose (PDX) and galactooligosaccharides (GOS); 7g/kg of diet). A different group of rats were fed control diet along with probiotic Lactobacillus rhamnosus GG (LGG). The probiotic was administered daily in the drinking water starting at P21. The viscero-motor response (VMR) to graded colorectal distension (CRD) was used as a method of assessing colonic sensitivity to mechanical stimulation in all rats. Serotonin, noradrenaline and dopamine levels were quantified in the frontal cortex, sub-cortex, brain stem and cerebellum in all groups at P60 using HPLC-based separation followed by fluorescent and/or electrochemical detection. **Results:** Intracolonic zymosan during the neonatal period resulted in visceral hyperalgesia in adult rats as evidenced by a higher VMR at CRD pressures >20mmHg. Supplementation with prebiotic (PDX/GOS) diet prevented the development of visceral hyperalgesia in zymosan treated rats. Similarly, rats treated with LGG did not develop visceral hyperalgesia. Rats treated with LGG exhibited higher levels of serotonin, noradrenaline and dopamine in all brain regions examined compared to control. **Conclusions:** Neonatal colonic irritation with zymosan results in visceral hyperalgesia during adulthood that is prevented by consumption of the prebiotic (PDX/GOS) or the probiotic LGG. LGG significantly alters the level of neurotransmitters in brain regions that are involved in pain modulation.

**497 GASTROESOPHAGEAL REFLUX BURDEN, EVEN IN PATIENTS THAT ASPIRATE, DOES NOT INCREASE RISK OF HOSPITALIZATION.** Daniel R. Duncan, Janine Amirault, Heather J. Litman, Rachel L. Rosen, Boston Children's Hospital, Boston, MA

**Background:** In many institutions, prophylactic fundoplication is performed in neurologically compromised children who aspirate in an effort to prevent urgent pulmonary hospitalizations. However, there are no studies to determine if a higher reflux burden increases the risk for hospitalization, particularly in patients who aspirate. The aim of this study was to determine if rates of hospitalization were affected by reflux burden after adjusting for aspiration risk. **Methods:** We prospectively recruited a cohort of 70 pediatric patients who underwent multichannel intraluminal impedence with pH (pH-MII) and modified barium swallow (MBS) studies. Patients were followed for 1 year after the initial MBS to determine the number, length and types of hospitalizations. Hospitalizations were categorized into pulmonary or gastrointestinal. Hospitalization data are presented as mean number of days (standard error) and mean number of admissions (standard error). pH-MII testing was considered abnormal if the pH was <4 for >6% of the study time or if there were greater than 73 reflux episodes detected during the study time. Proximal reflux burden was calculated by summing the bolus clearance times of the most proximal sensor and dividing by the total study duration. A negative binomial regression model was fit to consider predictors of hospitalization days and admissions. **Results:** The mean age of patients in the study was 5.7 years (±0.5 years). Nineteen percent of patients had an abnormal MBS and twenty percent of patients had an abnormal pH-MII study. The median (interquartile range) number of acid, non-acid, pH only and total reflux episodes were 22 (12, 32), 16 (10, 32), 5 (2, 15) and 40 (25, 63). There was a statistically significant inverse relationship between reflux and total admission nights before adjusting for neurologic status (p=0.03); however, this was attenuated after adjusting for neurologic status (p=0.16). As shown in the table, there was no statistically significant relationship between reflux burden and total admissions after adjusting for aspiration by MBS and neurologic status. There were no statistically significant relationships between reflux burden and the number of urgent pulmonary admissions (p=0.86), total GI hospitalization days (p=0.11) or total pulmonary hospitalization days (p=0.56) before or after adjusting for neurologic status and aspiration risk. There were no urgent GI admissions in either of the groups. **Conclusions:** Even in aspirating children, reflux burden did not increase the risk of hospitalization. Based on these results, routine reflux testing, which is costly and often traumatic, cannot be recommended even in aspirating children, as the results do not impact clinically significant outcomes.
Comparison between reflux burden and hospital admissions

<table>
<thead>
<tr>
<th></th>
<th>&lt;73 Reflux Episodes</th>
<th>≥73 Reflux Episodes</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>Total number of admissions</td>
<td>2.7 (0.3)</td>
<td>2.0 (0.5)</td>
<td>0.24</td>
</tr>
<tr>
<td>Total number of urgent admissions</td>
<td>0.8 (0.3)</td>
<td>0.5 (0.4)</td>
<td>0.64</td>
</tr>
<tr>
<td>Total admission nights</td>
<td>5.8 (1.0)</td>
<td>3.5 (1.2)</td>
<td>0.17</td>
</tr>
<tr>
<td>Total urgent admission nights</td>
<td>2.3 (1.2)</td>
<td>1.1 (1.2)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Data are presented as means (standard error). Data are adjusted for aspiration risk and neurologic status.

Saturday, October 25, 2014
3:45 – 5:30pm
Research Session VIII – Nutrition

NASPGHAN Nutrition Prize

498 A LOW FODMAPS DIET AMELIORATES SYMPTOMS IN CHILDREN WITH IRRITABLE BOWEL SYNDROME: A DOUBLE BLIND, RANDOMIZED CROSSOVER TRIAL. Bruno P. Chumpitazi, Cynthia M. Tsai, Ann R. McMeans, Robert Shulman, Pediatrics, Baylor College of Medicine, Houston, TX

Background: A low FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet ameliorates gastrointestinal (GI) symptoms in adults with irritable bowel syndrome (IBS). We previously demonstrated efficacy of a low FODMAPs diet in a small, open-label pilot study. A rigorous dietary intervention trial evaluating the efficacy of a low FODMAPs diet in children has not been conducted to date.

Methods: Children, ages 7-17 yrs, with Pediatric Rome III IBS were enrolled. During a 7-d baseline period they recorded abdominal pain episodes (frequency and severity [0-10 scale]) and stooling characteristics using a validated diary. In addition, other associated GI symptoms (abdominal discomfort, bloating, flatulence, nausea, and heartburn) were captured. Following the baseline period, participants entered a randomized, double blind, crossover design in which either a high (0.7 g/kg/day; up to 50 g/d) or low (0.15 g/kg/day; up to 9 g/d) FODMAPs diet was provided for 48 hr. The provided diets were matched for overall number of calories. A minimum 5-d washout period occurred between dietary interventions. On the diets, children captured the same measures as during the baseline period. On the 2nd day of each dietary intervention period, subjects collected hourly breath hydrogen samples for up to 15 hr.

Results: Fifty-two children were enrolled of whom 33 completed both arms of the crossover trial. Of those completing the trial, 22 (67%) were female, and mean age was 11.5 ± 3.0 (SD) yrs. The number of calories consumed did not differ between the two intervention periods. Children had fewer daily abdominal pain episodes during the low FODMAPs period as compared to baseline (2.2 ± 2.0 vs 2.6 ± 1.8, respectively, P<0.01) but not during the high FODMAPs (2.4 ± 2.1) period. Mean pain severity decreased during both the low and high FODMAPs period compared to baseline (2.7 ± 2.5 and 2.7 ± 1.9, respectively, P<0.01). The proportion of children demonstrating a ≥50% decrease in abdominal pain frequency did not differ between the low FODMAPs (13/33) vs. high FODMAPs (11/33) periods. Similarly, there were no significant differences identified in pain characteristics or other measured GI symptoms when comparing the two intervention periods over 48 hours. However, during the 2nd day of the low FODMAPs vs. high FODMAPs period there was less bloating (P<0.05), less nausea (P<0.05), and trend toward decreased abdominal discomfort (P=0.08). Breath hydrogen production was lower on the low vs high FODMAPs diet (9355 ± 4075 vs 11013 ± 4467 ppm*min, respectively; P=0.05). Methane production did not differ between dietary intervention periods.

Conclusions: In children with IBS a low FODMAPs diet appears to: 1) Improve GI symptoms within 48 hr.; 2) Decrease breath hydrogen production vs. a high FODMAPs diet implying a change in gut microbiome metabolism.

499 THE IMPACT OF RAPID INFANT WEIGHT GAIN ON SUBSEQUENT CHILDHOOD OBESITY IN AN URBAN, LATINO COHORT. Jacob Robson, Sofia Verstraete, Melvin B. Heyman, Janet Wojcicki, University of California San Francisco, San Francisco, CA

Background: Disproportionate rates of childhood obesity are prevalent in urban minority populations, especially Latinos. Childhood obesity predicts adult obesity, as well as the early onset of obesity-related co-morbidities; this has led to an effort to identify early, potentially preventable, predictors of obesity. One identified predictor of obesity is rapid infant weight gain (RIWG), which is thought to influence adipocyte and hormonal set points throughout childhood and into adulthood. With Latino children at particularly high risk for obesity, we sought to analyze the impact of RIWG in infants with normal birth weights (2.5-4kg) in a large, urban cohort of Latino children, controlling for key confounding maternal and infant factors.

Design/Methods: Latina women were recruited during pregnancy at two hospitals in San Francisco for a prospective cohort study to evaluate predictors of childhood obesity. The primary predictor was RIWG, defined as change in
weight-for-age Z-score >0.67 standard deviations between birth and 6 months of age. The primary outcome was obesity (body mass index [BMI] >95th percentile) at 4 years of age. Chi-square and t-tests were applied to evaluate associations between maternal and infant factors and RIWG. Confounders of the relationship between RIWG and obesity were identified and controlled for in a logistic regression model.

**Results:** RIWG was documented in 84/174 (48%) of infants who were still in follow up at 4 years of age. Factors significantly associated with RIWG included female gender (p=0.03), lower birth weight (p<0.01), shorter gestational age (p<0.01) and later introduction of solids (p=0.02). In unadjusted analysis, RIWG was not associated with obesity at 4 years of age, although mean BMI percentile was higher in children with RIWG compared to those with normal weight gain (p<0.01). After adjusting for confounding maternal and infant factors, RIWG (OR 4.19, 95% CI: 1.41-12.49, p=0.01) and lower birth weight (OR: 2.73, 95% CI 1.44-5.18, p<0.01) were associated with obesity at age 4. Conversely, higher maternal age at childbirth (OR 0.95, 95% CI: 0.82-0.99, p=0.04) showed a slight negative association with obesity at age 4. Weight-for-age Z-score was a strong predictor of obesity, with a considerably stronger association for those born in the lower half (2.5-3.25kg) of the normal weight spectrum (OR 7.71, 95% CI: 2.35-25.37, p<0.01) than in the upper half (3.25-4kg) (OR 2.14, 95% CI 1.01-4.53, p=0.04).

**Conclusions:** Urban Latino infants who displayed rapid weight gain were at an increased risk of early childhood obesity. RIWG remained a key predictor of obesity after adjustment for factors known to modulate obesity, including breastfeeding, age solids were introduced, maternal depression and birth weight. This analysis is the first to show that RIWG is an important predictor of obesity across a wide spectrum of birth weights, not just among those with low/low-normal birth weight who display rapid catch up growth. These findings suggest a need for close monitoring of infant weight gain and development of interventions for those that display rapid gain prior to the 6-month visit.

Supported in part by NIH grants K01 DK080825 and T32 DK007762.

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**500 PIGLETS WITH NECROTIZING ENTEROCOLITIS HAVE ALTERED PLASMA BILE ACID PROFILES.**

Michaela C. Kollisch-Singule1, Steven R. Davis2, Randal Buddington3, 1General Surgery, SUNY Upstate Medical University, Syracuse, NY; 2Abbott Nutrition, Columbus, OH; 3Department of Health and Sport Science, University of Memphis, Memphis, TN

**Background:** Neonatal necrotizing enterocolitis (NEC) is a serious clinical problem that, once established, is refractory to treatment. NEC is associated with an altered microbiome, but a specific NEC microbiome profile has not been identified. We investigated if NEC is associated with an altered metabolic profile of the GI bacteria that could be used to predict and target infants at risk of developing NEC, with the focus on bile acid metabolism.

**Methods:** Premature piglets born at 92% of gestation were maintained on parenteral nutrition for 48h until T0h. Piglets were then randomized to feeding with infant formula that induces NEC (n=8) or colostrum that prevents NEC (n=9). Plasma samples were collected every 12 h until T72h and submitted for analysis using Metabolon's global metabolic profiling platform. Necropsies were performed at T72h and NEC grading was defined as: Absent (n=7), Mild (n=7) or Severe (n=3) and was based on small intestine gross pathology.

**Results:** There was a direct relationship between NEC severity and an increase in plasma levels of cholate, hyodeoxycholate, gamma-muricholate and 7-ketolithocholate levels (Table 1). Hyodeoxycholate achieved significance between Severe and Absent (RR 4.50;p<0.05). Piglets that developed Severe NEC also demonstrated increased hyodeoxycholate levels between T0h and T12h before clinical NEC was detected (RR 5.88;p<0.05).

**Conclusions:** The elevations in secondary bile acids associated with NEC 1) are suggestive of increased bile acid deconjugation by the GI microbiome or poor reabsorption by the ileum and 2) may serve as an early marker of NEC or may be a potential target for therapy. Ongoing evaluation of the metabolome data is being performed to search for other plasma-borne metabolites that can be used as biomarkers for early diagnosis of NEC.

**Bile Acid Profile of Piglets by NEC Severity**

<table>
<thead>
<tr>
<th></th>
<th>Bile Acid</th>
<th>Mild vs. None</th>
<th>Severe vs. None</th>
<th>Severe vs. Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Cholate</td>
<td>1.36</td>
<td>2.84</td>
<td>2.09</td>
</tr>
<tr>
<td>Secondary</td>
<td>Hyodeoxycholate</td>
<td>2.19</td>
<td>4.50*</td>
<td>2.05*</td>
</tr>
<tr>
<td>Secondary</td>
<td>Gamma-muricholate</td>
<td>1.30</td>
<td>3.20*</td>
<td>2.47*</td>
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<tr>
<td>Secondary</td>
<td>7-ketolithocholate</td>
<td>1.63</td>
<td>3.23</td>
<td>1.98</td>
</tr>
</tbody>
</table>

Table 1. Data reported as ratios of bile acids. *=0.05≤p≤0.10. ¶=p<0.05.
TOTAL PARENTERAL NUTRITION (TPN) CAUSES GUT MUCOSAL ATROPHY AND HYPERBILIRUBINEMIA: WE DESCRIBE A NOVEL ULTRA-MOBILE AMBULATORY MODEL. Ajay K. Jain, Joy X. Wen, Sumit Arora, Keith S. Blomenkamp, Abhineet Sharma, Shaz Iqbal, Jonathan Rodrigues, Victor Liou, Timothy A. Blaufuss, John P. Long, Jeffrey H. Teckman, Pediatrics, Saint Louis University, St Louis, MO

Background: Total Parenteral Nutrition (TPN) provides all nutrition intravenously. Though TPN therapy has grown enormously; it causes significant complications, including gut and hepatic dysfunction. In humans, TPN is provided in an ambulatory manner allowing complete mobility. Current models employ animal tethering which is much unlike human ambulatory TPN delivery. Hypothesis: We hypothesized that TPN can be delivered in an ambulatory fashion using ambulatory pumps and that TPN would cause gut and hepatic injury. Methods: Neonatal piglets were implanted jugular vein (JV), duodenal catheters (DC) which were exteriorized between the scapulae. Animals were fitted in dual pocket jackets. An ultra-mobile ambulatory pump was placed in one pocket and connected to JV or DC. Isocaloric TPN solution or swine milk was placed in ethylene vinyl acetate (EVA) bags in the other pocket. Bags were regularly replaced. Rigorous continuous wi-fi based video and scheduled monitoring was done. Daily weight and study samples were collected. Results: Mean daily weight gain (grams) for Enteral Fed control (EN) vs TPN animals, standard deviation (±SD) was 102.4±10.8, 91.03±12.1 respectively, (p<0.05). TPN caused significantly increased conjugated bilirubin level and hepatomegaly. Mean serum conjugated bilirubin (µmol/L) and (±SD) was 1.5±0.7 for EN and 6.3±2.8 for TPN, (p<0.05). Marked gut atrophy was noted with TPN. The mean gut weight as a percent of body weight, (±SD) was 4.30±0.26 for EN and 2.62 ± 0.48 for TPN (p<0.05). Catheter sites, surgical wounds healed well. All animals remained completely mobile. Conclusion: TPN was successfully delivered using ambulatory pumps establishing a model that closely replicates human TPN delivery and TPN related complications. Significant gut atrophy, hepatomegaly and bilirubin elevation were noted with TPN infusion.

Saturday, October 25, 2014
3:45 – 5:15pm

502 USE OF ENDOSCOPIC NEEDLE-KNIFE IN THE RESECTION OF UNUSUAL BRIDGING POLYP LESIONS IN A PATIENT WITH GENERALIZED JUVENILE POLYPOSIS SYNDROME. Quin Y. Liu, Russell Merritt, Vrinda Bhardwaj, Pediatrics, Children's Hospital Los Angeles/University of Southern California, Los Angeles, CA

Introduction: Juvenile polyposis syndrome (JPS) is characterized by multiple juvenile polyps throughout the gastrointestinal tract. Juvenile polyps usually are pedunculated and routinely removed with snare cautery. We encountered a patient with JPS with unusual polyp lesions that bridge one side of the intestinal lumen to the opposite side. We report a novel use of the endoscopic needle-knife to aid in the resection of these polyps.

Case and endoscopic technique description: A 9-year-old boy with tetralogy of Fallot and pulmonary stenosis status-post surgical repair with no family history of gastrointestinal polyps presented with chronic diarrhea, abdominal pain, growth failure and intermittent rectal bleeding. Physical exam reveals abdominal ascites and hepatosplenomegaly. Laboratory assessment revealed anemia, hypoalbuminemia, low protein S and C, and elevated stool alpha-1 antitrypsin levels indicating protein-losing enteropathy. Endoscopy was performed to evaluate the patient's GI bleeding. Upper endoscopy revealed numerous pedunculated polyps in the stomach and duodenum. The duodenum had several polyps that bridged one side of the intestinal lumen to the opposite side. The polyps appeared to have stalks on each side of the lumen. Colonoscopy also revealed numerous pedunculated polyps throughout the colon along with lumen bridging polyps like those in the duodenum. The sigmoid region had a polyp with 3 different stalks/attachments to the intestinal lumen. The polyps appeared to have stalks on each side of the endoscopy revealed numerous pedunculated polyps in the stomach and duodenum. The duodenum had several polyps that bridged one side of the intestinal lumen to the opposite side. The polyps appeared to have stalks on each side of the lumen. Colonoscopy also revealed numerous pedunculated polyps throughout the colon along with lumen bridging polyps with greater than one stalk were consistent with juvenile polyps. Erosions, chronic and acute inflammation and granulation tissue formation were present. There was no evidence of dysplasia or malignancy. Genetic evaluation of the patient was negative for SMAD, FAP, STK 11 and other markers for known polyposis syndromes.

Discussion: Although cancer risk with JPS is relatively low, screening for dysplasia and removal of suspicious or symptomatic polyps is recommended. Juvenile polyposis syndrome with polyp lesions consisting of two or three stalks is rarely seen. Such lesions present a challenge to the endoscopist who is monitoring and treating such patients. In JPS patients with these unusual bridging polypoid lesions, use of the endoscopic needle knife can facilitate snare polypectomy.
503 NIGHT OUT FOR STEAK AND BAND: INNOVATIVE USE OF THE MULTIPLE BAND LIGATOR IN ENDOSCOPIC MANAGEMENT OF ESOPHAGEAL FOOD BOLUS IMPACTION. Joelle Roskens, Sarah Matchan, Angela Deubel, Stephen Nanton, Pediatrics, Avera McKennan Hospital, Sioux Falls, SD

Esophageal food bolus impaction usually occurs in association with underlying esophageal motility or structural pathology. The impacted food bolus often consists of meat and may cause partial or complete esophageal obstruction. Patients with total esophageal obstruction are unable to manage secretions and require emergent intervention. Patient with esophageal food impaction without complete obstruction may be managed with urgent endoscopy.

A variety of tools are available for the endoscopic management of food bolus impaction depending on the texture of the food bolus. These tools include; retrieval net, friction-fit adaptor, banding cap and polypectomy snare. En bloc removal is often desired, however, the food extraction often requires a tedious piecemeal approach, which is often time consuming requiring multiple passes of the endoscope.

A push technique in which gentle pressure is applied to the center of the food bolus in an attempt to push the bolus into the stomach may also be attempted. However, care must be applied due to the high incidence of esophageal abnormalities associated with food impactions.

We describe our approach to the management of esophageal food bolus impaction in a 17 year old male with a 4 hour history of food bolus impaction while eating steak that presented with significant drooling and inability to manage oral secretions and complained of a foreign body sensation in his mid chest. Initial attempts at food bolus extraction using foreign body forceps, retrieval net and suction technique using banding cap resulted in only piece meal extraction. We therefore devised a variation of the banding cap technique in which the proximal aspect of the food bolus was suctioned into the banding cap and multiple band ligators were deployed onto the food bolus itself to form a secure anchoring point. A retrieval snare was then applied directly on to this anchor and after gentle traction, the entire 5 cm long food bolus was extracted en bloc.

Our technique of directly banding the food bolus was not previously described. The band of ligators prevents the retrieval snare from slicing through the food bolus when tension is applied. Our technique may represent an important addition to the therapeutic options for en bloc extraction of esophageal food bolus impaction especially those which are harder in texture, such as steak. It appears to be more effective than applying suction alone as used in the friction-fit adaptor or banding cap technique.

Our banding technique for esophageal food bolus extraction utilized the skills that most endoscopists already possess and the technique can be applied to both adult and pediatric patients. Further studies are needed to ascertain the utility and efficacy of our technique.

504 PEDIATRIC PER-ORAL ENDOSCOPIC MYOTOMY (POEM) FOR ACHALASIA. James Wall1, Stephanie Chao1, William Berquist1, 2, Pediatric Surgery, Lucile Packard Children's Hospital Stanford, Stanford, CA; 1Gastroenterology, Lucile Packard Children's Hospital Stanford, Stanford, CA

Introduction: Per-oral Endoscopic Myotomy (POEM) is a transmural endoscopic surgical technique that is gaining widespread adoption in the management of adult achalasia. The endoscopic approach offers excellent access to the muscular wall of the esophagus enabling division of the abnormal circular fibers. The procedure offers the benefits of being incisionless, preserving the outer longitudinal esophageal muscle fibers and avoiding a hiatal dissection.

Functional luminal imaging measures the diameter and pressure of the esophagus allowing intraoperative assessment of the endoscopic myotomy effect on the gastroesophageal junction.

Methods: 3 pediatric POEM procedures were performed at our institution under IRB approval. The average age of the patients was 16 years 10 months. 2 patients underwent intraoperative luminal imaging.

Results: POEM was completed in all 3 cases without major complications. All patients had a decrease in Eckardt scores at 1-month follow-up. Functional imaging of the gastroesophageal junction demonstrated an increase in minimum cross-sectional area from 22mm² pre-operatively to 55.5mm² postoperatively and an increase in distensibility index from 1.07mm²/mmHg preoperatively to 2.55mm²/mmHg postoperatively.

Conclusion: POEM is technically feasible in the pediatric population by pediatric specialists. Initial follow-up reveals symptomatic relief in all patients. Long-term follow-up is needed to characterize the outcomes of POEM in pediatric esophageal motility disorders. Expanding advanced endoscopic interventional skills by pediatric specialists is important to develop less invasive options for childhood diseases.

505 B-CELL LYMPHOMA PRESENTING WITH RECTAL BLEEDING IN A PEDIATRIC PATIENT WITH PROTEIN LOSING ENTEROPATHY. Quin Y. Liu, Russell Merritt, Vrinda Bhardwaj, Pediatrics, Children's Hospital Los Angeles/University of Southern California, Los Angeles, CA

Introduction: Protein losing enteropathy (PLE) is a complex disorder characterized by enteric protein loss, often associated with cardiovascular abnormalities, particularly those with elevated right sided venous pressure. Presenting signs and symptoms of PLE include abdominal bloating, ascites, pleural effusions, diarrhea, edema, and failure to

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SUCCESSFUL SMALL BOWEL ENTEROSCOPY AND DILATION FOR INFLAMMATORY JEJUNAL STRICTURE IN FIBROSTENOTIC CROHN’S DISEASE. Diana G. Lerner, Bhaskar Gurram, Joshua Noe, Medical College of Wisconsin, Milwaukee, WI

Background: Small bowel dilation with/without steroid injection has been reported to be safe and surgery sparing for stricturing Crohn's disease. It is unknown if this technique is useful in inflammatory strictures and limited data is available on length of dilation and maximal diameter of dilation needed for symptom resolution in the pediatric population.

Case Report: 14-year-old male presents with acute small bowel obstruction requiring a resection of 40 cm of proximal ileum and distal jejunum. Post operatively; he is started on Cimiza 400 mg sub-Q every month. He did well for one year and then developed abdominal pain and poor weight gain. Labs showed increasing CRP. MRE was done and showed 6 cm of concentric wall thickening, enhancement and restricted diffusion at the terminal ileum and 7 cm area of jejunum. Enteral therapy was discussed but he was reluctant to start and 6-MP at 1mg/kg was added to Cimzia as well as budesonide 9 mg daily. Multiple subsequent MRE studies showed progression of small bowel disease. Eight months prior to procedure MRE showed small bowel dilation. Patient continued to experience nausea, vomiting, and post-prandial abdominal pain. He was started on 40 mg of prednisone and the 6-MP dose was increased and optimized. Symptoms improved until steroids were weaned. Three months prior to procedure MRE showed progressive narrowing and G tube was placed for enteral nutrition therapy. However two weeks after starting the therapy patient did not tolerate the rate and was admitted with concerns of acute small bowel obstruction. He underwent a single balloon enteroscopy under fluoroscopic guidance. Small ulcers were seen in the proximal small bowel with otherwise normal mucosa. Mid to distal jejunum he was found to have very dilated small bowel and an inflammatory ulcer causing a near complete obstruction. Fluoroscopy was used to document no passage of contrast through the stricture. Enteroscope was then slowly passed through the stricture with minimal resistance. Stricture was measured at 5 cm in length. Post stricture bowel appeared normal. Diameter of the enteroscope with the splinting tube is 13.2 mm. Scope was withdrawn slowly and minimal amount of bleeding was seen. CRE balloon was then used to dilate the stricture to 10mm and then to a maximal diameter of 11 mm and pressure was held for one minute each time. When using CRE balloons it is possible to see through the balloon if the endoscope is pushed up to the balloon at the time of the dilation. Post dilation, contrast easily passed through the stricture. Patient was observed overnight and was able to tolerate his enteral feeds at 150cc/hr. He was discharged home and has been doing well to date on Cimiza, 6-MP and general diet.

Conclusion: Stricture dilation was successful in improving symptoms of small bowel obstruction, quality of life and preventing further surgical intervention. Further multicenter studies are needed to evaluate this surgery sparing technique as a primary intervention for pediatric stricturing Crohn's disease.
507 ENDOSCOPIC CLOSURE OF GASTROCUTANEOUS FISTULAS: USE OF AN OVER THE SCOPE CLIP (OTSC). Shelly Rustagi, Mary K. Boruta, Robert E. Kramer, Pediatric Gastroenterology, Hepatology and Nutrition, University of Colorado School of Medicine, Aurora, CO

When gastrostomies are present for more than 8-12 months, there is a 22-44% risk of development of a persistent gastrocutaneous fistula following removal of the gastrostomy tube. A persistent gastrocutaneous fistula can result in leakage of gastric contents with resulting skin breakdown and discomfort. There are numerous modalities available to attempt closure of gastrocutaneous fistulas including surgery, medical management and endoscopic interventions. The most common endoscopic therapy to close gastrostomies is use of endoclips to approximate the edges of the fistula. A newer modality for endoscopic closure of gastrostomies is use of over the scope clips (OTSCs), which have been reported to have up to a 91.7% success rate of resolving gastrointestinal fistulas. We report two cases of gastrocutaneous fistula closure with use of an over the scope clip device. Through the presentation of the cases, we demonstrate the endoscopic technique of closing gastrostomy fistulas with over the scope clipping through the assistance of suction, twin grasper device and anchoring device. We also exhibit evolution of a gastrocutaneous fistula following OTSC with follow-up endoscopy. This video highlights a newer modality of endoscopic closure of a gastrostomy. OTSC closure of gastrocutaneous fistulas may be a less invasive and more cost effective alternative to surgery.

508 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT IN CHILDREN. Robert E. Kramer, 1Pediatrics, University of Colorado, Aurora, CO; 2Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital Colorado, Aurora, CO

Percutaneous endoscopic gastrostomy placement is one of the core interventional procedures performed by pediatric gastroenterologists and carries a relatively high risk of complications. The risk of early complications has been reported to be as high as 41% while the risk of late complications as high as 52%. The volume of these procedures, however, can be limited, making proficiency and comfort with these procedures a challenge. Up to 42% of training programs studied do not offer training in performance of PEG placement. The purpose of this video, therefore, is to provide a brief visual reference for endoscopists that can be easily reviewed prior to performing this procedure, as well as used in the training of fellows. Review of the indications, contraindications and post-endoscopy management of PEG insertion is beyond the scope of this video. Instead, the focus is on providing a step-by-step guide for PEG insertion, while highlighting potential pitfalls.