
The diagnostic value of upper endoscopy (EGD) to detect positive histology in relation to symptoms has not been adequately investigated. Hyams JS reported that 62% of his EGDs cohort had normal histology (JPGN 2000).

**Aim:** to evaluate the correlation between symptoms and histology in children undergo the first diagnostic EGD.

**Method:** A retrospective chart review of the first diagnostic EGD in children (2006- 2011) was performed. Demographic, symptoms and histology were recorded. Mucosal biopsies from the esophagus, stomach and duodenum were available in all patients. Children with the diagnostic criteria of chronic abdominal pain were excluded.

**Results:** 728 endoscopy charts were reviewed. Symptoms distribution was: abdominal pain (64%), N&V (23%), FTT (6.4%), GI bleed (6%), and dysphagia (5.6%). Pathology distribution was: gastritis (56%), esophagitis (37%), duodenitis (11%), EoE (10%), and H. pylori-gastritis (2%) (Table 1). In 260 (36%) procedures, no pathology was found in none of the biopsies (esophagus, stomach or duodenum). The sensitivity and specificity to detect mucosal pathology for any symptom ranged between 56- 68% and 34- 40%, respectively, with no significant differences among the symptoms (Table 2).

**Conclusion:** In over a third of our EGD's no mucosal pathology was found. The accuracy rate to detect pathology was approximately 80% for abdominal pain, but was below 50% for all other presenting symptoms. With increasing cost of EGDs, cost analysis calculation is needed in order to assess the diagnostic and economic value of this procedure in children with various GI symptoms.

Table 1: Presenting symptoms and histology

<table>
<thead>
<tr>
<th>Histology</th>
<th>AbPain</th>
<th>N&amp;V</th>
<th>FTT</th>
<th>GI bleed</th>
<th>Dyspha.</th>
</tr>
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<tbody>
<tr>
<td>Negative</td>
<td>146 (31%)</td>
<td>61 (36%)</td>
<td>19 (40%)</td>
<td>19 (43%)</td>
<td>15 (36%)</td>
</tr>
<tr>
<td>Positive</td>
<td>321 (69%)</td>
<td>107 (64%)</td>
<td>28 (60%)</td>
<td>25 (57%)</td>
<td>26 (64%)</td>
</tr>
<tr>
<td>Total: 728</td>
<td>467 (64%)</td>
<td>168 (23%)</td>
<td>47 (6.4%)</td>
<td>44 (6%)</td>
<td>41 (6%)</td>
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</table>

Table 2: Accuracy of symptoms to detect positive histology

<table>
<thead>
<tr>
<th></th>
<th>Sen (%)</th>
<th>Spe (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Acc (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abd pain</td>
<td>68</td>
<td>40</td>
<td>67</td>
<td>42</td>
<td>79.9</td>
</tr>
<tr>
<td>N&amp;V</td>
<td>63</td>
<td>34</td>
<td>22</td>
<td>75</td>
<td>41.1</td>
</tr>
<tr>
<td>FTT</td>
<td>59</td>
<td>34</td>
<td>5</td>
<td>92</td>
<td>35.9</td>
</tr>
<tr>
<td>GI bleed</td>
<td>56</td>
<td>34</td>
<td>5</td>
<td>92</td>
<td>35.5</td>
</tr>
<tr>
<td>Dysphag.</td>
<td>56</td>
<td>34</td>
<td>5</td>
<td>94</td>
<td>36.2</td>
</tr>
</tbody>
</table>

ASSESSMENT OF HISTOLOGICAL ADEQUACY IN PEDIATRIC ENDOSCOPIC ESOPHAGEAL BIOPSY SAMPLES.

Ghanim Aljomah1, Humaira Hashmi1, Rafał Kozielski2, Ricardo A. Arbizu1, Robert D. Baker1, Susan S. Baker3, Pediatric Gastroenterology, University at Buffalo, Buffalo, NY; 2Pathology Department, University at Buffalo, Buffalo, NY

**PURPOSE:** Different esophageal biopsy techniques might play a role in the overall histological adequacy. This study compares the use of the single-bite technique, versus the double-bite technique, to assess the histological quality of endoscopic esophageal biopsies.

**METHODS:** Six hundred eighty four esophageal biopsies were obtained via esophagogastroduodenoscopy in 108 pediatric patients (2-18 years of age). Two hundred eighty two biopsies (47 patients) were obtained by the double-bite technique and 366 (61 patients) by the single-bite technique. The length, thickness, orientation, fragmentation and overall adequacy of the histological specimen were evaluated. Blinded pathologist scored the biopsies using a minimum score of 1 (poor) and a maximum score of 3 (excellent). The overall adequacy score was calculated as the sum of the scores.

**RESULTS:** In the single -bite group, the average score for length was (2.02), thickness (2.15), orientation (2.67), fragmentation (2.34) and overall adequacy (9.17). In the double-bite group, the average score for length was (1.95), thickness (2.12), orientation (2.61), fragmentation (2.37) and overall adequacy (9.04). No statistical significance was found in the length, thickness, orientation, fragmentation or the overall adequacy between the two groups (P>0.05).

**CONCLUSIONS:** There is no difference between single-bite and double-bite biopsy techniques in the assessment of histological quality of the esophageal biopsies.
EOSINOPHILIC ESOPHAGITIS IN CHILDREN: OUR EXPERIENCE IN CENTRAL AND NORTH EASTERN SOUTH CAROLINA. Rathna Amarnath, MD, Malathi Amarnath. MS, Karen Goon-Johnson. APNP, Nirav Patel. MD, University of South Carolina School of Medicine, Columbia SC 29203. Rathna P. Amarnath, 1Palmetto Health Children’s Hospital, Columbia, SC; 2University of South Carolina School of Medicine, Columbia, SC

BACKGROUND: Eosinophilic esophagitis (EoE) is a clinicopathologic disorder characterized by the presence of eosinophils in the esophageal mucosa, leading to esophageal dysfunction. Kapel and colleagues’ national database report of EoE indicated no diagnosed cases of EoE in South Carolina. We report our experience with the diagnosis and treatment of EoE over a four year period, including the prevalence and incidence of EoE in children in central and northeastern South Carolina.

METHODS: A retrospective chart review was performed, including all children between the ages of 0-18 years between March 2009 and February 2013 with a diagnosis of EoE. All children who fit FIGERS definition of EoE were included. Data was collected, including age, gender, duration of symptoms, symptoms, endoscopic findings (gross and histologic), treatment, and response to treatment. Incidence and prevalence was calculated using the 2010 US census data for children <18 yrs of age (338,500).

RESULTS: A total of 104 children were included (mean age was 8±0.8 yr), General annual incidence was 7.68 per 100,000. Prevalence of 30.7/100,000 for the four years of analysis. The incidence increased significantly from 1.7/100,000 in 2009 to 11.8/100,000 in 2012 (P=0.99 ). There were 72Male: 29 Female. Presenting symptoms included 17.3% with reflux, 29.8% with vomiting, 44.2% with abdominal pain, 8.7% with food impaction, 30.8% with dysphagia, and 3% with other symptoms (including cough, feeding refusal, and weight loss).

Mean duration of symptoms was 12.9±13.08 months (13.65±14.6 months in children ≤7 years of age and 12.6±11.8 months in children >7 years). Gross endoscopic findings included 26% with white exudates, 49% with linear furrows, 1% with both, 24% with erythematous mucosa, 7.7% with normal-appearing mucosa, and 1% with esophageal rings. Histologically, 1.9% of patients were found to have ≤15 eosinophils per high power field (Eo/hpf), 30.8% had 15-30 Eo/hpf, and 67.3% had >30 Eo/hpf. For treatment, 37.3% of patients were treated with topical steroids, 30.8% with dietary intervention, 14.4% with a combination of both, and 24% with a proton-pump inhibitor alone. While 16.3% of our patients did not follow up, 63.5% of patients reported a good clinical response to treatment. Erythematous mucosa and normal mucosa was more common in ≤7 yr age group (P <0.016, and 0.014 respectively).

CONCLUSIONS: Our data analysis shows high incidence of EoE in South Carolina compared to the literature and the incidence is significantly increasing, possibly due to increased recognition of the problem. Presentation, findings, and treatment response is similar to previous reports in the literature.

PEDIATRIC EOSINOPHILIC ESOPHAGITIS IN WASHINGTON, DC METROPOLITAN AREA. Vahe Badalyan, Seema Khan, Gastroenterology, Hepatology, and Nutrition, Children’s National Medical Center, Washington, DC

Background: Epidemiologic data show that the incidence of pediatric eosinophilic esophagitis (EoE) is rising and that it is more prevalent among Caucasian boys. A different pattern may exist in certain regions of the United States, particularly those with high proportions of non-white and foreign-born populations.

Aim: To describe the demographic and clinical characteristics of pediatric EoE in the ethnically diverse referral population of the DC metro area.

Methods: We compiled epidemiologic and clinical data for children who were referred to the specialized EoE clinic between December 2011-May 2013 at Children’s National Medical Center. Washington, DC.

Results: We reviewed records of 59 children (76% boys) evaluated in the clinic (mean age 8.2 years, range 1-20 years). Thirty-five (57%) were non-white, of which 24 (68%) were African-American. The average age at the first clinic visit was 5.8 years (SD 4.8 yr) with presumed first symptom onset at an even earlier age. Vomiting was the predominant symptom (52%) among children who presented under age of 4 yr, followed by poor weight gain/weight loss (21%), and feeding difficulties/aversion (17%). Abdominal pain was the most common complaint (33%) among children who presented at ≥4yr of age, and was followed by dysphagia/regurgitation (28%), vomiting (18%), and food impaction (10%).

In the available first endoscopy and biopsy reports, gross abnormalities were noted in 34 cases (57%), with furrowing and white exudates/edema reported in 44% and 38% of cases, respectively. Initial biopsies showed >15 eos/hpf in >71% of cases. In 15 cases (25%) endoscopy was grossly normal. Seven (46%) of these children were aged ≤2 yr at the time of the endoscopy. Prospectively, children had an average 5 clinic visits and 3 endoscopies over an average of 20.5 mo of follow-up in the EoE clinic. At the time of their last clinic visit, 49 children (83%) were receiving one or more therapy for EoE, most commonly, dietary restriction (58%), acid suppression (56%), elemental formula (24%), and swallowed steroids (20%).

Among children with both first and latest endoscopy reports available (n=34), histological improvement was noted in 19 (56%) children. The various therapies for this group were restricted diet in 74%, acid suppression regimen in 74%, and swallowed steroids in 37% children preceding the latest endoscopy.

Conclusions: Our data provides a unique insight into the demographics and prevalence of EoE in predominantly non-white children. EoE is an important diagnosis in non Caucasian children akin to the white population. Further studies are needed to assess long term efficacy of therapies, outcomes and natural history of these children, and compared to other geographic locations. We speculate that epigenetic factors may be influential in the striking prevalence of EoE in this group.

DOES HELICOBACTER PYLORI PROTECTS AGAINST EOSINOPHILIC ESOPHAGITIS IN CHILDREN? Yoram Elitsur1, Baraa Alabd Alrazzak1, Yulia Dementieva2 1Pediatrics, Gastroenterology, Marshall University, Huntington, WV; 2Mathematics, Emmanuel College, Boston, MA

The rate of Eosinophilic esophagitis (EoE) in children is increasing while the rate of Helicobacter pylori (Hp) infection is decreasing in children from developed countries. EoE is closely related to allergy while Hp infection is closely related to poor hygienic conditions. In countries with poor hygienic conditions, allergy is low (hygienic theory) and Hp infection is high. The opposite epidemiological data may suggest a "protective" effect between both diseases. Todate, this relationship has never been investigated in children.
**AIM:** To investigate the relationship between Hp infection and EoE in children.

**Material & Methods:** A retrospective analysis of all first diagnostic endoscopic procedure (2007-2012) performed in our gastroenterology clinic was reviewed. Chronological data and histologic diagnoses were collected. Biopsies from the esophagus and stomach (antrum, body) were available in all the charts irrespective of mucosal appearance. Hp diagnosis was determined by histology (H&E, Giemsssa, CLO-test). EoE diagnosis was established after patients failed adequate PPI therapy and when high number of eosinophils (>15 eos/hpf) was documented at the distal/mid esophageal biopsy.

**Results:** A total of 966 charts were available for review. The mean age and M:F ratio was 11.3 y and 1:1.18, respectively. Esophagitis, idiopathic gastritis, EoE, and Hp infection was detected in 268 (28%), 480 (50%), 62 (6%), and 31 (3%), respectively. The association between Hp infection and esophageal GER, gastritis, and EoE is described in the following Table.

**Conclusion:** No significant association (Phi Coefficient) was noted between Hp infection and EoE disease (p = -0.024). Positive association was found between Hp infection and gastritis (p = 0.183) and between Hp infection and GER (p = 0.294). We hypothesize that the low rate of EoE and Hp infection in our population is responsible for the lack of association between both diseases.

### Hp infection and EoE

<table>
<thead>
<tr>
<th></th>
<th>EoE</th>
<th>Gastro</th>
<th>GERD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count (%)</td>
<td>1 (3)</td>
<td>32 (100)</td>
<td>31 (97)</td>
</tr>
<tr>
<td>Fisher exact p-Value</td>
<td>0.716</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Phi Coefficient (p-Value)</td>
<td>-0.024 (0.461)</td>
<td>0.183 (&lt;0.0001)</td>
<td>0.294 (&lt;0.0001)</td>
</tr>
</tbody>
</table>

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**6** **MICRORNA-21 AS A POTENTIAL NON-INVASIVE BIOMARKER FOR EOSINOPHILIC ESOPHAGITIS IN CHILDREN.** Deepali V. Sawant, Weiguo Yao, Zachary Wright, Cindy Sawyers, Sandeep K. Gupta, Mark H. Kaplan, Alexander L. Dent, Indiana University School of Medicine, Indianapolis, IN

**INTRODUCTION:** MicroRNAs (miRs) have emerged as useful non-invasive biomarkers for different Th2-type allergic disease states such as asthma and EoE. miR-21 can promote Th2 responses by two different pathways. First, miR-21 can repress IL-12 gene expression, thus inhibiting Th1 responses and favoring Th2 responses. Second, miR-21 can directly promote Th2 differentiation in a T-cell intrinsic manner, by increasing Gata3 and IL-4 expression at early points after T cell activation. miR-22 appears to play a role in malignant conditions.

**AIM:** To study expression of miR-21 and its utility as a non-invasive biomarker for EoE.

**METHODS:** Quantitative PCR was used to assay miR-21 and miR-22 in esophageal biopsies and sera from controls and EoE (>15 eosinophils/hpf on esophageal biopsies) pediatric subjects.

**RESULTS:** 36 children were enrolled (18 children in each group with mean age 7 years). Atopy was present in 63% of controls and 83% of EoE subjects. miR-21 expression was increased an average of 50-fold (in esophageal biopsies) and 30-fold (in sera) in EoE group compared to controls. miR-21 expression up-regulation was independent of degree of eosinophilic inflammation on esophageal biopsies or presence/absence of atopy. miR-22 expression in esophageal biopsies of EoE group was similar to controls; miR-22 was not detected in sera of either group.

**CONCLUSIONS:** miR-21 was upregulated in esophageal biopsies and sera of EoE patients compared to controls; this was independent of atopy. Our preliminary results suggest miR-21 as a potential sera-based non-invasive biomarker for EoE which is a significant unmet need in care of children with EoE who often undergo multiple endoscopies. Future studies will need to assess effects of treatment and histological resolution of EoE on miR21 expression.

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**7 NEOCATE® NUTRA IS AS EFFECTIVE AS SUCRALOSE AS A DELIVERY VEHICLE FOR ORAL VISCOS BUDENSONIDE TO TREAT EOSINOPHILIC ESOPHAGITIS IN CHILDREN.** Elizabeth J. Hait¹, John Lee², Ari Fried³, Peter D. Ngo¹, Douglas McDonald², Eitan Rubinstein¹,¹Gastroenterology, Boston Children’s Hospital, Boston, MA; ²Allergy & Immunology, Boston Children’s Hospital, Boston, MA

**Background:** Oral viscous budesonide (OVB) using sucralose (eg: Splenda®) as a delivery vehicle has become an attractive therapeutic option for children with eosinophilic esophagitis. However, many families are wary of giving the artificial sweetener in high doses to their children.

**Specific Aim:** To determine if OVB mixed with Neocate® Nutra, a hypoallergenic nutritional supplement, is at least as efficacious as OVB mixed with sucralose at healing eosinophilic esophagitis.

**Methods:** IRB approved retrospective chart review of patients with well documented allergic eosinophilic esophagitis (EoE) treated with OVB at the Boston Children's Hospital Eosinophilic Gastrointestinal Disorder program between June 2008 and June 2013. Primary outcome measured was change in peak eosinophil count to less than 15 eosinophils per high powered field (HPF) after at least 4 weeks of OVB therapy.

**Results:** Forty-six children were treated with OVB mixed with Neocate, a hypoallergenic nutritional supplement, and 14 were treated with OVB mixed with Nutra. The two groups were not significantly different in their demographic (race, age, gender) and clinical (initial eosinophil count, proton pump inhibitor use, or concomitant dietary elimination) characteristics. The comparisons were performed using Wilcoxon test and Fisher's exact test for continuous and categorical covariates, respectively.
On follow up endoscopy, 30 out of 46 patients on sucralse and 13 out of 14 patients on Nutra had peak eosinophil counts of <15/HPF.

To compare treatments with Nutra and sucralse, we used logistic regression with the outcome defined as the success of treatment. A priori, we defined treatment with Nutra to be non-inferior to sucralse if the odds ratio (OR) of treatment success with Nutra as compared to sucralse were above 0.67 with 95% confidence. The OR of success with Nutra as compared to sucralse was 6.28 (95% CI: 0.74, 52.90). Therefore, we conclude non-inferiority of Nutra. None of the other covariates had a statistically significant (at p-value=0.05) association with the treatment success.

Conclusion: We demonstrate that OVB mixed with Neocate® Nutra is at least as effective as OVB mixed with sucralse at treating children with allergic eosinophilic esophagitis. Neocate® Nutra is an innovative, effective, and palatable mixing agent to create a viscous budesonide slurry for families who prefer not to use the standard recipe with sucralse.

ALOX15: A NEW MARKER TO HELP DISTINGUISH BETWEEN EOSINOPHILIC ESOPHAGITIS AND GASTROESOPHAGEAL REFUX DISEASE? Michael Herzlinger1, Andres Matoso2, Danisha Allen1, Sonja Chen1, Jason Ferreira1, Renee Monahan1, Vincent Mukkada1, Lelia Noble2, Dongfang Yang1, Shamlal Mangray1, Murray Resnick2

1Pediatric Gastroenterology, Nutrition, and Liver Diseases, Hashbro Children's Hospital, Warren Alpert Medical School of Brown University, Providence, RI; 2Pathology, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI; 3Gastroenterology, Rhode Island Hospital, Warren Alpert Medical School of Brown University, Providence, RI

BACKGROUND: Eosinophilic esophagitis (EoE) is a chronic, allergen-mediated, inflammatory condition affecting the esophagus. Currently, there is no "gold standard" test for EoE. Diagnosing EoE is complicated by clinical and histological overlap with gastroesophageal reflux disease (GERD). Consensus guidelines suggest that the presence of ≥15 eosinophils per high power field (HPF) in at least one esophageal biopsy meets pathologic criteria for EoE, though uncertainty remains when distal and proximal esophageal eosinophil counts are discrepant. Clinicians would benefit from a more reliable method of distinguishing these conditions. One such candidate marker is arachidonate 15-lipoxygenase (ALOX15), an enzyme involved in inflammation and fibrosis. We recently demonstrated the presence of ALOX15 by immunohistochemistry in 95% of EoE patients, but 0% of GERD patients or healthy controls. However, inclusion into this study was limited to only those with definitive diagnoses. In the current study, our goal was to determine if ALOX15 may be useful in diagnostically challenging cases.

METHODS: Pediatric patients with ≥15 eosinophils per HPF in esophageal biopsies were identified via retrospective search of our institution's pathology database from the years 2009 to 2011 (N=73). The sample was categorized into two groups: 1) "equivocal cases" (N=30), as defined by the presence of ≥15 eosinophils per HPF in the distal esophagus, but ≤15 eosinophils per HPF in the proximal esophagus, and 2) "unequivocal cases" (N=43), in which both distal and proximal esophageal biopsies contained ≥15 eosinophils per HPF. Patients with candida esophagitis, a non-eosinophilic inflammatory condition, were also identified (N=15), and served as a comparison group. Immunohistochemistry for ALOX15 was performed and results were correlated with clinical parameters, which included patient symptoms, history of atopy, endoscopy findings, and response to therapy (i.e. acid suppression, topical steroid, or elimination diet).

RESULTS: Of 30 equivocal patients, 15 (50%) were classified clinically as EoE, 10 (33%) as GERD, and 5 (17%) as undetermined. ALOX15 expression was significantly higher in EoE compared to GERD (93% vs. 50%; P=0.02; Table 1). Of 43 unequivocal patients, 39 (91%) were classified clinically as EoE, 1 (2%) as GERD, and 1 (2%) as undetermined. Within this group, expression of ALOX15 was similar in EoE and GERD patients (90% vs. 66%; P=0.29). ALOX15 expression was absent in candida esophagitis patients (0/15, 0%).

CONCLUSION: When multiple levels of the esophagus are involved, ALOX15 immunohistochemistry does not significantly contribute to the classification of patients with esophageal eosinophilia. However, when only the distal esophagus is involved, ALOX15 immunohistochemistry is a useful diagnostic tool to better classify these ambiguous patients, allowing for a more appropriate therapeutic approach.

Table 1: Equivocal Cases (N=30)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>ALOX15 Positive</th>
<th>ALOX15 Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>EoE</td>
<td>15 (50)</td>
<td>14 (93)</td>
</tr>
<tr>
<td>GERD</td>
<td>10 (33)</td>
<td>5 (50)</td>
</tr>
</tbody>
</table>

P value = 0.02 NS

THE MINIMALLY INVASIVE ESOPHAGEAL STRING TEST MEASURES CHANGES IN MUCOSAL INFLAMMATION IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS DURING TREATMENT: A LONGITUDINAL STUDY. Katie Amsden1, Amir Kagalwalla1,2, Preeth Alumkal1, Sergei Ochkur2, James Lee2, Glenn Furuta1, Steven J. Ackerman3

1Department of Pediatrics, Division of Gastroenterology, Hepatology & Nutrition, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 2Department of Pediatrics, John H. Stroger Hospital of Cook County, Chicago, IL; 3Depts of Biochemistry and Molecular Genetics, and Medicine, College of Medicine, University of Illinois at Chicago, Chicago, IL

Background: Endoscopy with biopsy is currently the only method to assess disease activity in eosinophilic esophagitis (EoE). During treatment with food elimination/reintroduction, children require multiple endoscopies with biopsy, an invasive procedure that is burdensome to families in both cost and lost days of school/work. We recently reported the Enterostest, a minimally invasive string-containing capsule, could be used to quantify esophageal eosinophil inflammation in children with EoE(1). This minimally invasive Esophageal String Test (EST) may be a useful tool to monitor disease activity in EoE. We hypothesize that the EST can be used to follow
esophageal inflammatory changes that occur during EoE treatment.

Methods: Secondary data analysis was performed following our prospective EST trial to identify longitudinal changes in eosinophil biomarkers in subjects performing multiple ESTs. Our analysis identified 5 children that performed an EST (ranging 1-12hrs) at least twice at Ann & Robert H. Lurie Children's Hospital of Chicago. All subjects were on a food elimination diet for treatment, requiring multiple endoscopies to identify the specific causative food(s) antigens. Eosinophil-derived granule protein (EDGP) biomarkers were measured by ELISA in string and biopsy extracts, providing correlations between string and biopsy biomarker levels with the gold standard peak eosinophil counts performed on esophageal biopsies.

Results: Four EDGPS (MBP1, CLC/Gal-10, EDN and EPX) were measured in both EST samples and biopsy extracts. Each biomarker showed correlation with EoE disease status, with levels increased in active disease (≥15 eos/hpf) and decreased during disease remission (<15 eos/hpf). Eosinophils per high power field decreased 96.9% from active disease to remission. Similarly, EDGP biomarkers showed a decrease with disease remission in EST and biopsy extracts respectively, MBP1 (80.2%/90.1%), CLC/Gal-10 (84.8%/74.7%), EDN (79.5%/91.1%) and EPX in EST (98.3%). Significant correlations (Spearman's) between esophageal eosinophil counts and MBP1 levels in EST samples (r=0.753, p=0.031) and EPX levels in EST samples (r=0.805, p=0.029) were identified. Similarly, there were significant correlations between eosinophil counts with CLC/Gal-10 levels in biopsy extracts (r=0.872, p=0.002) and EDN in biopsy extracts (r=0.879, p=0.009). As well, EDGP biomarker levels in EST samples were significantly correlated with one another, MBP1 with EDN (r=0.929, p=0.003). Similarly, EDGP biomarker levels in biopsy extracts significantly correlated with one another, CLC/Gal-10 with EDN (r=0.929, p=0.003) and CLC/Gal-10 biopsy extracts (r=0.893, p=0.007) and EDN biopsy extracts (r=0.821, p=0.023) with EPX in the EST.

Conclusion: Despite the small sample size, EST-captured EDGP biomarkers highly reflect significant changes in response to treatment over time in the same patient. These findings support continuation of our prospective study to determine the EST’s capacity to identify changes in disease status in response to treatment in EoE.

10* PREVALENCE OF ENDOSCOPIC ABNORMALITIES IN PATIENTS REFERRED FOR REFRACTORY FEEDING PROBLEMS. Mitchell Katz, 1Peds Gastroenterology, CHOC Children's, Orange, CA; 2Pediatrics, UCI Medical Center, Orange, CA

Introduction: Feeding problems are a common reason for referral to a pediatric gastroenterologist. Determining when to perform endoscopy is an important question. At CHOC Children's Hospital (CHOC), a multidisciplinary feeding program has been established for intense treatment of children with severely disordered feeding behavior or for weaning from gastrostomy tube dependency. A larger than expected percentage of patients referred to The CHOC Children's Feeding Program were diagnosed by upper endoscopy (EGD) to have gastroesophageal reflux and eosinophilic esophagitis (EoE). With this in mind, the purpose of this study is to evaluate endoscopy outcomes of patients referred to CHOC's multidisciplinary feeding program in an attempt to guide pre-evaluation screening for children with complex feeding problems.

Methods: A retrospective chart review identified 121 patients (mean age = 60 months) referred to The Feeding Program in 2011-2012. Sixty-five patients underwent EGD with biopsy. A convenience sample of 95 age-matched patients referred for EGD with biopsy from the general GI clinic, during the same interval, was used as controls. Prevalence of abnormal biopsy results were compared between the two groups. Prevalence rates of EoE were compared between groups and with published findings.

Results: 65 Feeding Program patients had an EGD with biopsy. Of these, 27 patients had normal biopsies and 38 (58.5%) patients had abnormal findings. Twenty patients (30.8%) had reflux esophagitis, 9 patients (13.8%) showed EoE, 10 patients (15.4%) demonstrated gastritis, and 1 patient was positive for H. pylori gastritis.

In the age-matched control group 57.9% had abnormal biopsies. Reflux esophagitis was found in 28.4% of patients, EoE in 6.3% of patients and gastritis in 22.1% of patients.

In a study by Sorser SA et al. (J. of Gastroenterol. 2013 Jan;48(1): 81-5) the prevalence of EoE from all reported pediatric EGDs taken from 2001-2006 was shown to be 5.8%. A Meta analysis by Soon IS et al. (J Pediatr Gastroenterol Nutr. 2013 Mar) found the prevalence of EoE in children undergoing EGD for any reason to be 2.5%, 5.1%, 6.4%, and 23% in different studies. Combining these studies yields a prevalence of 195/4331 (4.5%).

Conclusion: In a group of patients referred exclusively for treatment of feeding problems, 58.5% of patients had abnormal EGD biopsy results. This was similar to patients referred from a general GI clinic for endoscopy, where there was a high index of suspicion of pathology.

Of particular interest, the incidence of EoE was more than doubled in the disordered feeding group compared to controls and triple published prevalence. When evaluating a patient with complex feeding problems, an EGD with biopsy is an essential part of the diagnostic assessment.

Hepatobiliary/Transplant

21 HOME-BASED SCREENING FOR BILIARY ATRESIA USING INFANT STOOL COLOUR CARDS IN CANADA: QUEBEC FEASIBILITY STUDY. Najma Ahmed1, Veronique Morinville1, Cindy Ibberson1, Lajos Kovacs2, Janusz Kaczorowski3, Bryan Stirling2, Jean Paul Coller2, Richard Schreiber2, 1McGill University, Montreal, QC, Canada; 2University of British Columbia, Vancouver, BC, Canada; 3Universite de Montreal, Montreal, QC, Canada

Aims: Biliary atresia (BA) manifests in the first few weeks of life as jaundice with pale/acholic stools. Optimal outcome with Kasai portoenterostomy (KP) is achieved when this is performed at ≤60 days of life. The use of an infant stool color card (SCC) screening program in Taiwan has successfully eliminated all KP > 90 days. A recent study in British Columbia (BC) indicated that a passive distribution of SCC led to high utilization rates (59-94%) and cost-effectiveness. We report the experience and generalizability of the SCC screening strategy in another province.
Methods: The study was conducted at St. Mary's Hospital, Montreal, QC. Families discharged from the maternity ward before 14 days of age were given an instruction and opt-out consent document, and a postage-paid SCC, containing a series of six photo images of different stool color. They were instructed by ward nurses to monitor their newborn's stool color daily for 21 days by comparing the stool color to the SCC, and then complete and mail the SCC to the study centre. Phone surveys to families who did not return their cards were used to estimate the total card utilization rate (cards returned + cards not returned but utilized).

Results: During the 201 study days, there were 2281 births. Of the 2250 infants eligible for the study, 99.9% were enrolled. The SCC return rate was 63%. Three families who reported transient abnormal stool color were contacted with no further action necessary. No cases of BA were identified. Attempts were made to contact 233 families who had not returned their cards. All 118 families who completed the phone survey had used the SCC. Conservative and optimistic estimates for total card utilization were 82% and 100% respectively.

Conclusions: The high enrollment rate in this SCC screening study suggests strong family support of this simple screening process. The overall high SCC card return and utilization rates demonstrate reliability and reproducibility for a home-based BA screening strategy in another provincial jurisdiction. The results lend support for a Quebec SCC program to improve outcomes of children with BA.

22 PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE IN ADOLESCENTS WITH POLYCYSTIC OVARY SYNDROME. Mrouge Sobaihi1,2, Yogita Malan2, Evelyn Constantin1,2, Helen Bui1,2, Najma Ahmed1,2, 1Pediatrics, Montreal Children's Hospital, Montreal, QC, Canada; 2McGill University, Montreal, QC, Canada

Background: Polycystic ovary syndrome (PCOS) is an endocrine disorder characterized by hyperandrogenism and oligo-anovulatory cycles. Women with PCOS are at an increased risk of the metabolic syndrome independent of obesity and hyperinsulinism. Furthermore, some adult studies have suggested that PCOS may be an independent risk factor for non-alcoholic fatty liver disease (NAFLD). To date there are no data on the prevalence of NAFLD in adolescents with PCOS.

Aim: To assess the prevalence of NAFLD in adolescents with PCOS as defined by elevated liver enzymes using 3 cut-off values and to determine risk factors for NAFLD in this population.

Methods: A retrospective chart review of adolescents followed in the endocrinology clinic at the Montreal Children's Hospital between 1999-2009 with PCOS was conducted. The diagnosis of PCOS was based on the Rotterdam consensus criteria. Clinical information including anthropometric data and laboratory data (liver enzymes, lipid profile, glucose and insulin) were abstracted. BMI z-scores were calculated for each patient and insulin resistance was calculated using the homeostasis model assessment (HOMA-IR). Patients were considered to be obese if their BMI z-score was >2. The prevalence of elevated alanine aminotransferase (ALT) levels was examined at three different cut-off values.

Results: 140 patients (mean age 15.96 years) with PCOS were identified. Of these, 79 subjects (51.9%) had liver enzymes measured and were included in our study. Mean BMI z-score was 1.53. 35 patients (44.3%) had insulin resistance (elevated HOMA-IR), and of these 16 (45.7%) were obese. Using 3 different cut-offs, NAFLD prevalence values were determined. At an ALT ≥ 45 U/L, prevalence of NAFLD was 10.1%, at an ALT ≥ 37 prevalence was 26.7% and at an ALT ≥ 22 prevalence was 72.2%. Using the standard ALT cutoff of 45 U/L, of the 8 patients with an elevated level, 3 were obese (BMI Z-score ≥ 2) and 5 had a normal BMI. Three of the eight (37.5%) patients with an elevated ALT also had insulin resistance as indicated by an elevated HOMA-IR and 3 (37.5%) had a normal HOMA-IR.

Conclusion: Our data suggest that a significant proportion of adolescent girls with PCOS have abnormal liver enzymes suggestive of hepatic steatosis. Furthermore, this appears to be present in girls with PCOS independent of their BMI. As this is a retrospective study, corroborating data such as imaging were not available, however, it suggests the need for further study of the incidence of NAFLD in adolescents with PCOS.

23 ROLE OF ALCOHOL IN THE PATHOGENESIS OF NAFLD. Ghanim Aljomah1, Susan S. Baker1, Wensheng Liu1, Rafal Kozieliski2, Robert D. Baker1, Lixin Zhu1, 1Pediatric Gastroenterology, University at Buffalo, Buffalo, NY; 2Pathology Department, University at Buffalo, Buffalo, NY

Purpose: Non-alcoholic steatohepatitis (NASH) is a serious form of nonalcoholic fatty liver disease (NAFLD). It is characterized by hepatic steatosis, inflammation, and variable degrees of fibrosis. NASH and alcoholic steatohepatitis share many histological features. The increased gene expression of alcohol-catabolism related genes in NASH was reported in children, suggesting that alcohol may play a role in NASH. Our previous studies suggest that gut microbiome is a source of endogenous alcohol. The purpose of this study is to examine the gene expression of alcohol-catabolism related genes in simple steatosis patients, in comparison to NASH patients and normal controls and to determine the role of alcohol in the natural progression of NASH.

Methods: NASH was diagnosed according to Kleiner's criteria. The mRNA expression of alcohol-catabolism related genes (ADH4, ADH1C, CYP2E1 and Catalase) in the livers of normal controls, simple steatosis and NASH patients were examined by quantitative real-time PCR (qRT-PCR). ANOVA test was applied to analyze the data.

Results: There was a statistically significant difference in mRNA expression of the alcohol related genes among the three groups (p < 0.05, ANOVA) for ADH4, ADH1C, CYP2E1 and Catalase. The gene expression of (ADH4, ADH1C, CYP2E1 and Catalase) was higher in NASH and simple steatosis compared to NC (p < 0.05). No statistical significance was found between the simple steatosis and the NASH patients.

Conclusions: Increased expression of alcohol metabolizing genes suggests that alcohol metabolism is elevated in patients with NASH and with simple steatosis. Alcohol metabolism may contribute to the pathogenesis of steatosis and steatohepatitis in a mechanism similar to the pathogenesis of alcoholic steatohepatitis.
Background: We have recently developed a new histologic score, the PNHS, to categorize nonalcoholic fatty liver disease (NAFLD) into NASH (the aggressive form) and not NASH for inclusion in pediatric clinical trials. PNHS was developed in a cohort of Italian children. The aim of this study was to validate the use of PNHS in the diagnosis of pediatric NAFLD in a large cohort of North American children with biopsy-proven NAFLD and compare it to the NAFLD activity score (NAS).

Methods: Consecutive children with biopsy-proven NAFLD from 5 major US centers were included in this study. The diagnosis of NASH was established by an experienced liver pathologist and the PNHS and NAS were calculated for each patient. Spearman correlation coefficients were used to evaluate correlations between PNHS and histological features. ROC analysis was performed to assess the role of PNHS in diagnosing NASH and distinguishing between patients with and without certain histological characteristics.

Results: A total of 108 pediatric patients with NAFLD were included; 13 had simple steatosis and 95 had definitive NASH. Mean age was 13 ± 3.3 years and 63% were male. Subjects with definitive NASH had higher BMI and AST compared to those without (p< 0.05 for both).

The mean PNHS in the NASH group was 94.9 ± 8.9 compared to 12.9 ± 23.4 in not NASH group, p= 0.001. PNHS correlated with the presence of NASH according to pathologist diagnosis with a sensitivity of 90.5% and specificity of 92.3% for PNHS of ≥ 85 compared to a sensitivity of 50.5% and specificity of 100% for NAS of ≥ 5. PNHS had an excellent area under the ROC curve (AUC) of 0.97 for diagnosing NASH. PNHS also correlated with the individual histologic features of NASH with the highest correlation being with Ballooning (r=0.72 (0.59,0.85)).

Conclusion: There is a high level of agreement between categorization of NAFLD cases using the PNHS and the pathologist's diagnostic determination. Our results supports the use of PNHS in future therapeutic trials in children.

25 DOES A DECREASE OF AT LEAST 5% IN POST-LIVER BIOPSY HEMATOCRIT PREDICT THE DEVELOPMENT OF COMPLICATIONS IN CHILDREN AND YOUNG ADULTS? Amal Aqul1, Sarah Harney1, Paul Mitchell2, Maureen M. Jonas1, Gulraiz Chaudry,1 Pediatric Gastroenterology and Hepatology, Boston Children's Hospital/ Harvard Medical School, Boston, MA; 2Clinical Research Center, Boston Children's Hospital/ Harvard Medical School, Boston, MA

Background: Percutaneous liver biopsy (PLB) is an important tool used to evaluate liver disease. It can be obtained by different techniques: "blind," with pre-biopsy ultrasound (US) localization, or with real-time guidance using either US or CT. A recent study showed that most pediatric gastroenterologists refer their patients to interventional radiologists (IR) for real-time guided PLB. A NASPGHAN Medical Statement recommends observing patients at a medical facility for at least 6 hours post-PLB. Additionally, a post-procedure drop of hematocrit (HCT) by 5% or more is suggested as evidence of occult hemorrhage.

Aim: To determine whether a decrease in HCT by at least 5% following US-guided PLB predicted complications in a pediatric/young adult cohort.

Methods: This is a retrospective analysis of patients 0-21 years of age who underwent US-guided PLB at Boston Children's Hospital (BCH) between 1/2002 and 6/2009. Charts were reviewed for age, sex, platelet count (<75 vs ≥75 K/mm3), INR (<1.3 vs ≥1.3), the presence of findings on routine end-of-procedure US examination and symptomatic complications requiring an intervention. The association of a HCT drop of ≥5% and asymptomatic post-PLB abnormalities was examined in subjects who had only 1 biopsy by Fisher exact test. The association of a HCT drop of ≥5% and symptomatic complications was examined in the entire cohort and corrected for within subject variability by a generalized estimating equation.

Results: 564 US-guided PLBs were performed on 450 patients. 384 (85%) had only one biopsy. The mean age was 10.5±6.5 years (range 0.1-21.6). The indications for PLB were: chronic liver disease (n=196, 35%), evaluation of a transplanted liver (n=109, 19%), staging of viral with (n=108, 19%), iron quantification (n=71, 13%), focal liver abnormality (n=53, 9%), and other parenchymal liver disease (n=27, 5%), 51 (11%) patients had asymptomatic subcapsular hematoma on routine end-of-biopsy US examination, 36 of which had only 1 biopsy (36/383, 9%) and were the analysis cohort. A decrease in HCT of ≥5% did not correlate with the occurrence of asymptomatic subcapsular hematoma (P=0.11). These findings remained when adjusted for pre-PLB platelet count and INR. 11 (2.4%) patients (12 biopsies) had symptomatic complications including bleeding (n=4, 0.9%), pain (n=3, 0.7%), and pneumothorax, bronchospasm, fever, tachycardia, and hypotension (1 each). A drop in HCT of ≥5% was not associated with symptomatic complications (P=0.15). The influence of pre-PLB platelet count and INR on this association could not be examined in this group because of the small number of complications.

Conclusion: Symptomatic complications are very uncommon after US-guided PLB in children and young adults. A decrease in the post-PLB HCT of ≥5% did not predict development of complications. Further analyses, already underway, are required to evaluate the association of complications with the number of needle passes, comorbidities, and the degree of liver fibrosis. The timing of complications, with respect to the 4 hour observation period following PLB routinely used at BCH, will also be assessed.
D-AMINO ACID OXIDASE AND PEPTIDOGLYCAN RECOGNITION PROTEIN-2 GENE EXPRESSION IN PEDIATRIC NON-ALCOHOLIC STEATOHEPATITIS.

Ricardo A. Arbizu, Susan S. Baker, Wensheng Liu, Robert D. Baker, Lixin Zhu, Digestive Diseases and Nutrition Center, SUNY at Buffalo, Buffalo, NY

Background: Non-alcoholic steatohepatitis (NASH) is the progressive form of non-alcoholic fatty liver disease. Accumulating evidence suggests that the gut microflora may play a role in NASH pathogenesis through bacterial metabolites (e.g. ethanol) and bacterial cell components, facilitated by increased gastrointestinal (GI) tract permeability. D-amino acids (DAA) are major components of both Gram positive and Gram negative bacterial cell wall peptidoglycan which are not found in human proteins. D-amino acid oxidase (DAO) is a liver enzyme that catalyzes the oxidative deamination of DAA yielding an imino acid, an α-keto acid, ammonium and hydrogen peroxide. Peptidoglycan recognition protein-2 (PGLYRP-2) is a liver secreted protein that recognizes and hydrolyzes bacterial peptidoglycan to produce DAA. Studies on the impact of bacterial cell components on NASH pathogenesis are limited to the lipopolysaccharide/toll-like receptor pathways. We hypothesize that bacterial cell wall components may play a role in the pathogenesis of NASH by increasing oxidative stress. Therefore, we examined the expression of genes related to the metabolism of bacterial cell wall components in NASH livers.

Methods: Pediatric patients with histologic diagnosis of NASH were included. The gene expression of DAO and PGLYRP-2 in NASH livers and normal controls (NC) were examined by microarray analysis and confirmed by quantitative real time PCR (qRT-PCR). Unpaired student t-test was performed to analyze the differences between NASH and control groups. A p value less than 0.05 was considered statistically significant.

Results: Microarray data showed that the gene expression of DAO (NASH/NC=8.3, p=0.0039) and PGLYRP-2 (NASH/NC=8.4, p=0.014) were elevated in NASH patients compared to NC. Similar results were observed by qRT-PCR analysis for both DAO (NASH/NC=4.8, p=0.0002) and PGLYRP-2 (NASH/NC=9.0, p=0.0017).

Conclusions: The gene expression of both DAO and PGLYRP-2 is increased in pediatric NASH patients compared to NC. We speculate that hydrogen peroxide, a product of DAO, contributes to the pathogenesis of liver damage in NASH by increasing oxidative stress and that bacterial cell wall components (DAA, peptidoglycan) derived from the gut play a role in NASH.

PREVALENCE AND OUTCOME OF NON-ALCOHOLIC FATTY LIVER DISEASE IN ADOLESCENTS UNDERGOING WEIGHT LOSS SURGERY.

Kathleen Corey, Takara Stanley, Joseph Misraji, Christina Scirica, Janey Pratt, Alison Hoppin, Madhusmita Misra, Mass General Hospital, Boston, MA

Objectives: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of liver disease among adolescents. However, screening for and diagnosis of NAFLD is infrequent even among high risk individuals. We sought to evaluate the frequency of NAFLD diagnoses in patients referred to the Mass General Weight Center and the true prevalence of NAFLD and nonalcoholic steatohepatitis (NASH) based on histology. We also evaluated metabolic differences in patients with and without NASH and the frequency of NASH resolution after weight loss surgery (WLS).

Methods: We performed a retrospective evaluation of 27 patients referred for WLS during which liver biopsies were performed. Results: NAFLD was under recognized in our patients. Despite their severe obesity, only 2 patients (7.4%) had been previously diagnosed with NAFLD. However, liver biopsy revealed that 18 patients (66.7%) had NAFLD, and of those, 10 patients (37.0%) had NASH and 11 (40.7%) had fibrosis stage ≥1. One patient had advanced fibrosis.

Conclusions: NAFLD and NASH patients had persistently elevated aminotransferase levels despite significant weight loss, suggesting ongoing NASH.
Metabolic Characteristics of NASH and Non-NASH Patients

<table>
<thead>
<tr>
<th></th>
<th>Non-NASH (n=17)</th>
<th>NASH (n=10)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Age, (years)</td>
<td>19.4 (16-22)</td>
<td>18.3 (15-22)</td>
<td>0.27</td>
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<tr>
<td>Gender</td>
<td>3M/14F</td>
<td>2M/8F</td>
<td>0.88</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td>0.24</td>
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<tr>
<td>Asian</td>
<td>0 (0%)</td>
<td>2 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>3 (17.6%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>4 (23.5%)</td>
<td>3 (30.0%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>8 (47.1%)</td>
<td>5 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (11.8%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>BMI, (kg/m2)</td>
<td>51.5 (42.6-71.8)</td>
<td>54.7 (38.8-67.2)</td>
<td>0.35</td>
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<tr>
<td>ALT, (U/L)</td>
<td>26.4 (11.0-69.0)</td>
<td>30.3 (17.0-53.0)</td>
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</tr>
<tr>
<td>Glucose, (mg/dL)</td>
<td>87.1 (74-107)</td>
<td>98.4 (74-134)</td>
<td>0.06</td>
</tr>
<tr>
<td>Insulin, (uU/mL)</td>
<td>21.9 (6-37)</td>
<td>42.8 (16-83)</td>
<td>0.02</td>
</tr>
<tr>
<td>HOMAIR</td>
<td>4.6 (1.3-8.0)</td>
<td>11.3 (3.3-26.2)</td>
<td>0.02</td>
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<td>HbA1C</td>
<td>5.4 (4.7-6.3)</td>
<td>5.9 (5.3-7.4)</td>
<td>0.01</td>
</tr>
<tr>
<td>LDL, (mg/dL)</td>
<td>109.3 (69-172)</td>
<td>79.0 (42-132)</td>
<td>0.02</td>
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<tr>
<td>Type 2 Diabetes Mellitus, (%)</td>
<td>1 (5.9%)</td>
<td>2 (20.0%)</td>
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<td>Obstructive Sleep Apnea, (%)</td>
<td>8 (47.1%)</td>
<td>8 (80.0%)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

28 HEPATIC FIBROSIS POST LIVER TRANSPLANT IN THE LONG TERM OUTCOME. USEFULNESS OF FIBROSCAN AS A GUIDING STUDY IN CHILDREN. Daniel E. D'Agostino1,2, Gustavo H. Boldrin1,2, Maria C. Sanchez1,2, Joaquin Solari1, Victoria Fernandez de Cuevas1,2, 1Pediatric Gastroenterology-Hepatology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 2Department of Pediatrics, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

PURPOSE: The liver fibrosis may threaten the graft in the long term post liver transplantation (LT). The Measuring stiffness with fibroscan can help diagnose of fibrosis. However when and how often it should be performed remains uncertain. Liver biopsy is the gold standard study in the assessment of graft fibrosis.

Aim: This study compare the performance of fibroscan and liver biopsy in liver transplant children in the long follow up.

*METHOD: We prospectively assessed the performance of transient elastography in 23 patients after 5 years post liver transplant. Children underwent both liver biopsy and transient elastography. The grade of liver fibrosis (METAVIR score) obtained by biopsy was compared to liver stiffness measured by fibroscan. They were divided into two groups according to the time since liver transplantation: G I (5 to 10 years after LT), G II (> 10 years after LT).

*RESULTS: 23 patients were prospectively included, 12 boys (52.17%). Mean time since LT was 13.72 ± 4.9 years (r 5.6-23.9y). G I: 8 patients, mean time since LT 8.36 years (r 5.6-9.9y) G 2: Group II: 15 patients, mean time since LT 16.58 years (r 10.3-23.9y). Liver stiffness values ranged from 2.9 to 72.0 kPa. The optimal cutoff value was 7.8 kPa for F>1. The area under the receiver operator characteristic curve for the diagnosis of fibrosis (F>1) by transient elastography was 0.82, 95% CI 0.61-0.99, positive predictive value 0.86, negative predictive value 0.67, 86.67% sensibility, 75% specificity. No statistical difference was found in liver stiffness measured by fibroscan can between G1 (8.27 ± 3.59 kPa) and G2 (11.32 ± 7.13 kPa) (p<0.272).

*CONCLUSION: *These data suggest that transient elastography is a simple, noninvasive and reliable tool to assess liver fibrosis in patients after liver transplantation in children. A fibroscan value higher than 7.8 kPa should determine the need to perform a liver biopsy. Further validation in larger populations is needed.

29* IMMUNOSUPPRESSION-FREE REMISSION IN PEDIATRIC AUTOIMMUNE HEPATITIS: A POPULATION-BASED STUDY. Mark R. Denneau, Linda Book, Stephen Guthery, M. Kyle Jensen, University of Utah, Salt Lake City, UT

Introduction: Limited data exist on outcomes in pediatric autoimmune hepatitis (AIH), particularly sustained immunosuppression-free remission (SIFR).

Methods: We retrospectively reviewed all pediatric AIH patients in the region from 1986-2011 using population-based methods and followed them from time of diagnosis until outcomes of biochemical remission on immunosuppression and SIFR. The definition of SIFR required at least one year of biochemical remission on immunosuppression, normal histology on biopsy before medication discontinuation, and subsequent remission through the end of all follow-up.

Results: We identified 56 AIH-patients (62.5% female, median age 11.1 years [IQR: 5.7-14.4], 8.9% type II, followed for median 5.6 years [IQR: 2.8-8.6]). Baseline cirrhosis was present in 14.0% and primary sclerosing cholangitis in 21.4%. Coexisting non-hepatic autoimmune disease occurred in 37.5% including inflammatory bowel disease (IBD) in 19.6%, celiac in 14.3%, and thyroiditis in 13.5%. Celiac and thyroid screening occurred in 50 and 66% of AIH patients, respectively. Biochemical remission on immunosuppression was achieved in 76.4% of all AIH patients by median 1.2 years [IQR:0.4-3.6]; 23.1% of these experienced a subsequent relapse.
Discontinuation of immunosuppression was attempted in 16 stable patients and was successful in 87.5% (median age 8.9 years [IQR: 3.5-17.9]) at discontinuation, treated for median 2.0 years [IQR: 1.3-3.5] after diagnosis, all with type I AIH) with SIFR through median 3.4 years [IQR: 2.6-5.8] of follow-up. Excluding patients with IBD who were on immunosuppression independent of liver disease, the probability of achieving SIFR within five years of AIH diagnosis was 41.6% (95%CI: 25.3-62.9). Baseline patient features associated with inability to achieve biochemical remission on immunosuppression or SIFR were elevated INR, positive anti-neutrophil cytoplasmic antibody titer, cirrhosis and/or the presence of a non-hepatic autoimmune diagnosis.

Conclusions: We identified an 87.5% rate of successful discontinuation of all immunosuppressive medications in carefully-selected pediatric AIH patients from a population-based cohort. SIFR is an achievable goal for many AIH patients, especially those with type I disease in stable biochemical remission on immunosuppression.

30  **IN VIVO ULTRASOUND IMAGING OF MICROCIRCULATION IN HEPATIC STEATOSIS USING MICRO MARKER NON-TARGET CONTRAST AGENT.** Vasantha L. Kolachala1, Rong Jiang1, Carlos Abramowsky3, Allan Kirk2,4, Nitika A. Gupta1,2, 1Pediatric Gastroenterology and hepatology, Emory University, Atlanta, GA; 2Transplant services, Children's Healthcare of Atlanta, Atlanta, GA; 3Surgery, Emory University, Atlanta, GA; 4Pathology, Emory University, Atlanta, GA

Background: Incidence of Non alcoholic fatty liver disease (NAFLD) is on the rise. Swollen steatotic hepatocytes cause sinusoidal distortion and impairment of hepatic microcirculation that leads to the development of hepatocellular dysfunction and portal hypertension. Thus, quantitative non invasive hemodynamic investigations of steatotic livers provide important diagnostic and therapeutic implications. Aim: To determine the effect of fat on hepatic vascular flow in mice with hepatic steatosis compared to lean mice using the small animal live imaging Vevo 2100 digital high-frequency ultrasound imaging method. Methods: C57BL/6 mice were fed a high fat diet (HFD) for 12 weeks and the onset of hepatic steatosis was determined by Oil red O staining of liver tissue. Sinusoidal spaces were quantified by histomorphometry using Image Pro software. Arterial blood flow was evaluated using Vevo 2100 high frequency, digital, linear array, color doppler machine. Rate of perfusion, blood flow and blood volume were analyzed by intravenous injection of gas-filled microbubbles (1.0x10^{7} /50 ul) into mice using vivoCQ software from VisualSonics (Canada). Results: A significant reduction in intra sinusoidal space in HFD mice (HFD: 7151 ± 1336 vs lean: 19800 ± 1692 pixel^2 p<0.0001) was noted. Ultrasound analysis demonstrated reduced sinusoidal perfusion rate (HFD 10.4 ±1.6 vs lean 4.4±0.5 sec p<0.005) and perfusion index (HFD 11.4±2.7 vs lean 54.2±20.07 p<0.02) in HFD mice. Using this bolus perfusion model we have also demonstrated significant reduction in blood volume (HFD: 19.0±4.3 vs lean: 103.2±32.0 p<0.01), blood flow (HFD 4.7±1.4 vs lean 77.7±35.4 p<0.02) in HFD mice with concurrence in a Resistive index indicator of resistance in the hepatic artery (HFD: 0.58±0.02 vs lean 0.46 ±0.04 p<0.03). Conclusion: Hepatic steatosis leads to impaired microcirculation as evidenced by reduced perfusion rate, blood flow and blood volume. We demonstrate that, murine ultrasound color doppler and bolus perfusion model is a non- invasive, potentially clinically relevant tool to determine perturbations in microcirculation of the hepatic steatosis and can provide the ability for intervention studies in various genetically modified models to determine the mechanism of hemodynamics during Ischemia reperfusion Injury.

31* **PROGRAMMED CELL DEATH PROTEIN (PD1) PLAYS A DYNAMIC ROLE IN CELL DEATH DURING ISCHEMIA REPERFUSION INJURY (IRI) IN HEPATIC STEATOSIS.** Vasantha L. Kolachala1, Rong Jiang1, Carlos Abramowsky3, Allan Kirk2,4, Nitika A. Gupta1,2, 1Pediatric Gastroenterology and hepatology, Emory University, Atlanta, GA; 2Transplant services, Children's healthcare of Atlanta, Atlanta, GA; 3Surgery, Emory University School of Medicine, Atlanta, GA; 4Pathology, Emory University School of Medicine, Atlanta, GA

Introduction: Hepatic steatosis, a common clinical problem leads to increased hepatocellular death when exposed to IRI. Though the role of PD1 as a critical inhibitory member of the CD28 family crucial for T cell activation is emerging in various clinical scenarios such as transplant, sepsis, hepatitis and autoimmunity, its role is not well studied in IRI in hepatic steatosis. Aim: To determine the role of PD1 in IRI of a hepatic steatosis. Methods: Male C57BL/6/ Wild type (WT) and PD1-KO mice were fed a high fat diet (HFD), lean control mice were fed on standard chow and subjected to IRI. Hepatic and splenic T-cells were subjected to flow- cytometry for CD3, CD4, CD8, CD4+/PD1+ and CD8+/PD1+. ALT, cytokines, chemokines were measured in serum and Liver tissues were examined for necrosis, apoptosis and PD-1 ligand PD-L1 and PD-L2 quantification. Results: HFD mice showed increased body weight (WT-HFD 42±1.2, PD1-KO HFD, 41.5±1.8, vs lean 24.6 ±0.6 grams p<0.0001) and presence of hepatic steatosis. After IRI, necrosis and serum ALT were increased 24 hrs after reperfusion in HFD mice compared to lean (365.9±73 WT, vs lean 61±9.7 IU/ml p<0.009). Pre-IRI percent PD1+ CD4+ T-cells were not significantly different (HFD: 41.05±15.55 vs lean: 30.4±11.0 p<0.57). However, at 72 hours after IRI, PD1+ CD4+ T-cells were upregulated on hepatic T-cells of HFD mice (HFD-IRI: 61.6±5.2 vs lean-IRI: 36.08±3.6 p<0.009). Similar findings were seen in splenic T-cells after IRI in hepatic mice vs lean mice (44.4±3.8 vs 28.1±3.6, p<0.01). Lean mice did not show any of these changes post IRI : (28.6±3.6 vs 19.98±3.57, p<0.15). In HFD post IRI there was no difference in CD8+/PD1+ T-cells. PD1 ligand PD-L1 was decreased in HFD mice. Additionally, PD1-KO mice fed on HFD showed no protection from IRI as demonstrated by severe necrosis, significant increase in ALT (PD-KO HFD: 304.67±47.97 vs PD1-KO: lean 73.33 IU/ml), CXCL1/KC (HFD- IR 215± 21.07 vs PD1-KO HFD: 396.5 ± 76.33, p<0.03) and T cell chemoattractant MIG (HFD-IRI 50.67±2.8 vs PD1-KO HFD: 233.9 ± 9.99, p<0.04). IL-6 was increased in both HFD -WT: 102.7± 27.2 and PD1-KO: 65.5±14.8 vs lean IR 18.3 ±3.4, p<0.01). Conclusions: With increased cell death, there is an increase in CD4+/PD1+ hepatic and splenic T-cells after IRI in hepatic steatosis. Concurrent decrease in ligand, leads to loss of inhibitory effect of PD1, with resultant activation of T cells. This is confirmed by increased hepatocellular damage seen in HFD-PD1KO mice undergoing IRI. This profiles a unique signature, which can be targeted for therapeutic intervention for mitigating hepatocellular injury in hepatic steatosis.
32 LEVELS OF PAI-1 AND ITS CORRELATION WITH METABOLIC IMPAIRMENT IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE RECEIVING HIGH FRUCTOSE OR GLUCOSE BEVERAGES: PRELIMINARY RESULTS FROM A FOUR-WEEK CLINICAL TRIAL. Jeffrey Holzberg1, Ran Jin2, Ngoc-Anh Le2, Miriam B. Vos1,2. 1Medical School, Emory University, Atlanta, GA; 2Pediatrics, Emory University, Atlanta, GA

Introduction: Nonalcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease in children. Recent research has suggested increased fructose consumption as a risk factor for the insulin resistance, hypertension and dyslipidemia seen in NAFLD. Plasminogen Activator Inhibitor-1 (PAI-1) production has been proposed as a key step in this pathway. The purpose of this study was to examine the relationship between fructose consumption, PAI-1 levels and markers for insulin resistance and dyslipidemia in children with high risk of NAFLD.

Methods: 49 Hispanic overweight and obese children aged 11-18 years with high daily consumption of sugar-sweetened beverages were recruited throughout the state of Georgia. All participants underwent an anthropometric assessment, magnetic resonance imaging for hepatic fat content, and a fasting blood sample collection to correlate PAI-1 levels with various metabolic markers. 21 of these children underwent a 4-week, double-blinded, parallel armed intervention study, consuming 36 ounces of either fructose- or glucose-sweetened beverages daily. PAI-1 levels were measured with ELISA and compared at baseline, two weeks and four weeks using repeated measures ANOVA.

Results: Among the 49 children, PAI-1 was found to be significantly higher among those with high hepatic fat compared to low hepatic fat (p-value 0.003). Additionally, there was a significant correlation between PAI-1 and visceral adipose thickness (p-value 0.04), adipose-IR (p-value 0.001) and CRP (p-value 0.01). Within the fructose arm of the intervention group (n=9), PAI-1 was measured in the serum at 47.3 ± 7.8, 48.7 ± 5.9, and 49.5 ± 7.0 ng/mL at baseline, two weeks and four weeks, respectively. Within the glucose group (n=11), PAI-1 was measured at 51.3 ± 6.7, 48.0 ± 9.7, and 50.9 ± 8.0 ng/mL at baseline, two weeks and four weeks, respectively. Using repeated measures ANOVA, the level of PAI-1 over time was not significantly affected by the type of supplement, (F-test = 1.59, p-value = 0.2).

Conclusion: Levels of PAI-1 appear to be positively correlated with hepatic fat and insulin resistance. There appears to be no significant difference in the levels of PAI-1 over the four week period between children who consumed fructose or glucose beverages. Further studies with a larger sample size are needed to more closely analyze this trend.

33 HYPERKINETIC GALLBLADDER IN THE PEDIATRIC POPULATION. Patrick M. Jones, Marian Pfefferkorn, Pediatric Gastroenterology/Hepatology/Nutrition, Riley Hospital for Children at IU Health, Indianapolis, IN

BACKGROUND: Biliary dyskinesia is a disorder increasingly recognized in children in which gallbladder emptying is impaired, presumably because of chronic acalculous cholecystitis. It is traditionally diagnosed when gallbladder ejection fraction (GBEF) is less than 35% on hepatobiliary scintigraphy. Treatment is with cholecystectomy, although studies evaluating long term outcomes have shown mixed results. Anecdotally, we have seen patients with very high GBEF values who go on to cholecystectomy and subsequently have resolution of their pain. There are few, if any, data about the possible entity of hyperkinetic gallbladder.

OBJECTIVES: We wanted to describe the patients at our institution with very high GBEF values, by recording their symptoms, radiologic and endoscopic testing performed, and pathology results of their gallbladder if they went for cholecystectomy.

METHODS: The nuclear medicine radiologist provided the medical record numbers of all patients ages 20 and younger who had a GBEF >80% on HIDA scan in the previous ten years. A retrospective chart review was then conducted to collect demographic data, symptoms, other testing performed, and pathology results if they had cholecystectomy.

RESULTS: Forty nine patients (39 female, 10 male) had GBEF values greater than 80%. Of these, nine patients (18%) had cholecystectomies. Eight out of nine gallbladder specimens showed chronic cholecystitis (four in association with cholelithiasis, four without stones).

CONCLUSIONS: Our results are limited by lack of follow up data on whether the patients who had cholecystectomies had improvement in their pain, so prospective studies are needed in the future. However, our results do suggest that a GBEF greater than 80% may not be normal but may signify underlying gallbladder pathology. We are currently collecting large numbers of pediatric patients who had HIDA scans so that we compare rates of cholecystectomy and pathology results of patients with low (<35%), normal (35-80%), and hyperkinetic (>80%) ejection fractions.

Intestinal/Colonic Disorders – Inflammatory Bowel Disease

50 THE CHARACTERISTICS OF PEDIATRIC-ONSET INFLAMMATORY BOWEL DISEASE AT A JAPANESE CHILDREN’S HOSPITAL: COMPARISON TO EUROKIDS DATA USING PARIS CLASSIFICATION. Katsuhiro Arai, Hirotaka Shimizu, Chisa Ogura, Rie Funayama, Kenji Hosoi, Akira Matsui, Medical Specialty, National Center for Child Health and Development, Setagaya, Japan

Background: Patients with inflammatory bowel disease (IBD) have been increasing worldwide including children. The characteristics of pediatric-onset IBD have been reported mainly from North America and Europe, and pediatric data from Asia has been limited.

Methods: A cohort of 100 children with IBD at National Center for Child Health and Development (NCCHD) in Japan was retrospectively reviewed. The characteristics of ulcerative colitis (UC) and Crohn's disease (CD) in this cohort were analyzed using the Paris Classification. The results were compared to those of EUROKIDS data.

Results: 59 children with UC, 39 children with CD, and 2 children with indeterminate colitis were identified. The comparison of disease characteristics to EUROKIDS according to the Paris classification were summarized in the following tables.

Conclusion: The characteristics of pediatric-onset IBD in Japan appeared similar to those reported by EUROKIDS study. However, There were more L2, and less B2/B3 in our CD children compared to that of EUROKIDS. Multicenter prospective registry study is warranted to
Age at diagnosis: A1a (0-<10y), A1b (10-<17y), A2 (17-40y), Disease extent at diagnosis: E1 (ulcerative proctitis), E2 (left-sided UC, distal to splenic flexure), E3 (extensive, hepatic flexure distally), E4 (pancolitis, proximal to hepatic flexure), S1(ever severe: PUCAI ≧ 65), G1 (Impaired linear growth)

## Ulcerative Colitis

<table>
<thead>
<tr>
<th></th>
<th>A1a</th>
<th>A1b</th>
<th>A2</th>
<th>E1</th>
<th>E2</th>
<th>E3</th>
<th>E4</th>
<th>S1</th>
<th>G1</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC (NCCHD)</td>
<td>27.1</td>
<td>69.5</td>
<td>3.4</td>
<td>8.7</td>
<td>10.5</td>
<td>10.5</td>
<td>70.2</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>UC (EUROKIDS)</td>
<td>26</td>
<td>68</td>
<td>6</td>
<td>5</td>
<td>18</td>
<td>9</td>
<td>69</td>
<td>N/A</td>
<td>N/A</td>
</tr>
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</table>

## Crohn's Disease

<table>
<thead>
<tr>
<th></th>
<th>A1a</th>
<th>A1b</th>
<th>A2</th>
<th>L1</th>
<th>L2</th>
<th>L3</th>
<th>L2+L4a</th>
<th>L3+L4a</th>
<th>L3+L4a+L4b</th>
<th>B1</th>
<th>B2</th>
<th>B3</th>
<th>B2B3</th>
<th>P</th>
<th>G1</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD (NCCHD)</td>
<td>26%</td>
<td>69%</td>
<td>5%</td>
<td>10.3%</td>
<td>28.2%</td>
<td>28.2%</td>
<td>10.3%</td>
<td>12.8%</td>
<td>10.3%</td>
<td>87.1%</td>
<td>7.7%</td>
<td>2.6%</td>
<td>2.6%</td>
<td>12.8%</td>
<td>32</td>
</tr>
<tr>
<td>CD (EUROKIDS)</td>
<td>20%</td>
<td>80%</td>
<td>7.9%</td>
<td>18.2%</td>
<td>27.7%</td>
<td>4.1%</td>
<td>14.3%</td>
<td>4.3%</td>
<td>82%</td>
<td>12%</td>
<td>5%</td>
<td>2%</td>
<td>9</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

Disease location at diagnosis: L1 (distal 1/3 ileum ± limited cecal disease), L2 (colonic), L3 (ileocolonic),L4a (upper disease proximal to Ligament of Treitz), L4b (upper disease distal to Ligament of Treitz and proximal to distal 1/3 ileum)

Disease behavior at diagnosis: B1 (non-stricturing/non-penetrating), B2 (stricturing), B3 (penetrating), P (perianal disease)

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**51 CHANGES IN VITAMIN D-RELATED MINERAL METABOLISM FOLLOWING INFlixIMAB INDUCTION IN CROHN'S DISEASE.** Marianne Augustine1, Mary Leonard2, Meena Thayu1, Robert Baldassano1, Justine Shults3, Michelle Denburg2, 1Division of Gastroenterology, Hepatology and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA; 2Division of Nephrology, The Children's Hospital of Philadelphia, Philadelphia, PA; 3Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, PA

**Background:** We recently showed that incident Crohn's disease (CD) was associated with 25(OH)D and 1,25(OH)2D deficiency and relative hypoparathyroidism that resolved over time, suggesting that inflammatory cytokines may suppress parathyroid hormone (PTH) and the renal 1-α-hydroxylase. A recent study suggested that fibroblast growth factor-23 (FGF23) may be a contributing factor. The aim of this study was to assess short-term changes in vitamin D-related mineral metabolism in CD following induction with anti-tumor necrosis factor (TNF)-α therapy.

**Methods:** 87 CD participants (5-39 years of age, 61% male, and 17% black) were evaluated prior to and 10 weeks post infliximab induction. Serum concentrations of vitamin D metabolites [25(OH)D, 1,25(OH)2D, 24,25(OH)2D], PTH, FGF23, interleukin (IL)-6, and TNF-α were measured at each visit. Paired t-tests or sign rank tests were used to determine changes over time. Multivariable generalized estimating equation (GEE) regression analysis was used to examine correlates of PTH and 1,25(OH)2D at each visit.

**Results:** Following infliximab, there were significant decreases in concentrations of inflammatory markers (IL-6, TNF-α, ESR and CRP) and in pediatric CD activity index (PCDAI). At baseline, 36% of participants were classified as moderate to severe, as compared to 1% at 10 weeks. PTH and 1,25(OH)2D concentrations increased significantly, while 25(OH)D, 24,25(OH)2D and FGF23 did not change significantly. [table] In GEE analysis, higher IL-6, TNF-α, ESR and CRP were associated with lower PTH concentrations (all p <0.001), adjusted for corrected calcium and 25(OH)D. Higher PTH was associated with higher 1,25(OH)2D concentrations at each visit adjusted for 25(OH)D (p <0.001). In models adjusted for 25(OH)D, higher levels of all inflammatory markers were associated with lower 1,25(OH)2D concentrations. However, with the exception of CRP, when PTH was added to these models, the inflammatory markers were no longer significantly associated with 1,25(OH)2D.

**Conclusions:** Inflammation was associated with lower PTH and 1,25(OH)2D concentrations. Following infliximab induction, there was an increase in PTH and 1,25(OH)2D concentrations without concomitant changes in 25(OH)D and FGF23, confirming the suppressive effects of inflammation on PTH and thereby renal activation of vitamin D.
Measures of Vitamin D-Related Mineral Metabolism and Inflammation Following Infliximab Induction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Week 0</th>
<th>Week 10</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCDAI</td>
<td>28 ± 15.9</td>
<td>12 ±8.90</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>7.2 (5.1, 10.3)</td>
<td>1.7 (1.1, 2.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>12.4 (6.0, 24.9)</td>
<td>4.9 (2.6, 9.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>1.1 (0.5, 2.6)</td>
<td>0.5 (0.3, 0.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>24.5 (12.40)</td>
<td>9 (4,15)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PTH (pg/mL)</td>
<td>21.0 (14, 33)</td>
<td>30 (20, 40)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FGF 23 (pg/mL)</td>
<td>29.4 (23.8, 37.2)</td>
<td>31.8 (23.8, 40.8)</td>
<td>0.22</td>
</tr>
<tr>
<td>Corrected Calcium (mg/dL)</td>
<td>4.98± 0.10</td>
<td>5.04 ± 0.07</td>
<td>0.75</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.79 ±0.58</td>
<td>4.2 ±0.44</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1,25(OH)2 D (pg/mL)</td>
<td>41.7 (31.6, 58)</td>
<td>48.1 (38.2, 60.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>25(OH)D (ng/mL)</td>
<td>25.2 (17.1, 35.0)</td>
<td>26.2 (19.6, 33.1)</td>
<td>0.50</td>
</tr>
<tr>
<td>24,25(OH)2D (ng/mL)</td>
<td>3.1 (1.9, 4.5)</td>
<td>3.1 (2.0, 4.4)</td>
<td>0.72</td>
</tr>
</tbody>
</table>

PCDAI, Pediatric Crohn's Disease Activity Index for participants less than 22 years of age.

52 INFLAMMATORY BOWEL DISEASE AMONGST SOUTH ASIAN IMMIGRANTS TO CANADA AND THEIR CHILDREN: A POPULATION-BASED COHORT STUDY. Eric I. Benchimol1,2, Douglas G. Manuel2,3, David R. Mack1, Geoffrey C. Nguyen1,2, Teresa To4,5, Nassim Mojaverian5, Pauline Quach1,2, Jennifer L. Gommerman5, Kenneth Croitoru6, Astrid Guttmann1,2, 

BACKGROUND: Canada has amongst the highest incidence of IBD in the world. IBD is most common in westernized nations and less common in South Asia (SA) based on reports from India. Small studies have demonstrated high incidence of IBD in immigrants from SA to the United Kingdom and Vancouver, Canada. In recent years, SA has become the leading source of immigrants to Canada. We assessed the incidence of IBD in both immigrants to Canada from SA and their Canadian-born children to determine the role of the Canadian environment in disease development.

METHODS: The Ontario Crohn's and Colitis Cohort (OCCC) is a population-based surveillance system derived from health administrative data using validated algorithms to identify all patients diagnosed with IBD in Ontario, Canada (1994-2009). The OCCC was linked to the records of immigrants landing in Canada after 1985. Incidence of IBD was calculated per 100,000 person-years of follow-up. We calculated adjusted relative incidence ratio (RIR) with 95% confidence intervals (CI) to compare incidence in SA immigrants and their children, immigrants from other regions, and non-immigrants (reference group). Analyses were stratified by age of onset (pediatric <18y; adult 18-64y), and disease type (Crohn's or UC).

RESULTS: In Ontario, there are 68,260 people with IBD of whom 3553 (5.2%) are immigrants. 23.7% of immigrants originated from South Asia (SA) based on reports from India. Small studies have demonstrated high incidence of IBD in immigrants from SA to the United Kingdom and Vancouver, Canada. In recent years, SA has become the leading source of immigrants to Canada. We assessed the incidence of IBD in both immigrants to Canada from SA and their Canadian-born children to determine the role of the Canadian environment in disease development.

CONCLUSIONS: Incidence of IBD in SA immigrants to Canada is low and comparable to immigrants from other regions (predominantly from east Asia). However, incidence in Canadian-born children of SA immigrants is comparable to the children of non-immigrants. This suggests that birth in Canada confers elevated risk of IBD in those of SA origin. Further research will identify the biological changes in immigrants and their children which confers IBD risk, as well as the age at which exposure to the Canadian environment results in the greatest risk.
Incidence of IBD in immigrants and their children.

<table>
<thead>
<tr>
<th></th>
<th>Pediatric IBD</th>
<th>Adult IBD</th>
<th>Children of Immigrants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># new diagnose</td>
<td>Total populat</td>
<td>PYS</td>
</tr>
<tr>
<td>South Asian Immigrants</td>
<td>31</td>
<td>106,338</td>
<td>570,717</td>
</tr>
<tr>
<td>Immigrants from Other Regions</td>
<td>111</td>
<td>369,951</td>
<td>2,139,931</td>
</tr>
<tr>
<td>Non-Immigrants</td>
<td>3825</td>
<td>4,547,173</td>
<td>37,217,447</td>
</tr>
</tbody>
</table>

PYs: Person-years of follow-up; CI: confidence intervals.

53 INCIDENCE OF PEDIATRIC INFLAMMATORY BOWEL DISEASE IN ONTARIO, CANADA (1994-2009): POPULATION-BASED ESTIMATES FROM THE ONTARIO CROHN'S AND COLITIS COHORT. Eric I. Benchimol1,2, Astrid Guttmann3,4, David R. Mack1, Geoffrey C. Nguyen4,5, Nassim Mojaverian1, Pauline Quack1,2, Douglas G. Manuel1,2,5
1CHEO Inflammatory Bowel Disease Centre, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, University of Ottawa, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; 3Department of Paediatrics, University of Toronto, Toronto, ON, Canada; 4Zane Cohen Centre for Digestive Research, Division of Gastroenterology, Mount Sinai Hospital, Toronto, ON, Canada; 5Ottawa Hospital Research Institute, Ottawa, ON, Canada
BACKGROUND: Ontario, Canada has amongst the highest reported incidence and prevalence of pediatric-onset inflammatory bowel disease (IBD) in the world (1). Between 1994-2005, incidence was noted to be increasing in children <10y, primarily attributed to increasing incidence of Crohn's disease (CD), not ulcerative colitis (UC). We aimed to update these estimates and assess age-specific incidence of pediatric IBD from 1994-2009.

METHODS: The Ontario Crohn's and Colitis Cohort is a population-based surveillance cohort derived from health administrative data. All patients with IBD in Ontario, Canada. Children <18y diagnosed with IBD were identified and classified as CD, UC or unclassifiable using validated algorithms (1). Age- and sex-adjusted incidence was calculated (with 95% confidence intervals (95%CI) by gamma distribution), using age-appropriate standard populations for each age group. Statistical trends over time were determined using Poisson regression analysis and reported as percentage change over the 16 years of analysis.

RESULTS: Between 1994 and 2009, 4374 children were diagnosed with IBD in Ontario (2561 CD, 1509 UC, 304 unclassifiable with available data). The yearly at-risk population ranged from 2.52 to 2.74 million children. Incidence increased from 9.4 (95%CI 8.2-10.8) to 13.1 (95%CI 11.8-14.6) per 100,000 children (P<0.0001). CD incidence increased from 5.2 to 8.0 per 100,000 between 1994-2009 (P<0.0001), and UC incidence rose from 3.9 per 100,000 in 1994 to a peak of 4.8 per 100,000 in 2006 (P<0.0001). Percentage change in incidence between 1994-2009 are reported for each age group in the table below.

CONCLUSIONS: The incidence of IBD, CD and UC continue to rise in Ontario. While previous research (1) reported significant increases only in children under 10 and only in CD, recent estimates from the Ontario Crohn's and Colitis Cohort demonstrated significantly increased incidence in almost all age groups, both in CD and UC.

Change in incidence of IBD in Ontario, Canada (1994-2009).

<table>
<thead>
<tr>
<th></th>
<th>IBD</th>
<th>Crohn's</th>
<th>UC</th>
</tr>
</thead>
<tbody>
<tr>
<td>6mo-4yr</td>
<td>+56.8% (P=0.11)</td>
<td>+51.0% (P=N/A)*</td>
<td>+38.1% (P=0.95)</td>
</tr>
<tr>
<td>5-9y</td>
<td>+65.7% (P&lt;0.0001)</td>
<td>+59.9% (P=0.0003)</td>
<td>+57.9% (P&lt;0.0001)</td>
</tr>
<tr>
<td>10-14y</td>
<td>+34.1% (P&lt;0.0001)</td>
<td>+36.3% (P=0.002)</td>
<td>+38.9% (P=0.09)</td>
</tr>
<tr>
<td>15-17y</td>
<td>+25.1% (P=0.009)</td>
<td>+12.1% (P=0.006)</td>
<td>+27.4% (P=0.03)</td>
</tr>
</tbody>
</table>

*P value not available due to overdispersion.
DELAY IN DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE IN NEW ZEALAND CHILDREN. Sophie McFarlane1,2, Jonathan Bishop1,2, 1Dunedin School of Medicine, University of Otago, Dunedin, New Zealand; 2Department of Paediatrics, Child and Youth Health, University of Auckland, Auckland, New Zealand. 

Introduction: There is often significant delay in the diagnosis of inflammatory bowel disease (IBD) in childhood. This may be related to the relative rarity of pediatric IBD, a lack of awareness by primary and secondary care and/or the protean manifestations of the condition. Delayed diagnosis is associated with an increased symptom burden and the risk of poorer long-term outcome. Particular challenges are faced in New Zealand due to the low population density, limited access to tertiary paediatric gastroenterology and widely varying referral pathways.

Methods: Starship Children's hospital is one of two paediatric gastroenterology units nationally and provides tertiary care for children from New Zealand's North Island.

A retrospective review of medical records of children diagnosed with IBD in Starship over a five year period was performed. We assessed the recorded delay in diagnosis and investigated potential associated factors, including epidemiological factors, disease-related factors and the nature of the referral pathway. A questionnaire was also completed by families, which provided comparative data from families relating to symptom onset and date of diagnosis.

Results: 61 children (25F, 36M) were diagnosed in the period studied. 43 (70%) had Crohn's disease, 18 (30%) ulcerative colitis or IBDU. IBD was more prevalent in higher socioeconomic groups.

The median time from symptom onset to diagnosis was 6 months. However, in 17 patients (28%), the time to diagnosis was greater than 1 year.

Statistically significant delays in diagnosis were associated with older age ($p = 0.05$), higher socioeconomic group ($p = 0.01$) and increasingly complex referral pathways ($p < 0.001$).

There was poor correlation between time to diagnosis documented in medical records and reported by families.

Conclusion: The results are comparable with international studies and demonstrate a considerable diagnostic delay in children presenting with IBD in New Zealand. This study highlights the need for increased awareness of the condition in primary and secondary care and the value of developing standardised, streamlined referral pathways. The findings of increased delay in older children and those from higher socioeconomic groups have not been previously described and warrant further investigation.

BIOLOGIC AGENTS ARE NOT ASSOCIATED WITH EXCESSIVE WEIGHT GAIN IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE. Rachel Chevalier, Felicity T. Enders, Seema Kumar, Jeanne Tung, Mayo Clinic, Rochester, MN

Background: Children with inflammatory bowel disease (IBD) are frequently underweight at the time of diagnosis. The use of anti-tumor necrosis factor (anti-TNF) agents in other autoimmune diseases (psoriasis, spondyloarthropathies) has been associated with excess weight gain. We examined whether children with IBD treated with anti-TNF agents also gain weight excessively.

Methods: We performed a retrospective chart review of pediatric patients treated with anti-TNF therapy prior to 18 years of age seen at our institution between January 1, 1996 and December 31, 2011. Demographics, type of IBD, disease activity at onset of anti-TNF therapy, and concomitant steroid use were collected. Anthropometric data was collected for anti-TNF initiation, 3, 12, and a median of 21.5 months later. Based on CDC growth charts, weight and height data were transformed into z-scores by age and gender, and changes in growth and BMI were expressed as a change in z-score.

Results: During the study period, 151 children received anti-TNF therapy. Of these, 42 (76% Crohn's, 19% ulcerative colitis, 2% indeterminate colitis) had sufficient follow-up for inclusion. The median age was 14.6 years (44.2% male). We had 80% power to detect excessive weight gain occurring in at least 8% of patients. At initiation of anti-TNF therapy, the mean weight z-score was -0.50 (± 1.18), while the mean BMI was -0.38 (± 1.15). After 3 and 12 months of biologic therapy, changes in weight and BMI z-scores were not significant. At last follow-up, however, the change in weight z-score was 0.40 ($p<0.004$, 95%CI 0.14-0.66) while change in BMI z-score was 0.30 ($p<0.03$, 95%CI 0.05-0.56). Female patients had a change in weight z-score of 0.39 ($p=0.04$, 95%CI 0.04-0.74) and BMI z-score of 0.41 ($p<0.02$, 95%CI 0.09-0.74). The majority of patients (36, 88%) were treated with corticosteroids during the study period. There was no difference between IBD subtypes.

Conclusions: One year after initiating biologic therapy, children with IBD do not experience excessive weight gain. Female patients may experience excessive weight gain beyond one year of treatment.

VB15, A DISSOCIATIVE STEROIDAL ANALOGUE, IS EFFECTIVE AT REDUCING INTESTINAL INFLAMMATION. Jesse Damsker2, Blythe C. Dillingham2, Soheil Sadri1, Christopher Heier2, Kanheboyina Nagaraju2,3, John McCall2, Eric P. Hoffman2,3, Erica K. Reeves1, Anthony Sandler2, Laurie S. Conklin1, Sheikh Zayed Institute for Pediatric Surgical Innovation, Children's National Medical Center, Washington, DC; 2Research Center for Genetic Medicine, Children's National Medical Center, Washington, DC; 3Reveragen Biopharma, Rockville, MD

BACKGROUND: Glucocorticoids are used frequently to induce remission and treat refractory Inflammatory Bowel Disease (IBD). Despite their effectiveness, severe side effects, such as osteoporosis, growth inhibition, and muscle atrophy limit long-term use. The anti-inflammatory properties of glucocorticoids are believed to be mediated by inhibition of pro-inflammatory transcription factors such as NFκB, while glucocorticoid side effects are the result of transcriptional activation of genes with glucocorticoid responsive elements (GREs) in their promoter regions. VB15, a dissociative steroid analogue, lacks the capacity to induce GRE-mediated transcription, but has been shown to inhibit NFκB activity in multiple cell types, including muscle and lung cells. We hypothesize that VB15 may also inhibit NFκB activity in intestinal epithelial cells and reduce inflammation in two mouse models of IBD.

METHODS: To test the effect of VB15 on NFκB activity in vitro, human primary intestinal epithelial cells were treated with VB15, prednisolone, or vehicle control and subsequently stimulated with TNFα. The expression of NFκB-inducible genes was then measured by RT-PCR. To assess the anti-inflammatory capacity of VB15 within the context of IBD, two widely used acute mouse models—dextran
Background: Anemia is the most common systemic complication of inflammatory bowel disease (IBD) with significant negative impact on quality of life and cognition in children regardless of disease activity. While iron deficiency is the main contributor, iron therapy is underutilized due to poor tolerance of oral formulations and concerns about hypersensitivity reactions to parenteral formulations, particularly iron dextran. Iron sucrose (IS), the most widely used and well-studied intravenous iron supplement in adults with IBD, is also a potential alternative, not yet systematically studied in children with IBD.

Objective: Review response of anemia and iron indices to standard doses of IS in pediatric IBD patients to aid design of prospective studies for dose optimization.

Methods: Medical records of patients followed by the author with diagnosis of IBD, who received IS during 2012 were reviewed. There were 12 patients, ages 10-18 years, 10 with Crohn's disease, and 2 with ulcerative colitis; all except 2 in clinical remission throughout treatment. Vitamin B12 and folate deficiencies were ruled out. Indications for IS: Ferritin <30 (considered consistent with iron deficiency in IBD patients without evidence of active disease) with or without anemia and/or microcytosis (Hb and/or MCV < mean -2SD for age), and difficulty taking oral iron supplements. Average doses per IS infusion: 2.5-3.4 mg/kg; maximum single dose: 200 mg; one treatment cycle: 2 IS infusions, 1 week apart. Of the 48 IS infusions administered, results from 36 infusions are included in the analysis. Summary and Conclusions: Within recommended dose limits (max. 200 mg/infusion) intravenous IS is safe in children with IBD. Two IS infusions of 2.5-3.5 mg/kg, max. 200mg/dose, given 1 week apart lead to normalization of ferritin in the majority of iron deficient IBD patients.

Further studies are needed to determine optimal dosing schedules and establish the proper role of intravenous IS in treatment of iron deficiency in children with IBD.

57 INTRAVENOUS IRON SUCRose FOR TREATMENT OF IRON DEFICIENCY ANEMIA IN PEDIATRIC INFLAMMATORY BOWEl DISEASE. Istvan Danko, UW-Madison, Madison, WI

Background: Anemia is the most common systemic complication of inflammatory bowel disease (IBD) with significant negative impact on quality of life and cognition in children regardless of disease activity. While iron deficiency is the main contributor, iron therapy is underutilized due to poor tolerance of oral formulations and concerns about hypersensitivity reactions to parenteral formulations, particularly iron dextran. Iron sucrose (IS), the most widely used and well-studied intravenous iron supplement in adults with IBD, a potential alternative, has not been systematically studied in children with IBD.

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Further studies are needed to determine optimal dosing schedules and establish the proper role of intravenous IS in treatment of iron deficiency in children with IBD.

58 MANAGEMENT OF INTRA-ABDOMINAL ABSCESES IN CHILDREN WITH CROHN'S DISEASE: A 10-YEAR RETROSPECTIVE REVIEW. Jennifer L. Dotson1, Hillary Bashaw2, Benedict Nwomeh3, Wallace Crandall4

1Division of Pediatric Gastroenterology, Hepatology and Nutrition, Nationwide Children's Hospital, Columbus, OH; 2Pediatric Residency, Nationwide Children's Hospital, Columbus, OH; 3Division of Pediatric Surgery, Nationwide Children's Hospital, Columbus, OH

Background: Complications of Crohn's disease (CD) may include intra-abdominal abscesses (IAA), which often result in hospitalization, surgery and increased cost. There is a paucity of primary research and practice guidelines regarding optimal management in children. The study objectives were to assess the IAA management practice and outcomes at our institution and to facilitate the development of a local IAA diagnosis and treatment algorithm.

Methods: We conducted a retrospective medical record review for all pediatric patients with Crohn's disease who developed an IAA at Nationwide Children's Hospital from January 1, 2000 - April 30, 2012. Results: 27 cases of IAA were identified. The mean age at IAA diagnosis was 15.6 years, 17 (67%) female, and median CD duration of 2.8 months. Patients received several initial imaging studies (≤3 days from date of admission). 23 (85%) patients received a CT, 11 (41%) abdominal x-rays, 10 (37%) ultrasound, and 4 (15%) had a MRI. The median number of imaging studies was 2, with a range of 1-3. Follow up imaging studies during the index hospitalization included 12 (44%) CT, 9 (33%) ultrasound, 8 (30%) x-rays, and 3 (11%) MRI. The median number of follow up imaging studies was 3, with a range of 0-5. The average number of days from initial imaging to first follow up imaging study was 8.5 days. For initial management, 18 patients received only medical therapy, 8 underwent percutaneous drainage (PD) and 1 had surgery. Patients in the PD group had larger abscesses (7.5cm, p=0.031) compared to the medical (3.7cm) and surgical (4.9cm) groups. Central lines were placed in all patients in the PD group, in 10 (56%) patients in the medical group and none in
59 EPICUTANEOUS TOLERANCE INDUCTION TOWARDS THE TREATMENT OF GASTROINTESTINAL DISEASES.
David Dunkin1, Leticia Tordesillas2,3, Hugh Sampson2,3, Lloyd Mayer4, M. Cecilia Berin2,3; 1Pediatric Gastroenterology, The Icahn School of Medicine at Mount Sinai, New York, NY; 2Pediatric Allergy and Immunology, The Icahn School of Medicine at Mount Sinai, New York, NY; 3Immunology Institute, The Icahn School of Medicine at Mount Sinai, New York, NY

Background: Crohn's disease patients have an inherent defect in inducing T regulatory cells (Treg) via the gut. When generated externally in response to food antigen and infused into patients, Tregs are able to suppress inflammation in Crohn's disease. Epicutaneous tolerance induction has the potential to be used as a therapy by inducing Tregs but without the risk of the side effects present with oral and infused therapies. Additionally, epicutaneous exposure has been shown to block allergic inflammation in the gut of mice. We, therefore, examined the ability to induce epicutaneous and its mechanisms towards the goal of inducing gut homing of Tregs and bystander suppression of inflammation in Crohn's disease.

Methods: Mice were exposed epicutaneously daily for 5 days to the food antigen α-lactalbmin (ALA) 1mg. Then, two different models were utilized to assess suppression of Th2 or Th1 responses. For Th2 responses, mice were immunized with ALA systemically with alum. ALA-specific immunoglobulins in serum were determined by ELISA. Mice were then challenged orally or systemically, and anaphylaxis was assessed by symptoms and body temperature. For Th1 suppression, mice were immunized with ALA locally in the hock with CFA/IFA. Ex-vivo cytokine production by draining LNs was assessed by ELISA. The mechanism of tolerance induction was explored by determining the impact of repeated Ag exposure on DC phenotype and Treg development.

Results: Daily epicutaneous exposure to ALA induced tolerance as demonstrated by the inability to subsequently induce a Th2 response in one model: suppression of ALA-specific IgE formation and lack of symptoms upon challenge; and by suppression of Th1 responses in another model: ALA-specific IFN-γ. Repeated Ag exposure induced migration of Langerin+ DCs to the draining LN and proliferation of Tregs in both the draining LN and mesenteric LN.

Conclusion: The skin is an important route of tolerance formation upon epicutaneous ALA exposure. Our experimental model shows the relevance of epicutaneous exposure for the induction of Tregs. Potential exists to utilize epicutaneous Treg induction to suppress inflammation in the gut.

60 PREDICTORS OF RESPONSE TO INFliximAB IN PEDIATRIC FISTULIZING AND NON-FISTULIZING PERIANAL CROHN'S DISEASE: A GETAID PÉDIATRIQUE STUDY.
Claire E. Dupont-Lucas1, Catherine Le Gall2, Jérôme Viala3, Christine Martinez-Vinson1, Sheila Viola1, Anne Breton1, Cécile Talbott1, Alain Morali1, Alain Dabadie1, Raphaëlle Maudins2, Jean-Louis Giniès1, Thierry Lamireau1, Nicolas Caron1, Valérie Bertrand1, Claire Speyckerelle1, Laurent Michaud1, Céline Roman1, Valérie Triolo1, Stéphanie Willo1, Audrey Vanrenterghem1, Clara Cremilleux1, Nadège Thomassin1, Cécile Pelatant1, Corinne Albert1, Frank Ruemmelé1, Département de Pédiatrie, Centre Hospitalier Universitaire (CHU) de Caen, Caen, France; 2Service Hépato-Gastro-Entérologie pédiatrique, Hôpital Femme Mère Enfant, Lyon, France; 3Service Gastroentérologie et Nutrition pédiatriques, Hôpital Robert Debré, Paris, France; 4Service Gastroentérologie et Nutrition pédiatriques, Hôpital Armand Trousseau, Paris, France; 5Unité hépatologie, gastroentérologie et nutrition pédiatriques, Hôpital des enfants, Toulouse, France; 6Service Gastroentérologie et Nutrition pédiatriques, Hôpital Necker Enfants Malades, Paris, France; 7Service de médecine infantile, Hôpital d'enfants de Brabois, Vandoeuvre-lès-Nancy, France; 8Service de médecine de l'enfant et l'adolescent, CHU Hôpital Sud, Rennes, France; 9Service de Pédiatrie, CHU de Dijon, Dijon, France; 10Clinique de l'adolescent et service des grands enfants, CHU d'Angers, Angers, France; 11Gastroentérologie pédiatique, Hôpital des enfants, Bordeaux, France; 12Service pédiatrie générale, CHU de Clermont-Ferrand, Clermont-Ferrand, France; 13Service de Pédiatrie, Groupe Hospitalier du Havre, Le Havre, France; 14Service de Pédiatrie, Groupe Hospitalier de l'Institut Catholique de Lille, Lille, France; 15Unité de gastro-entérologie, hépatologie et nutrition, Hôpital Jeanne de Flandres, Lille, France; 16Service Hépato-gastro-entérologie et nutrition, endocrinologie et néphrologie pédiatriques, Hôpital de la Timone, Marseille, France; 17Service de Pédiatrie, CHU de Nice, Hôpital L'Archet 2, Nice, France; 18Service de médecine infantile, Hôpital Clocheville, Tours, France; 19Service Pédiatrie médicale et Médecine de l'adolescent, CHU d'Amiens, Amiens, France; 20Service de Pédiatrie générale, CHU de Besançon, Besançon, France; 21Clinique Universitaire Pédiatrique, CHU de Grenoble, Grenoble, France; 22Service de Pédiatrie, Centre Hospitalier du Mans, Le Mans, France; 23Unité d'Epidémiologie Clinique, URC Robert Debré, INSERM CIE 5, Paris, France

Objective: To identify predictors of perianal lesions' healing after one year of infliximab (IFX) treatment in pediatric perianal Crohn's disease (CD), and predictors of loss of response during the year of follow-up, among initial responders.

Patients and methods: We performed a retrospective chart review of all pediatric patients treated with IFX between 2000 and 2011 for perianal CD, not including patients who had only superficial fissures and skin tags, or who had received IFX previously for luminal disease. Patients were recruited by pediatric gastroenterologists participating in the Groupe d'Études Thérapeutiques des Affections pédiatriques.
Inflammatory Bowel Disease Collaborative Research Group. Response was monitored after induction therapy and at one year of follow-up, with or without maintenance therapy. Complete response was defined as closure of all fistulas and complete healing of ulcers. Partial response was defined as a reduction of 50% or more from baseline in the number of draining fistulas or partial healing of ulcers. Treatment was considered to have failed if the perianal lesions were identical to baseline or if the patient had discontinued IFX before one full year of treatment due to adverse events or lack of efficacy.

Results: 103 patients from 23 French hospitals were included. Sixty-two percent were male. Median age of first IFX infusion was 13.6 years (range, 1.4 - 18.4), and median duration of CD was 9.8 months (range, 0 - 75.9). Seventy-nine patients (77%) had fistulas/abscesses and 24 patients (25%) had a cavitating ulcer with or without associated fistula/abscess. 88 patients (85%) responded to induction therapy (37 partial / 51 complete). At one year, 76 patients (74%) were responders (22 partial / 54 complete). Predictors of one-year response using a multivariable logistic regression model were: a number of fistulas of ≤ 1 per patient (OR: 4.36, 95% CI: 1.33 - 14.31, p=0.015) and baseline Harvey-Bradshaw index ≤ 5 (OR:3.28, 95%CI: 1.14 - 9.46, p=0.028). The presence of perianal lesions at diagnosis of CD was not associated with one-year response (p=0.21), nor were surgical drainage before initiation of IFX in patients with abscesses or combined therapy with an immunosuppressant during the year of treatment with IFX (p=0.89). Predictors of relapse during the year of follow-up among initial responders, using a multivariable cox regression model, were: CD duration < 10 months at initiation of IFX (OR: 2.97, 95% CI: 1.25 - 7.06, p=0.001) and number of fistulas > 1 per patient (OR: 3.50, 95% CI: 1.46 - 8.41, p=0.007). Neither surgical drainage before IFX nor concomitant medication with antibiotics, corticosteroids or immunosuppressants were associated with relapse during the year of follow-up.

Conclusion: A number of fistulas of less than 2, a CD duration of more than 10 months and a baseline Harvey-Bradshaw index of less than 5 were independent predictors of response to infliximab in pediatric perianal CD. Combined therapy with immunosuppressant or surgery did not change the outcome of IFX treatment in these patients.

61 INFORMATION NEEDS FOR PEDIATRIC IBD PATIENTS AND THEIR PARENTS. Dawn R. Ebach, Pediatrics, University of Iowa, Iowa City, IA

Background: It is important for patients to understand their disease and treatment options in order to fully participate in decision making and to improve adherence to recommendations.1 To better anticipate patient needs investigating how patients learn about their disease and whether the sources of information are accurate is needed. In addition, there can often be a disconnect between what a physician feels is important information and what the patient wants to know. A 2011 study in adults revealed that 24% of patients were dissatisfied in the information they received and that there was information that they wanted and were not provided such as about prognosis or self-management.2

Methods: A questionnaire obtained from an ongoing IRB approved study of shared decision making aids was analyzed. Pediatric IBD patients between 8-20 and their parents were invited to participate if they were newly diagnosed or were having a change in therapy. Results: A total of 34 subjects (15 mothers, 6 fathers, and 13 patients) completed the questionnaire. Eleven of the patients had been recently diagnosed and 4 had the diagnosis for at least 1 year. Two patients had ulcerative colitis and 13 had Crohn’s disease. The internet website (16/34, 47%), Learning from friends or family member (7/34, 21%), computer applications (4/34, 12%) or videos (5/34, 15%) were the most common source of previous knowledge of IBD (17 patients) and a close family member or no previous knowledge was 24 patients (25%) had a cavitating ulcer with or without associated fistula/abscess. 88 patients (85%) responded to induction therapy (37 partial / 51 complete). At one year, 76 patients (74%) were responders (22 partial / 54 complete). Predictors of one-year response using a multivariable logistic regression model were: a number of fistulas of ≤ 1 per patient (OR: 4.36, 95% CI: 1.33 - 14.31, p=0.015) and baseline Harvey-Bradshaw index ≤ 5 (OR:3.28, 95%CI: 1.14 - 9.46, p=0.028). The presence of perianal lesions at diagnosis of CD was not associated with one-year response (p=0.21), nor were surgical drainage before initiation of IFX in patients with abscesses or combined therapy with an immunosuppressant during the year of treatment with IFX (p=0.89). Predictors of relapse during the year of follow-up among initial responders, using a multivariable cox regression model, were: CD duration < 10 months at initiation of IFX (OR: 2.97, 95% CI: 1.25 - 7.06, p=0.001) and number of fistulas > 1 per patient (OR: 3.50, 95% CI: 1.46 - 8.41, p=0.007). Neither surgical drainage before IFX nor concomitant medication with antibiotics, corticosteroids or immunosuppressants were associated with relapse during the year of follow-up.

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Ranks of Topics

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Patients ranked topics from 1-10 with 1 being the topic they were most interested in and 10 with least interest. Numbers in parentheses after topics refers to the number of patients who selected this topic. Some patients did not rank.

62 **USE OF DECISION MAKING AIDS FOR IBD THERAPY. Dawn R. Ebach, Pediatrics, Univ. of Iowa, Iowa City, IA**

Background: It is important for patients to understand their disease and treatment options in order to fully participate in decision making and to improve adherence to recommendations. Shared decision making aids are tools designed to provide information about patient options for complex decisions. This study involved evaluating the use of a booklet designed to provide information about efficacy, risks, and benefits of various IBD therapies.

Methods: An IRB approved quasi-randomized study evaluated the use of visual aids (VA) in therapeutic decision making as compared to discussion of therapy without the use of aids (control) in patients with newly diagnosed IBD or for those facing change in therapy. A pre-test consisting of 10 true/false and 10 multiple choice questions about IBD was administered. The physician then used a booklet with written and graphical information in their discussion of therapeutic in those with in the VA group and no booklet was used in the control group. The same test was then given and a satisfaction survey completed.

Results: The control group had 13 parents and 9 patients. The VA group had 7 parents and 4 patients. Pretest scores for the control group was 71% and for and 79% for VA. Posttest scores were 80% for control and 82% for VA. P=0.2082 for the change in score between groups. Overall patients were satisfied with either method of explanation. 87.5% of the VA group strongly agreed with the statement "I felt like I was included in decision making but only 73% of the control group strongly agreed (p=0.6378). However, 25% of the VA group strongly disagreed with the statement "I wish that more visual aids were used by doctors and only 12.5% of the control group agreed or strongly agreed with the statement "I wish doctors used visual aids." (p=0.21)

Conclusion: Subjects were overall satisfied with their doctor's explanation of therapy for IBD in both groups. The method used did not show any differences in knowledge obtained. It is possible that since the same physicians were enrolling patients in both groups the amount and quality of information given did not differ, thus leading to no differences in knowledge or satisfaction. Further studies about long term disease control and medication adherence with use of decision making aids would be beneficial.


63 **THIOPURINE MONITORING IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW. Anastasia Konidari2, Antonios Anagnostopoulos2, Laura J. Bonnett2, Munir Pirmohamed2, Wael El-Matary2**

1Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada; 2University of Liverpool, Liverpool, United Kingdom

Background: Thiopurines are widely used for maintenance of remission in children with inflammatory bowel disease (IBD). Current evidence of the importance of thiouprine metabolite and peripheral blood count monitoring for assessment of therapeutic response and thiopurine toxicity is controversial.

Aim: To systematically review the evidence on the utility of thiopurine metabolite and peripheral blood count monitoring in assessing therapeutic response and thiopurine induced haematologic and hepatic toxicity in children with IBD.

Methods: Medline, Embase, Cochrane Central Register of Controlled trials and www.clinicaltrials.gov. were searched. Randomised controlled trials (RCTs), cohort studies and large case series were eligible. Primary outcome was the clinical usefulness of routine thiopurine metabolite and peripheral blood count monitoring in assessing therapeutic response and toxicity in children with IBD. Secondary outcome was to investigate a possible correlation between these markers.

Results: Sixteen studies of variable quality were included (n=1093). None of the studies were RCTs. While high 6TGN levels were not consistently associated with leucopenia, a positive correlation between 6TGN levels and optimal clinical outcome was frequently reported. Several studies supported the use of high 6MMP levels as an indicator of hepatotoxicity.

Conclusion: Thiopurine metabolite testing does not safely predict therapeutic response or thiopurine toxicity. Current evidence does not support routine metabolite monitoring but a combination of metabolite and white blood count testing may be useful for safe dose escalation in cases with suboptimal response. Leucopenia is not necessary for achievement of optimal therapeutic response. Well designed RCTs and identification of additional surrogate markers of thiopurine efficacy and toxicity are required.

64 **HEPATITIS B IMMUNITY AND RESPONSE TO VACCINATION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE IN WEST VIRGINIA. Maria G. Lopez-Marti, Yoram Elitsur, Marshall University, Huntington, WV**

Immuno-compromised children, such as children with inflammatory bowel disease (IBD) are at risk of HBV infection and reactivation. Almost half of patients with IBD had no baseline immunity to HBV and up to 14 % could not mount an effective immune response after booster vaccination (Moses J. 2012). The status of HBV vaccination in IBD children from rural West Virginia has never been reported.

Aim: To investigate HBV exposure and immunity in a cohort of IBD children and examine the response to HBV vaccine in the non-immune patients.

Methods: A retrospective chart review of pediatric patients treated for IBD was performed. Hepatitis B surface antigen (HBsAg) and antibody (HBsAb) were checked. Patients found to be non-immune for HBV, received a booster vaccination series and the immune status was rechecked, per routine clinical care.

Results: A total of 31 patients with IBD were analyzed. The mean age was 14.5 years; 14/31 (45%) were female. Twenty five (81%) patients were diagnosed with Crohn's disease and 6 (19%) patients had ulcerative colitis. Immunomodulator drugs were used in all patients including: prednisone (n=17), azathioprine (n=9), infliximab (n=13), and adalimumab (n=7). Twenty patients had no HBV immunity, of whom 7 (35%) had prior documentation of HBV vaccine in infancy.

Conclusions: The majority of our IBD children lack protective antibodies and are at risk of HBV infection, even those with history of vaccination at infancy. Two doses of HBV vaccine provided protective immunity for most of our patients, in spite of the
immunosuppressive therapy. Assessment of the HBV immunity status in children with IBD is vital, and revaccination is recommended to ensure full protection in these high risk patients.

Vaccination status in children with IBD

<table>
<thead>
<tr>
<th>Results</th>
<th>No. pts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg negative</td>
<td>31 (100)</td>
</tr>
<tr>
<td>HbsAb at baseline Positive (immune)</td>
<td>11 (35)</td>
</tr>
<tr>
<td>HbsAb at baseline Negative (non-imm)</td>
<td>20 (65)</td>
</tr>
<tr>
<td>Booster vaccination</td>
<td>16 (65)</td>
</tr>
<tr>
<td>Post vaccination testing</td>
<td>13 (81)</td>
</tr>
<tr>
<td>HBsAb positive (immune)</td>
<td>12 (92)</td>
</tr>
<tr>
<td>HBsAb negative (non-imm)</td>
<td>1 (8)</td>
</tr>
</tbody>
</table>

65 A RETROSPECTIVE ANALYSIS OF ANEMIA IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE.

Laurence Feinstein1, Laurie S. Conklin2, 1Pediatrics, Children's National Medical Center, Washington, DC; 2Gastroenterology, Hepatology, and Nutrition, Children's National Medical Center, Washington, DC

Background: Iron deficiency anemia (IDA) is common in children with Inflammatory Bowel Disease (IBD), but there is no standardized method of treatment. It is often assumed that remission of disease will lead to resolution of anemia. Oral iron supplementation is a common practice. However, there are studies that support the futility of this method of supplementation during active intestinal inflammation. We hypothesized that a significant number of patients would be anemic at diagnosis and remain anemic one year after diagnosis, with or without iron supplementation. Methods: We retrospectively reviewed the IBD database at CNMC for patients diagnosed between 2008-2011 and recorded the following: demographics, disease type, hemoglobin at diagnosis and at 1 year (9-15 months), iron studies at diagnosis and at 1 year, iron supplementation (yes or no), transfusion, and method of supplementation. Anemia was defined as < 2.5% of the normal hgb range based on age and gender (NHANES 1988-1994). IDA was defined as ferritin <30 g/L when CRP was <10 mg/L, or a ferritin <100 g/L when the CRP >10 mg/L and/or transferrin saturation <16%, based on published IBD guidelines. Data was recorded and analyzed using Microsoft Excel. CRP and ESR were used as surrogate markers of disease activity. Patients with incomplete data were excluded from this preliminary analysis. Results: Data from 69 patients were analyzed. Demographics: 51% female, 38% Black, 53% Caucasian, 60% CD, 35% UC, 5% unclassified. No patient had a known hemoglobinopathy. At diagnosis, 51/69 (74%) of patients were anemic. At 1 year, 28/69 (40%) remained anemic. 61% of persistently anemic patients had normal CRP at 1 year. Of the anemic patients at diagnosis, 35 had complete iron studies and 29/35 (82%) had IDA. Of 28 patients that were persistently anemic at 1 year, 10 had complete iron studies and 7/10 (70%) had iron deficiency anemia. 5 of the 18 remaining patients without iron studies had a microcytic anemia with normal inflammatory markers. Of the 51 patients that were anemic at diagnosis, 36 were treated with enteral iron, 15 were not, and 1 was treated with parenteral iron sucrose. 17/36 (47%) remained anemic at 1 year despite treatment with iron. 7/15 (48%) remained anemic at 1 year with no iron treatment. By the end of 1 year, a blood transfusion was received by 21% of patients who were anemic, and 22% of those who were not. There were no gender or race trends noted. Discussion: Our preliminary data indicate that many IBD patients remain anemic at 1 year, despite normal inflammatory markers or oral iron supplementation. This retrospective analysis lacks data on dosing and adherence. However, a large number of patients that remained anemic at 1 year seem to have IDA based on available data (iron studies, MCV, inflammatory markers). Prospective studies are needed to determine the best approach to treat IDA in children with IBD. The role and timing of parenteral iron administration in pediatric IBD needs further study.


66 THE DETECTION OF INFLAMMATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS: THE ROLE OF FECAL CALPROTECTIN.

Alice Foster1, Brian Bressler2, Kevan Jacobson1, 1Pediatric Gastroenterology, B.C Children's Hospital, Vancouver, BC, Canada; 2Gastroenterology, University of British Columbia, Vancouver, BC, Canada

Background: Fecal calprotectin (FC) is a calcium binding protein found in the cytoplasm of neutrophils, monocytes and macrophages. FC levels can be used as a marker of inflammation in Inflammatory Bowel Disease (IBD) patients. The aim of this study is to explore the current use of FC at our pediatric hospital, and to assess the impact of FC results on patient management.

Methods: We performed a retrospective chart review of all IBD patients who had an FC level checked between January 2012 and January 2013. Demographic information, laboratory values and the indications for checking FC were collected. We documented any change in patient management that occurred as a result of the FC value.

Results: Thirty-six patients were included in our review. Twenty-nine of the patients (81%) were found to have FC levels greater than 200 μg/g indicating active ongoing inflammation. Twelve of twenty-nine patients (41%) with elevated FC levels had normal routine blood work screening (including erythrocyte sedimentation rate and c-reactive protein). The FC level resulted in management changes in 23/36 patients (64%).

Conclusion: FC was a valuable screening test for inflammation in children with IBD in our center. FC detected inflammation in a subgroup of patients with otherwise normal screening inflammatory markers. FC also provided new information to the physician that frequently resulted in a change in management.
**Objective:** Although polymorphisms of the NOD2 gene predispose to the development of ileal Crohn's disease (CD), the precise mechanisms of this increased susceptibility remain unclear. Previous work has shown that transcript expression of the Paneth cell (PC) antimicrobial peptides (AMPs) α-defensin 4 and α-defensin related sequence 10 are selectively decreased in Nod2−/− mice (Kobayashi et al, 2005). Because α-defensins can modulate gut microbial communities, Nod2-mediated regulation of these molecules may be an important factor in CD pathogenesis. However, the specific mouse background used to demonstrate the regulatory effects of Nod2 on the α-defensins is unclear. In light of recent work suggesting that mouse strain strongly influences PC antimicrobial activity, we sought to characterize PC AMP function in Nod2−/− mice on a pure C57BL/6 (B6) background. We hypothesized that Nod2−/− B6 mice would also display reduced AMP expression and activity. **Design:** Wild-type (WT) and Nod2−/− (KO) B6 mice were crossed to generate Nod2+/− heterozygous animals, which were then interbred to produce WT and KO littermates. Littermates of the same sex were housed together until sacrifice. Ileal AMP expression was assessed via real-time PCR, acid urea polyacrylamide gel electrophoresis, and mass spectrometry. PCs were enumerated using flow cytometry. Functionally, α-defensin bactericidal activity was evaluated using a gel-overlap antimicrobial assay. Ileal and fecal microbial composition was determined using 454-sequencing of the bacterial 16S gene. **Results:** WT and KO B6 mice displayed no significant differences in mRNA expression of global PC AMP classes (P > 0.6) or specific α-defensins (P > 0.1). At the protein level, AU-PAGE and mass spectrometry analyses revealed identical α-defensin peptide profiles between WT and KO mice. Moreover, the bactericidal activity of PC α-defensins extracted from WT versus KO mice was equivalent when tested against commensal and pathogenic bacterial strains. For our microbial analysis, we generated a total of 132,740 fecal and 39,756 ileal mucosal 16S rRNA sequences of appropriate quality. Principal coordinates analysis revealed that the cage the mice were housed in had a stronger effect on microbial community composition than did the WT or KO genotype (at a 10% false discovery rate). **Conclusions:** Our data demonstrate that Nod2 does not directly regulate PC antimicrobial activity in B6 mice. This raises concerns with the commonly accepted hypothesis that NOD2 dysfunction leads to attenuated PC microbicidal activity, which in turn alters the composition of the gut microbiota, thereby predisposing to the development of CD. We also show that previously reported Nod2-dependent influences on gut microbial composition may be overcome by environmental factors, such as co-housing with WT littermates. Ultimately, if we hope to modulate intestinal microbial communities as a treatment strategy for CD, it will be imperative to override the impact of host genetics on the gut microbiota. The homogenization of the intestinal microbiota of KO mice and their WT littermates suggests that strong environmental pressures may supersede gene-based influences on gut microbial composition.

**68 LOW 25-HYDROXY VITAMIN D LEVELS ARE NOT ASSOCIATED WITH ACTIVE INFLAMMATORY BOWEL DISEASE.** Bhaskar Gurram1, Rebecca Joekel1, Diana G. Lerner1, Pippa Simpson1, Praveen S. Goday1, 1Pediatrics-Gastroenterology, Medical college of Wisconsin, Milwaukee, WI; 2Department of Pediatrics-Division of Quantitative Health Sciences, Medical College of Wisconsin, Milwaukee, WI

Introduction: Patients with inflammatory bowel disease (IBD) are at risk of vitamin D deficiency. There is some evidence that vitamin D deficiency is associated with active disease. Aims/Background: To determine the vitamin D status and evaluate the correlation of vitamin D levels with disease activity in patients with IBD.

Method: All IBD patients with serum vitamin D levels measured from May 2005 to April 2010 were included. Vitamin D deficiency was defined as plasma 25-hydroxy vitamin D levels ≤ 20ng/L and Vitamin D insufficiency was defined as plasma 25-hydroxy vitamin D levels 21 to 30. Disease activity was determined based on physician global activity (PGA).

Results: 232 patients with IBD had their plasma vitamin D measured. Of these, 71 patients (30.6%) were vitamin D deficient, 74 (31.9%) had vitamin D insufficiency while 87 (37.5%) were vitamin D sufficient. There was no significant difference in the prevalence of vitamin D deficiency or insufficiency between Crohn's disease (CD), ulcerative colitis (UC) and indeterminate colitis. Contrary to previously published data, we found no significant association between vitamin D supplementation or 25-hydroxy vitamin D levels and disease activity. However, 25-hydroxy vitamin D levels were higher in patients on supplementation (p=0.08).

Conclusion: In patients with IBD, supplementation with vitamin D potentially increases the 25-hydroxy vitamin D levels but there was no correlation between low vitamin D levels and disease activity.

Table 1

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Vitamin D ≤30ng/mL (%)</th>
<th>Mean Vitamin D levels ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>232</td>
<td>145 (62.5)</td>
</tr>
<tr>
<td>CD</td>
<td>183</td>
<td>117 (63.9)</td>
</tr>
<tr>
<td>UC</td>
<td>33</td>
<td>19 (57.6)</td>
</tr>
<tr>
<td>IC</td>
<td>16</td>
<td>6 (37.5)</td>
</tr>
<tr>
<td>On supplements</td>
<td>140</td>
<td>80 (57.1)</td>
</tr>
<tr>
<td>Not on supplements</td>
<td>67</td>
<td>48 (71.6)</td>
</tr>
<tr>
<td>Quiescent disease(inactive)</td>
<td>123</td>
<td>71 (57.7)</td>
</tr>
<tr>
<td>Active disease (mild, moderate, severe)</td>
<td>98</td>
<td>65 (66.3)</td>
</tr>
</tbody>
</table>
69  COMBINATION THERAPY WITH CYCLOSPORINE AND CYTAPHERESIS FOR INDUCING REMISSION IN STEROID-RESISTANT PEDIATRIC ULCERATIVE COLITIS. Shin-ichiro Hagiwara, Mitsuru Kubota, Ryusuke Nanbu, Seiichi Kagimoto, Division of General Pediatrics, Saitama Children's Hospital, Saitama, Japan

Background and Aim: Various treatment options, including cyclosporine (CsA), infliximab, and tacrolimus, exist for inducing remission in steroid-resistant pediatric ulcerative colitis (UC). Although CsA is effective for inducing remission in severe/fulminant pediatric UC, some patients still require emergent colectomy. Leukocytapheresis (LCAP) is a recent nonpharmacological therapy introduced to treat UC.

In Japan, Tomomasa et al. showed that LCAP was well tolerated both in children and adults. We evaluated the efficacy and safety of CsA and cytapheresis (CAP) combination therapy while inducing steroid-resistant pediatric UC remission.

Methods: Pediatric patients with steroid-resistant UC treated using CsA and CAP combination therapy at Saitama Children's Medical Center were investigated retrospectively.

Results: A total of 10 patients aged 9 -15 years with moderate (n = 5), severe (n = 4) and fulminant (n = 1) steroid-resistant UC were included. All patients had pancolitis, but emergency colectomy was avoided in 9. The stool frequency/hematochezia score decreased significantly from 5.6 ± 1.3 before treatment to 0.9 ± 1.9 after treatment. In addition, the pediatric UC activity index decreased significantly from 70.5 ± 12.5 to 8.5 ± 20.2 and the endoscopic findings also showed improvements. Moreover, the steroid dose decreased from 1.2 ± 0.4 mg/kg before treatment to 0.5 ± 0.3 mg/kg after treatment. All patients experienced CAP-associated adverse effect, such as decreased hematocrit, hemoglobin level, and platelet concentration, but none of these were severe. The estimated cumulative colectomy-free rate was 70% at 1 year and 20% at 2 years after the combination therapy.

Conclusion: The present study showed that the combination of CyA and CAP was well tolerated in children with steroid-resistant UC. This combination therapy may be a new treatment option for this disorder. Future studies should focus on identifying the best combination therapy for inducing remission in steroid-resistant pediatric UC.

Intestinal/Colonic Disorders – Non – Inflammatory Bowel Disease

80  TESTING FOR FAT SOLUBLE VITAMINS DEFICIENCY IN PEDIATRIC PATIENTS WITH CELIAC DISEASE: UNNECESSARY AS ROUTINE. Mohamad Imam1, Youssef Ghazzawi2, Joseph A. Murray3, Imad Absah1,2, 1Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; 2Pediatric Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN

Background: Celiac disease (CD) is a common immune based disease, triggered by gluten. Fat soluble deficiencies were common in the earlier decades when most patients presented with frank or indeed severe malabsorption, more recent presentations are milder. The frequency of fat soluble deficiencies in more recently diagnosed patients has not been described.

Aim: To identify the frequency and clinical predictors of fat soluble vitamins deficiency in children with celiac disease.

Methods: We conducted a retrospective chart review of patients with a confirmed diagnosis of celiac disease and who had fat soluble vitamin levels measured at diagnosis between 1995 and 2012 at Mayo Clinic. Patients’ demographics, fat soluble vitamins levels and pertinent clinical factors at the time of diagnosis were collected.

Results: Eighty eight patients were included in the final result analysis. Fifty six patients (63.6%) were females and 32 patients (36.4%) were males with the average age at diagnosis being 12.8 ± 3.8 years in females and 13 ± 3.6 years in males. Average BMI was 16.7 ± 3.4 and the most common reported symptoms were abdominal pain and diarrhea seen in 49 patients (55.7%) and 30 patients (34.1%) respectively. Family history of celiac disease was reported in 32 patients (36.4%). Average vitamin levels were 7.5 ± 2.0 mg/l, 32.8 ± 9.6 mg/dl, 334.5 ± 109.9 mcg/dl for vitamin E, 25-hydroxyvitamin D and vitamin A respectively. No patients had vitamin A or D deficiency.

81  EPCAM IN CELIAC PATHOPHYSIOLOGY - VARIABLE EXPRESSION AT THE TIME OF INITIAL DIAGNOSIS CORRELATES WITH SEROLOGIC FINDINGS. Seth Septer1, Samuel Aquilina2, Jurgen Gerada1, James Degaetano2, Thomas M. Attard3,2, 1Gastroenterology, Children's Mercy Hospital, Kansas City, MO; 2Pediatrics, Mater Dei Hospital, B‘Kara, Malta; 3Internal Medicine - Gastroenterology, Mater Dei Hospital, B‘Kara, Malta

BACKGROUND: Epithelial cell adhesion/activating molecule (EpCAM/CD326) has been implicated initially as a tumor-associated antigen and more recently in the pathogenesis of congenital Tufting Enteropathy, a disorder that shares several histopathologic similarities with celiac disease (CD). Herein we studied the expression of EPCAM in duodenal and colonic biopsies in newly diagnosed pediatric celiac patients.

METHODS: Fourteen consecutive pediatric patients (8F mean,SD; 9.1, 4.1 years) diagnosed with celiac disease since 2009 and followed at Mater Dei Hospital (MDH) were included in the study. Clinical, laboratory-serology, endoscopic and histologic findings from their initial presentation and follow up were accrued from the clinical chart. Immunohistochemistry on paraffin-embedded tissue from the initial diagnostic endoscopy was performed as previously described (1) using EPCAM antibody (1:300, Cell Signaling Technology). Statistical analysis was performed using SigmaStat®.

RESULTS: EPCAM immunostaining (IH) in our patients with Celiac varied considerably between patients and was independent of all demographic variables studied, clinical presentation, and the reported histologic severity on duodenal biopsy (Marsh score - Table 1). One patient exhibited strongly positive staining whereas half the patients exhibited negative staining; comparable to our group of tufting
enteropathy patients reported previously (2).

High (>100 U/ml) tTG IgA titres prior to initial endoscopy-biopsy correlated with negative EPCAM IH (PPV 87.5%; 95% CI: 47.38 % - 97.93 %). Initial EPCAM IH positivity was highly predictive of normalization of tTG IgA level upon follow up on GFD (PPV 100.00 %; 95% CI: 47.95 % to 100.00 %).

**DISCUSSION:** Our preliminary data suggests that EPCAM is variably expressed (or degraded) in pediatric celiacs at presentation, the relationship appears independent of histologic severity but correlates with the initial serologic findings and serologic response to therapy. This suggests a pathophysiology role in a subgroup of patients. Although there are several putative mechanisms, further studies are needed to define the implications of EPCAM expression in pediatric CD.

**References:**

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**82 Fecal Calprotectin is Raised in Pediatric Patients with Eosinophilic Enteropathy.**

**Kevin D. Borg2, James Degaetano2, Thomas M. Attard1,2, 1Gastroenterology, Children's Mercy Hospital, Kansas City, MO; 2Pediatrics, Mater Dei Hospital, B’Kara, Malta**

**BACKGROUND** Calprotectin; a intracytoplasmic leukocyte protein can be assayed from stool and is construed as surrogate marker for inflammatory enteropathic processes. Fecal Calprotectin (FC) is established in the diagnosis and surveillance of Inflammatory Bowel Disease; its relevance to the diagnosis of other, including allergic enteropathies is undefined. Herein we studied the correlation between FC levels done prior to endoscopy-colonoscopy and the histopathologic findings upon biopsy and subsequent diagnosis of allergic - eosinophilic enteropathy.

**METHODS** The study design was a retrospective case-control series with unmatched consecutive patients seen at our institution (MDH) and who had undergone FC assay prior to EGD-Colonoscopy which showed either 1. normal histology, 2. eosinophilic enteropathy defined as inflammatory changes including greater-than-normal tissue eosinophilia (>35 - 50 / HPF) or 3. histopathologic findings consistent with IBD upon biopsy. Subjects accrued were further defined upon chart review as having been correspondingly diagnosed with either 1. Functional GI Disorder (FGID), 2. Allergic-Eosinophilic Enteropathy including colitis, or 3. IBD through standard diagnostic criteria, or were excluded from further analysis.

**RESULTS** Between 2009 and 2013; 134 pediatric patients (<16years) were studied by FC determination 32 had gastrointestinal endoscopy with biopsy with prior FC determination; of these 5 had tissue eosinophilia described as moderately or markedly increased and associated with variable inflammatory changes. In 6 patients with IBD, FC was obtained prior to endo-colonoscopy. Differences between the three groups are summarized in Table 1; patients with Eosinophilic Enteropathy were significantly younger than patients with IBD (P = 0.0022) and the mean FC in patients with Eosinophilic enteropathy was significantly higher than controls (P=0.0008) and comparable to levels in IBD patients. FC > 100ug/g feces was highly predictive of enteropathy in non-IBD pediatric patients (PPV 83.3% NPV 100%)

**CONCLUSIONS:** Fecal Calprotectin is a non-invasive, easily performed, cost-effective diagnostic test in the investigation of chronic diarrhea and in children with suspected allergic - eosinophilic enteropathy. Eosinophilic enteropathy needs to be included in the differential diagnosis of elevated FC in children.

Fecal Calprotectin in control / Eosinophilic Enteropathy and IBD

<table>
<thead>
<tr>
<th></th>
<th>Control (FGID)</th>
<th>Eos. Enteropathy</th>
<th>IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (gender)</strong></td>
<td>16 (M:10)</td>
<td>5(M:2)</td>
<td>6(M:3)</td>
</tr>
<tr>
<td><strong>mean age (SD) / years</strong></td>
<td>5.6 (4.5)</td>
<td>3.0(3.3)</td>
<td>11.8 (3.1)</td>
</tr>
<tr>
<td><strong>mean FC (SE) / ug/g of feces prior to EGD / COL</strong></td>
<td>52.5 (53.6)</td>
<td>532(223)</td>
<td>658(215)</td>
</tr>
</tbody>
</table>

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**83 Current Standard in Pediatric Gastroenterology Fellowship Training in Interpretation of Capsule Endoscopy.**

**Nadia M. Hijaz1, Seth Septer1, Thomas M. Attard2, 1Gastroenterology, Children's Mercy Hospital, Kansas City, MO; 2Pediatrics, Mater Dei Hospital, B’Kara, Malta**

**Background:** Pediatric Gastroenterologists are increasingly expected to be proficient in the interpretation of wireless capsule endoscopy (CE) in children. Although consensus positions on fellowship training in adult gastroenterology have been published (ASGE / ESGE), no analogous resource is in place for pediatric trainees.

**Aim:** to define current standard and formal structure of training of Pediatric Gastroenterology Fellows in reading and interpreting CE
studies in the United States and Canada.

Methods: An e-mail questionnaire was developed that qualified inclusion of key components of CE training based on published ASGE guidelines(1) on credentialing physicians to perform CE studies. This tool was sent to 64 pediatric GI fellowship program directors / assistants and to 45 adult GI fellowship program directors identified through the respective professional associations (NASPGHAN, AGA, ACG). Responses were categorized by components of training program present as well as comments by the respondents.

Results: 25/64(39%) pediatric and 36/45(80%) adult program directors or program coordinators responded; 38% adult compared to 4% pediatric programs reported having a formal GI capsule endoscopy module as part of the training program, trainees were required to attend a hands-on course as part of their training in 27% adult and 8% pediatric programs. The CE module in ACG Universe was most often quoted as a useful resource. A specific number of CE studies to be read were a requisite in 66% adult and 8% pediatric programs. When specified, trainees were required to interpret 10 - 25 studies. 5.5% adult and 12% pediatric programs required trainees to present journal club or other formal didactic presentation whereas 30.5% adult and 33% pediatric programs required faculty to present didactic material. Comments received spanned the gamut from questioning the need for any formalized training in CE interpretation (2 pediatric programs) through the description of a highly structured CE module including defined hands-on cases, training course, regular CE journal club/lecture (2 adult programs).

Discussion: A larger proportion of adult gastroenterology training programs emphasize CE training as part of the curriculum, require trainees to attend a hands-on course as part of their training and have a specified number of procedures to be performed by trainees. The didactic exposure on CE performance and interpretation appears comparable across programs. A more formalized approach to CE training may be required as credentialing in pediatric trainees more closely aligns with that in adult program graduates.


84 DURATION OF SPECIALIZED FORMULA USE FOR THE TREATMENT OF ALLERGIC PROCTOCOLITIS AND COW MILK PROTEIN ALLERGY. Vishal Avinashi, Kamran Sadiq, BC Children's Hospital, Vancouver, BC, Canada

Introduction: Cow's milk protein allergy is a relatively common problem amongst infants. Presentations include a variety of symptoms including bloody stools, diarrhea, vomiting, irritability and failure to thrive. Semi-elemental formulas are often used when there is no response to dietary manipulations and elemental formula is used for more severe cases that do not respond to semielemental formulas. While there is general agreement that the natural history allows for general improvement in the first couple of years, less information is available about the length of time specialized formulas are required, which is of interest to families, funders and health care professionals.

Hypothesis: Patients with proctocolitis presenting with bloody stool and the absence of diarrhea and vomiting will have a shorter duration of specialized formulas.

Methods: A retrospective chart review will be performed on cases which require semi-elemental and elemental formula use for the treatment of CMPA. Cases from 2004 to 2011 will be reviewed from applications to the Home Enteral Nutrition (HEN) program which is the sole program in the province which funds elemental feeds. In order to be eligible for elemental formula through the program, the patient must have failed a semi-elemental formula.

Results: In total there were 120 cases of CMPA. Of those 67 had a diagnosis proctocolitis with the presence of blood in stools and the absence of vomiting. There was an equal distribution of males and females amongst those affected with CMPA. The average age at onset of those with proctocolitis was 4.1 months with a range from 15 days to 27 months, Median 2.7 months (vs. 5 months for other CMPA). Amongst those with proctocolitis, 75 percentage required the use of elemental therapy (vs. 83% with other CMPA). The average duration of use was 12.5 months for patients with proctocolitis with a range of 3 months to 36 months (vs. 11.1 months (range 2 - 24 months) for other CMPA). In our series of patients with proctocolitis only 27% percent were improved by one year of age (vs. 28%), however 69% were free of formula at 18 months (vs. 72%). 87 percent of children with proctocolitis were off elemental/semielemental formula by two years of age and 96% percent by three years of age (vs. 91% and 98% in other CMPA).

Conclusion: The vast majority of children with even severe CMPA are off specialized formulas by two years of age. There is no obvious duration difference in proctocolitis vs. other forms of CMPA.

85 PREVALENCE OF ISOLATED DISACCHARIDASE DEFICIENCIES IN PEDIATRIC PATIENTS. Maricruz Crespo1, Virginia M. Baez Socolro1, Hong Li1, Judy Splawski1, Thomas J. Sferda1, Reinaldo Garcia1, 1Peds Gastroenterology, University Hospitals, Cleveland, OH; 2Center for Clinical Investigation, Case Western Reserve University, Cleveland, OH

Background: The digestion of carbohydrates is mediated by a complex process. Duodenal mucosal disaccharidases play a vital role in the degradation of carbohydrates. An enzymatic deficiency might result in gastrointestinal symptoms including diarrhea. Abnormal duodenal disaccharidase activities and associated symptoms have been reported in children, but the prevalence and clinical significance is not completely understood.

Methods: A retrospective study was conducted in 2862 esophagogastroduodenoscopies performed at UH Rainbow Babies & Children's Hospitals (Cleveland, Ohio) during 2008 - 2010. Symptoms, diagnoses, and disaccharidases activities (DAs) were obtained from medical records. DAs were measured at JOLI Diagnostic (Williamsville, NY).

Results: DAs were determined in 1214 patients (42% of those undergoing esophagogastroduodenoscopy). Histologically normal duodenal biopsies were present in 1141 patients with measured DAs; of those with normal histology disaccharidase deficiencies (based upon normal ranges reported by the contract laboratory) were found in 580 patients (51%). Lactase deficiency was the most common (568 patients, 50%), followed by maltase (48 patients, 4.2%), and sucrase (2 patients 0.1%). Prevalence of lactose deficiency was 40 % in caucasian patients and 70 % in african-american patients and other ethnicities. Diarrhea was reported in 321 patients with measured DAs and normal histology. In those with diarrhea, there was no significant difference in the number with or without disaccharidase deficiency (48% with deficiency versus 52% without deficiency).
Conclusion: In all patients undergoing esophagogastroduodenoscopy, disaccharidase deficiency is common (50%). Prevalence of maltase and sucrase is very low. Also the prevalence in white patient appears to be higher than reported in previous studies. Enzyme deficiency was not more prevalent in those patients with diarrhea.

EMERGING PATTERNS OF DUODENAL SUCRASE ISOMALTASE DEFICIENCY IN A NATIONAL COHORT. Susan S. Baker1, Christine M. Roach1, Bridget Adams1, Bruno Chumpitazi2, Buford L. Nichols2, 1Pediatrics-N&GI, SUNY Digestive Diseases and Nutrition Center, Women and Children's Hospital, Buffalo, NY; 2Pediatrics-N&GI, Baylor College of Medicine, Houston, TX
Sucrase-isomaltase Deficiency (SID) may be congenital and classically is clinically recognized by deficient sucrase (<15 U) associated with normal lactase (>10 U) enzyme activities on assay of duodenal biopsies. However SID may also be secondary and clinically SID may be associated with abnormal lactase and other α-glucosidase activities. Objective: To determine the frequency and pattern of SID among a large population of children and adults undergoing duodenal disaccharidase activity evaluation in routine clinical practice. Method: Complete disaccharidase assays were obtained on 27,860 biopsies between 2005 and 2010 using the Dalqvist method. The statistical lower limits used to define deficiencies were calculated as Mean-1SD: (Sucrase < 26 U; Maltase < 100 U; Palatinase < 5; Lactase < 10 U). Pandisaccharidase deficiency (PDD) was defined as low activity of all enzymes. Results: Isolated lactase deficiency was most common and increased with age from 14% at age 2 yrs. to 55% of biopsies over 40 yrs. SID was recognized by deficient sucrase, maltase and palatinase activities and could be subdivided in 2 groups: Severe SID with Sucrase <=15 and Moderate SID with Sucrase>15 but <23 U and with Lactase >10. The severe SID pattern made up 3% and the moderate pattern 8% of total sucrase deficient biopsies. The rates of severe and moderate SID as a portion of all sucrase deficiencies under the age of 4 were 7% and 13% respectively, versus 2% and 7% over 4 years. Of assays with sucrase <=15 U, 97% had maltase and palatinase deficiencies. In addition, 90% of all SID had lactase deficiency, for which age was a contributing factor. The age distribution of PDD was distinctive from that of SID, with a small rise at 1-2 years then a fall followed by a steady increase in frequency peaking at 17 years followed by another fall. PDD was present in both severe and moderate SID cases. Conclusion: SID is most commonly identified in young children, and is often associated with deficiencies in maltase and palatinase activity. SID is frequently associated with lactase deficiency, particularly with an increase in age of the subjects. The PDD enzyme age pattern is distinct from that seen in SID and requires further evaluation.

ARE THERE PRIMARY DUODENAL MALTASE DEFICIENCIES? Susan S. Baker2, Bridget Adams2, Christine M. Roach2, Bruno Chumpitazi2, Buford L. Nichols2, 1Pediatrics-N&GI, SUNY-Women and Children's Hospital, Buffalo, NY
Duodenal Maltase activities are commonly assayed on clinically obtained biopsies but are often difficult to interpret. A major reason is that Sucrase-isomaltase (SI) activities also hydrolyze maltose to free glucose. Another reason is that Maltase-glucosamylase (MGAM) also has very active maltase and oligoglucoside properties. Historically, some have argued that glycogen or maltooligosaccharide substrates are specific for MGAM but recent investigations have disagreed. Objective: Search for cryptic MGAM deficiencies in clinical mucosal biopsy assays. Method: Complete assays were obtained on 27,847 biopsies obtained during routine clinical practice between 2005 and 2010 using Dalqvist methods. The results were further classified by age at biopsy. The statistical lower limits were calculated as M-1SD: (Sucrase < 26 U; Maltase < 100 U; Palatinase < 5; Lactase < 10 U if under the age of 4). Results: 13% of the assayed biopsies had maltase deficiency (<100 U). 79% of maltase deficient biopsies also had sucrase deficiency (<26 U). The contribution to reduced activity of maltase by sucrose-isomaltase was estimated based on the slope of the regression line that best fits the plot of maltase vs. sucrase activities. Maltase and sucrase are highly correlated with an R-squared of 0.92. The formula for the regression line is [maltase U = (sucrase U * 2.2) + 40 U] Adjusted maltase-glucosamylase (adjMGAM) results were defined as maltase U less 2.2 * sucrase U. The average and standard deviation for adjMGAM were 43 U and 24 U, respectively. The lower limit for adjMGAM was defined as M-1SD or 19 U. Based on this methodology, 71% of maltase activity deficiency was attributable to sucrase deficiency. 4% of biopsies have adjMGAM deficiency regardless of lactase activity, but 82% would be excluded as primary maltase deficiency by abnormal lactase. 32% of maltase deficient biopsies had sucrase <15 U, but 90% did not meet the classic definition of congenital sucrase isomaltase deficiency due to adult type lactase activity which is common in older children (~50%). Six percent of biopsies had low Lactase (<10 U) and moderate Sucrase deficiency (>15-23 U) with low maltase and may represent secondary deficiency. 8% had pandisaccharidase deficiency (PDD, Lactase <10; Sucrase <26, Maltase <100 U). Conclusion: MGAM deficiency may be as common as sucrase deficiency assays. Primary MGAM deficiency can be suspected if Maltase is <100 U and lactase and sucrase activities are normal. Primary or secondary MGAM deficiency may occur with lactase deficiency. Secondary MGAM deficiency may be suspected in PDD and in older children with adult type lactase deficiency but normal sucrase activities.

ELEVATED CALPROTECTIN IN ISOLATED UPPER GASTROINTESTINAL TRACT PATHOLOGY. Elaine Barfield1, Debra Beneck2, Aliza Solomon1, 1Pediatric Gastroenterology and Nutrition, New York Presbyterian-Weill Cornell, New York, NY; 2Pathology, New York Presbyterian-Weill Cornell, New York, NY
Background: Calprotectin is a protein derived from neutrophil activation and plays a role in the regulation of the inflammatory process. Fecal calprotectin measurement is safe, sensitive and noninvasive and the value is elevated in both infectious and inflammatory conditions. As a surrogate marker of inflammation in the lower gastrointestinal (GI) tract, it is commonly used in inflammatory bowel disease (IBD) to assess efficacy of therapy and to predict flares. It is also used to differentiate IBD from functional GI disorders. The goal of this study is to determine whether calprotectin can be used as a surrogate marker of upper GI tract inflammation as well. Design: Using the outpatient electronic medical record, we identified 167 pediatric subjects who submitted stool for fecal calprotectin as part of a workup for various symptoms including abdominal pain, vomiting, dysphagia, failure to thrive, hematocrit, diarrhea and joint pain. All subjects underwent upper endoscopy and 102 subjects also had a colonoscopy. The mean number of weeks between calprotectin testing and upper endoscopy was 4.75. Subjects with IBD, systemic lupus erythematosus, rheumatoid arthritis, juvenile idiopathic
arthitis, psoriasis, cystic fibrosis, glomerulonephritis, pancreatitis, sepsis and cancer were excluded from the study. Calprotectin levels and endoscopic biopsy results were reviewed. Result: Of the 167 subjects who submitted stool samples, 65 (39%) had elevated calprotectin levels. 47 of these 65 underwent both colonoscopy and upper endoscopy. Of the 47 subjects, 27 (57%) had pathology in either the esophagus, stomach or duodenum with normal colonicoscopic biopsies. 8 of the 27 subjects with elevated calprotectin and normal colonicoscopic biopsies had esophagitis (30%); 3 (11%) had foveolar metaplasia in the duodenum (evidence of peptic injury); and 2 (7%) had hyperplastic/regenerative polyps in the gastric antrum. Among the other pathologic diagnoses were chemical gastropathy, chronic inactive gastritis and non-H. pylori-associated chronic active gastritis. 19/27 had pathology in one upper gastrointestinal site, 6/27 had pathology in two sites and 2/27 had pathology in the esophagus, stomach, and duodenum. Conclusion: While calprotectin is commonly used as a surrogate marker of inflammation in the lower GI tract, elevated calprotectin may be present in disorders of the upper GI tract that involve neutrophil activation as well. Our findings suggest that calprotectin may be used in the evaluation of upper GI pathology and should not be solely considered a marker of lower GI tract inflammation.

89*  TREATMENT WITH FECAL MICROBIOTA TRANSPLANTATION FOR CLOSTRIDIUM DIFFICILE IN IMMUNOCOMPROMISED CHILDREN. Mark G. Bartlett, Pediatric Gastroenterology, Mayo Clinic, Rochester, MN

Clostridium difficile is among the leading hospital-acquired infections in the United States. In the past decade there has been an increase in the incidence, severity, and recurrence rates of C. difficile infection (CDI) in children. Fecal microbiota transplantation (FMT) is being studied as an alternative to standard therapy with antibiotics for recurrent CDI. The existing literature demonstrates a 92% success rate for eradicating CDI by infusing intestinal microorganisms from a healthy donor via colonoscopy into a patient. Few studies have been completed in children and most protocols have excluded children who are immunocompromised.

At Mayo Clinic we have recently offered FMT to three immunocompromised patients who had suffered from multi-drug resistant CDI. The three children include a 6-year old with CHARGE syndrome and T-cell deficiency, a 12 year-old immunosuppressed after both heart and kidney transplantation, and a 3 year-old immunosuppressed after kidney transplantation. All three had copious amounts of foul-smelling diarrhea that was tested positive for C. difficile toxin and was resistant to multiple courses of antibiotics. We used parental donors in each case. The parent donors were tested for infectious diseases according to our protocols. Fresh parental stool samples were obtained and prepared for infusion just prior to the colonoscopies. The children were all treated with at least 10 days of oral Fidaxomicin up until the day of the FMT and then prepped for colonoscopy following our typical protocols with Polyethylene Glycol. In each case after FMT the diarrhea abated and the Clostridium difficile toxin was negative and remained negative 10 weeks after the FMT. Our preliminary results demonstrate that FMT is both safe and effective in immunosuppressed children. This finding is important since immunocompromised children are among the most vulnerable to recurrent CDI and are likely to benefit from availability of FMT.

90  STEP PROCEDURE IN PEDIATRIC SHORT BOWEL SYNDROME: 17 PROCEDURES IN 13 CHILDREN. Veronica Busoni1, Romina Mehaudy1, Daniel D’Agostino1, Pablo A. Lobos1, Rodrigo Sanchez Claria1, Fernando Frangi2, Marina Orsi1, 1Pediatric Gastroenterology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; *Pediatrics, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 2Pediatric Surgery, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; *Transplant Surgery, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Introduction: In the last decades, intestinal transplantation (ITx) has become a reality for children with short bowel syndrome (SBS), although its morbidity and mortality still remains high. Serial Transverse Enteroplasty Procedure (STEP) has been introduced to improve enteral tolerance avoiding the need for an ITx. We report herein our experience with this surgical procedure in children with SBS.

Methods: A cases series of children with SBS who underwent a STEP procedure was retrospectively analyzed from our database. Study period was March 2008 to April 2013. Indications for surgery were: TPN dependant patients, unable to achieve enteral autonomy with medical treatment, which also had significant bowel dilatation. Age, weight and underlying disease, TPN requirements, enteral volume tolerance, intestinal length before and after the procedure, surgical complications and outcome were analyzed.

Results: 50 pediatric patients were referred to our center during the study period. STEP procedure was performed in 13 patients (26%), with 4 re-STEPs. Mean age at surgery was 14.2 months (r: 5-32) and mean weight 7.830 kg (r: 3.8-17). Mean time interval between procedures in Re-STEP pts was 12 months (r: 10-17). Underlying disease: gastrochisis (6), atresia (6), and necrotizing enterocolitis (1). Mean increase in residual intestinal length was 29.9 cm (r: 9-75) or 59% (r: 24-130) of the initial length. Re-STEP procedures had a mean increase of 26% (r: 21.9-28.5). Follow up: 16.8 months (r:0.6-36). Complications (3): intraoperative shock assumed as latex allergy (1), intraperitoneal bleeding (2). No surgery- related mortality was recorded. 3 patients (23%) died secondary to infection, 6, 12 and 14 mo. post STEP. 7/13 pts (53.8%) are currently off TPN.

Discussion: Surgical intestinal rehabilitation through STEP technique has become a good alternative to rescue children with SBS. In our experience, it has been useful to enhance enteral tolerance and decrease TPN dependance. Although not exten from complications, STEP procedure is reproducible and may even avoid the need for ITx.

91  AN UNUSUAL CAUSE OF LEFT UPPER QUADRANT ABDOMINAL PAIN. Neil Copeland1, Donald Ta1, Raheel Khan1, April Lawson2, Ritu Walia2, 1Pediatrics, West Virginia University, Charleston, WV; 2Pediatric Gastroenterology, West Virginia University, Charleston, WV

Omental infarction (OI) is an uncommon but increasingly recognized cause of acute abdominal pain in children, with the great majority of cases presenting as significant right sided abdominal pain. To our knowledge there are only two cases presenting with a left sided OI reported in the pediatric literature. We report the case of a previously healthy obese 13 year old male who presented to the emergency room with a 6 day history of intermittent colicky abdominal pain located in the left upper quadrant (LUQ). There was no history of trauma, anorexia, nausea, vomiting, or diarrhea. Physical examination revealed tenderness to palpation in the LUQ without rebound, guarding, rigidity, or masses. CBC, CMP, and
coagulation profile were normal, with a mildly elevated ESR at 17 seconds. Stool for occult blood and calprotectin were normal. Cooked tomography (CT) scan revealed a hypodense, homogeneous mass with fat stranding in the left upper quadrant. Based on the radiological findings, a diagnosis of OI was made. The patient underwent conservative management with overnight hospitalization for pain control and was discharged the following day with improvement of symptoms. To our knowledge he has remained asymptomatic. Conclusion: Healthcare providers should be aware of the possibility of a left sided OI when presented with a child with complaints of acute left sided abdominal pain. The clinical symptoms when combined with CT findings allow for prompt diagnosis and conservative treatment; potentially avoiding unnecessary tests and surgical procedures.

92 A NOVEL METHOD OF QUANTIFYING SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO) USING DUODENAL BRUSHING. Chirajyoti Deb1, Devendra Mehta2, Janet M. Conrad2, Patrick Pignon2, Jeffrey A. Bornstein2, Karoly Horvath1,2, 1APH Pediatric Specialty Diagnostic Laboratory, Orlando Health, Orlando, FL; 2Pediatric Center for Digestive Health and Nutrition, Orlando Health, Orlando, FL.

Background: Small intestinal bacterial overgrowth (SIBO) is commonly diagnosed by hydrogen/methane breath test, although is often inaccurate. The current gold standard method of SIBO diagnosis is the quantitative culture of duodenal aspirate that is normally collected during esophagogastroduodenoscopy (EGD). Unfortunately, duodenal fluid is not always found in the lumen for sampling. In addition, the duodenal aspirates typically get contaminated with the oral and upper airway flora and gastric fluid or the fluid may have been recently secreted from pancreatobiliary system as a result of the EGD. We hypothesized that duodenal brushing specimens will contain the more appropriate microbial population, with less contamination from the upper airway flora for accurate detection of overgrowth. Methodology: Small intestinal aspirate and brushing samples were collected from the pediatric patients (age 1.5–17 years) undergoing medically indicated EGD. The small intestine was brushed using a cytology brush (Kimberly-Clark #60314). The brush tip was placed in a sterile tube and the fluid was collected aseptically. Calibrated loops (1 μl) were used to streak media plates. The colony-forming units (cfu) were counted and averaged from a set of plates grown under aerobic and anaerobic conditions, respectively.

Results: A total of 32 patients enrolled in this prospective pilot study had both duodenal fluid and brushing samples collected. Eight/27 had >10^4 cfu using aspirates compared with 10/27 using Brushing sample (P<0.001 Fishers). Using log10 transformation, the two methods were strongly correlated at 0.73 R2 (P<0.001 Pearson’s). The duodenal aspirates (mean 3x10^5) tended to have more cfu than corresponding brushing (mean 3X104). Receiver operating characteristic (ROC) curve showed at a cut off of cfu log10 4.4, equivalent to 2.5 x 10^4, sensitivity was 87.5% and specificity 95% for brushing. Under the aerobic and anaerobic growth conditions 56% and 59% of the brushing and 37% and 44% of the aspirate samples developed colonies on media plates. Duodenal aspirates had more oral flora than brushings. In contrast, brushing samples produced more microbial growth in tube liquid media corresponding to cultivable fastidious and facultatively anaerobic and microaerophilic organisms.

Conclusion: Duodenal brushing correlated well with duodenal aspirate for small bowel bacterial CFUs. The findings suggest brushings may be better than aspirates based on both higher levels of oral flora in aspirates, which may be contaminants and a better yield of fastidious and facultatively anaerobic as well as microaerophilic organisms with brushings. Further characterization of the microbiome using molecular methods is warranted.

93 APPLICATION OF A NOVEL QUANTITATIVE SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO) DIAGNOSTIC TEST THAT USES DUODENAL BRUSHING SAMPLES: A PRELIMINARY CLINICAL OUTCOME REPORT. Chirajyoti Deb1, Devendra Mehta2, Janet M. Conrad1, Sagar Mehta1, Sharon S. Carter1, Shaista Safder1, Tejas R. Mehta2, Reinaldo Figueroa-Colon2, Jeffrey A. Bornstein2, Karoly Horvath1,2, 1APH Pediatric Specialty Diagnostic Laboratory, Orlando Health, Orlando, FL; 2Pediatric Center for Digestive Health and Nutrition, Orlando Health, Orlando, FL; 3University of Michigan Medical School, Ann Arbor, MI.

Background: The current gold standard method of SIBO diagnosis by quantitative microbial culture uses duodenal aspirate. However, the duodenal fluid is not always available in the lumen to aspirate; it can get contaminated with oral and other gastrointestinal flora or get diluted and chemically laden due to sudden pancreatobiliary secretion. We developed a new quantitative microbial culture based SIBO diagnosis method that uses duodenal brushing samples as a better alternative to the duodenal aspirate, and ≥10^4 CFU/ml as the cut off value for SIBO in the duodenum was established. We aimed to study the clinical course of 100 patients with chronic abdominal pain using ROME III criteria and who underwent the new SIBO diagnostic test as part of their endoscopic evaluation. Preliminary data is submitted.

Methodology: Consecutive patients (age 5 to 17 years) who underwent duodenal brushings in search of bacterial overgrowth and had abdominal pain for more than 3 months with no specific endoscopic or sonographic findings were reviewed. Duodenal mucosal layer samples were collected using a ‘cytology brush’ (Kimberly-Clark #60314) during EGD. The droplets of fluid from brushes was extracted and plated on standard media for determining the microbial load and colony counts and subsequent identification performed as warranted. Clinical characteristics at the baseline were obtained.

Results: A total of 12 patients (male, n=9 and female, n=3) were identified so far who had chronic abdominal pain for at least past 3 months before testing for SIBO. These patients (n=12) with a history of abdominal pain did not have any other histopathological abnormality. None of the patients tested for SIBO were on proton pump inhibitor (PPI). Functional dyspepsia and functional abdominal pain were the most common patterns based on Rome III criteria. Four out of twelve (33%) patients were detected to be SIBO positive with a total microbial load of ≥10^4 CFU/ml. Constipation was noted for two (2/12; 17%), with one also SIBO positive. Symptoms of flatulence, diarrhea, or weight loss were not common in this entire group. Only one patient among the four SIBO positive cases (1/4; 25%) was severely lactase deficient. A range of enteric or oral flora was identified in the four SIBO positive, but none had overgrowth of bacteroides or yeast/fungi.

Conclusion: The preliminary retrospective chart review study on consecutive SIBO tested patients with chronic abdominal pain indicates that overgrowth may be common. A larger sample size as well as further follow up is planned to correlate with breath tests as well as
assess impact of this test on therapy and outcome. If a significant correlation between uncharacterized chronic abdominal pain with SIBO is confirmed, then SIBO with brushings may have an important role in the evaluation and management of chronic abdominal pain. We expect to continue and complete with chart review of a larger number of samples before the final presentation.

94 PREVALENCE AND SIGNIFICANCE OF COLORECTAL ADENOMA FOUND DURING COLONOSCOPY IN AVERAGE RISK CHILDREN, Victor Fox1, Sivan Kassif1, Hongyu Jiang2, Jeffrey Goldsmith3, 4Gastroenterology, Hepatology, and Nutrition, Boston Children's Hospital, Boston, MA; 2Clinical Research Program, Boston Children's Hospital, Boston, MA; 3Department of Pathology, Boston Children's Hospital, Boston, MA

Introduction: Colorectal adenoma (CRA) is the precursor lesion for most colorectal cancer (CRC), warranting early detection and removal to reduce morbidity and mortality. The prevalence of CRA in average risk adults age 20-30 yrs ranges from 1.7% to 4.1% and increases to 25% by age 50-60 yrs. In contrast, CRA is rarely encountered in patients younger than 20 yrs. The prevalence and significance of this lesion occurring in average risk children has not been studied. The primary aim of this study was to identify and characterize a cohort of children with colorectal adenoma discovered during colonoscopy for indications unrelated to suspected neoplasia. We defined these as average risk children. We planned to measure the prevalence of this lesion and to use the information as a basis for proposing future surveillance.

Methods: A retrospective review of medical records was conducted at a single pediatric hospital. Cases of colorectal adenoma were identified in patients younger than 20 years by searching pathology records from 1992 to 2012. Colonoscopy procedures performed during the study period were counted using billing data. Additional information collected included patient demographics, indication for colonoscopy, underlying medical conditions, family history, genetic testing, and polyp number, location, and histopathologic phenotype. Subgroup analysis was conducted to identify variations related to patient age and date of colonoscopy over the course of the study period.

Results: Twenty-eight patients were included in the INFANT cohort while twenty-seven patients constituted the historical control group. The most common etiologies of SBS included: necrotizing enterocolitis, intestinal atresia, gastroschisis and volvulus. Mean length of small bowel remaining after surgery was 115.6 ± 24.6 cm in the pre-INFANT group vs 112.3 ± 55 cm in the INFANT group (p=0.837), presence of ICV was also similar in both groups 19 (70.4%) vs 21 (75%), (p=0.7). There was no statistically significant difference in the proportion of infants who reached full enteral feeds (85.2% vs 85.7%, p=0.956) although patients in the INFANT cohort took longer to attain full enteral feeds (100.8 vs 158.5 days, p=0.014). There was no significant difference in terms of number of patients on home TPN (7.1% vs 14.8%, P=0.362). Overall mortality was less in the INFANT cohort but the difference was not statistically significant (7.1% vs 14.8%, P=0.362).

Conclusions: Our study demonstrates a trend towards an increased survival rate of patients with neonatal SBS since the creation of INFANT. Our data suggest that survival of patients who would have previously died possibly accounts for the longer PN duration and longer time to full enteral feeds in the INFANT cohort. Although the incidence of cholestasis was similar in both groups, mean peak bilirubin was lower in the INFANT group (116.6 ± 82.8 vs 181.6 ± 124.1, P=0.026). Overall mortality was less in the INFANT cohort but the difference was not statistically significant (7.1% vs 14.8%, P=0.362).

95 OUTCOMES OF PATIENTS WITH INTESTINAL FAILURE AFTER THE CREATION OF A MULTIDISCIPLINARY TEAM AT THE MONTREAL CHILDREN'S HOSPITAL. Sabrina Furtado, Najma Ahmed, Sylviane Forget, Ana Sant'Anna, Pediatrics, Division of Gastroenterology and Nutrition, McGill University, Montreal Children's Hospital, Montreal, QC, Canada

Background: Intestinal failure is defined as the inability to maintain energy, fluid, electrolyte and micronutrient balance using the enteral route. The most common cause of intestinal failure is Short Bowel Syndrome (SBS). SBS can be associated with mortality rates as high as 40%. Morbidity is also significant, with major impairment in quality of life for many that survive. The need to coordinate complex care and optimize management for this patient population led to the creation of a multidisciplinary team called INFANT: Intestinal Failure Advanced Nutrition Team. The purpose of this study was to assess and compare care and outcomes of two patient cohorts, before and after the creation of INFANT.

Methods: A retrospective chart review of all neonates diagnosed with intestinal failure at the Montreal Children's Hospital, 3 years prior to the creation of INFANT(2007-2009) was conducted. The outcomes of this group were compared with a cohort of neonates with the same diagnosis that were followed by our team for the first 3 years of its creation (2010-2012). Results: Twenty-eight patients were included in the INFANT cohort while twenty-seven patients constituted the historical control group. The most common etiologies of SBS included: necrotizing enterocolitis, intestinal atresia, gastrochisis and volvulus. Mean length of small bowel remaining after surgery was 115.6 ± 24.6 cm in the pre-INFANT group vs 112.3 ± 55 cm in the INFANT group (p=0.837), presence of ICV was also similar in both groups 19 (70.4%) vs 21 (75%), (p=0.7). There was no statistically significant difference in the proportion of infants who reached full enteral feeds (85.2% vs 85.7%, p=0.956) although patients in the INFANT cohort took longer to attain full enteral feeds (100.8 vs 158.5 days, p=0.014). There was no significant difference in terms of number of patients on home TPN (7.1% vs 14.8%, P=0.362) but the peak direct bilirubin was lower in the INFANT group (116.6 ± 82.8 vs 181.6 ± 124.1, P=0.026). Overall mortality was less in the INFANT cohort but the difference was not statistically significant (7.1% vs 14.8%, P=0.362).

Conclusions: Our study demonstrates a trend towards an increased survival rate of patients with neonatal SBS since the creation of INFANT. Our data suggest that survival of patients who would have previously died possibly accounts for the longer PN duration and longer time to full enteral feeds in the INFANT cohort. Although the incidence of cholestasis was similar in both groups, mean peak bilirubin was lower in the INFANT group, likely attributable to the increased use of omega-3 fatty acids parenteral lipid preparations. Continuing data collection on incoming patients in a prospective fashion will allow to further define improvements in outcomes for this patient population.
96 CONTEMPORARY EXPERIENCE TREATING SHORT BOWEL SYNDROME IN INFANTS AND CHILDREN: A THREE TERTIARY EUROPEAN CARE CENTRES REPORT. Fabio Fusaro1, Andrea Conforti1, Riccardo Coletta2, Antonella Diamanti2, Basem Khalil3, Dominique Hermans4, Chiara Grimaldi3, Giuliano Torre2, Pietro Bagolan2, Antonino Morabito1, 1Neonatal Surgery, Bambino Gesù Children's Hospital, Rome, Italy; 2Hepatology, Gastroenterology and Nutrition, Bambino Gesù Children's Hospital, Rome, Italy; 3Hepatobiliary and Transplant Surgery, Bambino Gesù Children's Hospital, Rome, Italy; 4Paediatric autologous bowel reconstruction and rehabilitation unit, Royal Manchester Children’s Hospital, Manchester, United Kingdom; 5Pediatric and Nutrition unit, Saint Luc Hospital - UCL, Brussels, Belgium

BACKGROUND: Intestinal failure (IF) is defined as the reduction of functional gut mass necessary to maintain health and growth in children. This severe condition should be secondary to neuromuscular intestinal disorders, severe protracted diarrhea or to short bowel syndrome (SBS). A variety of surgical conditions may lead to SBS during neonatal period. Aim of the present study is to report the experience of three tertiary care centers in treating infants and children affected by SBS with residual small bowel length between 10 and 40 cm.

METHODS: All patients treated for SBS between January 2009 and December 2012 at Royal Manchester Children's Hospital, Manchester (RMCH), at the Bambino Gesù Children's Hospital (OPBG), Rome and the St Luc Hospital (SLH), Brussels were included in the study. Patients enrolled presented residual bowel length between 10 and 40 cm. Multidisciplinary dedicated team followed up those patients, as part of an intestinal rehabilitation programme. Clinical outcomes and morbidity were evaluated as well as the TPN dependency.

RESULTS: During the study period, 31 patients (RMCH: 14, OPBG 13, SLH 4) were followed up for SBS, secondary to extensive bowel resection during neonatal period (7 necrotizing enterocolitis, 7 multiple intestinal atresia, 11 midgut volvulus, 6 gastrochisis). Mean residual bowel length was 21.5 cm (IQ range 11 cm to 36.50 cm); ileo-cecal valve was preserved in 19 patients (61%), and 17 patients received intestinal lengthening procedures (LILT, STEP 1, TAPERING 1, LILT + interposition 1, STEP + interposition 5, LILT + STEP 1, LILT + STEP + interposition 1). Mean final lengthening after procedure was 36 cm (+95%) (IQ range 30cm to 54cm). Overall, 12/31 children (38.7%) are actually out of TPN (p=NS), while 6 (19%) required less than 30% of their caloric needs from TPN. We observed one exitus secondary to central venous line sepsis.

CONCLUSION: Multidisciplinary approach to SBS should decrease the rate of TPN dependency even at short-term follow-up. Modern TPN protocol as well as the availability of surgical competences to lengthening procedures implemented outcomes in infants affected by this severe condition.

97 LARGE DELETION IN THE EPCAM GENE GIVING RISE TO THE MILDER PHENOTYPE OF CONGENITAL TUFING ENTEROPATHY. Jurgen Gerada2, Godfrey Grech1, Ruth Galdies3, Wilhelmina Cassar2, Christian Saliba1, Christian Scerri4, Sue Hill5, Mario J. Vassallo2, Thomas M. Attard4-1, 1Gastroenterology, Children's Mercy Hospital, Kansas City, MO; 2Internal Medicine - Gastroenterology, Mater Dei Hospital, B'Kara, Malta; 3Pathology, University of Malta, B'Kara, Malta; 4Department of Physiology and Biochemistry, University of Malta, B'Kara, Malta; 5Pediatric Gastroenterology, Great Ormond Street Hospital, London, United Kingdom; 6Pediatrics - Gastroenterology, Mater Dei Hospital, B’Kara, Malta

Background: Absent EpCAM gene product expression has been associated with congenital Tufting Enteropathy (CTE) and several associated point mutations within the EPCAM gene (chromosome 2p21) have been characterized. We have previously described a milder phenotype of this condition in a cohort of patients in the Maltese Islands. EpCAM staining was negative in all patients in this cohort, suggesting a defective EPCAM gene in the milder phenotype as well.

Aim: To identify the underlying genetic abnormality within the EPCAM gene responsible for the milder phenotype of CTE.

Methods: In the period 1985 - 2012, eight Maltese patients with CTE from six unrelated families were retrospectively identified and enrolled. Genomic DNA was extracted from peripheral blood. Primers for all nine exons within the EPCAM gene were designed and optimized. PCR products were amplified, checked on a gel, purified and sequenced. To sequence exon 4 - exon 6 region, the PCR product was purified from the gel and ligated in a TA Vector. The ligated products were transformed into DH5α bacteria and cultured on ampicillin-containing agar plates. The cultured DNA was extracted, sequenced and analysed. All DNA sequences were compared with controls.

Results: Genetic analysis of the EPCAM gene in the first four Maltese CTE patients revealed a homozygous 1773bp deletion, starting from 1170bp downstream of exon 4, up to 721bp upstream of exon 6 and thus involving all of exon 5, in all four patients. Two of these patients are siblings and the other two are unrelated. Genotyping of the other four patients is underway but the PCR product corresponding to this region, as analyzed by gel electrophoresis, showed identical bands in another two patients.

Conclusion: A novel mutation in the EPCAM gene, consisting of a large deletion involving all of exon 5, was found to be responsible for the milder phenotype of CTE in the Maltese cohort and paradoxically appears to give rise to a milder phenotype. This is the first report of a deletion in the EPCAM gene of CTE patients and may provide insight on genotype-phenotype correlates of the disorder and its specific molecular-genetic mechanisms.

References:
98  QUALITY ASSESSMENT, DEVELOPMENT AND OUTCOMES IN PEDIATRIC GASTROENTEROLOGY: COLONOSCOPIC CECAL AND TERMINAL ILEAL INTUBATION RATES. Kiranmai Gorla1,2, Thirumazhisai Gunasekaran1,2, James Berman3, Zach Jones1, 1Pediatrics, Advocate Children's Hospital, Park Ridge, IL; 2Pediatrics, Children's Hospital at University of Illinois, Chicago, IL; 3Pediatrics, Loyola University Medical Center, Maywood, IL

Introduction: Despite increased emphasis on quality assessment in endoscopic performance, no data from actual clinical practice in pediatric gastroenterology has been published. Meaningful use of EHRs includes quality assessment reports of endoscopic procedures. Hospitals, training programs and the public are increasingly looking for reliable data on physician quality. Cecal intubation rate has been suggested as one such quality indicator. This Quality Improvement data should serve as a catalyst for improving assessment of colonoscopic performance in Pediatric Gastroenterology.

Aims: 1. Development of reporting tools and use of those tools for assessment of performance in pediatric colonoscopies. 2. Comparison of results to established adult data and national benchmarks.

Methods: A total of 1293 consecutive colonoscopies performed by 6 faculty gastroenterologists at three different facilities over a 2½ year period (January, 2010 - April, 2013) were reviewed. A customized database search using software included in the Provation (Wolters-Kluwer, Minneapolis, MN) and Endopro (Pentax-USA, Montvale, NJ) reporting systems was converted into a spreadsheet format. We worked with the technical support staff of these two reporting systems to optimize the data reports. We measured trends in overall and individual cecal and ileal intubation rates. We analyzed the trends that impact these rates including colonoscopic findings and prep quality, and the quality of documentation of cecal intubation. A random sample of physician documentation of ileal intubation was cross-checked with pathology reports to confirm presence of ileal histology.

Results: Intubation rate for the cecum was 95.74% (1238) and the terminal ileum was 85.3% (1103) in our cases. There was no variation in success rates when analyzed by physician or site of care. Poor prep quality was responsible for 38.15% and mucosal inflammation for 15.78% of failures to reach the terminal ileum. In the rest of the cases the failure of TI intubation was other/not documented. The median number of colonoscopies per physician per year was 69 and none of the physicians performed more than 200 per year. Type of bowel prep, sedation method and endoscopic assistant were not analyzed as a part of this study.

Conclusion: 1. Our pediatric GI Group's Cecal Intubation rates are higher than the adult national benchmarks (90%). 2. No correlation was noted between Cecal and Ileal Intubation rates and number of colonoscopies performed per physician per year. 3. No correlation was noted between Cecal and Ileal Intubation rates and years of experience post-fellowship. 4. Endoscopy QI can be obtained by custom programming the tools in the electronic reporting systems that are readily available. 6. In the absence of established pediatric national benchmarks, we believe our outcomes can be considered to represent acceptable standards.

99* THE EFFECTS OF LACTOFERRIN SUPPLEMENTATION ON THE INTESTINAL MICROBIOTA OF PREMATURE INFANTS RECEIVING PROBIOTICS. Kelly Grzywacz1,4, Ibrahim Mohamed2, Keith J. Barrington3, David R. Mack2,4, Alain Stintzi1; 1Department of Pediatric Gastroenterology Hepatology and Nutrition, CHU Sainte Justine, Montreal, QC, Canada; 2Department of Neonatology, CHU Sainte Justine, Montreal, QC, Canada; 3Department of Pediatric Gastroenterology Hepatology and Nutrition, Children's Hospital of Eastern Ontario (CHEO), Ottawa, ON, Canada; 4Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, ON, Canada

Introduction: Lactoferrin is the major whey protein in mammalian milk and is an important component of the innate immune system. It has been reported to exhibit anti-inflammatory properties, antibacterial activity and to support the growth of beneficial bacteria in the gut. Objective: To compare the stability and diversity of the intestinal microbiota of premature infants receiving probiotics with and without lactoferrin supplementation.

Patients and 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 FloraBABYTM, a probiotic mixture of Bifidobacterium and Lactobacillus +/- 100 mg of bovine lactoferrin. Clinical information such as mode of delivery, antibiotic use, and type of milk ingested, was collected to correlate patient factors with the microbiota. Meconium was collected followed by one stool sample each week for the first month of life. DNA was extracted from each stool sample 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. All further analysis was performed using DNA analysis tools such as; Novoborode, Prinseq, QHIME, and Galaxy.

Results: Thus far we have analyzed the sequencing results of 73 samples representing the intestinal microbiota of 29 of the targeted 70 infants in the study. Enterobacteriaceae had the highest relative abundance in all samples (46.2%), which is consistent with the current literature on the intestinal biota of premature babies. Statistical analysis using a one-way ANOVA revealed no significant difference in the diversity (Shannon Index, Chao1, and number of observed species) of the intestinal microbiota between the two groups. No difference in the relative abundance of Lactobacillus (10.1%) or Bifidobacterium (2.8%), the 2 strains in FloraBabyTM, was seen between the 2 groups. When samples were grouped by week of postnatal life, we found a higher relative abundance of the Klebsiella genus (34.4% versus 5.3%) in our combined lactoferrin/probiotic group and a higher relative abundance of the Clostridiales order (14.9% versus 1.2%) in the probiotic alone group at week 4.

Conclusion: Based on our interim data, we are unable to show a more diverse and stable intestinal microbiota in infants receiving both probiotic and lactoferrin supplementation compared to probiotic alone.
Motility/Functional Gastrointestinal Disorders

115  THE RELATIONSHIP BETWEEN RUMINATION SYNDROME PHENOTYPE AND BEHAVIORAL TREATMENT OUTCOME. Anthony Alioto1,3, Nicole Dempster1,3, Rose Schroedl1,3, Mary Montgomery2,3, Desalegn Yacob2,3, Hayat Mousa2,3, Carlo Di Lorenzo2,3, 1Pediatric Psychology and Neuropsychology, Nationwide Children's Hospital, Columbus, OH; 2Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH; 3Pediatrics, The Ohio State University, Columbus, OH

Introduction: Rumination Syndrome presents with various phenotypes (e.g., rumination immediately after ingestion, rumination after completion of a meal). Several approaches to treatment have been suggested in the literature and shown to provide benefit. Characteristics of individuals with different phenotypes have not been described, nor has a differential response to treatment. The purpose of the current chart review was to determine if differences exist between rumination phenotypes and their responsiveness to behaviorally-based treatment.

Method: Chart reviews were conducted of the first 45 adolescent patients in an intensive interdisciplinary behaviorally-based inpatient program for rumination syndrome at a large Midwestern pediatric hospital. Data obtained included rumination phenotype (i.e., Type 1 rumination = rumination immediately after ingestion; Type 2 = rumination after completion of meal), age, duration of rumination, enteral feeding usage prior to admission, dyspeptic symptoms, presence of a mental health diagnosis, and outcome variables (meeting nutritional discharge goals, having enteral feeds discontinued, days admitted to the program).

Results: Type 1 patients did not differ from Type 2 patients with regard to age, duration of rumination prior to admission, or body mass index. Rumination type was not associated with the presence of a mental health diagnosis, patients' ability to meet nutritional discharge goals, or discontinuation of enteral feeds during treatment. Type 1 patients were more likely to come into treatment with enteral feeding and required a longer hospitalization to reach their treatment goals.

Conclusion: There do not appear to be identifiable patient or illness factors related to the specific presentation of rumination. Patients with more "severe" rumination (i.e., Type 1) do respond to behaviorally-based treatment, but appear to require longer admissions to reach goals. Future research will examine if rumination phenotype is related to long-term outcomes.

Patient and Outcome Variables by Rumination Type

<table>
<thead>
<tr>
<th></th>
<th>Type 1 (N=13)</th>
<th>Type 2 (N=32)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (Years)</td>
<td>17.2</td>
<td>16.1</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Duration or Rumination (Months)</td>
<td>18.2</td>
<td>13.5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>20.1</td>
<td>20.7</td>
<td>NS</td>
</tr>
<tr>
<td>Number with Mental Health Diagnosis</td>
<td>5 (38%)</td>
<td>16 (50%)</td>
<td>NS</td>
</tr>
<tr>
<td>Number Entering Program on Enteral Feeding</td>
<td>12 (92%)</td>
<td>11 (34%)</td>
<td>p = .001</td>
</tr>
<tr>
<td>Mean Number of Dyspeptic Symptoms</td>
<td>1.5</td>
<td>2.1</td>
<td>NS</td>
</tr>
<tr>
<td>Met Nutritional Treatment Goal</td>
<td>11 (85%)</td>
<td>28 (88%)</td>
<td>NS</td>
</tr>
<tr>
<td>Discontinued Enteral Feeding</td>
<td>10 (83%)</td>
<td>9 (82%)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Days of Treatment</td>
<td>13.7</td>
<td>9.4</td>
<td>p &lt; .05</td>
</tr>
</tbody>
</table>

116  MMPI-A RESPONSE PROFILES IN ADOLESCENTS WITH RUMINATION SYNDROME. Nicole Dempster1,3, Anthony Alioto1,3, Rose Schroedl1,3, Mary Montgomery2,3, Hayat Mousa2,3, Desalegn Yacob2,3, Carlo Di Lorenzo2,3, 1Pediatric Psychology and Neuropsychology, Nationwide Children's Hospital, Columbus, OH; 2Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH; 3Pediatrics, Nationwide Children's Hospital, Columbus, OH

Introduction: While adolescent rumination syndrome has been described in the literature, little research has explored the psychological profiles of these patients. The present study aimed to examine psychological factors in this population and explore the relationship with treatment outcome.

Method: Of patients seen in a large Midwestern hospital for interdisciplinary inpatient treatment for rumination syndrome, adolescents between the ages of 13-18 (N = 30) completed the Minnesota Multiphasic Personality Inventory - Adolescent (MMPI-A) as part of standard care. MMPI-A t-scores were considered elevated if $t \geq 65$. Chart reviews gathered data on rumination severity, age, BMI, duration of rumination, mental health diagnoses, and if patients met nutritional intake goals.

Results: Our sample's MMPI-A profiles were valid, though 50% reported an elevated K scale which indicatess a defensive approach to completion of the measure. Elevations on the K scale were not related to any variables of interest. On the MMPI-A clinical scales, the highest mean t-scores were (in order) hysteria (scale 3), hypochondriasis (scale 1), and depression (scale 2). The frequency of significantly elevated scales in the sample was 54%, 30%, and 40%, respectively. Elevated hypochondriasis and hysteria scales were not related to variables of interest; however, elevated depression scales were (see table). Specifically, those with elevated depression scales were more likely to be older, have more months of rumination prior to admission, and have a diagnosis of anxiety. Elevated MMPI-A depression scale also was related to longer inpatient admissions and more severe rumination. The depression scale was not related to patients' BMI or number of dyspeptic symptoms. A diagnosis of depression was not related to an elevated depression scale. Elevated MMPI-A scales were not significantly related to meeting caloric intake goals during admission in the program.

Conclusion: Greater reported psychological distress is present in patients with more severe rumination. These patients experienced longer...
duration of rumination pre-treatment. Although patients with higher reported psychological distress did benefit from behaviorally-based treatment, they tended to take longer to reach treatment goals. Future research will examine if MMPI-A psychological profiles are related to long-term outcomes.

Patient and Outcome Variables by MMPI-A Depression Scale

<table>
<thead>
<tr>
<th>Patient and Outcome Variables</th>
<th>Elevated MMPI-A Depression Scale (N = 9)</th>
<th>Non-Elevated MMPI-A Depression Scale (N = 21)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (Years)</td>
<td>16.67</td>
<td>15.19</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Mean Duration of Ruminating (Months)</td>
<td>35.11</td>
<td>16.76</td>
<td>.01</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>20.57</td>
<td>20.52</td>
<td>NS</td>
</tr>
<tr>
<td>Number with Anxiety Diagnosis</td>
<td>5 (56%)</td>
<td>2 (1%)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Number Entering Program on Enteral Feeding</td>
<td>5 (56%)</td>
<td>36%</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Number of Dyspeptic Symptoms</td>
<td>1.89</td>
<td>2.14</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Days of Treatment</td>
<td>11.56</td>
<td>8.19</td>
<td>&lt; .05</td>
</tr>
</tbody>
</table>

117 PREVALENCE OF ABDOMINAL PAIN PREDOMINANT FUNCTIONAL GASTROINTESTINAL DISORDERS IN JORDANIAN SCHOOL CHILDREN. Eyad M. Altamimi1, Mohammad Al Safadi2, 1Pediatric, Mu'tah University, Alkarak, Jordan; 2Qatar Red Crescent, Tripoli, Lebanon

Introduction: Recurrent abdominal pain is a common complaint in children. Significant portion of them are of functional origin. This study aimed to assess the prevalence of Abdominal pain predominant FGID and its types in Jordanian school children.

Patients and Methods: This is a school - based survey at south Jordan. Information regarding abdominal pain characteristics, bowel habits and associated symptoms were collected using the self-reporting form of The Questionnaire on Pediatric Gastrointestinal Symptoms—Rome III Version (QPGS-RIII) - The official Arabic translation -. Classes from academic years (grades) 6-8 were selected. All students in selected classes, present during the day of the survey, were included. The questionnaire was distributed in the class rooms in an examination setting. Children were given unlimited time to fill the questionnaire, verifications were provided by the researchers.

Results: 500 Questionnaires distributed, 454 returned answered (91%). 451 included in the analysis, 229 (50.8%) were males. The average age of participants was 12.7 yrs (11-15 yrs). 116 (25.7%) had abdominal pain - predominant FGD. 79 (68%) of them were females. 47 (10.6%) had Irritable Bowel Syndrome (IBS). 36 (8%), 17 (3.8%), 11 (2.4%) and 5 (1.1%) had abdominal migraine, functional abdominal pain, functional abdominal pain syndrome and functional dyspepsia, respectively.

Conclusion: Abdominal pain predominant FGD becomes a major health issue in our society. One out of four children between 11 and 15 years has at least one abdominal pain predominant FGD. IBS is the most common type. Females are affected more than males.

118 EFFECT OF BLADDER FILLING AND VOIDING ON INTRA-ANAL PRESSURE PROFILES IN CHILDREN

Lusine Ambartsumyan1, Anees Siddiqui2, Stuart Bauer2, Samuel Nurko2, 1Center for Motility and Functional Gastrointestinal Disorders, Boston Children's Hospital, Boston, MA; 2Urology, Boston Children's Hospital, Boston, MA

Background: Many children with voiding dysfunction have associated constipation and fecal incontinence. The coexistence of defecation and voiding disturbances in children significantly affects their quality of life. The physiological relationship between the lower urinary tract (LUT) and the anorectum in children is not well understood. Adult studies report variable alterations in anorectal function with bladder filling. The effect of bladder filling and voiding on anorectal function and intra-anal pressure characteristics in children has not been studied. Aim: To observe the effect of bladder filling and voiding on parameters of anorectal function. Methods: Children with urinary dysfunction were referred to Boston Children's Hospital Urodynamic Center for further evaluation. They were prospectively enrolled to undergo a combined Urodynamic (UDS) and Anorectal Manometry (ARM) study. A specially designed system to capture simultaneously anorectal pressure changes and urodynamic parameters were employed. ULD and anorectal physiological parameters were measured during the micturition cycle of bladder filling and voiding. Results: 10 children (mean age, 113.7 ± 18.7 months, 3 male, 7 female) were prospectively enrolled. All 10 children had voiding dysfunction of which 7 had urinary incontinence, 9 children had functional constipation, and 6 had "overflow" fecal incontinence. Bladder pressures significantly increased from 0.07 ± 0.9 cmH20 at start of bladder fill to 42.4 ± 4.3 at void (p<0.05). There was an increase in abdominal pressures from start of fill to void (p=0.24). Intra-anal pressures significantly decreased from 68.0 ± 2.1 at start of bladder fill to 49.7 ± 7.3 at void (p<0.05) (See Table). During bladder filling intra-anal pressures decreased at 25th (p=0.03) and 50th (p=0.06) percentile of total volume of bladder fill. Conclusion: Intra-anal pressures decrease during bladder filling. There was also a significance decrease in intra-anal pressures during voiding. This is the first time that intra-anal relaxation during bladder filling and voiding has been described in children. We speculate that there may be an inhibitory influence from the urinary system to the anorectum during the micturition cycle. These may explain some of the associations observed between urinary and fecal incontinence.

Voiding Dynamics
119* ENTERIC INFLAMMATION-DERIVED NEUROGENESIS IN RODENTS AND HUMANS. Jaime Belkind-Gerson1,2, Ryo Hotta2, Sarah A. Miller2, Aaron Zuckerman2, Allan M. Goldstein2, 1Pediatric Neurogastrology, MGH, Boston, MA; 2Pediatric Surgery, Massachusetts General Hospital, Boston, MA

Introduction: Structural changes in the ENS have been reported in human inflammatory bowel disease. Both Crohn's disease and ulcerative colitis have been associated with hyperganglionosis, including increased neurons and glial cells. These observations and others suggested that inflammation may contribute to increased numbers of enteric neurons. However, initial reports of experimental intestinal inflammation described acute neuronal loss with or immediately after inflammation. While ENS neurogenesis has been shown in vitro, its demonstration in vivo has been limited and has not been observed in healthy adult rodents. Replacing abnormal or injured neurons through endogenous neurogenesis would offer a novel approach to treating intestinal neuropathies.

Methods: To study neurogenesis in vivo, we used the DSS colitis model in adult mice, a well-studied model of mucosal and submucosal inflammation. We then looked for neurogenesis in full-thickness colonic biopsies of patients with different causes of colitis including: ulcerative colitis, Crohn's disease and C. Difficile infection.

Results: Four to 8 weeks after DSS colitis had resolved, despite the fact that DSS causes inflammation limited to the mucosa and submucosa, we found significantly more myenteric neurons in the distal colon. We examined neuronal proliferation using the mitosis marker Phospho-histone H3 (PH3) and found that starting at 4 weeks after colitis, 8-10% of Hu C/D+ cells (neurons) in the myenteric plexus were PH3-immunoreactive. This DSS-induced increase in neuronal proliferation led to an increase in the total number of neurons compared to control colon (p<0.05). In the analyzed samples from human patients with colitis, we found that 2-5% of enteric neurons were undergoing mitosis. No neuronal proliferation was present in control, non-inflamed samples.

Conclusions: These observations suggest that in rodents and humans, inflammation may contribute to post-natal enteric neurogenesis.

120 PARADOXIC PUBORECTALIS CONTRACTION IN CHRONICALLY CONSTIPATED CHILDREN DIAGNOSED BY 3D HIGH-DEFINITION ANORECTAL MANOMETRY. Jaime Belkind-Gerson1, Claire Zar-Kessler1, Brad Kuo1, 1Pediatric Neurogastrology, Massachusetts General Hospital, Boston, MA; 2GI Unit, Massachusetts General Hospital, Boston, MA

Introduction: Paradoxic Puborectalis Contraction (PPC) is a common cause of dyssynergic defecation in adults may require pelvic physical therapy/biofeedback. In children, it is a condition seldomly detected due to the difficulty in making the diagnosis, as it typically requires defecography or electromyographic testing. Both of these are unavailable in many centers. The objective of the study was to determine the incidence of PPC using 3D ARM in chronically constipated children.

Methods: Retrospective review of 3D Anorectal Manometry studies (ARM) done on 86 chronically constipated children aged 5-19 (Rome 3). During ARM, the beardown maneuver (BDM) was performed with both, an uninflated and an inflated balloon to 20, 40 and 60ml. The puborectalis sling-elicited pressure on the anal canal could be identified in a posterior-proximal location during BDM. It could also be distinguished from the pressure exerted by the anal sphincters distally. If the puborectalis constricted the posterior anal canal (the puborectalis sling does not exert pressure on the anterior wall), occluding the lumen by more than 25% during the BDM, the diagnosis of PPC was made.

Results: of 86 total children (45 fem / 41 male) PPC was found in 23 (27%) (13 fem / 10 male). PPC was easily identified during the BDM in 3D ARM. Two patients additionally underwent defecography where the PPC was confirmed. Of the 23 patients, balloon expulsion test was done in 22 and 15 with PPC could not expel balloon in 1 min, thus 69% could not expel the balloon. This is in contrast with children with a normal ARM, who have 14% rate of unsuccessful balloon expulsion.

Conclusion: PPC is common in chronically constipated children of both sexes. 3D Arm is a promising way to evaluate the puborectalis function during BDM in this population. We found that children with PPC identified by 3D ARM had higher rates of failing the balloon expulsion test compared to those with a normal ARM. This information is clinically relevant for therapy as PPC may require pelvic physical therapy/biofeedback or the application of Botulinum toxin.

121 CORRECTED RECTO-ANAL PRESSURE DIFFERENTIAL DURING HIGH-DEFINITION ANO-RECTAL MANOMETRY IN CONSTIPATED CHILDREN AND ITS CORRELATION TO THE BALLOON EXPULSION TEST. Jaime Belkind-Gerson1, Claire Zar-Kessler1, Brad Kuo1, 1Pediatric Neurogastrology, MGH, Boston, MA; 2GI Unit, Massachusetts General Hospital, Boston, MA

Introduction: Dyssynergic defecation is common in constipated adults and children, but its mechanisms are difficult to study. The balloon expulsion test (BET) is helpful to detect outlet obstruction and is normal in 94% of children with a normal anorectal manometry (ARM) (Belkind-Gerson, JPGN, 2013). However it does not provide the cause of the mechanistic defect. The bear-down maneuver (BDM) during ARM is used in adults to explore the presence of dyssynergic defecation and whether there is an abnormality of rectal or anal canal pressures during defecation. However, the BDM has not been studied in pediatrics.

Aims: To investigate if the values obtained from the BDM in chronically constipated (CC) children correlates with BET and if it provides additional clinically important information.

Methods: Retrospective review of 21 CC children (7-19 yrs) (Rome 3) with 3D-ARM and BET. A normal BET in children occurs when a 60 ml filled balloon was passed in ≤ than 60 seconds (Belkind-Gerson, JPGN, 2013). The corrected rectal pressure was determined as the

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Start of Bladder Fill</th>
<th>Void</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-anal pressures (mmHg)</td>
<td>68.0 ± 2.1</td>
<td>49.7 ± 7.3</td>
<td>0.047</td>
</tr>
<tr>
<td>Bladder pressures (cmH2O)</td>
<td>0.07 ± 0.9</td>
<td>42.4 ± 4.3</td>
<td>0.005</td>
</tr>
<tr>
<td>Abdominal pressures (mmHg)</td>
<td>9.4 ± 3.4</td>
<td>21.4 ± 11.2</td>
<td>0.241</td>
</tr>
</tbody>
</table>
total pressure in rectal sensor minus balloon pressure from air inflation to 60 ml. This is due to the fact that the rectal sensor is contained within the balloon. The BDM was also done with 60 ml of air in balloon. Sufficient time was allowed for anal accommodation after balloon inflation. The corrected recto-anal pressure differential (cRAPD) is a measure of coordinated defecation and takes into account rectal pressure (thrust) and anal canal relaxation. It is calculated as: corrected rectal pressure - anal canal pressure. Normal values are not available in children, but in adults it is -41(6) mmHg (Noelting, Am J Gastro 2012).

Results: Total 21 children, all performed the BDM test successfully. Nine expelled balloon during the BET, 12 did not. In 3 patients, no rectoanal inhibitory relaxation (RAIR) was found at 60 ml. These 3 could not expel balloon at BET. The range of corrected rectal pressures during BDM was 4 to 96 mmHg (av: 38), the range of anal pressure during BDM was 40 to 196 mmHg (av 109) and the range of cRAPD was -18 to -182 mmHg (av: -69). If the cRAPD was <-60 mmHg, 8/9 failed BET (89%) (lack of anal canal relaxation). If the cRAPD was >= -60 mmHg, 8/12 passed the balloon in BET (67%). In the 4/12 that did not pass the balloon, the corrected rectal-pressure was 25 mmHg or less suggesting low rectal thrust effort during defecation.

Conclusions: 1) The BDM test can be done in children 7 yo or older. 2) Dynamic testing using BDM with balloon inflation in pediatrics gives better insight of pathophysiology of outlet obstruction (anal vs rectal pressure abnormalities). 3) Patients that do not have a RAIR at 60 ml may have outlet dysfunction and have an abnormal BET. 4) When the RAPD is less than -60 mmHg, there is a high likelihood that the balloon will not be passed during BET. 5) The information obtained during BDM may be valuable for planning pelvic physical therapy as well as anal Botox use.

122 ARE NEONATAL STRESS EVENTS RISK FACTORS FOR DEVELOPMENT OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN? Christian G. Boggio Marzet1, Christian Palacios Perez1, Maria Luisa Deforel1, Carmen Vecchiarelli2, Cecilia Baston2, Graciela Rodriguez3, 1Pediatric Gastroenterology, Hospital "Dr.I.Pirovano", Buenos Aires, Argentina; 2Neonatology, Hospital "Dr. I.Pirovano", Buenos Aires, Argentina; 3Neonatology, Otamendi Clinic, Buenos Aires, Argentina

Background: Functional gastrointestinal disorders (FGID) affect 15-20% of the general pediatric population. A model of altered stress response is believed to play an important role in the development of FGID.

Aim: To analyze the presence of neonatal stress events (NSE) as risk factors for the development of functional gastrointestinal disorders (FGID) in children 5 to 15 years.

Methods: retrospective cohort study. Population: children aged 5 to 15 of the Pirovano Hospital and Otamendi Clinic in Buenos Aires city. Sample was divided in two groups: Group I (GI): with exposure to NSE and group II (GII): no exposure. Both groups answered a survey on FGID. Items considered: age, sex, birth weight, gestational age and neonatal stress events (endotracheal intubation, nasogastric tube, canalization, phototherapy) and FGID analyzed.

Results: Sample = 50 patients in each of the cohorts. No statistically significant differences between the two cohorts (GI/GII) by sex distribution (48% vs 56% males [Z proportion Test p=0.42]) and x age (8.81 +/- 2.52 vs 8.39 +/-2.79 [t Test p=0.42]). Global FGID: 24% (26% GI 95% CI 13.8-38.1 and GII 22% 95% CI 10.5-33.4 with no significant differences [Z proportion Test p=0.63]). GI x gestational age did not present differences according to presence or absence of FGID (31.38 vs 32.27 weeks t Test p=0.40). While the x z-score for weight had lower value for those who presented FGID within the GI (-0.42 vs -0.12) this difference was not significant respect to those without FGID (t Test p=0.17). The NSE most viewed were canalization, endotracheal intubation and nasogastric tube (100% vs 94%) and were not associated with FGID (Fisher Test p=0.60).

Conclusions: This study cannot support enough evidence to show the association between FGID in children and adolescents and presence of NSE. Further research would be necessary on this issue involving more patients and that explore in particular the impairment of the birth weight as a possible risk factor associated.

123 PEDIATRIC ESOPHAGEAL HIGH-RESOLUTION MANOMETRY: APPLICATION OF THE CHICAGO CLASSIFICATION FOR ACHALASIA IN CHILDREN. John M. Hollier, Eric Chiou, Pediatrics, Baylor College of Medicine, Houston, TX

Background: Achalasia is divided into 3 distinct subtypes using the Chicago classification for high-resolution manometry (HRM) in adults. Pediatric HRM data are sparse and classification of pediatric achalasia based on HRM parameters has not been established. The aim of this study was to apply the adult Chicago classification criteria to a pediatric cohort of achalasia and to compare clinical and manometric characteristics between the 3 subtypes.

Methods: Clinical and manometric data were collected in a retrospective study of pediatric patients diagnosed with achalasia by HRM at Texas Children's Hospital from 2007 to February 2013. Esophageal pressure topography was used to analyze gastroesophageal junction (GEJ) resting and relaxation pressure, upper esophageal sphincter (UES) resting and relaxation pressure, and esophageal body motility. Achalasia was classified according to the 3 Chicago classification subtypes.

Results: Using HRM, achalasia was diagnosed in 17 pediatric patients; median age was 13.6 (6-17) years. The most frequent symptoms were vomiting (70.6%) and dysphagia (58.8%). Applying the Chicago classification, 35% of patients were classified as type I, 47% classified as type II, and 18% as type III. There were no significant differences between subtypes in terms of age, gender, ethnicity, or clinical symptoms. There was a trend towards higher median UES resting pressure in type III patients (125 mmHg) compared to type I (67.6 mmHg) and type II (51.5 mmHg) patients. GEJ resting and relaxation pressures did not differ significantly between the 3 groups.

Conclusion: The Chicago classification for achalasia can be applied to pediatric achalasia patients. Similar to adult studies, type II achalasia with pan-esophageal compression was found to be the most common subtype. Further studies are needed to understand the clinical significance of these subtypes in children, such as differences in response to therapy.
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**LOW FERMENTABLE SUBSTRATE DIET IN CHILDREN WITH IRRITABLE BOWEL SYNDROME: PILOT EFFICACY AND MICROBIOLOGICAL PREDICTORS OF RESPONSE.** Bruno P. Chumpitazi1, James Versalovic2, Emily B. Hollister2, Cynthia M. Tsai2, Ann McMeans1, Ruth A. Luna1, Robert J. Shulman1, 1Pediatrics, Baylor College of Medicine, Houston, TX; 2Pathology, Baylor College of Medicine, Houston, TX

A low fermentable substrate diet (LFSDD) has demonstrated efficacy in reducing gastrointestinal (GI) symptoms in adults with IBS, though not all respond. The efficacy of a LFSDD in children with irritable bowel syndrome (IBS) is unknown. We sought to determine whether a LFSDD decreases abdominal pain frequency in children with IBS and factors determining efficacy of the diet.

**Methods:** Children with Pediatric Rome III-defined IBS completed a 1-wk baseline period on their habitual diet followed by a 1-wk LFSDD intervention. Participants were informed they would be taught one of two potential diets, although all participants were taught the same LFSDD by a dietitian. Measurements during baseline and LFSDD intervention included: A Pain/Stool Diary (capturing the number of pain episodes, stool frequency, and stool form using the modified Bristol Stool Form Scale for children), breath hydrogen/methane production, whole intestinal transit time, and stool microbiome composition analysis. Responders were defined as having ≥50% decrease in abdominal pain frequency.

**Results:** Eight children (4 girls), mean age 9.0 ± 3.6 yrs were enrolled and completed the LFSDD. Baseline vs LFSDD Diet: As a group, overall pain frequency, pain severity, and pain related interference with activities decreased, with a trend toward fewer bowel movements but no differences in stool form. There were no changes in breath hydrogen or methane production, or intestinal transit time. Trends toward increased abundances of Clostridiales and decreased abundance of Bacteroidetes were observed during the LFSDD. Responders vs Non-responders: Four children (50%) were identified as responders. There were no differences between responders and non-responders with respect to baseline pain frequency, stool frequency, stool form, hydrogen, or methane production. During the LFSDD, responders produced less hydrogen than non-responders (P<0.05), without differences between the groups in stooling characteristics or methane production. Responders (n=3) and non-responders (n=3) with constipation-predominant IBS could be separated by principal components analysis based on the relative species abundance of their baseline gut microbiota. Responders were characterized by increased abundance of taxa belonging to the genera Sporobacter (P<0.05) and Subdoligranulum (P<0.02) and decreased abundance of taxa belonging to Bacteroides (P<0.05) relative to nonresponders. In addition, other differences in microbiome composition between responders vs. non-responders were identified during the LFSDD.

**Conclusions:** A LFSDD was effective in decreasing abdominal pain frequency in children with IBS. Those children who had ≥50% reduction in pain frequency had less hydrogen production and a different stool microbiome composition vs. those who did not respond to the LFSDD suggesting that gut microbiome makeup may predict LFSDD efficacy in childhood IBS.

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**LACTASE AND SUCRASE DEFICIENCIES IN CHILDREN WITH CHRONIC ABDOMINAL PAIN.** Khalil I. El-Chammas, Sara Williams, Adrian Miranda, Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI

Introduction: While low lactase activity is the most common of all small intestinal disaccharidase deficiencies, it has been suggested that lactose elimination in some children with lactase deficiency does not improve abdominal pain (1). The frequency of sucrose and/or lactase deficiencies in children with chronic abdominal pain (CAP) has not been well established. We aimed to evaluate disaccharidase levels in patients with CAP and hypothesized that: 1) a majority of patients with CAP have abnormal levels of one or more disaccharidas, 2) sucrase as well as lactase is abnormally low in patients with CAP, and 3) CAP patients with abnormally low disaccharidase levels have different clinical characteristics compared to those with normal levels. Method: The study was approved by the Children's Hospital of Wisconsin (CHW) institutional review board. Patients presenting to the CHW pediatric gastroenterology clinic between 2005 and 2011 with a primary complaint of abdominal pain prospectively completed a detailed demographic, history and symptom questionnaire. A retrospective chart review was performed to obtain disaccharidase levels and histology of endoscopic biopsies. The CAP cohort included those with at least one month of abdominal pain and non-diagnostic endoscopic biopsies. Patients with eosinophilic esophagitis, peptic ulcer disease, pancreatitis, celiac disease or inflammatory bowel disease were excluded from the study. Results: A total of 203 CAP patients were included. The mean age was 11.5 years (SD 3.1) and 32.5% of the patients were male. The percentages of abnormally low disaccharidase groups and clinical features. Conclusions: A large proportion of patients with CAP have deficiencies in lactase and sucrase. Low lactose diet alone in these patients may not be sufficient to alleviate symptoms. Bowel frequency, consistency, or location of pain was no different between groups, suggesting that these clinical features cannot be used to predict deficiencies in lactase or sucrase in children with abdominal pain.


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**FRUCTOSE MALABSORPTION IN CHILDREN WITH DIGESTIVE AND/OR NUTRITIONAL DISORDERS.** Ulysses Fagundes-Neto, Adriana Chebar Lozinsky, Cristiane Boé, Ricardo Palmero Division of Pediatric Gastroenterology, Escola Paulista De Medicina - Universidade Federal De São Paulo (Epm-Unifesp), São Paulo, Brazil. Ulysses Fagundes-Neto, Pediatrics, EPM/UNIFESP, São Paulo, Brazil

Background: Fructose is a monosaccharide frequently present in natural and artificial juice fruits. When the concentration of fructose in
certain food is present in excess of glucose concentration some individuals may develop fructose malabsorption.

Objectives: to report the frequency of fructose malabsorption utilizing the Hydrogen Breath Test (HBT) in children with gastrointestinal and/or nutritional disorders.

Methods: Forty three patients, of both sexes (24 boys), aging 3 months to 16 years, median 2.6 years, were consecutively and prospectively investigated, recruited from the UNIFESP Pediatric Gastroenterology outpatient clinic, presenting clinical complains of gastrointestinal and/or nutritional disorders, such as: chronic abdominal pain, chronic diarrhea and failure to thrive, during the period from July 2011 through July 2012.

The patients were divided in two groups according to the major complaints, as follows: 1- irritable bowel syndrome (IBS): 16 patients; 2- Other digestive and/or nutritional symptoms: failure to thrive (FT) 10, food allergy 4, lactose intolerance 3, celiac disease (CD) 1 and giardiasis 1 patient.

All patients underwent the HBT utilizing the following carbohydrates: glucose, fructose, lactose and lactulose, as part of the routine investigation of the digestive/absorptive function.

After an overnight fasting the patients ingested an oral carbohydrate load in a 10% aqueous solution, in the following doses: lactose 2g/body weight (maximum 25 grams), glucose and fructose 1g/body weight (maximum 12 grams) and lactulose 20 grams. The expired breath samples were collected in the fasting state to measure the H2 baseline value. After the ingestion of the carbohydrate load.

Breath samples were collected every 15 minutes during the first hour and every 30 minutes in the second hour of the test, in order to complete in total 2 hours for each test. Malabsorption was considered when there was an increase of >20 ppm of H2 over the fasting level, and intolerance was diagnosed if gastrointestinal symptoms would appear.

Results: Fructose malabsorption was characterized in 13 (30.2%) patients, and 1 (2.3%) patient also revealed lactose intolerance within the first 8 hours after the performance of the test. The 13 patients that presented fructose malabsorption and their respective diagnosis was, as follows: IBS 7, FAP 4, FT 1 and CD 1 patient. The analysis of the HBT utilizing the other carbohydrates (lactose, glucose and lactulose) showed the following results: lactose malabsorption 3, bacterial overgrowth syndrome in the small bowel 1. All the tests utilizing the glucose load showed normal results.

Conclusions: Patients with IBS and FAP were the main cause of fructose malabsorption in this group of patients.

127 PEPSIN IN SALIVA AS A BIOMARKER FOR ESOPHAGEAL REFUX COMPARED WITH 24-HOUR ESOPHAGEAL IMPEDANCE/PH MONITORING IN PEDIATRIC PATIENTS. John E. Fortunato1, Ralph B. D'Agostino2, Mark O. Lively3,

1Pediatrics, University of Colorado, Aurora, CO; 2Biostatistics, Wake Forest School of Medicine, Winston-Salem, NC; 3Biochemistry, Wake Forest School of Medicine, Winston-Salem, NC

Background: Measurement of pepsin from expectorated saliva/sputum and in bronchial alveolar lavage (BAL) fluid has been used to detect gastric aspiration. Pepsin in the oropharynx is a biomarker for gastroesophageal reflux (GER) in adults and children and can be measured in a non-invasive way by collection of saliva. We hypothesized that salivary pepsin is more prevalent in children with GER symptoms and correlates with proximal reflux events measured by impedance/pH monitoring (MII/pH). Aim: Assess pepsin in patients undergoing MII/pH for GER symptoms vs. asymptomatic controls and correlate the presence of pepsin in saliva with associated GER events during 24-hour esophageal MII/pH monitoring. Methods: Pediatric patients ages 1 month to 18 years (n=194) who were deemed clinically to require 24-hour MII/pH monitoring and healthy asymptomatic controls (n=45) were included. Saliva was collected by adsorption with eye sponges used in ophthalmic surgery. Pepsin was measured in saliva using an enzyme linked immunosorbent assay (ELISA) with a lower limit of quantification of 1.0 ng/mL pepsin. For MII/pH subjects, samples were collected: 1) immediately before catheter placement; 2) before and 30 minutes after meals (3 meals, 6 samples); and 3) upon awakening. For controls, a single sample was collected during a well-child exam visit. The pepsin score was defined as the sum of the number of pepsin-positive samples provided by each patient. Results: Of all the oropharyngeal samples collected, 56.2% (663/1179) of saliva samples were pepsin-positive in MII/pH patients compared to only 9.1% (4/44) of control subjects. Pepsin scores correlated with distal MII events (r=0.19, p=0.01), proximal MII events (r=0.24, p=0.001), and symptom index (SI) (r=0.21, p=0.005). Distal MII events also positively correlated with the SI, (r=0.47, p<0.0001). Pepsin was positive in 82% of refluxes for patients on a PPI and 84% for those not on a PPI during testing. The majority (86%) of saliva samples were obtained within one hour of the most recent reflux event. The average pepsin concentration of samples obtained within 30 minutes of a MII reflux event was 37 ng/mL versus 11 ng/mL for samples obtained between 31 and 60 minutes.

Conclusion: Measurement of salivary pepsin is a non-invasive way to screen for patients with oropharyngeal reflux. Pepsin concentration in saliva appears to decrease rapidly after 30 minutes giving a limited window for optimal detection. The weak correlation between pepsin and MII/pH suggests that pepsin is a more sensitive indicator for proximal or laryngopharyngeal reflux than MII/pH as impedance sensors were limited to the proximal esophagus below the upper esophageal sphincter. Future studies using pepsin and MII to measure both GI and respiratory clinical outcomes after treatment of GER are needed to determine the clinical significance of these diagnostic tools.

128 GASTROINTESTINAL SYMPTOMS IN PREGNANT TEENAGERS. Rafael Guerrero-Lozano, Nubia Farias, Catalina Puello, Karina Rubio, Ricardo Rubio, Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia

Introduction: During pregnancy many women report increased gastrointestinal symptoms, which in the case of adolescents may represent concern for expectant mothers and their families.

Gastrointestinal manifestations have been associated with physiological changes resulting from hormonal levels, and not just with physical effects caused by pregnancy. Symptoms may be individually expressed according to emotional conditions.

Objective: To determine the frequency of gastrointestinal symptoms in a group of pregnant teenagers.

Methods: Descriptive study in a cohort of 117 pregnant teenagers attending health activities. A survey was conducted regarding incidence and evolution of upper and lower gastrointestinal symptoms before and during gestation.

Participants signed their consent. Information was managed in Excel.
Results: We included 98 women aged 16.1 ± 1.1 years, and gestational age 23 ± 7 months, corresponding to 84% of program attendees in a year.

Overall, 13.3% reported digestive problems prior to pregnancy and 7.1% appearing during it; however, the frequency of symptomatic participants was clearly higher when asked about specific manifestations. Previously symptomatic mothers improved by 3.1%, while 4.1% worsened during pregnancy. About half (51%) had symptomatic evolution of <2 years; 8.2% had consulted for listed symptoms before and 29.6% during pregnancy.

Pre-pregnancy symptoms were epigastric pain (22.4%), belching (19.4%), hiccups (14.3%), diarrhea (13.3%), colic (12.2%), early fullness (9.2%), nausea (8.2%), anal pain or burning (8.2%), heartburn (7.1%), vomiting (6.1%), blood in stools (5.1%), other abdominal pain (4.1%), flatulence (4.1%), fecal soling (4.1%), hematemesis (1%), blackish stools (1%).

During pregnancy, mostly during the first trimester, symptoms were: vomiting (67.3%), nausea (65.3%), heartburn (59.2%), early fullness (40.8%), other abdominal pain (28.6%), epigastric pain (27.8%), colic (22.4%), retro-sternal pain (15.3%), anal pain or burning (14.3%), blackish stools (13.3 %), belching (12.2%), hiccups (10.2%), hematemesis (7.1%), blood in stools (6.1%), diarrhea (6.1%), fecal soling (1 %).

Stool frequency was suggestive of constipation in 13.3% before and 14.3% during pregnancy. Stool quality was considered normal in 73.5 and 65.3% and compatible with constipation in 23.5 and 28.6% before and after gestation, respectively.

Previous symptoms worsened as follows: constipation (5 of 13), heartburn (2 of 7), epigastric pain (5 of 22), early fullness (2 of 9).

Improved symptoms were: vomiting (3 of 6), early filling (4 of 9) diarrhea (5 of 13), epigastric pain (8 of 22), hiccups (5 of 14).

Conclusions: In adolescents, pregnancy induces and increases upper and lower gastrointestinal symptoms, evident mostly from the first trimester. In particular, in addition to vomiting, dyspeptic symptoms appear or increase. Constipation increases and with it some associated symptoms. In general, frequency of clinical manifestations in this study is higher than that reported in older pregnant women.

129 FUNCTIONAL GASTROINTESTINAL SYMPTOMS IN 10 TO 18 YEAR-OLD SCHOOL CHILDREN WITH OBESITY IN BOGOTA. Rafael Guerrero-Lozano, Lina Martinez, Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia

Obesity has been considered a precipitating factor of functional gastrointestinal disorders (FGID).

Objective: To establish the frequency of symptoms and FGID in obese children.

Methods: 792 children aged 10 to 18 years, from 6 schools, were included. The self-completed questionnaire designed by the Rome III committee was used. FGID frequency was established using the criteria currently in force. Population was considered normal when body mass index (BMI) was between -1 and 1, overweight when BMI was between >1 and ≤2 SD; obese when it was> 2 SD.

Results: 39 (4.9%) children were obese and 153 (19.3%) overweight; 482 (60.9%) had normal and 118 (14.9%) low BMI. FGID were suspected in 306 (38.6%), as follows: 194 (63.4%) in children with normal BMI, 61 (19.9%) in children with overweight and 13 (4.2%) in obese children.

The most common FGID were: functional abdominal pain, irritable bowel syndrome and functional constipation, with no statistical evidence of association with nutritional status.

Conclusion: Unlike other publications, the study population did not show a larger proportion of children with FGID in overweight and obese population.

130 MULTICHANNEL INTRAESOPHAGEAL IMPEDANCE PATTERN OF CHILDREN WITH AEROPHAGIA.

Celine Halb, Martine Pomerleau, Christophe Faure, CHU St Justine, Montréal, QC, Canada

Aim of the study: Aerophagia in childhood is defined by the Rome III criteria with two or more criteria including air swallowing, abdominal distention because of intraluminal air or repetitive belching and/or flatus. The aim of this study was to determine the multichannel intrasophageal impedance (MII) pattern in children suffering from aerophagia.

Methods: We compared the MII tracings of children suffering from aerophagia according to Rome III criteria (3 girls, mean age 10.4 years) to 5 control children (3 girls, mean age 8.6 years).

Results: There was no difference for the total number of LS and MS between the 2 groups. However, the total number of AS in patients with aerophagia was significantly higher than in controls (26 per hour vs. 5.5 per hour, P<0.05) although the number of AS was similar in the 2 groups in the recumbent position. SGB was found only in patients with aerophagia (2.6 per hour vs. 0 per hour, P<0.01).

Conclusion: Children suffering from aerophagia have a specific MII pattern with an increased frequency of air swallows and supragastric belching as compared to controls. MII may be used as a tool to confirm diagnosis of aerophagia in children.

131 RETINALDEHYDE DEHYDROGENASE ENZYMES REGULATE COLON ENTERIC NERVOUS SYSTEM STRUCTURE AND FUNCTION.

Elizabeth Wright-Jin1, John R. Grider2, Gregg Duester3, Robert O. Heuckeroth2, 1Pediatrics, Washington University School of Medicine in St. Louis, St. Louis, MO; 2Developmental, Regenerative and Stem Cell Biology, Washington University School of Medicine in St. Louis, St. Louis, MO; 3Physiology, Virginia Commonwealth University, Richmond, VA; Development and Aging Program, Sanford-Burnham Medical Research Institute, La Jolla, CA

The enteric nervous system (ENS) forms from neural crest-derived precursors that colonize the bowel before differentiating into a network of neurons and glia that control intestinal function. Retinoids are essential for normal ENS development, but the role of retinoic
acid (RA) metabolism in development remains incompletely understood. Because RA is produced locally in tissues where it acts by stimulating RAR and RXR receptors, RA signaling during development is absolutely dependent on the rate of RA synthesis and degradation. RA is produced by three different enzymes called retinaldehyde dehydrogenases (RALDH1, RALDH2 and RALDH3) that are all expressed in developing bowel. To determine the relative importance of these enzymes for ENS development, we analyzed whole mount preparations of adult (8-12 week old) myenteric and submucosal plexus stained with NADPH diaphorase (neurons and neurites), anti-TuJ1 (neurons and neurites), anti-HuC/HuD (neurons), and anti-S100β (glia) in an allelic series of mice with mutations in Raldh1, Raldh2, and Raldh3. We found that Raldh1−/−, Raldh2+/-, Raldh3+/- (R1KOR2HetR3Het) mutant mice had a reduced colon myenteric neuron density, reduced colon myenteric neuron to glia ratio, reduced colon submucosal neuron density, and increased colon myenteric fibers per neuron when compared to wild type (WT; Raldh1WT, Raldh2WT, Raldh3WT) mice. These defects are unlikely to be due to defective ENS precursor migration since R1KOR2HetR3KO mice had increased enteric neuron progenitor migration into the distal colon compared to WT during development. RALDH mutant mice also have reduced contractility in the colon compared to WT mice. These data suggest that RALDH1, RALDH2 and RALDH3 each contribute to ENS development and function.


EVALUATION OF LIQUID GASTRIC EMPTYING IN CHILDREN WITH FUNCTIONAL DYSPESIA. Nadia M. Hijaz, Robin E. Pearce, Susan M. Abdel-Rahman, Craig A. Friesen, Bridgette L. Jones, Gregory L. Kearns.

ASSESSMENT OF THE 13C-ACETATE BREATH TEST IN CHILDREN WITH FUNCTIONAL DYSPESIA AND DELAYED GASTRIC EMPTYING. Nadia M. Hijaz, Robin E. Pearce, Susan M. Abdel-Rahman, Craig A. Friesen, Bridgette L. Jones, Gregory L. Kearns.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FD (Mean+/− SD)</th>
<th>CONTROLS (Mean +/− SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1/2 (min)</td>
<td>112.94</td>
<td>25.27</td>
<td>0.95</td>
</tr>
<tr>
<td>Tmax (min)</td>
<td>55</td>
<td>13.23</td>
<td>0.004*</td>
</tr>
<tr>
<td>Cmax(delta over baseline, %)</td>
<td>38.24</td>
<td>10.61</td>
<td>0.38</td>
</tr>
<tr>
<td>DPHmax(Dose%/h)</td>
<td>13.81</td>
<td>0.97</td>
<td>0.045*</td>
</tr>
<tr>
<td>PDRmax(%)</td>
<td>8.71</td>
<td>1.60</td>
<td>0.006*</td>
</tr>
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</table>

Derived kinetic parameters for the breath test described in Mean and Standard deviation SD. * P<0.05.
compare gastric liquid emptying (GE) utilizing standard 13C-acetate breath test (ABT) parameters as well as parameters derived from a pharmacokinetic approach between FD patients with delayed GE versus normal GE determined by standard scintigraphy.

**METHODS:** Twenty-three FD patients, ages 5-17 years underwent simultaneous assessment of GE using a liquid test meal by scintigraphy and 13CO2 breath test samples (produced from administered 13C-acetate) collected from 0 to 120 min. FD patients were subdivided into 2 groups: delayed GE (N=16; 9 females; mean age 14.1 ± 2.4 years) and normal GE (N=7; 5 females; mean age 13.7 ± 3.3 years) determined by the gold standard, scintigraphy half emptying time. The 13CO2 versus time profiles were fit using traditional pharmacokinetic analyses. Means were compared using independent T test.

**RESULTS:** The time to the maximum concentration of 13CO2 [Tmax] produced from the acetate breath test and the concentration of 13CO2 at T max [C max] differed significantly between groups. (See table) However, the half emptying time [T1/2] as measured by ABT, the metabolic speed in dose per hour to Tmax [DPH max], and the cumulative percent of drug recovery to the [PDRmax] were not significantly different between both groups. See table.

**CONCLUSION:** The parameters, C max and T max, derived from pharmacokinetic analyses of 13C-acetate breath test differ between patients with functional dyspepsia and delayed liquid emptying as compared to those with normal gastric emptying. Future studies are necessary to determine the physiologic and therapeutic significance of these parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>FD with Delayed GE (Mean+/− SD)</th>
<th>FD with normal GE (Mean +/- SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1/2(min)</td>
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<td>67.37</td>
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</tr>
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<td>T max(min)</td>
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<td>C max(Δ over baseline,%)</td>
<td>31.98</td>
<td>10.16</td>
<td>0.02*</td>
</tr>
<tr>
<td>DPH max(Doase %/h)</td>
<td>14.9</td>
<td>4.28</td>
<td>0.13</td>
</tr>
<tr>
<td>PDR max(%)</td>
<td>6.7</td>
<td>3.06</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Derived kinetic parameters for the breath test described in mean and Standard Deviation SD. * P <0.05.

**Pancreas/Cystic Fibrosis**

**135 PEDIATRIC USAGE OF A BILIARY ENDOPROSTHESIS FOR GI AND PANCREATOCBILIARY DISEASE.** Douglas S. Fishman1, Richard Kellermayer1, Monica Lopez1, Thaddeus D. May1, Isaac Raijman2, 1Pediatric Gastroenterology, Texas Children's Hospital, Houston, TX; 2Digestive Associates of Houston, Houston, TX; 3Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX

Introduction: The Viabil® stent (Gore®, Flagstaff, AZ, USA) is a fully covered metal stent (FCMS) with a non-porous liner that provides a barrier to tissue ingrowth. Pediatric usage of this stent has not been reported. We have previously described the use of Viabil® for pancreatic pseudocysts in adults. We present the use of this stent in a pediatric series of patients with pancreaticobiliary and gastrointestinal disease. Patients And Methods: Retrospective review of four cases. (Table 1) Two patients were female, ages 13-16 (median 14). FCMS were placed over a .035 inch hydrophilic wire in gastric wall (n=2), pyloro-duodenal junction (n=1) and biliary tree (n=1). The indications for stent placement were pancreatic pseudocyst (n=2), refractory pyloric stricture (n=1) and post-liver transplant anastomotic stricture (n=1). Endoscopes used included: Pentax 2970 (n=1) upper endoscope, Olympus linear echoendoscope (n=1) and the Pentax duodenoscope 3490 TK (n=3). Fluoroscopy was employed in all cases, and endoscopic ultrasound was used in conjunction in one case. Effectiveness was rated on a 1-3 point scale (3 highest). Results: Stent deployment and removal was successful in all four cases. Mean stent duration was 39.5 days. All stents were patent at time of removal. Complete pseudocyst eradication was demonstrated by ultrasound in the two cases. In case 3, the stent was placed as a bridge to surgery, and in case 4, short term usage of the stent was effective, but removed due to unrelated medical issues. There were no complications associated with stent use. Conclusions: Viabil® use is promising in pediatric patients with non-malignant GI disease. Stents were highly effective in the treatment of pancreatic pseudocysts with resolution of cysts and stent patency. The advantages of Viabil® include ease in deployment and removal. Further studies are needed to delineate the range of indications in pediatric patients of FCMS.

**Patient Demographics**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Indication</th>
<th>Associated Procedures</th>
<th>Duration of stent (days)</th>
<th>Success</th>
<th>Complications</th>
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<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>Pancreatic pseudocyst (26cm x 20cm)</td>
<td>EGD with cyst-gastrostomy</td>
<td>71</td>
<td>+++</td>
<td>None</td>
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<tr>
<td>2</td>
<td>14</td>
<td>pseudocyst (12 cm x 10.9 cm)</td>
<td>EGD with cyst-gastrostomy</td>
<td>61</td>
<td>+++</td>
<td>None</td>
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<td>3</td>
<td>16</td>
<td>Refractory pyloric stricture</td>
<td>Pyloric dilatation</td>
<td>14</td>
<td>+</td>
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<td>4</td>
<td>13</td>
<td>Biliary stricture post-OLT</td>
<td>ERCP with biliary dilatation</td>
<td>14</td>
<td>++</td>
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</tr>
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</table>
Background: Infant mortality was the norm when cystic fibrosis (CF) was initially recognized in 1938, however, current approaches in therapy have led to prolonged life expectancy and better understanding of the extra-pulmonary manifestations of the disease with CF liver disease (CFLD) emerging as the number two cause of mortality and up to 65% of all patients showing some sign of hepatic injury during their lives. Despite improved recognition of CFLD, we still understand little about why fibrosis, and ultimate cirrhosis, occurs in only a select number of patients with a predilection to occur during childhood. Mouse models for CF are available, but have yet to adequately model the clinical patient. Some of the changes seen in CF livers mimic those seen in response to inflammation, yet mechanistic connections between CF pathophysiology in the lung, and those in the liver, remain elusive. We hypothesize that intra-tracheal infection in CFTR-/- mice leads to altered inflammatory signaling in the liver.

Methods: Gut spared 2 month old CFTR-/- mice (Cftrtm1Unc Tg(FABPCFTR)-1law/J) were infected with Pseudomonas aeruginosa via an intra-tracheal inoculation at a dose of 75μL of 4.9×10^6 cfu/ml. CFTR-/- and wild type (WT) littermates were analyzed as observational controls. Livers were collected at 18hours post infection. RNA was isolated and qRTPCR performed from tissue to determine hepatic RNA levels of inflammation-sensitive target genes.

Results: Preliminary data shows a hepatic phenotype after intra-tracheal inoculation of Pseudomonas aeruginos. The expression of sinusoidal bile acid exporter BSEP is up regulated by 48% after intra-tracheal inoculation along with a 50% decrease in expression of the canalicular bile acid exporter BSEP. These changes are similar to those seen in direct hepatic inflammatory models. At baseline, a 26% decrease in expression of apical bile acid transporter ASBT, as well as a 320% increase in OST-β expression, supports an increased inflammatoty state as well as increased bile acid concentration in CF mice compared to their WT littermates.

Conclusions: To our knowledge, this is the first study showing a hepatic phenotype expressed after intra-tracheal infection with an infectious agent and is a model that more closely resembles human clinical patients supporting a role for inflammation in CFLD. Changes in bile salt transporter expression at baseline also suggest a contributory role for bile acid retention in the pathophysiology of CF liver.

Background: Acute pancreatitis (AP) is a common problem in pediatrics, with an incidence that is rising over the last two decades. Data on management and physician practice patterns are lacking. We designed a survey with the purpose to identify the variances in management of uncomplicated AP. Methods: We surveyed pediatric gastroenterologists (GI) (total 25), and non-GI pediatric practitioners comprised of Hospitalists and Emergency Department physicians (total 59) at our 587-bed tertiary care pediatric referral center (Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio). Internet-based survey instrument SurveyMonkey (Palo Alto, CA) was used for survey enrollment and to collect responses. Responders included 19 of 25 (76%) GI physicians, and 49 of 59 (83%) non-GI physicians. Responses to individual questions were summarized by group, (the number of physicians who chose the answer), and percentages within each group. Comparisons of responses between GI and non-GI physicians were made using a Fisher's exact test for binomial proportions. P-values reported are two-sided. A p-value < 0.05 was considered statistically significant. The Fisher's test was used to compare the proportions of answers between the two groups. Representative graphs display response rate (percentage) in each category for relevant questions. Results: Practice patterns varied greatly within the same group of physicians, as well as between GI and non-GI physicians in the clinical management of AP. Labs ordered for first attack and recurrent attacks varied between GI and non-GI physicians (p<0.05). Imaging modalities ordered included ultrasound (US), Computed Tomography (CT) scan and plain films; 85% of GI physicians order an US compared to 49% of non-GI physicians (p<0.05). Pain medication choices varied between physicians but didn't reach statistical significance (p=0.08). The majority of physicians start narcotic pain medications for patients with pancreatitis. Non-GI physicians are more likely to use NSAIDs and acetaminophen than GI physicians. Intravenous fluids (IV) rates
varied between the two groups (p<0.001). Non-GI physicians begin at lower rates (1-1.5x maintenance) of IV hydration on AP patients when compared to GI physicians (1-2x maintenance). There was a trend to delay enteral feeding for patients with pancreatitis until pain was improved by most physicians and the mode of nutrition preferred varied between physicians. Conclusion: There exists a wide variance in practice management between GI and non-GI practitioners for children with AP. Prospective studies defining optimal management of pediatric pancreatitis are needed to guide care and improve outcomes for this patient population.

139 LONG-TERM NUTRITIONAL OUTCOMES OF GASTROSTOMY TUBE FEEDING IN CHILDREN WITH CYSTIC FIBROSIS. Ashley Falzone1, Sarah S. Lusman2, 1Institute of Human Nutrition, Columbia University, New York, NY; 2Department of Pediatrics, Columbia University, New York, NY

BACKGROUND: Cystic fibrosis (CF) is the most common fatal autosomal recessive disorder in Caucasians and is increasingly recognized in non-white populations. Better nutritional status in patients with CF correlates with better pulmonary function and increased survival. Due to pancreatic insufficiency, gastrointestinal dysfunction and increased energy expenditure, many children with CF do not meet the recommended goal of a BMI at or above the 50th percentile for age. Previous studies have shown that supplemental feeding through gastrostomy tubes (GTs) in children with CF is effective in improving nutritional status after six months and one year of tube feedings. It is not known whether this improvement is maintained over a longer period of time after gastrostomy tube placement.

OBJECTIVE: The purpose of the study was to investigate long-term nutritional outcomes of GT placement.

METHODS: We performed a retrospective study of 12 pediatric patients with CF who had GTs placed between January 2002 and January 2012 and who had at least 6 months of follow-up data. Height, weight, and BMI were obtained from medical records for visits corresponding to 1 month, 6 months, 1 year, and each subsequent year after GT placement, until the end of the study period. Nutritional status was expressed as BMI percentile for age.

RESULTS: All 12 patients had GTs placed due to weight loss or difficulty maintaining weight. The average time of follow-up after GT placement was 4.0 years (SD=2.1, range=0.6-6.2). The average age at the time of GT placement was 6.1 years (SD=4.8, range=0.6-11.9), and the average BMI percentile was 13.3 (SD=10.5, range=1-32). The average BMI percentile one year after GT placement was 46.5 (SD=27.2), the average two years after placement was 57.3 (SD=35.0). By the end of the follow-up period, 9 out of 12 patients had a positive change in BMI percentile (mean=36.9, SD=32.19). The average change in BMI percentile from the time of placement was 20.6 at one month, 30.8 at 6 months, 59.5 at one year, and 44.3 at 2 years. While none of the patients had a BMI at or above the 50th percentile at the time of GT placement, 7 patients met this goal during the follow-up period, and 6 of those maintained BMI above the target until the end of follow up.

CONCLUSIONS: Due to the well-established link between improved nutritional status and lung function in CF, effective nutritional interventions in CF can optimize survival. Our data is consistent with previous studies that show improved nutritional status in patients receiving supplemental feedings via GTs. Because 6 of the 7 patients who met the BMI percentile target maintained their BMIs until the end of the study period, our data suggests that GT placement supports long-term improvement in nutritional status in children with CF.

140 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN CHILDREN: TRENDS WITHIN THE UNITED STATES FROM 2000 TO 2009. Chaitanya Pant1, Thomas J. Sferra1,2, Bradley A. Barth3, Abhishek Deshpande4, Anil Minocha2, Waqar A. Qureshi2, Mojtaba Olyaee5, Michael P. Anderson1, 1UH Rainbow Babies & Children's Hospital, Cleveland, OH; 2University of Oklahoma Health Sciences Center, Oklahoma City, OK; 3University of Texas Southwestern Medical Center, Dallas, TX; 4Case Western Reserve University School of Medicine, Cleveland, OH; 5Louisiana State University Health Sciences Center, Shreveport, LA; 6Baylor College of Medicine, Houston, TX; 7University of Kansas Medical Center, Kansas City, KS

Background: Data pertaining to the number of diagnostic and therapeutic endoscopic retrograde cholangiopancreatography (ERCP) procedures performed in children are very limited with the absence of large-scale studies. The objective of this study was to investigate the volume of ERCPs performed in hospitalized children in the United States.

Methods: Data were obtained from the Kids' Inpatient Database (KID), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality for the years 2000 to 2009. We used ICD-9-CM procedural and diagnostic codes to identify cases in which an ERCP was performed and cases with pancreatitis and gallbladder or biliary disease. Data were weighted to generate national-level estimates. Comparisons were made using Chi-square analysis with corresponding odds ratios (ORs) and confidence intervals (CIs). Trend analysis was performed using the Cochran-Armitage test for linear trend. For the years included in this study (2000, 2003, 2006, and 2009) the HCUP-KID contains between 7,291,032 and 7,370,203 weighted total pediatric cases reported from between 2,784 and 4,121 hospitals.

Results: From 2000 to 2009, there were 22,153 pediatric (ages 1-20 years) cases (i.e. individual hospitalizations) in which an ERCP was performed. Children who had undergone ERCP were more likely to be female (82.6 vs 60.8%; OR 1.89; CI 1.84, 1.95). Of all the children undergoing an ERCP, 1,533 (6.9%) children were coded as undergoing both a diagnostic and therapeutic ERCP, 6,372 (28.8%) a diagnostic, and 17,314 (78.2%) a therapeutic procedure. The number of diagnostic ERCPs decreased from 2,047 in 2000 to 1,161 in 2009 representing an overall decline of 43%. Therapeutic ERCPs increased from 3,290 in 2000 to 5,572 in 2009 (69% increase). There was a significant decreasing trend for diagnostic and increasing trend for therapeutic ERCPs (P<0.001 for each analysis). These trends were present in all age groups (P<0.001). Seventy-eight percent of diagnostic ERCPs and 82% of therapeutic ERCPs were performed in the 16-20 year age group. During the period studied, the number of cases within the KID with pancreatitis increased 55% and those with gallbladder or biliary increased 43% (significant overall increasing trend for pancreatobiliary disease during the period studied, P<0.001).

Conclusions: Our results demonstrate a significant increasing trend for therapeutic ERCPs in hospitalized children in the United States. Children who underwent ERCP as compared to hospitalized children who did not were older and more likely to be female and Hispanic. Each of these demographic features have a direct association with pediatric gallbladder disease and pancreatitis. Also, there was a coincident increasing trend in pancreatobiliary disease. Future studies should address more completely the relationship between
increasing trends in pancreatobiliary disease and ERCP in children and how advances in endoscopic techniques might have affected the number of procedures performed in children.

141 A NON-INVASIVE METHOD OF ASSESSING PANCREATIC VOLUME LOSS IN EXPERIMENTAL PANCREATITIS INJURY MODELS USING MICRO-MRI. Jose Paredes1, Katie L. Lemon1, Tanveer A. Javed2, Eric Ludwick2, Sameh S. Tadros3, Kimimasa Tobita4, Sohail Z. Husain1, 1Pediatrics, University of Pittsburgh, Pittsburgh, PA; 2Radiology, University of Pittsburgh, Pittsburgh, PA; 3Developmental Biology, University of Pittsburgh, Pittsburgh, PA

Experimental pancreatitis and the resulting dynamic changes in pancreas size are primarily assessed at the current time by having to euthanize a large cohort of animals at varying time points. However, in clinical practice, patients with pancreatitis routinely undergo non-invasive cross-sectional imaging of the pancreas. Thus the purpose of the current study was to assay pancreatic volume, which is a gross parameter that changes during severe pancreatic injury, using the non-invasive imaging modality of micro-magnetic resonance imaging (MRI). Using a powerful 7 Telsa Bruker MRI system, T1 weighted images were performed of the abdomen in whole-fixed mouse with continuous slices in three standard planes--axial, transverse, and coronal. The contour of the pancreas was traced using Vitrea software and then transformed into a 3D reconstruction, from which volumetric measurements were calculated. The volumes were compared to a gold standard, which was a 3D reconstructed image from the dissected pancreas ex vivo. We found that on MRI the pancreas of the mouse could be easily identified and, using a fat attenuation protocol, could be well-differentiated from peri-pancreatic fat. Remarkably, the volumetric calculations between the in situ and ex vivo gold standard differed by less than 5%. These initial results point to the feasibility of reliably tracking changes in pancreatic size using MRI in experimental models of pancreatic disease, with the use of fewer animals. The bedside to bench approach, once perfected, can be expanded to yield novel, non-invasive imaging modalities for pancreatic disease to take back to the bedside.

142 SERUM FIBROBLAST GROWTH FACTOR 21 IS ELEVATED IN ACUTE PANCREATITIS IN HUMANS. Vivek K. Shenoy1,2, Kristin M. Beaver1, Sarah N. Flier1, Fjolliott M. Fisher1, Jyoti Ramakrishna1, Eleftheria Maratos-Flier1

Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA; 2Pediatric GI & Nutrition, Floating Hosp for Children/Tufts Med Ctr, Boston, MA; 3Pediatrics, Floating Hosp for Children/Tufts Med Ctr, Boston, MA

Background: Fibroblast Growth Factor 21 (FGF-21) is a recently discovered hormone shown to improve metabolic parameters in animal models of diabetes and obesity. Although most research has focused on FGF-21 in the liver, the hormone is most highly expressed in the acinar pancreas. There is sparse data on the role of FGF-21 in the exocrine pancreas apart from a recent report suggesting that FGF-21 is protective in a mouse model of pancreatitis.

Methods: Subjects admitted from May to September 2012 to the Beth Israel Deaconess Medical Center (BIDMC) were prospectively enrolled by screening inpatient census lists and the electronic medical record for patients with a suspected diagnosis of pancreatitis. To be included in the study, subjects had to meet 2/3 criteria: abdominal pain, lipase >3 times the upper limit of normal, and CT findings suggestive of pancreatitis. Exclusion criteria included preexisting malignancy. Serial serum aliquots were obtained throughout the course of hospitalization from discarded serum specimens obtained for clinical indications. Definitions from the Atlanta Symposium were used to grade pancreatitis severity. FGF-21 levels were analyzed using a commercially available enzyme-linked immunosorbent assay. Approval was obtained through the Institutional Review Board of BIDMC.

Results: FGF-21 levels peaked at various points during the course of hospitalization and were significantly greater than baseline FGF-21 levels (1601 pg/mL vs. 477 pg/mL, P < 0.05). Twenty out of the 26 subjects experienced at least a twofold increase in FGF-21 levels; on average, FGF-21 levels increased sixfold during the course of hospitalization. Higher absolute and relative changes in FGF-21 were associated with ICU admission and length of hospital stay, but FGF-21 levels were otherwise not associated with severity of disease. We also observed a statistical trend towards an inverse correlation between body mass index (BMI) and FGF-21 levels. There was no correlation between FGF-21 and lipase levels. There was no association between FGF-21 levels and fatty liver disease or diabetes.

Conclusions: Serum FGF-21 is significantly elevated in acute pancreatitis. During acute pancreatitis, FGF-21 levels appear to become uncoupled from several factors that have been previously shown to affect serum levels of this hormone. A blunted FGF-21 response to pancreatic injury in subjects with a higher BMI may partially explain why obesity is a risk factor for susceptibility to and increased severity of pancreatitis.

143 POST-ERCPC PANCREATITIS IN CHILDREN AND ADOLESCENTS. David Troendle1, Omana Abraham2, Bradley A. Barth3, 1UT Southwestern Medical Center, Dallas, TX; 2Children's Medical Center, Dallas, TX

Background: Clinically significant pancreatitis is the most common complication following ERCP and is known to contribute to significant morbidity and health care costs in the adult population. The prevalence and severity of post-ERCP pancreatitis in the pediatric population remains inadequately defined. This is important because the baseline condition of the pancreas and the indications for ERCP in children may be different than in adults with pancreatic disease. Our aim was to assess the prevalence and severity of clinically significant pancreatitis following ERCP and to identify high risk patients who may be appropriate for prophylactic therapy.

Methods: A retrospective review was performed of all pediatric patients followed at UT Southwestern Medical Center undergoing ERCP between January 2008 through May 2013. Demographic information, pre-operative data, and intra-operative data were collected to identify potential risk factors for developing post-ERCP pancreatitis. Post-operative data out to 2 weeks was reviewed to identify patients who developed post-ERCP pancreatitis and define the severity of the episodes. The 2010 ASGE lexicon for adverse events was utilized to define all episodes of pancreatitis and their severity. The Fisher exact test was utilized to compare groups for univariate analysis.

Results: 206 ERCPs were performed on 152 unique patients over the 5 year study period. Post-ERCP pancreatitis was experienced after 18 procedures (prevalence 8.7%). 13 of the cases were mild, 4 were moderate, and 1 was severe. There was no mortality. On univariate analysis, performing ERCP for pancreatic vs biliary indication and having a therapeutic procedure vs a diagnostic one did not increase the risk of pancreatitis. Female gender (p=0.04) and history of recurrent pancreatitis (p=0.04) were risk factors for post-ERCP pancreatitis.
whereas a history of obesity, sickle cell disease, chronic pancreatitis, acute pancreatitis in the week preceding ERCP, and normal bilirubin at time of the procedure did not reach significance. Performance of a minor papillotomy (p=0.03), attempting placement of a pancreatic stent (0.0001), placing a pancreatic stent (0.0001), pancreatic duct cannulation (p=0.0001) and pancreatic duct injection (p=0.0001) were identified as risk factors for post-ERCP pancreatitis. Performing a biliary sphincterotomy, a pancreatic sphincterotomy and involvement of a trainee did not reach significance.

**Conclusions:** Clinically significant pancreatitis is a relatively common complication after ERCP. Female gender, history of recurrent pancreatitis, performance of a minor papillotomy and pancreatic duct manipulation increase the risk of post-ERCP pancreatitis in pediatric patients. Patients with these risk factors may represent a suitable target population for abortive prophylactic measures.

**Nutrition/Nutrition Support**

151 **A RARE CASE OF FAMILIAL PERIODIC HYPOKALEMIC PARALYSIS IN 2 YEAR-OLD PATIENT.** Baraa Alabd Alrazzak, Basel Katerji, M. Samhar Alali, Tarek Husien, Susan Flesher, Mary S. Payne, Marshall University, Huntington, WV

Introduction: Periodic hypokalemic paralysis is a rare medical condition that presents with sudden attacks of generalized weakness associated with a low potassium level in the plasma. It is an autosomal dominant inherited defect in calcium or sodium ion channels, in muscular membrane. The first paralysis attack usually presents at late childhood or teenage years. In this case a 2-year-old male presented with first attack of periodic hypokalemic paralysis which is very rare at this age.

Case: A 2 year-old previously healthy male was admitted to the hospital for a sudden onset of lower extremity weakness and refusing to bear weight. Prior to this attack, the patient was acting himself with no fever, seizures, neurologic defects, respiratory distress, vomiting or diarrhea; no previous spells reported before. He maintained a normal level of consciousness during the attack. PMH was unremarkable except for a mild viral URI a week prior to the presentation. The patient was not on any medication. Allergies, PSH and birth history were also unremarkable. The family history revealed a similar attack in the father at age 16 which has resolved completely. Physical exam showed proximal muscle weakness in the lower extremities with muscular strength 1/5 bilaterally, deep tendon reflexes were diminished also but other than that was unremarkable. Potassium level was noted to be 2 and bicarb was 17 at time of presentation, other studies including EKG, CBC, electrolytes, Mg, renal function test, urinalysis and electrolytes in urine were normal. The potassium was corrected slowly over 36 hours and this was accompanied by marked improvement of the weakness with no complications. The patient was discharged home on low carb diet in addition to potassium supplementation to prevent future attacks.

Conclusion: Even though Familial Periodic Hypokalemic Paralysis is a rare medical problem; physicians should be familiar with the presentation, diagnosis and management of this condition and should have a high index of suspicion even in children younger than 5 years. Dietary modifications with a low carb diet as well as potassium supplementation and potassium sparing diuretics are essential to prevent future attacks.

152 **FRUCTOSE RESTRICTED DIET IMPROVES QUALITY OF LIFE IN CHILDREN WITH DIETARY FRUCTOSE INTOLERANCE.** Tara Harwood, Lisa Feinberg, Sarah Worley, Naim Alkhouri, Pediatric Gastroenterology and Nutrition Support, Cleveland Clinic, Cleveland, OH

**Background:** Incomplete fructose absorption can result in gastrointestinal distress symptoms in children which may impact their quality of life; however, this has not been formally studied. The aims of this study were to quantitatively evaluate gastrointestinal symptoms and quality of life in children with dietary fructose intolerance and determine the effect of fructose restricted diet on these measures.

**Methods:** 38 subjects 8 to 18 years old with a positive hydrogen breath test indicating fructose intolerance were included. The subjects drank 2 grams of fructose sugar per every 1 kg of body weight, with a maximum amount of 50 grams fructose sugar. Hydrogen was collected every 30 minutes over two hours. A hydrogen production of >20 ppm indicated a positive test. Upon completion of a positive breath test, participants completed a Peds Quality of Life Inventory (PedsQL) and a Peds Gastro Scale symptom scale (GSS). A dietitian provided specific instruction for the patients to follow a two-week fructose restricted diet. After the two weeks, dietitian called patients and administered a post-intervention PedsQL/GSS.

**Results:** The median age was 12.2 (10.4, 15.1) years and 58% were female. Children with fructose intolerance had a mean GGS score of 47.2/100 (+14) and a mean PedsQL score of 75/100 (+13.3). GSS score improved from a mean of 47.2 (+14) to 72.8 (+15.5) after the two-week dietary intervention (p value < 0.001). Furthermore, subjects significantly improved on their total PedsQL score 4 out of the 5 PedsQL subscales (physical, emotional, school function, and psychosocial) (p value < 0.001 for all).

**Conclusion:** Fructose restricted diet can significantly improve quality of life in fructose intolerant children.

153 **METABOLIC SYNDROME COMPONENTS (METSS) COMPONENTS IN OBESE SCHOLARS AND ADOLESCENTS.** Erika F. Hurtado-López1,2, Rosa Ortega-Cortes4, Alfredo Larrosa-Haro1, Ana L. López-Beltran4, Xochilt Trujillo-Trujillo3, 1Gastroenterology, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; 2Nutrition, Instituto de Nutricion Humana, Guadalajara, Mexico; 3Facultad de Medicina, Universidad de Colima, Colima, Mexico; 4Endocrinology, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico

**OBJECTIVE:** To identify the frequency of MetSx components in obese scholars and adolescents.

**PATIENTS AND METHODS:** One-hundred and twenty-five obese children and adolescents were studied at an Obesity Clinic of a 3rd level pediatric hospital. The MetSx components evaluated were: blood pressure, waist circumference, acantosis nigricans, glucose, high-density lipoprotein, triglyceride, insulin, HOMA, uric acid, AST and ALT. liver and ovary ultrasound were performed to search for fatty liver and polycystic ovaries.

**RESULTS:** Mean age was 12.2 years, 54% were females. The percentage of the MetSx components were: Waist circumference >90 percentile 98%, acantosis nigricans 86%, insulin resistance 73%, HOMA elevated 64% increased uric acid 64%, hiperinsulinism 58%,
increased triglyceride 54\%, high blood-pressure 50\%, fatty liver 15\%, polycystic ovary 3\%; 52\% presented criteria for MetSx. CONCLUSIONS: The prevalence of MetSx in children in population studies is 2-8.5\% and it increases to 14.5-60\% in obese. This variability seems dependent on geographic and ethnic factors and it is particularly high in Latin America. Our results underline the priority of performing primary and secondary intervention trials in our high-risk population.

154 **EARLY COW MILK FEEDING AND TYPE I DIABETES MELLITUS IN SCHOOLERS AND ADOLESCENTS.** Edna F. Villagran-Garcia\(^2\), Erika F. Hurtado-López\(^1,2\), Edgar M. Vázquez-Garibay\(^2\), Alfredo Larrosa-Haro\(^2\), Rogelio Troyo-Sanromán\(^2\), \(^1\)Gastroenterology, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; \(^2\)Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud. Universidad de Guadalajara, Guadalajara, Mexico

**BACKGROUND:** Exposure to environmental factors such as lack of vitamin D and introduction of cow milk before the first year of age could trigger alterations in the immune system, favoring the development of diabetes mellitus type 1 (DM 1).

**OBJECTIVE:** To evaluate the association of early feeding with cow’s milk with the occurrence of DM1 in scholars and adolescents.

**PATIENTS AND METHODS:** This case control study included 150 school-age children and adolescents, 75 cases (DM1) and 75 healthy controls. The mean age was 11.2±6.3 years, 51\% were males. Dependent variable: DM1. Independent variable: cow’s milk (raw or pasteurized) feeding before 12 months. Statistics: Chi square, OR and 95\% CI.

**RESULTS.** Thirty-four percent of controls and 25\% of cases was exclusively breast-fed. Twenty one percent of DM1 patients received cow’s milk before 12 months versus 7\% of controls (OR 3.4, 95\% CI 1.2-12.7). Comparison of subjects that were fed with a standard infant formula (21\%) with the 7\% fed with cow’s milk also showed statistical differences (OR 3.2 95\% CI 1.1-10.3).

**CONCLUSION:** In the current series, early feeding with cow’s milk (raw or pasteurized) milk was associated with a higher frequency of DM1. This association should be ratified in prospective studies.

155 **ESTABLISHMENT OF ENTERAL AUTONOMY IN CHILDREN WITH INTESTINAL AGANGLIONOSIS.** Harsh Kothari, Ajay Kaul, Samuel Kocoshis, Gastroenterology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

**Aim:** To determine nutritional outcomes in children with intestinal aganglionosis (IA) who have intestinal failure (IF).

**Methods:** We mined our institutional database to identify children with IA who had IF. Intestinal failure was defined as requiring >60 consecutive days of parenteral nutrition after initial surgery. We analyzed demographic, clinical, anthropometric and nutritional parameters. The end point was death, transplantation or latest data available.

**Results:** Eighteen patients were identified: 13 males (72\%), 13 Caucasian (72\%). These were divided into those that were still in IF or had small bowel transplantation (n=8), (group A) and those that attained enteral autonomy (n=10), (group B). Family hx of intestinal aganglionosis was found in 3 of 8 patients in group A and none in group B. Estimated gestational age, comorbid conditions and number of abdominal surgeries were similar in the 2 groups. Median age at diagnosis was 20 months in group A and 5 months in group B. There were 2 subjects with colonic aganglionosis and 6 with colonic and small intestinal aganglionosis in group A compared to 4 and 6 respectively in group B. Mean ganglionated small bowel length was 69 cm in group A and 108 cm in group B. Median ostomy duration (beforeakedown) was 28 months in group A and 13 months in group B. Median age and height for age were at 49th and 24th percentile in group A and 10th and 15th in group B. Median BMI was 17 in group A and 15 in group B. Median time on parenteral nutrition was 49 months in group A and 9 months in group B. Median age at which subjects in group B attained enteral autonomy was 10 months. 3 patients in group A underwent small bowel transplantation and 1 still requires PN due to severe GVHD 3 months small bowel post transplantation.

**Conclusion:** In this series, shorter ganglionic bowel length, delay in diagnosis, and genetic predisposition appear to be related to unfavorable outcomes. However, comorbid conditions seem to play little role in outcome. Persistent fluid and electrolyte disturbances mandated prolonged use of tpn or ivf even in some patients with isolated extensive colonic aganglionosis. Clinicians caring for patients with extensive aganglionosis should be prepared to use prolonged parenteral nutrition to ensure adequate growth and metabolic balance for their patients.

156 **HIGH ENERGY INTAKE COMPARED TO FAO/WHO ENERGY REQUIREMENTS FOR AGE ADJUSTED TO HEIGHT IN MUCOPOLYSACCHARIDOSES PATIENTS WITH ENZYME REPLACEMENT THERAPY.** Liliana Ladino\(^1\), Erika Ochoa\(^1\), Natalia Sepúlveda\(^1\), Laura Moreno\(^1\), \(^1\)Departamento Nutrición y Bioquímica, Pontificia Universidad Javeriana, Bogotá, Colombia; \(^2\)Departamento Nutrición y Bienestar Integral, Instituto Tecnológico y de Estudios Superiores de Monterrey, México D.F, Mexico

Little is known about nutritional status and dietary intake of patients with mucopolysaccharidosis (MPS). Short stature and delayed puberty have been described, but not explained; however, improvement has been seen when enzyme replacement therapy is started, especially at a younger age.

**Aim:** The objective of the present study was to determine dietary intake in MPS patients with enzyme replacement therapy in Colombia, and compared them to a paired-healthy population as well as with the energy requirements recommended by WHO/FAO 2001.

**Methodology:** Forty-eight subjects were recruited (24 MPS patients referred to a nutrition private practice in different cities of Colombia and 24 healthy and eutrophic controls paired by age and gender). Twenty-four hour dietary recalls of three non-consecutive days were recorded and analyzed. Weight and height were also recorded for MPS patients.

**Results:** All MPS had short stature and 91.3\% suffers from overweight or obesity according to BMI for age adjusted to height. Dietary analysis showed a significantly lower energy intake than healthy controls (p=0.0137); when compared to FAO/WHO Energy Requirements for chronological age and sex, MPS patients had a significantly lower intake (p=0.0008); and when compared to requirements to age adjusted to height, their intake was significantly higher (p=0.0101). Protein and lipid intake was lower than healthy controls, explaining the differences in energy intake. Minerals like sodium and potassium are also lower than their healthy counterparts.

**Conclusion:** The short stature in MPS disease is believed to be related to a combination of joint contracture, bone growth plate...
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Plenary Session I

Fellow Research Award

161 INITIATION OF MURINE SCLEROSING CHOLANGITIS INVOLVES EFFECTOR LYMPHOCYTES AND REGULATORY T CELLS. Alexandra Merchise, Julia Simmons, Celine S. Lages, Maha Almanan, Wyjuan Zhang, Claire Chougnier, Kenneth Setchell, Pranavkumar Shivakumar, Alexander Miethke. Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; Molecular Immunology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Hepatic lymphocytes in sclerosing cholangitis (SC) are recognized as effector cells of bile duct (BD) destruction. In a recent trial of oral vancomycin in children with SC and colitis, improvement of liver disease was associated with expansion of regulatory T cells (Tregs). Tregs represent a subset of CD4+ T cells which control adaptive and innate immunity and protect from autoimmune disorders.

Mechanisms by which Tregs affect hepatobiliary injury in SC are unknown. Here, we examine the role of Tregs during initiation of biliary injury in Abcb4−/− mice, which lack expression of the canalicular membrane phospholipid (PL) flopase mdr2. Methods: The phenotype of early murine SC was characterized by determination of PL and bile acid levels in bile and plasma with mass spectrometry, colorimetric plasma ALT measurement, and analysis of liver histomorphology on H&E and Trichrome sections. For quantification and localization of Tregs, cytometry, SYBR green RT PCR, and immunohistochemistry (IHC) were performed in 8- and 14-day double transgenic Abcb4−/− Foxp3/GFP Treg reporter mice compared to Abcb4+/+ Foxp3/GFP mice. Results: At 8 days, total bile PL levels were decreased in Abcb4−/− mice as expected (407 vs 157mg/L in Abcb4+/+, p<0.04). Elevated plasma bile acid levels (TMCA: 86 vs 28mg/mL; p=0.01; TCA: 261 vs 98mg/mL; p=0.01, in Abcb4−/− vs controls, respectively), increased BD profiles, and perportal inflammatory infiltrates on H&E indicate that SC begins during this neonatal period. Fibrosis was not detected by Trichrome staining. Within 6 days, at day 14 of life, liver injury worsened as shown by expanding perportal infiltrates and prominent BD epithelial injury on H&E and significantly elevated ALT levels in Abcb4−/− and Foxp3xFoxp3 double transgenic mice (318 vs 62 IU/L in Abcb4+/+, p=0.02). Progression of SC was associated with dramatic increase in number of NK and CD8 cells at 14 days (8.9 vs 4.1x10^5 NK+CD3−/100mg tissue; p=0.001; 3.2 vs 0.4x10^3 CD8+CD3+/100mg, p=0.001, in Abcb4−/− vs +/+ controls, respectively). Importantly, expansion of CD8 and NK cells as putative effector cells in the initiation of SC was accompanied by rapid population of the liver with Tregs (7.9 vs 3.6x10^3 of CD25+Foxp3+ in Abcb4−/− vs +/+). Increased Tregs was linked to upregulation of mRNA expression of Tgfβ, a cytokine important for Treg homeostasis. Anti-GFP IHC showed that Tregs were present in the periportal infiltrates. In order to test the hypothesis that Tregs constrain hepatobiliary injury, Tregs were depleted by injection of 100ug of CD25-antibody at 7 and 12 days. Importantly, a reduction of Tregs at day 14 (1.3 vs 7.3x10^3 Tregs/100mg liver in IgG2a-treated Abcb4−/− mice; p<0.001) was associated with a rise in ALT (790 vs 450 IU/L in IgG2a-treated controls; p=0.04). Conclusion: Initiation of SC in young Abcb4−/− mice is linked to hepatic expansion of CD8 and NK cells which is accompanied by upregulation of Tgfβ expression and a surge of Tregs. An aggrivated SC phenotype following Treg depletion may indicate an important inhibitory role of this CD4+ subset in control of immune-mediated injury during early SC.

Research Session I – Pediatric Pancreatic Disorders

162 ACUTE RECURRENT AND CHRONIC PANCREATITIS IN CHILDREN: THE FIRST REPORT FROM INSPIRE CONSORTIUM. Aliye Uç, Monika Ahuja, Bradley Barth, Melena D. Bellin, Heath Davis, Peter R. Durie, Brian Finley, Douglas S. Fishman, Steven Freedman, Cheryl Gariepy, Matthew Giefer, Tanja Gonska, Mel Heyman, Ryan Himes, Sohail Z. Husain, Soma Kumar, Veronique Morinville, Keith Y. Ooi, John Pohl, Sarah J. Schwarzenberg, David Troendle, Steven Werlin, Michael Wilschanski, Mark Lowe, University of Iowa, Iowa City, IA; UTSW, Dallas, TX; University of Minnesota, Dallas, MN; The Hospital for Sick Children, Toronto, ON, Canada; Baylor College of Medicine, Houston, TX; Beth Israel Deaconess Medical Center, Boston, MA; Nationwide Children's Hospital, Columbus, OH; Seattle Children's Hospital, Seattle, WA; UCSF, San Francisco, CA; Children's Hospital of Pittsburgh, Pittsburgh, PA; McGill University, Montreal, QC, Canada; UNSW, Sydney, NSW, Australia; University of Utah, Salt Lake City, UT; Hadassah Medical Center, Jerusalem, Israel; MCW, Milwaukee, WI

Background: Although acute pancreatitis (AP) is usually self-limiting, a subset of children develops acute recurrent pancreatitis (ARP) or progresses to chronic pancreatitis (CP). The lives of these patients are dramatically altered by multiple hospital admissions, physical, emotional and social stress. The epidemiology, etiologies, pathogenesis, natural history and outcome of these disorders in childhood are not well-understood.

Objective: We created a multi-center consortium, INSPIRE (International Study group of Pediatric Pancreatitis: In search for a cure) to collect clinical and demographic information in a well-phenotyped cohort of children with ARP and CP. Our ultimate goal is to create a prospective registry of clinical data accompanied by the systematic collection of biological samples in this cohort for future studies.

Results: From 9/1/12 to 6/1/13, we enrolled 172 patients with ARP or CP, <19 years of age, (52% F). Most were Caucasian (86%). Approximately 75% of patients reported episodic pain of severe intensity and ~25% constant pain of variable intensity. Clinical evaluation led to a diagnosis of CP in 48 patients. Gene mutations were found in 58 (28 PRSS1; 21 CFTR on either allele, 11 on both alleles; 13 SPINKI; 3 CTRC) of 87 children tested. Obstructive factors were found in 39 children; pancreas divisum was the leading cause in this category. Toxic/metabolic diagnoses were sporadic (no hypercalcaemia, no cigarette smoking, 4 passive smoking, 5 medication-related, 3 alcohol use, 3 hyperlipidemia, 2 propionic acidemia). Four children had autoimmune pancreatitis. Idiopathic
pancreatitis was diagnosed in 25 patients. Evaluation is ongoing for the remaining cases. 119 reported recurrent attacks of AP (20.2±9 per patient) and hospitalizations (6.7±1.1 per patient). Children with ARP or CP missed 5.5±0.8 school-days per month.

**Conclusions:** We are successfully engaged in a unique collaborative cohort study to conduct studies in children with ARP and CP. Early data reveal that genetic and obstructive factors are the main causes of ARP and CP in children. Alcohol, a common cause in adults, was infrequent in our pediatric patients. ARP and CP significantly impact the lives of affected children. Our future goal is to define the natural history of these diseases in children, to determine responses to medical, endoscopic or surgical interventions, and to begin to investigate the role of genetic modifiers on disease onset and outcome.

On behalf of INSPIRE Consortium, supported by NIH R21 DK096327, CTSA 2UL1 TR000442-06

<http://www.icts.uiowa.edu/content/acknowledging-nih-following-public-access-policy-guidelines-citation-publication> and REDCap

163 GASTROINTESTINAL SYMPTOMS BEFORE AND AFTER TOTAL PANCREATECTOMY WITH ISLET AUTOTRANSPLANTATION AND THE ROLE OF PANCREATIC ENZYME DOSING. Jill Crosby1, Melena D. Bellin1,2, David Radosevich2, Srinath Chinnakotta1, Ty B. Dunn3, Timothy L. Pruett4, Martin L. Freeman4, Gregory J. Beilman5, Sarah J. Schwarzenberg1, 1University of Minnesota Amplatz Children's Hospital, Minneapolis, MN; 2University of Minnesota, Minneapolis, MN; 4Schulze Diabetes Institute, Minneapolis, MN

Objective Complete exocrine enzyme insufficiency following total pancreatectomy with islet autotransplantation (TPIAT) necessitates exogenous enzyme replacement to prevent gastrointestinal (GI) symptoms and malnutrition. Little is known about the prevalence and severity of their GI symptoms, and what factors contribute to poor treatment response. We assessed the prevalence and duration of GI symptoms before and after TPIAT and the impact of enzyme dosing on symptoms. Methods 70 pre- and post-operative questionnaires were collected from 31 subjects ages 6-18 years (13.9 ±3.5 years, 17/31 female) who underwent TPIAT for treatment of chronic pancreatitis between 2006 and 2011 at the University of Minnesota. Self-reported frequency and severity of GI symptoms (diarrhea, steatorrhea, constipation, weight loss, and whether GI symptoms interfered with their daily life, but not pain), enzyme dose, and glycemic lability was collected. A mixed models approach was used to compare the proportion of patients reporting symptoms at each follow up time point versus baseline prevalence. Logistic regression was used to analyze the relationship between enzyme dose and adherence on the presence or absence of GI symptoms, and the association of glycemic variability with GI symptoms. Results Diarrhea was common (47-87% across the two years), but was not affected by surgery. Surgery did not impact prevalence of weight loss. Two years after surgery, constipation had decreased. Steatorrhea increased significantly 6 months after surgery (28% to 87%, p=0.008), then declined. The interference of GI symptoms on daily activity was the same before and after surgery. Presence of GI symptoms did not vary with enzyme dose, although some subjects were receiving less than or greater than recommended doses. Glycemic variability was associated with steatorrhea. Conclusion Although our previous work demonstrates improvement in abdominal pain after TPIAT, GI symptoms are common after surgery and are not related to pancreatic enzyme dose. Glycemic lability is associated with steatorrhea, suggesting that poor response to enzyme replacement therapy may contribute to more difficult to manage diabetes in these patients. Patients often are on enzyme doses that are higher or lower than recommended.

164 PREVALENCE OF MECONIUM ILEUS AS A PHENOTYPIC MARKER FOR THE SEVERITY OF CFTR MUTATIONS. Tanja Gonska1,2, Annie Dupuis1, Katherine Keenan1, Marcy Sontag1, Carlo Castellani1, Marco Cipolli1, Lutz Naehrlich1, Ruslan Dorfman1, Chelsea Taylor2, Lei Sun2, Keith Y. Ooi2,5, Johanna Rommens1, Lisa Strug1, Peter R. Durie1,2

1Research Institute, The Hospital for Sick Children, Toronto, ON, Canada; 2Department of Pediatrics, University of Toronto, Toronto, ON, Canada; 3Department of Epidemiology, University of Colorado, Aurora, CO; 4Department of Pediatrics, University of Verona, Verona, Italy; 5Pediatric Pulmonology, Justus-Liebig-University, Giessen, Germany; 6Geneyouin Inc, Maple, ON, Canada; 7Department of Biostatistics, University of Toronto, Toronto, ON, Canada; 8School of Women's and Children's Health, Medicine, University of New South Wales, Sydney, NSW, Australia; 9Sydney Children's Hospital Randwick, Sydney, NSW, Australia; 10Department of Molecular Genetics, University of Toronto, Toronto, ON, Canada

Introduction: We use the meconium ileus (MI) trait, as a very early disease complication in cystic fibrosis (CF) patients, to evaluate for genotype-phenotype relations in CF. We calculated meconium ileus prevalence scores (MIP) for the most frequent CFTR mutations as the ratio between CF patients with MI and all CF patients (MI and no MI). Initial analysis focused on patients carrying F508del on one allele allowing each mutation on the second allele to be assigned a MIP score.

Methods: MIP scores were established by chart review using a Canadian cohort (representing 70% of the Canadian CF population; n=2492) sampled for ongoing modifier studies in CF. MIP scores were compared to those derived from other registries including the US CF Foundation (US; n=43,432), Italy (I; Veneto/Trentino/Alto Adige) (n=1,786) and Germany (G; n=3,596). The pancreas insufficient prevalence (PIP) score was calculated based on chart review of pancreatic sufficient CF patients using the same Canadian cohort (Ooi Gastroenterol 2011). Hierarchical linear regression analysis was used to look for effects of MIP on lung function measured FEV1 and nutritional status expressed as BMI.

Results: The overall prevalence of MI (16%) was very similar to that observed in other registries 17% (US), 10.4% (IT), 20% (G). In the Canadian population the different mutations showed variable MIP scores ranging from zero to 0.31. Those with high PIP scores (high prevalence of "pancreas insufficiency") showed a wide range of MIP scores (0.06 to 0.31), whereas mutations with low PIP scores (low prevalence of "pancreas insufficiency") showed a MIP score of zero (r2=0.7, p=0.0002). MIP scores for each mutation in the other registries were remarkably similar to those observed in the Canadian database (e.g. Canada and US r2=0.8, p=0.001). Preliminary analysis shows that the MIP score, but not the actual MI status, effects FEV1 (p=0.02) as well as BMI z-scores (p=0.02).

Conclusion: Preliminary results demonstrate considerable variation of MIP score among different CFTR mutations following the same trend as the corresponding PIP scores.

MIP scores may help to more accurately predict the genotype/phenotype correlations of CFTR mutations at the severe end of the
spectrum. This knowledge is essential in studies investigating the role of modifier genes in CF, but also in studies comparing clinical outcomes within the CF population.

<table>
<thead>
<tr>
<th>CFTR mutation</th>
<th>MIP score (#of patients with specific mutation)</th>
<th>PIP score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Canada</td>
<td>US</td>
</tr>
<tr>
<td># with F508del</td>
<td>2,117</td>
<td>27,494</td>
</tr>
<tr>
<td>G542X</td>
<td>0.31 (72)</td>
<td>0.29 (976)</td>
</tr>
<tr>
<td>621+1G&gt;T</td>
<td>0.24 (88)</td>
<td>0.25 (369)</td>
</tr>
<tr>
<td>F508del</td>
<td>0.22 (1260)</td>
<td>0.27 (15391)</td>
</tr>
<tr>
<td>G551D</td>
<td>0.08 (53)</td>
<td>0.15 (979)</td>
</tr>
<tr>
<td>G85E</td>
<td>0.06 (24)</td>
<td>0.14 (979)</td>
</tr>
<tr>
<td>3849+10kbC&gt;T</td>
<td>0.00 (14)</td>
<td>0.05 (299)</td>
</tr>
</tbody>
</table>

na: too few patients (<10) to calculate MIP score

165 A RAPID AND RELIABLE SEGMENTATION-BASED AUTOMATED SOFTWARE FOR MEASURING ACINAR DROPOUT DURING PANCREATITIS. John F. Eisses1, Amy Davis2, Akif B. Tosun3, Cheng Chen3, Jia Guo3, John Ozolek2, Gustavo Rohde4, Sohail Z. Husain1, 1Pediatrics, University of Pittsburgh, Pittsburgh, PA; 2Pathology, University of Pittsburgh, Pittsburgh, PA; 3Biomedical Engineering, Carnegie Mellon University, Pittsburgh, PA

Pancreatitis leads to varying degrees of pancreatic obliteration and subsequent recovery. At present, the histological measurement of recovery is tedious and operator-dependent, requiring manual assessment of acinar area on serial pancreatic sections. In this study, we utilized a novel computer-generated learning algorithm to come up with a rapid and consistent method of analyzing acinar content. The algorithm works by learning differences in pixel intensities from input examples provided by expert pathologists. Hematoxylin and eosin-stained pancreatic sections were obtained in mice recovering from a 2-day, hourly caerulein hyperstimulation protocol. An expert pathologist then established a gold standard, known as the ground truth, in which discrete areas of acinar versus non-acinar tissue were labeled in 20 sections at various stages of injury and recovery. These sections were used as training data. The software results were validated by the expert pathologist by applying the algorithm to a different group of sections. In normal, non-injured pancreatic sections, the software demonstrated close agreement with the ground truth in identifying acinar tissue area (2.4% +/- 0.01% less area with the software; p=0.43). However, in recovering tissue (3 days post-caerulein hyperstimulation) the software reported about 8.8% +/- 5.7% less acinar area (p=0.04). Surprisingly, on detailed morphological examination, the discrepancy was primarily because the software outlined acini and excluded inter-acinar edematous stroma with greater precision. Although further iterations and validation of the computer learning are necessary, the results indicate that the software will be of great potential benefit to both clinicians and researchers in quantifying pancreatic acinar dropout in the injured and recovering pancreas, and it may hold promise in reliably screening specimens for more complex pancreatic processes.

Poster Session II
Poster of Distinction*

Esophagus/Stomach

166 HOW DOES ESOPHAGUS LOOK ON BARIUM ESOPHAGRAM IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS? Abdulrahman A. Al-Hussaini1, Amany Abozaid2, 1Pediatrics, King Saud bin Abdulaziz University for Health Specialities, King Fahad Medical City, Division of gastroenterology, Riyadh, Saudi Arabia; 2Department of Radiology, King Fahad Medical City, Riyadh, Saudi Arabia

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

Methods and materials: We identified children diagnosed with EoE in our center from 2004 to June 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 patients who underwent barium swallow study within 1 week prior to upper endoscopy, were included in the study. Clinical, radiologic, and endoscopic data were collected by retrospective chart review.

Results: During the study period, 45 pediatric EoE patients were diagnosed (age range 1-14 years, median 8 years; 33 males); 20 cases had barium swallow study done as part of the diagnostic approach of dysphagia (age range 1.5-12 years; median 8 years). Ten children had abnormal radiologic findings of esophagus (50%): rings formation (n=5), diffuse irregularity of mucosa (n=6), fixed stricture formation (n=3), and narrow-caliber esophagus (n=6). Barium swallow study failed to show ring formation visualized on upper endoscopy in 7 patients.

In conclusion: Barium esophagram is frequently normal in pediatric EoE. With the exception of stricture formation and narrow-caliber esophagus, our
data show poor correlation between radiologic and endoscopic findings. Therefore, in children with dysphagia in the absence of an esophageal stricture, endoscopy and biopsy are indicated for further evaluation.

167 RISING TRENDS IN EOSINOPHILIC ESOPHAGITIS IN CHILDREN, FIVE YEARS STUDY FROM THE CENTRAL REGION OF SAUDI ARABIA. Asaad Assiri1,2, Anjum Saeed1, Mohammad El Mouzan1, Ahmed Al Sarkhy1, Yassin Hamid1,1 Pediatrics, King Saud University, Riyadh, Saudi Arabia; 2Pediatrics, Dr. Suleman Al-Habib Medical Group, Riyadh, Saudi Arabia

Eosinophilic esophagitis (EoE) is an immune/antigen mediated inflammatory condition of the esophagus. It's an emerging disease in the children and adults as with better understanding of biology of the eosinophils, their functions and association with various gastrointestinal disorders. The aim of this study was to observe the clinical presentation and frequency of eosinophilic esophagitis (EoE) among Saudi children at two tertiary care hospitals, Saudi Arabia.

Methods: The data base of children admitted or seen during the period from Jan 2008 till Dec 2012 in two tertiary care hospitals, one public and one private and diagnosed as EoE were enrolled in this study. All children below 18 years were included excluding children with reflux esophagitis. The diagnosis was made on clinical presentation, physical examination, hematological and radiological findings and confirmation by endoscopy with histopathology.

Results: A total of 22 children were found to have EoE with a mean age of 8.3 years (< 18 years). There were 14 males and 8 females. Major presentation was dysphagia in 15 (68.1%) children followed by vomiting in 11 (50%). Description of dysphagia revealed difficulty swallowing solids and impaction of food in the center requiring some fluid to push it down and sometime feel comfortable by vomiting. Five children had abdominal pain mainly in the epigastric area in addition to dysphagia and vomiting. Five children were also asthmatic, four were allergic to some food like peanuts, and fish but none of children had history of diarrhea. Family history of EoE or stricture was negative especially in parents. Physical examination was unremarkable in all the children except two children who were failure to thrive and present under the age of 2 years. Peripheral eosinophilia was present in 6 (33.3%) children with a mean of 8.98 % (range 7-28%). Barium contrast was done in 16 children, showed narrowing of lower esophagus but without any hold up of contrast in 3 children and irregular outline of lower esophagus in 2 children. Endoscopic examination evidenced typical ring appearance in 4 children with stenosis, linear furrowing was present in 3 children and moderate to severe esophagitis in 11 children. Three children required dilatation. Antral nodularity was present in only one case. Histopathology confirmed eosinophilic esophagitis in all the children as reported eosinophils more than 20 HPF. In addition one child was positive for eosinophilic gastroenteritis and celiac disease and one for helicobacter pylori infection.

Conclusion: EoE is not an uncommon presentation in children with dysphagia and should be considered as one of the top differentials with reflux esophagitis.

Key Words: Children, eosinophilic, esophagitis.

168 A NOVEL TECHNIQUE IN ESOPHAGEAL STRUCUTE DILATION: USING THE MALONEY DILATOR WITH DIRECT ENDOSCOPIC VISUALIZATION. Michele Cho1,2, Thirumazhisai Gunasekaran1,2, James Berman1,2

1Pediatric Gastroenterology, Center for Children's Digestive Health, Park Ridge, IL; 2Advocate Children's Hospital, Park Ridge, IL

Esophageal strictures in pediatrics occur in a variety of conditions including complications of congenital esophageal atresia repair, peptic and eosinophilic esophagitis, and caustic ingestion. Treatment of these strictures involves dilation with either bougie or balloon dilators. The two types of bougie dilators currently being used include tungsten-filled bougie dilators (Maloney) and wire-guided polyvinyl dilators (Savary). The Maloney dilator is traditionally passed blindly through the stricture or passed with the guidance of fluoroscopy. The risk of perforation is higher when a Maloney dilator is passed blindly versus under fluoroscopic guidance. We describe the use of the Maloney dilator in a novel way, which decreases the risk of perforation and avoids the use of ionizing radiation. To date, we have seen no other reports of using the Maloney dilator in this manner. In our case, a 10 month old female with a history of esophageal atresia and tracheo-esophageal fistula had surgical correction shortly after birth. She developed dysphagia at six months of age and an upper GI series demonstrated an esophageal stricture at the anastomotic site. Upper endoscopy was performed and dilation of the stricture successfully completed. Instead of passing the Maloney dilator blindly or under guidance of fluoroscopy, as traditionally done, we passed the dilator under direct endoscopic visualization. The Pentax EG-1690K neonatal scope was passed into the esophagus and positioned proximal to the stricture. Once this was well visualized, a second physician or technician held the endoscope in place while the endoscopist passed the dilator through the stricture. Serial dilations were done starting with the 18 Fr. dilator, subsequently increasing in size to 20, 22, 24 and 26Fr. The method was safe and effective and there were no complications. Passing the Maloney dilator under endoscopic guidance is safer than passing the dilator blindly as there is direct visualization of the dilation site throughout the procedure. It also saves the child from ionizing radiation as fluoroscopy is not needed. This method is less time consuming than using the Savary dilator, which requires multiple steps. We found this method to be a safe and easy way of dilating an esophageal stricture. Future prospective data is needed to measure success rates and outcomes using this method compared to traditional use. Conclusion: Using the Maloney bougie dilator with direct endoscopic visualization is a novel method of dilating esophageal strictures in children.

169 IS ESOPHAGEAL IMPEDANCE BASELINE AND TIME OF ACID EXPOSURE DIFFERENT IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS COMPARED TO THOSE WITH GASTROESOPHAGEAL REFLUX? Judith Cohen Sabban1, Gabriela Donato Bertoldi1, Romina Mehauy1, Silvia Christiansen1, Maria Davila1, Marina Orsi1,1 Hospital Italiano, Buenos Aires, Argentina; 2Hospital Garrahan, Buenos Aires, Argentina

Esophageal impedance baseline (IB) reflects the integrity of the esophageal mucosa. Acid exposure (AET) decreases esophageal impedance baseline. Histological features differ in children with eosinophilic esophagitis (EoE) from those with gastroesophageal reflux esophagitis(GERD).

Aim: To analyze if the IB and AET in children with esophagitis due to EoE are different to those due to GERD.

Material & Methods: Review of MII tracings performed between May 2008 and May 2013 in children diagnosed with EoE or GERD. All
patients underwent upper endoscopy with multiple biopsies followed by a 24 hr MII-pH study. Esophageal histology was reported by two independent pathologists in a blinded manner. MII tracings were analyzed manually by two physicians using Sandhill software. Mean IB was measured retrospectively by 6 channel impedance testing at every hour for 24 h impedance-pH recording, excluding swallows and reflux. T-test and Mann Whitney tests were used for statistical analysis. Patients were divided into two groups: EoE and GERD. Results: Tracings from 34 children were evaluated; 25 boys, mean age: 9.75yrs (r 6-16yrs); EoE:6, GERD:28. There was no significant statistical difference between groups when comparing IB in all impedance channel and AET (p>0.248) (Table). Conclusions: Despite histopathological and etiological differences between groups, in this small group of patients IB and AET is similar to each other.

Mean baseline impedance in each channels

<table>
<thead>
<tr>
<th>Channel</th>
<th>EoE (Omhs) (X±SD)</th>
<th>GERD (Omhs) (X±SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Channel 1</td>
<td>2341.3 ± 641.07</td>
<td>3122.5 ± 812.99</td>
<td>0.065</td>
</tr>
<tr>
<td>Channel 2</td>
<td>2239.8 ± 544.68</td>
<td>2233.1 ± 542.20</td>
<td>0.981</td>
</tr>
<tr>
<td>Channel 3</td>
<td>2310.2 ± 319.34</td>
<td>2508.1 ± 650.75</td>
<td>0.476</td>
</tr>
<tr>
<td>Channel 4</td>
<td>2352.3 ± 551.80</td>
<td>3503.9 ± 1457.4</td>
<td>0.068</td>
</tr>
<tr>
<td>Channel 5</td>
<td>2132.2 ± 1134.7</td>
<td>2396.3 ± 1347.9</td>
<td>0.659</td>
</tr>
<tr>
<td>Channel 6</td>
<td>1947.3 ± 1192.1</td>
<td>2196.9 ± 1131.0</td>
<td>0.631</td>
</tr>
</tbody>
</table>

170 EVALUATION OF TOLL-LIKE RECEPTOR ACTIVATION BY H. PYLORI LPS AND LIVE BACTERIA FOR INITIATION OF THE HOST INFLAMMATORY RESPONSE. Sana Iqbal, Thomas G. Blanchard, Steven Czinn, Pediatrics, University of Maryland School of Medicine, Baltimore, MD

The Gram-negative bacterium Helicobacter pylori (H. pylori) colonizes the human gastric mucosa of over half the world's population. Infection can cause dyspepsia, and it is an etiologic agent of peptic ulcer disease and gastric cancer. Although less than 20% of infected individuals will develop H. pylori-associated diseases, the large number of infected individuals make H. pylori a significant pathogen. The mechanisms by which H. pylori induce inflammation and disease remains poorly understood, but interaction of the bacteria with toll-like receptors (TLRs) on white blood cells represents an important immune activation step. TLR2, which is bound my peptidoglycans present in bacterial cell walls, has been reported to be the primary TLR in host recognition of H. pylori. Whereas TLR4 typically recognizes bacterial LPS, H. pylori LPS has only weak TLR4 stimulation activity. There are several reports however that implicate H. pylori LPS signaling through TLR2. The purpose of the present study was to use highly purified preparations of H. pylori LPS to determine whether such TLR2 activation occurs in the absence of membrane contaminants. HEK 293 cells were transfected with plasmids for the expression of either TLR2 or TLR4 in addition to a reporter plasmid encoding alkaline phosphatase under the NFκB promoter. Cells were stimulated with either whole bacterial lysate antigen or with LPS purified from one of two H. pylori reference strains, J99 and 26695. Supernatants were collected and combined with a colorimetric alkaline phosphatase substrate, and cell stimulation was measured by optical density. TLR-expressing HEK cells, and control HEK cells carrying only the reporter plasmid failed to respond to stimulation with either bacterial lysate or purified LPS. TLR2-expressing cells, but not TLR4 expressing cells responded to bacterial lysate with significant levels of alkaline phosphatase. Neither TLR2 or TLR4 expressing cells responded to H. pylori LPS. Although some alkaline phosphatase activity was detected in supernatants from TLR4 expressing cells, these levels were not significantly different that control cells. LPS from both strains of H. pylori were then tested at multiple concentrations ranging from 10 ng/ml to 1µg/ml, but TLR2 stimulating activity was not detected. We also identified 12 clinical isolates of H. pylori that were negative for the cag pathogenicity island which encodes the IL-8 inducing type four secretion system (TFSS). Despite the ability of H. pylori to strongly stimulate TLR2, these strains failed to induce IL-8 when co-cultured with the human gastric epithelial AGS cell line suggesting that while H. pyloric can induce IL-8 production by epithelial cells via the TFSS, TLR activation in the host occurs primarily by antigen presenting cells.

171 USE OF PROTON PUMP INHIBITORS IN THE PEDIATRIC INPATIENT SETTING; A RETROSPECTIVE CHART REVIEW. Arieda Gjikopulii, Joanne Lanzo, Gia Bradley, David Tuchman, Jennifer Liao, Pediatrics, The Herman and Walter Samuelson Children's Hospital at Sinai, Baltimore, MD

INTRODUCTION: We assessed the trends in proton pump inhibitor (PPI) use in a community hospital pediatric inpatient unit, to evaluate if their use complies with evidence-based indications and to identify predictors associated with non-indicated use.

METHODS: A 3-year retrospective medical chart review was performed of all non-ICU, pediatric inpatients, ages 1-18 years, placed on a PPI during their hospital admission. Data collected included demographics, admitting service, concurrent use of steroids or NSAIDs and discharge diagnoses. Pediatric indications for PPI use are gastroesophageal reflux disease, peptic gastric or duodenal ulcer, H. pylori eradication, erosive esophagitis, NSAID-induced gastropathy, upper GI bleeding and hypersecretory conditions.

RESULTS: 270 patients from 5725 total admissions (4.7 %) received a PPI. Mean age was 8.6±6 years and mean length of stay was 5.2±5.4 days. 197 patients (73%) had a PPI initiated upon admission, 67(25%) during admission and 6(2%) at discharge. Based on discharge diagnoses only 85 patients (31.5%) had an indication for PPI use; ‘gastroesophageal reflux’ was the most common indication in 64 of those patients (75.3%). Concurrent administration of steroids was noted in 109 patients (40%) and around the clock (ATC) NSAIDs in 14 patients (5.2%). The association between concurrent use of steroids or ATC NSAIDs and non-indicated use of PPIs was not statistically significant (p=0.109 and 0.325 respectively). 54 subjects (20%) of the total 270 were PICU transfers and 53 (19.6%) were admitted under the Hematology/Oncology (H/O) service. There is a statistically significant relationship between these 2 groups and non-indicated use of PPIs.
PPI (p<0.05).
CONCLUSION: Our study shows that although a small portion of pediatric inpatients received a PPI (4.7%), only 31.5% of the cases had a clear indication. The association of concurrent use of steroids or ATC NSAIDs and non-indicated PPI use was not statistically significant. However, there was noteworthy non-indicated PPI use among PICU transfers and among those admitted under the H/O service. The above observations could be used in targeting specific areas of improvement.

172 **SUBGROUPS OF EOSINOPHILIC ESOPHAGITIS (EOE) IN CHILDREN AND ADOLESCENTS: IS THERE A DIFFERENCE IN THE ENDOSCOPY, HISTOLOGY, RESPONSE TO TREATMENT AND OUTCOMES?** Vimal Gunasekaran1, James Berman1, Alan Schwartz2, Kiran Gorla1, Sue Weides1, T’s Gunasekaran1, 1Advocate Children’s Hospital-Park Ridge, Park Ridge, IL; 2University of Illinois Chicago, Chicago, IL; 3Loyola Medical Center, Maywood, IL

Aim: Compare the clinical features, endoscopy findings, histology, response to treatment and outcomes of children and adolescents of the four subgroups of EoE patients seen at a specialized EoE Clinic.

Methods: A retrospective study was done on patients diagnosed with EoE, made as per the consensus guidelines 2011. They were grouped based on the primary symptom into EoE - D (dysphagia), EoE - AP (abdominal pain), EoE, GERD/vomiting, and EoE, failure to thrive (FTT)/feeding difficulty. Features captured and compared were: physical findings, CBC, CMP, esophagogram, upper gastrointestinal endoscopy, histology of the distal and mid esophagus, duodenum and antrum. Treatments were: dietary modifications and topical steroids or a combination, PPI was continued in some, and symptomatic outcomes were recorded as: improved, worsened or same. Data entered into Access and analysis was done using SPSS.

Results: A total of 157 patients were seen in the EoE Clinic between 1/2007- 6/2012. There were no major differences in the CBC, CMP, and esophagogram was normal in patients who had the study. See Table 1

Conclusion:
1. EoE- D and EoE- AP were the two largest groups and EoE- FTT the smallest.
2. More than half of all groups of patients had visible endoscopic findings of EoE (chisq(1)=24, p<.001); there was no significant difference in the rate of findings among the groups (chisq(3)=8.4, p=.19).
3. Most patients with EoE, had 26-50 eos/hpf both in the distal and proximal biopsies, except for EoE-FTT group,. (chisq(3)=68, p<.001).
4. Groups differed in the treatments most frequently prescribed; EoE-D and EoE- GERD groups are more likely to receive steroids alone and the EoE-AP group is more likely to receive combined therapy (chisq(6)=18.4, p=.03).
5. Groups differed in the likelihood of clinical improvement, with the EoE-D group most likely to show improvement (chisq(6)=15, p=.018).
6. PPI use was used in a limited number of patients.

Subgroups of EoE

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Endoscopy (%)</th>
<th>Eos/HPF Distal 15-25, 26-50, 51-75, &gt;75 (%)</th>
<th>Eos/HPF Mid 15-25,26-50,51-75, &gt;75 (%)</th>
<th>TX MEDS (%)</th>
<th>TX Diet (%)</th>
<th>TX Diet +MEDS (%)</th>
<th>No TX (%)</th>
<th>Improved (%)</th>
<th>Worsened (%)</th>
<th>No Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EoE-D</td>
<td>62</td>
<td>49 (79)</td>
<td>8/31/6/9 (13/50/10/15)</td>
<td>11/28/7/4 (18/45/11/6)</td>
<td>44 (71)</td>
<td>5 (8)</td>
<td>8 (13)</td>
<td>5 (8)</td>
<td>45 (72)</td>
<td>13 (21)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>EoE-AP</td>
<td>63</td>
<td>39 (61)</td>
<td>25/25/5/5 (40/40/10/10)</td>
<td>21/27/4/5 (33/43/6/8)</td>
<td>37 (58)</td>
<td>2 (3)</td>
<td>21 (33)</td>
<td>3 (5)</td>
<td>31 (49)</td>
<td>14 (22)</td>
<td>17 (27)</td>
</tr>
<tr>
<td>EoE-GERD</td>
<td>28</td>
<td>18 (64)</td>
<td>4/18/0/0 (14/64/0/14)</td>
<td>4/15/3/1 (14/53/11/3)</td>
<td>25 (89)</td>
<td>1 (3.6)</td>
<td>1 (3.6)</td>
<td>1 (3.6)</td>
<td>16 (57)</td>
<td>8 (28)</td>
<td>4 (14)</td>
</tr>
<tr>
<td>EoE-FTT</td>
<td>4</td>
<td>3 (75)</td>
<td>2/2/0/0 (50/50/0/0)</td>
<td>4/15/3/1 (14/53/11/3)</td>
<td>2 (50)</td>
<td>0</td>
<td>2 (50)</td>
<td>0</td>
<td>1 (25)</td>
<td>2 (50)</td>
<td>1 (25)</td>
</tr>
</tbody>
</table>

*Visible endoscopic findings; vertical lines, white patches, rings and crepe paper appearance.

173 **PANTOPRAZOLE DESENSITIZATION IN A PATIENT WITH OVERLAP EOSINOPHILIC ESOPHAGITIS AND GASTROESOPHAGEAL REFUX DISEASE.** Elizabeth J. Hait1, Eitan Rubinstein1, Ari Fried2, Anahita Dioun2, John Lee2

1Gastroenterology, Boston Children’s Hospital, Boston, MA; 2Allergy & Immunology, Boston Children’s Hospital, Boston, MA

Background: We describe a pediatric patient with confirmed eosinophilic esophagitis (EoE), gastroesophageal reflux disease (GERD) and anaphylaxis to proton pump inhibitors (PPIs) whose disease was refractory to treatment. He successfully underwent allergic desensitization to pantoprazole resulting in control of his esophageal inflammation.

Case Report: Our patient was initially diagnosed with EoE at 19 months of age with endoscopy showing severe esophagitis and peak eosinophil count of 50 per high power field (HPF). He was prescribed lansoprazole which caused a pruritic rash and agitation. He was changed to omeprazole which resulted in urticaria and vomiting.

Allergy skin testing revealed positive prick tests to both omeprazole and pantoprazole. He was started on an elimination diet and showed clinical improvement. Subsequent endoscopy revealed a peak eosinophil count of less than 10 eosinophils/HPF. At 5 years of age, his symptoms recurred and repeat endoscopy revealed recurrent esophagitis (peak eosinophil count: 70 eosinophils/HPF). His therapy was modified to high dose ranitidine (~10 mg/kg), topical fluticasone and diet limited to potato and...
RESULTS: Our cohort consisted of 12 children, 75% female, with a median age of 14.0. Only 4 (33%) children had prior knowledge of collection techniques.

Collection Aid® and active saliva (AS) collection (Salimetrics Oral Swab®). After collection of saliva samples, the participants

METHODS: Saliva samples were collected from children aged 5-18 years, using a passive drool (PD) technique (Salimetrics Saliva

eosinophils count on esophageal biopsy was observed at 32.5 hpf. Eotaxin-3 mean concentration levels on EoE patients, was 39.45pg/ml,

Results: Our EoE population consisted of 9 males (75%) and 3 females (25%). The mean age of these patients was 6.8 years. Mean
eosinophil count < 10/HPF). It has remained asymptomatic, continues to tolerate pantoprazole, and is in the process of expanding his diet.

Conclusion: This is the first report of allergic desensitization to pantoprazole. We also documented the utility of skin prick testing for evaluation of PPI hypersensitivity.

174 CHILDREN PREFER SALIVA TESTING OVER BLOOD TESTS EVEN IF IT IS MORE EXPENSIVE. Samir S. Shah1, Girish Hiremath1, German Vargas3, Carla M. Davis2, Sridevi Devaraj3, Anthony Olive1, 1Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX; 2Pediatric Immunology, Allergy and Rheumatology, Baylor College of Medicine, Houston, TX; 3Pathology, Baylor College of Medicine, Houston, TX

BACKGROUND & AIMS: Saliva is an emerging medium for health and disease surveillance, as well as personalized care. Collection and evaluation of saliva is well-accepted to identify disease-specific diagnostic and prognostic biomarkers among adults, but in children its role is less well-known. We investigated the awareness and acceptability of saliva testing and preference between saliva collection techniques among children.

METHODS: Saliva samples were collected from children aged 5-18 years, using a passive drool (PD) technique (Salimetrics Saliva Collection Aid®) and active saliva (AS) collection (Salimetrics Oral Swab®). After collection of saliva samples, the participants responded to a series of questions related to their knowledge and acceptability of saliva testing and their experiences for the two collection techniques.

RESULTS: Our cohort consisted of 12 children, 75% female, with a median age of 14.0. Only 4 (33%) children had prior knowledge of saliva testing for any condition. Eleven (92%) of them preferred the AS method, and only 1 (8%) participant preferred PD. On average, it took 141±92.1 seconds for the patients to collect 1 mL of saliva via PD. All 12 participants reported no pain or discomfort with either technique. Eleven (92%) children reported that they believed saliva testing would be accepted by other children. Finally, 11 (92%) participants stated they would prefer a saliva test even if it costs more than a blood test.

CONCLUSIONS: A majority of the children were not aware of using saliva to detect systemic conditions. However, collection and use of saliva for health and disease surveillance was well-accepted and preferred over blood testing in children. The AS technique was favored over PD collection. Saliva collection may be a useful diagnostic technique in a pediatric population.

175 EOSINOPHILIC ESOPHAGITIS AND EOTAXIN-3 LEVELS: IS IT WORTH IT? Carlos A. Camacho, Cristina Jimenez, Vyilma Velazquez, Jose Torres, Pediatrics, Hospital Episcopal San Lucas, Ponce

Background: Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder characterized by eosinophilia in esophageal mucosa that causes feeding difficulties, regurgitation, vomiting, abdominal pain, dysphagia, and food impaction. Diagnosis is currently made by gastroscopy and biopsy but there is no efficient, non-invasive, cost effective method to monitor disease progression. The diagnostic criterion of EoE is the presence of more than 15 eosinophils/ high-power fields on esophageal mucosa biopsies. Studies of esophageal tissue suggest that eotaxin-3, which is a systemic immune indicator for the presence of eosinophils, has a pathological effect.

Objectives: Describe the demographic characteristics of pediatric patients diagnosed with eosinophilic esophagitis in a Puerto Rican population. Compare serum Eotaxin-3 levels in patients diagnosed with EoE, GERD, allergies and healthy controls.

Method: This is a case control study, in which records were reviewed from 2010-2013 of EoE, GERD, allergic and healthy controls patients from an Allergist and Pediatric Gastroenterology office. A sample of blood was withdrawn from our four groups and quantified with the The Quantikine Human Eotaxin-3 Immunoassay. Statistic analysis was made with SPSS for ANOVA analysis.

Results: Our EoE population consisted of 9 males (75%) and 3 females (25%). The mean age of these patients was 6.8 years. Mean eosinophils count on esophageal biopsy was observed at 32.5 hpf. Eotaxin-3 mean concentration levels on EoE patients, was 39.45pg/ml, which demonstrates a two fold difference over the mean concentration of the other three groups combined. (p value by ANOVA = 0.03). Contrary to published data our allergic patients did not demonstrate elevated Eotaxin-3 levels.

Conclusion: Consistent with other published case series, patients with EoE were predominantly male with an average age of 6.8 years. In EoE patients, Eotaxin-3 concentration did not correlate directly with the eosinophil count in biopsies. Although the highest Eotaxin-3 serum levels were found in the same group. As we expected, we were able to observe that the patients with EoE presented higher statistically significant levels of Eotaxin-3 than the other groups, also patients with GERD showed lower levels of Eotaxin-3 as compared to EoE patients. Contrary to the published literature, our allergic patients did not demonstrate elevated Eotaxin levels.
**Hepatobiliary/Transplant**

186  **MS275, A CLASS I SPECIFIC HISTONE DEACETYLASE INHIBITOR, IMPROVES METABOLIC AND INFLAMMATORY MARKERS AND DECREASES HEPATIC STEATOSIS IN DIET AND GENETIC MODELS OF MURINE OBESITY.** Elizabeth L. Yu1,2, Michael Downes1, Ronald M. Evans1, 1Pediatric Gastroenterology, Hepatology and Nutrition, UCSD, La Jolla, CA; 2The Salk Institute for Biological Studies, La Jolla, CA

**BACKGROUND/AIMS:** Histone deacetylase inhibitors (HDACi), already used clinically as oncologic therapy, have demonstrated anti-inflammatory properties. Anti-inflammatory properties include an increase in lymphocyte apoptosis in murine models of colitis, suppression of inflammatory cytokines in murine models of autoimmune neuritis and decreased IL-1 and IL-6 expression in murine models of colitis. Given these anti-inflammatory effects, we hypothesized that HDACi therapy may be hepatoprotective in non-alcoholic fatty liver disease (NAFLD).

**METHODS:** Two murine models of obesity were utilized - diet induced obesity (DIO) and genetic-induced obesity (OB/OB or leptin deficient mice). In the DIO cohort, WT (wild type) mice were fed a high fat diet (HFD) for 14 weeks. WT mice fed regular chow were used for comparison. After histologic confirmation of non-alcoholic steatohepatitis (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. For the OB/OB cohort, mice were treated with 4 weeks of daily IP injections of PBS or MS275. During this period, we followed weight trends, metabolic and inflammatory markers, and at the end of the study, evaluated hepatic histology.

**RESULTS:** Internal consistency reliability for the PeLTQL was excellent (Cronbach's alpha 0.85). There were 129 parent-child pairs that independently filled out the PeLTQL. Fifty-seven percent of patients were female, with mean age 13.4±2.8 years for the sample (biliary atresia 50%; acute liver failure 12%; other cholestatic 13%; fulminant 5%; metabolic 5%; tumour 8%; other 9%). Patients were drawn from 4 countries (36.4% Canada, 22.5% US, 20.2% UK, 20.9% Australia). There was a significant difference between parent and patient ratings of HRQOL on the PeLTQL overall (64.2±12.6, 69.2±13.5, p < .001), the Coping and Adjustment (62.3±15.8, 67.1±16.4, p = .001) and Social Emotional Domain (66.2±14.9, 71.4±16.0, p = .000), but not on the Future Health Domain (71.2±16.6, 68.7±18.1, p = .125). There were no significant differences between male (n = 14) and female (n = 115) parents' ratings of their child's QOL. There were also no significant differences between parents' or patients' ratings of QOL for younger (child age 8-12 years) vs. older (child age 13-17 years) children. There was no effect of gender on children's quality of life across age strata. However, for the younger age strata (n = 57), patients and parents views were more closely aligned, as there were no significant differences between QOL ratings on PeLTQL overall or domains. The SCARED and CDI-S had significant interactions with PeLTQL overall, where higher anxiety or depression was related to higher discordance between parent and patient ratings (p < .01). Patients scores on the PedsQL and the PeLTQL were highly correlated (r = .68, p < .001). There was a significant different between parents (70.5±18.5) and patients' (74.2±19.0) scores on the PedsQL (p = .01).

**CONCLUSION:** The results show a pattern of parental underestimation of their children's QOL on the PeLTQL and PedsQL. Concordance seems to differ as a function of child age, where higher concordance was found with younger children.  

**187 PARENT'S JUST DON'T GET IT! PARENTAL UNDERREPORTING OF QUALITY OF LIFE IN PEDIATRIC LIVER TRANSPLANTATION.** Anthony R. Otley1, Amy Grant1, David Nicholas3, Anil Dhawan1, Nada Yazigi3, Looi Ee3, Susan Gilmour4, Michael Stormon1, Vicky Ng1, 1Pediatrics, Division of Gastroenterology, Dalhousie University, Halifax, NS, Canada; 3Pediatrics, King's College Hospital, London, United Kingdom; 4Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 5Pediatrics, The Children's Hospital at Westmead, Sydney, NSW, Australia; 6Pediatrics, Royal Children's Hospital, Brisbane, QLD, Australia; 2Pediatrics, Stollery Children's Hospital, Edmonton, AB, Canada; Social Work, University of Calgary, Calgary, AB, Canada; 3Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada

**INTRODUCTION:** Research has shown high-concordance between parent-proxy and child ratings of health-related quality of life (HRQOL), though parents tend to undereport more subjective domains.

**AIM:** To compare HRQOL ratings of pediatric post-liver transplant patients (LT) to their parents' on the Pediatric Liver Transplant Quality of Life Questionnaire (PeLTQL) and its related domain scores: Future Health, Coping and Adjustment, Social Emotional.

**METHODS:** LT patients (8-18 years) completed the 26 item, and their parents completed a proxy version of the PeLTQL (higher scores = higher HRQOL). Similarly patients and parents completed the PedsQL Generic questionnaire. Patients completed the PeLTQL at baseline and at 6 months post-LT. Parents independently filled out the PeLTQL. There were no significant differences in age, gender, or domains. The SCARED and CDI-S had significant interactions with PeLTQL overall, where higher anxiety or depression was related to higher discordance between parent and patient ratings (p < .01). Patients scores on the PedsQL and the PeLTQL were highly correlated (r = .68, p < .001). There was a significant different between parents (70.5±18.5) and patients' (74.2±19.0) scores on the PedsQL (p = .01).

**CONCLUSION:** The results show a pattern of parental underestimation of their children's QOL on the PeLTQL and PedsQL. Concordance seems to differ as a function of child age, where higher concordance was found with younger children. Child anxiety and depression may also be related to increased discordance.

**188 NORMAL RANGE FOR ALT, AST IN OTHERWISE HEALTHY 1-11 MONTH OLD INFANTS IN STUDIES OF GASTROESOPHAGEAL REFLUX (GERD).** William Treem1, Peter Hu2, Sheldon Sloan3, 1Pediatric Center of Excellence, Janssen Pharmaceutical Research and Development, L.L.C, Raritan, NJ; 2Established Products, Janssen Research and Development, Raritan, NJ; 3Established Products, Janssen Research and Development, Raritan, NJ

**BACKGROUND AND AIM:** The normal range of serum ALT in adults and adolescents has been redefined downward by eliminating subjects with known and potential asymptomatic liver disease. We sought to define the normal range of ALT, AST in a population of otherwise healthy infants participating in studies of GERD.

**METHODS:** In 2 global studies of Rabeprazole in 1-11 month old infants, we conducted a
post-hoc analysis of baseline ALT, AST collected pre-study in local laboratories. Medical history, concomitant medications, baseline fasting serum glucose and weight were assessed. Premature infants; patients previously in the NICU; and those with genetic/metabolic disease, intrauterine infection, twin-twin or blood transfusion, hemoglobinopathy or hemolysis, chronic organ system disease, surgery, prolonged jaundice, acute infection or exposure to potentially hepatotoxic drugs within two weeks of ALT, AST testing were excluded (EC) from the “normal” included (IC) cohort. Infants of diabetic mothers, and those with baseline glucose ≥ 6.0 mmol were also excluded; as were those with weights for age > 97% or < 2.3%. Acetaminophen exposure was allowed up to 72 hr prior to ALT, AST testing provided it was not given continuously for > 24 hr. Descriptive statistics [mean ± SD, median, range (5%-95%)] were generated for the entire group; and the IC, the EC, and for subgroups divided by gender, race, and age (1–<6m; 6–<12m). The 95% was defined as the upper limits of normal (ULN). Results: 405 infants were evaluated (59% male). After exclusion, 312 infants remained in the IC (57% m) with 93 in the EC (66% m). In the entire group (n=405); the mean ± SD ALT value was 31±18 [median=26 (range=15–66)]; and the mean ± SD AST was 41±15 [median=38 (range=25–67)]. In the IC, the mean ALT value was 31±18 [median=26 (range=14–68)]; and the mean AST =41±15 [median=38 (range=25–65)]. There were no significant differences between the IC and the EC. Using these ranges, 4.8% of those in the IC exceeded the ULN for ALT and 4.8% for AST; and in the EC, 4.3% and 4.4% exceeded the ULN for ALT and AST respectively. Because values were similar in IC and EC, all subjects were included in subgroup analyses. There were no statistically significant gender differences for either ALT or AST; although ALT trended higher in males (n=238) than females (n=167) (p=0.092). Values were similar for white, AA, and Hispanic or Latino infants. ALT also did not differ significantly between age subgroups although the mean/median values did trend downward with increasing age (p=0.140). AST showed a statistically significant increase with increasing age during the first year (p=0.012). Conclusions: The mean/median and ULN (>95%) for ALT in otherwise normal infants with GERD are all approximately twice those seen in adults and adolescents, and persist higher throughout the first year of life. Unlike adults or adolescents, there is no significant reduction in the ULN of ALT in female infants compared to males. These ALT, AST parameters can be used to more accurately define chronic liver disease and drug-induced liver injury in infants 1-11 months of age.

189 **THE PREVALENCE AND SPECTRUM OF ABNORMAL LIVER BIOCHEMISTRY IN A LARGE COHORT OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE.** Pamela L. Valentino1,2, Brian M. Feldman2,3, Thomas D. Walters1,2, Anne M. Griffiths1,2, Simon C. Ling2,3, Eleanor Pullenayegum2, Binita M. Kamath1,2, 1Division of Gastroenterology, Hepatology, and Nutrition, Hospital for Sick Children and the University of Toronto, Toronto, ON, Canada; 2Department of Pediatrics, University of Toronto, Toronto, ON, Canada; 3Division of Rheumatology, Hospital for Sick Children and the University of Toronto, Toronto, ON, Canada; 4Child Health Evaluative Sciences, Hospital for Sick Children and the University of Toronto, Toronto, ON, Canada

Background: There is scant literature regarding abnormal liver biochemistry (LB) in inflammatory bowel diseases (IBD). We sought to determine the prevalence, spectrum and clinical associations of abnormal LB in children with IBD.

Methods: A random sample of 300 children with IBD was retrospectively ascertained from the IBD database at the Hospital for Sick Children in Toronto. Serial LB measurements from the time of IBD diagnosis and onwards were evaluated to detect abnormalities and a Kaplan-Meier time to event analysis was performed. Cox-proportional hazards models identified clinical variables associated with abnormal LB.

Results: IBD in this population was classified as Crohn disease in 163 (54%), ulcerative colitis in 100 (33%), and IBD-Undefined in 37 (12%), with a median duration of follow-up of 2.8 years (interquartile range [IQR]: 1.5, 4.8 years). 297/300 patients (99%) had LB abnormalities. Kaplan-Meier time to event analysis was performed. Cox-proportional hazards models identified clinical variables associated with the increased development of abnormal LB included: steroid use (hazard ratio [HR] 1.8 [CI 1.1, 2.9], p=0.012), antibiotic use (metronidazole or ciprofloxacin, HR 1.7 [CI 1.1, 2.9], p=0.016), and Exclusive Enteral Nutrition use (EEN, HR 2.4 [CI 1.2, 4.8], p=0.0017). The association between abnormal LB and medication use was more pronounced at a biochemistry threshold of ≥2xULN with a HR of 3.7 for steroid use (CI 2.1, 6.3, p<0.0001) and 2.4 for antibiotics use (CI 1.2, 4.3, p=0.004). There were no significant associations between methotrexate use and abnormal LB, and infliximab had a protective effect (HR 0.56 [CI 0.32, 0.98], p=0.043).

Conclusions: Abnormal LB is a prevalent problem in pediatric IBD occurring in 53% of this cohort within the first 3 years after diagnosis. However, the degree of abnormal LB is typically mild, and not persistent, and the development of chronic liver disease is a relatively rare event. Substantial elevations in LB are associated with steroid, antibiotic, and EEN use, which may be markers for IBD exacerbations. These data suggest that conservative observation is appropriate for most children with IBD and abnormal LB, in whom costly and invasive investigations are unnecessary.

190 **NOVEL APPROACH TO DISTINGUISH PRIMARY FROM SECONDARY 5BETA-REDUCTASE (SRD5B1) DEFICIENCY BY URINARY STEROID ANALYSIS.** Tatsuki Mizuochi1,2, Tadahiro Yanagi1, Keiko Homma3, Yoshitaka Seki1, Hajime Takei4, Hiroshi Nittou4, Tomonobu Hasegawa4, Akihiko Kimura1,1Pediatrics and Child Health, Kurume University School of Medicine, Kurume, Japan; 2Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 3Central Clinical Laboratories, Keio University Hospital, Tokyo, Japan; 4Institution of Bile Acid, Junshin Clinic, Tokyo, Japan; 5Pediatrics, Keio University School of Medicine, Tokyo, Japan

Background: 3-Oxo-delta4-steroid 5beta-reductase (5beta-reductase) deficiency represents one of the key bile acid synthesis defects with distinctive findings of neonatal cholestasis and hyper-3-oxo-delta4 bile aciduria. 5beta-reductase enzyme not only regulates bile acid synthesis but is also involved in steroid hormones metabolism in the liver. 5beta-reductase deficiency manifests as two distinct types of disease: a primary 5beta-reductase deficiency (Primary) associated with the SRD5B1 gene mutation, and a secondary 5beta-reductase deficiency (Secondary) without any mutations. Secondary is usually initiated by fulminant liver failure occurring from multiple etiologies...
such as neonatal hemochromatosis (NH). Distinguishing Primary from Secondary is difficult by established parameters including GGT, serum total bile acids, and GC-MS based urinary bile acid analysis. Currently, SRDSB1 gene analysis is the only diagnostic method. Aim: To investigate whether urinary steroid analysis can distinguish patients with Primary from Secondary.

Methods: We examined 11 patients who presented with cholestatic jaundice, normal or slightly elevated GGT, and hyper-3-oxo-delta4 bile aciduria by urinary steroid analysis of both cortisol and cortisone including 5beta-tetrahydrocortisol (5beta-THF) and 5beta-tetrahydrocortisone (5beta-THE), using GC-MS. These patients were previously diagnosed as having Primary (n=3), NH (n=3), and Secondary as a result of liver failure except NH (Secondary-non-NH, n=5).

Results: The levels of urinary 5beta-THF (normal range: 0.2-3.5 mg/g Cr) and 5beta-THE (normal range: 1.6-18.5 mg/g Cr) were 0.001 and 0.014 mg/g Cr in Primary, 0.068 and 0.104 mg/g Cr in NH, and 0.363 and 2.231 mg/g Cr in Secondary-non-NH, respectively (Primary vs. Secondary-non-NH, p<0.05). We were able to clearly distinguish Primary from Secondary-non-NH by urinary steroid analysis. Our results also suggest that affirmative diagnosis and distinction of Primary from NH should rely not only on urinary steroid analysis but also on clinical course of the disease and abdominal MRI to diagnose those children with NH.

Conclusion: Our study demonstrates that urinary steroid analysis can efficiently be used to distinguish primary from secondary 5beta-reductase deficiency.

191* EFFECT OF INHIBITING HEPATIC MONOACYLGLYCEROL ACYLTRANSFERASE 1 ON DEVELOPMENT OF NONALCOHOLIC STEATOHEPATITIS (NASH). Nisreen Soufi, Angela M. Hall, Brian N. Finck, Geriatrics and Nutritional Sciences, Washington University, Saint Louis, MO

Nonalcoholic steatohepatitis (NASH) is associated with metabolic syndrome and is a major cause of liver morbidity. The incidence of NASH is higher in obese patients and the condition has been affecting an increasing number of children over the last decade. It is likely that abnormalities in hepatic lipid metabolism are involved in the etiology of NASH. However, many pathogenic mechanisms leading to liver injury remain unknown. Monoacylglycerol acyltransferase (MGAT) is an enzyme in the triglyceride synthesis pathway and functions to convert monoacylglycerol to diacylglycerol, which has been linked to hepatic steatosis and liver injury. We have recently shown that the expression of genes encoding MGATs is upregulated in the livers of patients with NAFLD. In mice, hepatic Mogat1 expression, which encodes MGAT1 is strongly induced by high fat diet feeding. Antisense oligonucleotides (ASOs) were used to knockdown the expression of Mogat1 in obese mouse liver and were found to improve hepatic insulin resistance. We next sought to investigate the role of Mogat1 on the development of diet-induced NASH by placing 7 week old mice on either a control low fat diet, or a diet containing high levels of trans fat (40%), fructose (20%), and cholesterol (2%) for 5 weeks. After that, mice were given biweekly intraperitoneal injections of ASO to knockdown Mogat1 (or scrambled ASO control) for 3 weeks. The low fat group received a control ASO. The high transfat, fructose and cholesterol diet induced hepatic steatosis, low grade inflammatory changes, and fibrosis. As expected, Mogat1 ASO treatment successfully suppressed Mogat1 expression in the liver. Mice that received Mogat1 ASO had a significant decrease in hepatic triglycerides, a significant decrease in collagen 1a (a fibrotic marker) gene expression, and tended to have expected, Mogat1 ASO treatment successfully suppressed Mogat1 expression in the liver. Mice that received Mogat1 ASO had a significant decrease in hepatic triglycerides, a significant decrease in collagen 1a (a fibrotic marker) gene expression, and tended to have reduced expression of macrophage markers and TNF alpha in the alpha. Conclusion: Inhibition of Mogat1 expression may improve hepatic steatosis and fibrosis in mice on a high fat/high fructose diet. Targeting hepatic MGAT activity may be a potential therapy for treating NASH in children with the hopes of preventing long-term complications.

192 DOES VITAMIN E IMPROVE THE OUTCOMES OF PEDIATRIC NAFLD? SYSTEMATIC REVIEW AND META-ANALYSIS. Ahmed Sarkhy1, Abdulrahman Al-Hussaini2, Valerio Nobili3, 1Gastroenterology unit, Pediatric department, King Khalid University hospital, King Saud University, Riyadh, Saudi Arabia; 2Gastroenterology unit, Pediatric department, Children's hospital, King Fahad Medical City, King Saud bin Abdulaziz University for Health sciences, Riyadh, Saudi Arabia; 3Liver Research Unit, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy

Background & objectives: To systematically evaluate the efficacy of adjuvant vitamin E on the outcomes of non-alcoholic fatty liver disease (NAFLD) and/or non-alcohol steatohepatitis (NASH) in children

Methods: We searched MEDLINE, PUBMED, EMBASE, the Cochrane CENTRAL Register Controlled Trials and the Cochrane database of systematic reviews over the period between January 1969 and September 2012 for studies that examined the role of adjuvant vitamin E given at any dose or duration, alone or in combination with other interventions on the outcome of pediatric NAFLD. The outcomes are alanine aminotransferase (ALT) normalization and histological improvement.

Results: Five randomized trials were eligible to be included in our analysis with total number of 270 participants. There was no statistically significant difference in the effect of adjuvant vitamin E on normalizing serum ALT (RR= 1.18, CI =0.92-1.53, P = 0.77 for heterogeneity, I² = 0 %). Sensitivity analysis showed that using higher doses of vitamin E, a longer duration of therapy or adding vitamin C did not change the effect on the measured outcome. Only two studies looked at histological changes as an outcome. We observed substantial heterogeneity between the two studies.

Conclusions: Our meta-analysis did not find a significant effect of adjuvant vitamin E over the placebo in normalizing serum ALT. Data on the long-term effect of adjuvant vitamin E on histological improvements in NAFLD patients are still lacking. Larger, well-designed randomized controlled trials (RCTs) in children with histological endpoints are still needed to answer this question.

193 BILIARY COMPLICATIONS FOLLOWING PEDIATRIC LIVER TRANSPLANTATION. Bridget Whitehead1, Saeed Mohammad2, Stanley Kim1, James Donaldson1,3, Jared Green1, Estella M. Alonso1,2, 1Northwestern University Feinberg School of Medicine, Chicago, IL; 2Division of Gastroenterology, Hepatology and Nutrition, Ann & Robert Lurie Children's Hospital of Chicago, Chicago, IL; 3Division of Radiology, Ann & Robert Lurie Children's Hospital of Chicago, Chicago, IL

Biliary strictures are a common complication following liver transplantation leading to increased morbidity and graft loss. We studied characteristics of biliary strictures their impact on patient and graft survival, and treatment success using interventional radiological techniques and surgery.
Methods: We retrospectively identified 78 patients with biliary strictures diagnosed between August 1997-March 2013. This was an expansion of a previously published report on stricture treatment and outcomes. Initial therapy for strictures included percutaneous cholangiogram with dilation and stent placement. Successful therapy was defined as the absence of recurrent strictures over 5 years of follow up. Stricture recurrence was treated by repeat stenting, and surgical revision was reserved for patients who failed stenting twice. Seven patients were excluded due to treatment outside of standard therapy. The remaining 71 patients were divided by, interval from transplant to stricture diagnosis: early (<3 months) or late (>3 months) and by era of stricture occurrence (1997-2003, and 2003-2013). Demographics, details of therapy and health outcomes were collected. Results: Of 71 patients, 57% were female, 50% had biliary atresia, 76% received reduced/split grafts and the median follow up was 5.5 years. Median age at transplant was 16 months and the median interval between transplant and stricture was 10 months. 93% of grafts had a Roux en Y anastomosis. Nineteen patients (26.71%) were retransplanted, 11 (15.5%) had abnormalities of the hepatic artery and 73% had anastomotic strictures. Initial stenting succeeded in 33 patients (46.5%) while 47% who had a second stent required surgical revision. Median follow up after successful first stent or surgical revision was 71 months and 37 months respectively. We found no differences between patients with early and late strictures with respect to gender, primary disease, stricture location, graft type, transplant type, and graft failure. Conclusions: We report outcomes of the largest pediatric cohort of post-transplant biliary stricture patients. Success with initial stenting has improved in the more recent era. Patients with an intrahepatic stricture were less likely to have successful radiologic treatment. There were no significant differences in outcomes for early vs late strictures. Percutaneous treatment with balloon dilation and stenting leads to favorable outcomes in the majority of patients; however biliary strictures remain an important risk factor for graft dysfunction and death.

### Treatment Outcomes for Early and Late Cohort

<table>
<thead>
<tr>
<th>Transplant-Stricture Interval</th>
<th>Number of Subjects</th>
<th>Stent 1 Success</th>
<th>Stent 2 Success</th>
<th>Surgical Revision Success</th>
<th>Graft Failure</th>
<th>Deceased</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3 months</td>
<td>22</td>
<td>50% (11)</td>
<td>36% (4)</td>
<td>50% (1)</td>
<td>17% (4)</td>
<td>13% (3)</td>
</tr>
<tr>
<td>&gt; 3 months</td>
<td>49</td>
<td>45% (22)</td>
<td>30% (8)</td>
<td>57% (8)</td>
<td>19% (9)</td>
<td>18% (9)</td>
</tr>
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</table>

### Significant Factors with Respect to Stricture Type and Era of Stricture Occurrence

<table>
<thead>
<tr>
<th>Variables</th>
<th>Stricture Type</th>
<th>P value</th>
<th>Era</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Anastomotic/Intrahepatic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary disease biliary atresia</td>
<td>48%</td>
<td>52%</td>
<td>NS</td>
<td>51.4%</td>
</tr>
<tr>
<td>Split/Technical variant graft</td>
<td>82.6%</td>
<td>52.6%</td>
<td>0.01</td>
<td>68.6%</td>
</tr>
<tr>
<td>Successful initial stent</td>
<td>57.7%</td>
<td>16%</td>
<td>0.02</td>
<td>31.4%</td>
</tr>
<tr>
<td>Graft failure</td>
<td>17.3%</td>
<td>21%</td>
<td>NS</td>
<td>25.7%</td>
</tr>
<tr>
<td>Surgical revision</td>
<td>19.2%</td>
<td>31.6%</td>
<td>NS</td>
<td>34.3%</td>
</tr>
<tr>
<td>Intrahepatic stricture</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>40%</td>
</tr>
</tbody>
</table>

### Infection as an Independent Risk Factor for Gastrointestinal Bleeding in Biliary Atresia.

Daniel M. O'Connell, Estella M. Alonso, Lee M. Bass, Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL

Gastrointestinal (GI) bleeding from esophageal varies, gastric varices, and portal gastropathy is a significant source of morbidity and mortality in children with biliary atresia (BA), cirrhosis, and end stage liver disease. Bacterial infection in adult patients with cirrhosis is associated with failure to control bleeding and early re-bleeding. Studies in adult cirrhotic patients pose a role for infection as a causative factor in an initial variceal bleed. This may be due to impaired reticuloendothelial clearance of endotoxin leading to intravascular activation of cytokines, nitric oxide, platelet-activating factor, and leukotrienes. No such studies have been performed in a population of children with BA. We hypothesize that concurrent infection is an independent risk factor associated with GI bleeding in children with portal hypertension.

Methods: We performed a retrospective chart review of data extracted from the electronic medical record (EMR) and related data sources of all patients with BA at our institution between 2004 and 2012. Diagnostic codes, procedure codes, medications, and lab values were extracted from the EMR to help classify episodes of GI bleeding, infection, and presence of portal hypertension. Infection was defined as a diagnostic code denoting bacterial or viral infection. Portal hypertension was defined as prior to diagnostic codes for splenomegaly or thrombocytopenia or either splenomegaly or thrombocytopenia and a complication of portal hypertension (ascites, esophageal varices, hepatoportal syndrome, or hepatopulmonary syndrome). Patients were included in the analysis until liver transplant (LT). Statistical analysis performed using Fisher's exact test was used to analyze contingency tables generated by the data.

Results: Eighty-six patients with BA were identified. Forty-two patients had a LT during the period of analysis. Fifty-eight patients had an infection related diagnosis prior to LT. Fifteen patients had a diagnosis of GI bleed. 73% (11/15) patients with a GI bleed had an infection related diagnosis within 2 weeks prior to bleeding episode. 27% (4/15) patients had a GI bleed not associated with infection. There was no statistically significant difference between GI bleeding and infection based on these data. Associations between portal...
hypertension and infection and portal hypertension and bleeding were all non-significant. No difference was noted between groups with regards to ALT, AST, Total Bilirubin, INR, or platelet count. Presence of ascites was significantly related to incidence of GI bleeding (p<0.005). LT-free survival was significantly less in the infection and bleeding group compared to the infection alone group (p=0.002).

**Conclusions:** The majority of bleeding episodes in our BA patients were associated with an infection related diagnosis however our study was not powered to show a statistically significant difference. The strong association between comorbid bleeding and infection and early LT may indicate a sicker cohort of patients. Prospective studies with adequate sample size should be performed to ascertain the true association between infection and GI bleeding in BA.

195* PREDICTORS OF TRANSFUSION REQUIREMENTS DURING PEDIATRIC LIVER TRANSPLANT IN THE STUDIES OF PEDIATRIC LIVER TRANSPLANTATION (SPLIT) REGISTRY. Daniel M. O'Connell1, Wendy Yin2, Ravinder Anand1, Riccardo Superina1, Estella M. Alonso1, 1Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL; 2The EMMES Corporation, Rockville, MD; 3Department of Surgery, Ann & Robert H. Lurie Children’s Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL

Liver transplantation (LT) is a technically complex and high-risk operation frequently requiring high volume blood transfusion. Intraoperative transfusions are inversely related to post-LT survival in adults and multivariate analysis of SPLIT data demonstrates an association between amount of intraoperative blood transfused and risk of patient death (HR 1.026 per 100 ml transfused). The predictors of transfusion requirements in this cohort have not been previously examined.

**Methods:** Recipients of primary LT with available data for transfusion volumes were included. Packed red blood cell and cell saver volumes were combined and expressed in ml/kg. Nine variables were hypothesized a-priori as predictors of transfusion volume: primary diagnosis, ICU status, era of transplant, age of recipient, type of graft, PELD score, length of operation, INR, and platelets. Descriptive statistics and univariate analysis were conducted.

**Results:** 2937 patients were identified. The median age at LT was 1.9 y (IQR 7.7). The sample was 52.9 % female and 40% had a diagnosis of biliary atresia. 25% were in the ICU at the time of transplant. The mean transfusion requirement was 56.6+/-89.4 ml/kg, 555 subjects (18.9%) received no transfusions. The mean operative time was 6.8+/-.2.4 hours.

Transfusion volume was classified into 4 categories based on ml/kg: 0, >0 - < 45, 45 - <90, and ≥90 to facilitate univariate analysis. All variables were significant at a p value of < .001, see table.

**Conclusions:** All 9 variables explored were significantly related to transfusion volume. Patients with higher acuity, ie higher PELD, higher INR, and ICU location require more blood. Also, patients <6 months, those with biliary atresia, and technical grafts have higher requirements.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>%</th>
<th>0</th>
<th>&gt;0-&lt;45</th>
<th>45-&lt;90</th>
<th>≥90</th>
<th>p value</th>
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<td></td>
<td></td>
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<tr>
<td>Biliary Atresia</td>
<td>1184</td>
<td>40.3</td>
<td>16</td>
<td>34.5</td>
<td>25.8</td>
<td>23.7</td>
<td>&lt;.0001</td>
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<td>Other Cholestatic or Metabolic</td>
<td>821</td>
<td>28</td>
<td>23.6</td>
<td>43.2</td>
<td>16</td>
<td>17.2</td>
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<tr>
<td>Fulminant Liver Failure</td>
<td>408</td>
<td>13.9</td>
<td>16.7</td>
<td>53.7</td>
<td>17.6</td>
<td>12</td>
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<tr>
<td>Cirrhosis</td>
<td>191</td>
<td>6.5</td>
<td>21.5</td>
<td>55.5</td>
<td>14.1</td>
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<td>Other</td>
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<td>11.3</td>
<td>18.6</td>
<td>49.2</td>
<td>17.1</td>
<td>15</td>
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<td><strong>ICU Status</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>750</td>
<td>25.5</td>
<td>17.7</td>
<td>38</td>
<td>20.3</td>
<td>24</td>
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<tr>
<td>No</td>
<td>2180</td>
<td>74.2</td>
<td>19.1</td>
<td>44.3</td>
<td>20.2</td>
<td>16.4</td>
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<tr>
<td><strong>Transplant Era</strong></td>
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<td></td>
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<tr>
<td>1995-2001</td>
<td>1087</td>
<td>37</td>
<td>16.7</td>
<td>40.6</td>
<td>22.4</td>
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<tr>
<td>≥2002</td>
<td>1850</td>
<td>63</td>
<td>20.2</td>
<td>43.8</td>
<td>18.9</td>
<td>17.1</td>
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<tr>
<td><strong>Age</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt; 6 months</td>
<td>256</td>
<td>8.7</td>
<td>16.8</td>
<td>21.5</td>
<td>23</td>
<td>38.7</td>
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<tr>
<td>6-11 months</td>
<td>714</td>
<td>24.3</td>
<td>13.7</td>
<td>24.5</td>
<td>29</td>
<td>32.8</td>
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</tr>
<tr>
<td>1-4 years</td>
<td>966</td>
<td>32.9</td>
<td>20.1</td>
<td>44.6</td>
<td>20.1</td>
<td>15.2</td>
<td></td>
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<tr>
<td>5-12 years</td>
<td>599</td>
<td>20.4</td>
<td>22.9</td>
<td>55.9</td>
<td>14.4</td>
<td>6.8</td>
<td></td>
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<tr>
<td>≥13 years</td>
<td>401</td>
<td>13.7</td>
<td>20.7</td>
<td>63.6</td>
<td>11.5</td>
<td>4.2</td>
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<tr>
<td><strong>Type of Graft</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live</td>
<td>454</td>
<td>15.5</td>
<td>20.7</td>
<td>32.4</td>
<td>22.9</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Cadaveric Whole</td>
<td>1582</td>
<td>53.9</td>
<td>21.4</td>
<td>53.4</td>
<td>15.7</td>
<td>9.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Cadaveric Reduced</td>
<td>494</td>
<td>16.8</td>
<td>10.7</td>
<td>26.5</td>
<td>26.9</td>
<td>35.8</td>
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<tr>
<td>Cadaveric Split</td>
<td>380</td>
<td>12.9</td>
<td>15.8</td>
<td>32.1</td>
<td>26.3</td>
<td>25.8</td>
<td></td>
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<tr>
<td><strong>PELD Score</strong></td>
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<td></td>
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<tr>
<td>&lt;0</td>
<td>539</td>
<td>18.4</td>
<td>26</td>
<td>57.3</td>
<td>11.5</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td>0-&lt;10</td>
<td>571</td>
<td>19.4</td>
<td>20.3</td>
<td>52</td>
<td>18</td>
<td>9.6</td>
<td></td>
</tr>
<tr>
<td>10-&lt;20</td>
<td>674</td>
<td>22.9</td>
<td>14.7</td>
<td>40.9</td>
<td>24.2</td>
<td>20.2</td>
<td></td>
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</tbody>
</table>
196  INCREASE IN DE NOVO FOOD ALLERGIES AFTER PEDIATRIC LIVER TRANSPLANTATION. Marie-Jeanne Lebel, Hugo Chapdelaine, Fernando Alvarez, Anne Des Roches, Louis Paradis, CHU Sainte-Justine, Montreal, QC, Canada

Background and Objective: Post-transplant acquired food allergy (TAFA) is an uncommon but serious complication of organ transplantation. This study was undertaken to compare the incidence of food allergy in cyclosporine (CsA) and tacrolimus (FK 506)-treated children post liver transplantation and their characteristics to identify risk factors.

Patients and Methods: The medical charts of all patients who underwent liver transplantation at our institution were reviewed. Data collected included indication and age at transplant, immune suppression protocol, presence of food allergy, onset and type of symptoms, allergens, maximum eosinophil count and total IgE.

Results: Between 1985 and 2010, 218 liver transplantsations were performed on 188 pediatric recipients, of which 154 were included in the study. Three patients (3%) of the 102 receiving CsA developed food allergy, compared to 9 (17%) in the 52 tacrolimus-treated patients, the latter exceeding the incidence of food allergy reported in the general population (Relative Risk 5.88; 95 % CI: 1.66-20.81). All patients who developed FA underwent transplantation before the age of three. In that age group, the incidence of TAFA was 29% (9/31) in the tacrolimus treated children in comparison to 7% (3/41) in the CsA group (RR 3.97; 95% CI: 1.17-13.45). Eosinophilia was present in 81% of children receiving tacrolimus compared to 54% in the CsA group (P=0.002).

Conclusions: We observed a statistically significant increase incidence of food allergy in tacrolimus treated-children following a liver transplant compared to CsA and those under the age of three at the time of the transplant are particularly vulnerable. The underlying process is still unknown and probably multifactorial.

197  HIGH RATE OF NON-ADHERENCE TO IMMUNOSUPPRESSIVE MEDICATION BY SELF-REPORT IN ADOLESCENT LIVER TRANSPLANT RECIPIENTS. Rebecca McKenzie, William Berquist, Kenneth Cox, K. T. Park, Iris Litt, Stanford, Palo Alto, CA

Introduction: Non-adherence to immunosuppressive medication is a common problem in adolescent liver transplant recipients. Previous studies lack data from self-reported non-adherence using a validated measure in this population. Methods: Adolescent liver transplant patients (Ages 12-21) >6 months post-transplant were eligible for the study. Participants completed a questionnaire on-line or in person that included the 5-item Basel Assessment of Adherence to Immunosuppressive Medication Scale (BAASIS), which evaluates self-reported adherence to anti-rejection medication over a 4 week period. Results: A total of 25 patients, 6 male and 19 female, completed the questionnaire. A total of 15 patients (60%) were non-adherent based on the BAASIS scale. 12 patients (48%) had missed a single dose of their medication in the last 4 weeks. 4 patients (16%) admitted to having skipped two more doses of anti-rejection medication in a row at least twice or three times during the last month. 9 patients (36%) reported having taken their anti-rejection medications more than 2 hours before or after the recommended dosing time. In 6 of the 9 patients (67%), this occurred 2-3 times last month and every 2-3 days in one patient. 1 patient admitted to altering the prescribed amount of the anti-rejection medication without physician advice. No patients admitted to completely discontinuing medication over the last month. Using a scale from 0-100 with 100 as perfect adherence, patient scores ranged from 35-100% with 91% as the average (+/- 15.36 SD). Conclusions: Patient-reported non-adherence to immunosuppressive medication occurs at a high prevalence in adolescent liver transplant patients. This included reports of missed doses, alterations in administration schedule and changes in prescribed doses of medication. Our study highlights the importance of evaluating adherence to immunosuppressive medications at each clinic visit to optimize medical management and outcomes for these patients.

198  SINGLE-CENTER EXPERIENCE WITH ANIDULAFUNGIN IN PEDIATRIC LIVER TRANSPLANT PATIENTS. Mary Elizabeth M. Tessier, Daniel Leung, Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine/ Texas Children's Hospital, Houston, TX

Introduction: Fungal infections are more common in immunosuppressed and critically ill patients. Anidulafungin is a novel echinocandin antifungal with a good safety profile in adults. Anidulafungin is not metabolized but is biotransformed in plasma leading to its favorable pharmacokinetic profile, causing neither hepatic nor renal toxicity. Additionally, it has no impact on immunosuppressant medication levels (i.e. tacrolimus and cellcept) in adult solid organ transplant patients. In pediatric studies, it is well-tolerated at a loading dose of 1.5mg/kg/day followed by 0.75mg/kg/day. Although anidulafungin theoretically has favorable parameters for use in critically ill children with hepatic dysfunction, little is known about anidulafungin's clinical usefulness and safety in pediatric liver transplant patients. We report the safety profile and clinical outcomes of four children with significant liver disease treated with anidulafungin.

Methods: Anidulafungin was initiated in four critically ill children in the pediatric ICU at the above dose. Two patients awaiting transplant and two recently transplanted patients were started on anidulafungin due to acute decompensation and concern for occult fungal infection. Three of the four patients had chronic liver failure. Liver disease was due to biliary atresia (n=2), hepatoblastoma (n=1), and chronic rejection (n=1). On-treatment creatinine, ALT, tacrolimus levels, survival and clinical outcomes were analyzed. Spearman's correlation was performed to evaluate the differences in ALT, creatinine, and survival.

Results: Anidulafungin was well tolerated and showed no signs of hepatic or renal effects. There was no significant difference in median change in ALT (6.5 U/L) during treatment (p=0.2). Tacrolimus levels fluctuated in all newly transplanted patients, a common phenomenon. However, in the previously transplanted patient, tacrolimus levels were consistent. No alterations in creatinine were noted, with a median change over treatment of 0.1mg/dL, also non-significant (p=0.2). One patient had transient elevation of creatinine...
following removal from dialysis which improved while still on anidulafungin. Significant neurological improvement was noted in one child with severe encephalopathy, improving from grade III to I. Overall, no patient experienced an adverse effect from anidulafungin, and all patients exhibited a good clinical outcome with 100% survival at the end of treatment.

Conclusion: Anidulafungin is a safe alternative antifungal in pediatric liver transplant patients. In our single-center experience, four patients demonstrated clinical improvement without hepatic or renal toxicity. Further pediatric studies with anidulafungin are needed, but our experience suggests there will be positive outcomes.

Table 1. Evolution of ALT, Creatinine, and Survival during Anidulafungin Therapy

<table>
<thead>
<tr>
<th>Patient</th>
<th>Δ ALT (U/L)</th>
<th>Δ Creatinine (mg/dL)</th>
<th>Alive</th>
<th>Duration of Antifungal (days)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26</td>
<td>0.03</td>
<td>yes</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>-21</td>
<td>0.16</td>
<td>yes</td>
<td>21</td>
<td>NS</td>
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<td>14</td>
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<td>45</td>
<td>-0.24</td>
<td>yes</td>
<td>26</td>
<td>NS</td>
</tr>
<tr>
<td>Median</td>
<td>6.5</td>
<td>0.1</td>
<td>100%</td>
<td>18</td>
<td></td>
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</tbody>
</table>

199  RECENT REPLACEMENT THERAPY IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS WITH HEPATORENAL SYNDROME. Cindy E. Parsons, Linda Book, Raoul Nelson, M. Kyle Jensen, Pediatric Gastroenterology, University of Utah, Salt Lake City, UT; Pediatric Nephrology, University of Utah, Salt Lake City, UT.

Introduction: Limited data on short and long-term outcomes from renal replacement therapy (RRT) in pediatric liver transplant (LTx) patients exists. The aim of this study was to identify risk factors for RRT in pediatric LTx recipients with hepatorenal syndrome (HRS) and describe outcomes.

Methods: We conducted a single center, case control study of all LTx recipients who required RRT for HRS from 1999 to 2011. Controls were LTx recipients matched on age, diagnosis, and LTx date who did not receive RRT. We collected data from the electronic medical and pharmacy records, blood bank, and paper charts.

Results: We identified 8 RRT cases and 24 controls [mean age 7.7 (0.5-19.8years) vs. 6.0(range: 0.6-18.2years), p=0.6]. 4 of 8 cases were <1year old with weight (5.6-6.6kg). The most common LTx indication for cases and controls was biliary atresia (50 vs. 54%). Cases had higher M(P)ELD scores at listing (26 vs. 16, p=0.01) and lower GFR (median 15 vs. 102, p<0.0001) at RRT initiation or LTx.

Ascites, GI bleeding and infestations occurred at higher rates in cases than controls: [(100 vs. 54%, p=0.03), (100 vs. 46%, p=0.01), (88 vs. 33%, p=0.01)]. Cases received vancomycin more frequently than controls (75 vs. 21%, p=0.01) and had a higher rate of toxic vancomycin troughs as well (38 vs. 0%, p=0.01). Cases received RRT a mean 64 days (range: 3-355days). Case mortality rate was 3/8 (37.5%) compared to 0% in controls. Death occurred at 1, 26, & 346 days post-LTx. RRT-infants required 0-3 dialysis catheters replacements.

Cases and controls had similar length of follow up: median (3.2, range: 1.5-7.6years) vs. (4.9, range 0.2-11years, p=0.3). After LTx, cases and controls had similar GFR [(83 vs. 99, p=0.2), (77 vs. 93, p=0.3), (80 vs. 107, p=1), and (97 vs. 114, p=0.1)] at 1, 6, 12months and latest follow-up. Of 6 surviving cases, 4 required anti-hypertensives and diuretics 1month post-LTx, but at most recent follow-up only 1 case required antihypertensive therapy and 0 needed diuretics.

Conclusions: RRT is feasible, even in small infants. Survival is lower in RRT patients than controls, but appears acceptable. Survivors after RRT have similar renal function to controls within 1 month of transplant that persists at long-term follow-up. More studies are needed to assess risk factors for RRT and outcomes in LTx recipients with HRS.

200  FURTHER STUDIES OF ω-3 FATTY ACID (ω3FA) IN PREVENTING HEPATIC STEATOSIS IN A MURINE MODEL OF PARENTERAL NUTRITION-ASSOCIATED LIVER DISEASE (PNALD): THE ROLE OF PPARα AND PPARγ. Esther N. Prince, Farrah B. Lazare, William R. Treem, Jiliu Xu, Jahangir Iqbal, Xiaoyue Pan, Joby Josekutty, Meghan Walsh, Virginia Anderson, Mahmood Hussain, Steven M. Schwarz, Pediatric Gastroenterology, SUNY Downstate Medical Center, Brooklyn, NY; 2Cell Biology, SUNY Downstate Medical Center, Brooklyn, NY; 3Johnson and Johnson, Pharmaceutical Research and Development, Titusville, NJ; 4Pediatric Gastroenterology, Winthrop University Medical Center, Mineola, NY; 5Pathology, SUNY Downstate Medical Center, Brooklyn, NY.

Background: ω3FAs attenuate PNALD. However, mechanisms underlying ω3FA's protective role are still unknown. Several molecular mediators are known to be involved in the pathogenesis of hepatic steatosis. Absent or decreased activity of microsomal triglyceride transfer protein (MTP), a rate-limiting intracellular chaperone responsible for assembly and secretion of apoB100-containing VLDL, has been correlated with hepatic lipid accumulation. Both expression and functional activity of MTP increase via PPAR-α activation. PPAR-α is a nuclear receptor regulating transcription of genes for key enzymes promoting hepatocellular β-oxidation and lipid clearance. PPARγ is also involved in regulating fatty acid storage and glucose metabolism. ω3FAs, MTP, PPAR-α and PPAR-γ have not been elucidated. In work presented previously, we showed that hepatic triglycerides (TG) and MTP activity increased in mice fed oral, fat-free PN solution (PN-O), PN-O + intraperitoneal (IP) ω6FA-predominant supplements (PN-ω6) and PN-O + IP ω3FA (PN-ω3), when compared with Chow fed controls. PN-O and PN-ω6 groups accumulated significantly greater amounts of TG, when compared with PN-ω3 mice. Objective: To determine the potential roles of PPARα and PPARγ in mediating the protective effect of ω3FAs in a murine model of PNALD. Methods: 129S4/SvJaePparatm/Gonz/J PPAR-α knockout mice (PPARα KO) were fed chow and water (controls), PN-O, PN-ω6, or PN-ω3. Hepatic TG was assessed after 19 days. In order to examine the role of PPARγ, wild-type and PPARα KO groups received the PN-ω6
regimen and were gavage fed (every other day) either pioglitazone, a thiazolidinedione derivative and selective PPAR-γ agonist, or vehicle. Results: Hepatic TG levels of PPARα KO animals were significantly increased in PN-O, PN-ω6 and PN-ω3 when compared with wild-type controls. TG levels in PN-ω3 animals were similar to controls and significantly lower when compared with PN-O and PN-ω6. Hepatic lipid content, both in wild-type and in PPAR-α knockout animals receiving PN-ω6, was not significantly altered by pioglitazone. Conclusions: 1. PN induces TG accumulation in wild type and in PPAR-α KO mice; 2. Hepatic TG accumulation is reduced in PN-fed wild type and PPAR-α KO mice given IP ω3FAs; 3. Activation of PPARγ by pioglitazone agonist does not ameliorate TG accumulation in PN-fed mice. Speculation: Prevention of steatosis by ω3FA is independent of both PPAR-α and PPARγ pathways. To clarify PNA LD pathogenesis and mechanisms underlying the protective role of ω3-FA, future studies should focus on molecular pathways involved in hepatic lipid homeostasis other than MTP, PPARα and PPARγ.

201* ANALYSIS OF DIFFERENTIAL GENE METHYLATION IN LIVERS FROM BILIARY ATRESIA PATIENTS UNCOVERS A POTENTIAL ROLE FOR PLATELET-DERIVED GROWTH FACTOR (PDGF). Steven F. EauClaire1, Shuang Cui1, Zenobia Cofer1, John Tobias2, Cecilia Kim1, Hakon Hakonarson1, Randolph P. Matthews1, 1Division of GI, Hepatology, and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA; 2Molecular Profiling Facility, University of Pennsylvania, Philadelphia, PA; 3Center for Applied Genomics, The Children's Hospital of Philadelphia, Philadelphia, PA.

Objectives: We have previously demonstrated that inhibition of DNA methylation leads to developmental biliary defects and that cholangiocytes from patients with biliary atresia (BA) demonstrate DNA hypomethylation. Inhibition of DNA methylation generally leads to increased expression of genes, as lack of the epigenetically tagged methylcytosines allows transcription factor binding and activation of the hypomethylated gene. We hypothesized that gene expression changes resulting from DNA hypomethylation contribute to the pathogenesis of BA.

Methods: We isolated DNA from livers of BA patients, as well as disease control and non-disease control patients, obtained at transplant. We then performed a methylation microarray study on these samples, using the Illumina HumanMethylation450 BeadChip, from which we can determine the relative methylation of over 450,000 sites thought to be important in gene regulation. Selected positive candidates were confirmed using pyrosequencing, and we examined expression of the top 4 candidates using quantitative PCR. Differential protein expression of the top candidate, PDGF, was performed using immunofluorescence of patient samples. We then examined the importance of increased PDGF in mediating biliary defects by injecting PDGF peptide into developing zebrafish larvae and examining biliary development using cytokeratin immunostaining.

Results: Analysis of the methylation microarray in toto confirmed our previous findings showing decreased DNA methylation in BA livers, as there was a highly statistically significant bias towards hypomethylated sites (chi-square 893.1, p<10E-20). The 4 most highly hypomethylated genes - PDGFA, ZEB2, ARHGEF10, and ADAP1 - demonstrated increased expression by quantitative PCR. There was increased protein expression of PDGF in cholangiocytes in BA patients. Finally, injection of PDGF-AA peptide into developing zebrafish larvae led to biliary defects, supporting a scenario in which overexpression of PDGF-AA leads to biliary damage. Conclusions: Inhibition of DNA methylation may be an important pathogenic mechanism in BA, as manipulation of differentially methylated genes found in BA livers can elicit biliary defects in an animal model.

202 HIGH-VERSUS LOW-DOSE STEROIDS AFTER LIVER TRANSPLANTATION IN CHILDREN: THE CONS WITHOUT THE PROS. Massimiliano Paganelli1, Mona Beaunoyer2, Michel Lallier2, Fernando Alvarez1, 1Gastroenterology, Hepatology and Nutrition, Ste-Justine Hospital, Montreal, QC, Canada; 2Surgery, Ste-Justin Hospital, Montreal, QC, Canada.

Corticosteroids have been the mainstay of immunosuppression since the early days of liver transplantation. Steroid-free protocols have recently been proposed as an interesting alternative to reduce side effects while decreasing the risk of rejection. Nevertheless, the majority of adult and pediatric transplantation centers worldwide are still using immunosuppression protocols combining calcineurin inhibitors with corticosteroids. Two different steroids regimens were used at our institution for induction of immunosuppression: low-dose (1 mg/kg) up to year 2007 and high-dose (2.5 mg/kg) ever since. Full dose was maintained until normalization of liver enzymes, and then tapered over 3 months. All patients received calcineurin inhibitors. In this study we compared children receiving low-dose (group 1) and high-dose (group 2) corticosteroids, and evaluated the incidence of acute and chronic rejection, infections, arterial hypertension and glucose intolerance in the first year post-transplant. Of 69 children transplanted from January 2002 to June 2012 at Ste-Justine Hospital, 59 (32 males, 27 females) had >1-year follow-up. Twenty-three and 36 patients were included in group 1 and 2, respectively. The two groups were comparable in terms of age at transplantation (median of 2 and 2.3 years, respectively) and M/F ratio, whereas more subjects in group 1 (60.1%) than in group 2 (30.5%) were transplanted for biliary atresia (p<.05). All but one patient in group 1 received tacrolimus as calcineurin inhibitor. Basiliximab was used in 3 children from group 1 and 29 from group 2 (p<.001). Acute rejection developed in 52.2% and 50% of patients in group 1 and 2, respectively (p=NS), for a total of 15 acute rejection episodes in group 1 (1.3 episodes/patient) and 32 in group 2 (1.8 episodes/patient). Chronic rejection, defined as chronic allograft parenchymal damage or vanishing bile duct syndrome, developed in 4.3% and 13.9% of patients, respectively (p=NS). Arterial hypertension complicated the early post-transplant course of 65.2% of children in group 1 and 72.2% in group 2 (p=NS), whereas glucose intolerance was seen in 8.7% and 16.7% of patients, respectively (p=NS). Viral infections affected group 1 more often than group 2 (65.2% vs. 38.9%, p<.05), but no difference was noted for CMV and EBV infection/reactivation. Although bacterial infections were as frequent in group 1 as in group 2, significantly more fungal infections were registered in group 2 (30.6% vs. 8.7% in group 1, p<.05).
Stronger immunosuppression during the early post-transplant period has been implicated in the failure to develop long-term graft tolerance. Our data show that higher doses of steroids during the induction of immunosuppressive treatment do not confer protection against acute or chronic rejection, and this despite the more frequent concomitant addition of basiliximab. Moreover, higher doses of corticosteroids are associated with a higher risk of developing side effects such as fungal infections, glucose intolerance and arterial hypertension. Overall, these data support the use of low-dose steroid regimens for the induction of immunosuppression after liver-transplantation.

203 WITHDRAWN

204 IS VITAMIN A LEVEL FRIEND OR FOE IN NEONATAL SEPSIS-ASSOCIATED CHOLESTASIS? Hanifah Oswari, Windy Setyawati, Idham Amir, Jose R. Batubara, Fatima S. Alatas, Child Health Department, University of Indonesia, Jakarta, Indonesia

Background: Neonatal sepsis-associated cholestasis (NSAC) is still a major problem in developing countries, resulting in prolonged morbidity, hospitalization and increase mortality in neonates with septicemia. Previous study reported that biochemical liver parameters have a prognostic value in NSAC. Antioxidants were also thought to be involved in inflammatory process of sepsis. However, there are still few reports regarding the role of biochemical liver parameters and antioxidants in the development and the outcome of NSAC.

Therefore, we aim to investigate whether antioxidants (zinc, vitamin A and vitamin D) and biochemical liver parameters (bilirubin, AST, ALT and gamma-glutamyltransferase/GGT) have a prognostic value in the development of NSAC and the outcome of NSAC.

Method: This is a prognostic study with cohort prospective method during December 2011-December 2012. Eighty neonates were consecutively included to this study, out of 225 neonates with proven sepsis, who were hospitalized during the study period. Fifty neonates developed cholestasis (NSAC group) and 30 sepsis neonates without NSAC (non-NSAC group). NSAC group further divided into 2 groups (NSAC with good prognosis and poor prognosis). Their antioxidants level and biochemical liver parameters were evaluated at the time when sepsis was proven by blood culture result (median 3 days; range: 3-9 days), after sepsis symptoms were observed, then compared between each groups.

Results: Mean onset of cholestasis was 6.3 days (SD: 2.45) from the first sepsis symptoms were observed (at the time of blood culture was taken). There are no statistical differences found in the level of zinc, vitamin A and D between NSAC and non-NSAC group. Antioxidants levels have no prognostic value in the development of NSAC. However, AST level > 51U/L and direct bilirubin > 0.3 mg/dL have prognostic value in the development of NSAC, RR 8.57 (95% CI:2.22 to 33.19), P=0.002 and RR 14.31 (95% CI:1.29 to 158.45), P=0.03, respectively. In NSAC group, vitamin A deficiency (retinol< 0.697 μmol/L) was found in 23 neonates with good prognosis and 11 neonates with poor prognosis (P=0.044). Vitamin A deficiency has a higher possibility to have good prognosis for the outcome of NSAC, RR 0.16 (95% CI 95%; 0.04 to 0.63), P=0.009. In addition, low GGT (< 85.5 U/L) was found in 2 neonates with good prognosis and 7 neonates with poor prognosis (P=0.025). Low GGT was also found to have a higher possibility to have poor prognosis for the outcome of NSAC, RR 13.16 (95% CI 95%; 2.07 to 83.65), P=0.006.

Conclusion: AST level >51U/L and direct bilirubin >0.3 mg/dL have prognostic value in the development of NSAC. Vitamin A deficiency has been demonstrated to have a good prognostic factor for the outcome of NSAC. While low GGT level has been demonstrated to have a poor prognostic factor for the outcome of NSAC.

Keywords: Antioxidant, biochemical liver parameter, cholestasis, neonatal septicemia, neonatal sepsis-associated cholestasis

205 SCREENING AND PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE IN OVERWEIGHT AND OBESE PEDIATRIC PATIENTS: SINGLE CENTER EXPERIENCE. Sarah Fleet1, Haamid Chamdawala2, John C. Rausch1, Faith Ihekweazi1, Joel E. Lavine1, Nadia Ovchinsky1, 1Pediaiatrics, Columbia University, Morgan Stanley Children's Hospital of New York-Presbyterian, New York, NY; 2Mailman School of Public Health, Columbia University, New York, NY; 3Pediatrics, Baylor College of Medicine, Texas Children's Hospital, Dallas, TX

Non-alcoholic Fatty Liver Disease (NAFLD) is the most common cause of liver disease in children, and its rise has been related to the increasing prevalence of obesity. The exact prevalence of NAFLD in children is unknown as a result of impracticality of screening liver biopsies. Alanine aminotransferase (ALT) is a non-specific marker of liver injury used as a surrogate marker for NAFLD. Screening for liver disease in overweight and obese children has been suggested by expert committees. We aim to determine the screening rate for NAFLD in overweight and obese children and to describe the prevalence of NAFLD in a unique mixed-race Latino population served by the center's clinics.

Methods: All pediatric patients 4 to 19 years old with a BMI ≥ 85th percentile over a period of two years were identified using ICD-9 codes for overweight or obesity. Outpatient records were reviewed for demographics, anthropometric and clinical data. Body mass index (BMI) was calculated using weight and height measurements. BMI Z-score was determined according to gender, age and sex. As demographic data was largely incomplete, data from latest census was used for the population of the Washington Heights-Inwood community. Patients were defined as "screened" for NAFLD if ALT was measured for routine screening purposes. Patients were determined to be at risk for NAFLD if ALT ≥ 40 U/L. Data was analyzed using Statistical Analysis System (SAS), by logistic and linear regression analysis, where appropriate.

Results: Of 2325 overweight or obese patients identified, 740 patients, or 31.8%, were screened with ALT. Of those screened, 39 patients, or 5.3% were found to have elevated ALT. Males were more likely to have elevated ALT (6.6% vs 3.8%, p=0.09). Mean BMI z-score was 2.1. Increasing ALT levels were associated with increasing BMI z-scores (p = 0.0014) even in patients with normal ALT as well as increasing insulin levels (p =.04). 6 of 39 patients with elevated ALT (15.4%) were referred for further evaluation. 74% of the community population identified themselves as Latino, of whom 72% described themselves as Dominican.

Conclusion: Less than a third of all patients identified by the providers as overweight or obese were screened for NAFLD and only 15% of those with abnormal ALT were further referred for an evaluation. The high mean BMI z-score suggests that children with lower BMI may not be recognized as obese by the providers. In addition, ALT cut-off value used may be too high, as normal values have not been
established in children. Therefore NAFLD may be under-diagnosed in our pediatric clinics. Higher BMI z-scores were associated with increasing ALT values, suggesting that those with more severe obesity may be at higher risk of having NAFLD. The prevalence of elevated ALT (5.3%) among screened patients was lower than other population-based estimates of NAFLD in overweight children. This is the first time the prevalence of NAFLD has been studied in a largely Dominican American population of mixed-race ethnicity (owing heritage to Africa and Europe). Dominican children, even when obese, may be at less risk of developing NAFLD.

206 SEVERE AND RAPID DISEASE COURSE IN THE NATURAL HISTORY OF LYOSOMAL ACID LIPASE (LAL) DEFICIENCY. Simon Jones1, Yassil Valayannopoulos2, Donna Bernstein3, Martin Bialer3, Anil Dhawan4, Chris Hendriks5, Chester B. Whitney6, Maryam Bankazemi7, Alicia Chan8, Ornella Guardamagna9, Julian Raiman10, Iman Gamal11, Laila Selim11, Stephen Cederbaum12, Maja Di Rocco13, Jennifer Domn13, Greg Enns13, David Finegold14, Jay Gargus15, Oasma Zak16, Stephen Eckert17, Eugene Schneider18, Anthony G. Quinn19, Central Manchester and Manchester Children’s Hospital NHS Foundation Trust, Manchester, United Kingdom; 2Ref Cen EME, Necker-Enf Maladies Hospital, Paris, France; 3North Shore Long Island Jewish Hospital, Manhasset, NY; 4Kings College Hospital NHS Foundation Trust, London, United Kingdom; 5Birmingham Children’s Hospital NHS Foundation Trust, Birmingham, United Kingdom; 6University of Minnesota, Minneapolis, MN; 7New York Presbyterian Hospital, New York, NY; 8University of Alberta Health Services Edmonton, Alberta, AB, Canada; 9University of Turin, Turin, Italy; 10The Hospital for Sick Children, Toronto, ON, Canada; 11Cairo University Children’s Hospital, Cairo, Egypt; 12University of California-Los Angeles, Los Angeles, CA; 13Istituto Giannina Gaslini-Ospedale Pediatrico, Genova, Italy; 14Vanderbilt Children’s Hospital, Nashville, TN; 15Stanford University School of Medicine, Stanford, CA; 16Children’s Hospital of Pittsburgh, Pittsburgh, PA; 17University of California - Irvine Medical Center, Orange, CA; 18Ain Shams Hospital, Cairo, Egypt; 19Synageva BioPharma Corp., Lexington, MA

Introduction: Lysosomal Acid Lipase (LAL) Deficiency is a rare, autosomal recessive disorder caused by mutations in the LIPA gene, which encodes the enzyme responsible for lysosomal hydrolysis of cholesteryl esters and triglycerides. LAL Deficiency in infants, also known as Wolman Disease, manifests in the first few months of life and usually leads to death within the first year of life. These patients develop malabsorption, hepatosplenomegaly, liver failure, adrenal calcifications, cytopenias, and growth failure as per case reports, but no systematic study of LAL Deficiency in infants has been undertaken. This is the first natural history study of a large multinational group of LAL deficient patients less than 2 years of age.

Methods: Demographic and clinical information on LAL deficient patients were collected utilizing clinical chart data abstractions and summarized.

Results: Of the 36 patients, 17 were White, 8 Asian, 11 other or unknown, and at least 37% had no family history of consanguinity. More than two-thirds developed symptoms before 2 months of life. Median ALT and AST values were elevated prior to diagnosis (64 and 109 U/L) and increased further where longitudinal data were available prior to death (144 and 333 U/L). Median bilirubin values were normal at the time of diagnosis (0.9 mg/dL) and increased slightly prior to death (1.3 mg/dL). 26 patients had growth failure (defined as weight decrease across 2 major centiles and/or weight below 10th percentile with no weight gain for ≥2 weeks) and/or loss of 5% of birth weight after 2 weeks of age) on standard weight-for-age-for-growth chart within the first 6 months of life. The median age (range) for all patients (n=36) at symptom onset, at diagnosis, and at death were 1.0 month (0 - 6.0), 2.6 months (1.0 - 17.7), and 3.7 months (1.4 - 46.3) respectively. Transplantation was attempted in 10 patients (median age at time of transplant was 5.5 months); 9 underwent hematopoietic stem cell transplant (HSCT) with 7 dying before 9 months of age, one dying at 26.9 months and another at 46.3 months. The 10th patient (HSCT & liver transplant recipient) died at 37.3 months.

Conclusion: LAL Deficiency in infants has a rapidly progressive clinical course and nearly universal mortality during the first year of life.

207 EOSINOPHILIC ESOPHAGITIS IN PEDIATRIC LIVER AND INTESTINAL TRANSPLANT PATIENTS. Rajasekhar Bodicharla1, Jennifer Garcia2, Philip Ruiz3, Lesley J. Smith4, 1Pediatrics, Univ Miami, Miami, FL; 2Pathology, University of Miami, Miami, FL

Introduction: Eosinophilic esophagitis (EoE) is increasingly recognized in the pediatric transplant (Tx) population. Liver (LI) and intestinal Tx patients (I/MVT) may have an increased risk of EoE because of immune imbalance leading to a Th2 response favoring an eosinophilic inflammatory response.

Objective: To determine the prevalence of EoE in esophageal biopsies (bx) in LI and I/MVT recipients at a single transplant center in comparison to a group of non-tx recipients without immunosuppression (ISP) or deficiency.

To compare the degree of ISP in each group to determine whether increasing tacrolimus exposure or number of ISP agents used leads to an increased eosinophilic response in the esophagus.

Methods: There were 472 pediatric Tx recipients between ages 0-18 yrs from April 2000 to August 2012. Of these 181 were I/MVT and 291 were LI recipients. 128 patients underwent esophageal bx and the bx reports were reviewed retrospectively for EoE. Based on inclusion and exclusion criteria and pathological slide availability, only 79 subjects had available biopsy slides for re-review. These esophageal biopsies were reviewed by a skilled tx liver and GI pathologist. The charts were reviewed for tacrolimus (Tac) levels and dosage, other ISP agents and clinical information including known allergies. The Tac exposure was calculated by calculating the area under the curve (AUC) based on the previous 3 months of Tac levels in ng/L.

Results: Among the Tx subjects (n=128), 12 patients were found to have EoE by pathological records. Of the 12 patients with EoE, only 1 new patient was identified based on the pathology re-review. In LI patients undergoing upper endoscopy (n=64), 5 were found to have EoE compared to 7 subjects in the I/MVT group (n=64). Only 3 subjects from the non-Tx (n=128) comparison group had EoE. The disease rate in the Tx group as a whole was 9.3% and in the non-Tx comparison group was 2.4% (two-tailed p= 0.03, odds ratio of 4.3 (95% CI 1.18-15.66, p = 0.026)). The prevalence among the LI recipients was 7.8% and among the I/MVT recipients was 10.9 % which was not significant (P=0.7, CI- 0.23 to 2.78). When the bx samples were reviewed again by our pathologist, only 7 Tx patients (from N=79) were found to have EoE. There was no significant difference in average Tac exposure between each transplant group. There was no statistical difference in the disease rates between LI and MVI ( p=0.1349). Mean age from transplant to development of EoE was 5.3
years with range of 2-13.1 years. There were no significant gender-related differences. Mean Tac exposure in transplant patients who developed EoE was 83.9 ng/dL and in patients who did not develop EoE was 56.4 (p <0.0001). Only 1 patient had EoE in the matched comparison group (n=79). The number of ISP agents used was not significant in determining the esophageal eosinophilic response and steroid use was not clearly protective.

Conclusion: There is an increased risk of EoE in pediatric LI and I/MVT patients compared to non-Tx patients mostly likely due to exposure to tacrolimus favoring a Th2 response, with a clear association between tacrolimus exposure and the eosinophilic response in esophagus.

208 CONGENITAL ABSENCE OF GALLBLADDER - A CASE REPORT AND REVIEW OF THE LITERATURE. Anshu Maheshwari, Katryn Furuya, Pediatric gastroenterology and Hepatology, AI dupont hospital, Wilmington, DE

15 month old male presented to his pediatrician for failure to thrive. As part of his initial evaluation, he was found to have elevated transaminases. Initial biochemical analyses revealed: aspartate aminotransferase: 225 U/L, alanine transaminase: 312 U/L, alkaline phosphatase: 396 U/L, total bilirubin: 0.2 mg/dl, albumin: 4.2 gm/dl, hemoglobin: 11.5 g/dl, platelet count: 268 K/UL, prothrombin time and partial thromboplastin time were normal. He was then referred to the hepatology clinic at our institution were it was initially felt that his elevated transaminases may have been secondary to a viral illness and thus, repeat testing was done which showed improvement in his transaminases. He was clinically asymptomatic and on physical examination his liver was soft and palpable 1.5 cm below the costal margin, and his spleen was not palpable. At the same time an abdominal ultrasound showed non-visualization of the gallbladder and slightly heterogeneous echotexture of the liver without focal abnormalities. The gallbladder and common bile duct were not identified. There was no intra-hepatic biliary ductal dilatation. A magnetic resonance cholangiopancreatography confirmed the absence of the gallbladder.

Discussion: Congenital Agenesis of the Gallbladder (CAG) is a rare malformation. It was first reported by Lemery in 1701. Currently, only 400 cases have been reported worldwide. Most cases of CAG defined in literature have been described in adults. We report only the fifth case of CAG to be diagnosed in early childhood. Therefore, CAG represents a rare anomaly of the biliary system.

It likely results from an embryologic defect in the development of the hepatobiliary bud and can occur with other associated malformations like biliary atresia and duodenal atresia. However, there are families in which the condition has occurred in several members, suggesting that there are familial hereditary forms of CAG. Symptoms have been reported in 23% of cases, and CAG has almost always been misinterpreted as cholecystitis with cystic duct obstruction or as sclero-atrophic gallbladder, therefore leading to unnecessary surgery.

Intestinal/Colonic Disorders – Inflammatory Bowel Disease

226 USE OF THE EMERGENCY DEPARTMENT IN PEDIATRIC INFLAMMATORY BOWEL DISEASE. Edward J. Hoffenberg1, Jacqueline Fridge2, Ian Leibowitz3, Marc Tsou4, Dana Dykes4, Michael Kappelman6, Richard Colletti7, 1Pediatrics-GI, University of Colorado Denver School of Medicine, Aurora, CO; 2Pediatric Gastroenterology, Northwest Pediatric Gastroenterology, LLC, Portland, OR; 3Inova Pediatric Specialty Center, Inova, Fairfax, VA; 4Pediatric Gastroenterology, Children's Hospital of The King's Daughters, Norfolk, VA; 5Pediatric Gastroenterology, Cincinnati Children's Medical Center, Cincinnati, OH; 6Pediatric Gastroenterology, University of North Carolina at Chapel Hill school of Medicine, Chapel Hill, NC; 7Vermont Children's Hospital, University of Vermont College of Medicine, Burlington, VT

Introduction: ImproveCareNow is a collaborative learning health care system aiming to optimize the care of Pediatric IBD patients. A sub-group has begun to investigate areas of overuse and misuse of health care resources, initially focusing on Emergency Department (ED) visits. We sought to determine factors leading to ED visits, and whether they might be preventable in a health care system with optimal care coordination and access to care.

Methods: Records were reviewed of 4-5 consecutive ED visits by pediatric IBD patients from each of 6 different centers. Prior to review, a list was developed of 35 potential factors, grouped into 9 categories, that could lead to ED visits. For each ED visit, the reviewing physician indicated the likely and most important factors for each visit; judged its medical necessity and whether the ED visit might be avoided in a more optimal health care system.

Results: Data on 29 ED visits from 27 unique patients was obtained. Diagnoses were ulcerative colitis in 8, Crohn's disease in 17 and indeterminate colitis in 2. Of ED visits, 62% led to admission (21% were pre-planned). The most important factors leading to ED visits were time after 4pm or weekend/holiday, 93%; disease severity or course, 90%; health care provider referral to ED, 66%; and patient self-referral, 45% (Table). The medical necessity of the ED encounter was felt to be definitely or probably not necessary for 24% (7 of 29) visits. In an optimal care delivery system, about 50% of ED were felt to be avoidable.

Conclusions: Physician analysis of ED visits in pediatric IBD suggests that a significant proportion may be avoided. Optimizing the health care system for improved access to specialty care may reduce ED visits.
Factors Associated with ED Visit

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<td>Day or Time</td>
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<td>Disease Severity or Course</td>
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<td>Provider Referral</td>
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### MARIJUANA USE IN ADOLESCENTS AND YOUNG ADULTS WITH AND WITHOUT INFLAMMATORY BOWEL DISEASE.

**Analice S. Hoffenberg**, Christian Hopfer, Jay Markson, Tory Garling, Jose Guerrero-Baez, Edward J. Hoffenberg, Psychiatry, University of Colorado Denver School of Medicine, Aurora, CO; Childrens Medical Center, PC, University of Colorado Denver School of Medicine, Denver, CO

**Background:** Cannabis has been proposed to have anti-inflammatory effects in inflammatory bowel disease (IBD). Use of marijuana (MJ) is common among adolescents and young adults and Colorado has recently legalized its use. We sought to determine the frequency of and motivations for use of MJ in our pediatric IBD center population.

**Methods:** We designed a cross-sectional pilot study using validated questionnaires to investigate substance use patterns among pediatric patients with (IBD), and without IBD (noIBD). Recruitment was from a pediatric IBD center patient population and from an urban private primary care outpatient office. Electronic surveys included PUCAI, sPCDAI, CIDI supplement which assesses both substance use and substance use disorders. Questions on MJ lifetime use (yes/no), patterns of use in the last 12 months (how often, Likert scale) and motivations of use (35 multiple choice items) were analyzed. At completion of the survey, all subjects received substance use counseling information.

**Results:** Surveys were completed by 65 IBD and 100 noIBD subjects. The groups were similar for gender but the IBD group was younger (16.3 vs 17.0 y) and more likely to be Caucasian (Table). No significant differences were found in lifetime MJ use between the two groups (31% IBD vs. 40% non-IBD; OR (95% CI)= 0.67 (0.34-1.29); p= 0.2284), but adolescents with IBD exhibited a more intense use of MJ (> 1x/week) than other adolescents (OR (95% CI)= 3.54 (1.14-11.05); p=0.0258). There were no differences in regard to MJ use motivations, except for physical symptoms help. IBD adolescents endorsed items reflecting MJ use to help with physical problems more often than other adolescents (Kruskal-Wallis test, p=0.0349).

**Conclusion:** Our data suggests that adolescents and young adults with IBD use MJ as often as, but more intensely than their peers without IBD. A motivational factor seems to be self-medication. Patients with IBD may be at higher risk for future substance use disorders. Care providers may consider screening for substance use. The utility of non-addictive cannabinoid compounds in improving physical symptoms of IBD needs further study.

MJ use in IBD and non-IBD adolescents and young adults

<table>
<thead>
<tr>
<th></th>
<th>IBD (n=65)</th>
<th>non-IBD (n=100)</th>
<th>p, OR (95% CI)</th>
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<tr>
<td>Age in yr, SD</td>
<td>16.3, 1.7</td>
<td>17, 2.8</td>
<td>0.0378</td>
</tr>
<tr>
<td>% Caucasian</td>
<td>48</td>
<td>55</td>
<td>NS</td>
</tr>
<tr>
<td>Ever used MJ (% yes)</td>
<td>88</td>
<td>65</td>
<td>0.0012</td>
</tr>
<tr>
<td>Use more than weekly (% yes)</td>
<td>31</td>
<td>40</td>
<td>0.2284, OR 0.67 (0.34-1.29)</td>
</tr>
</tbody>
</table>

### ADDRESSING BARRIERS TO INFLUENZA VACCINATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD).

Kathleen Huth, Eric I. Benchimol, Mary Aglipay, Kristen Moran, David R. Mack, Department of Pediatrics, University of Ottawa, Ottawa, ON, Canada; Children's Hospital of Eastern Ontario IBD Centre, Ottawa, ON, Canada

**Background:** International guidelines recommend annual influenza vaccination for immunocompromised children with IBD. Objectives: We sought to understand influenza vaccination practices in pediatric IBD patients, perceived barriers to vaccination, and strategies to increase vaccine uptake in this population.

**Study Design:** We conducted a survey of parents and patients aged ≥14 years at the CHEO IBD Centre from September 2012 through
March 2013. Descriptive statistics were used to determine annual influenza vaccination and reasons for non-vaccination. T-tests and Fisher's exact tests were used to determine the association between patient characteristics and their decision to vaccinate every year or most years. Results: 180 of 183 parents approached (98%) completed the survey along with all 108 adolescents. Mean patient age at study time was 13.8 ± 3 years, mean time from diagnosis was 3.3 years, 63% were males, and 66% had Crohn disease. 74% of patients were using immunomodulator medications or biologic agents. Only 34% of patients reported obtaining influenza vaccination annually. Reasons for non-vaccination included a perceived lack of benefit (29%), concerns about adverse events (19%), and needle aversion (18%). Additional barriers identified by patients included inconvenience (22%) and concerns of worsening IBD symptoms (17%). Most families (91%) reported they would obtain influenza vaccination if their physician provided evidence of its benefit, and 73% would obtain the vaccination if offered during IBD clinic visits. Vaccination of family members (P<0.001) and greater number of years since diagnosis (P=0.04) were factors associated with influenza vaccination in patients. Use of immunomodulators did not influence vaccination attitude. Conclusions: Influenza vaccination rate is low in IBD patients at risk for influenza complications. Providing education on vaccine safety may address some barriers faced by families, and concomitant influenza vaccination during IBD clinic visits may increase uptake.

229 USE OF A TEMPLATE IMPROVES DOCUMENTATION OF KEY ELEMENTS OF THE CLINICAL ENCOUNTER IN THE PATIENT WITH INFLAMMATORY BOWEL DISEASE (IBD). Esther J. Israel, Kristen Solemina, George H. Russell, Sarah M. Henderson, Pediatric Gastroenterology, Massachusetts General Hospital, Boston, MA

Introduction: Substantial variation occurs in the care of patients with pediatric Inflammatory Bowel Disease (IBD) resulting in inconsistencies in care delivery. The standard clinical encounter session is a challenge to the documentation of important elements for the care of the IBD patient. Consistent and easy to access documentation of key clinical components for the care of patients with IBD is also critical to our participation in ongoing improvement efforts such as the ImproveCareNow Quality Improvement Collaborative (ICN).

Methods: An 8-person quality improvement work team agreed to improve the variability of documentation of the IBD patient. After agreeing on the key clinical components for documentation at each visit for an IBD patient, based on the "bundle" required by ICN, the IBD Summary Sheet, an electronically embedded template with 5 key clinical measures was created. The defined measures included kinetic factors which require re-documentation at each visit such as disease activity, nutritional status and growth status, and static factors which are more stable, such as the Montreal disease classification and the last PPD. Findings: A chart review served as the source of preliminary baseline data. A chart review tool was used to review 200 randomly selected electronic medical record charts from 20 practitioners in the Pediatric GI practice seen over the preceding year. The five elements were documented with the following frequencies: 20% for PPD status, 48% for the location of disease involvement; IBD phenotype in 12%, disease activity in 8%, and nutritional parameters 88% of the time. A composite measure of all 5 components showed that not one patient had all of the components of the "bundle" documented. Using prioritization methodology, an IBD Summary template in the electronic medical record was chosen by the working group as the tool to be tested for better documentation. During a 4 week intervention period, the template was used in 76% of IBD patients seen by the 8 practitioners in the working group. Documentation of the composite bundle was 100% in those patients with the template. Subsequently, other elements of the encounter have been added to the template with excellent compliance. This effort has been expanded to the entire 26 member professional staff. This template has facilitated our division's participation in ICN with 83% of our IBD population, numbering 700, now enrolled. Compliance with the use of the IBD Summary sheet is presently at 82% of encounters for these IBD patients. Summary and Conclusions: A change in the process of documentation from a free style note to the readily available and accessible template should facilitate accurate documentation for these purposes.
clinical assessment and PCDAI or PUCAI. 18 Patients had high FC levels (>200 μg/g), 11 Crohn’s disease and 7 Ulcerative colitis. Patients. In 15 out of 18 patients with elevated FC, the management plan was change on the basis of the FC result, significant at p<0.05. These included repeat colonoscopy, additional diagnostic imaging or intensification medical treatment. CONCLUSIONS: Our study has shown that FC correlates well with the disease activity in pediatric IBD patients. Patient management plans were changed in the majority of patients with elevated FC levels. Further study is required to determine whether changes improved patient outcomes.

231 ROLE OF PERCUTANEOUS DRAINAGE IN THE MANAGEMENT OF INTRA-ABDOMINAL ABSCESSES IN PEDIATRIC CROHN'S DISEASE. Jess L. Kaplan1, Brian Pugmire2, Mayureewan Taphey2, Peter Hahn3, Daniel Doody3, Debra Gervais2, Harland Winter1, Michael S. Gee3, 1Division of Pediatric Gastroenterology, MassGeneral Hospital for Children, Boston, MA; 2Department of Radiology, Massachusetts General Hospital, Boston, MA; 3Department of Pediatric Surgery, Massachusetts General Hospital, Boston, MA

BACKGROUND/AIMS: Intra-abdominal abscesses (IAA) are a well-known complication of penetrating Crohn's Disease (CD) and occur with regularity in the pediatric population. Percutaneous drainage (PD) has been shown to be a safe and effective method for the treatment of CD-related abscesses in adults, but few studies have evaluated its success in the children specifically. We present data from a retrospective review of 26 cases of pediatric CD patients who underwent PD for CD-related abscesses.

METHODS: We retrospectively reviewed the medical records of 26 patients (age < 21 years) with CD who underwent PD of IAA at Massachusetts General Hospital between 1995 and 2012. Success of PD was defined as (1) no surgery within one year of drainage with resumption of IBD-related medical therapy within 8 weeks of the time of drainage or (2) surgical bowel resection following drainage with no evidence of residual abscess on imaging or at surgery. Various patient characteristics (gender, age, abscess size and volume, affected bowel segment, and need for repeat PD) were analyzed using the Fisher exact test to assess for factors associated with treatment success or failure.

RESULTS: The average age of the patients at the time of treatment was 17.5 years (range 10-20 years) with a male to female ratio of 15:11. Average disease duration at the time of IAA was 30 months (range 0-108 months). 10/26 (38%) patients had associated strictureing disease behavior. Twenty-one of 26 (81%) IAA were spontaneous and 5 of 26 (19%) were post-surgical. Medications at the time of IAA diagnosis included 5-aminosalicylates (46%), prednisone (34%), immunomodulators (34%) and biologics (12%). The majority of PD procedures (85%) were CT-guided. Using the criteria listed above, 19 of the 26 patients were classified as having undergone successful drainage, six were classified as treatment failures, and one patient could not be classified, giving a treatment success rate of 73%. Six patients required additional PD procedures and two required surgical drainage of IAA after initial PD. Seven patients resumed immunosuppressive medications within 8 weeks of PD. Among the multiple factors analyzed, large abscess volume (>100cc) was the most strongly associated with PD treatment success but did not reach statistical significance (p = 0.13).

CONCLUSION: Percutaneous image-guided drainage is an effective treatment for CD-related intra-abdominal abscesses in pediatric patients and should be considered in their management. Abscess size, location and number do not seem to have an effect on treatment success. PD may obviate the need for more invasive surgical drainage and allows for brisk resumption of immunosuppressive medications after drainage.

232 COMPLEX BACTERIOTHERAPY IN PEDIATRIC GASTROINTESTINAL DISORDERS. Richard Kellermayer1, Dorotty Nagy-Szakal1, Sabina A. Mir2, Ruth A. Luna2, Milena Pitashny2, Emily Hollister2, Deborah Schady2, Samir Shafi1, Jason M. Reynolds1, Monica E. Lopez2, Caroyl L. Gilbert1, Mark A. Gilger1, James Versalovic1, 1Section of Pediatric Gastroenterology, Baylor College of Medicine, Houston, TX; 2Department of Pathology, Baylor College of Medicine, Houston, TX; 3Section of Pediatric Anesthesiology, Baylor College of Medicine, Houston, TX

BACKGROUND & AIMS: Recent studies have shown the efficacy of complex bacteriotherapy, such as fecal microbiota transplantation (FMT), for the treatment of antibiotic-refractory Clostridium difficile infection (CDI). Serial FMTs have been indicated to potentially cure chronic inflammatory intestinal disorders, such as ulcerative colitis (UC) as well. This therapeutic option has been rarely explored in children. METHODS: Colonoscopic FMT was given in one UC-associated and one community acquired CDI case under IRB approved protocols. Serial FMT was administered in 4 cases of biologic agent- or immunomodulator-dependent UC with concomitant withdrawal of conventional treatments. The fecal microbiome was studied by 454 pyrosequencing of the bacterial 16S rRNA gene. RESULTS: A single FMT treated the community acquired case of CDI. Three FMTs were required to provide persistent (over 4 week) clearance of C. difficile in the patient with moderately active UC. Within the UC trial, one patient could not retain the enemas and was excluded from the study. One patient was successfully weaned off infliximab to mesalamine and is in remission for over 5 months. Another steroid dependent patient who was for 4 weeks without treatment after FMTs is now in clinical remission on oral mesalamine after a minor flare. One patient remains in clinical and histological remission off of any therapy for over 6 weeks after the FMTs. FMT induced significant microbiome changes indicating its effects to go beyond simple engraftment of the donor microbiota. CONCLUSIONS: Complex bacteriotherapy is a promising treatment modality for pediatric CDI and UC. Further studies are required to elucidate the long term safety and efficacy of this therapy.

233 SEASONAL VARIATIONS IN PEDIATRIC IBD INCIDENCE. Ali Khalili, Gilian Tam, Reinaldo Garcia, Zili Zhang, Thomas Sferra, Judy Splawski, Pediatric GI, University Hospitals. Cleveland, OH

Background: Inflammatory Bowel Disease (IBD) is a chronic, immune-mediated disease of the gastrointestinal tract. The etiology of IBD still remains unclear but thought to be a combination of genetic and environmental factors. Numerous infectious agents including viruses have been linked to the development and exacerbation of IBD. Many pathogens such as viruses and allergens have seasonal variations. Conflicting data have been reported about the seasonal variation of IBD. We hypothesized there is a seasonal variation in the incidence of IBD here at Rainbow Babies and Children's Hospital (RBC).

Objectives: To evaluate for seasonal variations in the onset of pediatric IBD.
Methods: This was a retrospective study of all the patients who underwent colonoscopy in RBC from January 2008 to December 2010. We included all the pediatric patients (<21 yrs old). Patients with previous history of IBD and non-IBD colitis were excluded. We obtained patient's demographics (age, gender), date of visit prior to colonoscopy and date of scope. Biopsy results were categorized into normal and abnormal groups. We used Chi-square and logic regression analysis.

Results: There were a total of 1347 colonoscopies and 1069 patients, where 960 patients had no IBD and 99 had a new diagnosis of IBD. Median age was 13 years and 55.5% were female. The incidence of IBD was 9.3%. Patients were significantly more likely to develop IBD between the ages of 13-15 years (P=0.003). IBD was 2.5 times more likely with 95% CI (1.3-4.5) to occur in summer season (between July to September) compared to winter time. This seasonal variation was also significantly noted in the incidence of ulcerative colitis.

Conclusions: Our results demonstrated a seasonal variation in the incidence of pediatric IBD here in RBC with a peak in summer time. These finding can perhaps be due to environmental factors, such as viruses and allergens that also have seasonal variations.

234 ANTI-INFLAMMATORY EFFECT OF BUTANOL PURIFIED CHINESE HERBAL FORMULA FAHF-2 AND ITS PURIFIED COMPOUNDS ON PBMCs OF PEDIATRIC CROHN'S DISEASE SUBJECTS. Joanne Lai, Changda Liu, Ying Song, Clare Ceballos, Nan Yan, Keith Benkov, Xiu-Min Li, David Dunkin, 1Pediatric Gastroenterology, Mount Sinai School of Medicine, New York, NY; 2Pediatric Allergy & Immunology and Jaffe Food Allergy Institute, Mount Sinai School of Medicine, New York, NY

Background: Crohn’s disease is a form of inflammatory bowel disease characterized by chronic inflammation of the gastrointestinal tract and causes significant morbidity in the pediatric population. Since current IBD treatments may lead to serious side effects, there is a growing interest in complementary treatments. Food Allergy Herbal Formula-2 (FAHF-2) has been used historically in China to treat colitis, providing the basis for investigating its anti-inflammatory effects in children with CD. Prior studies confirm the ability of FAHF-2 to inhibit production of the pro-inflammatory cytokine tumor necrosis factor-α (TNF-α) by peripheral blood mononuclear cells (PBMCs) from children with UC. To ease clinical study, we generated butanol purified FAHF-2 (B-FAHF-2), which reduces daily oral consumption by 80%. Ganoderic acid C1 and β1 (GA-C1 and GA-β), which were isolated from ganoderma lucidum in B-FAHF-2, inhibited TNF-α production by a murine macrophage cell line.

Methods: PBMCs were isolated from 24 pediatric subjects (13 CD, 11 control), cultured with B-FAHF-2 60µg/mL, GA-C1 40µg/mL, GA-β 40µg/mL, or dexamethasone 10-5µM/mL, in the presence of lipopolysaccharide (LPS) or anti-CD3/CD28 stimulation. TNF-α production in culture supernatants was measured by ELISA.

Results: As seen in FAHF-2, B-FAHF-2 as well as GA-C1 and GA-β inhibited the production of TNF-α (p<0.05) by PBMCs derived from pediatric CD and control subjects in a non-cytotoxic manner when cells were stimulated by LPS and anti-CD3/CD28. This inhibition of TNF-α production in response to both stimuli was similar to the effect of dexamethasone, which served as a positive control. Conclusions: B-FAHF-2, GA-C1 and GA-β derived from FAHF-2, suppress TNF-α production by PBMCs from CD subjects to a similar extent as dexamethasone. These active compounds have the potential to be used as treatments for CD. Further research will test B-FAHF-2, GA-C1 and GA-β on blood and biopsy specimens from a larger sample size of pediatric IBD subjects, evaluate efficacy in murine models of colitis, and determine their mechanism of action.

235 INFLAMMATORY BOWEL DISEASE ACTIVITY AND DISTRIBUTION IN CHILDREN WITH AND WITHOUT PRIMARY SCLEROSING CHOLANGITIS. Laura Lascurain, Mark R. Deneau, Stephen Guthery, M. Kyle Jensen

University of Utah, Salt Lake City, UT

Introduction: That interplay between primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD) is poorly described in children. Adult series describe a milder clinical course and higher prevalence of pancolitis and rectal-sparing in IBD patients with PSC. We compared clinical and endoscopic disease activity, and colonic disease distribution in pediatric IBD patients with and without PSC.

Methods: We identified all patients in the region with pediatric-onset IBD and PSC from 1986-2011 using population-based methodology. We matched each PSC-IBD case with 3-4 controls of the same IBD phenotype (ulcerative colitis (UC) or Crohn's disease). We reviewed medical records and endoscopy images on all patients. We assigned physician's global assessment (PGA) to all patients, and Mayo endoscopic severity scores to UC patients, at diagnosis and one year later. We followed patients until time of diagnosis or 1 year after.

Results: We identified 39 cases of IBD with PSC (median age 14.2 [IQR 9.9-16.7] years, 66.7% male), and 137 cases without PSC (median age 14.1 [IQR 11.4-16.8] years, 55.5% male). 88.0% had UC, 12% had CD. Median disease activity was similar between both groups on all measures: initial Mayo score (2 vs. 2), 1yr Mayo score (2 vs. 2), proportion with improved Mayo score (23.5% vs. 15.7%), proportion with worsened Mayo score (61.8% vs. 56.2%); initial PGA score (2 vs. 2), 1yr PGA score (1 vs. 1), proportion with improved PGA score (35.9% vs. 27.0%), and proportion with worsened PGA score (35.9% vs. 54.7%), in those with and without PSC, respectively. Five year colectomy-free survival was 81.8% (95%CI 63.0-91.6) in those with PSC, and 74.9% (95%CI 65.7-82.0) in those without PSC. Disease distribution was similar between groups, with pancolitis in 87.1% vs. 72.7% and rectal-sparing in 22.6% vs. 16.4% in patients with PSC and without PSC, respectively. p=NS for all comparisons.

Conclusions: No difference existed in the clinical activity, endoscopic activity or colonic distribution of IBD in a population-based cohort of pediatric IBD patients with and without PSC. Liver disease from PSC does not appear to affect the phenotype of IBD in children.

236 DECOMPOSING PCDAI INTO CONSTITUENT COMPONENTS IN THE ANALYSIS OF BODY COMPOSITION IN PEDIATRIC CROHN'S DISEASE. Dale Lee, James D. Lewis, Robert Baldassano, Mary Leonard

1Pediatric Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 2Gastroenterology, University of Pennsylvania, Philadelphia, PA; 3Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA

BACKGROUND: Crohn's disease (CD) activity can be an important driver of changes in both lean mass (LM) and fat mass (FM). PCDAI is a validated measure of disease activity and broadly used in clinical studies. In this study we decompose PCDAI into history,
lab, and exam components, and assess associations between individual components and both LM and FM.

METHODS: Subjects ages 8-21 years, with >6 months since CD diagnosis, and a bone mineral density <25th % for age were eligible. Over 24 months, leg LM (excluding bone) and whole body FM were assessed using DXA. Race and sex-specific z-scores for LM and FM were generated relative to age, and then adjusted for leg-length and height z-scores respectively (LM-Z, FM-Z) to account for differences in body size and maturation. At each visit, anthropometry, Tanner stage, PCDAI, medications, and caloric intake were assessed. Physical activity was measured with accelerometers worn for one-week intervals quarterly. PCDAI scores (range 0-100) were decomposed into history (0-30), lab (0-20), and examination (0-50) components. "Examination" was then further decomposed into "physical" (0-30) and "growth" (0-20). Generalized estimating equations were used to assess determinants of changes over time in LM-Z and FM-Z.

RESULTS: This study enrolled 138 subjects with a median (range) disease duration of 2.7 (0.5-11.8) yrs. At baseline 62% of subjects had inactive CD (PCDAI<10), 33% mild activity (PCDAI 11-30), and 5% moderate-to-severe CD (PCDAI>30). Over 24 months, the proportion of children with moderate-to-severe disease decreased to 2% (p=.04), systemic glucocorticoid use decreased from 13 to 6% (p=.04), and anti-TNF-α medication use increased from 31 to 41% (p<.005). The table below demonstrates adjusted associations between PCDAI (and decompositions) and LM-Z and FM-Z, respectively. LM-Z was negatively associated (p<.05) with each PCDAI component, even with all components included in the same model. FM-Z was not associated with total PCDAI (p=.07), but the lab component of PCDAI was negatively associated (p=.005 and .01, respectively). Excluding subjects with no potential to receive points for delayed "growth" (females >=15 and males >=18 yrs), our analysis produced similar results.

CONCLUSION: History, lab, and examination are individual components of PCDAI that were all independently associated with LM-Z. Total PCDAI is not associated with FM-Z, but the "lab" component of PCDAI was associated. PCDAI is potentially limited by a physical exam component that considers growth velocity in some adolescents who are done growing, but this did not alter results in our analysis.

Table: Multivariate longitudinal models for leg LM and whole body FM Z scores

<table>
<thead>
<tr>
<th>Model</th>
<th>Covariates</th>
<th>LM-Z model</th>
<th>FM-Z model</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>PCDAI</td>
<td>Beta-coeff</td>
<td>p-val</td>
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<tr>
<td>Model 1:</td>
<td></td>
<td>-0.016</td>
<td>&lt;.005</td>
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<td>Model 2:</td>
<td>PCDAI—history PCDAI—labs PCDAI—exam</td>
<td>-0.008 -0.028 -0.027</td>
<td>.03 &lt;.005</td>
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<tr>
<td>Model 3:</td>
<td>PCDAI—history PCDAI—labs PCDAI—exam (physical)</td>
<td>-0.008 -0.029 -0.019 -0.030</td>
<td>.02 .01 &lt;.005</td>
</tr>
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</table>

**Models adjusted for study visit, physical activity quartile, % expected energy intake, race, tanner stage, age, sex

237 LAB MONITORING FOR IBD PATIENTS ON INFlixIMAB - COST REDUCTION BY STANDARDIZATION OF CARE. Diana G. Lerner1, John Grantham2, Joshua Noe3, Steven Werlin1. 1Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI; 2Business Intelligence and Data Warehousing, Children's Hospital of Wisconsin, Milwaukee, WI

Background: Infliximab, the first in the class of anti-TNF monoclonal antibodies, was approved for treatment of Crohn's disease in 1998. Due to novelty of this medication and patient convenience, routine blood monitoring was done at every infusion. No published recommendations exist to guide this practice. Newer anti-TNF-α medications (adalimumab, certiluzimab) are administered at home and blood work is ordered less frequently. We developed an algorithm of anti-TNF-α medications to be administered at home and a protocol to guide this practice. Newer anti-TNF-α medications (adalimumab, certiluzimab) are administered at home and blood work is ordered less frequently.

Aims: 1. To identify the frequency and content of routine blood work ordered by 15 pediatric gastroenterologists 2. To standardize this practice by clinical necessity and cost consciousness.

Methods: The records of all patients who received infliximab infusions between October 2010 and October 2012 at the Children's Hospital of Wisconsin were identified via Sunrise Clinical Manager (Allscripts) (n=200). Analysis was completed for patients who received infliximab for at least 12 months (n=95). All blood work associated with infusions was evaluated for frequency and types of labs ordered. A subcommittee of IBD specialists was formed for the development of standard monitoring recommendations based on literature review and the known side effect profile of infliximab.

Results: The mean time between infusions was 48 +/- 11.7 days. All physicians ordered lab tests with each infusion but the nature and cost of labs varied between physicians (table 1). The mean billed per year on blood monitoring was calculated at $562 per visit and $5129 per patient per year (range 2742-8979). The IBD committee proposed to standardize practice in clinically stable patients and obtain a complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) with every other infusion. This does not include the annual recommended labs done at our institution (ALT, 25-hydroxy vitamin D, iron studies, creatinine). Anticipated per patient cost for regular blood monitoring after the implemented guidelines will be reduced $295.75 per lab draw. Retrospective analysis of 95 patients indicated that the proposed modification has the capacity to decrease healthcare utilization in blood monitoring by 75% ($496,278.75 to $122,440.50 per year).

Conclusion: Implementation of the new protocol will standardize care for patients on infliximab and eliminate costs associated with unnecessary blood monitoring. This model can be applied to patients with other chronic diseases and serve to improve the value of care provided by medical professionals.
Percent of Physicians Ordering Infliximab Monitoring Labs at Each Price-Point

<table>
<thead>
<tr>
<th>Percent of physicians ordering labs at each price point</th>
<th>Labs ordered</th>
<th>Cost of lab panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>41%</td>
<td>CBC, ESR, LFT</td>
<td>$483</td>
</tr>
<tr>
<td>25%</td>
<td>CBC, CMP, ESR, CRP</td>
<td>$748</td>
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<tr>
<td>25%</td>
<td>CBC, CRP, ESR, LFT</td>
<td>$565</td>
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<tr>
<td>8%</td>
<td>CBC, ESR, CRP, Albumin, ALT, BUN</td>
<td>$385</td>
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</tbody>
</table>

Complete Blood Count with differential (CBC), Erythrocyte Sedimentation Rate (ESR), Complete Metabolic Profile (CMP), C-Reactive Protein (CRP), Liver Function Tests (LFT)

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DIAGNOSTIC IMPLICATION OF INTESTINAL WALL THICKENING BY COMPUTERIZED TOMOGRAPHY SCANS IN A PEDIATRIC EMERGENCY DEPARTMENT. Ross Malitz, John W. Ibrahim, Farrah Lazare, Tuvia Marciano, Donald Brand, Fred Daum, Pediatrics, Winthrop University Hospital, Mineola, NY

Objective: To determine what percentage of children seen at Winthrop University Hospital (WUH) with intestinal wall thickening by Computerized Tomography (CT) scan have Inflammatory Bowel Disease (IBD) defined by endoscopy/histology.

Methods: A chart review was conducted at Winthrop University Hospital (WUH), Mineola New York. Subjects were 5 to 18 years of age seen in the Pediatric Emergency Department at Winthrop University Hospital (WUH) from January 1, 2007 through July 6, 2012 who had abdominal CT scans of the abdomen and pelvis were done. Patients with a history of IBD, appendicitis, trauma or cystic fibrosis requiring lipase supplementation were excluded. 108 charts meeting the inclusion criteria were reviewed. Endoscopy/histology data confirming the diagnosis of IBD were noted.

Results: 58/108 (54%) subjects were seen by a pediatric gastroenterologist at WUH. 25/58 (43%) had upper and lower endoscopy. 8/25 (32%) were diagnosed with IBD.

Conclusion: The total number of patients diagnosed with IBD (7.4%), represents the least number of children in this study who might have IBD. Despite limitations of this study, the prevalence of IBD in children with intestinal wall thickening is high enough to warrant a prospective study.

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ROLE OF RECTAL EXAM IN SCREENING FOR INFLAMMATORY BOWEL DISEASE. Christopher J. Moran¹, Jess L. Kaplan¹, Peter Masiakos², Harland Winter¹, ¹Pediatrics, MassGeneral Hospital for Children, Boston, MA; ²Pediatric Surgery, MassGeneral Hospital for Children, Boston, MA

BACKGROUND: Pediatric inflammatory bowel disease (IBD) often presents insidiously, and the optimal set of non-invasive screening testing remains unclear. As serum and stool inflammatory markers and antimicrobial antibodies become more widely available, the reliance on physical examination diminishes. We hypothesized that the value of a rectal exam in the initial screening for IBD in children contributes to the diagnosis. METHODS: The medical records of consecutive patients undergoing endoscopic evaluation for possible IBD were reviewed for laboratory values (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), platelets, hematocrit, and albumin) and documentation of rectal exam (perianal examination and occult blood testing) prior to the day of endoscopic evaluation. Standard limits of normal lab values were used to determine abnormal values (with the exception of hematocrit in which age-specific normal values were used). The sensitivity and specificity of individual laboratory tests were determined. An abnormal rectal exam was defined as either occult blood or any perianal disease. Multi-variate logistic regression was performed to determine which laboratory values and rectal exam results would best predict IBD. RESULTS: We identified 335 patients (49 Crohn's disease, 24 ulcerative colitis, 12 IBD-U, 250 non-IBD). 61.2% had a complete rectal exam prior to their diagnostic procedure, including 67.1% (57/85) of IBD patients and 59.2% (148/250) of non-IBD patients. In the cohort of patients with all labs drawn and a complete rectal exam performed (41 IBD patients and 78 non-IBD patients), the sensitivity and specificity of ESR were 46.3% and 92.3%, CRP were 51.2% and 91.0%, hematocrit were 48.8% and 57.7%, albumin were 19.5% and 98.7%, and platelets were 33.8% and 95.5% for IBD. The sensitivity and specificity of rectal exam was 65.9% and 72.0%. After logistic regression modeling of 119 patients (41 IBD and 78 non-IBD patients), the rectal exam was the best predictor of IBD. CONCLUSION: Complete rectal exams (including stool guaiac) are not routinely performed as part of the initial evaluation for IBD. The rectal exam remains a key predictor that should be included in initial screening for pediatric IBD.

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WHOLE EXOME SEQUENCING IN VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE. Christopher J. Moran¹, Judith Kelsen¹, Jess L. Kaplan¹, Mariah Baril-Dore³, Lili Schindelar¹, Batya Vais§, Barbara Kirschner⁴, Robert Baldassano², Ramnik Xavier³, Harland Winter¹, Mark J. Daly⁵, ¹Pediatrics, MassGeneral Hospital for Children, Boston, MA; ²Pediatric Gastroenterology, Children's Hospital of Philadelphia, Philadelphia, PA; ³Pediatrics, Sheba Children's Medical Centre, Tel Hashomer, Israel; ⁴Pediatric Gastroenterology, University of Chicago/Comer's Children Hospital, Chicago, IL; ⁵Gastroenterology, Massachusetts General Hospital, Boston, MA; ⁶Broad Institute of Massachusetts Institute of Technology and Harvard University, Cambridge, MA; ⁷Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, MA

BACKGROUND: Meta-analyses of genome-wide association studies (GWAS) have now identified single nucleotide polymorphisms in >160 genes that are associated with risk for developing inflammatory bowel disease (IBD). GWAS of pediatric IBD have identified a smaller number of SNPs associated with risk of pediatric IBD, although the majority of patients studied in those cohorts are adolescent-onset patients. Recent reports of loss-of-function mutations in interleukin-10 (IL-10), IL-10 receptor (IL-10R), and x-linked inhibitor of apoptosis (XIAP) have strengthened the interest in investigating the genetic causes of very early onset IBD as these patients may...
EPIGENETIC SEPARATION OF ULCERATIVE COLITIS IN TREATMENT NAIVE CHILDREN. Dorottya Nagy-Szakal, R. A. Harris, Sabina A. Mir, Else Frank, Reka Szidgeti, Jess L. Kaplan, Jiri Bronszky, Antone Opekun, George D. Ferry, Harland Winter, Richard Kellermayer, Department of Pediatrics, Baylor College of Medicine, Texas Children's Hospital, Houston, TX; Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX; Department of Computer Science, University of Waikato, Hamilton, New Zealand; Department of Pathology, Baylor College of Medicine, Houston, TX; Department of Pediatrics, Mass General Hospital for Children, Boston, MA; Department of Pediatrics, Charles University and University Hospital Motol, Prague, Czech Republic; Department of Gastroenterology, Baylor College of Medicine, Houston, TX

BACKGROUND & AIMS: Inflammatory bowel diseases (IBD) are emerging globally, supporting the hypothesis that environmental factors may play a role in their pathogenesis. Epigenetic changes can occur in response to environment. Epigenetic processes, such as DNA methylation, have been implicated in the pathogenesis of IBD. We evaluated colonic mucosal DNA methylation in association with gene expression in treatment naive pediatric IBD. METHODS: DNA methylation from transverse colonic biopsy specimens was examined by Infinium HumanMethylation450 BeadChip Kits in a discovery cohort (10 control patients [C], 10 patients with Crohn disease [CD], and 4 patients with ulcerative colitis [UC]) as well as a validation cohort (13 C, 4 CD, 5 UC). Methylation changes were validated by bisulfite pyrosequencing at select loci. Machine learning was employed to determine methylation based differential diagnostic algorithms. UC specific gene expression was interrogated in a subset (5 C and 5 UC) of adjacent samples by Affymetrix GeneChip PrimeView Human Gene Expression Arrays. RESULTS: There was a significant and consistent DNA methylation separation of untreated pediatric UC in the discovery and validation cohorts (4277 CpG sites; FDR<0.01) compared to controls. Following single nucleotide polymorphism (SNP) filtering, machine-learning-identified the top 2 CpG sites differentiating UC from control in the discovery cohort of UC in the discovery and validation cohorts (4277 CpG sites; FDR<0.01) compared to controls. Following single nucleotide polymorphism (SNP) filtering, machine-learning-identified the top 2 CpG sites differentiating UC from control in the discovery cohort and performed with an AUC=0.967 (p-value=0.001) in the validation cohort. The UC-linked, SNP-filtered methylation changes showed an association with the expression of 438 genes. CONCLUSIONS: A significant epigenetic separation of untreated pediatric UC in transverse colonic mucosa was observed. These findings may have etiologic, diagnostic and therapeutic relevance for IBD.

EFFECTIVENESS AND COST-EFFECTIVENESS OF FECAL CALPROTECTIN IN DIAGNOSIS OF PEDIATRIC INFLAMMATORY BOWEL DISEASE. K. T. Park, Nick Clark, Zhuo Yang, Center for Health Policy / Primary Care Outcomes Research, Stanford University, Palo Alto, CA; Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Stanford University, Palo Alto, CA; Center for Healthcare Policy and Research, University of California, Davis, Davis, CA

Background & Aims: The level of fecal calprotectin (FC) can predict the onset of inflammatory bowel disease (IBD) with high accuracy and precision. We evaluated the cost-effectiveness of using measurements of FC to identify children who require endoscopic confirmation of IBD. We compared pediatric results with our previous analysis in adult patients.

METHODS: We constructed a decision analytic tree to compare the cost-effectiveness of measuring FC before endoscopy examination with that of direct endoscopic evaluation alone. A second decision analytic tree was constructed to evaluate the cost-effectiveness of FC cut-off levels of 100 µg/g vs 50 µg/g (typically used to screen for intestinal inflammation). The primary outcome measure was the incremental cost required to avoid 1 false-negative result using FC level to diagnose new-onset IBD.

RESULTS: In children, FC screening saved $300/patient but delayed diagnosis for 4.8/61 patients with pediatric IBD, among 100 screened patients. If endoscopic biopsy analysis remained the standard for diagnosis, direct endoscopic evaluation would cost an additional $6250 in children to avoid 1 false-negative result from FC screening. Sensitivity analyses showed that cost effectiveness of FC screening varied with the sensitivity of the test and the pre-test probability of IBD in children. Pre-test probabilities for IBD of <65% in children made FC screening cost-effective, but cost ineffective if the probabilities were >78%. Compared to the FC cut-off level of 100 µg/g, the cut-off level of 50 µg/g cost an additional $43 but yielded 6.1 additional accurate diagnoses of IBD per 100 screened children.

CONCLUSIONS: Screening patients with measurements of calprotectin is effective and cost-effective in identifying those with IBD on a per-case basis when the pretest probability for IBD is <65% for children. Compared to our prior analysis in adults, the utility of FC screening is slightly less in children than in adults. Increasing the FC cut-off level to >50 µg/g increases diagnostic accuracy without substantially increasing total cost.
METABOLIC ANALYSIS OF EXHALED BREATH TO IDENTIFY VOLATILE ORGANIC COMPOUNDS (VOCS) IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE AND IRRITABLE BOWEL SYNDROME. Nishaben Patel1, Katharine Eng1, Frank Cikach1, David Grovë2, Lori Mahajan1, Raed Dweik2, Naim Alkhouri1, 1Pediatric Gastroenterology, Cleveland Clinic, Cleveland, OH; 2Respiratory Institute, Cleveland Clinic, Cleveland, OH

Background: Distinguishing inflammatory bowel disease (IBD) from functional causes of abdominal pain, such as irritable bowel syndrome (IBS), can be challenging. Children with IBD often undergo unnecessary endoscopic, histologic, and radiographic tests which are costly, invasive, and can result in diagnostic uncertainty. The aim of this study was to analyze the exhaled human breath for volatile organic compounds and develop a simple noninvasive screening test to distinguish IBD from IBS.

Methods: An IRB approved prospective study was conducted at a tertiary center. Patients (age range, 5-21 years) with documented IBD and IBS were recruited from the Pediatric Gastroenterology Clinic. The diagnosis of IBD was confirmed by endoscopic, histologic, and radiographic data. The diagnosis of IBS was established using the Rome III criteria. Exhaled breath was collected and analyzed using a selective ion flow tube (SIFT-MS) to identify new markers or patterns of IBD.

Results: 75 patients were included in the study (62 with IBD and 13 with IBS). Compared to the IBD group, the IBS group was significantly younger (12.7± 3.6 vs. 15.7± 3.4 years), had a higher mean BMI percentile (75.2% vs. 53.7%), and more likely to be Caucasian (100% vs. 88%); p < 0.05 for all. Approximately 80% of the IBD cohort was in remission based on standardized pediatric IBD activity index tools. Routinely analyzed VOCs for SIFT-MS quantification showed significant increases in exhaled 2-propanol, benzene, carbon disulfide, dimethyl sulfide, 2-nonen in patients with IBD (p value < 0.001) (Table 1). Discriminant analysis via stepwise variable selection of mass scanning ion peak data demonstrated three ion peaks (2-propanol, O2+28+, O2+50+) can discriminate between children with IBD and those with IBS with good accuracy (p < 0.0001).

Conclusion: Exhaled breath analysis maybe a promising non-invasive screening method to distinguish children with IBD from children with IBS. Exhaled 2-propanol, benzene, carbon disulfide, dimethyl sulfide, 2-nonen are novel biomarkers that are significantly elevated in the breath of children with IBD as compared to children with IBS. We provide pilot data to support the hypothesis that a unique breathprint can be demonstrated for IBD and IBS in the exhaled metabolome.

Table 1: Exhaled Volatile Organic Compound Concentrations (all in parts per billion) in IBD and IBS groups

<table>
<thead>
<tr>
<th>VOCs</th>
<th>Median [25%,75%] ppb</th>
<th>Median [25%,75%] ppb</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>IBD</td>
<td>IBS</td>
</tr>
<tr>
<td>2-propanol</td>
<td>115.5 [84.5, 139.1]</td>
<td>49.3 [35.1, 74.1]</td>
</tr>
<tr>
<td>Benzene</td>
<td>2.09 [1.7, 2.6]</td>
<td>1.3 [1.1, 1.4]</td>
</tr>
<tr>
<td>Carbon disulfide</td>
<td>1.7 [1.2, 2.3]</td>
<td>1.1 [1.0, 1.4]</td>
</tr>
<tr>
<td>Dimethyl sulfide</td>
<td>1.2 [0.9, 1.4]</td>
<td>0.6 [0.5, 1.0]</td>
</tr>
<tr>
<td>2-nonen</td>
<td>1.8 [1.4, 2.6]</td>
<td>1.2 [0.9, 1.6]</td>
</tr>
</tbody>
</table>

Significant increases were demonstrated in exhaled 2-propanol, benzene, carbon disulfide, dimethyl sulfide, 2-nonen in patients with IBD compared to patients with IBS.

RISK FACTORS FOR UNDER DOSING THIOPURINES IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Analise Peleggi, Leslie Higuchi, Jessica Kerr, Rajat Moman, Tracee Saslovsky, Lori Hartigan, Jenifer Lightdale, Gastroenterology, Hepatology and Nutrition, Children's Hospital Boston, Boston, MA

Azathioprine (AZA) and 6-mercaptopurine (6MP) are thiopurines that can be dispensed as either suspensions or 50-mg tablets to treat children with inflammatory bowel disease (IBD). As measured by ImproveCareNow (ICN), a national learning healthcare system dedicated to improving the quality of pediatric IBD healthcare, thiopurine dosing in children should be adjusted in line with individual body weight and thiopurine methyltransferase (TPMT) activity. Although precise dosing may be possible with suspensions, patients using fixed-dose tablets may be at risk for inexact dosing. Aim: To identify patient risk factors for insufficient dosing of thiopurines, as defined by the Collaborative's "Model Care" guidelines. Methods: We reviewed the Population Management Report (dated 5/17/13) of all patients consented and enrolled in ICN at Boston Children's Hospital to identify the total number who had a TPMT profile recorded and who were taking a thiopurine at their most recent clinic visit. Per ICN protocol, we excluded patients who were prescribed allopurinol, infliximab, alendrinab, and certozilumab, as well as those with unknown TMPT status. Target doses were determined by TPMT profile: For patients with intermediate activity, target doses of AZA were defined as ≥1.0mg/kg/day and target doses of 6MP were ≥0.5mg/kg/day. For normal-high TPMT activity: target doses of AZA were ≥2.0mg/kg/day and target doses of 6MP were ≥1.0 mg/kg/day. All patients were characterized in terms of age, gender, weight, TPMT profile and disease activity, as well as drug type and formulation (suspension or tablet). Results: Of 609 patients actively enrolled in ICN at our institution, 185 (103 (56%) male; median age 17 years (IQR 14, 19); weight 58.5kg (IQR: 51, 69)) were eligible for the thiopurine metric, with the great majority using tablets (98%), and most taking 6MP (95%). 73/185 (40%) were identified as not receiving Model Care thiopurine doses. Comparing patients who received Model Care vs. not, there were no differences in median age (17 yrs vs.16, p=0.9), gender (57% male vs. 53%, p=0.6), TPMT activity (90% normal-high vs. 86%, p=0.4), use of AZA (5% vs. 4%, p=0.7), disease activity (83% inactive disease vs. 84%, p=0.9), or use of tablets (98% vs. 97%, p=0.6). 29/73 (40%) of patients not receiving Model Care were within 0.1mg/kg of their target dose. Taking TPMT activity and drug type into account, patients ≥50kg were receiving on average 0.2mg/kg less drug per day than their lighter counterparts. They were also more likely to be under their target dose (89% vs. 11%, p=0.001). Discussion: Most patients at our institution...
on thiopurine therapy for IBD were teenagers who weighed more than 50kg. Both teenagers and younger patients were more likely to use tablet formulations of thiopurines, which are difficult to split into precise doses. Patients weighing >50kg were at risk for under dosing per Model Care standards.

245 ILEAL POUCH ANAL ANASTOMOSIS IN CHILDREN WITH CHRONIC ULCERATIVE COLITIS (CUC): LONG TERM RESULTS AND QUALITY OF LIFE IN 202 CHILDREN OVER 33 YEARS. Stephanie F. Polites1, D. D. Potter1, Christopher R. Moir1, Abdalla E. Zarroug1, Michael C. Stephens2, Jeanne Tung3, W. S. Harmsen4, Emily S. Pavey4, John H. Pemberton4, 1Division of Pediatric Surgery, Mayo Clinic, Rochester, MN; 2Division of Pediatric Gastroenterology, Mayo Clinic, Rochester, MN; 3Division of Biostatistics, Mayo Clinic, Rochester, MN; 4Division of Colon and Rectal Surgery, Mayo Clinic, Rochester, MN

Objective: Ileal pouch anal anastomosis (IPAA) is the surgical treatment of choice for patients with chronic ulcerative colitis (CUC). In the pediatric population, short-term outcomes of IPAA are excellent. Our aim was to define outcomes and satisfaction with IPAA, over the long term, in children with CUC.

Methods: Between 1980 and 2009, all patients undergoing IPAA before or at age 18 years were included. Prior to 1991, patients were identified using surgical case logs and provided with a standardized, previously published, questionnaire through a survey center. After 1991, patients were enrolled in a prospective database and followed using annual questionnaires. Functional outcomes, complications, and quality of life were assessed.

Results: 202 children underwent IPAA for CUC. 175 (87%) returned questionnaires. The median age at IPAA was 16 years with median follow-up of 15 years. 97% had a functioning pouch at last follow-up. Bowel function is summarized in Table 1. Occasional incontinence was reported in 91 out of 166 (55%) patients; however, frequent day- and night-time incontinence occurred in only 5 of 166 (3%) patients. 70% of patients had at least one episode of pouchitis. Quality of life measures were excellent at 25 years. Sexual life and the ability to work remained stable over follow-up, whereas social activities began to decline slightly after 25 years.

Conclusion: IPAA for pediatric CUC is effective and durable over the long term. Importantly, quality of life is maintained or improved for 25 years.

Bowel function following IPAA

<table>
<thead>
<tr>
<th></th>
<th>5 years n=83</th>
<th>10 years n=65</th>
<th>20 years n=27</th>
<th>30 years n=6</th>
<th>All-time n=165</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day-time stools, median</td>
<td>5.0</td>
<td>5.0</td>
<td>6.0</td>
<td>7.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Night-time stools, median</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>2.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Median number of day-time and night-time stools are reported at 5, 10, 20, and 30 years following IPAA. Median number of stools for all-time is also reported.

Intestinal/Colonic Disorders – Non – Inflammatory Bowel Disease

256 INTRACELLULAR COBALAMIN METABOLISM DEFECT MANIFESTS WITH PROTEIN LOSING ENTEROPATHY. Nadia M. Hijaz, William O. San Pablo, Pediatric Gastroenterology, Children's Mercy Hospital and Clinics, Kansas City, MO

Combined methylmalonic acidemia and homocystinuria is an inborn error of intracellular cobalamin metabolism where there is enzyme-bound cobalamin reductase is absent in the cytosol or the mitochondria. Elevated methylmalonic acid (MMA) and homocysteine with decreased methionine production are the biochemical hallmarks of this disorder. Cobalamin defects have been associated with haemolytic uremic syndrome, severe gastropathy, and a single case of cobalamine C defect complicated with a protein losing enteropathy (PLE). We report the second case of inherited cobalamine defect in associated with PLE. The patient is a six months old female former 34 weeks gestation who is exclusively breast fed presented with few weeks history of projectile vomiting and failure to thrive (weight and Height below 3%). Her initial newborn screen is unremarkable. Her examination revealed a poorly nourished baby, with normal exam otherwise except for mottled skin.

Admission investigations revealed borderline low haemoglobin of 10.1 g/dl (normal range 10.5 -13.5), elevated aspartate aminotransferase (AST 132) and alanine aminotransferase (ALT 65), hypoproteinemia ( total protein 3.9 gm/dL;normal range 6.2 - 8.30) and hypoalbuminemia (albumin 2.2 gm/dL;normal range 2.7 - 5.6). Other liver function test and renal function were normal, with no proteinuria. Testing for ammonia, coagulation profile and LDH and uric acid were all in the normal range. An abdominal ultrasound, upper GI gastrointestinal series, and head ultrasound didn't reveal any pathology. Because of her hypoalbuminemia, a stool for alpha 1 antitrypsin was obtained and found to be grossly elevated at 585 mg/dl (normal range<54). Hepatic virological studies were negative.

Further biochemical evaluation demonstrated elevated urinary and plasma quantitative methylmalonic level was (5.04 nmol/mL ; normal range < 0.4) , homocystine ( 34.3 mcmol/L; normal range 3.3-8.3) and low plasma methionine 6mcmol/L (9-42) mcmol/L. Serum vitamin B12 levels were above the normal range>2000 pg/ml. A presumptive diagnosis of cobalamin F deficiency was made and the patient was started on injected hydroxocobalamin (1 mg every other day), betaine (0.5 g twice a day) and folicic acid (10 mg daily). Her vomiting and her growth improved considerably and she gained 1.6 kg in 2 months. Her anemia and MMA levels normalized dramatically within few weeks of therapy. The patient didn't have upper or lower endoscopy to evaluate for the source of protein loss especially due to her rapid clinical improvement.

In summary we describe a second case of a cobalamine defect presenting with PLE. The etiology of the PLE in our patient remains undetermined. The prompt response to treatment, however, suggests the same metabolic defect in the epithelial mucosa of gastrointestinal GI tract.
257 ONE-DAY COLONOSCOPY PREPARATION IS EFFECTIVE AND SAFE IN CHILDREN. Rima Jibaly1,2, Pat Vijitakula2, Jenny LaChance1,2. 1Hurley Medical Center, Flint, MI; 2Michigan State University, East Lansing, MI

Introduction: Pediatric colonoscopy preparation requires a method that is effective, yet well tolerated. Two-day cleanout with polyethylene glycol without electrolytes has been shown to be an effective method for colonoscopy preparation among children. Shorter dosing preparations, however, have been used successfully with adults. There is little examination of the effectiveness of a 1-day preparation for children. This study examines the effectiveness of a 1-day preparation for children.

Methods: Data were collected via chart review for pediatric patients who had a one-day at home colonoscopy preparation between 3/2010 and 8/2012. The preparation consisted of polyethylene glycol or magnesium citrate. Dosing depended on age and weight. Demographic information, colonoscopy indication, and side effects were obtained. Preparation quality was determined by whether the cecum and terminal ileum were reached. Colonoscopy photos obtained were rated on a 4-point effectiveness scale.

Results: Data were reviewed for 165 children who had a colonoscopy. Mean age was 11.3 years. Majority were female (62.5%) and Caucasian (84.7%). Abdominal pain was the most common presenting system (67.3%). The cecum was reached in 95.2%, and the terminal ileum was reached in 90.3% of the cases. Majority of photos (68.1%) were clear of any material or had clear fluid. Only 8.1% of photos showed significant fecal matter. Three children had to have a repeat colonoscopy. No adverse events were reported by parents.

Conclusions: A one-day preparation for colonoscopy for children appears to be safe and effective. This preparation minimizes the procedure's impact for the child and allows for less school to be missed.

258 A CROSS SECTIONAL STUDY OF INTESTINAL MICROBIOME IN CHILDREN WITH CYSTIC FIBROSIS. Nagraj Kasi1, Casey Morrow2, Matthew Stoll4, Janaina Nogueira1, Reed Dimmitt1, Meredith Hitch1, William T. Harris3

1Pediatric Gastroenterology, University of Alabama Birmingham, Birmingham, AL; 2Cell, Developmental and Integrative Biology, University of Alabama Birmingham, Birmingham, AL; 3Pediatric Pulmonology, University of Alabama Birmingham, Birmingham, AL; 4Pediatric Rheumatology, University of Alabama Birmingham, Birmingham, AL

Background: Children with Cystic fibrosis are prone to intestinal dysbiosis secondary to recurrent antibiotic use, disease related intestinal dysfunction and a high fat diet. In children with Cystic fibrosis, neither the intestinal microbiome nor its relation to clinical manifestations have been well studied. The aim of our cross sectional study was to demonstrate intestinal dysbiosis in children with CF.

Methods: In our cross sectional study, we compared the diversity and composition of the fecal microbiome in children with Cystic fibrosis between 3-18 yrs to their healthy controls (CF 10, controls 9). The bacterial species and gene content of the stool specimens were characterized by using culture independent 16S rRNA gene sequencing technology. All children in the CF group were on antibiotics within eight weeks of enrolment into the study.

Results: CF patients had a significantly lower microbial diversity compared to healthy controls as measured by Shannon index (p=0.008) and Simpson index (p=0. 011). Within the CF group, weighted and unweighted UniFrac analysis of the microbiome showed significant diversity. At the phylum level, the relative abundance of Actinobacteria, Bacteroidetes, and Proteobacteria was higher in the CF population while the relative abundance of Firmicutes was less than controls; these differences, however, were not statistically significant. Enterobacteriaceae species were were significantly abundant in the CF group compared to controls (CF 1.0±1.9, Controls 0.05±0.1, p=0.0080).

Conclusions: Our study supports the theory of intestinal dysbiosis in children with Cystic fibrosis. The significant diversity within the CF group can be accounted for by the type of antibiotic at the time of recruitment. A longitudinal study to correlate the changes in intestinal microbiome with nutrition (BMI), vitamin deficiency, pancreatic enzyme dosages and other intestinal manifestations of CF, will provide with therapeutic options in the management of CF.
Comparison of biodiversity of bacteria in stool samples of cystic fibrosis (CF) and controls

<table>
<thead>
<tr>
<th></th>
<th>CF (n=10)</th>
<th>Control (n=9)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Mean overall diversity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shannon index</td>
<td>4.4±1.2</td>
<td>6.1±0.6</td>
<td>0.0080</td>
</tr>
<tr>
<td>Simpson index</td>
<td>0.82±0.12</td>
<td>0.95±0.02</td>
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<tr>
<td>Mean % by phylum</td>
<td></td>
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<tr>
<td>Actinobacteria</td>
<td>6.4±12.1</td>
<td>1.6±2.1</td>
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<tr>
<td>Bacteroidetes</td>
<td>25.6±22.5</td>
<td>16.7±10.3</td>
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<tr>
<td>Firmicutes</td>
<td>66.2±22.5</td>
<td>80.1±9.9</td>
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<tr>
<td>Proteobacteria</td>
<td>1.7±1.7</td>
<td>0.8±0.7</td>
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<tr>
<td>Verrucomicrobia</td>
<td>0.1±0.001</td>
<td>0.6±0.1</td>
<td>0.2218</td>
</tr>
</tbody>
</table>

p-value Estimated from Wilcoxon ranked sums test

259 COMPLIANCE AND EFFICACY OF A STANDARD LAXATIVE PROTOCOL IN CHILDREN WITH AUTISM SPECTRUM DISORDER. Ahmed Arshad, Natasha Warikoo, Ajay Kaul, Gastroenterology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

INTRODUCTION: Conventional treatment for functional constipation in neuro-developmentally intact children includes disimpaction, use of laxatives, and behavioral and biofeedback therapy. Compliance with this conventional regimen is challenging in children with Autism Spectrum Disorder (ASD).

AIM: To test the compliance and efficacy of a standard laxative protocol in children with ASD.

METHODS: The institutional database was screened to identify children with a formal diagnosis of ASD who attended the gastroenterology clinic for children with special needs at our hospital for a presenting symptom of constipation. They had all been treated unsuccessfully by their primary care physician and none were toilet trained. After confirming the diagnosis of functional constipation (Rome III criteria), parents were explained the pathophysiology and compliance with treatment stressed. They were all put on a standard 3-step laxative protocol: initial bowel clean out with oral laxatives, maintenance on a combination laxative treatment (Polyethylene glycol 3300 and senna) and repeat bowel clean out once a month. No additional behavioral strategies were recommended. The child was either followed up in clinic or the family contacted by phone to evaluate changes in frequency of bowel actions, soiling and behavior.

RESULTS: Seventeen children met the inclusion criteria including twelve males and five females. The mean age at presentation to the GI clinic was 9 years. The mean duration of follow up was 10 months (10 in clinic and 7 by phone). Fourteen children were compliant with the treatment protocol and showed an increase in number of bowel actions, decrease in frequency of soiling and improvement in behavior. Chi-square analysis showed that treatment failure was only seen in non-compliant children (p < 0.001). Eleven children were using constipation-inducing medications for co-morbid conditions, however no significant association was found between medication use and response to treatment (p= 0.21).

CONCLUSIONS: Parental counselling and compliance with our standard laxative protocol was critical in the success of the management of functional constipation in children with ASD. Medical management may be necessary before instituting behavioral therapy for toilet training in children with ASD.

260 KNOCK-DOWN OF CONGENITAL TUFTING ENTEROPATHY GENE, EPCAM, EXHIBIT BARRIER DYSFUNCTION AND ION TRANSPORT DEFECTS IN INTESTINAL EPITHELIAL CELLS. Philip Kozan, Ron Marchelletta, Mamata Sivagnanam, Pediatrics, University of California, San Diego, San Diego, CA; UCSD, San Diego, CA

Congenital tufting enteropathy (CTE) is one of several intractable diarrheas of infancy. CTE is an autosomal recessive disorder that presents in the first few months of life with chronic watery diarrhea and impaired growth. The diagnosis of CTE is made with the recognition of villous changes of the epithelium of the small intestine. Typical findings include total or partial villous atrophy and crypt hyperplasia. The characteristic findings are focal epithelial tufts in the duodenum and jejunum. These tufts are composed of enterocytes with rounding of the plasma membrane which results in teardrop-like configurations. Mutations in the gene that encodes for EpCAM (Epithelial cell adhesion molecule) appears to be responsible for the presentation of CTE. In effort to study the absence of intestinal fluid salvage in patients that are homozygous for mutant EpCAM, a knock-down cell line derived from T84 intestinal cell line transfected with EpCAM specific shRNA was established. Western blot and confocal microscopy confirmed the EpCAM Knock-down (KD) phenotype of the cell line. Studies using the KD-EpCAM cell line revealed transepithelial resistance (TER) significantly attenuated (Student’s Unpaired T-test, p<0.05, 377.25±22.10 ohms/cm2) when compared to control (897.00±90.70 ohms/cm2). Furthermore, Ussing chamber studies revealed that forskolin-simulated KD-EpCAM cell line exhibit a significant reduction in short-circuit current (ΔIsc, 8.24±0.14 ohms/cm2) when compared to control (69.64± 12.99 mA/cm2). Our data suggest that CTE mediated diarrhea may result from a combination of barrier dysfunction and ion transport defects thereby reducing the ability of the intestine of afflicted patients to salvage fluid.

261 PERSISTENT DIARRHEA OF INFANCY: ASSOCIATION TO ENTEROPATHOGENS, CARBOHYDRATE INTOLERANCE, PROTEIN ALLERGY/HYPERSENSITIVITY AND MALNUTRITION. Alfredo Larrosa-Haro, Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico
BACKGROUND: Prevalence of persistent diarrhea of infancy (PDI) in Mexico has diminished in the last three decades. However, pediatricians and pediatric gastroenterologists require updated information regarding the factors associated to PDI for a reasonable care of their patients.

OBJECTIVE: To report de frequency and type of etiologic associated factors in infants with PDI.

PATIENTS: Seventy-eight consecutive infants <24 months with PDI seen at a GI Clinic are reported. The evaluation time after the PDI onset was 27.6 days (SD 5.7). METHODS: Fresh stool smear (0.9% saline) and Kinyoun smear; semi-quantitative stool reducing substances; stool cultures (eosin- methylen blue agar, MacConkey, SS/V cholerae & Campy-bap) were done to search for enteropathogens and carbohydrate intolerance. Protein allergy/hypersensitivity was diagnosed by means of a two-week suppression/challenge trial. Nutritional status was evaluated with the Waterlow criteria.

RESULTS: The overall Mean age was 8.9 months (SD 4.8). The enteropathogens isolated were: Campylobacter jejuni 25 (32.6%), Salmonella enterica 6 (7.7%), Cryptosporidium parvum 6 (7.7%), E. coli O157:H7 4 (5.1%), Giardia lamblia 3 (3.8%), Shigella spp 2 (2.6%); overall isolation was 59.5%. Carbohydrate intolerance: Lactose 31 (39.7%), glucose polymers 4 (5.1%). Protein allergy/hypersensitivity: Cow’s milk 26 (33.3%), soy protein 4 (5.1%), extensive hydrolyzates 2 (6.6%). Mild acute malnutrition (weight/height median %) was found in 15 (19.2%).

DISCUSSION: In the current series PDI was a syndrome triggered by an enteropathogen and associated to a high proportion of carbohydrate intolerance and formula protein allergy/hypersensitivity.

262 EOSINOPHILIC COLITIS IS ASSOCIATED WITH FUNCTIONAL CONSTIPATION IN CHILDREN. Min Yang1, Tie-Fu Fang1, Mei-Wan Chao1, Cui-Ping Liang2, Pei-Yu Chen1, Yong-Mei Zeng1, Lan-Lan Geng1, Si-Tang Gong2, Ding-You Li2, 1Gastroenterology, Guangzhou Women and Children's Medical Center, Guangzhou, China; 2Pediatric Gastroenterology, Children’s Mercy Hospital, Kansas City, MO

Background: Food allergy has been shown to be associated with chronic functional constipation as well as eosinophilic gastrointestinal disorders. However, the incidence of constipation in children with eosinophilic colitis is not known.

Aim: To investigate the association between eosinophilic colitis and functional constipation in children.

Methods: Children underwent colonoscopy from January 2011 to December 2012 were enrolled prospectively at Guangzhou Women and Children’s Medical Center. Clinical manifestations, laboratory tests, colonoscopy findings and mucosal pathological features of children with biopsy-proven eosinophilic colitis were analyzed. As a control, an on-site questionnaire survey of healthy children was conducted in the well-child clinic. The prevalence rates of functional constipation in healthy and eosinophilic colitis children were compared.

Results: A total of 246 children underwent colonoscopy procedures, with 19.5% (48/246) patients diagnosed with eosinophilic colitis (mucosal eosinophils ≥ 20/hpf), aged between 5 months to 14 years old. The main clinical manifestations were abdominal pain, bloating, hematochezia, diarrhea, nausea, vomiting, fecal incontinence, constipation and poor appetite. 25% (12/48) patients had peripheral eosinophilia and 41.7% (20/48) had increased serum total IgE. Eight children with eosinophilic colitis met the Rome III criteria for the diagnosis of functional constipation, with the prevalence rate of 16.7% (8/48). Questionnaire survey of 1551 consecutive healthy children, aged 3 months to 14 years old, showed that 62 children met the criteria for the diagnosis of functional constipation, with the prevalence rate of 4.1%. The prevalence rate of functional constipation in children with eosinophilic colitis were significantly higher than that in healthy ones (χ² =17.85, P=0.000).

Conclusions: Eosinophilic colitis is associated with increased functional constipation in children. A further multicenter study with a large sample size would be needed to confirm our finding.

263 SEQUENTIAL VERSUS STANDARD TRIPLE THERAPY FOR HELICOBACTER PYLORI INFECTION IN CHINESE CHILDREN: A MULTICENTER, OPEN-LABLED, RANDOMIZED CONTROLLED TRIAL. Jing Huang1, Liya Zhou2, Lanlan Geng1, Mei-Yang1, Xi-Wei Xu1, Zhao-Lu Ding1, Meng Mao1, Zhi-Ling Wang1, Si-Tang Gong1, Ding-You Li1, 1Gastroenterology, Guangzhou Women and Children's Medical Center, Guangzhou, China; 2Pediatric Gastroenterology, Children’s Mercy Hospital, Kansas City, MO

Background: Studies have showed that 10-day sequential treatment regimen achieved higher Helicobacter pylori (H. pylori) eradication rate than standard triple therapies. However, no data were available about the efficacy of a 10-day sequential therapy in Chinese children with H. pylori infection.

Aim: To compare a 10-day sequential therapy and standard triple therapy in Chinese children with H. pylori infection.

Methods: A prospective, multicenter, open-label, randomized controlled trial was conducted in four tertiary medical centers in China. Children with H. pylori gastritis were randomly assigned to a 10-day sequential therapy consisting of omeprazole and amoxicillin for five days followed by omeprazole, clarithromycin and metronidazole for the remaining five days, or 7-day or 10-day standard triple therapy comprising of omeprazole, amoxicillin and clarithromycin. H. pylori eradication was assessed by means of a two-week suppression/challenge trial. Nutritional status was evaluated with the Waterlow criteria.

Results: A total of 360 patients were included. The eradication rate achieved with the 10-day sequential therapy was significantly higher than either the 7-day or 10-day standard triple treatment, either by the intention-to-treat analysis (81.4% vs. 61.9% or 67.7%, P <0.05) or per protocol analysis (89.7% vs. 70.8% or 77.8%, P <0.05). Conclusions: The 10-day sequential regimen was significantly more effective than standard 7-day or 10-day triple regimens in eradicating H pylori infection in Chinese children.

264 DOWNREGULATION OF AQUAPORIN 1, 4 AND 8 EXPRESSION OF THE COLON IS ASSOCIATED WITH ROTAVIRUS DIARRHEA IN A MOUSE MODEL. Huan Chen1, Mei-Wan Chao1, Min Yang1, Pei-Yu Chen1, Lan-Lan Geng1, Si-Tang Gong1, Ding-You Li1, 1Gastroenterology, Guangzhou Women and Children's Medical Center, Guangzhou, China; 2Pediatric Gastroenterology, Children’s Mercy Hospital, Kansas City, MO

Background: Aquaporins (AQPs) play an important role in cell function and fluid homeostasis. However, no studies have evaluated the
expression of AQPs in rotavirus-induced diarrhea.

Aim: The present work is to determine the expression of AQP1, AQP3, AQP4 and AQP8 in jejenum, ileum and colon in a mouse model of rotavirus-induced diarrhea.

Methods: 3-4 days old mice were given 100 ul rotavirus strain SA11 through intragastric feeding needles. The control mice were fed with 100 ul virus-free cell culture medium. Symptoms were observed and histological analysis was performed. Western blot was used to determine the expressions of aquaporins 1, 3, 4, 8 in jejenum, ileum and colon of mice.

Results: After rotavirus infection, the intestinal epithelial cells showed cytoplasmic vacuolation, villous malalignment and atrophy. The expression of AQP1 was significantly reduced in ileum and colon of mice after SA11 virus exposure compared with untreated controls (P<0.05). Likewise, the expression of AQP4 and AQP8 protein were significantly decreased in colon of the SA11 virus-infected mice (P<0.05). However, the expression of AQP3 protein was significantly increased in colon of the SA11 virus-infected mice compared to the controls (P<0.01).

Conclusion: Rotavirus strain SA11-induced diarrhea is associated with a down-regulation of AQP1 protein in ileum and AQP1, AQP4, and AQP8 protein in colon.

265 PROSPECTIVE STUDY OF EDUCATIONAL CARTOON ON PEDIATRIC BOWEL PREP QUALITY AT TIME OF COLONOSCOPY. Elizabeth C. Maxwell1,2, Marsha Simmons2, Linda Franklin1, Janis Arnold1, Harpreet Pall1,2, 1Gastroenterology, Hepatology, and Nutrition, St. Christopher's Hospital for Children, Philadelphia, PA; 2Department of Pediatrics, Drexel University College of Medicine, Philadelphia, PA; 1Gastroenterology, Hepatology, and Nutrition, Boston Children's Hospital, Boston, MA

Background: Success of colonoscopy is highly dependent on thorough completion of bowel preparation. Barriers to completing bowel prep adequately include understanding the importance and instructions. The aim of this study was to evaluate if addition of an educational cartoon to the standard PEG-3350 bowel prep instructions would objectively improve the quality of the bowel prep and patient experience. Methods: Patients were recruited from the outpatient Gastroenterology clinic at St. Christopher's Hospital for Children in Philadelphia. Eligibility criteria included age 7-14 years, English-speaking, and scheduling of a first time outpatient colonoscopy. Patients were randomized to a control group receiving standard bowel prep instructions, or the intervention group receiving an additional educational cartoon. To objectively rate the quality of the bowel prep on the day of the procedure, the blinded endoscopist completed a numeric Ottawa scale (0-14, with 0 being the best score). A questionnaire rating the experience of the bowel prep process was also completed by the family. Results: Data from 21 patients was analyzed. Mean Ottawa score in the intervention group compared with controls was not significantly different (mean scores 3.6 and 3.18, respectively; p=0.35). Level of education was significantly correlated with a better Ottawa score overall (rho=0.449, p=0.041). Level of education was significantly correlated with a better Ottawa score in the control group (rho=0.658, p=0.028). Both groups of patients reported a positive experience with the bowel prep. Conclusion: In the study population quality of bowel preparation is good overall. Objective quality of bowel preparation was not improved when a supplemental educational cartoon was used. There may be benefit to further investigation of this educational cartoon in parents with less than college level education in a larger population of patients. Small sample size was a limitation of this study.

266 INTESTINAL LYMPHANGIECTASIA (IL) IN A CHILD WITH VERBAL APRAXIA & MALABSORPTION WHOSE NEUROLOGICAL SYMPTOMS IMPROVED WITH VITAMIN E THERAPY. Barbara McElhanon1, Marilyn Agin2, Claudia Morris2, 1Division of Pediatric Gastroenterology, Hepatology and Nutrition, Emory University School of Medicine, Atlanta, GA; 2Emergency Medicine, Emory University School of Medicine, Atlanta, GA; 3Developmental Behavioral Pediatrics of New York, New York, NY

Purpose: IL is a rare disorder characterized by hypoalbuminemia, edema, & immune dysregulation due to dilation of intestinal lymphatics & resultant lymph leakage into the gastrointestinal (GI) tract. Hypogammaglobulinemia, hypocholesterolemia, & trace element deficiencies (def) may occur. Diarrhea and steatorrhea may lead to malabsorption, mild immune def, growth retardation, and significant fat soluble vitamin (vit) def with clinical consequences. In particular, vit E def is known to cause neurological symptoms which overlap with the following 2 disorders. Verbal apraxia is a motor-planning disorder than impacts coordination. Dyspraxia is a motor-planning disorder than impacts coordination.

Methods: A 9 year old boy with a history of VA, dyspraxia/poor coordination, hypotonia, decreased pain sensation in his extremities, decreased deep tendon reflexes, poor proprioception, asthma, eczema, many food/environmental/drug allergies, short stature, poor weight gain, chronic GI symptoms including diarrhea, constipation, pale to acholic stools, severe GERD in infancy, steatorrhea, fat malabsorption, recurrent rectal prolapse, carnitine, vit D def, zinc def, iron def, mild edema of hands/feet/chest, persistently low cholesterol (< 90 mg/dL), low albumin, macrocytosis with elevated methylmalonic acid suggesting B12 def, mild elevation of transaminases, recurrent ear & skin infections, disseminated molluscum contagiosum, recurrent oral thrush & small intestine bacterial overgrowth (SIBO) was one of a case series of 187 children described with a novel syndrome of allergy, apraxia & malabsorption (Morris/Agin 2009, Alternative Therapies in Health & Medicine) whose neurologic symptoms related to speech, coordination, muscle tone, & pain sensation dramatically improved with dose-dependent vit E supplementation first introduced at age 3, titrated up to 200 mg/kg/day. An elemental diet was initiated to treat the SIBO in 2011 with dramatic improvement in GI symptoms, normalization of stool, weight gain from 2nd to 75th %ile, improved albumin levels, & improved cholesterol levels. Medically refractory oral thrush resolved within 2 weeks of elemental diet. Reintroduction of food brought on a return of GI symptoms, weight loss, thrush, & drop in cholesterol.

Results: Video Capsule Endoscopy revealed classic endoscopic features of IL, dilated lacteals which appear as white nodules, throughout the jejenum. Additionally, mild duodenal inflammation was seen.

Conclusions: Primary intestinal lymphangiectasia is an uncommon cause of protein-losing enteropathy in children. The prevalence of IL in children with VA, dyspraxia, and/or autism spectrum disorders is unknown, but may help explain case reports of dramatic improvement in neurologic and GI symptoms to nutritional interventions in a subgroup of these children. IL creates an environment vulnerable to SIBO & may lead to neurological sequelae of vit E def. Apraxia may be a symptom of this clinical phenotype that could help identify children who require a malabsorption work-up & nutritional therapy. More research is needed.
267  **THE ROLE OF DUODENAL BULB BIOPSIES IN THE DIAGNOSIS OF CELIAC DISEASE.** Jonathan Moses, Thomas Plesec, Barbara Kaplan, 1Pediatric Gastroenterology, Cleveland Clinic Children's, Cleveland, OH; 2Pathology and Laboratory Medicine, Cleveland Clinic, Cleveland, OH

**Background:** Celiac disease is an autoimmune disorder in which ingestion of gluten causes intestinal inflammation and a variety of gastrointestinal symptoms. Gold standard for diagnosis of celiac disease is upper endoscopy with biopsies. Recent guidelines have recommended routine biopsies should include samples from the duodenal bulb. Our aim was to evaluate the diagnostic utility of duodenal bulb biopsies in the diagnosis of celiac disease.

**Methods:** This was a retrospective chart review of celiac disease patients 5-21 years of age who had separate duodenal bulb and distal duodenal biopsies at time of diagnosis. Exclusion criteria were patients who had only one set of biopsy specimens from the duodenum. Demographic, laboratory [complete blood count (CBC), complete metabolic panel (CMP), and celiac antibodies] and endoscopic data was collected. Patients with abnormal duodenal bulb biopsies (Marsh 3 grading on histology) were divided into two groups: 1) normal distal duodenal biopsies and 2) Marsh 1 findings in the distal duodenal biopsies.

**Results:** Data were collected on 27 patients. 67% of the patients were female, 100% were Caucasian and mean age was 9.6 years (±5.1). 6 of 27 patients (22%) had abnormal visual endoscopic findings in the duodenal bulb and normal endoscopic findings in the distal duodenum. CBC and CMP were normal in 82% of the patients. 2/27 patients (7%) were in group 1 and 5/27 patients (19%) were in group 2. Overall, bulb biopsies contributed to the diagnosis of celiac disease in 7/27 patients (26%).

**Conclusion:** Duodenal bulb biopsies contributed to the initial diagnosis of celiac disease in 26% of patients, with 7% of patients having diagnostic findings only in the duodenal bulb. These findings are in line with recent guidelines and obtaining duodenal bulb biopsies should be part of routine practice for establishing the diagnosis of celiac disease.

268  **RISK FACTORS FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN.** Maribeth R. Nicholson, Isaac P. Thomsen, C. B. Creech, Kathryn M. Edwards, Pediatrics, Vanderbilt University School of Medicine, Nashville, TN

**Background:** Clostridium difficile is an increasingly common cause of diarrhea in children. While most patients respond to initial therapy, there is a high rate of recurrence within 2 months of therapy with about 20% of pediatric patients experiencing recurrence. Although adult studies have identified concurrent antibiotics, the use of proton pump inhibitors, and older age as independent risk factors for recurrent Clostridium difficile infection (CDI), no studies have been published to date in children.

**Objective:** Identify risk factors for recurrent CDI in children

**Study Design:** We conducted a retrospective cohort study of pediatric patients ages 1-18 years with CDI from January 1st 2007 through December 31st 2011 at Monroe Carell Jr. Children’s Hospital at Vanderbilt. Demographic, clinical, and laboratory data on all CDI patients were collected. Patients were excluded if they had no documented diarrhea, if they were not treated for CDI, or if there was inadequate documentation to determine recurrence.

**Results:** We have reviewed 181 medical records of which 128 (71%) met inclusion criteria. Fifty five patients (43%) were female and 73 (57%) were male. The median age was 9 years (range 1-17). Of the 128 patients with CDI, 23 (18%) experienced recurrence and 9 of those 23 (40%) experienced multiple recurrences. Patients with a larger number of antibiotics used (by class) in the 30 days prior to primary CDI were more likely to experience recurrent CDI (3.04 vs. 2.07 antibiotic classes in patients with and without recurrence, P=0.0058). Patients using acid blockers were more likely to experience recurrence with a recurrence rate of 24% in those using acid blockers versus 10% in those not using acid blockers (P=0.04). The odds ratio for the use of acid blockers was 2.91 (95% CI= 1.038,8.13, P=0.04). Patients on immunosuppressants were more likely to suffer from recurrent CDI, with a recurrence rate of 28.5% in those using immunosuppressants versus 8% in those not using immunosuppressants (P=0.002). The odds ratio for the use of immunosuppressants was 4.8 (95% CI= 1.70,13.4 P= 0.002). Patients with hospital-acquired disease were more likely to experience recurrence with rates of 30% versus only 12.5% of patients with non-hospital acquired disease experiencing recurrence (P=0.02). The odds ratio for this exposure was 3.0 (95% CI= 1.2, 7.5 P=0.02).

**Conclusions:** The use of acid suppressing agents, increased exposure to antibiotics (by number of classes), and the use of immunosuppressive agents in the 30 days prior to initial CDI increased the risk of recurrent disease in the pediatric host. Pediatric patients with hospital-acquired CDI were also more likely to experience recurrence.

269  **GASTROINTESTINAL MANIFESTATIONS IN CHILDREN WITH COMMON VARIABLE IMMUNE DEFICIENCY.** Mohammad Osman, Chaitanya Pant, Thomas Sferra, 1Oklahoma University Health Sciences Center, Oklahoma City, OK; 2Case Western University Hospitals, Cleveland, OH

**Aim of the study:** Identify the association of gastrointestinal disorders with CVID.

**Materials and methods:** We used the Healthcare Cost and Utilization Project Kids' Inpatient Database (HCUP-KID) sponsored by the Agency for Healthcare Research and Quality to obtain the data for this study. We identified hospital discharge that contains the ICD9 code for CVID. ICD-9 diagnostic codes were used to identify additional co-morbid gastrointestinal diagnoses in patients with CVID. To assess the association of CVID with additional co-morbid gastrointestinal diagnoses, an analysis including high-dimensional propensity scores was performed. High-dimensional propensity scores were generated by regression analysis of patients with CVID based on demographics (age, gender, race, insurance status, geographic location of care, year of discharge and median household income). Patients with an indication of CVID (cases) were matched by high-dimensional propensity score, using a matching algorithm, to patients who did not have CVID (controls), with a 1:5 matching ratio. Odds ratios (ORs) and 95% confidence intervals (CIs) are reported to identify the association of CVID with associated co-morbid gastrointestinal diagnoses.

**Results:** There is a marked increase in the risk of: Giardiasis [OR 31.8], malabsorption [OR 18.4], Celiac disease [OR 11.8], and hepatitis [OR 10] in CVID patients than in non CVID cohort. Liver diseases excluding hepatitis are one of the commonest gastrointestinal disorders in children with CVID with a prevalence of 6% (OR=5.58, CI=4.4-7). Diarrhea and Intestinal infection follow in the order of
Motility/Functional Gastrointestinal Disorders

286 NEURAL PROCESSING OF SOMATIC PAIN IN SUBJECTS WITH GASTROINTESTINAL SYMPTOMS AND DISEASE. Jeannie Huang1,2, Irina Strigo1, Laura Terrones1, Elena Kosheleva1, Walter Kaye1, 1Pediatrics, University of California, San Diego, La Jolla, CA; 2Gastroenterology, Rady Children's Hospital, San Diego, CA; 3Psychiatry, University of California, San Diego, La Jolla, CA

Interception is the brain system by which afferent signals from the body affect human emotion, sense of well-being, and behavior. Brain regions including the thalamus, anterior cingulate cortex (ACC), and insula (INS) are involved in interception. Prior research has demonstrated that persons with irritable bowel syndrome (IBS) demonstrate altered neural processing of visceral pain signals. Recent data suggest that altered somatic pain processing may also affect outcomes in IBS.

Objective: To determine if neural processing of somatic pain stimuli differs between IBS, inflammatory bowel disease (IBD), and control subjects.

Methods: Subjects underwent periods of anticipated and actual thermal pain stimuli and simultaneous blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI). Briefly, subjects were cued to anticipate painful heat of low or high intensity during fMRI. fMRI data were analyzed for the difference in BOLD response to high compared to low painful stimulus during both anticipation and stimulation periods. Subjects answered surveys evaluating alexithymia, anxiety, depression, and pain catastrophizing. Group data were compared using ANOVA.

Results: 8 IBD (4F, 4M, 18±1y), 7 IBS (6F, 1M, 17±1y), and 8 healthy control (5F, 3M, 20±1y) subjects underwent the protocol. Increased activation within interception brain areas (thalamus, ACC, and right ventral anterior INS) was seen in IBS as compared to IBD and control subjects during anticipation of somatic pain stimuli. fMRI signals between groups did not differ significantly during pain stimulation.

IBS subjects scored significantly higher on pain catastrophizing measures [rumination (p=0.02), magnification (p<0.05), and helplessness (p<0.001)] compared to other groups. Between-group differences in anxiety were also observed, with IBS subjects scoring the highest on frequency with 5% prevalence for each. None of our CVID patients had the diagnosis of H pylori infection, although atrophic gastritis was reported in 0.4% of CVID patient with OR=3.8 (CI1.5-9.32). IBD was a common finding in 3.4% of patients, with increased incidence of 6.22 times than controls (OR 6.22, CI=4.55-8.49)

Conclusion: GI disorder is a common association with CVID in the pediatric age group as described in adult patients. Some disorders are more common in pediatric patients, while others are rare or less common. Knowledge of this association can assist practitioners in diagnosis of CVID in patients presenting primarily with a GI manifestation.

270 DUODENAL HEMATOMA FOLLOWING EGD: A CASE SERIES AND COMPARISON WITH BLUNT ABDOMINAL TRAUMA-INDUCED DUODENAL HEMATOMA. Benjamin A. Sahn1, Neha J. Dadhania2, Michael L. Nance1, Sudha A. Anupindi2, Petar Mamula1, 1Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 2Drexel University College of Medicine, Philadelphia, PA; 3General Surgery, Children's Hospital of Philadelphia, Philadelphia, PA; 4Radiology, Children's Hospital of Philadelphia, Philadelphia, PA

Introduction: Duodenal hematoma (DH) is a well-recognized, rare complication of esophagogastroduodenoscopy (EGD) with duodenal biopsy and uncommon, but better described following blunt abdominal trauma (BAT). Published case reports suggest this complication of EGD occurs more frequently in children than adults, however the incidence remains undefined. We aimed to describe DH incidence post EGD and to compare its features to those post BAT.

Methods: Medical, radiologic, and trauma surgical databases at The Children's Hospital of Philadelphia were searched for the diagnosis of duodenal hematoma from 2000-2012. Data included medical history, time to development of symptoms, imaging studies, medical and surgical management, and length of hospital stay. The total number of EGDS with duodenal biopsy was identified to determine the incidence of DH following EGD.

Results: During the 13-year study period 26,905 EGDS with duodenal biopsies were performed. Duodenal hematoma developed after 13 procedures. (0.0005%, 95% CI 0.0002-0.0007). Four patients (31%) had a transplant history (bone marrow, heart, 2 liver). Presenting symptoms included abdominal pain (11 patients, 85%), non-bilious (6) and bilious vomiting (2). These developed within 24 hours in 9/13 (69%) patients, while all presented by 72 hours post endoscopy. Anti-coagulation medications were taken by 3/13 (2 aspirin, enoxaparin)

Conclusion: In a 13-year study period, 13 cases of EGD complicated by duodenal hematoma were identified, for an incidence of 1:2,070
anxiety scales among evaluated groups (p<0.04). IBS subjects also scored higher than IBD and control subjects on the alexithymia measure (p<0.0001). There were no significant group differences appreciated on the depression rating.

Conclusions: Our data demonstrate altered somatic pain processing in IBS. Individuals with IBS demonstrate significantly altered neural processing of anticipated somatic pain stimuli along the interoception pathway as compared with IBD and control groups. IBS subjects also demonstrate increased emotional lability as compared to IBD subjects and controls. Our results suggest that neural processing of pain signals from both visceral and somatic origins is altered in IBS.

Table 1. BOLD fMRI signals according to brain region and subject group during Somatic Pain Anticipation.

<table>
<thead>
<tr>
<th>Brain Region</th>
<th>Volume</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>F-statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Thalamus</td>
<td>1408</td>
<td>-4</td>
<td>-12</td>
<td>8</td>
<td>4.9</td>
</tr>
<tr>
<td>Left ACC</td>
<td>1408</td>
<td>-8</td>
<td>31</td>
<td>37</td>
<td>4.5</td>
</tr>
<tr>
<td>Right Insula</td>
<td>960</td>
<td>33</td>
<td>11</td>
<td>-4</td>
<td>5.1</td>
</tr>
<tr>
<td>Right Cuneus</td>
<td>832</td>
<td>27</td>
<td>-83</td>
<td>30</td>
<td>5.7</td>
</tr>
<tr>
<td>Right Inferior Temporal Gyrus</td>
<td>704</td>
<td>56</td>
<td>-43</td>
<td>-18</td>
<td>4.6</td>
</tr>
<tr>
<td>Right Middle Temporal Gyrus</td>
<td>1984</td>
<td>36</td>
<td>-4</td>
<td>-32</td>
<td>5.1</td>
</tr>
</tbody>
</table>

*Based on Group by Cue effects from Linear Mixed Effects Model with Group (HC, IBD, HC) and cue (high pain, low pain) as factors and age as covariate

287 Efficacy of Lubiprostone for Treating Functional Constipation in Children and Adolescents in an Open-Label, Multicenter Study. Paul Hyman1, Carlo Di Lorenzo2, Taryn Joswick3, Ryuji Ueno4,5, 1Louisiana State University and Children’s Hospital, New Orleans, LA; 2Nationwide Children's Hospital, Columbus, OH; 3Sucampo Pharma Americas, LLC, Bethesda, MD; 4Sucampo AG, Zug, Switzerland; 5Sucampo Pharmaceuticals, Inc., Bethesda, MD

Background: Treatments for functional constipation, such as enemas and laxatives, may be challenging to administer or are not recommended for long-term use. The oral ClC-2 chloride channel activator lubiprostone (LUBI) increases intestinal fluid secretion, enhances gastrointestinal motility, and increases the frequency of spontaneous bowel movements (SBMs). This prospective study evaluated the efficacy of LUBI in children and adolescents.

Methods: Patients ≥12 kg and ≤17 y of age with functional constipation (<3 SBMs/week) participated in this 4-wk, open-label, multicenter trial. Treated patients (N=124) received LUBI 12 mcg once daily, 12 mcg twice daily (BID), or 24 mcg BID based on age and weight. The primary endpoint was change from baseline (CFB) in SBM frequency at week 1. In this analysis, CFB in SBM frequency over the 4-wk study was evaluated by Wilcoxon signed-rank tests for subgroups ranging from young children (age <6 y) to adolescents (age 12-17 y).

Results: Mean CFB in SBM frequency improved at week 1 in all age and weight subgroups, reaching statistical significance in children <6 y, children 6−11 y weighing 24-35 kg and ≥36 kg, and adolescents (Table). The CFB improvements in SBM frequency were generally maintained at weeks 2-4. In children <6 y and adolescents, 46.7% and 42.6%, respectively, experienced an SBM within 24 hours after the first dose. In the weight subgroups of children 6−11 y, 15.4%−38.1% experienced an SBM within 24 hours.

Conclusion: Lubiprostone increased SBM frequency in children with functional constipation across age ranges from young children to adolescents, and 35% reported a first SBM within 24 hours of treatment initiation.

Mean SBM Frequency After Lubiprostone Treatment

<table>
<thead>
<tr>
<th>Children &lt;6 y</th>
<th>Children 6-11 y</th>
<th>Adolescents 12-17 y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12-23 kg</td>
<td>24-35 kg</td>
</tr>
<tr>
<td>Number of Patients</td>
<td>n=15</td>
<td>n=13</td>
</tr>
<tr>
<td>Baseline</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Wk 1 CFB</td>
<td>1.69*</td>
<td>0.34</td>
</tr>
<tr>
<td>Wk 2 CFB</td>
<td>1.41*</td>
<td>1.26</td>
</tr>
<tr>
<td>Wk 3 CFB</td>
<td>1.17*</td>
<td>1.54</td>
</tr>
<tr>
<td>Wk 4 CFB</td>
<td>1.52*</td>
<td>1.56*</td>
</tr>
</tbody>
</table>

*P<0.05 and †P≤0.01 vs baseline.

288 Is Colonic Manometry Useful in the Pre-Surgical Evaluation of Children with Intractable Idiopathic Constipation? Giulia Brisighelli1, Jose M. Garza1, Monica Holder2, Jason S. Frischer2, Marc Levitt3, Belinda Hsi1, Ajay Kaul1, 1Gastroenterology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 2Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: Idiopathic constipation is the most common functional defecation disorder in children. There is no consensus on the optimal
management of these patients which leads to variability in their work up and treatment. 

Aim: Can colonic manometry predict non responders to maximal medical treatment and guide surgical intervention?

Material and Methods: Data from 18 children with severe idiopathic constipation referred to the Colorectal Center at CCHMC were analyzed. Each patient had a contrast enema (CE) and colonic manometry (CM).

Results: The mean age was 10.3 years with 11 females and the mean duration of symptoms was 47 months. 67% of patients had fecal incontinence. 

Contrast enema showed colonic redundancy in all patients and colonic dilation in 14 patients: 11 with segmental rectosigmoid dilation and 3 with pancolic dilation.

Colonic manometry was abnormal in 6 patients; 4 had distal colonic motor abnormality (all had megarectosigmoid on CE) and 2 had total colonic inertia (both had pancolic dilation on CE).

All patients were treated with senna-based stimulant laxatives according to the protocol used at the Colorectal Center. Ten of 18 patients underwent colonic resection. These included 5 of the 6 patients with abnormal manometric findings (in which the CE showed rectosigmoid dilation in 3 and diffuse colonic dilation in 2). One patient, with abnormal CM and dilated rectosigmoid, refused surgery despite recommendation by the team. In the 3 patients with rectosigmoid dilation and abnormal manometry that had a resection, the length of colonic dysmotility was consistent with the length of colonic dilation seen on the contrast enema. In the two patients with total colonic dilation, the CM showed total colonic inertia: one patient underwent a subtotal colectomy and the other a descending colon resection. This patient later underwent a subtotal colectomy because he was still incapable of having voluntary bowel movements with laxatives.

Five patients with a normal CM underwent resection in order to reduce the high dose of laxatives needed to accomplish complete evacuation. On CE, 1 had a dilated colon throughout, 2 had sigmoid dilation and 2 had normal colonic caliber. All these patients subsequently reduced their daily laxative need and did not require further interventions.

The remaining 8 patients that did not have surgery were maintained successfully on a daily laxative regimen (dose determined after completion of the bowel management program).

Conclusion: In our series, an abnormal colonic manometry correlated with colonic resection. CM is consistent with the CE in the work-up of patients with segmental dilation of the rectosigmoid colon and CM may not be necessary. Prospective studies enrolling larger numbers of children are underway at our center to further delineate the role of colonic manometry in the pre-surgical evaluation of children with intractable idiopathic constipation.

**289 ROLE DEFECOGRAPHY IN EVALUATION AND TREATMENT OF COLONIC DYSMOTILITY IN CHILDREN.**

Basavaraj Kerur, Kanchan Kantekure, Silvana Bonilla, Bruce Orkin, Alejandro Flores, Pediatrics, Floating Hospital for Children, Boston, MA; Division of Pediatric Gastroenterology & Nutrition, Floating Hospital for Children, Boston, MA; Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; Department of Pathology and Laboratory Medicine, Tufts Medical Center, Boston, MA; Department of Colorectal surgery, Rush University Medical Center, Chicago, IL

Background: Chronic intractable constipation (CIC) due to colonic dysmotility is a troublesome disorder. Management can be challenging and includes medications, enemas and surgical management in selected cases. Role of defecography in management of CIC is not clear.

Method: Medical records of pediatric patients with CIC seen at a tertiary care center (2005 to 2012) were reviewed. Demographic variables, diagnostic investigations, medical management and surgical management including outcome after surgery were collected. Clinical outcome was defined using the Rome III Criteria. Defecography results were interpreted as normal or abnormal.

Results:

14 patients (10 males) were included in the study. Age range was 10-21 years. 11 patients underwent cecostomy, 1 patient underwent subtotal colectomy and 2 were treated medically. At follow-up 10 patients underwent total abdominal colectomy with ileorectal anastomosis (TAC-IRA), 1 had total colectomy with ileostomy, 1 had partial colectomy with colorectal anastomosis. Findings on anorectal manometry, barium studies and gastric motility did not correlate with choice of surgical intervention. Colonic motility studies were consistent with colonic neuropathy in 10 patients. All patients with abnormal colonic motility had some form of surgical intervention. 13 patients had defecography studies. Defecography was abnormal in most patients with abnormal colonic motility studies. Defecography was consistent with isolated pelvic floor dysfunction in 1 patient, abnormal motility and anatomy in 1 patient, pelvic floor dysfunction and abnormal motility in 2 patients and isolated abnormal motility in 5. Defecography study was normal in 5 patients. On follow up of 10 patients with TAC-IRA, 3 had incontinence. 7 patients were continent with frequent bowel movements.

Conclusion:

Defecography may be useful test prior to surgical intervention in patients with CIC. Defecography results were abnormal in most patients with abnormal colonic motility studies. Defecography may help in understanding the pathophysiology of defecation disorders in children. IRA may be a safe and useful intervention in a subset of patients when other treatment options have failed.

**290 CHRONIC NAUSEA OF CHILDHOOD AS A PRIMARY VERSUS SECONDARY SYMPTOM.** Katja Kovacic, Adrian Miranda, Gisela Chelimsky, Pippa Simpson, B. U. Li, Division of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI; Division of Quantitative Health Sciences, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI

Background: Chronic nausea is a prevalent and often debilitating symptom in pediatric functional gastrointestinal disorders (FGIDs). Yet, the literature on chronic nausea of childhood is extremely sparse. Although chronic idiopathic nausea is a diagnostic category in the adult Rome III criteria, the pediatric Rome criteria do not recognize it.

Objectives: To characterize children with a primary symptom of unexplained chronic nausea and compare them to children with secondary nausea associated with functional abdominal pain (FAP). To classify all patients according to pediatric Rome III criteria.
Methods: This was a retrospective chart review of 45 children, followed in an outpatient pediatric GI clinic, and suffering from a primary complaint of chronic nausea (CN group). These were compared to prospectively collected data on 49 children, suffering from FAP and nausea as a co-morbid symptom (AP group). Pediatric Rome III criteria were applied to all subjects.

Results: The majority of patients in the CN and AP groups were adolescent Caucasian females. Mean age was 14.4 years (SD=2.18) in the CN group vs. 12.2 years (SD=2.87) in the AP group (p< 0.0001). Most of the subjects in the CN group had severe, daily (88%) and constant (60%) nausea, many with peak morning intensity (19 or 51%). Fewer patients in the AP group had daily (26%) and constant (31%) nausea. In the CN group, 31 (69%) suffered from chronic headaches and 19 (42%) met Rome criteria for abdominal migraines (AM). 32 (71%) of CN patients had a family history of migraine headaches (versus 22% in the AP group). 12 (27%) of the CN patients met criteria for CVS and 24 (53%) were either diagnosed or had symptoms of postural orthostatic tachycardia syndrome (POTS).

Subjects in both groups suffered from fatigue, anxiety, school and sleep problems but these were more common in the CN group. Of those tried on amitriptyline, response rates were similar: 19 (59%) of CN patients and 19 (61%) of AP patients had some response. There was no significant difference between the two groups for meeting FD and IBS criteria: 40% of CN vs. 41% of AP subjects met FD criteria and 18% of CN vs. 24% of AP subjects met IBS criteria. More CN than AP patients met CVS (p< 0.0001) and AM (p< 0.003) criteria. In the CN group, CVS and AM frequently clustered.

Conclusion: Chronic nausea of childhood is a poorly described disorder. Patients with a primary as opposed to a secondary complaint of chronic nausea are more likely to be Caucasian, older adolescent females, suffer from severe, daily nausea and significant co-morbid conditions. Many of them have a family history of migraine headaches, features of POTS, AM and/or CVS. Chronic nausea is a major, disabling symptom that requires increased recognition as a separate entity. Future studies on treatment may need to focus on managing co-morbid symptoms including dysautonomia and migraine.

Diagnostic workup

<table>
<thead>
<tr>
<th>Extensive lab workup</th>
<th>CN group n (%)</th>
<th>AP group n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>36 (80*)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Extensive imaging workup</td>
<td>37 (82**)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>EGD</td>
<td>41 (93)</td>
<td>37 (84)</td>
</tr>
<tr>
<td>EGD normal</td>
<td>40 (98)</td>
<td>37 (100)</td>
</tr>
</tbody>
</table>

*p< 0.0001, **p< 0.0001

291 **JOINT HYPERMOBILITY SYNDROME - A RISK FACTOR FOR PEDIATRIC FUNCTIONAL GASTROINTESTINAL DISORDERS.** Katja Kovacic1, Tom C. Chelinsky2, Adriane Rozmarynowski3, Asima Husain2, Manu Sood1, Pippa Simpson1, Melodee Nugent1, Gisela Chelinsky4, Center for Pediatric Neurogastroenterology, Motility, and Autonomic Disorders, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI; 2Department of Neurology, Medical College of Wisconsin, Milwaukee, WI; 3Division of Quantitative Health Sciences, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI; 4Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI

Background: The prevalence of joint hypermobility is about 11.7% in Western populations. Children with joint hypermobility syndromes (e.g. Ehlers-Danlos) commonly seek medical advice for musculoskeletal pain and are also at risk of cardiac valve abnormalities. Joint hypermobility syndromes have been associated with functional gastrointestinal disorders (FGIDs), orthostatic intolerance and fibromyalgia in adults. We hypothesize that children who refractory FGIDs and orthostatic intolerance will have higher prevalence of joint hypermobility.

Aim: To evaluate the prevalence of joint hypermobility in children referred to a tertiary care Neurogastroenterology and Autonomic Disorders clinic.

Methods: We conducted a retrospective chart review of 66 new patients seen in the Neurogastroenterology and Autonomic disorders clinic at Children's Hospital of Wisconsin in one year (Feb. 2012- Feb. 2013). All patients had joint hypermobility evaluation by the validated Beighton scoring system. We also collected detailed history and examination findings for relevant co-morbidities such as: migraine headaches, nausea, sleep disturbances, fatigue and dizziness. Objective data on postural orthostatic tachycardia syndrome (POTS) by tilt-table test and fibromyalgia tender point scores were analyzed in all subjects.

Results: 45 children had Beighton scores and tilt table test for POTS as part of their clinical evaluation and were included in the study. The mean age was 14.6 years (range 10-19); 80% were females. 29 (64.4%) of subjects met Rome III diagnostic criteria for any pain-associated FGID, 61% of the subjects met Rome III criteria for irritable bowel syndrome (IBS) and 34% met criteria for functional dyspepsia (FD). Joint hypermobility was present in 21 (51%) and fibromyalgia in 9 (20.9%) of subjects versus 11.7% and 6% respectively in the general population (p<0.001 and p=0.004). Compared to population studies in healthy children, the prevalence of joint hypermobility and fibromyalgia in our cohort was significantly higher. In the subgroup with IBS, 35.7% had hypermobility and 18.8% had fibromyalgia (p<0.001, p=0.001 respectively compared to general population). In the FD group, 70% had hypermobility and 50% had fibromyalgia (p<0.001, p=0.001 respectively compared to general population). POTS was diagnosed in 1/4th of our subjects, and the vast majority suffered from co-morbid disorders such as migraine headaches, dizziness, sleep disturbances, fatigue and dizziness. Objective data on postural orthostatic tachycardia syndrome (POTS) by tilt-table test and fibromyalgia tender point scores were analyzed in all subjects.

Conclusion: The high prevalence of joint hypermobility in our cohort may be a clue to an underlying pathophysiology involving connective tissue disorders in children with pain-associated FGIDs. The link between FGIDs and joint hypermobility is well recognized in adults. Children with joint hypermobility may be at a higher risk of developing pain-associated FGIDs and dysautonomia. Lack of recognition of these systemic symptoms may contribute to difficulties in successful medical management. We recommend screening children with FGIDs and symptoms of autonomic dysfunction for joint hypermobility using the Beighton scoring system, which can be
292 **CONSTIPATION AND SOILING DISORDERS: EFFECTS ON QUALITY OF LIFE IN A PEDIATRIC POPULATION.**

Alan Silverman, Katja Kovacic, Mana Sood, Center for Pediatric Neurogastroenterology, Motility, and Autonomic Disorders, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI

Background: Encopresis, an elimination disorder characterized by recurrent soiling episodes, affects 1% to 7.5% of the population. Approximately 80% to 95% of children with encopresis have a history of constipation. Previous studies have shown that children with constipation in isolation of other symptoms endorse lower quality of life compared to healthy controls, children with IBD, and children with gastro-esophageal reflux. Other work has shown that children with fecal soiling have lower emotional and social functioning. The aim of this study was to assess the relative effects of constipation with and without soiling on quality of life (QoL) and on general functioning.

Methods: This was a multi-center, prospective study with data from outpatient constipation clinics in five large regional children's hospitals. Children who met Rome III criteria for chronic constipation were included. Parents completed a demographic form, the PedsQL-Parent Report, the PedsQL-Family Impact Module (FIM), the Functional Disability Inventory-Parent Version (FDI), and the Pediatric Inventory for Parents (PIP). Children ages 12-18 years completed the PedsQL-Child Version, the Functional Disability Inventory-Child Version, and the Pediatric Symptom Checklist (PSC)-Youth Report.

Results: Families of 440 children ages 2-17 years (SD±3.7 years) completed questionnaire packets (53% male). 184 children had constipation in exclusion of other symptoms, 226 children had constipation with fecal incontinence, 14 children had constipation with irritable bowel syndrome, and 14 had fecal incontinence without constipation. Approximately 50% of the sample reported difficulty or failure to achieve toilet training for bowel movements. Another 40% reported moderate to large soiling events occurring multiple times weekly to daily. Severity of soiling was negatively, yet strongly associated with measures of QoL including measures of family impact (FIM-Total, F = 7.84; FIM-PHRQL, F = 4.70; FIM-FF, F = 6.62), measures of Parent QoL (FDI-Total, F = 5.69), and a measure of general QoL (PedsQL Total, F = 4.29). Older children tended to have worse reported QoL than their younger counterparts. Severity of soiling was significantly associated with a measure of physical function (FDI-Total Score, F = 3.11), a physical functioning problem scale (FDI-Total Difficulty, F = 9.26), and a measure of general functioning (PSC Total, F = 7.30). Frequency of soiling was significantly associated with only FDI-Total Score, (F = 2.89).

Conclusion: Children with constipation have lower perceived quality of life when compared with same age peers. A child's severity of constipation in exclusion of other symptoms, 226 children had constipation with fecal incontinence, 14 children had constipation with irritable bowel syndrome, and 14 had fecal incontinence without constipation. Approximately 50% of the sample reported difficulty or failure to achieve toilet training for bowel movements. Another 40% reported moderate to large soiling events occurring multiple times weekly to daily. Severity of soiling was negatively, yet strongly associated with measures of QoL including measures of family impact (FIM-Total, F = 7.84; FIM-PHRQL, F = 4.70; FIM-FF, F = 6.62), measures of Parent QoL (FDI-Total, F = 5.69), and a measure of general QoL (PedsQL Total, F = 4.29). Older children tended to have worse reported QoL than their younger counterparts. Severity of soiling was significantly associated with a measure of physical function (FDI-Total Score, F = 3.11), a physical functioning problem scale (FDI-Total Difficulty, F = 9.26), and a measure of general functioning (PSC Total, F = 7.30). Frequency of soiling was significantly associated with only FDI-Total Score, (F = 2.89).

293 **FEFal EXCRETION OF REDUCING SUBSTANCES IN INFANTS WITH DYSCHEZIA.** Alfredo Larrosa-Haro1, Laura E. Flores-Fong2, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2División de Pediatría, Hospital Civil de Guadalajara Dr. Juan I, Menchaca, Guadalajara, Mexico

BACKGROUND: Lactose intolerance has been proposed as an associated factor to infantile colic. Under this assumption, several infant formulas with low or without lactose are used widely.

OBJECTIVE: To explore the association of dyschezia with the fecal excretion of reducing substances (RS).

PATIENTS AND METHODS: Eighty-five infants <12 weeks were included in this cross-sectional study; 45 were seen at a GI clinic for colic associated to dyschezia (Rome III) and 40 controls were attended at a General Pediatrician office for control consultation. Overall median age was 5 weeks. About one-half of each group received human milk (HM) exclusively and the remainder received a standard lactose infant formula (SLIF). Infants fed with HM or SLIF were not included. Reducing substances (Clinitest®) were tested in fresh stools in all subjects.

RESULTS: Dyschezia was more frequent in girls (p=0.007). There was no association between the HM or SLIF feeding with dyschezia (p=0.919). RS were identified in both study groups as well as in both feeding types and were inversely related to age (r= -0.4, p<0.001). SR were present in the stools of 49.4% HM and 16.5% SLIF. RS in stools were not associated to dyschezia (p= 0.107).

CONCLUSIONS: It is interesting the finding of RS in healthy infants on HM or SLIF as an age-related condition. Our observations do not support the association of RS in stools with dyschezia.

294 **PREDICTION MODEL OF DYSCHEZIA IN INFANTS SINCE THE STOOL OUTPUT PATTERN: CASE-CONTROL STUDY.** Alfredo Larrosa-Haro1, Laura E. Flores-Fong2, Jesus Naress-Cisneros3, Rocio Macias-Rosales4, Carmen A. Sánchez-Ramírez5, Mariana Gómez-Nájera6, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 3División de Pediatría, Hospital Civil Dr. Juan I, Menchaca, Guadalajara, Mexico; 4Servicio de Gastroenterología y Nutrición, Hospital General 16, Instituto Mexicano del Seguro Social, Torreón, Mexico; 5Servicio de Gastroenterología y Nutrición, UMAE Hospital de Pediatría CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; 6Facultad de Medicina, Universidad de Colima, Colima, Mexico; 7Hospital de Gineco-Pediatría 48, Instituto Mexicano del Seguro Social, León, Mexico

BACKGROUND: Outpatient attention of infants <3 months who cry before passing stools is a frequent circumstance for pediatricians and gastroenterologists; however, this condition has not been validated.1 This study attempts to predict dyschezia since the stool output pattern.

OBJECTIVE: To achieve a predictive model for dyschezia since the stool output pattern.

PATIENTS AND METHODS: One-hundred and fifty controls seen at a General Pediatrician office and 150 infants with dyschezia (cases, Rome III) attended in five GI Clinics were included. An ad hoc instrument designed to evaluate quantitatively and qualitatively the stool pattern was applied to the infant's parents. Protein allergy was ruled out by cow's milk protein suppression for two weeks.
RESULTS: Overall group age was 9.3 weeks (SD 2.4), 49.2% were females. Cases (controls): onset of crying 2.8 weeks (controls: no crying reported as a problem), stool output/day 1.9 ± 1.8 (controls 3.1 ± 2.2, p=0.013), week-days passing stools 4.9 ± 2.8 (controls 6.7 ± 0.7, p=0.002). In infants with diarreha the proportion of infants with hard stools was higher, the proportion of soft stools was lower (p=0.031), the stools were darker (p=0.017) and bad smelling (p<0.001). The predictive factors included in the logistic regression model included Bristol 1-3 (OR 7.9, 95% CI 2.6-24.3), < 5 passing stools/week (OR 5.1, 95% CI 2-12.8) and < 2 stools/day (OR 2.3, 95% CI 1.1-4.8).

DISCUSSION: In this series a clear association of a constipation-like stool output pattern with diarreha was identified. These findings may suggest an underlying motility disorder.


295 FUNCTIONAL CONSTIPATION COEXISTING WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): PREVALENCE AND RESPONSE TO ADHD TREATMENT. James Lewis, Kelli Brown, Yoram Elitsur, Pediatrics, Joan C Edwards School of Medicine at Marshall University, Huntington, WV

BACKGROUND: Although the comorbidity of learning disorders and behavior problems with ADHD is well established, there is little data on the coexisting medical complication of functional constipation. The response of functional constipation to ADHD treatment is unknown.

OBJECTIVE: To determine the incidence of functional constipation in newly diagnosed pediatric patients with ADHD and to evaluate response to ADHD treatment.

MATERIALS AND METHODS: From June 2010 to May 2012 parents of newly diagnosed ADHD patients were prospectively recruited to complete a written survey documenting the presence of two or more Rome III criteria for functional constipation. All patients subsequently received multimodal treatment for ADHD by one physician following current evidence-based guidelines. Parents of patients diagnosed with functional constipation were then re-surveyed by telephone in late 2012. Pre and post treatment scores were based on the number of positive criteria present.

RESULTS: Of the 252 patients initially surveyed, 55 (22%) met criteria for functional constipation. Of the total, 41 (75%) had a history of painful or hard stools, 39 (72%) had a history of large diameter stools that obstructed the toilet, 28 (51%) had 2 or fewer defecations in the toilet per week, 22 (40%) had a history of retentive posturing and 20 (37%) had one or more episodes of fecal incontinence per week. Twenty seven patients (49%) participated in the telephone follow up survey. Results in table.

CONCLUSIONS: Functional constipation is a common coexisting conditions in pediatric patients with ADHD and should be addressed in evaluation and treatment protocols. The symptom severity of functional constipation improves with treatment for ADHD.

<table>
<thead>
<tr>
<th>Constipation Severity Score (0-5) n=27</th>
<th>Mean + Standard Deviation</th>
<th>p-Value Student t-test</th>
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</thead>
<tbody>
<tr>
<td>Pre-Treatment</td>
<td>3.04 ±0.82</td>
<td>0.00023</td>
</tr>
<tr>
<td>Post-Treatment</td>
<td>1.88±1.21</td>
<td></td>
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</tbody>
</table>

296 THE COST OF CARE FOR CHILDREN WITH GASTROPARESIS. Peter L. Lu, Erin Schaffner, Tala Alhajj, Beth Skaggs, Carlo Di Lorenzo, Hayat Mousa, Division of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Nationwide Children's Hospital, Columbus, OH

Background: The cost of care for adults with gastroparesis (GP) has been increasing over the past two decades as the number of hospital admissions for GP steadily rises. Information about the cost of care for children with GP is limited. Our aim is to evaluate the cost of hospital care for pediatric patients with GP.

Methods: A retrospective review of data from the Pediatric Health Information System (PHIS) was performed. All patients with a hospital admission diagnosis of GP based on ICD9 code with a discharge date between January 1, 2004 and June 30, 2012 were included in our study. Demographic information, number and cost of hospital admissions and emergency department (ED) visits, and additional diagnoses were recorded. Data was compared using chi-square analysis.

Results: A total of 3,829 patients were included (55% female, 29% 0-2y, 22% 3-8y, 25% 9-14y, 24% 15-21y). The number of admissions rose from 263 in 2004 to 1,007 in 2011, with a total cost increase from $18,912,420 to $103,859,663. The average cost per admission rose from $71,910 to $103,137. The annual number of ED visits rose from 6 to 63 visits, with a total cost increase from $7,060 to $151,594. The average cost per visit rose from $1,176 to $2,406. The most common additional hospital diagnoses were gastroesophageal reflux (38%), functional gastrointestinal disorders (FGIDs, 18%), and diabetes (6%). Hospitalization costs were higher among patients diagnosed with both GP and an FGID, with 41% of admissions costing more than the 75th percentile of GP admission costs ($92,212) compared to 21% among those with GP without an FGID.

Conclusion: In the first evaluation of the cost of GP in children, we have found that hospital-related costs for care of GP in children are significant and increasing dramatically. Not only is the number of hospital encounters rising, but the cost of each encounter is increasing as well. When compared to recent adult studies, the average cost of admission for GP is much higher in children. This is important information given the increasing recognition of pediatric GP and the growing emphasis on cost-effective evaluation and management of children with functional and motility disorders. Further studies are needed to evaluate the outpatient cost of care for GP and to compare the cost-effectiveness of various treatment options.
297  SHARED CARE: A QUALITY IMPROVEMENT INITIATIVE TO OPTIMIZE PRE-REFERRAL MANAGEMENT OF PEDIATRIC CONSTIPATION BY PRIMARY CARE PROVIDERS. Daniel Mallon1, Louis Vernacchio1, Alan Leichtner1, Jessica Kerr2; Richard Antonelli2,2, Samuel Nurko1, Jenifer Lightdale2, 1Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; 2Pediatric Physician's Organization at Children's, Boston Children's Hospital, Brookline, MA; 3Children's Hospital Integrated Care Organization, Boston Children's Hospital, Boston, MA

Shared Care is an initiative involving Boston Children's Hospital (BCH) and the Pediatric Physicians' Organization at Children's (PPOC), a large network of community-based primary care providers (PCPs). In Shared Care, sub-specialists provide PCPs with education, decision support tools, pre-referral management recommendations, and access to advice.

Aim: To assess the impact of Shared Care on referral rates and pre-referral management for pediatric constipation.

Methods: We reviewed all PCP charts of patients 1-18 years seen by a BCH gastroenterologist (GI MD) and diagnosed with constipation who were referred from 18 PPOC practices in the 6-month periods before and after implementation of Shared Care. Charts were assessed for documentation of constipation, as well as 4 key management recommendations: (1) dietary modifications (2) behavioral interventions (if age ≥3 years), (3) laxative use, and (4) fecal disimpaction (if indicated).

Results: Among children seen in the PCP practices during the study periods, a smaller proportion was referred to a GI MD and diagnosed with constipation after implementation vs. before (32 / 27,365 [0.12%] vs. 51 / 27,792, [0.21%], p=0.01). The average duration of PCP management prior to referral increased after implementation (9.1 vs. 5.2 months, p=0.09). There were no significant differences between groups in median age (5.9 vs. 8.3 years; p=0.2), sex (44% vs. 48% male, p=0.7), or proportions with PCP-documented constipation, (72% vs. 76%, p=0.6), or fecal incontinence (16% vs. 14%, p=0.8). No significant differences were found in the proportions of patients receiving any or all key management recommendations prior to referral.

Conclusions: Early analysis suggests Shared Care led to decreased referrals of children with constipation. This change appeared unrelated to population differences or incorporation of key recommendations, but there was a trend towards longer PCP pre-referral management.

Further study of factors affecting PCP referrals to GI MDs and more robust educational interventions to promote management recommendations are needed.

298  GASTROINTESTINAL DISORDERS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS: A META-ANALYSIS & COMPREHENSIVE REVIEW OF THE LITERATURE. Barbara McElhanon1, William Sharp2,3, 1Division of Pediatric Gastroenterology, Hepatology and Nutrition, Emory University School of Medicine, Atlanta, GA; 2Department of Pediatrics, Emory University School of Medicine, Atlanta, GA; 3Feeding Disorders Program, Marcus Autism Center, Children's Healthcare of Atlanta, Atlanta, GA

Gastrointestinal (GI) disorders have been observed in children with autism spectrum disorders (ASDs). This interest is propelled by now refuted evidence of "autistic enterocolitis", as well as high prevalence of food selectivity, increased interest in the use of parent-mediated diets, and a sense of urgency to identify factors which contribute to the etiology of ASD. Much remains unknown regarding the prevalence and topography of GI concerns in ASD. Summaries of the literature have involved qualitative reviews and/or expert opinion, including a consensus statement from Buie et al. (Pediatrics, 2010) which concluded children with ASD have at least the same amount of GI problems as typical children while also recognizing the need for more high-quality evidence-based research. This meta-analysis represents the first attempt to rigorously evaluate and quantitatively integrate empirical studies comparing the prevalence of GI problems in children with ASD.

The objective is to determine whether studies in the existing research literature provide empirical evidence of GI concerns in children with ASD versus control groups.

We conducted a systematic review and meta-analysis in accordance with guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. We searched Medline, PsychINFO, and PubMed databases (Jan 1980 to Sept 2012), reviewed reference lists, and conducted ancestral and online first searched in English language journals for eligible studies. Two researchers independently coded all extracted information using a standardized protocol with >90% agreement. We calculated effect sizes and associated 95% confidence intervals using a random-effects model and conducted heterogeneity tests, assessment of bias, and sensitivity analyses.

Results suggest children with ASDs are more likely to experience at least one GI concern compared to non-ASD peers (OR=1.4) and non-ASD siblings (OR=6.16). Constipation and diarrhea were the most frequent and statistically significant symptoms reported in this population (OR= 3.08 & 3.11 respectively). This study supports the observation that GI issues occur more frequently in children with ASDs. At a minimum, pediatricians should screen these children for GI problems. Corroborating with a recently published research agenda in Pediatrics 2012 by Coury et al., future research should expand on these findings through prospective population-based prevalence studies, identification of certain phenotypic subsets of children with ASDs most likely to have GI problems, increased uniformity in the assessment of GI problems, measuring change in ASD features related to GI problems, identifying opportunities and testing for early interventions.

299  EFFICACY OF KETOTIFEN IN CHILDREN WITH FUNCTIONAL DYSPEPSIA. Vajiheh Modaresisaryazdi1, Zeinab Safaei Ardakani1, Zafja Modarres1, Bahar Pakseresht1, 1Shohada Hospital, Social Security Organization, Yazd, Islamic Republic of Iran; 2Medical School, Shiraz University of Medical Sciences, Shiraz, Islamic Republic of Iran; 3Ashma and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran; 4Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Islamic Republic of Iran

BACKGROUND: Ketotifen is a mast cell stabilizer and useful in children with allergic diseases such as asthma and allergic rhinitis. It is also reported that Ketotifen could improve intestinal symptoms in patients with irritable bowel syndrome. The aim of this study was to evaluate the therapeutic effects of ketotifen on children suffering from functional dyspepsia.

PATIENTS AND METHODS: Thirty-two patients (aged 4-10yr) with functional dyspepsia who underwent diagnostic
gastroduodenoscopy with visual appearances of lymphoid hyperplasia and no other specific finding and histological report of nonspecific chronic duodenitis were enrolled and randomized into two groups. Both groups received specific dietary elimination, group (k) (15 patients) was also given Ketotifen (K) once daily (adjusted according to body weight, 50 mcg/kg/dose), whereas a placebo (P) was given to group P for 3 months. Primary outcome including frequency of abdominal pain, and parental perception regarding patient quality of life and side effect of treatment were assessed during treatment protocol.

RESULTS: 73% children (11 out of 15) in group (k) and 52% (9 out of 17) in group (p) were symptom free by the end of 2 months. No significant adverse effect of therapy was observed during the study.

CONCLUSION: These data demonstrate that oral ketotifen is effective and safe for use in treatment of children with functional dyspepsia and nonspecific chronic duodenitis.

300 TREATMENT OF ACHALASIA: A LONG TERM FOLLOW UP. Claudio Morera1,2, Samuel Nurko3, Leonel Rodriguez4, Steve Fishman4, 1Center for Motility and Functional Gastrointestinal Disorders, Boston Childrens Hospital, Boston, MA; 2Pediatric Gastroenterology, Boston Medical Center, Boston, MA; 3Surgery, Boston Childrens Hospital, Boston, MA

Achalasia is a rare esophageal motor disorder in infancy. The treatment goal is to release the functional obstruction of the lower esophageal sphincter. Scarce studies exist evaluating long-term outcomes after different therapeutic options for pediatric achalasia.

Methods: Retrospective chart review of patients with achalasia. Patients were divided in groups according to treatment received.

Results: Sixty nine patients were evaluated (34 male). Average age was 12 ± 4.6 years and average duration of symptoms before diagnosis was 23 ± 12 months. Symptoms at presentation included dysphagia 85%, regurgitation 59%, chest pain 22%, cough 21.7%, and weight loss 18.8%. Average follow up time was 24 ± 25 median 12 months (0.5 to 82 months). Treatment options included pneumatic dilatation (D) and surgical myotomy (S). The average number of treatments per patient (D or S) was 2.7 ± 1.9.

A total of 44 patients started treatment with dilatation (D group), and 29 had a surgical myotomy (S group). Dilatation group: 35/44 (79.5%) had only repeated D as therapy. Of those, 76.6% received 3 or less dilatations (average time between treatments of 17 ± 15.6 median 13.5 m). The rest of the patients (23.4%) had 4 or more dilatations; 9/44 (20.4%) eventually underwent S after an average of 2.9 ± 1.2 median 3 dilatations. Follow up after last treatment was obtained in 16/35 (46%) of the D patients that only had dilatation (average time 20.77 months) and in 7/9 (77.7%) of those that underwent surgery after dilatation (average 34.3 months). All reported being either "asymptomatic" or "markedly improved". No perforations were seen.

Surgical group: A total of 29 patients had surgical myotomy. Classic laparoscopic Heller myotomy with fundoplication (HM+FP) was done in 13 patients and thoracoscopic Heller myotomy without fundoplication (THM) in 16 patients. 20/29 started with surgery and 9 had surgery after failed dilatation. From the patients that started with surgery 11 had surgery with no further treatment and 9 needed dilatations after surgery. From the 9 patients with S after D, 5 needed further dilatations. Dilatation after surgery due to recurrence of symptoms was done in 48.3% (14/29) patients, distributed in 4/16 THM vs. 10/13 HM+FP, p = 0.006. One patient needed fundoplication surgically undone and another needed a repeat myotomy. No perforations or other major complications were reported. Follow up data was available in 20/29 (69%) patients (average time 26.6 m). All were reported as either "asymptomatic" or "markedly improved". Time of symptoms before diagnosis was 31.2 ± 34 months in patients with surgery vs. 15.7 ± 13.7 months in patients with only dilatation, p = 0.0001. Age of presentation, symptoms, or follow up time was not statistically different between treatment groups.

Conclusion: Repeated dilatations seem to be effective in the treatment of achalasia in children with more than a 75% response. Most patients control their symptoms with 3 dilatations or less. Surgery was very effective, but 55% required D after surgery, with those after HM needing less post op interventions than THM+FP.

Patients that needed surgery had longer evolution time before diagnosis.

301* MULTICHANNEL INTRALUMINAL IMPEDANCE REFERENCE VALUES FOR INFANTS AND CHILDREN. Hayat Mousa1,2, Frederick W. Woodley1,2, Marina Orsi1, Rodrigo S. Machado1, Jolie Benner1, Catherine Chao2, Beth Skaggs1, Mark Alhajj1, Tala Alhajj1, Carlo Di Lorenzo1,2, 1Gastroenterology, Nationwide Children's Hospital, Columbus, OH; 2Pediatrics, The Ohio State University, Columbus, OH

Background: While combined multichannel intraluminal impedance/esophageal pH monitoring (MII-pH) has become widely used for assessing gastroesophageal reflux (GER) in the pediatric population, there are no reference values with which to distinguish normal from abnormal results. Specific Aim: To identify a reference range of AGER and non-acid GER (NAGER) impedance values for infants and children. Methods: We evaluated MII-pH tracings for patients referred for GER assessment. We excluded patients who had AGER Indices greater than 50% of the upper end of normal by pH probe standards (i.e. >6% for children >12 months and >3% for infants ≤12 months), had a positive association of GER with symptoms, were on anti-reflux medications and/or had a fundoplication prior to the study. We also excluded studies with durations shorter than 20 hours. Values calculated included AGER, NAGER, and All Reflux % time, AGER, NAGER, All Reflux episode frequency, % proximal AGER and NAGER, median bolus clearance time (BCT) and longest episode. The upper end of normal (UEN) was established at the 90th percentile. Results: Study population consisted of 33 infants (14F/19M, median age 4.8 months [range 3 days-12 months]) with a median AGER Index of 2.2% (range 0.2-5.9%) and 70 children (22F/48M, median age 7.3 yrs [range 1.3-17yrs]) with a median AGER Index of 1.1% (range 0-3.0%). For infants (≤ 12 months), the UEN for total %Time AGER, NAGER, and All Reflux was 1.26, 1.82, and 2.42, respectively. For AGER, NAGER, All Reflux frequency, the UEN was 42, 60, and 86, respectively. The UEN for %proximal AGER and NAGER was 81 and 82%, respectively. The
302  **FOOD REFUSAL IN CHILDREN.** Sirish K. Palle, Karen Crissinger, Pediatrics, University of South Alabama, Mobile, AL

Background: Feeding difficulties are common in infants and young children and generally involve organic versus behavioral etiologies. Numerous studies have evaluated behavioral food refusal, but few have evaluated organic causes.

Objectives: To characterize feeding difficulties in children <10 years old and to evaluate the presentation, diagnostic work-up, management, and outcome of these children.

Methods: After IRB approval was obtained, children <10 years of age with a diagnosis of food refusal or feeding difficulties between 2000 and 2010 from the USA Pediatric GI database were identified. Data were collected via retrospective chart review. For children with GI diagnoses, they were divided into groups of CMPI/EoE (cow's milk protein intolerance & eosinophilic esophagitis), peptic disease (GE reflux, esophagitis, gastritis, & duodenitis), and motility disorders (delayed gastric emptying & constipation). Data were compared among age groups of 0-1 year, 1-4 years, and 4-10 years. STATA 12 software was utilized for statistical analysis with comparisons made via student t test or Fischer exact test as appropriate.

Results: Seventy-two children with food refusal or feeding difficulties were identified with 56% boys, 44% girls, 76% Caucasian, 20% African American, and 31% preterm. The mean age of onset of symptoms was 10 months and the mean age of presentation to the GI Clinic was 23 months with 38% 0-1 y.o., 51% 1-4 y.o., and 11% 4-10 y.o. Approximately 40% of children had weight for length <25th % at initial evaluation. GI diagnoses accounted for 83% and behavioral 17%. Of the 60 children with GI diagnoses, 32% were in the CMPI/EoE group, 33% were in the peptic disease group, and 35% were in the motility disorders group. Cow's milk protein intolerance was more common in infants compared to older children 58%. Constipation and motility problems were more common in children ages 1-4 years compared to other ages 62%.

Conclusions: Most children presenting to the Pediatric GI Clinic with food refusal have a gastrointestinal, rather than behavioral, explanation for their food refusal. Thus, referral for GI evaluation is recommended as an initial step to evaluate feeding difficulties rather than referral for behavioral management.

303  **PREVALENCE OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN THE OBESE AND OVERWEIGHT CHILDREN AS COMPARED TO NORMAL WEIGHT CHILDREN.** Uma P. Phatak1, Alexandra Friedman1, Gabrielle Guetta2, Dinesh Pashankar2, 1Yale University, New Haven, CT; 2Colgate University, Hamilton, NY

Background: Obesity has reached epidemic proportions in both adult and pediatric populations. Previous pediatric studies suggest an association between obesity and functional gastrointestinal disorders (FGIDs) such as functional constipation, irritable bowel syndrome, and functional abdominal pain. However, these studies are limited by retrospective study design, small sample size, and/or lack of suitable controls. We hypothesize that FGIDs are more prevalent in the obese and overweight children as compared to normal weight children.

Aim: To compare the prevalence of FGIDs such as functional constipation (FC), functional abdominal pain (FAP), functional abdominal pain syndrome (FAPS) and irritable bowel syndrome (IBS) between obese/overweight children and normal weight children using a cross-sectional study design.

Methods: Healthy children between the ages of 4-18 years were eligible for recruitment from the Yale Pediatric Primary Care clinic, Yale Adolescent clinic and a local private practice in Orange, CT. Only children presenting to the clinics for a well visit, immunizations or counseling were eligible to be enrolled. Children or parents were interviewed using a questionnaire based on the ROME III standardized criteria for diagnosing FGIDs. Medical records were reviewed to collect information about height, weight, body mass index (BMI), chronic medical conditions and medication use. Children were classified into obese, overweight and normal weight based on their BMI for age/gender. Data were analyzed to compare the prevalence of FC, FAP, FAPS and IBS between obese/overweight children and normal weight children.

Results: A total of 450 children (45% males) were recruited. There were 191 (42%) obese/overweight children and 259 (58%) normal weight children. There was no significant difference between mean age and gender between the obese/overweight and normal weight children. Caucasians were significantly more likely to be normal weight than obese/overweight. FAPS, FC, IBS were significantly more prevalent in the obese/overweight children than in the normal weight children (table). 44% of obese/overweight children had at least one FGID as compared to 28% of normal weight children (p=0.0004).

Conclusions: FGIDs such as FAPS, FC, IBS were significantly more prevalent in the obese/overweight children as compared to the normal weight children. Almost, one in two obese/overweight children had at least one FGID.
Comparison of prevalence of FGIDs in obese/overweight children and normal weight children.

<table>
<thead>
<tr>
<th></th>
<th>Obese/overweight children</th>
<th>Normal weight children</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAP (%)</td>
<td>13 (6.8)</td>
<td>15 (5.8)</td>
<td>0.69</td>
</tr>
<tr>
<td>FAPS (%)</td>
<td>37 (19.2)</td>
<td>25 (9.7)</td>
<td><strong>0.005</strong></td>
</tr>
<tr>
<td>IBS (%)</td>
<td>31 (16.1)</td>
<td>18 (6.9)</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>FC (%)</td>
<td>43 (22.3)</td>
<td>37 (14.3)</td>
<td><strong>0.03</strong></td>
</tr>
<tr>
<td>Any one FGID (%)</td>
<td>84 (44)</td>
<td>72 (28)</td>
<td><strong>0.0004</strong></td>
</tr>
</tbody>
</table>

* = significant p value (<0.05)

304 **PATIENT-REPORTED STARCH MALDIGESTION IN CSID.** Aileen De Jonge, Brandi Rabon, Heather Elser, QOL Medical, LLC, Raleigh, NC

Background: Congenital Sucrase-Isomaltase Deficiency (CSID) is a carbohydrate malabsorption disorder. Recent studies establish poor starch digestion in CSID patients, possibly due to low maltase levels on disaccharidase assays and in an in vitro study, sucrase-isomaltase was highly active in starch glucogenesis. Coexisting starch and sucrase malabsorption complicate CSID diet management, stressing the need to understand the prevalence of starch intolerance in CSID patients. Online CSID patient support groups (Yahoo!, c. 2002, 167 members & Facebook, c. 2012, 92 members) eagerly provide feedback and were surveyed for the prevalence of starch malabsorption.

Methods: Three polls asking patients about carbohydrate intolerances were conducted. The groups' administrator initiated 30-day polls using groups' built-in poll options, identified individual voters per poll, and consolidated votes from non-duplicated voters for a poll consensus.

Results: Results demonstrated a high prevalence of self-reported starch malabsorption in CSID patients. Three polls showed 80-100% of patients reported coexisting starch intolerance. (Table 1). Of 42 distinct voters in 3 polls, 55% report starch and sucrase intolerance, 36% report starch, sucrase, and lactose intolerance, and 9% report sucrase intolerance only. Poll consensus shows 91% of surveyed CSID patients report coexisting starch intolerance.

Conclusion: Starch digestion is reported as universally poor in CSID patients. The polls may contain a self-selection bias, since patients with starch intolerance may respond more readily. Some patients/poll responders who participate in these online support groups have historically reported coexisting starch intolerance. Therefore, the polls themselves were not viewed as creating a bias, but instead captured relevant starch information not previously shared with the medical community. Patient reports of coexisting CSID starch intolerance should be considered in order to evaluate and communicate appropriate dietary changes and treatment requirements for CSID patients.

305 **ASSOCIATION BETWEEN ANTRODUODENAL MOTILITY AND GASTRIC EMPTYING IN CHILDREN WITH UPPER GASTROINTESTINAL SYMPTOMS.** Sergio Pinillos1,2, Sean Trauernicht1,2, Samuel Nurko1, Leonel Rodriguez1,2

1Gastroenterology, Children's Hospital Boston, Boston, MA; 2Pediatrics, Hospital Infantil, Mexico, Mexico; 3Pediatrics, Hospital Sant Joan De Déu, Barcelona, Spain

Background: The association between antroduodenal manometry (ADM) and gastric emptying time by scintigraphy (GET) in children is unknown. We present our experience in children with upper gastrointestinal symptoms that underwent both GET and ADM. Methods: Children referred to a tertiary care center for evaluation and management of upper gastrointestinal symptoms refractory to conventional medical therapy undergoing ADM and GET within 3 months of each other. Variables evaluated from the ADM included the change of antral motility from fasting to the post-prandial state and also after erythromycin (EES) challenge. Abnormal responses (antral post-prandial hypomotility and absent antral response to EES) were defined as a change in motility index (MI) of <15% and also visually analyzed by 2 expert physicians. Delayed GET was defined as >60% retention at 1 hour. We used chi square for proportions to compare the proportions of normal and abnormal ADM and GET. Results: A total of 151 children were included, median age was 8.3 years (0-21 years) and 53% were female. Of those, 91/151 (60%) subjects had post-prandial hypomotility and 30/151 (20%) had no antral response to erythromycin. A total of 90/151 (60%) patients had delayed GET. We found no association between the change of antral motility during fasting to the post-prandial period (both by change in MI and visual diagnosis) and GET (p=0.62 and 0.25, respectively) but we found an association between delayed GET and lack of increase in antral motility after EES stimulation (both by change in MI and visual diagnosis, p=0.03 and 0.04, respectively). There was also a significant difference between the antral fasting and both post-prandial and post-EES MI. Information on response to therapy was available in 80 subjects. Of those, 65 received metoclopramide with only 3 responding favorably and 18 (27%) reporting side effects, EES was used in 26 and only 1 responded successfully, 8 out of 30 using domperidone reported improvement and 7 out of 31 using tegaserod had a successful outcome. Of the 8 responding to domperidone, all had delayed GET and 7 of those had normal EES response. Of the 7 that responded to tegaserod 6 had delayed GET and 4 of those 6 had normal EES response. Conclusions: Delayed GET is associated with abnormal response to EES and not with antral post-prandial hypomotility. Antral response to EES seems to be associated with response to some prokinetics. Further studies are needed to assess the role of GET and ADM in predicting response to therapy and outcome of children with upper gastrointestinal symptoms.
PUREED BLENDED DIET BY GASTROSTOMY TUBE (PBGT) USED IN GT-FED PATIENTS WITH AND WITHOUT NISSEN FUNDOPICATION (NF). Karla J. Au Yeung, Laura Davis, Tiffani Hays, Pediatrics, Johns Hopkins Hospital, Baltimore, MD

Daily vomiting and retching is distressful to patients and their parents. The PBGT has been reported as a strategy in feeding clinics for management of retching symptoms in GT-fed children who have a NF with the possibility of improving oral intake. There has been no comparison of PBGT in patients without NF or who have gastrointestinal (GI) dysmotility. METHODS: We conducted a retrospective chart review of patients who were managed with PBGT from January 2012 to May 2013. Patients were given individualized recipes and plans for initiation and advancement appropriate for their calorie and protein needs. Diets were evaluated for macro and micronutrient provision using ESHA, a food nutrient analysis software program. Growth was monitored in all patients on the diet and nutrient provision adjusted according to individual needs. Comparison was made between patients who had a GT alone and GT with NF. RESULTS: Twenty-six patients presented for initiation of PBGT. Parents of 6/26 (23%) patients declined after receiving teaching. Twenty patients started on the PBGT diet, 12 (60%) with GT/NF and 8 (40%) with GT alone. Elemental formula was the previous diet for 5/20 (25%); thus, a recipe was created for food allergies. Prematurity history was present in 7/20 (35%). Ages at initiation ranged from 14 months old (prematurity corrected to 10 months) to 13 years old. Symptoms leading to initiation of the PBGT included frequent episodes of vomiting, gastroesophageal reflux, or retching with no medical or surgical etiology that were unresponsive to standard medical management. Prematurity accounted for 58.3% of patients with GT/NF. Genetic syndromes and anomalies of the GI tract, with chronic GI dysmotility, accounted for 62.5% of the GT group. Tolerance of feeds was documented by continuation of the diet, decreased vomiting and/or retching episodes, and normal growth. In the GT/NF group, 100% showed tolerance and in the GT group, 87.5% (paired t-test, p = 0.63). Overall, retching and vomiting greatly improved from multiple episodes per day to a few episodes per week in both groups. Parents of 6 patients chose to maintain overnight continuous feed while using PBGT during the day for parental ease. Bowel movements were stable with the diet except for 3 (15%) patients who experienced constipation that resolved with appropriate therapy. Overall, oral feeds during the follow-up period improved in 9 patients (45%), 3 off GT now, who did not enter an intensive feeding program yet. Parents preferred this diet to commercially available tube feeding formulas because it was perceived as being more natural. During this time period, there were no admissions related to the diet, and no reports of unresolved tube clogging. In conclusion, with a highly trained pediatric nutritionist and very close follow-up, we were able to safely implement individualized PBGT diet plans which were tolerated in GT-fed patients with and without NF as well as GI dysmotility. The PBGT diet offers another option for patients with chronic vomiting and/or retching not responding to standard medical management.

CARBOHYDRATE (CHO), PROTEIN AND FAT INTAKE OF HEALTHY PAKISTANI SCHOOL CHILDREN IN A 24 HOUR PERIOD. Sina Aziz1, Kehkashah Hossain2, 1Pediatrics, KMDC, Karachi, Pakistan; 2Nutrition, Sindh Institute of urology and transplantation, Karachi, Pakistan

Objective: To determine the frequency of CHO, Protein and fat intake in 24 hours, by Pakistani school children (of different socioeconomic and cultural background) 6 to 16 years of age.

Methods: A cross-sectional study with multistage stratified sampling was done in a nationwide survey of Higher Education Commission (HEC, Ref no: 20-441/R&D/2008). Study was conducted from 2006-2009. Growth Centile charts have been published (JPMA 2012; 62:367-77). This is the final paper of the completed project and includes data on the nutritional status (quality and quantity of CHO, protein and fats) taken by healthy schoolchildren in a 24 hrs recall (breakfast, brunch, lunch, tea time, dinner and bed time). Food records of the 11,237 school children were subjected to USDA food exchange List. Results: School children 6 to 16 years of age, from different area of Pakistan took higher amount of CHO (range 60 to 74%) than the normal requirement; Protein (10 to 12%) and fat (18 to 32) were less than the normal requirement for age. (Table 1) Table 2 shows the percentage of CHO, protein and fat taken by the schoolchildren at various times in 24 hours Conclusion: Schoolchildren overall from Pakistan were taking a deficient amount of protein and fat in their daily diet as documented by a 24 hour recall method. CHO intake was higher than normal. Table 1: Percentage of CHO (carbohydrate), protein and fat taken by the schoolchildren in 24 hours, from Balochistan, Pakhtoonwala, Punjab and Sindh (and Karachi). Karachi has been described separately, being the largest city of Pakistan with the maximum population

<table>
<thead>
<tr>
<th>Area</th>
<th>No of school children</th>
<th>CHO %</th>
<th>Protein %</th>
<th>Fat %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baluchistan</td>
<td>1000</td>
<td>69</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>Pakhtoon</td>
<td>2,168</td>
<td>57</td>
<td>11</td>
<td>32</td>
</tr>
<tr>
<td>Punjab</td>
<td>1,792</td>
<td>61</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td>Sindh</td>
<td>3,577</td>
<td>67</td>
<td>11</td>
<td>22</td>
</tr>
<tr>
<td>Karachi</td>
<td>2,700</td>
<td>63</td>
<td>11</td>
<td>26</td>
</tr>
<tr>
<td>Sum and %</td>
<td>11,237</td>
<td>65</td>
<td>11</td>
<td>24</td>
</tr>
</tbody>
</table>
Table 2: Percentage of CHO (carbohydrate), protein and fat taken by Pakistani children, in 24 hours at breakfast, brunch (10 to 11 am), lunch (avg 1 pm), Tea time 4 to 5 pm, Dinner 7 to 8 pm and bedtime (half hour before sleep) 9 to 10 pm

<table>
<thead>
<tr>
<th>Time</th>
<th>CHO (%)</th>
<th>Protein (%)</th>
<th>Fat (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast</td>
<td>60</td>
<td>8</td>
<td>32</td>
</tr>
<tr>
<td>Brunch</td>
<td>68</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Lunch</td>
<td>74</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Tea time</td>
<td>61</td>
<td>8</td>
<td>32</td>
</tr>
<tr>
<td>Dinner</td>
<td>72</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Bedtime</td>
<td>43</td>
<td>2</td>
<td>55</td>
</tr>
<tr>
<td>Sum &amp; %</td>
<td>74</td>
<td>11</td>
<td>23</td>
</tr>
</tbody>
</table>

308 THE EFFECT OF A LOW CALORIE, NUTRIENT DENSE FORMULA ON THE USE OF MODULAR NUTRITION SUPPLEMENTS IN CHILDREN WITH DEVELOPMENTAL DISABILITIES. Amy Kluge1, Maureen B. Huhmann2, Darin Brannan1, 1The Children's Center, Bethany, OK; 2Clinical Sciences, Nestle Health Sciences, Florham Park, NJ

Introduction: Subgroups of pediatric patients with neurological impairments or neuromuscular disorders expend very little energy and are susceptible to excessive weight gain. Many of these children are dependent upon enteral tube feedings to meet all or part of their nutritional needs and may need to maintain an energy intake of less than 800 kcal/day. As standard enteral formulas for children traditionally meet protein and energy needs for children in approximately 1000 calories, these formulas are often manipulated to meet protein and other nutrient requirements without exceeding energy needs. This may involve the use of a base enteral formula plus additives such as protein modulars, vitamins, minerals and water. The objective of this study was to assess the impact of a low calorie, high protein, micronutrient enhanced enteral product on types and quantities of modular nutrition supplements required to meet nutritional needs.

Methods: Children aged 1-13 years old with development disabilities who were currently tolerating enteral feeding, and clinically assessed to have low energy needs for their age (based on a history of maintaining 50-90th% weight-for-age on the Kennedy Kreiger Growth Charts while consistently receiving less than their estimated energy requirement) were enrolled in this 24-day prospective study of a low calorie enteral formula. Following consent and enrollment, data were collected on tolerance, use of modular nutrition supplements, time to prepare formula for administration and adverse events. For the first three days, this data was collected while the subjects were receiving their usual enteral nutrition (EN) regimen. Then, for 21 days, subjects received the low calorie EN formula and the same data points were retrieved.

Results: Sixteen children aged 1-12 years (median age 4.69y) were enrolled in the study. Caloric goals were met 97% of time on the study formula in all patients and 12 patients had energy needs met 100% of the time. The remaining four patients met 61-95% of goal on the days when 100% of goal was not met. Prior to initiation of the study formula all subjects were receiving at least one modular supplement or water, and 94% were receiving two or more. Modulars included protein supplements, multivitamins, vitamin D, calcium and free water. Following initiation of study formula no additional water or modular supplements were used to meet the patients' nutrient and fluid needs. There was no difference in time to prepare the formula between the two formulas (1.64 vs. 2.03 minutes). There were no serious adverse events that occurred during the course of the study. No abnormal stool patterns, episodes of vomiting, or other signs of intolerance were documented.

Conclusions: A reduced calorie, nutrient dense enteral formula used in a population of hypometabolic, developmentally disabled children was safe and well tolerated. This product, which met the nutritional requirements of the children, and eliminated the need for formula manipulation, offers a tailored approach to the needs of hypometabolic children requiring tube feeding.

309 EXCLUSIVE ENTERAL NUTRITION FOR PEDIATRIC CROHN DISEASE - THE PATIENT AND CAREGIVER EXPERIENCE. Deirdre M. Burgess1, Scott Nightingale1,2, Elizabeth Notaras1, Milena Heinsch1,2, Eileen Guest1,2, Gay Woodhouse1, Katie Marks1, Diane Carmody1, Caron Blumenthal1, Paediatric Gastroenterology, John Hunter Children's Hospital, Newcastle, NSW, Australia; 1University of Newcastle, Newcastle, NSW, Australia; 1Paediatric Gastroenterology, Sydney Children's Hospital Network, Sydney, NSW, Australia

Background: Exclusive Enteral Nutrition (EEN) is an effective yet underutilized therapy for the induction of remission in pediatric Crohn disease. We aimed to elicit patient and caregiver experience with EEN to determine factors that may influence uptake and compliance to therapy.

Methods: Separate focus groups involving patients and caregivers with experience of EEN were undertaken. Semi-structured open-ended questions were used to guide discussion and to elicit participants' experiences with EEN, the difficulties encountered, and suggestions to improve therapy provision. Transcript summaries underwent thematic analysis achieving concept saturation and trustworthiness.

Results: Of 62 invited families, 16 patients (6 to 17 years) and 17 parents attended. Completion of >6 weeks of EEN using oral polymeric formula was achieved in 85% of participating patients. Seven major themes were identified: Sensory attributes including taste, temperature, volume, texture and satiety; Effectiveness of therapy; Practicalities such as cost, convenience, ease of use at school; Education provided prior to commencing, perceived attitudes of healthcare providers to EEN, experiences of other patients and families, internet resources, and the education of siblings, peers and schools around EEN; Support such as regular contact with medical team, parental and peer encouragement, access to support networks and to social workers and psychologists; Social and family impact including...
emotional reactions of child, impact on household routines, feelings of isolation and being different, impact on celebrations; Empowerment including patient/family involvement and autonomy in decision making to commence EEN.

Conclusions: Patient and caregiver experiences with EEN suggest a variety of themes which are likely to influence uptake of, and adherence to this therapy. Attention to these themes may allow for improved delivery and wider use of this effective therapy.

310 FIRST REFERENCE CURVES OF WAIST CIRCUMFERENCE FOR 14-TO 18 YEAR-OLD BRAZILIAN ADOLESCENTS IN COMPARISON TO INTERNATIONAL VALUES. Giovani P. da Costa, Fabio A. Lopez, PEDIATRICS - NUTROLOGY, UNIFESP - Federal University of São Paulo, SÃO PAULO, Brazil

Background: A multitude of studies have clearly demonstrated the close relation between central obesity, expressed by waist circumference (WC) and cardiovascular events in the paediatric scenario. There is a tendency for worldwide creation of population based specific reference curves, but in our country it is usual to use international data as standards, with special consideration to the American ones. Therefore the objective of the present study is to develop the first age- and gender-specific reference curves for waist circumferences in a Brazilian population of adolescents and compare those with international ones.

Methods: The design of the study was cross-sectional. A total of 1,842 adolescents (1,001 boys and 841 girls) aged 14-18 years were included in the study. The subjects were divided according to their gender. Waist circumference, using a standardized procedure, was measured with the patient in a standing position, having the level of the umbilicus as the target, using a constant tension tape to measure its value to the nearest 0.1 cm. After the Anthropometric measurements the age- and gender-specific waist circumference reference curves were constructed and smoothed with Cole's LMS method. The median curves (50th Percentile) were then used as a comparison to similar studies in other countries: USA, UK, Australia, Turkey, China, Cyprus, The Netherlands and Spain.

Results: In both genders we have identified a marked increase in waist circumference with age. For girls, the 50th to 90th percentile curves for WC had a sharp increase between 14 and 15 years, respectively, and then show a tendency to plateau after this age, whereas for boys, these curves had a persistent increase with age, until the age of 18 years.

Graphical comparison of the median curves with international standards shows clearly that each population compared follow a unique path throughout the ages. And it is observed that the Brazilian male adolescents follow the American ones until close to 17 years old, when our population surpass them abruptly. The same is observed to the female adolescent population, where we find an abrupt ascension of the 50th percentile comparatively to the American.

In comparison to other countries, we observe the same behaviour, in males and females, where Brazilian adolescents have a higher waist circumference value than the rest of the compared population as we approach the 17 year-old age marker. One exception was shown with the feminine values as compared to the Kuwaitian values, where the Brazilian female group was not higher. These study data can sum up to the existing international reference values for waist circumference of adolescents and can be used as an important tool for public health considerations.

Conclusion: Having compared the present data with those found in other countries, we can conclude that our waist circumference values were significantly higher, especially than the American standards, which are extensively used in Brazil. Our study results trigger concerns regarding the high WC values found among our adolescent groups and urges further studies.

311 MOVING FROM TUBE TO ORAL FEEDING IN MEDICALLY FRAGILE NON-VESAL TODDLERS: INITIAL FINDINGS FROM A RANDOMIZED CONTROLLED TRIAL. Ann M. Davis¹, Sarah Edwards², Amanda Bruce³, Hayat Mousa⁴, Jose Cojin⁵, Kelsey Dean¹, Paul Hyman⁵, ¹Pediatrics, University of Kansas Medical Center, Kansas City, KS; ²Children's Mercy Hospitals & Clinics, Kansas City, MO; ³University of Missouri Kansas City, Kansas City, MO; ⁴Nationwide Children's, Columbus, OH; ⁵New 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 megestrol 3 mg/k BID. After 5 d of megestrol tube feedings are reduced by 1 h/d. To date, 14 subjects have enrolled, and 9 have completed across three sites. The primary outcome variable is percent Kcal obtained orally. Because the study is ongoing, subjects and researchers remain blind to group assignment (amitriptyline vs. placebo). At baseline subjects were obtaining most of their calories via tube (M = 67%, SD = 17%). At the end of the intervention, subjects who completed the protocol consumed 100% of their calories orally. These initial data suggest that amitriptyline may not be a necessary component of a multidisciplinary protocol for food refusal in young children.

312 ASSOCIATION OF THE INTESTINAL MICROBIOME WITH OBESITY AND COMORBIDITIES IN CHILDREN. Jaria Chowdhury², Vincent Mortellaro², Carroll Harmon¹, Beverly Haynes¹, Casey Morrow¹, Ranjit Kumar³, Reed A. Dimmitt², ¹Pediatrics, University of Alabama at Birmingham, Birmingham, AL; ²Surgery, University of Alabama at Birmingham, Birmingham, AL; ³Microbiology, University of Alabama at Birmingham, Birmingham, AL

Background: Comparison of the intestinal microbiota in normal and obese adults has revealed differences in bacterial composition and diversity. Little is known about the impact of the microbiome on pediatric obesity and its complications.

Methods: We analyzed the fecal microbiomes of 11 obese children (mean BMI%tile 98.51) and 3 normal (mean BMI%tile 80.33) children. Samples were analyzed using PCR with primers for the 16SrDNA region and analyzed using Nextgen sequencing. Correlations and non-parametric analyses were used; significance p<0.05.

Results: We found that bacteria in the Firmicutes phyla are more abundant in normal controls (81%) than obese children (64%).

E 90
Firmicutes were the dominant phylum in 9 obese patients and all 3 controls. There was a trend toward more Bacteroidetes in obese patients (32% versus 16%). Linear regression shows a trend towards increasing BMI as the ratio of Bacteroidetes increases. (R² = 0.223) There was a positive correlation between an increasing Firmicutes ratio and vitamin D deficiency (p = 0.01). Higher Firmicute population trended towards a higher microbiome diversity (p = 0.15). Children with an increasing Bacteroidetes population trended towards a negative correlation with diversity (p = 0.0253). Children with high ALT (NASH) correlated with low diversity (p = 0.05).

Conclusion: We found that morbidly obese children may have different microbial profile than non-obese controls, in terms of complexity and diversity.

### 313 WHAT ARE THE PARAMETERS OF AVOIDANT/RESTRICTIVE FOOD INTAKE DISORDER IN CHILDREN?

**Douglas Field, Yekaterina Belousov, Harclerode Whitney, Keith Williams, Penn State Hershey Childrens Hospital, Hershey, PA**

**Introduction:** The classification of childhood feeding disorders has long been identified as being problematic and various proposals have been made for revision of the diagnostic criteria for shortcomings of the current system. A new classification, Avoidant/Restrictive Food Intake Disorder (ARFID) has been suggested to improve both clinical utility and provide a diagnosis for persons previously excluded from other feeding or eating diagnoses. The goal of the current paper is to examine the utility of this new ARFID classification with a sample of children referred to a multi-disciplinary feeding program.

**Method:** Participants included 421 children ranging in age from 4 to 219 months referred to a multi-disciplinary pediatric feeding program. A chart review was conducted for all children referred to the feeding program. The variables included in this study were obtained from a standard set of information routinely collected for all children referred.

**Results:** The majority of the children did meet the diagnostic criteria for ARFID. Most of the children were not underweight, however, there were significant numbers who were either tube fed (70) or receiving oral supplements (158). Gastrointestinal diseases were common and seen more often than other medical problems.

**Conclusions:** More children referred for feeding problems are identified with the proposed criteria for ARFID than the current DSM-IV diagnostic system. This may allow more children with feeding problems to receive treatment. This new diagnosis still has shortcomings which will be discussed.

### 314 PARENTAL STRESS LEVELS IN AN OUTPATIENT PEDIATRIC FEEDING CLINIC.

**Mark Fishbein¹, Kathryn Benton², William Struthers³, Pediatrics, Feinberg School of Medicine at Northwestern University, Chicago, IL; ²Pediatrics, Cadence Health, Winfield, IL; ³Psychology, Wheaton College, Wheaton, IL**

**Introduction:** Feeding disorders are common among children. Symptoms vary but may include slow weight gain, difficulties with food textures, picky eating and extreme food selectivity. Multidisciplinary feeding clinics are available regionally. Since established guidelines are not established for referral, there is little known regarding characteristics of this population. We speculate that increased parental stress, resulting from disruptive mealtimes, is principally responsible.

**Methods:** Eligible subjects included primary caretakers of children ages 2 to 6 years referred to an interdisciplinary outpatient feeding disorder clinic at Cadence Health in Winfield, Illinois. The group was subcategorized according to the presence or absence of caretaker-reported comorbidities including cerebral palsy, autism spectrum disorder, seizure disorder, facial structure defect, GERD, developmental delay, failure to thrive, oral dysphagia, food allergies or intolerance, and genetic syndrome. An equivalent sized sample of caretakers of age-matched children from the general population was recruited randomly from local general pediatric practices. The group was subcategorized according to the presence or absence of a non-referred feeding problem in the index child. Data collected included demographics, feeding characteristics, childhood eating behavior index (CEBI), and parental stress index (PSI-SF).

**Results:** A total of 144 participants comprising feeding disorder (n=72) and control (n=72) were enrolled. The age range of children with feeding disorder was between 24-30 months and controls were 4 years. There were 18 (25%) children with feeding disorder without comorbidities and 54 children (75%) with feeding disorder and at least one comorbidity. Controls had shorter mealtimes than their counterparts with feeding disorders (p<0.001). Eight children (11.1%) with feeding disorders took more than one hour to complete a meal. Among feeding disorders groups, children without comorbidities tended to have more prolonged mealtimes than children with comorbidities (p=0.06). The CEBI and PSI scores were higher in the feeding disorder group than the control group; CEBI (109.62±14.61 vs. 84.92±11.68, p<0.0001), PSI total (86.71±26.36 vs. 63.99±13.9, p<0.0001). There was a stepwise progression of PSI from control to feeding disorder w/o comorbidity to feeding disorder with comorbidity (see table).

**Conclusion:** Prolonged mealtimes and increased parental stress are characteristic of the children and parents attending outpatient feeding clinic. Both factors should be considered by primary care physicians when triaging children with feeding disorders.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=72)</th>
<th>Feeding disorder w/o comorbidity (n=18)</th>
<th>Feeding disorder w/ comorbidity (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEBI</td>
<td>84.92 (11.68)⁶</td>
<td>111.56 (11.38)⁶</td>
<td>108.97 (15.58)⁶</td>
</tr>
<tr>
<td>PSI</td>
<td>63.99 (13.9)⁶</td>
<td>75.28 (19.34)⁶</td>
<td>90.52 (27.41)⁶</td>
</tr>
</tbody>
</table>

a<b, p<0.001; c<d<e, p<0.05

### 315 FOOD CONSUMER CHARACTERISTICS IN A LOW SOCIOECONOMIC URBAN POPULATION: AN INFLUENCE ON THE OBESITY EPIDEMIC?

**Mark Fishbein¹, Siva Balasubramanian², Pediatrics, Feinberg School of Medicine at Northwestern University, Chicago, IL; ²Stuart School of Business, Illinois Institute of Technology, Chicago, IL**

**Introduction:** Environmental factors, including increased availability and consumption of non-nutritious food items, are believed to be major contributors to the obesity epidemic. The supermarket, as a point of service for food consumers, represents a potential site of
intervention to improve health. In this study, food consumer characteristics are compared among adult subjects according to their self-perceived weight status to determine distinguishing factors that may facilitate future treatment strategies.

Methods: Parents or caretakers of children attending a public high school in Humboldt Park (urban high school in Chicago IL) were provided with a questionnaire containing information regarding their food consumer characteristics and demographics. Humboldt Park has a population of 41,212 with a median household income of $29,245. Racial background is predominantly African American and Hispanic. Food consumer characteristics were categorized according to impulsive buying (predisposition toward unplanned or spontaneous purchases), behavior control (control of behaviors promoting good health), motivation to process nutrition information (desire to seek information likely to improve nutrition outcomes for food purchases), and health status (excellence of current health). Self-perceived weight status was determined by a 5 point single item scale with response choices including underweight, a little underweight, about the right weight, a little overweight, or overweight. Student's t-test was performed to compare food consumer characteristics between individuals with self-perceived "right" weight and lower vs. overweight.

Results: Study participants (n = 466, 83M, 383F) had a mean age of 38.7 years. Average grocery expenditure was $401 per month. Self-perceived weight status was underweight (n=13), a little underweight (n=20), about "right" weight (n=182), a little overweight (n=183), and overweight (n=57). Cronbach's coefficient alpha was 0.70 or above for all scales. There was no difference in impulsive buying and motivation to process nutrition information between weight groups. However, behavioral control (39.9 ± 6.0 vs. 36.8 ± 6.1, p<0.001) and health status (10.6 ± 2.3 vs. 8.5 ± 2.8, p=0.001) were both decreased in the overweight group.

Discussion: Food consumer characteristics vary according to weight status. Individuals viewing themselves as overweight also characterize themselves as less healthy and less capable of modifying behaviors that might promote their own good health, despite having similar motivation to process nutritional information. Interventions designed to empower and support this high risk population are necessary to alter current adverse behavioral patterns.

316 DYSLIPIDEMIAS AND BODY MASS INDEX IN CHILDREN. Rafael Guerrero-Lozano, Andrea Pérez, Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia

Introduction: Dyslipidemias constitute a cardiovascular risk factor present from childhood; they can be associated with unhealthy lifestyles, obesity and genetic factors.

Objectives: To determine the frequency of dyslipidemia in children and its relationship to body mass index (BMI); to determine the relationship between dyslipidemia and family history as well as feeding patterns.

Methods: From a population of 1103 school children aged 10-18 years, with obesity and overweight rate of 4.5 and 18.5%, respectively, 206 (54.3% females) 13.6±2.0 years of age, were randomized for measurement of total cholesterol (TC), HDL cholesterol (HDL), LDL cholesterol (LDL) and triglycerides (TG), after a 12-hour fast, using enzymatic colorimetry. Information was obtained on weight, height, BMI and demographics. Food frequency was surveyed via Internet. Data were processed in Excel 2007.

Results: Lipid profile (LP) was altered in 34.5%: TG 25.2, HDL 13.1, LDL 9.2, and CT 8.7%. Altered LP was found in 14.5% of overweight and obese children vs. 17.5% of those with normal BMI. CT: 163.4±29.4, 164.2±29.8, 164±29.6 mg/dL. TG: 96.2±55.2, 103.7±45, 122.8±77.8 mg/dL. LDL 99.8±25.0, 102.7±27.4, 103.7±23, 2 mg/dL. HDL: 52.2±13.2, 46.2±8.7, 41.5±10.4 mg/dL, all for normal BMI, overweight and obesity, respectively.

Children with dyslipidemia had family history of the latter in 52.1%.

Children with altered LP showed higher consumption of processed foods, and lower of fruits and vegetables. Consumption of fast food, soft drinks, industrial juices, dairy, and sweets was similar in children with normal and altered LP.

Conclusions: Total cholesterol levels are similar in overweight, obese and normal children. Triglycerides tend to be higher and HDL to be lower in children with overweight and obesity. Just over half of children with dyslipidemia have a family history of it. Children with altered lipid profile consume more processed foods and less fiber.

317 GROWTH AND NUTRITION IN CHILDREN WITH TRICHO THIODYSTROPHY. Emily Atkinson1, Diana Thiara1, Deborah Tamura1, John J. DiGiovanna2, Kenneth H. Kraemer2, Colleen Hadigan1, 1Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD; 2DNA Repair Section, Dermatology Branch, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, MD

Background: Trichothiodystrophy (TTD) is a rare autosomal recessive disorder of DNA repair characterized by defects in ectodermal tissues including short, brittle hair and ichthyosis, as well as impaired growth and development.

Study Design: Twenty-five patients with TTD were evaluated through a natural history study at the National Institutes of Health between 2001 and 2012. Retrospective and prospective data on nutritional status and height/weight were collected.

Results: In general, patients with TTD had considerable abnormalities in growth, with markedly low height-for-age and weight-for-age z-scores at initial evaluation which, in most cases, worsened over time. However, laboratory indices such as serum albumin, hemoglobin, and vitamins D and B12 were largely within normal limits. Patients who died during follow-up (n=5; mean age at death 9.6 yrs) had lower height-for-age z-scores (p=0.03), lower weight-for-age z-scores (p=0.006) and significantly increased heart rate (p=0.02) compared to the remainder of the cohort.

Conclusion: Children with TTD have markedly diminished weight-for-age and height-for-age relative to reference populations. Stunting may be a marker of increased mortality in TTD, but the cause of growth disturbances remains unclear.
### Growth and Nutritional Indices

<table>
<thead>
<tr>
<th></th>
<th>Mean Value ± SD</th>
<th>N</th>
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<tbody>
<tr>
<td>Sex (Male/Female)</td>
<td>15/10</td>
<td>25</td>
</tr>
<tr>
<td>Age at First Visit (years)</td>
<td>3.8 ± 2.5</td>
<td>25</td>
</tr>
<tr>
<td>Age at Last Visit (years)</td>
<td>6.4 ± 3.8</td>
<td>25</td>
</tr>
<tr>
<td>Height-for-age Z-score at First Evaluation</td>
<td>-2.75 ± 2.09</td>
<td>23</td>
</tr>
<tr>
<td>Height-for-age Z-score at Last Visit</td>
<td>-2.90 ± 2.45</td>
<td>23</td>
</tr>
<tr>
<td>Weight-for-age Z-score at First Evaluation</td>
<td>-2.60 ± 2.35</td>
<td>24</td>
</tr>
<tr>
<td>Weight-for-age Z-score at Last Visit</td>
<td>-3.24 ± 3.29</td>
<td>25</td>
</tr>
<tr>
<td>Change in Height-for-age Z-score</td>
<td>-0.73 ± 1.20</td>
<td>21</td>
</tr>
<tr>
<td>Change in Weight-for-age Z-score</td>
<td>-0.74 ± 1.52</td>
<td>24</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>3.8 ± 0.3</td>
<td>25</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>12.5 ± 0.9</td>
<td>24</td>
</tr>
<tr>
<td>25 OH Vitamin D (ng/mL)</td>
<td>34.5 ± 11.6</td>
<td>25</td>
</tr>
<tr>
<td>Vitamin B12 (pg/mL)</td>
<td>1165 ± 414</td>
<td>20</td>
</tr>
<tr>
<td>Serum Iron (μg/dL)</td>
<td>72 ± 26</td>
<td>20</td>
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### Research Session II – Liver Disorders

#### COMPLEMENT RECEPTOR DEPENDENT EFFECTOR FUNCTIONS REGULATE DUCT PATHOGENESIS IN EXPERIMENTAL BILIARY ATRESIA.

**Pranavkumar Shivakumar**, **Stephanie Walters**, **Kazuhiko Bessho**, **Reena Mourya**, **Rachel Sheridan**, **Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; Pathology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH**

**Background/Aims:** Biliary atresia (BA) is characterized by progressive inflammation of the extrahepatic bile duct (EHBD) culminating in biliary cirrhosis. Although we have assigned key roles to innate and adaptive immune responses in a mouse model of rotavirus (RRV)-induced experimental atresia, the role of complement activation in BA pathogenesis remains unexplored. We have previously shown elevated levels of serum C3a and C5a and complement receptor expression in livers after RRV challenge. Here, we hypothesize that C3aR and C5aR modulate hepatobiliary inflammation and mucosal injury.

**Methods:** Neonatal Balb/c wild-type (WT), C3aR-deficient (C3aR-KO) and C5aR-deficient (C5aR-KO) mice were challenged with saline or RRV soon after birth. C3aR/C5aR expression was quantified by flow cytometry using antibodies recognizing surface antigens. Intrahepatic gene expression was quantified by real-time PCR. Histology was performed using H/E-stained sections of EHBDs and livers. Cytolytic assays were performed using a murine cholangiocyte cell line (mCL) and intrahepatic NK cells from RRV-challenged mice. Genome-wide expression of datasets of human liver samples were generated for 64 infants with BA and 7 deceased-donor children as controls using GeneChip® Human Gene 1.0 ST Array.

**Results:** Flow cytometric analyses of WT intrahepatic lymphocytes at day 7 post RRV revealed increased population of NK cells expressing C3aR (saline=13.3±1.9, RRV=23.0±2.8%, P<0.001) and C5aR (saline=10.8±0.5, RRV=28.0±4.4%, P<0.0001) corresponding to duct injury. Strikingly, mCL showed higher levels of constitutive C5aR (38-44%) than C3aR (1.9-2.2%) expression. Challenging neonatal C3aR- and C5aR-KO mice with RRV, we observed growth failure, progressive jaundice and mortality akin to WT mice in C3aR-KO but not C5aR-KO mice. C5aR-KO mice resolved cholestasis by day 14 with improved long-term survival. Histological analysis of EHBDs and livers showed extensive inflammation, epithelial injury and portal expansion in C3aR-KO mice with preserved epithelial lining and normal parenchyma in C5aR-KO mice. Increased hepatic gene expression levels for Tnf-α, Il-1β and Tgf-β correlated with a worse outcome in C3aR-KO mice. Exploring mechanisms underlying C3aR/C5aR deficiency, we identified increased populations of Nkg2d+ NK cells specifically in livers of C3aR- (21.1±1.1%) but not C5aR-KO (5.7±1.3%, P<0.001) mice. Importantly, C5aR but not C3aR deficiency was associated with markedly reduced cytolytic activity of NK cells against mCL from day 7 (5-hrs, 1:10 effector:target ratio; C3aR-KO: 45.0±3.8%, C5aR-KO: 9.8±0.6%, P<0.0001) and day 14 (C3aR-KO: 46.4±4.1%, C5aR-KO: 3.3±2.4%; P<0.001) livers after RRV challenge. Examining the expression levels of human C3AR1 and C5AR1 in livers from BA patients at the time of diagnosis, we found increased expression of C3AR1 (1.86-fold; P=0.001) and C5AR1 (1.51-fold; P=0.041) over controls.

**Conclusions:** Our results assign an important role to complement receptor expression in the regulation of cellular and molecular activation leading to hepatobiliary injury in experimental atresia and uncover a potential target for therapeutic interventions.
**324 EVIDENCE FROM ZEBRAFISH AND PATIENTS THAT ADD3 IS A BILIARY ATRESIA SUSCEPTIBILITY GENE.**

Vivian Tang1, Ellen A. Tsai2,3, Nancy Spinner2,3, Randolph P. Matthews1,4, 1Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; 2Pathology and Laboratory Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; 3Genomics and Computational Biology Graduate Group, Children's Hospital of Philadelphia, Philadelphia, PA; 4Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA.

Objectives: Biliary atresia (BA) is a progressive fibro-inflammatory cholangiopathy affecting the intra- and extrahepatic bile ducts of neonates. Although BA is the most common identifiable cause of obstructive jaundice in infants, and is the leading indication for pediatric liver transplantation, the etiology remains elusive. We investigated the importance of genes identified in genome-wide association studies (GWAS) of BA patients using zebrafish. The Matthews lab has demonstrated the utility of the zebrafish system to test the functionality of genes identified in GWAS of biliary atresia (BA) by demonstrating that knockdown of gpc1 leads to biliary defects. Methods: A prior GWAS examined single-nucleotide polymorphisms in 200 Han Chinese BA patients and 481 ethnically matched controls. The strongest association was found for a region located between the XPNPEP1 and ADD3 genes on 10q24.2. Our genetic analysis confirmed the importance of this region in a separate cohort of patients.

To determine whether loss of xpnpep1 and/or add3a leads to biliary defects we performed knockdown studies of the respective genes using morpholino antisense oligonucleotides (MO). We then examined their biliary function using the lipider reader PED6, biliary development using cytokeratin immunostaining, and gene expression using quantitative PCR.

Results: We confirmed that xpnpep1 and add3a are expressed in the developing zebrafish liver. Knockdown of add3a led to decreased biliary function by PED6 screening, while xpnpep1 knockdown had only a mild effect. There were developmental biliary defects in the add3a morphants, as demonstrated by cytokeratin immunostaining. The transcription factor vmf1, implicated in biliary development, was significantly downregulated in add3a morphants but not xpnpep1 morphants. add3a morphants also demonstrated increased expression of gli2a, a Hedgehog target, which is consistent with prior studies of BA patients and of zebrafish models of BA such as gpc1 knockdown. Interestingly, knockdown of both add3a and gpc1 resulted in a synergistic disruptive effect on biliary development. Conclusions: While GWAS identified ADD3 and XPNPEP1 as potential BA susceptibility genes, our results suggest that ADD3 is likely the more important gene in this regard. Like gpc1, add3a acts via Hedgehog signaling, supporting a role for this important pathway in BA pathogenesis.

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**325 LONG TERM EFFECT OF SEBELIPASE ALFA IN PATIENTS WITH LYSOSOMAL ACID LIPASE (LAL) DEFICIENCY.**

Chester B. Whitley1, Simeon Boyadjiev2, Christopher Bourdon1, Stephen Eckert1, Bruce Kessler1, Vera Malinova1, Eugene Schneider2, Reena Sharma1, Christopher Twelves3, Vassilis Valayannopoulos4, Anthony G. Quinn1, 1University of Minnesota, Minneapolis, MN; 2Health Sciences North, Sudbury, ON, Canada; 3Salford Royal NHS Foundation Trust, Salford, United Kingdom; 4University of California-Davis, Sacramento, CA.

Background: Lysosomal Acid Lipase Deficiency (LAL Deficiency) is an autosomal recessive disorder which results in abnormal cholesteryl esters and triglycerides accumulation within the lysosome. Most patients present with dyslipidemia, elevated transaminases and/or hepatosplenomegaly with frequent progression to cirrhosis and early death. Patients' signs and symptoms may overlap with other disorders and as such maybe underdiagnosed or misdiagnosed. There are no approved pharmacological therapies that address the underlying disorder.

Methods: LAL-CL04, an ongoing phase 1/2 extension trial, evaluates the long-term effects of every-other-week IV infusions of 1 mg/kg or 3 mg/kg of sebelipase alfa (an investigational human recombinant human lysosomal acid lipase) in LAL deficient patients (n=8). Most patients were on stable background lipid-lowering therapy (statins or combination therapy).

Results: The rapid improvement in transaminase values to normal ALT and AST seen after initiation of treatment was maintained at 52 weeks with mean percent decreases from pre-treatment baseline of 56% and 40%, respectively (p=0.031). Additionally, patients had a mean improvement in liver volume of 14% and mean reduction in fat fraction of 55% (assessed by MRI) at week 52. All lipid parameters improved during the course of the first year of treatment, with additional benefit noted between week 24 and 52. The mean percent decreases for LDL, total cholesterol and triglyceride were 63%, 42% and 47% at week 52, respectively, with a mean increase in HDL of 29% (p=0.031 each). AEs were mainly mild and unrelated to sebelipase alfa. Two SAEs (cholestaticis and cholelithiasis) occurred in one subject and were deemed unlikely related to sebelipase alfa. Infusion-related reactions (IRRs) were uncommon. One patient had a moderate allergic-type IRR and has paused treatment pending skin testing. No anti-drug antibodies have been detected in any patient to date.

Conclusions: These results demonstrate that long-term, every-other-week dosing with sebelipase alfa produces sustained improvement in patients' transaminases and lipid profile. A global, randomized, placebo-controlled phase 3 trial to assess the safety and efficacy is underway (ARISE: NCT01757184).

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**326 DIFFERENTIAL EXPRESSION AND ROLE OF MICRONRNAS IN THE TOLEROGENIC PROPERTIES OF HEPATIC PLASMACYTOID DENDRITIC CELLS.**

Audrey H. Lau1,2, Liang Wei2, Xiumei Qu2, Sheri M. Krams2, 1Pediatrics, Division of Gastroenterology, Hepatology, and Nutrition, UCSF, San Francisco, CA; 2Surgery, Division of Transplantation, Stanford University, Stanford, CA.

Liver allografts are well tolerated and other solid organ allografts, such as the small intestine (SI) or kidney, when transplanted concurrently with livers, show improved graft outcomes. However, the mechanisms underlying "hepatic tolerance" have yet to be elucidated. Previous data show that liver dendritic cells (DC) can regulate immune responses and, compared to DC from lymphoid tissue, have diminished antigen presenting and immune stimulatory function. Current postulation to explain the differential properties of liver DC has been that functional differences between DC subsets including plasmacytoid (p)DC and myeloid (m)DC exist. Indeed, it has been
Hypothesized that immature pDC are inherently tolerogenic and data from multiple studies show that pDC play a unique and important role in the generation of tolerance. A recent paper examining pediatric patients who are rejecting SI transplant have a higher ratio of mDC to pDC, supporting a tolerogenic role for pDC. Our work confirms that hepatic pDC prolong cardiac allograft survival (p<0.01) in a murine model of cardiac transplantation compared to bulk and mDC. Using microarray analysis and confirmation with quantitative polymerase chain reaction, we investigated changes in specific microRNA (miR) - short (15-22 nucleotides) RNA molecules which can post-transcriptionally regulate messenger RNA transcripts - in hepatic pDC. mir-23b (p<0.01) and -181a (p<0.005) are significantly elevated in hepatic pDC compared to hepatic mDC and splenic DC (mDC and pDC). Using bioinformatic analysis, predicted mRNA targets (p<0.05) for these microRNA include SP1, MAPK1, JAK1, and IL12B. These data suggest that therapeutics which enhance mir-23 and mir-181a expression or decrease expression of specific targets may promote tolerance.

Saturday, October 12, 2013

Plenary Session II

Young Faculty Clinical Investigator Award

327 MUCOSAL HEALING IN CHILDREN WITH TREATED CELIAC DISEASE (CD). Imad Absah1,2, Joseph A. Murray1, Yousef Ghazzawi1, Alberto Rubiio Tapia2, 1Department of Pediatric Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; 2Department of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN

Background: CD is characterized by small bowel (SB) mucosal injury, comprising influx of lymphocytes into the epithelium, crypt hyperplasia, and villous atrophy. Pediatric data suggest complete mucosal healing after starting gluten-free diet (GFD), and current practice suggests that a repeat biopsy is rarely required. However recent adult data using endoscopic biopsies found substantial numbers failed to heal and this failure was associated with long term complications.

Aim: #1 Assess the rate of mucosal healing in response to a GFD in children with CD.

#2 Document the most common indications for 2nd SB biopsy in children with CD.

Methods: We conducted a retrospective chart review of pediatric patients with CD between 1997 and 2013. We included children age (0-18) with SB biopsy proven CD, who had 2nd SB biopsy. Demographics, symptoms, and histologic findings were recorded.

Results: Forty out of 222 (18%) children with CD had 2nd SB biopsy. Average age at diagnosis was 8.5 years ±4.5 SD, 14 were males (35.89%) and 27 (64.10%) females. On the 1st biopsy 26 patients (65%) had partial villous atrophy, 10 (25.64%) had complete villous atrophy, and 4 had increase intraepithelial lymphocytosis (IEL's). The most common indication for 2nd SB biopsy was abdominal pain in 20 patients (50%), diarrhea in 7, constipation in 4, follow up in 7, and persistent positive serology in 1.

Average time between 1st and 2nd biopsies was 24 months ± 22 SD. On the 2nd biopsy 25 patients (62.5%) showed complete resolution, 9 patients (22.5%) showed persistent IEL's and 6 patients (15%) had persistent SB injury. Only 1 patient was noncompliant with the GFD due to lack of symptoms. Out the 5 compliant patients 2 had mildly positive TTG with improved histology from complete to partial villous atrophy within 18 months average time between biopsies, and 3 had negative serology and complete villous atrophy. Only 2/20 (10%) patients with abdominal pain as an indication for the 2nd biopsy had persistent villous atrophy with negative serology. All patients with constipation as an indication for the 2nd biopsy had complete resolution. One out of the 7 patients with diarrhea as an indication for the 2nd biopsy had persistent villous atrophy with negative serology.

Conclusion: We found that 5/40 (12.5%) of the children with CD who underwent 2nd SB had persistent villous atrophy after 24 months on GFD. Abdominal pain was the most common indication for repeating the SB biopsies in children. Persistence of clinical symptoms pain, diarrhea, and constipation didn't correlate with the persistence of mucosal injury. Healing of symptomatic treated patients with CD is not universal but occurs much more frequently than adults.

Young Faculty Investigator Award

328 HISTAMINE DRIVES INNATE INFLAMMATORY DAMAGE IN ULCEURATIVE COLITIS. Joshua B. Wechsler1, Terrence A. Barrett1, Paul J. Bryce3, 1Pediatrics, Division of Gastroenterology, Hepatology, & Nutrition, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL; 2Medicine, Division of Gastroenterology & Hepatology, Northwestern Memorial Hospital, Chicago, IL; 3Medicine, Division of Allergy & Immunology, Northwestern Memorial Hospital, Chicago, IL

Rationale: Ulcerative colitis (UC), a subtype of Inflammatory Bowel Disease (IBD), is a chronic inflammatory disorder associated with inappropriate activation of the mucosal immune system. The underlying pathogenesis of UC is poorly understood but GWAS and animal studies have indicated that abnormal responses in both the innate and adaptive immune system contribute to disease pathogenesis. IBD patients have increased secretion of mucosal histamine, a bioactive amine best associated with allergic reactions, as well as excretion of a urinary metabolite, n-methylhistamine, both of which correlate with disease severity. Furthermore, animal studies utilizing experimental colitis models have suggested roles for histamine and its receptors (H1R-H4R) in promoting UC-like inflammation. Despite this, the mechanism remains unclear.

Initially, we examined the expression pattern of the histamine receptors in newly diagnosed UC patients and compared this to healthy controls. We found increased expression of H4R, but not H1R or H2R in biopsies from UC patients, thereby suggesting a potential role in pathogenesis.

To explore the requirement and role of H4R in both innate and adaptive immune responses in UC, we utilized two experimental models of colitis; oxazolone colitis, a delayed-type hypersensitivity response which has a prominent Th2-associated adaptive response, and DSS colitis, which is driven primarily by innate immune responses.

METHODS: Wildtype (WT) mice were compared to H4R Knockout (KO) or Histamine deficient (HDC KO) mice in oxazolone and DSS...
colitis. For oxazolone colitis, 8-10-week-old male mice were sensitized on the shaved abdomen with 3% oxazolone followed 7 days later by intrarectal administration of 1% oxazolone. For DSS colitis, 8-10 week-old female mice were fed 3.5% DSS for 6 days. Mice were monitored daily for weight loss, diarrhea, and rectal bleeding. Mice were euthanized after 3 days for oxazolone colitis and 9 days for DSS colitis. Colonic length was measured and colonic tissue was formalin fixed for H&E and IHC. RNA and protein were isolated from colonic lysates and analyzed by RT-PCR and ELISA respectively.

RESULTS: Compared to WT mice, H4R KO or HDC KO mice had significantly reduced weight loss, disease activity, colonic shortening, and histologic severity in either colitis model. H4R KO and HDC KO mice had significantly reduced colonic IL-6, CXCL1 (KC), & CXCL2 (MIP2α), molecules important for recruitment of neutrophils. In accordance, the colonic tissue of H4R KO mice had reduced infiltrating myeloperoxidase-staining neutrophils in the mucosa. Despite the significant impact on intestinal damage and overall health, H4R KO and HDC KO mice had a normal Th2 adaptive response in oxazolone colitis, characterized by normal expression of IL-4 and IL-13.

CONCLUSION: Our data suggests that the histamine/H4R pathway regulates colonic inflammation through regulation of the innate immune response via promoting neutrophil infiltration in the colonic mucosa through IL-6, CXCL1, and/or CXCL2. We are currently exploring the cellular source of histamine along with the critical mucosal cell involved in H4R signaling in the colitis response.

Research Session III – Nutritional Disorders

329  EFFECT OF AN EXTENSIVELY HYDROLYZED PROTEIN HUMAN MILK FORTIFIER ON THE GROWTH OF PRETERM INFANTS.  

Jae H. Kim1, Gary Chan2, Richard Schanler3, Sharon Groh-Wargo4, Reed Dinnitt5, Larry Williams6, Geraldine Baggs6, Bridget Barrett Reis6, 1Pediatrics, UC San Diego, San Diego, CA; 2University of Utah, Salt Lake City, UT; 3Cohen Children’s Medical Center of NY, New Hyde Park, NY; 4MetroHealth Medical Center, Cleveland, OH; 5University of Alabama, Birmingham, AL; 6Abbott Nutrition, Columbus, OH

Background: Multicomponent human milk fortifiers (HMF) are required to supplement the nutritional base of human milk for the best growth of preterm infants. More extremely low birth weight infants are surviving than in the past. These vulnerable infants increase the clinical need for human milk fortifiers with higher protein and reduced or absent microbial content (commercial sterility).

Objectives: The objectives of this study were to demonstrate that a newly formulated concentrated liquid versus standard powdered human milk fortifier would support growth and tolerance when added to human milk.

Methods: This was an unblinded randomized controlled multicenter study conducted on preterm infants receiving human milk supplemented with two randomly assigned human milk fortifiers (HMF), either a newly formulated HMF containing liquid extensively hydrolyzed bovine protein (LE-HMF) or a conventional powdered intact bovine protein HMF (Similac Human Milk Fortifier, PI-HMF) as control. The study population consisted of preterm infants ≤ 33 weeks gestational age with birth weights ranging from 700 to 1500 g who were enterally fed human milk. Infants were studied from the first day of human milk fortification when subject reached an intake of at least 100 mL/kg/day of human milk until day 29 after fortification began or hospital discharge, whichever came first. Anthropometric indices, feeding tolerance, serum biochemistries, enteral intake, and morbidity data were assessed.

Results: A total of 147 preterm infants were enrolled at 14 NICUs. There were 129 infants in a total intent-to-treat (ITT) population, with 75 of these infants in a strict evaluable (SEV) group with complete data to the end of the study. There was no statistical difference for the primary outcome of weight gain (g/kg/day) between the groups in the ITT or SEV analyses. Weight gain reported in the ITT analysis was 17.5 and 18.2 g/kg/day for the PI-HMF and LE-HMF, respectively. In the SEV subset of infants, the weight over the course of the study in the experimental group (LE-HMF) exceeded the control group (LE-HMF > PI-HMF, p=0.036) and those infants receiving LE-HMF reached 1800 g ~ 1 week sooner than the infants fed PI-HMF (19 versus 26 days, respectively; p = 0.049). In the ITT analyses no differences were seen with the secondary outcomes, length and head circumference (HC) gains (cm/week) but in the SEV subset of infants the length over the course of the study in the LE-HMF exceeded the PI-HMF (p= 0.029). The protein intake from fortified human milk was significantly higher in the LE-HMF group as compared to the PI-HMF group (3.9 vs. 3.3 g/kg/day; p< .0001). Both fortifiers were well tolerated with no significant differences in overall morbidity.

Conclusion: The improved growth, excellent tolerance and low incidence of morbidity outcomes point to the safety and suitability of this experimental HMF for preterm infants. Growth with this fortifier closely matches the recent recommendations for a weight gain of at least 18 g/kg/day.

330  SHORT BOWEL SYNDROME: 100% RESOLUTION OF CHOLESTASIS AND 99% SURVIVABILITY- MEDICAL MANAGEMENT AND NON-TRANSPLANT SURGICAL OPTIONS VS. INTESTINAL TRANSPLANTATION? Clarivet -. Torres1, Anthony Sandler2, Sona -. Sehgal1, Khan Muhammad3, Artis Krystal1, Roshnee Pennigton1, Carola Cerezo-Allen1, Parvathi Mohan4, 1Gastroenterology, Childrens National Medical Center-George Washington University, Washington, DC; 2Surgery, Children’s National Medical Center- George Washington University, Washington, DC

Eighty one parenteral nutrition dependent SBS patients were enrolled. Fifty one were males. Median age was 4 months. Median intestinal length was 40cm. The initial median daily caloric requirement by PN was 100%. Height, weight Z score, platelet, albumin, and direct bilirubin (DB) were obtained at the beginning and end of the study. Forty nine patients (61%) had hyperbilirubinemia, mean DB: 10 mg/dl (3-32mg/dl), 22 had liver biopsies (11 portal fibrosis, 7 Bridging fibrosis, 4 cirrhosis). All 49 patients with hyperbilirubinemia normalized their bilirubin over a mean time of 10 weeks. Forty one (81%) reversed their cholestasis while receiving PN, using soy bean intralipid (SBIL). Of the 81 patients, 25 had 30 lengthening procedures (9 Bianchi, 21 STEP), and 13 had ostomy in continuity due to severe dysmotility. Four were listed for intestinal transplant: 2 were transplanted with a bowel length of 4 and 10 cm of Jejunum. One listed patient was weaned off PN (DB: 12mg/dl now normal, 10cm of jejunum and half colon). The fourth listed patient is inactive with no signs of liver disease (DB 19mg/dl now normal, 10cm of jejunum and sigmoid colon).
One died of cardiac anomalies. Among the 78 remaining patients, the mean caloric requirements by PN decreased from 100% to 7.5% and 67 patients (86%) were weaned off PN over a median time of 4 months (1-60 months). All laboratory parameters showed improvement (p<0.0001). Overall survival was 99%.

Patients with SBS treated at CNMC reverse their cholestasis using SBIL effectively and in a shorter time compared with recent reports using Omegaven. With meticulous medical/surgical management, patients with advanced liver disease can improve their liver function and nutritional parameters with the ability to discontinue PN and avoid transplantation. Our IRP at CNMC has shown one of the best survivability rates (99%) for patients with SBS with medical and non-transplant surgical treatment. The treatment of SBS PN-dependent patients should be based on medical and non-transplant surgical options. Intestinal transplant should only be considered when those measures fail.

331 INCREASE IN ARGinine VASOPRESSIN IS ASSOCIATED WITH THE REDUCTION IN BLOOD PRESSURE IN PATIENTS WITH CHRONIC NAUSEA AND ORTHOSTATIC INTOLERANCE. John E. Fortunato1,2, Ashley L. Wagoner1, Hossam A. Shaltout1, Debra I. Diz1, 1Pediatrics, University of Colorado, Aurora, CO; 2Hypertension and Vascular Research Center, Wake Forest School of Medicine, Winston-Salem, NC; 3Neuroscience, Wake Forest School of Medicine, Winston-Salem, NC

Background: Orthostatic intolerance (OI) is a common finding in subjects presenting to the GI clinic with functional gastrointestinal disorders, particularly chronic nausea. Vasopressin (AVP) release is triggered by a fall in blood pressure (BP) and may cause nausea. Therefore, we studied the relationship between AVP and tilt-induced changes in BP in 48 children with chronic unexplained nausea and OI. Methods: The mean age was 15.2 (range: 10-18) years with 36 females and 12 males. A validated nausea questionnaire (nausea profile [NP]) reporting symptoms of OI and nausea was completed 2 weeks prior to undergoing tilt table testing. NP scores were obtained by calculating the percent of total points scored (actual score/153 X 100%). Subjects were in the supine position for 15 min before undergoing a 45 min upright tilt (from 0 to 70 degrees). Plasma AVP was measured in blood sampled immediately before and 15 min into upright tilt. Results: Of the 48 tilt tests: 29 patients tested normal and 19 had OI. OI was further classified as: postural orthostatic tachycardia syndrome (POTS; heart rate >120 bpm or increase by 40 bpm during first 10 min of tilt; n = 5), neurally mediated hypotension (NMH, decrease in systolic blood pressure [SBP] >20 mmHg or diastolic blood pressure [DBP] >10 mmHg during first 10 min of tilt; n =13), and neurocardiogenic syncope (NCS; n = 1). NP scores were higher among children with nausea and OI vs. those without OI (56% ± 5% vs. 40% ± 4%, respectively, p=0.01). Supine BPs did not differ between groups with only slightly higher AVP levels in OI vs. non-OI subjects (7 ± 4 pg/mL vs 2 ± 0.2 pg/mL, respectively, p = NS). During upright tilt, mean SBP was lower in OI vs. non-OI subjects (96 ± 5 mmHg vs 112 ± 4 mmHg, respectively, p=0.01); whereas, AVP was higher in OI vs. non-OI subjects, (57 ± 19 pg/mL vs. 27 ± 11 pg/mL, respectively, p=0.05). There was a negative correlation between AVP and both SBP and DBP during tilt (r= -0.29, p = 0.05 and -0.4, p = 0.01, respectively). Conclusion: These data reveal an acute increase in AVP in subjects with OI and nausea, perhaps as a compensatory factor in response to the hypotension associated with OI. The relationship between the increase in AVP and the nausea remains to be determined, but better understanding of the hormonal profile in these subjects may allow more effective treatment options for chronic nausea and OI.

Research Session IV – Basic Research in Inflammatory Bowel Disease

332 SLC11A1 POLYMORPHISM INCREASES THE RISK OF EARLY SURGERY IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Samantha Fish1, Zhi Wei2, Jonathan Bradfield1, Kernika Gupta1, Cassandra Spengler1, Ashley Martin1, Colleen Judge1, Louis Ghanem1, Hakon Hakonarson1, Robert Baldassano1, Judith Kelsen1, 1Pediatrics, University of Colorado, Aurora, CO; 2Hypertension and Vascular Research Center, Wake Forest School of Medicine, Winston-Salem, NC; 3Neuroscience, Wake Forest School of Medicine, Winston-Salem, NC

Background and Aims: Genome-wide association studies (GWAS) have identified over 160 single nucleotide polymorphisms (SNPs), associated with inflammatory bowel disease (IBD). These studies have generated insights into the mechanism of disease. However, the challenge remains in determining how genetic variation can result in the different phenotypic penetrance of the identified risk SNPs and how this translates into potential therapeutic strategies. We aim to correlate IBD risk SNPs to specific disease phenotype in our cohort of pediatric patients with IBD.

Methods: A pediatric cohort of 550 patients with IBD, including ulcerative colitis (UC), Crohn Disease (CD) and Indeterminant Colitis from 2003 to the present were genotyped by SNP microarray on the Omni Express platform. Of those, a random sample of 200 patients were phenotyped. Extensive metadata were collected including age of onset, disease phenotype, severity, disease location, disease behavior and progression to early surgery, defined as surgery within 2 years after diagnosis. We performed a targeted analysis of fifteen SNPs associated with innate immunity and epithelial defense. Statistical modeling was performed to quantify SNP phenotype associations. Statistical methods, through an additive effect of the candidate variants, included genotypic testing using the Fisher exact test for detecting variant association with the phenotype of our interest.

Results: After adjustment for multiple comparisons, there was a statistically significant correlation between the susceptibility loci in the SLC11A1 gene (rs2382817) and risk of early surgery (P=0.001584). The SLC11A1 polymorphism was identified in 41% of the 200 patients analyzed who progressed to early surgery. All but 1 of these patients had CD. Of the patients who went on to early surgery, 86% had granulomatous, strictureting disease requiring ileocecectomy or other small bowel resection. Conclusion: Susceptibility loci in the SLC11A1 gene is independently associated with progression to early surgery in our pediatric cohort of patients with IBD. Polymorphisms in this gene have been shown to increase the risk of tuberculosis and mycobacteria-associated disease, highlighting the importance of the interaction between environmental and bacterial contributions to inflammatory bowel disease. This may have important therapeutic implications in the treatment of IBD in the future, particularly in aggressive disease such as our cohort.
333 TRANSCRIPTION FACTOR C/EBPβ INFLUENCES REGULATORY T CELL FUNCTION AFFECTING THE DEVELOPMENT OF COLITIS. Pamela R. Puthoor, Colm B. Collins, Derek Strassheim, Edwin F. de Zoeten, Pediatrics, Children’s Hospital of Colorado University of Colorado Health Sciences Center, Aurora, CO

Inflammatory Bowel Disease (IBD) is a chronic destructive intestinal inflammatory condition that affects thousands of children worldwide. IBD is partly mediated by CD4+ T cells, including the proinflammatory Th17 cell. Anti-inflammatory Foxp3+ regulatory T cells (Tregs) play a crucial role in maintaining intestinal immune homeostasis producing IL-10 and other factors, which protect against the development of IBD. We note that the transcription factor CCAAT enhancer binding protein β (C/EBPβ) regulates IL-6 and TGFβ expression, both of which help direct the differentiation of naïve T cells into Treg or Th17 cells. We note that C/EBPβ expression is gradually diminished under Treg converting conditions suggesting that loss of C/EBPβ influences the development of Tregs. Therefore we hypothesized that C/EBPβ provides additional regulation for the development of Tregs and that loss of C/EBPβ may attenuate intestinal inflammation.

Using C/EBPβ-/- as well as C/EBPβloxp/loxpFoxp3cre mice we addressed multiple questions assessing the role of C/EBPβ in the development of colitis and the function of Treg cells. Using flow cytometry we analyzed C/EBPβ-/- (KO) versus wild type (WT) mice and determined that KO mice have increased numbers of native CD4+Foxp3+ Tregs. However, under both in vitro and in vivo Treg converting conditions, KO naïve T cells demonstrate decreased conversion to Tregs compared to WT naïve T cells. We next evaluated the suppressive function of C/EBPβ KO Tregs noting a significant loss of suppressive function with the lack of C/EBPβ. This increase in frequency of poorly functioning Tregs is believed to be reflective of the situation within the intestinal lamina propria of IBD patients. These data suggest that C/EBPβ is critical for Treg suppressive activity and therefore C/EBPβ may play a protective role in the development of colitis. Using C/EBPβloxp/loxpFoxp3cre Tregs in a T cell adoptive transfer model of colitis we addressed the question of the influence of C/EBPβ in Tregs. Mice that received C/EBPβ-deficient Tregs developed more severe colitis as compared to those that received WT Tregs. This again demonstrates that C/EBPβ may have a critical role to play in IBD pathogenesis.

In conclusion, we determined that loss of C/EBPβ decreased Treg function and thus potentiated colitis as opposed to ameliorating colitis. While there were increased numbers of native Tregs in the C/EBPβ-/- mice the defect appears to be in their function and their ability to be induced peripherally. This intriguing finding suggests that C/EBPβ may play a possible dual role in pro and anti-inflammatory mechanisms of inflammation. Further studies are required to fully assess this role and determine if this transcription factor can be targeted for treatment of IBD.

Poster Session III
Posters of Distinction*

334 POST-ENDOSCOPY FEVER IN CHILDREN: INCIDENCE AND IMPLICATIONS. Robert Kramer, Pediatrics, Aurora, CO

Background: Occurrence of fever in the period following endoscopy in children raises concerns about possible complicating infection or perforation and may lead to unanticipated evaluation.

Objectives: To review the incidence of post-endoscopy fever in a large cohort of pediatric endoscopies to determine the related risk of defined perforation or infection.

Methods: All post-endoscopy complaints via parent phone call, emergency department visits and hospitalizations were recorded over a 33 month period at a large, tertiary care, free-standing children's hospital and analyzed by complaint type.

Results: Out of a total of 6207 endoscopic procedures, a complaint was recorded in 180 cases (3.13%), with 38 of these being fever (21.11%). In 10 of these cases (26.2%) fever occurred after a therapeutic endoscopic procedure. The risk of fever following therapeutic endoscopy was 1.65% and 0.50% following diagnostic endoscopy (relative risk of 3.3). In 28 of these cases (73.68%) the patient was referred to the emergency department or admitted for further evaluation. In only 2 cases (5.26%) was there continued suspicion of possible perforation or other significant endoscopy-related infection after clinical evaluation, though there was no definitive evidence in either case. In 5 cases (13.2%) a non-endoscopy related source of infection was identified (coronavirus, pneumonia x 2, streptococcal pharyngitis, and viral upper respiratory infection). In 19 cases (50.0%) there was no source of fever identified but no clinical sequelae on follow-up. In 12 (31.6%) cases there was only expectant management, with subsequent resolution of symptoms. Therefore the incidence of significant endoscopy-related infection in this cohort was 0.03% and perforation was 0.0%.

Conclusion: In this cohort, fever was a relatively common occurrence following endoscopy in children and often resulted in unanticipated evaluation and increased healthcare costs, though the incidence of significant endoscopy-related infection was low. The majority of post-endoscopy febrile episodes resolved spontaneously and were not clearly related to endoscopic procedures.

335 OBSERVATIONAL COMPARISON OF FLUTICASONE VERSUS COW’S MILK ELIMINATION FOR THE TREATMENT OF EOSINOPHILIC ESOPHAGITIS. Patrice Kruszewski1, John Russo1, Elizabeth Erwin2, 1Pediatric Gastroenterology, Hepatology and Nutrition, Nationwide Childrens Hospital and the Department of Pediatrics, The Ohio State University, Columbus, OH; 2Pediatric Allergy, Nationwide Childrens Hospital and the Department of Pediatrics, The Ohio State University, Columbus, OH

BACKGROUND: Eosinophilic esophagitis (EoE) is a chronic allergic inflammatory condition defined by the presence of $\geq 15$ eosinophils per high power field (hpf) on esophageal biopsies. Current treatment for EoE includes acid suppression combined with swallowed corticosteroids and/or complicated dietary changes. Because a significant proportion of patients improve with dietary avoidance of cow’s milk alone, our objective was to compare outcomes after treatment with dietary elimination of this single food with a current standard
medical therapy.

METHODS: Newly diagnosed patients with EoE treated with acid suppression and fluticasone (n= 8) or acid suppression and elimination of cow’s milk (n=4) at Nationwide Children’s Hospital with repeat biopsies obtained after 8 weeks were compared. Quality of life (QOL) and symptoms were assessed using the validated PedsQL™ EoE. Complete histological response was defined as <5 eosinophils on follow-up biopsy whereas partial response was defined as having between 5 and 15 eosinophils on follow-up biopsy.

RESULTS: At diagnosis, the median age was 13 years (range 2-17 y; 65% male); mean esophageal eosinophil count was 56/hpf [standard deviation (std dev) 31]; and mean EoE module scores were 60 (std dev 14). There were no significant differences in baseline characteristics between the patients in the two treatment groups. The mean decrease in esophageal eosinophil count in patients treated with fluticasone was 45/hpf compared with 25/hpf in patients treated with milk elimination (p=0.4). Four patients treated with fluticasone were classified as responders (i.e. having less than five eosinophils/hpf on repeat biopsy) compared with one patient treated with diet (p=0.4). There were two partial responders in the fluticasone treated group and one partial responder in the milk elimination group. Mean EoE module scores improved by 4.8 points in patients treated with fluticasone as compared with 23 in patients treated with diet (p=0.2).

CONCLUSION: Cow’s milk elimination showed a trend toward greater improvement in quality of life and symptoms compared with fluticasone therapy. Histologic responses were not significantly better with fluticasone treatment. Thus, the simpler dietary regimen of cow’s milk elimination may be more desirable for a distinct subset of EoE patients who do not want to take long term medications.

336 **RISK FACTORS FOR HELICOBACTER PYLORI INFECTION AT AN URBAN TERTIARY CARE REFERRAL CENTER.** Nava Yeganeh1, Rebecca N. Dudovitz1, Charles A. Newcomes1, Jorge H. Vargas1, Elizabeth A. Marcus1,2, 3Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles, CA; 2VA Greater Los Angeles Health Care System, Los Angeles, CA

**Background:** _H. pylori_ infects the gastric mucosa of 50% of the world’s population, leading to gastritis, gastric and duodenal ulcer disease, and gastric cancer. Infection frequently occurs in childhood and persists lifelong without treatment. Treatment of infection resolves inflammation and reverses the risk of advanced disease. Co-morbid conditions requiring chronic use of PPIs, steroids, or NSAIDs impact risk for advanced disease and are independent indications for treatment of known infection. This is particularly relevant at tertiary care centers, where children with complex medical conditions are often managed on such medications. The aim of this study was to examine risk factors for _H. pylori_ infection in a medically complex, ethnically diverse patient population and to describe testing and treatment parameters in this environment, so that we can better understand how to prevent advanced disease in similar populations.

**Methods:** We performed a retrospective case control study comparing _H. pylori_-positive patients ≤21 years of age with negative controls at a large academic pediatrics institution. Each patient with a history of a positive _H. pylori_ test was matched with 3 randomly selected control patients who were tested for _H. pylori_ by the same method but with a negative result. Statistical analyses were performed in STATA to describe the population, as well as testing and treatment patterns. In addition, we performed logistic regressions evaluating predictors of _H. pylori_ disease.

**Results:** In 2012, of 118 stool antigen tests sent to our microbiology lab, 7 (6%) patients had positive results. Of the 4 urea breath tests (UBT) performed, 3 (75%) were sent as test of cure for previously diagnosed infection. On review of the stool antigen results, nine (28%) of our patients had recently received steroids, 5 (16%) had used NSAIDs, and 15 (47%) had used protein pump inhibitors. The mean number of comorbidities in our patient population was 4.6 concurrent diseases, with 2 transplant recipients. As compared to negative controls, our univariate logistic analysis suggested infected individuals were significantly more likely to be older age (16.8 yo infected group vs 11.9 yo in control group). We did not see any difference in rate of infection based on ethnicity, number of household members, family history of ulcers or daycare attendance. Of note, our clinicians appeared to test for _H. pylori_ in patients treated with fluticasone as compared with 23 in patients treated with diet (p=0.2).

**Conclusion:** The prevalence of _H. pylori_ infection in this tertiary care academic center was lower than expected. This may be related to different childhood exposures in the setting of chronic illness or testing practices among physicians. Clinicians should be educated on risk factors for disease and appropriate indications for testing and treating.

*Note: First 2 authors contributed equally.*

337 **ESOPHAGEAL WALL THICKENING AT SITES OF EOE ASSOCIATED STRICTURES.** Calies Menard-Katcher1,2, Kelley Capocelli3, Joanne Masterson1,2, Glenn Furuta1,2, Robert Kramer1,2, 1Section of Pediatric Gastroenterology, Hepatology and Nutrition, Gastrointestinal Eosinophilic Diseases Program, Children’s Hospital Colorado, Aurora, CO; 2Department of Pathology, University of Colorado School of Medicine, Aurora, CO; 3Department of Radiology, University of Colorado School of Medicine, Aurora, CO

**Introduction:** In some patients with eosinophilic esophagitis (EoE), remodeling can lead to a luminal narrowing that ultimately results in obstructive symptoms. Mechanisms of, and the extent of the esophageal wall involved in, this process are yet to be fully defined. Whether remodeling would occur significantly more at sites of histological inflammation. To assess the extent of remodeling in EoE patients with stricturing disease, we performed endoscopic ultrasound (EUS) along the esophageal wall at sites of narrowed and endoscopically normal mucosa and correlated these measurements with histological features of EoE.

**Methods:** We performed an observational study to measure esophageal wall thickness by EUS in EoE patients with esophageal stricture. Esophageal strictures were either identified at the time of endoscopy or on radiographic contrast studies. EUS was performed using the 12 MHz miniprobe and measurements [total wall thickness (TWT), combined mucosa submucosa thickness (MST) and muscularis propria thickness (MPT)] were taken proximal to, at the site of, and distal to the esophageal stricture. Histological assessment of mucosal biopsies was recorded and correlated with EUS findings.

**Results:** 6 patients (4 female, 5 to 17 years old, median age 13.3 years) underwent EUS at time of upper endoscopy for evaluation of history suggestive of stricture. All patients had been previously diagnosed with EoE based on current guidelines. One patient did not have...
EUS measurements at the level of the narrowing. In the remaining 5 patients, there was a trend towards an increased TWT at the level of stricture compared to the proximal and/or distal TWT (2.87 mm ± 0.59 vs 2.43 ± 0.67, p=NS). In three patients with MST and MPT measurements, MST was significantly greater at the site of stricture (1.72 mm) compared to proximal (1.35 mm, p < 0.04) and distal sites (1.23 mm, p < 0.01). There was a trend towards increased MPT at the level of stricture compared to proximal and distal sites; however this did not meet significance. Correlation of peak eosinophil count with TWT, irrespective of esophageal location, was poor (R2<0.6 [0.1 - 0.6]). There was; however, a strong positive linear correlation (R2 > 0.7) between peak eosinophil count and MST in the proximal and distal esophagus but not at the site of stricture.

Discussion: The lack of correlation of the combined mucosa submucosa thickness with mucosal eosinophilia at the level of stricture may represent chronic remodeling or missed capture of inflammation. Remodeled mucosa-submucosa that are thicker at sites of esophageal stricture compared to non-strictured sites likely indicate hyperplasia or fibrosis secondary to previous eosinophilic inflammation.

**338 A PROSPECTIVE, MULTI-CENTER, STUDY TO COMPARE THE POcone® WITH THE UBIT®-IR300 IN MEASUREMENT OF 13CO2/12CO2 RATIO IN BREATH SAMPLES COLLECTED FROM PEDIATRIC SUBJECTS WITH UPPER GASTROINTESTINAL SYMPTOMS.** Antone R. Opekun1,4, Victor M. Cardenas2, Jesse Reeves-Garcia2, Seigi Kitagawa1,4, Christina E. Lecea1,4, Bruno P. Chumpitazi1,4, Tao Wang, Pediatrics, Baylor College of Medicine, Houston, TX; 2School of Public Health, University of Texas, El Paso, TX; 3Division of Gastroenterology, Miami Children's Hospital, Miami, FL; 4Gastroenterology, Hepatology and Nutrition, Texas Childrens Hospital, Houston, TX; 5Otsuka America Pharmaceutical, Inc., Rockville, MD

**BACKGROUND:** Although 13C urea breath test (UBT) has been available in the United States for nearly 20 years for the diagnosis and post-treatment monitoring of H. pylori infection in adults in the clinical setting, the use of UBT in pediatric patients has been limited to clinical research studies only. The UBT-IR300, an older version of the instrument for BreathTek® UBT, was approved by the US FDA for pediatric use whereas the newer POcone instrument requires validation for use in pediatrics. **OBJECTIVE:** To compare the POcone to the UBT-IR300 in measuring 13CO2/12CO2 ratio in breath samples in identifying H. pylori infection and post-treatment response in pediatric subjects. **DESIGNH / METHODS:** This was a prospective, multi-center, comparison study involving pediatric subjects ages 3 to 17 years. Children with any of the upper GI symptoms (abdominal pain/discomfort, bloating, nausea, or vomiting, etc) were enrolled if the symptoms were suspected by the investigators to be potentially due to H. pylori. As part of the BreathTek® UBT procedure, breath samples were collected and were analyzed by both the POcone and UBT-IR300 Infrared Spectrophotometers, either at the site of patient care or at a central laboratory. Breath test results from the POcone and UBT-IR300 were converted to urea hydrolysis rates (UHR) using the web-based pUHR-CA before being compared. A UHR value of greater than 10 g/min is considered positive for H. pylori infection. Subjects tested positive in the initial visit were offered an H. pylori eradication therapy of investigator's choice and asked to return for retest at last 4 weeks after the completion of the eradication therapy. **RESULTS:** Among the 95 evaluable subjects for initial diagnosis, 24 tested positive and 71 tested negative. The correlation coefficient between the two instruments was 0.9997. Slopes and intercepts of the regular regression were 0.99 and -0.03, respectively. Nineteen of the H. pylori positive subjects returned for retesting after one course of eradication therapy: 10 (52.6%) had a positive retest value and 9 (47.4%) had a negative retest value. Agreement between the two instruments in identifying H. pylori infection status was 100% for all samples in this study, regardless if they were for initial diagnosis or for post-treatment monitoring. **CONCLUSIONS:** The POcone is comparable to the UBT-IR300 in the initial diagnosis and post-treatment monitoring of H. pylori infection in children. The high treatment failure rate observed needs to be further investigated.

**DISCLOSURE:** This study was supported by the Otsuka America Pharmaceutical, Inc., manufacturer of the BreathTek® UBT for H. pylori and distributor of the POcone® and UBT®-IR300 Infrared Spectrophotometers in the United States.

**339 A PILOT STUDY FOR THE USE OF FRACTIONATED EXHALED NITRIC OXIDE IN THE DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS.** Stephanie L. Page1, Chitra Dinakar2, 1Gastroenterology, Children's Mercy Hospitals & Clinics, Kansas City, MO; 2Allergy, Asthma, and Immunology, Children's Mercy Hospitals & Clinics, Kansas City, MO

Introduction: The diagnosis of Eosinophilic Esophagitis (EoE) remains complicated and invasive requiring general anestheisa for esophageal biopsies. Less invasive methods are needed for the diagnosis of EoE. Fractionated exhaled nitric oxide (FeNO) has been effective in both the evaluation and management of patients with asthma by monitoring eosinophilic inflammation. We hypothesize that FeNO can be used to measure esophageal eosinophilia and therefore provide an alternative method for diagnosis of EoE.

Methods: This was a prospective study evaluating subjects aged 6-17 years who were being evaluated for EoE via upper endoscopy. FeNO levels were obtained twice prior to endoscopy using NIOX MINO (Aerocrine Inc). Subjects were classified into groups by post procedure esophageal eosinophil density (study group ≥ 15/high power field (hpf), control group <15/hpf). Exclusion criteria included subjects with recent steroid use and persistent asthma. Average FeNO levels were correlated with peak esophageal eosinophil density. Atopy scores were collected and correlated with esophageal eosinophil and FeNO levels. A subset analysis included subjects with and without esophageal eosinophilia but who also had increased eosinophil densities in the stomach, small intestine, and/or large intestine with correlation performed to FeNO levels and atopy scores.

Results: 15/100 subjects were enrolled in the study group and 44/100 subjects were enrolled in the control group. 20 subjects did not have esophageal eosinophilia but did have downstream eosinophilia present and 10 subjects had both esophageal eosinophilia and downstream eosinophilia. In the study group, mean FeNO level was 19ppb (std dev 13, range 7-47ppb) and mean esophageal eosinophil density was 34 (std dev 14, range 15-55). In the control group, mean FeNO level was 19ppb, (std dev 20, range 6-118ppb) and mean esophageal eosinophil density was 1 (std dev 2, range 0-9). No statistically significant correlation was found between the average FeNO levels and esophageal eosinophil density (p=0.72). Atopy scores correlated with average FeNO levels in the control group (p=0.0003) but not with...
the esophageal eosinophilia group (p=0.31). Atopy scores correlated with downstream eosinophilia if esophageal eosinophilia was present (Pearson Correlation 0.88, p=0.0008) but not if esophageal eosinophils were absent (p=0.69).

Conclusion: Preliminary data does not show a correlation between exhaled nitric oxide and esophageal eosinophil levels. However, our study group is small and the study is ongoing. We did find a correlation between atopy scores and subjects with diffuse eosinophilia indicating increased allergic tendencies.

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**EXPRESSION OF PARP1 AND PARP14 IN BIOPSIES FROM CHILDREN WITH EOSINOPHILIC ESOPHAGITIS (EOE) COMPARED TO CONTROLS.** Kalyan Ray Parashette1, Purna Krishnamurthy2, Shreevrat Goenka2, Mark H. Kaplan1, Sandeep Gupta1,1 Pediatric Gastroenterology, Hepatology and Nutrition, Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, IN; 2Pediatrics, Wells Center for Pediatric Research, Riley Children's Hospital, Indiana University School of Medicine, Indianapolis, IN

INTRODUCTION: T-helper 2 (Th2) cell cytokines are linked to the pathogenesis of EoE, and induce expression of the eosinophil chemoattractants such as eotaxin through a STAT6 dependent mechanism. We previously identified that poly-ADP ribose polymerase -14 (PARP14) promotes the binding of STAT6 to its target genes and enhances STAT6 dependent transcription by acting as a transcriptional switch. Additionally, PARP1 regulates interleukin (IL)-5 expression in allergen-induced eosinophilia. PARP1 is also shown to regulate STAT6 signaling cascade.

AIM: To study PARP1 and PARP14 expression in esophageal biopsies from children with EoE and compare to controls.

METHODS: Esophageal mucosal biopsies were obtained from 18 controls (normal findings on EGD and absence of histological changes on biopsies of upper GI tract) and 17 patients with EoE (> 15 eosinophils/high power field) and analyzed for PAPRP1 and PARP14 gene expression by real-time PCR.

RESULTS: In control group (n=18), age range was 1.6 years to 16 years with mean age of 8.4 years. 50% were male. In EoE group (n=17), age range was 2.2 years to 17 years with mean age of 7.5 years. 53% were male.

We observed that the expression of PARP1 and PARP14 in esophageal mucosal biopsies was 5.7 and 9.8 fold higher respectively in EoE patients compared to controls. P-values however were not statistically significant (p-value 0.07 for PARP1 and 0.2 for PARP14). On further review of PARP14 data, one outlier in each group was noted. Reanalysis after exclusion of these two outliers showed statistically significant higher PARP14 expression in EoE children compared to controls (p-value 0.03.).

CONCLUSION: We found upregulation of PARP1 and PARP14 expression in esophageal biopsies from children with EoE and compare to controls. This further supports that EoE is a Th2 mediated process and these findings provide insight into the molecular mechanisms of EoE where PARP1 and PARP14

**341**  
**EOSINOPHILIC ESOPHAGITIS (EOE) IN PEDIATRICS: DYSPHAGIA PREDOMINANT AND ABDOMINAL PAIN PREDOMINANT, DIFFERENT PHENOTYPES OR DIFFERENT DISEASES?** Gautham Prabhakar1, T s Gunasekaran1,2, Alan Schwartz1, James Berman1,2, Kiran Gorla1,2,1 Advocate Children's Hospital-Park Ridge, Park Ridge, IL; 2University of Illinois Chicago, Chicago, IL; 2Loyola Medical Center, Maywood, IL

EoE in pediatric patients presents with myriad symptoms. Consensus statement classifies patients into 4 groups based on predominant symptom: Dysphagia(EoE-D), abdominal pain(EoE-AP),GERD and failure to thrive. Patients with EoE-AP appear to have a suboptimal outcome with standard treatment for EoE compared to EoE-D. Symptoms of EoE-AP are similar to functional abdominal pain(FAP). Aim: Compare clinical features, endoscopy (EGD)+bx, treatment and outcomes of EoE-AP with EoE-D and FAP. Method: Patients with EoE seen from 2007-2011 were stratified into consensus symptom groups. A concurrent cohort of FAP patients,selected at random, with clinical features of FAP and a normal EGD and bx were also included. Results of EGD, bx of duodenum, antrum, distal and mid esophagus were recorded. Treatment; diet, steroids or combination. Clinical outcome measured as improved, worsened or same. Symptoms entered into two-step cluster analysis, then clusters cross-tabulated with patient's diagnosis and discriminant functional (DF)analysis performed. Cross-table with Chi-squared compared clinical outcomes within each group and impact of treatment choice on clinical outcome for each group.

Results: EoE-D: n 68, 59 M, age 2- 17yr, mean 11.68. EoE-AP n 64, 49 M, age 1-17 yr, mean 9.43. FAP: n 61, 26 M, age 4-17 yr, mean 10.87. Cluster analysis identified two clusters with fair fit quality. Predictors of membership were AP and D. Cluster 1 included all patients with EoE-AP and FAP and 8 patients with EoE-D. Cluster 2 included remaining 57 patients with EoE-D. Based on symptoms, prior to EGD, analysis classified 81% of patients into the correct diagnosis. There was error distinguishing between EoE-AP and FAP. 36% of EoE-AP were misclassified as FAP and 12% of FAP were misclassified as EoE-AP. DF scores averaged -.33 (sd .26) for FAP patients, -.28 (sd 1.1) for EoE patients, and +2.9 (sd 1.4) for EoE-D patients. With treatment, EoE-D: 73% improved, 24% stable, 3% worsened. EoE-AP 51% improved, 23% stable, 25% worsened. FAP: 62% improved, 16% stable, 21% worsened; (p <.001) Stepwise DF analysis found improved outcome with nausea and food bolus and negatively with budesonide and eosinophils in the distal esophagus of 15-25 and 26-51/hpf, in both EoE groups. No specific treatments were associated with a greater rate of improvement overall or in any specific patient groups. Conclusion: EoE-AP patients completely overlapped with FAP, but not with EoE-D. EGD and bx were required to differentiate EoE-AP and FAP. EoE-D had better outcome than EoE-AP. Improved outcome was associated with nausea and food bolus and negatively with budesonide and eosinophils in distal esophagus. We postulate that patients with EoE-AP may have a different disease process than those with EoE-D. Further studies are required to elucidate if EoE-D and EoE-AP are two phenotypes of same disease or different diseases.
Concordance between endoscopic and histological findings at three segment of upper gastrointestinal tract discordance pattern is different. The need of routine biopsy following endoscopic study is suggested, however, it is necessary to conduct a discordance pattern is less and similar in both studies. Discussion: Although concordance in both studies is relatively high, the normal histology was higher in esophagus; normal endoscopic with abnormal histological finding was higher in stomach; in duodenum, level of endoscopic-histological was stomach. Endoscopic and histopathological studies revealed peptic esophagitis and reflux esophagitis respectively as the most frequent in esophagus. In stomach, endoscopic and histopathological findings were predominantly erosive gastropathy and chronic gastritis respectively. In few patients we observed duodenal abnormalities in both studies. The level of endoscopic-histological discordance in esophagus was: \( \kappa = 0.61 \) (CI95%: 0.49 to 0.73); in stomach: \( \kappa = 0.55 \) (CI95%: 0.41 to 0.69); and duodenum: \( \kappa = 0.77 \) (CI95%: 0.64 to 0.89). We observed different discordance patterns depending on the anatomic region: Endoscopic abnormality with normal histology was higher in esophagus; normal endoscopic with abnormal histological finding was higher in stomach; in duodenum, discordance pattern is less and similar in both studies. Discussion: Although concordance in both studies is relatively high, the discordance pattern is different. The need of routine biopsy following endoscopic study is suggested, however, it is necessary to conduct a prospective study to elaborate diagnostic algorithm for gastrointestinal pathology management in pediatric populations. Concordance between endoscopic and histological findings at three segment of upper gastrointestinal tract

<table>
<thead>
<tr>
<th>Histology</th>
<th>Esophagus</th>
<th>Stomach</th>
<th>Duodenum</th>
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<tr>
<td>Endoscopy</td>
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</tr>
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</tr>
<tr>
<td>Total</td>
<td>146</td>
<td>113</td>
<td>146</td>
</tr>
</tbody>
</table>

Kappa I 95%: \( \kappa = 0.61 \) CI: 0.49-0.73; \( \kappa = 0.55 \) CI: 0.41-0.69; \( \kappa = 0.77 \) CI: 0.64-0.89

Utility of gastric and duodenal biopsies in eosinophilic esophagitis.

<table>
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Utility of gastric and duodenal biopsies in eosinophilic esophagitis.

Selecting appropriate diagnostic studies is vital to provide safe and cost-effective care. Pediatric gastroenterologists typically obtain biopsies of the esophagus, stomach, and duodenum in the setting of diagnostic esophagogastroduodenoscopy (EGD) for upper GI symptoms. Diagnosis of eosinophilic esophagitis (EoE) is defined by histologic abnormalities in conjunction with characteristic clinical/endoscopic features. After initial diagnosis of EoE, repeat endoscopy with esophageal biopsy is frequently warranted to assess therapeutic response. There are no published studies or evidence-based guidelines regarding best practice for repeated esophageal biopsy after diagnosis of EoE. The aim of this study was to determine the frequency of gastric and duodenal biopsies performed after diagnosis of EoE was established, and to determine their diagnostic yield.

Methods: An electronic database at our medical center was used to identify patients diagnosed with EoE between 2010 and 2012. Inclusion criteria were availability of diagnostic and subsequent endoscopy procedure and pathology reports. Gross and histologic findings, as well as general clinical and demographic information, were collected and analyzed.

Results: Forty-three EoE patients were identified. Mean age at diagnosis was 9.9 +/- 5.5 years (range 1.2-20.2) and 33% were female. Most common presenting chief complaints were dysphagia (26%), vomiting (26%), abdominal pain (19%), and dyspepsia (12%). At the initial diagnostic endoscopy 95.3% of patients had esophageal biopsies including an average 2.1 gastric and 3.0 duodenal biopsies. Abnormal gastric histology (12.2% of all patients) was most frequently characterized as chemical gastritis and did not correlate with gross abnormalities (16.7%) in any patient. Abnormal duodenal histology (12.2%) correlated with gross abnormalities (4.8%) in only 1 patient. Two patients were diagnosed with celiac disease and EoE as a result of the initial diagnostic endoscopy. Mean time between initial and subsequent endoscopy was 5.0 months. At the subsequent endoscopy 86.0% of patients had esophageal biopsies including an average 1.8 gastric and 2.2 duodenal biopsies. Abnormal gastric histology (18.9%) was again most frequently characterized as chemical gastritis. Gross abnormalities (12.5%) correlated with abnormal histology in 3/5 cases. Abnormal duodenal histology (5.4%) was only identified in patients with known celiac disease and did not correlate with gross abnormalities (2.6%) in any patient.

Conclusions: Gastric and duodenal biopsies are frequently obtained during endoscopy subsequent to EoE diagnosis. Gross gastric and duodenal endoscopic abnormalities are rare in patients with EoE and infrequently correlate with histology. In the absence of known co-morbid intestinal disease, duodenal biopsies during subsequent endoscopy have no utility. Extraesophageal biopsies do not impact clinical care and potentially introduce unnecessary risk and expense. Prospective, multicenter studies of endoscopy practice and utility in patients with EoE should be conducted to validate our findings.
The TIF technique appears to be safe and effective in the pediatric population. There is a clear improvement in both the esophageal pH and the DeMeester score in pre-and post pH probe studies. All patients had a histologic improvement on biopsies done before and after the TIF. All patients were admitted to the Rocky Mountain Hospital for Children and observed overnight for possible complications. The intraluminal time for a pH of less than four on average decreased on average by 72%. The total DeMeester score done on pre-and post-TIF decreased on average by 69.9%. All patients had a histologic improvement on biopsies done before and after the TIF. All patients had a histologic improvement on biopsies done before and after the TIF. All patients had a histologic improvement on biopsies done before and after the TIF. All patients had a histologic improvement on biopsies done before and after the TIF.
346 CHILDREN WITH ESOPHAGEAL STRICTURE SECONDARY TO CAUSTIC INGESTION HAS DIMINISHED FAT STORES. Carmen A. Sánchez-Ramírez1, Alfredo Larrosa-Haro2, Maria del Carmen R. Macias Rosales3, 1Facultad de Medicina, Universidad de Colima, Colima, Mexico; 2Instituto de Nutrición Humana, Universidad de Guadalajara, Guadalajara, Mexico; 3Pediatric Gastroenterology and Hepatology, UMAE HP CMNO, Guadalajara, Mexico

BACKGROUND: Ingestion of acid and alkali substances frequently leads to gastrointestinal tract damage that clinically presents as dysphagia, strictures and acquired motility disorders.

AIM: To compare the nutritional status and growth, the energy and macronutrient intake in children with and without esophageal stricture secondary to caustic ingestion.

PATIENTS AND METHODS: A cross sectional study was carried out in 68 children. Their mean age was 78 months (45.3 SD), 26 (38.2%) were females. The independent variable was the presence/absence of dysphagia and/or stricture and the dependent variables the nutritional status, energy and macronutrient intake.

RESULTS: Thirty-eight out of 68 (55.9%) presented esophageal stricture and 24/68 (35.3%) developed dysphagia. Secondary GERD was identified in 19/68 (27.9%).

Energy and macronutrient ingestion had no significant differences between the study groups.

CONCLUSION: Although the anthropometric data related to body composition remained between -1 and +2 SD in both study groups, a significant difference in the fat stores attributable to esophageal stricture was demonstrated. The diet surveys were not sensitive to identify these differences. Although the impairment in the nutritional status is discrete, it should be considered for the nutritional intervention of these patients.

<table>
<thead>
<tr>
<th>Anthropometrical indicator</th>
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<th>DE</th>
<th>x</th>
<th>DE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight/height</td>
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<td>0.87</td>
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<td>0.003</td>
</tr>
<tr>
<td>Height/age</td>
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<td>1.05</td>
<td>-0.25</td>
<td>1.14</td>
<td>0.289</td>
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<tr>
<td>Mid arm circumference</td>
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<td>-0.41</td>
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<tr>
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<td>0.73</td>
<td>1.28</td>
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</tr>
<tr>
<td>Subscapular skin fold</td>
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<td>1.32</td>
<td>1.32</td>
<td>1.64</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arm fat area</td>
<td>-0.34</td>
<td>0.96</td>
<td>0.96</td>
<td>1.29</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

p= t Student between groups

347 ESOPHAGEAL (ESOPH) INVOLVEMENT IN EOSINOPHILIC GASTROINTESTINAL DISEASE (EGID) MIMICKS EOSINOPHILIC ESOPHAGITIS (EOE). Fernando J. Windemuller1, Simon S. Rabinowitz1, Virginia Anderson2, Haseeb Siddiqi3, Evan Grossman2, Raavi Gupta4, Frank Gress5, Steven M. Schwarz6, Hanh D. Vo1, 1Pediatric Gastroenterology, Hepatology & Nutrition, SUNY Downstate, Brooklyn, NY; 2Gastroenterology & Hepatology, SUNY Downstate, Brooklyn, NY; 3Pathology, SUNY Downstate, Brooklyn, NY; 4Cell Biology, SUNY Downstate, Brooklyn, NY

Introduction: Recent reviews on both the treatment of EGID and comprehensive diseases of the esophagus (Esoph) do not provide any specific recommendations to treat children who have esophageal involvement as part of EGID. In addition, the two most recent guidelines on EoE specifically differentiate and exclude the Esoph in EGID. This abstract describes the clinical features of the Esoph in two children with EGID.

Methods: The clinical features, endoscopic appearance of the Esoph, the eosinophils (eos) in the Esoph, the total wall thickness of the Esoph as determined by endoscopic ultrasound (EUS), and the presence or absence of subepithelial fibrosis (SE fibr), of two children with EGID are presented and compared to a group with active EoE (AEoE) and a group with EoE successfully treated who have attained remission (REoE).

Results: There is a substantial degree of overlap between the clinical features (chief complaints), the histopathologic findings, and the total wall thickness between the two patients with Esoph involvement as part of EGID and those with EoE.

Conclusions: The Esoph in EGID shares many features with EoE. Until formal treatment guidelines are published, practitioners caring for children with EGID should determine the presence and extent of esophageal involvement. If present, at the minimum EoE management protocols should be followed.

<table>
<thead>
<tr>
<th>Group</th>
<th>#patient (exams)</th>
<th>Chief complaints</th>
<th>Mid esoph Eos/hpf</th>
<th>Mid esoph EUS</th>
<th>Mid esoph SEfibr +/-</th>
<th>Distal esoph Eos/hpf</th>
<th>Distal esoph EUS</th>
<th>Distal esoph SEfibr +/-</th>
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</thead>
<tbody>
<tr>
<td>AEoE</td>
<td>11 (9)</td>
<td>1,8</td>
<td>33</td>
<td>2.1</td>
<td>2/4</td>
<td>47</td>
<td>2.3</td>
<td>2/5</td>
</tr>
<tr>
<td>REoE</td>
<td>5 (6)</td>
<td>1,7,8</td>
<td>1.3</td>
<td>1.75</td>
<td>0/1</td>
<td>2.3</td>
<td>1.8</td>
<td>0/1</td>
</tr>
<tr>
<td>EGID</td>
<td>2 (3)</td>
<td>1,3,4,8</td>
<td>67*</td>
<td>3.2</td>
<td>1/0</td>
<td>75</td>
<td>2.4</td>
<td>1/0</td>
</tr>
</tbody>
</table>

The table compares the mean values for esophageal features in EGID to a cohort of children with EoE. Chief complaints: dysphagia=1, odynophagia=2, chest pain=3, epigastric pain=4, pyrosis=5, emesis=6, cough=7, asymptomatic=8 *one patient had >150 eos/hpf but for determining mean, 150 was utilized EUS measurements are in mm
**348 MODES OF GASTROSTOMY PLACEMENT IN PEDIATRIC POPULATION AND COMPLICATION MANAGEMENT.**
Melawati Yuwono, Randall Holland, Stephanie Acierno, Mary Bridge Hospital and Health Center, Tacoma, WA

Gastrostomy tube (GT) allow delivery of nutrition and medications in children who can not maintain their needs with oral intake. GT can be placed either surgically, endoscopically or radiologically. We report two cases of newly endoscopic and radiologic placed GT tube were dislodged, which required endoscopic replacement. The placement was quick and easy without intubation nor general anesthesia. Methods: A retrospective study of children who required GT insertion was undertaken. Low profile GT was placed in 25 patients (6 endoscopic, 5 surgical and 14 fluoroscopically). Indications for GT tube placement were FTT, dysphagia and seizure disorder. There were 8 females and 17 males with range of 4 months to 19 years old. Two patients had perforation of the bowel and one had significant pain after fluoroscopic insertion. All three required surgical repair. Two patients had repeat GT placement after newly endoscopically and fluoroscopically-placed tube became dislodged. Another placement was abandoned when the stomach was noted to be abnormally positioned. Two surgically placed tube had repeat placement surgically after it became dislodged.

Summary: 1. MIC-key low profile button can be placed not only surgically, fluoroscopically but also endoscopically. It can be done safely as an initial feeding tube in children.
2. Complications related to tube placement in different methods are common including dislodgement.
3. Endoscopic visualization during replacement after early dislodgement may help avoid open surgery

**349 WITHDRAWN**

**Hepatobiliaries/Transplant**

**361 HISTOPATHOLOGY OF NONALCOHOLIC FATTY LIVER DISEASE IN MORBIDLY OBESE ADOLESCENTS.**
Ann Ming Yeh1, Melissa Hurwitz2, John Morton3, Matias Brazoni4, Neeraja Kambham1, 1Pediatric Gastroenterology, Stanford University, Palo Alto, CA; 2Pathology, Stanford University, Palo Alto, CA; 3General Surgery, Stanford University, Palo Alto, CA; 4Pediatric Surgery, Stanford University, Palo Alto, CA

Background: Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are highly prevalent in the obese pediatric population, but the data is incomplete on the significance of histopathology associated with NASH in children. Aims: To describe the spectrum of histopathology of NAFLD and NASH in morbidly obese adolescents undergoing bariatric surgery, and to correlate severity of steatosis, inflammation and fibrosis with laboratory data. Methods: A cross-sectional study was performed on 30 morbidly obese adolescents (60% non-Hispanic white), ages 15-20 years who underwent liver biopsy and gastric bypass or sleeve gastrectomy between the years of 2007 and 2012. Histopathology specimens were analyzed by one pathologist for features of NAFLD and NASH including NAFLD activity score (NAS), hepatosteatosis grade, fibrosis stage, inflammation. Biopsies were also categorized as Type I, Type II or mixed type NASH. Results: 56% (n=17) of patients had hepatosteatosis. Of the patients with steatosis, the mean NAS was 2.7. 18% of patients with steatosis had bland steatosis, 24% with Type I NAS, 18% with Type II NAS, and 41% with mixed type NASH and 43% had fibrosis. Mixed type NAS correlated with increased steatosis and fibrosis severity. No patients had grade 3 fibrosis or cirrhosis. Increased insulin resistance determined by the homeostasis model assessment of insulin resistance (HOMA-IR) correlated with higher steatosis grade (p=0.001) but not with fibrosis severity (p=0.56). AST, ALT, AST/platelet ratio, and hsCRP levels did not correlate with severity of steatosis, inflammation, or fibrosis. There was no difference in NAFLD or NASH severity in the Hispanic vs. non-Hispanic groups. Clinically silent steatosis and fibrosis were also highly prevalent in this population, where 53% (n=9) of patients with steatosis and 40% (n=4) of patients with fibrosis had a normal ALT (ALT < 60mg/dL).

Conclusion: NAFLD and NASH are highly prevalent in the morbidly obese adolescent population, but none of the cases presented with severe NASH or cirrhosis. In contrast to prior studies in children, mixed type NASH was more prevalent than either type I or type II NASH.

**362 IMPACT OF PEDIATRIC TRANSMISSION ON BURDEN OF HEPATITIS C VIRUS INFECTION.**
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Background and Aims: Hepatitis C virus (HCV) infection contributes to 350,000 deaths each year. The projected cost of management in adults between 2010 and 2019 is $10.7B (Karnsakul W. Ther Clin Risk Manag. 2009), and is projected to increase. At least 5.1% of the 3.5 million cases are children (Mitchell AE. Hepatology. 2010). Minimal attention has been paid to the impact of childhood acquisition of HCV to the overall burden of the disease. We performed a cross-sectional analysis within the lead-in phase of the Hepatitis C Antiviral Long-Term Treatment against Cirrhosis (HALT-C) Trial to assess the impact of childhood-acquired HCV infection on adult HCV.

Methods: The HALT-C trial included patients (n=1075) that had failed prior therapy with interferon (IFN) with or without ribavirin and had histologic evidence of advanced hepatic fibrosis. HALT-C trial protocol was studied. Self-reported duration of infection was analyzed. We identified subjects that acquired HCV infection at 18 years of age or younger (peds infected, PI) and compared them to those who acquired the infection at a later age (adult infected, AI). The prevalence of PI subjects in this cohort was calculated, and variables such as demographics, history of substance abuse, liver histology, and response to therapy were analyzed.

Results: 37.6% (n=404) of subjects in the HALT-C Trial acquired HCV during their pediatric years. The mean age of our two groups was found to be significantly different (PI 47 y/o vs AI 51 y/o; p=0.001). This was consistent with longer mean duration of infection found to be higher in the PI (32.6 vs. 25.4 years, P<0.0001). A greater percentage of males were noted in the PI (77% vs. 70%, p=0.009), but no difference found with concerns to race or ethnicity. A lower percentage of PI subjects had a history of diabetes (12.9% vs. 17.9%, p=0.03). PI subjects reported higher: alcohol abuse (62% vs. 46%, p=0.0001), alcohol dependence (23% vs. 16%, p<0.007), and usage of tobacco (15.6 vs. 13.5 mean ppy, p<0.048). There was a small but significant difference found in accordance to employment status, with a higher proportion of PI subjects working full time (68.5 vs. 63.7%) and fewer retired or at home (7.9 vs. 14.2%, p=0.02). Majority of...
subjects acquired infection with genotype 1 (88% vs. 90%). There were no found statistical differences in insulin resistance assessed through the homeostasis model assessment (HOMA), cholesterol, and triglycerides levels. In multivariate analysis, when adjusting for duration of infection, both PI and AI had similar inflammation and fibrosis while PI was associated with higher steatosis (t ratio = 2.77, p=0.006). Lastly, fewer subjects in the PI group underwent a 2 log drop of HCV RNA between baseline to week 20 (48% vs. 55%, p=0.02); however, no differences in virological clearance was found. Conclusion: HCV infection acquired in childhood constitutes an important subset of the total HCV infected population with advanced disease. The impact of pediatric HCV infection on the burden of HCV disease has likely been underestimated. Unique characteristics such as higher degree of steatosis among patients with childhood acquired HCV merit further investigation.

363  ASSESSING SEVERITY OF HEPATIC FIBROSIS IN CHILDREN ON LONG TERM PARENTERAL NUTRITION (PN) USING NON INVASIVE MARKERS VS. LIVER BIOPSY - A RETROSPECTIVE PILOT REVIEW. Farvathy Mohan1, Krystal Arts1, Carola Cerezo-Allen1, Pennington Rashme1, Christine Reyes1, Robert McCarter1, Clarivet - Torres1, Gastroenterology, Hepatology & Nutrition, Children's National Medical Center, Washington, DC; 2Anatomic Pathology, Children's National Medical Center, Washington, DC; 3Biostatistics and Informatics, Children's National Medical Center, Washington, DC

Treatment of intestinal failure includes long-term (PN), which can be associated with a spectrum of liver diseases- cholestasis, fibrosis, cirrhosis and hepatic failure which may occasionally require a liver transplantation. Assessing the stage of fibrosis is an important tool to predict the course of PN associated liver disease (PNALD). A liver biopsy is the standard tool; most non invasive markers/models for predicting fibrosis are not validated in children. Using routine laboratory data, several authors have constructed a simple model, aspartate transaminase (AST) to platelet ratio index (APRI), to predict fibrosis in chronic viral hepatitis, biliary atresia and PNALD (1-3). Our aim was to examine the spectrum of liver disease in PN dependant pediatric patients treated in the Intestinal Rehabilitation Program (IRP) at our institution from 2007 to now to use APRI and other laboratory values as correlates of fibrosis vs. liver histology. Methods: A chart review study of 15 PN dependent children who had liver biopsies was performed. Duration of PN to liver biopsy, laboratory data including serum AST, total Bilirubin (TB), platelet count at the time of biopsy were correlated with histological changes, specifically fibrosis (stage 0-4) (4). Results: The mean age at biopsy was 11.4 ± 9 months and duration of PN to biopsy 10 ± 9 months. The histologic changes in 15 biopsies included cholestasis in 10, portal fibrosis (stage 1, 2) in 7, bridging fibrosis (stage 3), steatosis and inflammation in 4 each and cirrhosis (stage 4) in 2. At biopsy AST ranged from 25-219 U/L (mean ± SD 89.3 ± 62), platelets 151-495 (103/µL) (291.8±100), TB 0.2-7.8 mg/dL (2.5± 2.8) and APRI 0.21-3.62 (0.84 ± 0.86). The APRI had a modest inverse correlation (r=-0.37, p=0.16) with biopsy stage but a strong correlation with TB (r=0.70, p=0.003). However TB did not correlate with biopsy stage. Conclusion: Significant liver disease with diverse histological findings including fibrosis and cirrhosis is associated with PNALD which may develop over a relatively short period. In this subset of patients on long term PN, routine laboratory values may be altered by concurrent medical conditions such as infections, fluid/electrolyte imbalance and medications, and cannot be used as surrogate non-invasive markers for assessing fibrosis to replace a liver biopsy. Further study of a larger cohort is necessary to ascertain the value of APRI or similar markers as a screening tool for fibrosis in this patient group with significant co-morbidities.


364A  DEVELOPMENT OF A TRANSLATIONAL MODEL OF CHRONIC LIVER INJURY IN EXPERIMENTAL BILIARY ATRESIA. James E. Squires, Pranavkumar Shivakumar, Kazuhiko Bessho, Stephanie Walters, Jorge A. Bezerra, Pediatric Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Purpose: Biliary atresia (BA) results in an obliterative cholangiopathy of infants affecting intra and extrahepatic bile ducts. Studies of extrahepatic ducts of rotavirus (RRV) challenged newborn mice uncovered key roles for the immune system in the regulation of epithelial injury and obstruction. But, poor survival beyond 10 days limits studies of progressive liver injury. Our aims were to develop a model of intrahepatic disease and examine whether tumor necrosis factor-alpha (TNFα) regulates chronic liver injury in experimental BA.

Methods: Newborn Balb/c mice received 20µL intraperitoneal injections of either normal saline, full-dose (1.5x10⁷ ffu) or decreasing doses of RRV on day 1 of life. Weight, survival, jaundice and the presence of acholic stools were recorded through day 21. Liver injury was examined by H&E and trichrome stain at days 7, 14 and 21. Real-time PCR was used to quantify pro-inflammatory cytokines: IFNγ, TNFα, IL-12p40, IL-1α, IL-1β, IL-6. Hepatic mononuclear cells were isolated and flow cytometric analysis was used to identify key populations including CD8 T and NK cells. TNFα was blocked in vivo by injections of 100 μg of anti-TNFα (XT3.11) antibodies beginning at the onset of jaundice (day 6) and continued every third day through day 21; IgG injected mice served as controls. The impact of blocking of TNFα was determined by histopathology. Results: Intracconversion of 0.5x10⁷ ffu (low-dose) RRV induced jaundice and acholic stools in 100% of mice by day 7. In 49%, symptoms were transient and the mice survived to day 21. Histologically, livers had periportal inflammation, bile duct proliferation, expansion of portal tracts and fibrosis. RNA quantification showed increased hepatic expression of the pro-inflammatory cytokines IFNγ, TNFα, IL-12p40, IL-1α and IL-1β (P<0.05, student's t-test) above saline control livers. Cytometric analysis of hepatic mononuclear cells uncovered a 2.5-fold elevation in CDS T-cells on day 7 (P<0.01) that increased to 3-fold on day 14 (P<0.001) compared with saline controls. NK cells had a 4-fold increase on day 7 (P<0.05) that grew to near 6-fold on day 14 (P<0.001). Hepatic cytokine, CD8 T and NK cell populations were similarly elevated in mice receiving low-dose or full-dose RRV. Importantly, CD8 T and NK cell elevations persisted through day 21 in low-dose RRV injected mice (P<0.01). Finally, livers from mice receiving TNFα blocking antibodies demonstrated a significant reduction in hepatic injury as demonstrated by decreased periportal inflammation and fibrosis. Conclusions: Low-dose RRV injection enabled improved survival and produced intrahepatic cholangiopathy thus constituting a novel mouse model of chronic cholestasis with molecular and cellular signatures akin to the traditional model of experimental BA. Exploring interventional strategies, we saw that blocking TNFα-dependent inflammatory circuits prevented progression.

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of intrahepatic injury. We speculate that this new model will provide mechanistic insight into the etiopathogenesis of chronic liver injury, guide further studies on intrahepatic disease progression and assist with development of therapeutic interventions to treat children with BA.

365* PRIMARY VS. SECONDARY PROPHYLACTIC THERAPY OF ESOPHAGEAL VARICES IN THE PEDIATRIC PATIENT: A 15 YEAR REVIEW OF ESOPHAGEAL BAND LIGATION AND SCLEROTHERAPY. Peter Rogers1,2, James Daniel1,2, Corey Schurman1, Ryan Fischer1,2, 1Gastroenterology, The Childrens Mercy Hospital, Kansas City, MO; 2University of Missouri-Kansas City, Kansas City, MO

Background: Variceal bleeding is a major complication of portal hypertension. Primary and secondary prophylaxis with esophageal band ligation (EBL) has shown clinical utility and safety in adults. However, controversy exists regarding EBL's efficacy and safety in pediatrics. This study compared 15 years of primary EBL to secondary EBL and/or sclerotherapy. Rebleeding within two weeks, complications, and outcomes were studied. Methods: This retrospective analysis evaluated 56 pediatric patients with esophageal varices from 1995-2010. 315 endoscopy reports were reviewed and varices were graded as mild, moderate, or severe. 21 patients had primary EBL, 21 patients had secondary EBL, 14 patients had secondary sclerotherapy, and 4 patients had initial sclerotherapy followed by EBL. The mean age for primary EBL patients was 11.36 years. The secondary EBL group had a mean age was 11.7 years. The sclerotherapy +/- EBL group had a mean age of 3.08 years. Patients with varices secondary to biliary atresia, cystic fibrosis, portal vein obstruction, metabolic diseases, and primary sclerosing cholangitis were included in the study. Results: The primary EBL group had no rebleeding occur after 68 separate EBL sessions performed. One patient had dysphagia post EBL, yet no other complications were present. In this group, 12 patients had complete control of their varicies, 4 patients underwent liver transplantation, 2 died of non-liver related causes, and 3 were lost to follow up. Six rebleeding episodes occurred in the secondary EBL; the group underwent 65 EBL sessions. This was significantly greater than the primary group (0% to 29%, p <.03). No other complications were present in this group. The secondary EBL group had 6 patients with complete control of their varicies, 5 underwent liver transplantation, 5 patients had splenorenal shunts, 2 had Meso-rex shunts, 2 died of non-liver related causes, and 1 was lost to follow up. The 14 patient sclerotherapy group +/- EBL had 5 patients with rebleeding. This group had 3 patients who had complete control of their varicies, 6 underwent liver transplantation, 3 had splenorenal shunts, and 3 were lost to follow up. Conclusions: Primary EBL is safe and effective in children and adolescents. Also, primary EBL significantly reduces variceal bleeding when compared to secondary EBL and/or sclerotherapy. One should consider surveillance endoscopy with potential primary EBL in pediatric portal hypertension management. Future investigation on the cost utility and efficacy of primary EBL compared to less invasive prophylaxis such as beta blockade needs to explored.

<table>
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366 IMPACT OF A NUTRITIONAL TREATMENT IN LOW WEIGHT CHILDREN WITH BILIARY ATRESIA BEFORE LIVER TRANSPLANT. Josefinna Martinelli1,2, Julia Gallo1,2, Guillermo Alonso1, Maria Camila Sanchez1,2, Daniel D’agostino1,2, 1Gastroenterology and Hepatology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 2Pediatrics, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Liver transplant (LT) is the treatment for children with biliary atresia (BA) with end-stage liver disease. BA is the most frequent cause of LT in children. Bad prognosis is associated with poor nutritional status. The aim of the study was to assess the nutritional impact of a 80% MCT containing formula in patients with BA listed for LT. Methods : We prospectively included BA patients listed for LT with a weight lower than 8 kg from July 2010 to May 2013. During the follow up weight, length, weight’s Z score and length’s Z score, triceps and subscapular skinfolds were measured at the beginning and every 30 days. All patients received enteral nutrition with a 80% TCM containing formula with an intake of 120 kcal/kg/day. Follow up ended once the transplant occurred or with patient's death. Results: Since the beginning of our LT program, 40 % of the LT performed were BA (121/303). Twenty four children with BA were listed from july 2010 to may 2013; 80% (19/24) underwent LT, 1 died before LT and 4 are still on waiting list; 63% (12/19) weighed less than 8 kg at the time of LT. Finally, eight patients (8/12) were included in the study (4 refused to receive enteral nutrition). Six of these patients (6/8) underwent LT with a survival rate of 100% (one died before transplant and one is still on waiting list). Mean time of follow was 62.5 days (r 29-97d) and mean age 8 months (r 5-22m). Initial mean weight was 7.02 kg (SD +/- 1.09) and mean length was 66.28 cm (SD +/- 4.1 cm). Delta weight Z score was 0.57 (p<0.04), delta length Z score was 0.07 (p<0.76), delta triceps folds was 0.35 (p<0.02) and delta subscapular skinfolds was 1.05cm (p<0.06). Conclusions: Nutritional assessment in these patients provides a significant challenge. Enteral nutrition with a 80% MCT containing formula may improve nutritional status. Further studies with a large number of patients will allow a better assessment and evaluation of this enteral formula.

367 USING HUMAN INDUCED PLURIPOTENT STEM CELLS TO MODEL LIVER DISEASE ASSOCIATED WITH CLASSIC MUTATIONS OF ALPHA-1 ANTITRYPSIN. Tamara Takeda1,2, Maria P. Ordonez1,2, Lawrence S. Goldstein1, 1UCSD, La Jolla, CA; 2Rady 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 outcome of various diseases. A classic example is AAT deficiency, a monogenic 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. There is no treatment for AAT deficiency, and liver transplantation is currently the only available therapeutic option for severely affected patients. Despite being the leading genetic cause of liver disease in children, AAT deficiency occurs infrequently when compared to sporadic liver diseases. The relatively low incidence of AAT deficiency makes it challenging to obtain insight into the genetic factors that may affect progression of disease from genome-wide association studies (GWAS). However, study of hepatocytes derived from human induced pluripotent stem cells (hiPSC) with classic (ZZ) mutations of AAT may overcome this limitation by identifying cellular phenotypes that correlate with clinical severity of disease in existing AAT deficient patients.

To date, we report generation of the first set of hiPSC lines from a clinically well-characterized cohort of AAT individuals with extreme degrees of liver disease and age-matched controls. For this purpose, we have reprogrammed fibroblasts from AAT (ZZ) patients without evidence of liver damage and those who have suffered a more aggressive course leading to end stage liver disease. These hiPSC lines robustly differentiate into cells that have hepatocyte morphology and express lineage-specific markers. AAT hiPSC-derived hepatocytes recapitulate the histopathologic hallmark of AAT deficiency, which is accumulation of PAS positive, diastase resistant globules. Furthermore, our preliminary analyses suggest that hiPSC-derived hepatocytes from AAT patients without liver disease have more polymeric AAT than those generated from AAT patients with significant liver disease. We are currently investigating pathways involved in clearance of mutant AAT, focusing on autophagy as a potential mechanism mediating heterogeneity of AAT-related hepatocyte injury.

Intestinal/Colonic Disorders – Inflammatory Bowel Disease

385 CAN POOR POUCH FUNCTION BE PREDICTED FOLLOWING ILEAL POUCH - ANAL ANASTOMOSIS (IPAA) FOR CHRONIC ULCERATIVE COLITIS (CUC) IN CHILDREN? Stephanie F. Polites1, D. D. Potter2, Christopher R. Moir2, Abdalla E. Zarroug3, Michael C. Stephens4, Jeanne Tung5, W. S. Harmsen1, Emily S. Pavey3, John H. Pemberton4, 1Division of Pediatric Surgery, Mayo Clinic, Rochester, MN; 2Division of Pediatric Gastroenterology, Mayo Clinic, Rochester, MN; 3Division of Colon and Rectal Surgery, Mayo Clinic, Rochester, MN; 4Division of Biostatistics, Mayo Clinic, Rochester, MN; 5Division of Colon and Rectal Surgery, Mayo Clinic, Rochester, MN

Objective: Most children after IPAA for CUC have satisfactory long term outcomes. Some however experience poor function, recurrent pouchitis and, rarely, pouch loss. The purpose of this study is to determine if there are pre-operative risk factors that can predict poor long term function.

Methods: All patients (<18 years) undergoing IPAA at our institution between 1980 and 2009 were included. Their medical records were reviewed for pre-operative information and post-operative outcomes, including chronic pouchitis and pouch loss. Quality of life and functional outcomes were determined by internally standardized questionnaires.

Results: 13 of 183 (7%) of patients experienced pouch loss, including pouch excision and/or permanent ileostomy. Increased number of pre-operative stools per day was the only pre-operative risk factor for pouch loss (p=0.03, OR = 1.1 per stool). Importantly, increased number of pre-operative stools per day was associated with many measures of poor IPAA function including frequent incontinence (p < 0.01, OR=1.1 per stool), restricted social activities (p=0.02, OR=1.1 per stool), and increased daytime stools per week in IPAA versus controls (p=0.02, OR=1.1 per stool). Duration of CUC prior to IPAA, pre-operative steroid use, pre-operative albumin levels, and number of operative stages were not associated with poor function (p > 0.05).

Conclusion: Increased number of pre-operative stools per day in children with CUC is a strong predictor of poor function postoperatively. Increased age was also associated with frequent daytime stools. Further study into the etiology of pouch loss is ongoing.

386* EOSINOPHIL-DERIVED PROTECTIN D1 ATTENUATES INFLAMMATORY RESPONSES IN EXPERIMENTAL COLITIS. Joanne C. Masterson1, Eoin N. McNamee2, Rachel Harris1, Lindsay Hosford3, Paul Jedlicka1, Ryo Iwamoto4, Sophie Fillon1, Elizabeth Jacobsen1, Cheryl Protheroe5, Holger K. Eltzschig5, Sean Colgan1, Makoto Arita1, James J. Lee1, Glenn Furuta5, 1Pediatric Gastroenterology, Hepatology & Nutrition, University of Colorado School of Medicine, Aurora, CO; 2Anesthesiology, University of Colorado School of Medicine, Aurora, CO; 3Pathology, University of Colorado School of Medicine, Aurora, CO; 4Medicine, University of Colorado School of Medicine, Aurora, CO; 5Health Chemistry, University of Tokyo, Tokyo, Japan; 6Biochemistry and Molecular Biology, Mayo Clinic, Scottsdale, AZ

BACKGROUND: Eosinophils are normal constituents of the colonic mucosa and increase significantly during disease states. While a number of studies suggest that eosinophils contribute to the pathogenesis of gastrointestinal inflammation, their role in intestinal health is not certain.

AIM: We sought to define the impact of resident baseline eosinophils in a mouse model of acute colitis to provide a greater understanding of the homeostatic role(s) of these granulocytes.

METHODS: Acute colitis (DSS) was induced in eosinophil competent wild type mice and three models of mice deficient of eosinophils. Physical, histological, cellular and molecular features were measured. Analysis of lipid mediators was completed in these cohorts and add-back experiments performed.

RESULTS: Eosinophil-deficient (PHIL) mouse models developed significantly worse colitis than their eosinophil competent wild type (WT) counterparts (Disease Activity Index: 4.4 points greater day 6, P<0.001; 2.5 points greater day 7, P<0.01; 3 points greater day 8, P<0.05, PHIL vs. WT respectively). Eosinophil-deficient mice also succumbed to significantly greater mortality (PHIL - 39% death rate vs. WT - 0% at 7 days). Upon harvest colonic length was found to be significantly shorter (44.3mm vs. 53.9mm, PHIL vs. WT respectively). Eosinophil-deficient mice also succumbed to significantly greater mortality (PHIL - 39% death rate vs. WT - 0% at 7 days). Upon harvest colonic length was found to be significantly shorter (44.3mm vs. 53.9mm, PHIL vs. WT respectively). Mice experimentally deficient in eosinophils by antibody mediated depletion or by bone marrow transplantation were also found to develop...
significantly worse colitis. Further analysis revealed a predominance of neutrophils in eosinophil-deficient mice (76.4% vs 45.7%, PHIL vs. WT respectively; P<0.05) and lipidomic array of colonic tissue identified a deficiency in protectin D1 (11.1 vs. 1.0 ng/g colon, PHIL vs. WT respectively, P=0.0001). Reconstitution of eosinophil-deficient mice with exogenous protectin D1 led to significant decrease of colitis histological scores (9.4 versus 16.5, PD1 treated PHIL vs. untreated PHIL respectively, P<0.01) as well as attenuated neutrophil infiltration (54.6% vs. 74.5%, PD1 treated PHIL vs. untreated PHIL respectively; P<0.01) and reduced expression of TNF-α (0.7 fold, P<0.05), IL-1β (0.3 fold, P<0.05), IL-6 (0.3 fold, P<0.05), and inducible NO synthase (0.7 fold, P<0.05).

CONCLUSION: These studies demonstrate that eosinophils exert a protective role in mouse colitis through the production of the anti-inflammatory lipid mediator protectin D1.

387 DEVELOPMENT OF A SELF-EFFICACY SCALE FOR ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE
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Pediatric inflammatory bowel disease (IBD) self-management is important for short and long term disease outcomes. Disease self-management fits well within the framework of social cognitive theory, which posits that a person carries a set of beliefs, known as self-efficacy, that affect his/her behavior and ability to perform certain tasks. Self-efficacy is a measurable and specific belief about one's ability to engage in the skills required to master a new challenge despite obstacles. IBD self-efficacy could be a valuable outcome measure for interventions aimed at optimizing self-management in pediatric IBD. The first step in this process is to develop a valid and useful measure. The aim of this qualitative study was to design a disease specific self-efficacy scale for adolescents with IBD.

Methods: Obtaining patient input is the first step outlined in the FDA guidelines for patient reported outcome instruments. A purposive sample of adolescents and young adults were recruited from an outpatient pediatric gastroenterology clinic and each participated in a semi-structured interview. Audio recordings of the interviews were transcribed and individually reviewed by a pediatric gastroenterology fellow (M.R.) and health psychologist (L.K.) for themes and commonalities related to the patients' perspective on IBD self-management that could be used to generate measures for future quantitative analysis. Specific item construction was performed through an iterative process, with the initial results being reviewed by a consensus panel consisting of 5 gastroenterologists and 2 health psychologists. The final 13-item scale was then reviewed by a subset of participants through cognitive interviews which addressed readability/clarity of the question, adequacy of the time frame referenced per question, clarity of answer choices and an opportunity to add choices, as well as think-aloud decision making around answers. Once these were complete, the questions were adjusted to reflect their feedback.

Results: A total of 21 patients and 7 parents participated in the interviews. The study sample was 38% female, 81% Caucasian, 67% had Crohn's disease, and 81% had not required surgery. Median age was 15 years old (range: 10-22 years old). The average duration of disease was a median of 2 years (range: less than 1 month to 12 years). The majority of patients were on immunomodulators at the time of the interview. Theme analysis and expert review yielded 13 items across 4 theoretical domains: managing medical care, managing daily life with IBD, managing emotions, and managing the future with IBD. Likert scales measured the extent to which the teens related to each statement; for example, "No matter where I am, I can find something I can eat" and "I know what to do when I think a flare is starting". Supporting its theoretical and likely construct validity, the item domains resembled those of an adult IBD self-efficacy scale which has been validated in clinical and population based samples.

Conclusion: A 13-item disease specific scale has been developed to assess self-efficacy as a predictor of self-management in adolescents with IBD. Further validation studies are currently underway.

388 EFFICACY OF ADALIMUMAB FOR TREATMENT OF PERIANAL FISTULA IN CHILDREN WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM IMAGINE 1.
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Objective: To evaluate adalimumab (ADA) efficacy on fistula closure and improvement in pediatric patients (pts) with moderately to severely active Crohn's disease (CD) enrolled in the randomized clinical trial IMAgINE 1.

Methods: Pts aged 6-17 years with baseline (BL) PCDAI >30 and CD resistant or intolerant to conventional therapy received open-label induction of ADA at weeks (wks) 0/2 as per body weight (≥40kg, 160/80mg; <40kg, 80/40mg). At wk 4, pts 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). Fistula closure (closure of all BL draining fistulae ≥2 consecutive visits) and fistula improvement (decrease ≥50% from BL in the number of draining fistulae ≥2 consecutive visits) were measured in pts with at least 1 draining fistula at screening and at wk 0. Non-responder imputation (NRI) was used for missing data.

Results: 19% (36/188) of pts had at least 1 draining fistula at BL. A greater proportion of pts receiving HD than LD ADA achieved fistula closure from wks 12-52, although the differences were not statistically significant (Table). Similar results were seen for fistula closure. Rates of fistula closure and improvement were stable over time in HD ADA-treated pts (NRI). Safety data for LD and HD ADA were previously reported1. No new safety signals were detected and no significant differences were observed between LD and HD ADA1.

Conclusion: Fistula improvement and closure were seen in children with moderately to severely active CD treated with ADA. Pts in both dosing groups achieved these benefits.


Proportion of ADA-treated pts with fistula closure or improvement
## LONG-TERM SAFETY OF ADALIMUMAB IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE.

**Objective:** The safety profile of adalimumab (ADA) in children with moderately to severely active Crohn's disease (CD) enrolled in the IMAgINE 1 trial up to week 52 was previously reported. Cumulative safety data including the on-going open-label extension (OLE) is presented here.

**Methods:** Patients (pts) who completed IMAgINE 1 had the option to continue in the on-going OLE. Adverse events (AEs) were monitored regularly and by spontaneous reporting. Rates of AEs were assessed per 100 patient-yrs (PY) of exposure for any pt enrolled in IMAgINE 1 and followed through the 31 July 2011 cut-off or up to 70 days after the last dose of ADA. Subgroup analysis by prior infliximab (IFX) use was also performed.

**Results:** 192 pediatric pts had received ADA for CD, totaling 304.1 PY of exposure. As of 31 Jul 2011, 29/192 (15%) pts had up to 3 yrs of exposure. The most common AE was injection site reaction; all were non-serious. The most common serious AE (SAE) was flare or worsening of CD. Rates of SAEs, infections and AEs leading to discontinuation were consistent with IMAgINE 1. SAEs were experienced by significantly more IFX-exposed pts than IFX-naïve pts (Table). No malignancies, TB, demyelinating disease, or deaths were reported.

**Conclusion:** Prolonged ADA treatment, up to 3 yrs, in children with moderately to severely active CD has a safety profile that is consistent with known ADA data and no new safety signals have been identified.

### Overview of Treatment-emergent Adverse Events (AE) as of 31 July 2011

<table>
<thead>
<tr>
<th>Any ADA N=192, 304.1PYs</th>
<th>IFX-naïve N=107, 199.7 PYs</th>
<th>Prior IFX N=85, 104.4 PYs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any AE</strong></td>
<td>Events (E/100PY)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Any AE</td>
<td>2414 (793.8)</td>
<td>107 (100)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>123 (40.4)</td>
<td>38 (35.5)</td>
</tr>
<tr>
<td>AE leading to discontinuation</td>
<td>64 (21.0)</td>
<td>22 (20.6)</td>
</tr>
<tr>
<td>Opportunistic infection (excluding TB)</td>
<td>2 (0.7)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Serious Infection</td>
<td>24 (7.9)</td>
<td>12 (11.2)</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>100 (32.9)</td>
<td>23 (21.5)</td>
</tr>
<tr>
<td>Hematologic AE</td>
<td>33 (10.9)</td>
<td>12 (11.2)</td>
</tr>
<tr>
<td>Hepatic AE</td>
<td>14 (4.6)</td>
<td>10 (9.3)</td>
</tr>
</tbody>
</table>

* *Aeromonas* infection and histoplasmosis disseminated; *p<0.05 IFX-naïve vs prior IFX (Fisher's exact test)
Background: Clostridium difficile infection complicates inflammatory bowel disease in children and adults. Increased hospitalizations have been reported due to recent hypervirulent c. difficile strains. National trends of c. difficile infections in hospitalized children and young adults with inflammatory bowel disease (IBD) are currently incomplete.

Methods: We explored the annual Nationwide Inpatient Sample (NIS) for IBD-related hospitalizations of children and young adults, ages 5-24, with c. difficile infections. We used census data to establish per-capita hospitalization rates and assessed nationally representative trends using variance weighted least squares regression. 95% confidence intervals were reported for nationally representative estimates. We examined length of stay and colectomy as markers of disease burden.

Results: Per capita rates of IBD hospitalizations with c. difficile infections increased from 0.6 (95% CI: 0.2-1.0) to 1.5 (95% CI: 1.0-1.9) per 100,000 individuals across the 10 years of study. Lengths of stay were relatively constant across time and were longer for hospitalizations with c. difficile infection (7.8-10.1 days) than without (5.1-5.6 days). Hospitalizations including c. difficile infection had consistently longer lengths of stay than those without (mean difference 3.8 days, 95 CI: 2.3-5.2). Throughout the study period, the proportion of IBD hospitalizations with c. difficile infection in which colectomy was performed varied (range: 2.8-10.3%). The proportion of IBD hospitalizations without c. difficile infections in which colectomy was performed steadily decreased (11.4% to 6.1%, Table 1).

Conclusion: Hospitalizations of children and young adults with c. difficile infection have increased in the United States over the past decade. Hospital burden is higher in IBD hospitalizations with c. difficile, indicating a continuing need for prevention and investigation. Table 1. Proportion of IBD Hospitalizations when a colectomy was performed, with and without c. difficile infections.

<table>
<thead>
<tr>
<th>Year</th>
<th>Proportion with c. difficile (95% CI)</th>
<th>Proportion without c. difficile (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>0.042 (0.000 - 0.089)</td>
<td>0.114 (0.096 - 0.131)</td>
</tr>
<tr>
<td>2002</td>
<td>0.078 (0.019 - 0.137)</td>
<td>0.112 (0.099 - 0.126)</td>
</tr>
<tr>
<td>2003</td>
<td>0.059 (0.009 - 0.108)</td>
<td>0.101 (0.087 - 0.114)</td>
</tr>
<tr>
<td>2004</td>
<td>0.100 (0.045 - 0.156)</td>
<td>0.104 (0.085 - 0.123)</td>
</tr>
<tr>
<td>2005</td>
<td>0.096 (0.045 - 0.147)</td>
<td>0.094 (0.082 - 0.106)</td>
</tr>
<tr>
<td>2006</td>
<td>0.064 (0.023 - 0.104)</td>
<td>0.078 (0.069 - 0.087)</td>
</tr>
<tr>
<td>2007</td>
<td>0.103 (0.046 - 0.161)</td>
<td>0.081 (0.071 - 0.092)</td>
</tr>
<tr>
<td>2008</td>
<td>0.060 (0.023 - 0.098)</td>
<td>0.088 (0.074 - 0.102)</td>
</tr>
<tr>
<td>2009</td>
<td>0.028 (0.004 - 0.051)</td>
<td>0.070 (0.056 - 0.084)</td>
</tr>
<tr>
<td>2010</td>
<td>0.047 (0.019 - 0.075)</td>
<td>0.061 (0.054 - 0.068)</td>
</tr>
</tbody>
</table>

MAGNETIC RESONANCE ENTEROGRAPHY (MRE) REMISSION DEMONSTRATING RADIOLOGIC HEALING PREDICTS IMPROVED OUTCOME IN PEDIATRIC CROHN'S DISEASE. Cary G. Sauer1,2, Jeremy Middleton1,2, Adina Alazraki2, Kiery Braithwaite2, Subra Kugathasan1,2, 1Emory University, Atlanta, GA; 2Children's Healthcare of Atlanta, Atlanta, GA

Background: Mucosal healing by endoscopy predicts clinical remission; however, small bowel Crohn's Disease (CD) is unreachable by conventional endoscopy. Magnetic resonance enterography (MRE) evaluates the small bowel and can detect active inflammation. The primary objective of this study was to determine if MRE remission predicts clinical remission in pediatric CD.

Patients and Methods: An IRB-approved study using our prospectively maintained Emory / Children's Healthcare of Atlanta Crohn's Disease MRE Database from 2008-2012 was performed. All patients with CD who underwent an MRE during treatment greater than 90 days after diagnosis of CD with at least one year follow-up after the MRE were included in the study and MRE data, clinical data, and physician global assessment (PGA) were recorded. MRE studies were grouped into "MRE remission" defined as absence of active inflammation and "MRE active inflammation" by a radiologist blinded to clinical care.

Results: A total of 79 MRE studies in unique CD patients were performed with at least one-year follow-up after MRE. 27 children demonstrated MRE remission with radiologic healing while 52 children demonstrated active inflammation on their MRE studies. There was no difference between groups in gender, race, disease duration or follow-up duration from MRE to last follow-up. There was no difference in treatment at initial MRE between groups and no difference in likelihood of MRE remission with different medications (immunomodulators vs biologics). At follow-up, there was a higher percentage of children on biologic medications but this did not reach statistical significance. In the MRE remission group 85.2% were in clinical remission at follow-up (median follow-up 1.9 years, range 1.0-4.1 years). In the MRE active inflammation group only 42% were in clinical remission at follow-up (median follow-up 2.6 years, range 1.1-4.5 years) despite treatment changes. MRE remission is associated with improved outcome as defined by increased likelihood of clinical remission (p=0.002) (Table 2).

Conclusions: MRE remission or radiologic healing predicted clinical remission at follow-up, with sustained clinical remission in 85% of children. MRE is an important outcome measure for children with small bowel CD beyond the reach of standard endoscopy and can be
used to document objective disease healing and predict clinical outcome.

### Treatment at Initial MRE and Follow-up Visit

<table>
<thead>
<tr>
<th>Treatment at Initial MRE</th>
<th>MRE Remission (n=27)</th>
<th>MRE Active Inflammation (n=52)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunomodulator</td>
<td>9 (33.3%)</td>
<td>18 (34.6%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Biologic</td>
<td>18 (66.7%)</td>
<td>34 (65.4%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment at Follow-up Visit</th>
<th>MRE Remission (n=27)</th>
<th>MRE Active Inflammation (n=52)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunomodulator</td>
<td>8 (57.1%)</td>
<td>6 (42.9%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Biologic</td>
<td>19 (29.2%)</td>
<td>46 (70.8%)</td>
<td></td>
</tr>
</tbody>
</table>

### Physician Global Assessment at Follow-up Visit

<table>
<thead>
<tr>
<th>PGA at Follow-up Visit</th>
<th>MRE Remission (n=27)</th>
<th>MRE Active Inflammation (n=52)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Remission</td>
<td>23 (85.2%)</td>
<td>22 (42.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Mild Disease</td>
<td>3 (11.1%)</td>
<td>16 (30.8%)</td>
<td></td>
</tr>
<tr>
<td>Moderate Disease</td>
<td>1 (3.7%)</td>
<td>9 (17.3%)</td>
<td></td>
</tr>
<tr>
<td>Severe Disease</td>
<td>0 (0%)</td>
<td>5 (9.6%)</td>
<td></td>
</tr>
</tbody>
</table>

392 **DISCORDANCE BETWEEN CLINICAL REMISSION AND MRE REMISSION IN PEDIATRIC CROHN’S DISEASE**

*Cary G. Sauer1,2, Jonathan Loewen2,1, Subra Kugathasan1,2, 1Emory University, Atlanta, GA; 2Children’s Healthcare of Atlanta, Atlanta, GA*

**Background:** Clinical remission using the Physician Global Assessment (PGA) or the Pediatric Crohn's Disease Activity Index (PCDAI) has been the primary outcome of studies and the goal of clinical care. However, recent data demonstrates that mucosal healing is an important predictor of improved clinical outcome. Interestingly, there is discordance between clinical disease indices and more objective endoscopy indices which evaluate mucosal healing. The primary objective of this study was to determine if clinical remission correlates with MRE remission in children with CD.

**Patients and Methods:** We completed an IRB approved prospective study to evaluate MRE in children in clinical remission. We offered children with CD who were in clinical remission (PGA remission, PCDAI <10) research MRE studies (supported by an institutional grant). MRE studies were read by a radiologist blinded to clinical data (JL) and grouped into MRE remission (no active inflammation) and MRE active inflammation.

**Results:** A total of 14 research MRE studies were performed in children with CD in clinical remission. Median PCDAI was 1.3 (range 0-10) and there was no correlation between PCDAI and MRE results. Treatment included biologic medications in 11 children and immunomodulator medication in 3 children. MRE results demonstrated active inflammation in 7 studies including 5 demonstrating only small intestine inflammation, 1 small and large intestine inflammation, and 1 only large intestine inflammation. Of those with active inflammation on MRE, 5 of 7 were being treated with biologic medications. Of those in MRE remission, 6 of 7 were being treated with biologic medications.

**Conclusions:** Despite clinical remission, half of research MRE studies demonstrated active inflammation. Clinical symptoms or lack thereof may not correlate with true disease or disease control. Silent active Crohn's Disease may be more common that previously considered and objective disease evaluation may be preferable to clinical symptoms in evaluating disease control.
THE EFFECT OF DISEASE KNOWLEDGE ON QUALITY OF LIFE IN CHILDREN WITH IBD. Alice Williamson1,2, Thomas Chen1,2, Brian Morris1, Maria-Stella Serrano1, 1Pediatrics, Ochsner, New Orleans, LA; 2Pediatrics, Tulane University, New Orleans, LA

BACKGROUND: The Inflammatory Bowel Diseases (IBD) include Crohn's Disease (CD) and Ulcerative Colitis (UC) and have as their hallmark characteristic a dysregulated inflammatory response. These diseases affect people of all ages with 25% of diagnoses made in childhood or adolescence. It has been noted that these patients generally have a lower quality of life (QoL) than their healthy peers even when the disease is in remission. It is unclear why this is the case. The currently prevailing view of diseases in general is that patients who have a solid understanding of their diseases will be better able to cope with their ailments and better adhere to medication regimens, thus, may have a higher QoL. This idea is controversial in IBD. Some studies suggest patient education on IBD may worsen QoL by inducing stress. Other studies have shown that patient education improves disease knowledge and patient satisfaction while also contributing to better outcomes, including better QoL. Our goal was to identify a relationship between knowledge and QoL.

METHODS: Patients with IBD, ages 9-19, filled out four questionnaires: 1) IBD-KID, 2) the IMPACT III Questionnaire; 3) Pediatric Crohn's Disease Activity Index (for Crohn's patients) or the PUCAI (for UC patients); and 4) the personal fact sheet, which included a demographics and medical history survey; past medical history from patient's previously-established medical record was also utilized. Data was stratified by disease severity as to control for differences in symptoms that would affect quality of life regardless of knowledge. Within these groups, data was analyzed, exploring any relationships.

RESULTS: 13 patients completed the study questionnaires. 12 patients had good or excellent QoL, and 11 of these patients had poor or fair knowledge of IBD.

CONCLUSION: Most of the patients in this study had good or excellent QoL while knowing little about their disease. This study was fairly limited to patients with minimal disease, and including patients with worse disease may illustrate a more evident correlation between disease knowledge and QoL.

QoL Compared to Knowledge of IBD in Patients with Quiescent or Mild Disease Severity

<table>
<thead>
<tr>
<th>Subject</th>
<th>Disease Duration</th>
<th>Medication</th>
<th>PCDAI</th>
<th>MRE Active Inflammation of Small Intestine</th>
<th>MRE Active Inflammation of Large Intestine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.32 year</td>
<td>6-Mercaptopurine</td>
<td>10</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>5.38</td>
<td>Adalimumab</td>
<td>0</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>1.63</td>
<td>Infliximab</td>
<td>0</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>3.55</td>
<td>Infliximab</td>
<td>0</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>2.55</td>
<td>Infliximab</td>
<td>7.5</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>5.08</td>
<td>Adalimumab</td>
<td>0</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>3.05</td>
<td>Infliximab</td>
<td>5</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>5.02</td>
<td>Infliximab</td>
<td>5</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>1.57</td>
<td>Infliximab</td>
<td>0</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>10</td>
<td>6.84</td>
<td>Azathioprine</td>
<td>10</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>11</td>
<td>3.69</td>
<td>Infliximab</td>
<td>0</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>4.50</td>
<td>Infliximab</td>
<td>0</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>13</td>
<td>3.65</td>
<td>Adalimumab</td>
<td>2.5</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>1.72</td>
<td>6-Mercaptopurine</td>
<td>2.5</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

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BACTEROIOTHERAPY IN PEDIATRIC CROHN'S DISEASE. David Suskind1,2, Ghassan Wahbeh1,2, Heather Vendettoli1, Singh Namita1,2, Dennis Christie1,2, 1Seattle Children's Hospital, Seattle, WA; 2Pediatrics, University of Washington, Seattle, WA

Crohn's disease is characterized by chronic intestinal inflammation in the absence of a recognized etiology. Evidence from human and animal studies support the theory that patients with Crohn's disease have a dysregulated immune response to an unknown trigger. Crohn's disease is also associated with dysbiosis of the fecal microbiome. The fecal microbiome may trigger the intestinal immune response in Crohn's disease. Fecal Microbial Transplant (FMT), by changing the fecal microbiome, may therefore be a potential therapeutic option for patients with Crohn's disease. To answer the question of tolerability and efficacy of FMT in pediatric Crohn's disease, six patients with mild or moderate disease activity as defined by Pediatric Crohn's disease activity index (PCDAI) of 10-29 were enrolled into this study. Each patient received initial evaluation (which included donor evaluation), stool transplantation, and post transplant evaluation. Throughout the study, study subjects were maintained on their pre-transplant regimen for management of their Crohn's disease. Post FMT subjects had follow-up at 2 weeks and 6 weeks. Pediatric Crohn's disease activity index (PCDAI) and C-reactive proteins were completed during each study visit. Side effects of FMT were assessed through diary cards provided to subjects. Six patients with Crohn's disease have been enrolled (3 male/3 female). Ages ranged from 12 - 19 years (16.5 ± 2.4 years). Patients tolerated FMT well, 3 patients had mild symptoms of gassiness and bloating the day after transplantation. Two weeks after FMT, 5 of the 6 patients were in clinical remission based upon PCDAI (table1). PCDAI scores were at baseline 19.2 ± 7.7, at 2 weeks post FMT 5 ± 3.16, and at 6 weeks post FMT 6.6 ± 4.1. C-reactive proteins for all patients either improved or did not change at week 2 (Table 2). The median C-reactive protein level at baseline was 2.6 ± 1.5 mg/dL, at 2 weeks post FMT 1.5 ± 0.7 mg/dL, and at 6 weeks post FMT 1.8 ± 1.0 mg/dL. This study is the first study to show that FMT for active Crohn's disease is well tolerated and improves both clinical and laboratory parameters associated with active Crohn's disease.

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Baseline 27.5</th>
<th>2 weeks post transplant 7.5</th>
<th>6 weeks post transplant 12.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 2</td>
<td>10</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Patient 3</td>
<td>15</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Patient 4</td>
<td>22.5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Patient 5</td>
<td>12.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Patient 6</td>
<td>27.5</td>
<td>2.5</td>
<td>7.5</td>
</tr>
</tbody>
</table>

PCDAI score: Remission(<10); Mild to Moderate(10-30); Severe(>30)

C-reactive Protein in Crohn's Patients receiving FMT

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Baseline 3.1</th>
<th>2 Weeks post FMT 1.1</th>
<th>6 Weeks post FMT 1.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 2</td>
<td>4.5</td>
<td>1.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Patient 3</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Patient 4</td>
<td>1.4</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Patient 5</td>
<td>1.9</td>
<td>1.6</td>
<td>2.3</td>
</tr>
<tr>
<td>Patient 6</td>
<td>4</td>
<td>2.7</td>
<td>2.4</td>
</tr>
</tbody>
</table>

* CRP results are in mg/dL. Normal ≤ 0.8.

PSYCHOLOGICAL FACTORS ARE MORE IMPORTANT THAN DISEASE ACTIVITY IN EXPLAINING PEDIATRIC CROHN'S DISEASE SYMPTOMS. Miranda A. Van Tilburg1, Robyn Claar2, Shelby Langer2, Dalia Sherif2, Bisher Abdullah2, Douglas Drossman1, Dennis Christie1, Joan Romano1, William Whitehead1, Ronal L. Levy1, 1UNC Center for Functional GI and Motility Disorders, University of North Carolina, Chapel Hill, NC; 2Mary Bridge Children's Hospital, Tacoma, WA; School of Social Work, University of Washington, Seattle, WA; gastroenterology, Seattle Children's Hospital, Seattle, WA

Background: Crohn's Disease (CD) is a chronic, relapsing inflammatory bowel disease. Symptoms wax and wane with inflammation. Although symptoms are a sign of inflammation, the occurrence and severity of symptoms may be driven by more than disease severity alone. The aim of the current study is to examine the role of inflammation and psychological factors in CD symptoms.

Methods: Participants were 125 children (57.1% boys, 86.5% Caucasian, mean age 13.9) with Crohn's Disease. All children completed measures of CD symptoms (Inflammatory Bowel Disease Questionnaire), Disability (Functional Disability Inventory) and psychological factors (Children's Depression Inventory, Multidimensional Anxiety Scale, Pain Response Inventory, Pain Beliefs questionnaire).

Results: Structural equation modeling was used to test the effects of inflammation and psychological factors (all measures combined into one latent factor) on CD symptoms. The hypothesized model showed adequate fit to the data: Chi2(df=8)= 12.04.29; p=0.15; RMSEA <
.05. Disease activity was not significantly associated with symptoms. Psychological factors (β=0.45, p<0.001) explained 42% of variation in CD symptoms. A similar model was run to test the effects of psychological factors and disease activity on disability. The hypothesized model showed adequate fit to the data: Chi2(df=8) = 9.5; p=0.30; RMSEA < .05. Both disease activity (β=0.01, p<0.01) and psychological factors (β=0.61, p<0.001) were significantly associated with disability explaining 36% of the variance. Larger coefficients for psychological factors compared to disease activity indicate that psychological factors have a much stronger association with disability. Conclusion: CD symptoms in children are not only driven by inflammation. Psychological factors explain 30-40% of symptoms and disability. Physicians need to be aware that symptoms severity is largely driven by psychological factors and may not always be a good indicator of disease activity.

**396 MEDICATION NON-ADHERENCE IMPACTS DISEASE SEVERITY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE.** George M. Zacur1, Shehzad A. Saeed1, Katherine L. Loreaux2,3, Joseph R. Rauchle2, Elizabeth R. Williams1, Wendy N. Gray2,3, Kevin A. Hommel2,3, 1Division of Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 2Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 3Center for Adherence and Self-Management, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Background: Adherence to the often complicated regimens used in the management of Inflammatory Bowel Disease (IBD) can be challenging for children and families. Adherence research in pediatric IBD has been predominantly descriptive, and the association between adherence and disease severity has not been significantly evaluated. This study examines the association between oral medication non-adherence and disease severity in pediatric patients with IBD. Methods: Participants included pediatric patients with a confirmed diagnosis of Crohn disease (CD), ulcerative colitis (UC), or indeterminate colitis (IC) who were prescribed aminosalicylates (ASA) and/or a thiopurine immunomodulator [6-mercaptopurine (6MP)/Azathioprine (AZA)] and received a Physician Global Assessment (PGA) during regular clinic visits over a contiguous 2-year period. Adherence rates were calculated based on pharmacy refill records. Non-adherence was defined as refilling <80% of prescribed medications. Physicians provided assessments of disease severity using the PGA as part of standard clinic procedure. The Short Pediatric Crohn's Disease Activity Index (shPCDAI) or Pediatric Ulcerative Colitis Activity Index (PUCAI) was calculated for each subject as an additional measure of disease severity. Chi-square and logistic regression were performed to assess the association between adherence and disease severity. Results: We analyzed 143 pharmacy records for 107 subjects (CD=78, UC=24, IC=5). Median age was 15 years. The overall refill frequency was 77%, and the prevalence of non-adherence was 49%. Individual refill frequencies for ASA and 6MP/AZA were both 77%. The prevalence of non-adherence to ASA and 6MP/AZA was 50% and 40%, respectively. As age increased, refill frequency decreased and non-adherence prevalence increased. Patients with CD were more non-adherent than those with UC. Patients taking ASA, 6MP/AZA, or both who were non-adherent were more likely to have worse disease severity than adherent patients (p<0.0001). When the shPCDAI and PUCAI were used as measures of disease activity, increased severity was again related to non-adherence to both ASA and 6MP/AZA (p<0.0001). When examining age, gender, diagnosis, and medication type as predictors of disease severity and as moderators of the association between adherence and disease severity, we discovered that this association was strongest for females with CD and weakest for males with UC (p<0.05). Conclusions: Non-adherence is prevalent in pediatric IBD. This study is the first to objectively assess the relationship between medication adherence and disease severity in pediatric IBD. The results suggest that poor adherence to both ASA and 6MP/AZA significantly predicts worse disease severity. This study should promote awareness concerning the impact of non-adherence on disease severity and encourage the continued development and use of early interventions aimed at improving adherence and quality of care. Cost of delivered care may also be influenced in that adherent patients may require fewer hospitalizations and acute care visits, decreased surgical interventions, and a reduced need for more expensive medications (e.g., biologics).

**397 ILEOCECAL RESECTION IN PEDIATRIC CROHN'S DISEASE.** George M. Zacur1, Brooke I. Schmelzle1, Jason S. Frischer2, Shehzad A. Saeed1, 1Division of Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 2Division of Pediatric General and Thoracic Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Background: Crohn's disease (CD) and Ulcerative Colitis (UC) comprise the two major groups of inflammatory bowel disease (IBD), which may present with chronic and relapsing episodes of inflammation of the gastrointestinal tract. Complications of CD include intestinal strictures, fistulae, abscesses and phlegmons, among others. While there is ample adult literature on post-operative outcomes after ileocolonic resection, pediatric literature is limited. This study examines the medical and surgical experiences, as well as post-operative outcomes in a cohort of pediatric patients with medically refractory CD who underwent ileoceccectomy. Methods: We conducted a retrospective review of pediatric patients with complicated CD who underwent ileocecal resection at our institution from 2004 to 2012. We evaluated demographic data, indications for surgery, surgical approach, post-operative complications, and post-operative measures of growth and laboratory improvement. Early and late complications were defined as occurring within 30 days of the resection and between 31 days and one year following the resection, respectively. Results: Forty-one children (25 males; 16 females) underwent ileocecal resection for medically refractory CD. Age at diagnosis ranged between 6.8 and 20.1 years with a median age of 13.9 years, and a median age at first surgery of 16.5 years. The mean time to surgery was 28.7 months from diagnosis. Fifty-one percent of the patients had a single indication for resection and 49% had multiple indications. Indications for ileocecal resection included stricture (75%), fistula (29%), abscess (17%), phlegmon (19%), perforation (12%), and refractory disease [pain, bleeding, poor growth, weight loss, persistent diarrhea (17%)]. Laparoscopic-assisted resection was performed the most (51%), and laparoscopic and open resections were performed 29% and 19% of the time, respectively. Eighty-eight percent of patients had a primary anastomosis, and 12% had an ileostomy with a subsequent anastomosis. The anastomosis was stapled 93% of the time and hand-sewn 7%. There were a total of seven early complications (3 abscesses, 1 obstruction due to adhesions, 2 wound infections, 1 DVT) and one late complication (abscissa). Average weight and height gain at approximately 6 months (range 3-8 months) post-operatively was 4.63kg and 2.3cm, respectively, and average hemoglobin and albumin increase was 1.45g/dL and 0.65g/dL, respectively. Conclusions: Crohn's disease presents with an unpredictable course, and
complications may require surgical intervention. Ileocecal resection can improve symptoms and disease course, as well as nutrition and growth.

398 WITHDRAWN

399 ANTIBODIES TO INFlixIMAB ARE ASSOCIATED WITH LOWER INFlixIMAB LEVELS AND INCREASED LIKELIHOOD OF SURGERY IN PEDIATRIC IBD. Naamah Zitomersky1, Benjamin Atkinson1, Kerri Fournier1, Paul Mitchell1, Lori Ashworth1, Scott Hauenstein1, Linda Heiner2, Emil Chuang2, Athos Bousvaros1, 1Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; 2Prometheus Labs Inc., San Diego, CA

Background: Studies suggest that the development of antibodies to infliximab correlates with loss of response or need to change medications in children with inflammatory bowel disease. However, pediatric data on the role of therapeutic drug monitoring with infliximab remain limited. We conducted a cross sectional study of trough infliximab levels and antibodies to infliximab in a group of patients currently receiving infliximab.

Methods: We measured trough infliximab levels and antibodies to infliximab (ATI) in 134 patients on infliximab. Serum was obtained immediately prior to the patient's infusion. The assays were performed by Prometheus Laboratories Inc. Clinical information gathered at the time serum was obtained included demographics, disease phenotype, duration of infliximab therapy, use of combination therapy (methotrexate or 6-mercaptopurine with infliximab), and surgery after starting infliximab.

Results: Assays were performed on 134 subjects currently receiving infliximab infusions (85 Male; mean age 17.3±4.3 years; 119 CD, and 15 UC). Fifteen subjects had been receiving infliximab for less than 6 months, 47 from 6 months to 2 years, 48 from 2-5 years and 24 for more than 5 years. At the time serum was drawn, 49 patients were receiving concomitant immunomodulators (7 on 6-mercaptopurine, 42 on methotrexate), compared to 85 on infliximab without an immunomodulator. Of our 134 patients, 27 (20%) had ATI levels ≥5 U/ml, and 14 (10%) had ATI levels ≥12 U/ml. Of patients with ATI ≥5 U/ml, 59% had infliximab levels <5 µg/mL; in contrast, only 14% of patients with ATI<5 U/ml had low infliximab levels (table, p <0.001). For patients with ATI ≥5 U/ml, the median infliximab level was 1.0 µg/mL (IQR 1.0-9.3), while for patients with ATI <5 U/ml, the median was 12.7 µg/mL (IQR 7.6-25), p <0.001. Ten (7%) patients (9 CD, 1 UC) underwent bowel resections after beginning infliximab infusions. Four of the 10 patients (40%) that underwent surgery had ATI ≥12 U/ml; in contrast, only 8% of patients that did not undergo surgery had ATI≥ 12 U/ml (p = 0.01). Combination therapy (immunomodulator and infliximab) did not correlate with either increase in level or reduction in antibody compared to monotherapy.

Conclusion: Antibodies to infliximab correlate with a reduction in infliximab level, and a higher risk of surgery in patients with IBD. Prospective monitoring of ATI and levels may help identify a patient group at higher risk of losing response.

Higher antibodies to infliximab (ATI) are strongly associated with lower infliximab levels

<table>
<thead>
<tr>
<th>ATI (U/ml)</th>
<th>Infl iximab level (µg/mL)</th>
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<tbody>
<tr>
<td></td>
<td>&lt;5 (n=107)</td>
</tr>
<tr>
<td>&lt;5 (n=31)</td>
<td>15</td>
</tr>
<tr>
<td>≥5 (n=103)</td>
<td>92</td>
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</tbody>
</table>

P<0.001

n=number of subjects

Intestinal/Colonic Disorders – Non – Inflammatory Bowel Disease

408 CELIAC DISEASE IS ASSOCIATED WITH INCREASED EXPRESSION OF ALTERNATIVELY SPliced FOXP3 Δ2 ISOFORM. Gloria Serena1,2, Anna Saponi1,3, Laura De Magistris1, Alessio Fasano1, 1MGH, Charlestown, MA; 2University of Maryland, Baltimore, MD; 3Seconda Universita’ degli studi di Napoli, Napoli, Italy

Background: Celiac disease (CD) is an autoimmune enteropathy triggered by gluten in genetically predisposed individuals. FOXP3 transcription factor is important for regulatory T cells (Treg) development and function. While several autoimmune diseases have been associated to reduced Tregs, CD patients show high FOXP3 expression. Two main alternatively spliced isoforms of FOXP3 have been described. While full length (FL) contains 11 exons and it is fully functional, the Δ2 lacks exon 2. This last isoform is thought to have a reduced suppressive function due to the missing RORγt binding site that plays an important role in regulating the differentiation between Th17 and Treg cells.

Aim: To detect if CD is associated to an impaired expression of the alternatively spliced isoform of FOXP3.

Methods: We extracted RNA from intestinal biopsies of 23 CD patients and 15 healthy controls (HC). Real-time (SYBRgreen) was run to detect gene expression of total FoxP3, its FL and Δ2 isoforms by using specific primers. Statistical significance was determined using the two-tailed non parametric Mann-Whitney test and p values < 0.05 were deemed significant.

Results: As expected CD patients showed a significantly increased expression of total FOXP3 (p = 0.01). While the analysis of FL isoform expression showed no difference between the two group of samples (p = 0.33), the Δ2 isoform appeared to be significantly more expressed in CD patients than in HC (p = 0.02).

Conclusions: As described in literature we found that total FOXP3 is significantly over-expressed in CD patients; however for the first
time we show that CD is associated with an increased expression of the Δ2 FOXP3. This isoform is thought to be less functional because it lacks the binding site for RORγt and therefore it can't negatively regulate the Th17 differentiation. Further studies need to be performed to better understand how the over-expression of Δ2 FOXP3 is related to the onset of CD.

409 RISK OF KIDNEY INJURY IN CHILDREN FOLLOWING ORAL SODIUM PHOSPHATE SOLUTION FOR BOWEL CLEANSING. Rebecca Castro, Santo Tomas Hospital, Manila, Philippines

Background: Adult case reports suggest a potential link between oral sodium phosphate and kidney injury, however, controlled studies are lacking. There are limited studies among children and no local reports yet in the Philippines.

Objectives: To determine the risk of kidney injury among pediatric patients admitted at a tertiary hospital who were given Oral Sodium Phosphate Solution (OPS) for bowel cleansing, to determine the demographic profile of patients, and to compare the renal status of those given bowel preparation with OPS and those not given OPS by urinalysis and serum creatinine level determination.

Methods: This is a randomized controlled trial involving patients aged 5-18 years given bowel preparation with informed consent from January 2011-January 2012. Subjects were divided into those given OPS and those given alternative bowel cleansing regimen (castor oil). Baseline and repeat urinalyses and serum creatinine including estimated creatinine clearance (ECC) were recorded.

Results: Twenty patients aged 5-14 years were included. All baseline and repeat urinalyses were normal. There was no significant difference in baseline and repeat creatinine and ECC of the non-OPS patients, (p = 0.798 and p = 0.884) and OPS patients (p = 0.054 and p = 0.085). There was no significant difference between the baseline creatinine and ECCs of the non-OPS and OPS groups (p value 0.867 and 0.622). There was a significant difference with the repeat creatinine values of the non-OPS versus OPS group (p = 0.042), however, there was no significant difference with the repeat ECC (p = 0.069).

Conclusion: Although transient electrolyte shifts may occur, OPS is not associated with untoward events in the majority. Adequate hydration prior to bowel cleansing is of utmost importance prior to its administration. For the period that this study was done, there was no recorded incident of kidney injury based on the parameters measured.

Keywords: Oral Sodium Phosphate Solution (OPS), bowel cleansing, children, creatinine

410 STRUCTURAL, CELLULAR AND FUNCTIONAL FEATURES OF NOVEL MUTANTS OF SUCRASE-ISOMALTASE IN CONGENITAL SUCRASE-ISOMALTASE DEFICIENCY. Birthe Gericke, Mahdi Amiri, Hassan Y. Naim, Department of Physiological Chemistry, University of Veterinary Medicine Hannover, Hannover, Germany

INTRODUCTION: Carbohydrates malabsorption in the small intestine and the subsequent symptoms, such as vomiting and osmotic diarrhea, are associated with the absence or reduced levels of brush border disaccharidases at the apical membrane of the enterocytes. Congenital sucrase-isomaltase deficiency (CSID) is a prominent form of carbohydrate malabsorption that is characterized by altered trafficking and function of sucrase-isomaltase (SI), a major disaccharidase that cleaves α-glycosidically linked disaccharides. CSID is an autosomal recessive disorder that is elicited by mutations in the coding region of SI and inherited as a homozygous or a compound heterozygous trait. Biochemical and cellular analyses of several mutations have established the phenotypes concept of CSID (I-VII) (Naim et al., JPGN 2012), which classifies CSID according to their cellular location and function of SI. While the outcome of CSID is all these cases is severe, it is currently unclear, whether a mild to severe gradient of CSID symptoms exists that would occur at a higher frequency in the human population.

EXPERIMENTAL PROCEDURES: In this study we have analysed the pathophysiology of 11 naturally occurring missense mutations of human SI gene in patients with suspected CSID (Table 1). These mutations are among 56 different abnormal alleles identified recently in 33 patients (Ulrich et al, JPGN 2012). The mutations were introduced into the cDNA encoding SI by PCR mutagenesis, expressed in COS-1 cells as an in vitro cellular model. The structural and biosynthetic features of the mutated SI proteins as well as their cellular localization and enzymatic function were assessed.

RESULTS: The biosynthesis and processing of 11 SI mutants as well as their intracellular localization in immunofluorescence images revealed three major classes of the mutated SI: a class that is processed and matures in a fashion similar to wild type SI, another class with delayed maturation and a third class of mutants was not capable of exiting the endoplasmic reticulum. Importantly, the functional analyses deviated from this general scheme, since the activities of sucrase and/or isomaltase of the normally processed mutants exhibited delayed maturation and a third class of mutants was not capable of exiting the endoplasmic reticulum. Importantly, the functional analyses deviated from this general scheme, since the activities of sucrase and/or isomaltase of the normally processed mutants were substantially reduced. The ER-blocked mutants on the other hand are entirely inactive.

CONCLUSIONS: The presence of several patterns of intracellular processing of SI and alterations in the function that vary from normal to absent clearly demonstrate that CSID is a more heterogeneous disorder and may occur at higher frequency in humans than initially thought.

<table>
<thead>
<tr>
<th>Amino acid</th>
<th>S594P</th>
<th>L741P</th>
<th>F875S</th>
<th>W931R</th>
<th>R1544C</th>
<th>Q307Y</th>
<th>D536V</th>
<th>R774G</th>
<th>C1531Y</th>
<th>W105C</th>
<th>F139Y</th>
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<tr>
<td>% Mature SI</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>44</td>
<td>56</td>
<td>16</td>
<td>82</td>
<td>71</td>
<td>71</td>
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<tr>
<td>% Sucrase activity</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>22</td>
<td>58</td>
<td>88</td>
<td>7</td>
<td>30</td>
<td>47</td>
<td>100</td>
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<tr>
<td>% Isomaltase activity</td>
<td>4</td>
<td>6</td>
<td>1</td>
<td>11</td>
<td>71</td>
<td>2</td>
<td>1</td>
<td>110</td>
<td>109</td>
<td>61</td>
<td>66</td>
<td>100</td>
</tr>
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Table1: Summary of the effects of mutations on the trafficking and enzyme activities of SI.
411* MUTANT MURINE EPCAM LEADS TO PROLIFERATION DEFECTS MIMICKING CONGENITAL TUFTING ENTEROPATHY. Matt Mcgeough, Carla Pena, James Mueller, Mamata Sivagnanam, 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 in vivo mouse model of CTE based on EpCAM mutations found in patients. Functional alterations were identified using FITC-dextran gavage permeability studies. BrdU was injected intraperitoneally into EpcamΔ4/Δ4 and EpcamWT/WT mice, which were then sacrificed at time points of 4 and 24 hours following injection. Histological sections were stained for BrdU. Proliferation index was calculated as the number of BrdU-labeled cells out of the first 10 cells per crypt-villus. Due to the highly dysmorphic intestinal pathology and villus atrophy seen in EpcamΔ4/Δ4 mice, the positively stained cell ratio was limited to the first ten enterocytes to normalize WT and MUT samples. To investigate migrational effects, counts of the number of cells and longitudinal distance from base of crypt to the furthest travelled positively stained enterocyte at 24 h were obtained.

EpcamΔ4/Δ4 mice show increased intestinal permeability (Fig 1A) and migration. Enterocyte proliferation was assessed using BrdU at a 4 hour time point following injection. EpcamΔ4/Δ4 mice demonstrate a significantly higher proliferation index than EpcamWT/WT (P=0.0222). To assess migration, BrdU positive cells were assessed at 24 hours. Though significant changes were not seen with traditional counting methods (Fig 1B, P=0.4833), analyzing location (Fig 1C, P=0.0041 4h, P=0.0252 24h) and distance of furthest traveled BrdU positive cell (Fig 1D, P=0.0077 4h, P=0.0272, 24h), EpcamΔ4/Δ4 mice revealed significantly higher migration of BrdU positive enterocytes as compared with EpcamWT/WT (Fig 1E). EpcamΔ4/Δ4 mice are viable with limited survival and show pathologic changes resembling CTE. Furthermore, mutation of Epcam leads to enhanced permeability and intestinal cell migration, uncovering underlying disease mechanisms.

412 DESMOID TUMORS ASSOCIATED WITH FAMILIAL ADENOMATOUS POLYPOSIS. Voytek R. Slowik1, Thomas Attard1, Hongying Dai1, Raj Shah1, Seth Septer1, 1Children's Mercy Hospital, Kansas City, MO; 2University of Missouri Kansas City, Kansas City, MO

BACKGROUND: Familial Adenomatous Polyposis (FAP) is a hereditary syndrome with a nearly 100% risk of colorectal cancer as well as extracolonic tumors and malignancy. Most affected individuals harbor a mutation in the APC gene on chromosome 5q21. Genotype-phenotype correlations have been explored for many extra-intestinal manifestations of FAP. One of the most common extra-colonic tumors is a fibromatous proliferative disorder called a desmoid tumor. Desmoid formation can complicate surgery, notably colectomy and entails significant morbidity and mortality. Herein we have pooled the published literature to define the clinical and genotypic correlates of desmoids formation in FAP, both in adults and children.

METHODS: PubMed was searched using Mesh terms corresponding to FAP/APC/Gardners and fibroma/desmoid; the product of this search (62 studies) was filtered for duplicate reports and same populations (11 studies). The remaining (51 studies) were screened for reports or series that included codon specific mutations (26 studies). These were then analyzed for demographic, clinical, and mutation information and placed in a study database (Excel/Access®). Desmoid-associated mutations were compared to the UMD Locus Specific Database to compare the adjusted, relative weight of specific mutations associated with desmoid tumors complicating FAP.

RESULTS: Literature search resulted in 51 peer reviewed publications that were abstracted for content; clinical and genetic testing was reported in 262 patients with desmoids. Gender was specified in 107 patients (63F) and males were significantly older than females at the time of desmoid diagnosis (35.3; 26.6 P=0.021). 24% of affected individuals were 18 years or younger at the time of diagnosis with the youngest at 3 weeks of life. Location of desmoids was reported in 177 patients - most were intra-abdominal (45%), abdominal wall (7%), head and neck (7%), paraspinal (5%), extremities (5%) and chest (4%). Codon mutation was specified in 262 affected individuals. Mutation in the APC gene from codon 1310 to 2011 encompassed 41% of all desmoids cases, and in the reference population 40% of the cases were reported in females and their location was intra-abdominal in nearly half of the cases. The risk for desmoids seemed to be fairly equal in females and males. The most common mutation found in the APC gene from codon 1310 to 2011 was 2.7% and 0.1% respectively)

Mutation in the APC gene from codon 1310 to 2011 encompassed 41% of all desmoids cases, and in the reference population 40% of the cases were reported in females and their location was intra-abdominal in nearly half of the cases. The risk for desmoids seemed to be fairly equal in females and males. The most common mutation found in the APC gene from codon 1310 to 2011 was 2.7% and 0.1% respectively.

CONCLUSION: Desmoids associated with FAP can be found in any age group, including children. In this series they were slightly more common in females and their location was intra-abdominal in nearly half of the cases. The risk for desmoids seemed to be fairly equal throughout the gene after correcting for the prevalence of mutations in the reference population.

413 GASTROINTESTINAL MANIFESTATION OF ROHHADNET SYNDROME. Vibha Sood1, Prita Mohanty1, Marilyn Brown1, Yi-horang Lee2, 1Division of Pediatric Gastroenterology and Nutrition, Golisano Children's Hospital, Rochester, NY; 2Department of Pediatric Surgery, Golisano Children's Hospital, Rochester, NY

Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, autonomic dysregulation, and neural tumor (ROHHADNET) is a newly described syndrome;

A previously healthy 6 year old African American girl presented with history of cyclical fevers, vomiting, abdominal pain, constipation and rectal prolapse. Parents reported frequent outbursts of anger associated with behavioral changes and hyperphagia over previous few months. On admission her examination was remarkable for fever, tachycardia, hypertension and agitated behavior; her weight was 38 kg (greater than the 95th percentile) with BMI at 95th percentile. Examination of the anus showed a large patulous opening with grade III rectal prolapse. Flexible sigmoidoscopy revealed thickened and irritated rectum. During the course of hospitalization she developed recurrent events of desaturations with increasing oxygen requirement, and subsequently required ventilatory support. She continued having rectal prolapse along with persistent fever, vomiting and agitated behavior. Computed tomography of the abdomen revealed a small adrenal mass, which was resected and determined to be a ganglioneuroma. Rectopexy was performed at the same time to prevent...
continual prolapse. Her constellation of symptoms fit the diagnostic criteria of a rare condition, rapid-onset obesity with hypothalamic dysfunction, hypothalamic-pituitary-endocrine dysfunction (ROHHAD).

Postoperatively, she continued to have temperature instability, electrolyte imbalances with metabolic alkalosis and dehydration. Subsequent to this she developed abdominal distension. CT scan of abdomen and pelvis showed extensive pneumatosis intestinalis throughout the small bowel. Exploratory laparotomy revealed liquefactive necrosis of the small bowel with adhesions. She underwent serial abdominal washout, extensive lysis of adhesions, transverse colectomy with a Hartmann's pouch and G tube placement. She continued to be in critical condition in the pediatric intensive care unit. Over the course of time, her symptoms deteriorated with increased requirement for cardio respiratory support and family elected not to continue with any further resuscitation.

Discussion:
Diagnostic criteria for ROHHADNET syndrome includes onset of alveolar hypoventilation after 2 years of age with evidence of hypothalamic dysfunction. It can present as obesity during early childhood, the autonomic symptoms can be thermal dysregulation, chronic diarrhea or long standing constipation. This case illustrates the gastrointestinal manifestation of this rare condition, including rectal prolapse and necrotizing enterocolitis. Despite aggressive medical and surgical therapy, patient ultimately died of cardiopulmonary failure from autonomic dysfunction.

**414 EOSINOPHILIC GASTROINTESTINAL INFLAMMATION IS A COMMON ENDOSCOPIC FINDING IN PEDIATRIC INTESTINAL FAILURE PATIENTS.** Danielle Stamm1, Elizabeth J. Haif2, Paul Mitchell1, Christopher Duggan1,2, 1Center for Advanced Intestinal Rehabilitation, Boston Children's Hospital, Boston, MA; 2Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; 3Clinical Research Center, Boston Children's Hospital, Boston, MA

Objective: To describe the prevalence and clinical features of gastrointestinal eosinophilic inflammation among pediatric patients with intestinal failure (IF).

Background: Previous case series describe a non-infectious, eosinophilic colitis in infants with IF. We hypothesized that eosinophilic inflammation of the gastrointestinal mucosa is common in IF, and sought to determine its prevalence and associated characteristics in a large cohort of IF patients.

Methods: Following institutional review board approval, the medical records of all patients followed in the BCH Center for Advanced Intestinal Rehabilitation who underwent GI endoscopy between January 1997 and May 2012 were reviewed. Clinical, pathologic, nutrition and laboratory data were collected.

Results: A total of 103 patients (mean (SD) age 5.0 (6.0) years, 53% male sex) underwent 207 GI endoscopy procedures with biopsy. Underlying diagnoses were not mutually exclusive and included necrotizing enterocolitis (34%), gastrochisis (21%), volvulus (18%), intestinal atresia (16%), Hirschsprung's disease (9%), pseudo-obstruction (6%), microvillus inclusion disease (5%) and other/combined (25%). The most common indications for endoscopy were emesis (31%), diarrhea (18%) and hematochezia (17%).

The overall prevalence of eosinophilic inflammation was 38/103 (37%). Considered by tissue type, eosinophilic inflammation was found in the esophagus of 17 of 81 subjects (21%), in the stomach of 3/81 (4%), in the duodenum of 4/81 (5%), in the ileum of 9/59 (15%) and in the colon/rectosigmoid of 17/67 (25%). IF patients with eosinophilic colitis were more likely than those without colitis to have presented with hematochezia (61% vs 20%, P = 0.004). IF patients with eosinophilic inflammation had significantly higher peripheral absolute eosinophil counts (median (IQR) 0.69 (0.40 - 2.01) k cells/microl) than those without this finding (median (IQR) 0.26 (0.16 - 0.52) k cells/microl, p = 0.001). There was no significant difference between the two groups in the prevalence of atopic disease. Despite the use of amino acid-based formula as the sole source of enteral nutrition prior to endoscopy, 7/20 (35%) of patients had evidence of eosinophilic inflammation in the colon.

Conclusions: Eosinophilic inflammation is a common endoscopic finding in children as well as infant IF patients, and is significantly associated with clinical symptoms of GI blood loss and peripheral eosinophilia. The observation of eosinophilic GI inflammation in the setting of a strict elemental diet suggests that further research is required to adequately understand the natural history and response to therapy of this common condition.

**415 IMPROVED PEDIATRIC ENDOSCOPY SUITE TIMELINESS THROUGH QUALITY IMPROVEMENT INTERVENTIONS.** Gitti Tomor1, Steven Choi2, Andrea Montalvo1, Sheila Sutton1, John J. Thompson1, Yolanda Rivas1, 1Pediatric Gastroenterology and Nutrition, Children's Hospital at Montefiore, Bronx, NY; 2Pediatric Cardiology, Children's Hospital at Montefiore, Bronx, NY

BACKGROUND: Pediatric endoscopic procedures are essential in the evaluation and treatment of gastrointestinal diseases in children. One strategy to increase supply of endoscopy services is to improve the efficiency of pediatric endoscopy suites. Although pediatric endoscopists are greatly interested in increasing efficiency and through-put in pediatric endoscopy units, there is scarcely any literature on this critical process.

AIM: Improve timeliness of pediatric endoscopy procedures at the Children's Hospital at Montefiore (CHAM).

METHODS: In June 2010 the Division of Pediatric Gastroenterology at CHAM formed a pediatric endoscopy quality improvement (QI) initiative aimed at improving start times of scheduled pediatric endoscopy procedures. The baseline percentage of cases starting on time and the length of delay for cases were measured. We identified patient-, equipment-, and physician-related causes for case delays.

Primary process interventions included: sharing physician data, revising the procedure forms, providing procedure education materials to patients/families, and routinely calling patients 24-48 hours prior to their procedure. Pareto charts, cause and effect diagrams, process flow mapping, and statistical process control charts were utilized for the project.

RESULTS: From June 2010 to December 2012 we were able to significantly decrease the 1st case endoscopy delay from an average of 16.5 to 10.25 minutes (p=0.0001), 2nd case delay from 38.49 to 24.8 minutes (p=0.01), 3rd case delay from 61 to 45 minutes (p=0.046),
and 4rd case delay from 78.5 to 51 minutes (p=0.05). Total delay time for the day decreased from 194.5 to 129.85 minutes, resulting in a reduction of 64.65 minutes (p=0.017). From June 2010 to August 2011 (pre-intervention period), an average of 36% of first endoscopy case started within 5 minutes, 51% within 10 minutes and 61% within 15 minutes of the scheduled start time. From September 2011 to December 2012 (post-intervention period), the percentage of cases starting within 5 minutes, 10 minutes, and 15 minutes increased to 47% (P=0.07), 61% (p=0.04) and 79% (p=0.01), respectively. There was no statistical difference in delays between different days of the week or between cases scheduled as inpatients or outpatients.

CONCLUSIONS: Applying quality improvement methods and tools helped improve pediatric endoscopy efficiency and significantly decreased total delays.

416 TYPE 1 DIABETES AND CELIAC DISEASE: ASSOCIATED COMORBIDITIES AND COMPLICATIONS - IS THIS A DIFFERENT POPULATION? Alexandra Tsouka, Esther Assor, Farid H. Mahmud, Margaret Marcon, Division of Gastroenterology & Endocrinology, The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Objective: To evaluate the rates of complications screening in a population with type 1 Diabetes and Celiac disease (T1D/CD) and to compare it with a population with Celiac Disease (CD) only.

Methods: We retrospectively reviewed the health charts of 41 pts with T1D and biopsy proven CD to evaluate anthropomorphics before and after diagnosis of CD, frequency and results of complication screening within 2 yrs from CD diagnosis in addition to follow-up patterns within 3 yrs post diagnosis. This population was then compared to a population with symptomatic CD only, randomly selected and matched for age and sex at time of CD diagnosis.

Results: CD was observed in 5% of established pts with T1D. Mean age at the time of CD diagnosis was 8.83 ± 3.4 yrs (range 3-16 yr) with a male: female ratio of 0.64. In the T1D/CD group symptoms were present at 47.5% and good to excellent adherence to a gluten-free diet was observed in 69% of pts, using a standardized assessment (as part of a previous study). Compliance was difficult to assess in the CD group due to lack of information in the health records. In the T1D/CD group, no differences were observed in height, weight and BMI z scores assessed at diagnosis and 1 yr later. Complication screening for anemia and liver function was tested for 29/41 & 15/41 (T1D/CD), and 39/41 & 24/41 (CD) pts, respectively. Vitamin D status was available for 10/41 (T1D/CD) & 18/41 (CD) pts with approximately 50% of both groups having a level of <70 nmol/L (70-250 nmol). Bone mineral density was assessed by Dual-energy X-ray Absorptiometry (DEXA) in 4/41 (T1D/CD) & 7/41 (CD) pts, 2/41 CD with z-score<-.2. In comparison with the CD group, pts with the dual diagnosis presented with higher z-scores for height, weight and BMI at the time of diagnosis and for height and BMI 1 yr post diagnosis (P<0.05). Family history for CD was significantly more present in the CD group (P= 0.007). CD pts were significantly more likely to receive anemia and liver function testing, within the first 2 yrs post diagnosis (P<0.05). Anemia testing revealed more abnormalities in the CD group. Pts with T1D/CD received significantly higher rates of thyroid autoimmunity screening. Bone screening and abnormalities were not significantly different in the two groups. Follow-up was equally variable in both groups with a median of 3 (range 0-4) visits with a gastroenterologist the first 3 yrs. Serology testing was significantly more frequently obtained in the T1D/CD group with a median of 3 (range 1-6) vs 2 (1-4) in the CD group.

Conclusions: In patients with T1D/CD and only CD, complication assessment was variable and negative for the majority. Rates of bone health assessment were suboptimal. Anemia and liver function were more routinely assessed in the CD group, which also presented with higher rates of anemia, whereas T1D patients were more likely to receive autoimmunity screening. There was no on-going routine assessment of compliance using a standardized method in either groups. We suggest the development of guidelines to standardize screening at presentation and in follow up for children with CD, both with and without concomitant T1D.

417 INVESTIGATION OF ORIENTATION OF DUODENAL BIOPSIES OBTAINED TO DIAGNOSE CELIAC DISEASE OVER AN 11-YEAR PERIOD. Brintha Vasagar1,2, Elaine Leonard Pupp1, Debby Santora1, Alessio Fasano1, 1Family Medicine, Spartanburg Regional Hospital, Spartanburg, SC; 2Pediatrics, Massachusetts General Hospital, Charlestown, MA; 3Pediatrics, University of Maryland Medical Center, Baltimore, MD; 4Mucosal Biology Research Center and Center for Celiac Research, University of Maryland School of Medicine, Baltimore, MD

Background: The number of cases of celiac disease continues to increase in part due to improvements in serologic testing and improved awareness. Though biopsy remains the gold standard for diagnosing celiac disease, the potential role of improved awareness and skills of pathologists has not been systematically investigated. Correct orientation is essential to proper interpretation of histopathology and subsequent diagnosis of celiac disease. Improved orientation over time would indicate pathologists have better knowledge and skill in correctly cutting and positioning biopsies leading to improved diagnosis. If the specimens obtained are poorly oriented, the rate of diagnosis may also be artificially low. Methods: In this retrospective study, the orientation on pathology slides of 691 duodenal biopsies taken between 2000 and 2011 were reviewed for a second opinion by a celiac specialist at the Center for Celiac Research to determine if celiac disease could be diagnosed from these biopsies. Results: The percentage of biopsies adequately oriented varied from 46.8% in 2001 to 73.1% in 2004, with a downward trend in correct orientation from 73.1% in 2004 to 50.0% in 2011. Biopsies performed in the private practice setting were slightly more likely to have correct orientation (64.8%) in comparison to the hospital setting (58.6%), but this difference was not statistically significant (p=0.1). Conclusions: This study showed that correct orientation of biopsies to adequately diagnose celiac disease only transiently improved during the last decade. Since biopsy remains the gold standard for diagnosing celiac disease, emphasis on correct cutting and positioning of biopsies may aid in the accurate diagnosis of celiac disease.

418 INTESTINAL PARASITES IN CHILDREN DIAGNOSED WITH CANCER FOR THE FIRST TIME IN CALI, COLOMBIA. Claudia J. Ortiz, Carlos A. Velasco, Carlos A. Portilla, Consuelo Rojas, Pediatrics, University of Valle, Cali, Colombia

Introduction: Intestinal parasites (IP) in children with cancer can be present in 42%, with frequent T. trichiura, A. lumbricoides, G. duodenalis, B. hominis and C. parvum. Objective: To determine the prevalence of IP in children under 13 years diagnosed with cancer the first time from the Hospital Universitario del Valle “Evaristo García” of Cali, Colombia, and potential risk factors. Methodology:
Prevalence study in 52 children with cancer. Were considered sociodemographic (age, sex, origin); clinical (symptoms, weight, height, BMI, Height/age), paraclinical (anemia, eosinophilia), environmental (intradomicilares animals) and hygiene (drinking water, hand washing) variables. Statistical analysis included estimation of the proportion of children with IP and their corresponding confidence interval 95%, estimate percentages, percentiles, means, medians and other descriptive measures with their corresponding standard deviations and ranges; univariate analysis; possible occurrence of association between the variables (ORs with confidence intervals at 95%), Fisher's exact test with a P value <0.05, two-tailed, significant and multiple logistic regression analysis. Results: There was a prevalence of 38.5% for IP (19.2% E. nana, 7.7% E. histolytica and E. coli, respectively, 5.8% B. hominis, and 3.8% G. duodenalis and T. trichiura, respectively), with an age of 5.9 ± 4.0 years. There was a predominance of the female gender, precedence from Valle, Colombia, present malnutrition, solid tumor, anemia, symptoms and poor environmental conditions. There were > opportunity to present IP, be outside of Cali, present failure to thrive, anemia and eosinophilia, and poor environmental conditions, and < opportunity to present IP, be eutrophic, male gender, having solid tumor, being asymptomatic and with good hygiene. The factors associated with IP were age and origin. Conclusion: About ¼ of the children presented IP, and it is found associated with > age and come out of Cali, Colombia.

419* GASTROINTESTINAL ENDOSCOPY COMPETENCY ASSESSMENT TOOL FOR PEDIATRIC COLONOSCOPY: (GIECAT-KIDS): A MULTI-CENTER VALIDATION STUDY. Catharine M. Walsh1,2, Simon C. Ling2,3, Petar Mamula4, Jennifer R. Lightdale5, Jeffrey J. Yu1, Thomas D. Walters2,3, Heather Carnahan1,6, 1The Wilson Centre, University of Toronto, Toronto, ON, Canada; 2Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 3Department of Paediatrics, University of Toronto, Toronto, ON, Canada; 4Division of Gastroenterology, Hepatology and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA; 5Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; 6Centre for Ambulatory Care Education, Women's College Hospital, Toronto, ON, Canada

BACKGROUND: There is no objective measure of competence in performing colonoscopy that has been validated rigorously in pediatrics. Such a tool is required to support competency-based education and to demonstrate trainees are progressing towards proficiency by attaining milestones. This multicenter study aimed to assess the validity and reliability of the Gastrointestinal Endoscopy Competency Assessment Tool for pediatric colonoscopy (GIECAT-KIDS); an instrument developed by 41 North American experts using Delphi methodology.

METHODS: The GIECAT-KIDS consists of a 7-item global rating scale (GRS) and an 18-item checklist (CL). Data were collected on 85 colonoscopy procedures performed by 45 endoscopists at three North American tertiary care institutions: 22 novices (defined as having performed < 50 procedures), 17 intermediates (50-250 procedures), and 6 experts (> 500 procedures). Each endoscopist was evaluated in real time, by an attending physician, performing 2 colonoscopies. A second observer rated a subset of procedures (n = 12) for assessment of inter-rater reliability. Construct validity was examined by comparing level of experience with the mean GIECAT-KIDS GRS and CL scores assigned to the first procedure performed by each endoscopist. Concurrent validity was assessed by correlating the mean GIECAT-KIDS GRS and CL scores assigned to the first procedure performed by each endoscopist with (a) endoscopy experience (number of previous colonoscopies performed); (b) cecal intubation rate; (c) terminal ileal intubation rate; and (d) physician global assessment of skill. Inter-rater reliability (IRR) was determined using intra-class correlation coefficient (ICC). Test-retest reliability was assessed by comparing the correlation of GIECAT-KIDS GRS and CL scores given for an endoscopist's first and second procedure.

RESULTS: Mean GIECAT-KIDS GRS and CL scores differed significantly between endoscopists based on their level of experience (p < 0.001). There was a significant positive correlation between mean GIECAT-KIDS GRS and CL scores and (a) number of previous colonoscopies performed (GRS: r = 0.81, CL: r = 0.73, p < 0.001); (b) cecal intubation rate (GRS: r = 0.84, CL: r = 0.73, p < 0.001); (c) terminal ileal intubation rate (GRS: r = 0.85, CL: r = 0.76, p < 0.001), and (d) physician global assessment (GRS: r = 0.94, CL: r = 0.84, p < 0.001). The ICC between raters was 0.76 for the GRS and 0.71 for the CL; demonstrating good inter-rater reliability. There was a significant positive correlation between each participant's mean GIECAT-KIDS GRS and CL scores for the first and second colonoscopy performed (GRS: r = 0.94, p < 0.05, CL: r = 0.83, p < 0.001), demonstrating high test-retest reliability.

CONCLUSIONS: This study provides evidence of the feasibility, validity and reliability of the GIECAT-KIDS as a measure of competence of clinicians performing colonoscopy on pediatric patients, and supports its use in the training and evaluation of pediatric endoscopists. Studies are ongoing to determine the validity of blinded video-taped assessments and its generalizability to the simulated environment.

420* GD3 GANGLIOSIDE PROTECTS RATS FROM ILEAL DAMAGE BY AUGMENTING MUCOSAL FOXP3+ T REGULATORY CELL RESPONSES IN AN EXPERIMENTAL MODEL OF NECROTIZING ENTEROCOLITIS (NEC). Jiliu Xu1, Virginia Anderson2, Steven M. Schwarz1, 1Pediatric Gastroenterology, Children's Hospital at Downstate, SUNY Downstate Medical Center, Brooklyn, NY; 2Pathology, SUNY Downstate Medical Center, Brooklyn, NY

Background and Objectives: NEC arises from exaggerated inflammatory response to bacterial invasion of immature intestinal barrier due to immature immune regulation. Gangliosides, glycosphingolipids rich in colostrum and in membrane microdomains, promote enteroctye growth and differentiation, and modulate Th1/Th2 responses. In an in vitro intestinal culture model of NEC, gangliosides have been shown to ameliorate intestinal injury by suppression of vasoactive mediators and proinflammatory cytokines. However, possible immunomodulatory mechanisms associated with this observation, as well as potential in vivo protective effects of gangliosides remain unclear. The present study evaluates the effects of dietary GD3, the predominant ganglioside in neonatal rat intestine, both on the clinicopathologic expression of disease, and on ileal Foxp3+ T regulatory cell immune responses in an experimental NEC model.

Methods: Newborn rats were gavage-fed formula (NEC) or formula supplemented with 15 μg/ml GD3 (GD3-NEC). Dam-fed (DF) littermates served as controls. NEC was induced by asphyxia and cold stress. At 96 h, ileal gross changes were evaluated, and histological severity of NEC was analyzed by a standard scoring system; ileal cytokine profiles, Foxp3 expression and Foxp3+ cell number were determined by a rat cytokine array kit, immunoblot and immunofluorescence staining, respectively.

Results: GD3 decreased the incidence, gross and histopathologic severity of NEC. Ileal Foxp3 expression and Foxp3+ cell numbers were...
significantly up in the NEC group compared with DF. GD3 increased ileal Foxp3 expression and Foxp3+ cell numbers, in association with up-regulation of anti-inflammatory mediators, IL-10, tissue inhibitor of metalloproteinases 1 (TIMP-1), and IL-1 receptor antagonist (IL-1ra) and with suppressed pro-inflammatory mediators including TNF-α, IL-6 and RANTES.

Conclusion: These data suggest that dietary GD3 protects newborn rats from NEC, in part, by augmenting mucosal Foxp3+ T regulatory immune responses. GD3 ganglioside may represent a promising dietary agent for developing novel therapeutic strategies for preventing and/or ameliorating NEC.

**ENDOSCOPY FOLLOWING PEDIATRIC INTESTINAL TRANSPLANT: A 22 YEAR SINGLE CENTER EXPERIENCE.**

Joanna Yeh1, Khiet D. Ngo3, Laura J. Wozniak1, Jorge H. Vargas1, Elizabeth A. Marcus1, Sue V. McDiarmid2, Douglas G. Farmer2, Robert S. Venick1, 1Department of Pediatric Gastroenterology, Hepatology, and Nutrition, UCLA, Los Angeles, CA; 2Department of Surgery, Liver and Intestinal Transplantation, UCLA, Los Angeles, CA; 3Department of Pediatric Gastroenterology, Hepatology, and Nutrition, Loma Linda, Loma Linda, CA

Background: Biopsies remain the gold standard in the diagnosis of intestinal transplant (ITx) rejection, and timely endoscopy with biopsy plays a pivotal role in patient management. There are few reports on endoscopic findings and outcomes in ITx. Herein, we describe a single center 22-year experience with pediatric gastrointestinal endoscopy in ITx recipients.

Methods: A retrospective review of a prospective database was performed that included all ITx recipients <18 yo transplanted between 1991 and 2012. All endoscopy and pathology reports were recorded. Standard statistical analysis was undertaken. IRB approval was obtained. 71 patients receiving 87 ITx were included in analysis. 54% were male and 46% were female. Median age at transplant was 2.8 years, and mean age at transplant was 4.7 years (+/- 4.3 years). Median follow up time was 42 months, and mean follow up time was 51 months (+/- 46 months). The 1 year graft survival was 79% and 5 year graft survival was 76%.

Results: The demographics and endoscopic complications are shown in Table-1. A total of 1539 endoscopic procedures within 868 sessions were performed. Combination EGD and ileoscopy was the most common procedure (35%) and increased stool output the most common indication (37%). Surveillance endoscopy was the 2nd most common indication (31%).

Conclusions: Endoscopy with biopsy is a major part of the care of ITx recipients. Multiple repeat procedures are required for diagnosis, treatment, and follow-up of therapy. The gross endoscopic appearance does not correlate well with histology. Complication rates are higher than in non-transplant cases but remain acceptable for this complex patient population. The existence of a noninvasive biomarker to reliably and efficiently detect rejection in ITx would decrease the need for frequent endoscopies.

Table 1. Clinical, Endoscopic, and Histologic Results

<table>
<thead>
<tr>
<th>Gender (M:F)</th>
<th>38:33 54% male 48% female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td>African American n=4 Asian American n=3 Caucasian n=32 Latino n=41 Other n=1</td>
</tr>
<tr>
<td>Median age at transplant</td>
<td>2.8 years</td>
</tr>
<tr>
<td>Mean age at transplant</td>
<td>4.7 years</td>
</tr>
</tbody>
</table>

| Total number of endoscopy procedures performed | 1539 |
| Total number of endoscopy sessions | 868 |
| Endoscopy types (n=868) | Ileoscopy=201 EGD=82 EGD+Ileo=300 Colonoscopy=49 EGD+Ileo+Colon=85 EGD+Colon=130 Ileo+Colon=21 |
| Indications (n=868) | Increased outputs=318 Surveillance=265 GI bleed=86 F/u rejection=83 Procedure=18 Obstructive symptoms=13 Other=85 |
| Sedation Types (n=868) | GETA=569 Conscious or deep sedation=299 |
| Complications (n=36) | GI bleeding=11 GI perforation=9 GI hematoma=6 Respiratory event=8 Gastric mucosa avulsion=1 Distension from retained air=1 |

Acronyms: EGD=esophagogastroduodenoscopy Ileo=ileo Colon=colonoscopy GETA=general endotracheal anesthesia

Motility/Functional Gastrointestinal Disorders

**URINARY TRACT INFECTION IN INFANCY IS A RISK FACTOR FOR CHRONIC ABDOMINAL PAIN IN CHILDHOOD.**

John Rosen, Alyssa Kriegermeier, Papa N. Adams, Miguel Saps, Pediatric Gastroenterology, Hepatology, and Nutrition, Ann & Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University, Chicago, IL

Chronic abdominal pain (CAP) and urinary tract infections (UTI) are common in children. Gastrointestinal infection often leads to CAP and functional gastrointestinal disorders (FGIDs) after infection resolves. UTI causes chronic pelvic and abdominal pain in murine models. Acute cystitis in neonatal rats leads to colonic hypersensitivity in adulthood. Pathogenesis of FGIDs is incompletely understood but adverse early life events seem to be key factors for their development. We hypothesized that UTI in infancy increases the risk of FGIDs in childhood.

Methods: Children 4-18 years with history of a single UTI in the first year of life were contacted at least 3 years after infection. Medical records of all subjects were reviewed for general demographic information, to confirm positive urine culture by transurethral
catheterization, and to identify infecting bacterial species and treatment regimen. Exclusion criteria included abnormal vesicoureterogram or renal ultrasound. Siblings of cases without a history of UTI served as controls due to similar genetic and socioeconomic background. Parents completed a validated survey (Questionnaire on Pediatric Gastrointestinal Symptoms - Rome III) by telephone for subjects and controls. Children meeting QPGS criteria were considered as FGID. Children meeting QPGS criteria but with pain less than once weekly were considered as CAP.

Results: 61 UTI cases and 58 sibling controls were identified. Age at UTI was mean 4.8 +/- 3.1 months and mean time since UTI was 9.2 +/- 3.0 years. At the time of survey, mean age of UTI cases was 8.9 years (5-16 yr, 38% male) and mean age of controls was 9.6 years (range 4-17 yr, 57% male). FGIDs were diagnosed in 6/64 (9%) cases, and 1/58 (2%) controls (P=0.11, Fisher 2-tailed test). CAP was identified in 10/61 (16%) cases and 2/58 (3%) controls (P=0.03, Fisher 2-tailed test). Gender predominance (female), infecting organism (E. coli), and treatment (3rd-generation cephalosporin) were similar in UTI cases with and without CAP.

Conclusion: We show for the first time that UTI is associated with chronic abdominal pain in childhood. We speculate that pelvic organ crosstalk explains our findings. Prospective and translational studies are needed to confirm our findings and investigate the mechanisms involved.

433  LONG-TERM EFFECT OF SURGERY ON THE RISK OF CHILDHOOD FUNCTIONAL GASTROINTESTINAL DISORDERS. John Roson, Meghan Barrett, Papa N. Adams, Miguel Saps, Pediatric Gastroenterology, Hepatology, and Nutrition, Ann & Robert H. Lurie Children's Hospital of Chicago, Feinberg School of Medicine, Northwestern University, Chicago, IL

The biopsychosocial model proposes that adverse early life events predispose children to functional gastrointestinal disorders (FGIDs). This is the last in our series of investigations on the role of surgical early life events (Sx) in the development of FGIDs. Our initial study showed higher FGID rates years after pyloromyotomy (PM). The design did not allow the identification of factors explaining this risk. Multiple PM factors may contribute (i.e. abdominal wall and/or gastric incision, nasogastric tube placement, anesthesia, antibiotics, parental hypervigilance or others). This study assesses the role of these factors in the risk of developing FGIDs.

Methods: Cases included children 4-18 years who underwent one of two minor Sx > 4 years prior: 1. abdominal wall Sx without gastrointestinal incision (umbilical hernia repair) or 2. non-abdominal Sx of similar complexity (myringotomy). Exclusion criteria: chronic systemic disease or other abdominal Sx. Siblings of cases without history of Sx served as controls due to their similar genetic and socioeconomic background. Parents completed the validated Questionnaire on Pediatric Gastrointestinal Symptoms - Rome III (QPGS-III) by telephone for cases and controls. Children meeting QPGS criteria were considered as FGID. Children meeting all QPGS criteria with exception of pain frequency (<1 week) were considered chronic abdominal pain (CAP).

Results: 220 children were recruited into the study. Umbilical hernia: 50 cases and 43 sibling controls. Age at survey: cases (12.9, range 5-18) and controls (11.7, range 4-18). FGIDs were diagnosed in 10/50 (20%) hernia cases and 2/43 (5%) controls (P=0.033). CAP was identified in 15/50 (31%) cases and 6/43 (14%) controls (P=0.083). Gender and time since Sx were similar in cases with CAP (60% female, mean 7.6 +/- 1.9 y, range 4.8-11) and without CAP (31% female, mean 7.9 +/- 2.6 y, range 4.9-13.7). Myringotomy: 75 cases and 52 sibling controls. Age at survey: cases (11.5 years, range 6-18) and controls (10.4 years, range 4-17). FGIDs were diagnosed in 7/75 (9%) cases and 1/52 (2%) controls (P=0.14). CAP was identified in 12/75 (16%) cases and 5/52 (10%) controls (P=0.43). Gender and time since Sx were similar in cases with CAP (42% female, mean 10.6 y, range 5.9-16) and without CAP (49% female, mean 10.7 y, range 6-18.1). To account for possible effect of surgical complexity or frequency, myringotomy cases were subdivided into single Sx, multiple Sx: tonsillectomy and/or adenoidectomy (33%), and complex Sx: cleft lip/palate repair (28%). Rate of FGID (P=1.0) and CAP (P=0.54) was similar among all myringotomy subgroups.

Conclusions: FGID rates were higher in children after hernia repair, but not after myringotomy. This suggests that anatomic location, but not complexity of surgery, may determine risk of FGIDs. Gastrointestinal incision is not required to increase the risk of FGIDs suggesting the possible role of visceral-somatic convergence in pathogenesis of childhood FGIDs after surgery. Animal and translational studies should confirm and determine the mechanisms explaining our findings.

434  FUNCTIONAL GASTROINTESTINAL DISORDERS DOMINATE PEDIATRIC GASTROENTEROLOGY OUTPATIENT PRACTICE. Audra Rouster1,2, David Silver2, John Gao2, Harris Rosenblum2, Landon Tomb2, Paul Hyman1,2, 1LSU, New Orleans, LA; 2Children's hospital of New Orleans, New Orleans, LA

Purpose of Study: Symptom-based diagnostic criteria have improved recognition and standardization of pediatric functional gastrointestinal disorders (FGIDs). We used Rome diagnostic criteria to determine the ratio of FGIDs to organic disease in outpatients.

Methods Used: We enrolled all new patients ≤18y referred to pediatric GI clinic over 11 mo. Subjects or parents completed a demographic survey and a validated Rome Diagnostic Questionnaire (QPGS-RIII for children ≥4 years or a new infant-toddler questionnaire) before visiting with a clinician. We recorded the chief complaint and clinician's diagnosis following the visit.

Summary of Results: We acquired data from 612 subjects (304 male), 368 subjects ≥4y, 244 subjects <4y, 364 white, 184 African American and 64 Other. There was no significant difference in frequency of FGIDs among racial groups or gender. Of those ≥4 years old, 273 (74%) met criteria for a FGID on the questionnaire. Of those <4 y, 147 (60%) met criteria for a FGID. One hundred and twenty six (20%) met criteria for 2 or more FGIDs. Common FGIDs included: IBS (25%), functional constipation (22%), abdominal migraine (10%), cyclic vomiting syndrome (8%), aerophagia (6%), functional dyspepsia (5%), infant regurgitation (5%), functional abdominal pain syndrome (5%). Of those who reported missing >15 school days/year, 58 of 64 met criteria for a FGID. Thirty six of 42 patients reporting a stress level of high met criteria for a FGID. IBS was evenly distributed between age groups (49 ages 4-8, 59 ages 9-13, and 49 ages 14-18), gender (73 males and 84 females), and race (28% of whites, 22% African American, 20% other). In 172 of 420 children meeting symptom-based criteria there was concordance between clinician and questionnaire diagnosis.

Conclusions: Over half of the new patients in pediatric GI clinic met symptom-based diagnostic criteria for one or more FGIDs. Satisfying symptom-based diagnostic criteria may facilitate diagnosis on the first visit saving the patient and the system from unnecessary tests and cost. Curriculum hours devoted to functional disorders should reflect their importance.
Physicians rely on patient reported outcomes (PROs) to diagnose and monitor progress of FAP. Validity of pediatric PROs in FAP has not been assessed. Persistence of abdominal pain (AP) despite medical treatment is common. Children who fail initial drug treatment are often recommended second drug or psychological therapy. Optimal time of treatment success/failure assessment is not defined. Establishing validity of patient AP reports and identifying predictors for early success/failure of treatment may allow improve care. Early gains (EG) based on measuring clinically significant change (CSC) scores, defined as changes on severity from baseline to end of first week of treatment predict response to psychotherapy in children. We examined the role of EG in AP intensity in assessing treatment response in FAP children. Method: 74 FAP children (8-17 y), who participated in a randomized clinical trial on efficacy of amitriptyline (AM) in FAP (negative study) completed daily AP reports (100 mm visual analog scale (VAS)) during run-in period and 4 weeks of treatment. In this study, we analyzed daily AP reports at baseline and after weeks 1-4 of trial. For each child, a "reliable change index" (RCI) for the VAS that accounts for test-retest reliability of AP reports was calculated. Patients with significant RCIs have < 5% chance that rate improvement is due to imperfect reliability of the AP measure. Results: Mean one-week test-retest reliability (mean r = .77) of VAS for the placebo group was used to determine CSC values and child RCIs. CSC for 100 mm VAS was 18.66 points. Two RCI values were calculated per child: EG from baseline to week 1 and improvement from baseline to week 4 (end of trial). Children achieving CSC for the whole trial: 16/37 AM group vs. 9/37 placebo group (p=.085). EG assessment: 19/74 children achieved EG and 55/74 did not. 19/19 (100%) children who achieved clinically significant EG, showed a clinically significant gain from baseline to week 4 (OR 9.0, 95%CI 3.1-25.9, p<.001). Only 6/55 (10.9%) children without clinically significant EG, showed gain at week 4. A clinically significant EG significantly predicted clinically significant gains in the whole trial (Chi-sq 33.5, p<.001). Children achieving EG were 4.2 times more likely to achieve CSC at end of trial. Children in AM group (35.1%) were more likely to achieve EG than placebo group (16.2%) (t = 3.47, p = .06). EG were associated with lower anxiety level at baseline (t = 2.74, p = .007), but not with initial pain level, somatization tendencies, depression, gender, or functional impairment. Conclusion: The use of CSC scores to calculate EG at the end of the first treatment week significantly predicts response to treatment in children with FAP. EG assessment use has the potential to provide an evidence based tool for treatment planning. EG use could be helpful in establishing time to follow up, optimize care and decrease suffering by helping in the decision to review treatment strategies in children failing treatment. The fact that children in AM group were more likely to achieve EG questions whether higher AM doses may show efficacy in treating FAP.

**Using ecological momentary assessment to identify potential pediatric chronic abdominal pain triggers**

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Objectives: Empirical data are limited regarding triggers of children's chronic abdominal pain. Furthermore, much of the relevant literature on pediatric pain more broadly is limited in its clinical utility by retrospective assessments and group-based approaches to data analysis. The present study aims to evaluate the potential of intraindividual variation for modeling, prospectively, associations between chronic abdominal pain (CAP) and potential triggers. Methods: Data regarding participants' abdominal pain and related symptoms, as well as the occurrence of potential psychosocial and health behavior triggers, were collected via electronic diary from 10 children aged 8-13 three times per day for two weeks. Hierarchical linear regression (HLM) techniques were applied initially to investigate commonalities among participants regarding relationships between an array of possible biological, psychological, and social triggers and the occurrence of abdominal pain in real-time. Within-person time series models were then used to estimate lead-lag relationships within and between potential triggers and abdominal pain symptoms for each child. Preliminary Results: Acute illness, fewer hours of sleep, negative affect, drinking soda, and eating spicy food were particularly strong predictors of pain occurrence across participants. However, time series analyses suggest that triggers may be idiographic even for these more "common" triggers, so global recommendations based on group-based analyses must be drawn with caution. More data are needed to explore the relationships between these perceived triggers and actual pain episodes for each child. Conclusions: Initial results suggest that children may experience some common pain triggers, while other triggers may be more idiographic, affecting only a few children. Furthermore, data have implications for improving the feasibility of ecological momentary assessment and the capacity of intensive time-series and intraindividual analytic methods to provide information relevant to improving patient care through targeted intervention.

**Use of hydroxyzine in treatment of episodic dyspepsia suggestive of atypical abdominal migraine or cyclic vomiting syndrome**

Carole Rudman, Mark J. Integlia, Harohalli Shashidhar, New Hampshire Hospital for Children, Elliot Hospital, Manchester, NH

Objective: Retrospective review of children who received hydroxyzine for gastrointestinal symptoms that suggest but do not meet criteria for cyclic vomiting syndrome (CVS) or abdominal migraine (AM).

Background: Established treatment guidelines exist for pediatric patients with AM or CVS, including use of cyproheptadine and amitriptyline. In practice, it is not uncommon to see children with episodic nausea and/or vomiting, upper abdominal pain/distress that do not meet criteria for either CVS or AM for severity and frequency of episodes. No recommended therapeutic approach exists for this subset of children, with often debilitating symptoms.

Patients and methods: 12 mos retrospective chart review of children prescribed hydroxyzine for episodic gastrointestinal symptoms with interval resolution and at least one follow up visit after initiation of therapy. Review included presenting symptoms, investigations, dose, adverse events and discontinuation of hydroxyzine, and concomitant medications at the time of initiating therapy.
Results: 21 children from 5-18 yrs, 17 females and 4 males. Table 1 summarizes the clinical features. Investigations included head MRI (3), UGI barium (4) RUQ ultrasound (7), upper endoscopy (8), celiac screening (14) and Lactose breath hydrogen test (1). Testing was unremarkable in all patients. Dose range of hydroxyzine was 10-25mg (0.5-2 mg/kg/d) as a single dose at night. One patient who was also on amitryptiline, discontinued hydroxyzine for hallucinations. Follow up ranged from 6 weeks to 12 mos. Other medications at the initiation of therapy: proton pump inhibitors or H2 receptor antagonists (10), amitryptiline, cyproheptadine, clonidine and sertraline (1 each). In one patient with overlapping features of GERD and episodic GI symptoms, PPI started concomitantly was discontinued within 6 weeks. All but one patient reported significant reduction in frequency and severity of nausea episodes with particular improvement in episodic vomiting. One patient who discontinued hydroxyzine while receiving oral corticosteroids experienced recurrent symptoms that resolved on restarting hydroxyzine. Hydroxyzine had no effect on concomitant headache frequency or severity.

Conclusion: Hydroxyzine appears to be an effective and well tolerated therapy when dyspepsia is present in association with features suggestive of AM/CVS spectrum (episodic pattern, nocturnal symptoms, associated headache, autonomic features and family history of migraine). Testing is unyielding and empiric acid suppressive therapy is not effective in this subset of children.

### Presenting symptoms and associated features

<table>
<thead>
<tr>
<th>Symptom</th>
<th>%age (N=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>85</td>
</tr>
<tr>
<td>Vomiting</td>
<td>47</td>
</tr>
<tr>
<td>Epigastric/mid abdominal pain</td>
<td>100</td>
</tr>
<tr>
<td>Nocturnal symptoms</td>
<td>62</td>
</tr>
<tr>
<td>Associated headache/migraine</td>
<td>57</td>
</tr>
<tr>
<td>Associated pallor during episodes*</td>
<td>23</td>
</tr>
<tr>
<td>History of motion sickness*</td>
<td>23</td>
</tr>
<tr>
<td>Family history of migraine</td>
<td>62</td>
</tr>
</tbody>
</table>

* Only those with specific mention in the chart

**438 BIOFEEDBACK IS AN EFFECTIVE TREATMENT FOR CHILDREN WITH DYSSYNERGIC DEFECTION.** Yamen Smadi¹, Shaista Safder¹, Ellen Tindal¹, Vaishali D. Mehta², Jeffrey A. Bornstein¹, Devendra Mehta¹, ¹Center For Pediatric Digestive Health and Nutrition, Orlando Health, Orlando, FL; ²Northwestern University, Evanston, IL

Introduction: Dyssynergic defecation (DD) is defined as paradoxical contraction or failure to relax the anal muscles during defecation and accounts for a large portion of functional constipation in children. Aim: To study the efficacy of biofeedback (BF) on the clinical outcome and the manometry dynamics of patients with DD who failed aggressive medical treatment for constipation. Methods: We retrospectively reviewed all patients who had DD and underwent at least three sessions of BF. All patients failed aggressive traditional management for constipation (dietary advice, scheduled toilet training, stool softeners and laxatives) for at least 3 months before they were referred for BF. Our standard anorectal manometry (ARM) protocol includes measuring RAIR, resting pressure, sensation threshold, urge threshold, push, squeeze and expulsion tests. Patients who failed Balloon expulsion test of 30-ml water-filled rectal balloon and had a paradoxical squeeze with push were diagnosed with DD. Patients were trained on effectively using abdomen and pelvic muscles to improve relaxation and pushing effort with the help of visual feedback accompanied by continuous encouragement from the therapist. Clinical outcome was obtained by reviewing the medical records and contacting the families by phone for long term follow up. Clinical outcome after at least three months from the last BF session was defined as 'resolution' if the patient experiences no soiling, 'improvement' if the soiling frequency is reported as less than once a week, and 'failure' if the soiling is reported as once a week or more . We compared manometry dynamics before and after the biofeedback by using T-test. Patients with anatomical abnormalities were excluded. Results: 62 patients, 42 males and 21 females (Age 5-16 years, mean 9.5) met inclusion criteria. Average number of sessions was 5 (3-11). 25 patients (40.3%) reported complete resolution of symptoms. 14 patients (22.5%) reported improvement (average soiling frequency: once every 17days, range: 8-60 days). 15 patients (24.15%) reported failure and 8 patients (12.9%) reported initial improvement then relapsed symptoms. Behavioral disorders were more common in the failure and relapse group compared to the resolution and improvement group (21% vs. 7.5% respectively; p 0.06). First sensation threshold, urge threshold, squeezes and push pressures significantly improved after biofeedback (P < 0.001) [see table]. Expulsion threshold was positive in 6% before BF compared to 36.5% after BF (p < 0.01). Conclusion: Biofeedback results in resolution and significant improvement of soiling episodes in majority of patients with DD who failed traditional management of constipation. BF improves the dynamics of ARM in children with DD regardless their clinical outcome. Long term follow up is warranted to monitor persistency of improvement.
**ALTERED BRAIN SENSORY MODULATION IN CHILDREN WITH IRRRITABLE BOWEL SYNDROME - A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY.**

**Manu R. Sood**, Xiaoyu Xu, Mark Kern, Alan Silverman, Reza Shaker, Gisela Chehinsky, Shi-Jiang Li, Division of Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI; Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI; Division of Gastroenterology, Medical College of Wisconsin, Milwaukee, WI

**Introduction:** Altered brain sensory processing is one of the mechanisms for hypersensitivity in adults with irritable bowel syndrome (IBS). Rectal barostat studies in children with IBS have reported pain at a lower rectal distention pressure (RDP) but brain processing of RDP afferent signal has not been studied in children with IBS. Functional magnetic resonance imaging (fMRI) has been used in adults to evaluate brain cortical activity during visceral stimulation such as RDP.

**Aim:** To evaluate brain activity during incremental RDP stimuli in healthy controls & IBS subjects using fMRI.

**Methods:** We studied 8 healthy controls & 7 IBS subjects. Prior to fMRI scans, the RDP perception threshold (liminal distension) was measured by computerized barostat delivered incremental RDP. fMRI scans were performed at liminal RDP and sub-liminal RDP (5-10 mmHg below liminal pressure). Subjects could not perceive rectal distention at sub-liminal RDP and this would eliminate brain cognitive and emotional processes involved with RDP afferent signal. The fMRI settings for signal acquisition & analysis were based on previous publications. We used ANOVA to measure differences in brain activation between controls and IBS subjects and p<0.05 was considered a significant difference and only significant results are reported in the abstract.

**Results:** Control vs. IBS subject mean (SD) age in years was 14.6 (1.6) yrs. vs. 15.3 (2) yrs. respectively. Control vs. IBS subject mean (SD) dual and subluminal RDP were 26 (5) vs. 22 (3) mmHg (p=n.s.) & 19 (5) vs.13 (5) mmHg (p=n.s.) respectively. fMRI data showed significantly greater activation in precuneus region in control subjects during subluminal stimulus. At liminal RDP stimulation right insula and right superior temporal gyrus and left cingulate cortex had less activity in IBS patients while right anterior cingulate had more activity. We have identified the cortical network associated with rectal distention (data not shown).

**Discussion:** The regions of cortical activation in our cohort are similar to previous reports in adults including reduction in regional activation in IBS. Attention to afferent stimulus has been reported as a very important factor in modifying sensor (pain) perception & hyper-vigilance can amplify pain perception. Our study design enabled us to specifically evaluate the difference in brain activation during sub-liminal RDP stimulus (subject did not perceive rectal distention & thus could not attend to it) and liminal RDP stimulus (distention the subject feels and therefore attends to). Precuneus & posterior cingulate regions have a pivotal role in conscious information processing, & greater activation of the precuneus region in controls vs. IBS subjects suggests that it might be involved in suppressing RDP stimulus from reaching awareness. The anterior cingulate cortex is involved in attention, motivation & modulation of emotional response to a sensory stimulus & greater activation in IBS subjects would suggest that IBS subjects might be hyper-vigilant & have different emotional response to rectal distension stimulus compared to controls.

**ALTERED BRAIN SENSORY MODULATION IN CHILDREN WITH IRRRITABLE BOWEL SYNDROME - A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY.**

**Manu R. Sood**, Xiaoyu Xu, Mark Kern, Alan Silverman, Reza Shaker, Gisela Chehinsky, Shi-Jiang Li, Division of Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI; Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI; Division of Gastroenterology, Medical College of Wisconsin, Milwaukee, WI

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rates. The regional variability and apparent importance of insurance coverage indicate that socioeconomic factors influence the diagnosis and treatment of this disorder.

Comparison of patient characteristics admitted in 2009 for biliary dyskinesia, cholelithiasis or appendicitis (KID Database from HCUP)

<table>
<thead>
<tr>
<th>Age Cohort</th>
<th>Biliary Dyskinesia (%)</th>
<th>Cholelithiasis (%)</th>
<th>Appendicitis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 years</td>
<td>4.1</td>
<td>2.0</td>
<td>0.1</td>
</tr>
<tr>
<td>1-4 years</td>
<td>3.8</td>
<td>3.1</td>
<td>5.6</td>
</tr>
<tr>
<td>5-9 years</td>
<td>6.9</td>
<td>7.0</td>
<td>27.7</td>
</tr>
<tr>
<td>10-14 years</td>
<td>36.2</td>
<td>25.9</td>
<td>40.0</td>
</tr>
<tr>
<td>15-17 years</td>
<td>49.0</td>
<td>61.9</td>
<td>26.5</td>
</tr>
<tr>
<td>Female</td>
<td>70.7</td>
<td>74.6</td>
<td>38.4</td>
</tr>
<tr>
<td>Payer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>34.8</td>
<td>52.7</td>
<td>36.6</td>
</tr>
<tr>
<td>Private insurance</td>
<td>58.9</td>
<td>37.0</td>
<td>54.4</td>
</tr>
<tr>
<td>Uninsured</td>
<td>2.1</td>
<td>5.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Other</td>
<td>4.2</td>
<td>4.7</td>
<td>3.4</td>
</tr>
<tr>
<td>Children's Hospital</td>
<td>40.6</td>
<td>38.1</td>
<td>30.3</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>12.6</td>
<td>16.3</td>
<td>18.1</td>
</tr>
<tr>
<td>Midwest</td>
<td>22.0</td>
<td>15.6</td>
<td>17.8</td>
</tr>
<tr>
<td>South</td>
<td>45.9</td>
<td>37.6</td>
<td>32.8</td>
</tr>
<tr>
<td>West</td>
<td>19.6</td>
<td>30.5</td>
<td>31.3</td>
</tr>
</tbody>
</table>

441 FUNCTIONAL GASTROINTESTINAL DISORDERS IN A PRIMARY CARE PEDIATRICS CLINIC: PREVALENCE AND COMORBIDITIES. Ronen E. Stein¹², Thomas Chelimsky², Hong Li¹, Carol Rosen¹, Gisela Chelimsky², ¹Rainbow Babies and Children's Hospital, Cleveland, OH; ²Medical College of Wisconsin, Milwaukee, WI; ³Case Western Reserve University, Cleveland, OH; ⁴The Children's Hospital of Philadelphia, Philadelphia, PA

Background and Objectives: There has been little research conducted to determine the interrelationship between functional gastrointestinal disorders (FGIDs) and other non-psychiatric comorbidities in the general pediatrics population. The aims of this study were to investigate the prevalence of FGIDs in the general pediatrics population and to identify the comorbid non-psychiatric symptoms in children meeting criteria for FGIDs.

Study Design: Patients between the ages of 9 and 17 were recruited from a large urban primary care practice and administered a questionnaire inquiring about FGIDs, Raynaud-like symptoms, urinary frequency, migraines, sleep disturbances, chronic body pain, chronic fatigue, syncope, and orthostatic symptoms. The questions about FGIDs were based on Rome III criteria.

Results: A total of 145 patients completed the questionnaire. Eleven participants (7.5%) fulfilled the criteria for an FGID. Raynaud-like symptoms (defined as fingers or toes turning white, red, or blue on cold exposure) and urinary frequency tended to occur more often in patients meeting criteria for FGIDs, although this association was not statistically significant (p = 0.07 and p = 0.11, respectively). Migraines were found in only one participant with an FGID (9%) and in 4.5% of participants without FGIDs (p = 0.43). No association was found between FGIDs and other symptoms like sleep disturbances, chronic body pain, chronic fatigue, syncope, or orthostatic symptoms.

Conclusion: There seems to be an association between FGIDs in the general pediatric population and other comorbidities such as Raynaud-like symptoms and urinary frequency. A study with a larger sample size will be needed to confirm the association.

442 ANXIETY SYMPTOMS, NOT DISEASE CHARACTERISTICS PREDICT QUALITY OF LIFE IN PEDIATRIC CYCLIC VOMITING SYNDROME. Sally Tarbell¹, B. U. Li², ¹Child Psychiatry, University of Colorado Anschutz Medical Campus, Aurora, CO; ²Division of Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI

Objective: To evaluate the relationship of anxiety to health related quality of life (HRQOL) in children and adolescents with cyclic vomiting syndrome (CVS).

Methods. Forty-two children aged 8-18 years diagnosed with CVS, and 47 parents completed Screen for Childhood Anxiety and Related Emotional Disorders (SCARED) and the child and parent proxy form of the PedsQL, a measure of health related quality of life.

Results. Twenty-nine percent of children (12/42) by self-report and 17% (8/47) by parent report met clinical cut-off for an anxiety disorder on the SCARED. Parent and child SCARED ratings were moderately correlated (ICC = .45, p = .001). Child rated HRQOL
Background: Congenital Sucrase Isomaltase Deficiency (CSID) is a disorder preventing sucrose digestion. Those affected have lifelong symptoms including chronic diarrhea, vomiting, flatulence, and abdominal pain. Known single nucleotide polymorphisms (SNPs) in the sucrase-isomaltase (SI) gene lead to a reduced or inactive protein and presence or absence of these SNPs can be easily determined using a high throughput genetic platform. Clinicians have difficulty distinguishing and diagnosing CSID from other gastrointestinal (GI) diseases with similar symptoms, and thus, a genetic test would reduce time to a CSID diagnosis and also confirm etiology.

Methods: Nineteen subjects were consented (11 cases and 8 controls) that included three pediatric cases (1 biopsy-confirmed CSID and 2 CSID siblings) and three pediatric controls. The genotyping by sequencing assay consisted of a panel of 66 oligonucleotide probes targeting the exons of the SI gene which contain 37 previously identified SNPs causal for CSID. DNA sequencing was done with the Illumina MiSeq sequencer.

Results: Forty-four variants were detected including 33 SNPs, 6 insertions, and 5 deletions. Overall, 75% of cases contained variants known to be causal for CSID except for three adult cases. In the pediatric subjects, the affected cases had heterozygous variants causal for CSID (Table 1) with varying degrees of GI symptoms and no causal variants in the control subjects (no false positives).

Conclusion: Rapid DNA sequencing is ushering a new era of genetic based diagnostics which can inform treatments for genetic based diseases such as CSID. The genotyping by sequencing approach is especially valuable in pediatric patients as it provides the ability to link non-specific GI symptoms to causal DNA variants which in turn identifies therapeutic options that can resolve symptoms and allow individuals to lead a normal life. We anticipate that variants detected here are responsible for most CSID cases; however the CSID GPS study is ongoing to replicate these results and potentially discover other causal variants.

Table 1: SI Variant Results for Pediatric Subjects

<table>
<thead>
<tr>
<th>Sample Number</th>
<th>Sample Type</th>
<th>GI Symptoms</th>
<th>AA Positions</th>
<th>AA Change 1</th>
<th>AA Change 2</th>
<th>Type</th>
<th>SNP Accession</th>
<th>Coordinate</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>Control</td>
<td>None Reported</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>14</td>
<td>Control</td>
<td>None Reported</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>15</td>
<td>Control</td>
<td>None Reported</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>16</td>
<td>Case</td>
<td>CSID diagnoses (diarrhea and bloating)</td>
<td>1073 1124</td>
<td>ASP, GLY</td>
<td>STOP, ARG</td>
<td>Het SNP</td>
<td>rs200451408</td>
<td>164737443</td>
</tr>
<tr>
<td>17</td>
<td>Case</td>
<td>None but avoids sweets</td>
<td>577 1073</td>
<td>GLY, VAL</td>
<td>ASP, GLY</td>
<td>Het SNP</td>
<td>rs121912615</td>
<td>164764786</td>
</tr>
<tr>
<td>18</td>
<td>Case</td>
<td>None Reported</td>
<td>1124</td>
<td>STOP, ARG</td>
<td>NA</td>
<td>Het SNP</td>
<td>rs121912616</td>
<td>164739053</td>
</tr>
</tbody>
</table>

(Het = heterozygous, SNP= single nucleotide polymorphism)
The rate of complete examination varied from 85% to 95% depending on procedure indication. Colonoscopy time was documented in 69.2% of cases.

Conclusions: Significant variations in the practice of pediatric endoscopy are apparent, despite the use of a computerized report generator. Measurement of quality indicators in clinical practice can identify areas for quality improvement.

445 CHARACTERIZATION OF THE DUODENAL MICROBIOTA OF CHILDREN WITH BACTERIAL OVERGROWTH AND CHRONIC ABDOMINAL PAIN, Melissa Van Arsdall1, Yuying Liu1, Marcela Zozaya-Hinchcliffe2, Valerie McMurtry2, Audrey Wang3, Michael Ferris1, J. M. Rhoods1, 1University of Texas Medical School at Houston, Houston, TX; 2Research Institute for Children, Children's Hospital of New Orleans, New Orleans, LA

Background: Dysbiosis has been shown in pediatric IBS using stool analysis. An increased prevalence of small intestinal bacterial overgrowth (SIBO) has also been suggested in pediatric IBS, functional dyspepsia (FD), and functional abdominal pain (FAP). However, molecular profiling of the small bowel microbiota of such children with SIBO has not been reported.

Aims: To characterize the duodenal microbiota of children with chronic abdominal pain and SIBO and to determine the relevance of SIBO and specific organisms to pain severity.

Methods: Ten children, ages 4-17 years, undergoing esophagogastroduodenoscopy (EGD), without exclusion criteria, and with Rome III symptom criteria for IBS, FD, or FAP were evaluated. At endoscopy, the duodenal aspirate was cultured and Abdominal Pain Index (API) and Wong-Baker FACES™ Pain scores collected. If no organic problem was found, subjects had a glucose breath test (GBT) within 10 days of the EGD. SIBO was defined as bacterial growth of >10^4 cfu/mL within 5 days of aspirate culture, a fasting breath H2 >20 ppm, or a rise of ≥12 ppm breath H2 or CH4 within 3 hours of glucose ingestion; 5 children had SIBO, while 5 had no SIBO. The remaining duodenal fluid was evaluated using deep pyrosequencing of the 16SrRNA gene and the Ribosomal Database Project (RDP) pyrosequencing pipeline; bacterial communities were clustered based on the relative % abundance of operational taxonomic units in each specimen.

Results: No significant differences were found between the 2 groups (SIBO vs. no SIBO) in age, sex, race, nutritional status, PPI use, or in the number of those with FD or FAP. More patients in the SIBO group had IBS than in the group without SIBO (3/5 vs. 0/5, p=0.038). Positive tests in the SIBO group were cultures (2), GBTs (4, 3/4 from IBS patients, p=0.033), and fasting breath H2 levels (2). Total bacteria quantified by qPCR showed no significant differences between the groups (median 2.4x10^3 [SIBO] vs. 1.9x10^3 [no SIBO], p=0.917). The predominant species in the entire sample were Prevotella (31%), Streptococcus (12%), Veillonella (8%), Fusobacterium (8%), Neisseria (7%), Porphyromonas (3%), and Haemophilus (2%), with no significant differences in their relative abundance, comparing the 2 groups. The following positive correlations were found: API score with Prevotella abundance in the SIBO group (Pearson’s r=0.955, p=0.011) and in IBS patients (r=0.998, p=0.039); FACES™ pain score with Prevotella abundance in those without SIBO (r=0.835, p=0.0469); PPI use with Streptococcus abundance (r=0.673, p=0.033). No other significant relationships were found in comparisons between positive tests for SIBO, total bacteria on qPCR analysis, % relative abundance of bacterial species, abdominal pain scores, and Rome III diagnoses.

Conclusions: In this preliminary analysis, oral flora predominate the duodenal fluid of children with IBS, FD, and FAP, both in those with SIBO and without SIBO. The GBT appears to be more often positive in IBS than in FD or FAP. Prevotella, but not SIBO, appears to correlate with abdominal pain severity. However, healthy controls and a larger sample size are needed for further study.

446 FUNCTIONAL GASTROINTESTINAL DISORDERS IN PANAMANIAN SCHOOL CHILDREN, Ricardo Chantis2, Miguel Saps3, Carlos A. Velasco1, 1Pediatrics, University of Valle, Cali, Colombia; 2Pediatrics, Hospital del Niño, Panama, Panama; 3Pediatrics, Lurie Children's Hospital of Chicago, Chicago, IL

Introduction: The prevalence of functional gastrointestinal disorders (FGDs) in Latin America has not been studied, except for Colombia which is the 27.3% being associated with biological, social and psychological. Objective: To determine the prevalence of FGDs in one public and one private school in Panama City, Panama in 2013, and to establish possible associations with risk factors for FGDs.

Methodology: Prevalence study in 102 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; univariate analysis; possible occurrence of association between the variables (ORs with their 95%) Fisher's exact test with a P value <0.05, two-tailed, significant and multiple logistic regression analysis. Results: There was a prevalence of 31.4% FGDs, with an average age of 9.4±1.6 years. The FGDs and symptoms were functional constipation (FC) in 14.7% (pain on defecation in 86.7%) and Irritable bowel syndrome (IBS) in 12.8% (improvement in symptoms to defecate in 83.3%). Predominantly in girls and private school. There > opportunity to present FGDs to be older, private school and the female gender. The only factor associated with FGDs was age. Conclusion: The prevalence of FGDs in Panamanian school children between 8 and 14 years in Panama City, Panama, was 31.4%, with the most frequent FC and possible risk factor for presenting FGDs, age.

447 FUNCTIONAL GASTROINTESTINAL DISORDERS IN ECUADORIAN SCHOOL CHILDREN, Edgar Jativa2, Carlos A. Velasco1, Miguel Saps3, 1Pediatrics, University of Valle, Cali, Colombia; 2Pediatrics, Universidad Internacional del Ecuador, Quito, Ecuador; 3Pediatrics, Lurie Children's Hospital of Chicago, Chicago, IL

Introduction: The prevalence of functional gastrointestinal disorders (FGDs) in Latin America has not been studied, except for Colombia which is the 27.3% and Panama which is 31.4%. Objective: To determine the prevalence of FGDs in public and private schools in Quito, Ecuador in 2013, and to establish possible associations with risk factors for FGDs. Methodology: Prevalence study in 417 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; univariate analysis; possible occurrence of association between the variables (ORs with their 95%) Fisher's exact test with a P value <0.05, two-tailed, significant and multiple logistic regression analysis. Results: There was a prevalence of 22.8% FGDs, with an average age of 12.0±1.8 years. The FGDs and symptoms were functional constipation (FC) in 11.03% (pain on defecation in 95.7%) and Irritable bowel syndrome (IBS) in 4.8% (change in frequency of stool in 90.0%). Predominated in boys and public school. There < opportunity to present FGDs to be public school and the male gender. The factors associated with FGDs were school and age. Conclusion: The prevalence of FGDs in Ecuadorian school children between 8 and 15 years in Quito, Ecuador, was 22.8%, with the most frequent FC and possible risk factor for presenting FGDs, age and school.

448** PREVALENCE BY ROME III CRITERIA IN SPANISH OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN 3198 SCHOOL CHILDREN IN SEVEN CITIES OF COLOMBIA, SOUTHAMERICA AND POSSIBLE RISK FACTORS. Carlos A. Velasco1, Diana Vinueza2, Jairo Moreno3, Luis G. Vinasco3, Miguel Saps2, 1Pediatrics, University of Valle, Cali, Colombia; 2Pediatrics, Lurie Children's Hospital of Chicago, Chicago, IL; 3Pediatrics, Clinica Colsanitas, Bogota, Colombia

Introduction: To determine the prevalence of FGDs in 3198 school children in private and public schools in Cali, Sotavento, Pereira, Cucuta, Soledad, Pasto and Bogota, Colombia, and to establish possible associations with risk factors for FGDs. Methodology: Prevalence study in 3198 school children. Were considered sociodemographic, family and clinics factors. Statistical analysis included estimation of the proportion of children with FGDs and corresponding CI95%, % percentiles, means, medians and other descriptive measures with their corresponding standard deviations and ranges; univariate analysis, possible occurrence of association between the variables (ORs with their CI95%), Fisher's exact test with a p value <0.05, two-tailed, significant, and multiple logistic regression analysis. Results: There was a prevalence of 27.3% for FGDs (14.07% functional constipation, 5.44% irritable bowel syndrome and 1.38% aerophagia) with a mean age of 11.3±2.2 years. Predominated in girls, of public school and with family dysfunction. There was < opportunity to present FGDs, in boys and there was > opportunity to present FGDs, to live in Cali, study at public school; without parents separated; not only child; without the presence of the FGDs in cohabiting child; without a history of dengue in the past year; and to be eutrophic. The factors associated with FGDs were city, sex, age, family dysfunction and history of dengue in the past year. Conclusion: The prevalence of FGDs in school between 8 and 19 years of seven Colombian cities was 27.3% (14.07% functional constipation), with possible risk factors city, sex, age, family dysfunction and history of dengue in the past year.

449** REFERENCE VALUES FOR CHEMICAL CLEARANCE OF ACID REFUX IN INFANTS AND CHILDREN. Frederick W. Woodley1,2, Rodrigo S. Machado1, Marina Orsf3, Jolie Benner1, Catherine Chao1, Carlo Di Lorenzo2,4, Hayat Mousa1,2, Maria Velasco1, Diana Vinueza2, Jairo Moreno3, Luis G. Vinasco3, Miguel Saps2, 1Pediatrics, Nationwide Children's Hospital, Columbus, OH; 2Pediatrics, The Ohio State University, Columbus, OH; 3Pediatrics, Federal University of Sao Paulo, Sao Paulo, Brazil; 4Pediatr Gastroenterology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 5Pediatric Gastroenterology, Inova Fairfax Hospital, Fairfax, VA

Background: Clearance of acid gastroesophageal reflux (AGER) is biphasic; a volume clearance [VC] phase is followed by a chemical clearance (CC) phase. During CC, the acidified esophageal mucosa is neutralized by swallowed saliva and/or secretions from esophageal submucosal glands. Using combined esophageal pH monitoring and multichannel intraluminal impedance (Imp/pH), 4 unique types of AGER can be detected; classic two-phase, single-phase, pH only events, and re-reflux events. Two-phase AGER episodes may be used to assess CC because VC and CC components during these events are clearly distinguished. Specific Aim: To analyze two-phase AGER episodes from Imp/pH tracings of infants and children in order to define a "reference" range of CC for these pediatric populations. Methods: We analyzed Imp/pH tracings for patients referred for GER assessment. We excluded tracings from patients who: 1) had AGER Indices less than 50% of the upper end of normal (i.e. >3% for children >12 months and >6% for infants ≤12 months), 2) had a positive temporal association of GER with symptoms, 3) were on anti-reflux meds at the time of the study, 4) had a fundoplication prior to the study, and 5) had studies shorter than 20 hours. CC was assessed using both the duration of CC as well as the rate (pH units per sec). The mean for both variables (duration and rate) was calculated for each subject and then the reference range of CC was defined by the interval from the 10th to 90th percentiles. Results: A total of 32 infants (13F/19M, median age 4.8 months [range 3 days-12 months]) with a median AGER Index of 2.2% (range 0.2-5.9%) and 59 children (18F/41M, median age 7.3 yrs [range 1.3-16 yrs]) with a median AGER Index of 1.2% (range 0-3.0%). For the infants, the normal range of CC duration and rate was 31.9-96.9s and 0.0238-0.118 pH units/sec, respectively. For the children, the normal range of CC duration and rate was 14.6-90s and 0.0464-0.267 pH units/sec, respectively. Conclusions: This study provides a range of CC values that was derived from infants and children who had AGER Indices that were less than half of that which is considered normal by pH probe standards, had no temporal association of GER with symptoms, were not taking anti-reflux meds, and had not had anti-reflux surgery prior to the study. These values may be used as a reference to identify infants and/or children who may be at risk of developing serious clinical manifestations due to delayed CC.

450* NASPGHAN GUIDELINES FOR FUNCTIONAL CONSTIPATION COMPARED TO THE CURRENT PRACTICES OF PEDIATRICIANS. Christine H. Yang1, Jaya Punati2, 1Pediatrics, Children's Hospital Los Angeles, Los Angeles, CA; 2Pediatric Gastroenterology and Nutrition, Children's Hospital Los Angeles, Los Angeles, CA

Constipation is a common pediatric problem, accounting for 3% of visits to pediatrics and 25% of referrals to gastroenterologists. The majority of children will not have an organic etiology, and are diagnosed with functional constipation. The Constipation Guideline Committee of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) has formulated guidelines for functional constipation and its management. The major components of treatment are identifying whether impaction is present, and if so, disimpaction, followed by maintenance therapy (dietary changes, behavioral interventions, close follow-up, and medication). However, since the latest revision of the guidelines in 2006, no studies have been done investigating how pediatricians apply these guidelines, and the practices of trainee pediatricians in particular have never been extensively examined. Therefore, the purpose of this study was to evaluate pediatricians' familiarity with the NASPGHAN guidelines, and how closely their approaches adhere to these
guidelines, with an emphasis on surveying trainee pediatricians. An anonymous multiple choice questionnaire was sent electronically via general pediatrics department and trainee physician mailing lists at seven major academic centers throughout California, as well as through the American Academy of Pediatrics Section on Medical Students, Residents, and Fellowship Trainees mailing list. 828 survey responses were received (649 trainees, 179 attendings); 692 were complete (533 trainees, 143 attendings). 83.9% reported being unfamiliar or slightly familiar with the NASPGHAN guidelines. The most common initial interventions for constipation without encepsis included increasing fluids (92.4%), increasing fiber (88.6%), prune/fruit juice (76.9%), behavioral interventions (72.6%), regular follow-up (53.7%), and reducing constipating foods (50.5%), with maintenance medication as the most common secondary intervention (56.3%). The most common initial interventions for constipation with encepsis included bowel clean-out (72.9%), maintenance medication (69.3%), increasing fluids (67.3%), behavioral interventions (66%), increasing fiber (64.9%), and regular follow-up (58.5%), with increasing medication as the most common secondary intervention (53.9%). Osmotics were the most commonly prescribed PRN (82.8%) and maintenance medications (97.7%), with stimulants prescribed PRN by 35.2% and as maintenance by 17%. 38.3% reported concern that osmotics could result in dependence, addiction, or electrolyte imbalances, compared to 71.4% for stimulants. Our results show that more education regarding the role of medication in the management of functional constipation is necessary; specifically, the use of medication along with behavioral interventions reducing time to remission, the necessity of disimpaction prior to maintenance therapy, and misconceptions regarding the side effects of osmotics and stimulants. Furthermore, given the lack of familiarity with NASPGHAN guidelines, finding ways to increase awareness of these guidelines among pediatricians would be beneficial and likely increase consistency in management.

451 FASTEST BOWEL CLEAN-OUT FOR CONSTIPATION? NASOGASTRIC GOLYTELY VERSUS MAGNESIUM CITRATE IN THE AMBULATORY SETTING, Lisa Philichi, Melawati Yuwono, Jennelle German, Mary Bridge Hospital and Health Center, Tacoma, WA

A bowel clean-out may be necessary for a constipated child's condition to improve. Home clean-outs can be unsuccessful and a more aggressive clean-out in the hospital setting may be required. The purpose of the study was to determine which bowel clean-out is faster: nasogastric GoLYTELY (polyethylene glycol-electrolyte solution) or oral magnesium citrate. METHODS: A retrospective chart review of 103 children with constipation was done to determine the time from the start of the clinic clean-out until abdominal radiograph (KUB) verification of successful stool evacuation occurred. The protocol was identical except intravenous fluid was given during GoLYTELY. The protocol included an initial KUB, Reglan (metoclopramide) for nausea and vomiting, food coloring added to the clean-out agent, and milk and molasses enemas. The second KUB was done after three colored liquid stools were passed. RESULTS: Forty-six of the children (45%) underwent the GoLYTELY clean-out and 57 (55%) drank magnesium citrate. Their age range was 1-18 years with an average age of 8. Forty-five were female and 59 male. The GoLYTELY children on average required 2.5 enemas and the magnesium citrate children 3. Both GoLYTELY and magnesium citrate initial KUBs ranged from rectal impaction to massive amount of stool throughout the colon with the most frequent being moderate colonic stool. The average time for a GoLYTELY clean-out took 5 hours 15 minutes (range: 3 hours 30 minutes -7 hours) and 5 hours 30 minutes for magnesium citrate clean-out (range: 2 - 8 hours). Seven (15%) of the GoLYTELY and 6 (10%) of magnesium citrate clean-outs did not achieve interval clearance of stool at the time of the second KUB. Vomiting was an adverse effect of both types of clean-outs and 7 (12%) magnesium citrate children were unable to drink the entire dose. CONCLUSION: The study findings indicate that both methods of clean-out take almost the same amount of time. Although magnesium citrate can be difficult for some children to drink, it is less costly, less invasive, and safer than nasogastric GoLYTELY. Furthermore, an oral magnesium citrate clean-out can be done at home.

455 PREDICTION OF WEIGHT/AGE SINCE GROWTH AND BODY COMPOSITION ANTHROPOMETRICAL INDICATORS IN APPROPRIATE AND SMALL FOR GESTATIONAL AGE PRETERM NEWBORNS, Edgar M. Vásquez-Garibay1,2, Yomé E. Larios del Toro3,4, Rogelio Troyo-Sanromán1, Alfredo Larrosa-Haro1, 1Unidad de Cuidados Intensivos Neonatales, 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

BACKGROUND: Weight/age has been the diagnostic axis of intrauterine growth retardation. Newborn anthropometrics has evolved and provides new ways to approach this condition.

OBJECTIVE: To achieve a predictive model of weight/height since growth and body composition anthropometrical indicators. PATIENTS AND METHODS: One-hundred and one very low birth-weight (VLBW) (<1,500g) preterm newborns were evaluated prospectively along 4 weeks in a Neonatal Intensive Care Unit. Fifty-seven were classified as appropriate for gestational age (AGA) and 44 as small for gestational age (SGA). They were managed under a parenteral/enteral nutrition protocol. Anthropometric measurements of growth and body composition were evaluated on admission and at days 7th, 14th and 30th. A multivariate linear model was achieved with weight/height as dependent variable.

RESULTS: Length/age deteriorated in both study groups along the 4 weeks. AGA length/age remained between -2 to -1SD in the first two weeks and dropped below -2SD at 30 days. SGA length/age was below -2SD at all measurements and dropped below -3SD at the 3rd week. In AGA newborns weight/age correlated significantly with height/age, weight/length, cephalic circumference/age, arm and thigh circumference/age. In SGA newborns significant correlations were identified with thigh circumference and slightly with weight/height. In AGA, the multiple regression model included all growth and body composition indicators along the four weeks. In SGA, the multivariate model included head, thigh and arm circumference.

CONCLUSIONS: SGA preterm newborns had actually smaller length and head circumference than their AGA peers. AGA preterm newborns remained with harmonic body composition and growth along the study.

Nutrition/Nutrition Support
456  EFFECTION OF AN INDIVIDUAL, BREASTFEEDING-FOCUSED COUNSELING ON EXCLUSIVITY OF BREASTFEEDING AT SIX MONTHS: A RANDOMIZED, CONTROLLED, SINGLE-BLINDED TRIAL. Rebecca Castro, Santo Tomas Hospital, Manila, Philippines

Background of the study: Breastfeeding is the best nutrition for infants. However, the prevalence of exclusive breastfeeding is low globally. There is much interest in the effectiveness of breastfeeding promotion interventions in improving breastfeeding outcomes.

Objectives: To assess the effect of an individual breastfeeding-focused counseling on exclusivity of breastfeeding at six months of age, to determine associations between exclusivity of breastfeeding at six months and maternal age, parity and educational attainment, and to identify the reasons why mothers stop exclusive breastfeeding before six months.

Methods: This is a prospective, randomized controlled trial involving 121 mother-infant pairs. Both groups received prenatal and postnatal breastfeeding counseling at the obstetrics ward and well-baby clinic, respectively. The intervention group received at least three additional individual breastfeeding-focused counseling by a trained health professional. All participants were assessed during the third and sixth month of age as to the infant's feeding. The prevalence of exclusive breastfeeding at six months of age was determined.

Maternal age, parity, educational attainment and its association with exclusivity of breastfeeding at six months were also determined and reasons for discontinuing exclusive breastfeeding were identified.

Results: The prevalence rate of exclusive breastfeeding was higher in the intervention group (47.1%) versus the control group (21.2%) (p-value=0.006). No significant associations were noted between maternal age, parity, mother’s education and exclusivity of breastfeeding at 6 months of age. Mothers discontinued exclusive breastfeeding in both the intervention and control groups due to the following reasons: the mother returning to work (50% vs 53.5%), perception of inadequacy of milk (39.3% vs. 44.2%), difficulty in breastfeeding (7.1% vs 2.3%) and separation of mother and infant (3.6% vs 0).

Conclusion: An individual, breastfeeding-focused counseling by a trained health professional increases the exclusivity of breastfeeding at six months of age. There were no associations between exclusivity of breastfeeding at six months and maternal age, parity and educational attainment. Mothers discontinued exclusive breastfeeding due to the mother returning to work, perception of inadequacy of milk, difficulty in breastfeeding and separation of mother and infant.

Keywords: breastfeeding-focused counseling, exclusive breastfeeding

457  EVALUATION OF A COMPUTER-BASED MALNUTRITION RISK SCREENING TOOL FOR PEDIATRIC HOSPITALIZED PATIENTS. Thomas Karagiozoglou-Lampoudi, Efstratia Daskalou, Dimitrios Lampoudis, Alexandra Karadima, Euthimia Daoula, Aggeliki Apostolou, Nutrition & Dietetics Department, Clinical Nutrition Laboratory “Christos Mantzoros”, Alexander Technological Educational Institute of Thessaloniki, Thessaloniki, Greece

Objective: To evaluate a digital scaled malnutrition screening tool (SMART) targeting to pediatric hospitalized patients.

Material & Methods: The SMART software was designed using Java, on the Netbeans platform. It calculates weight-for-age z-scores using the WHO Anthro and Epi Info software, and displays it in the form of a four level categorization. Data concerning 3 additional parameters is inserted by pressing the keys 0-4, corresponding to their severity. The validation procedure was performed assessing 500 patients (271 boys, 229 girls) aged 1 month-17 years old (mean age=4.11±4.38 years) at admission. BIA Phase angle (PhA) was measured to test the arbitrary scoring of SMART against an objective measurement. Criterion and construct validity as well as content and discriminative validity were assessed. Inter-observer agreement and agreement between SMART and other established pediatric scores were evaluated using Kappa coefficient.

Results: The SMART score displayed an inverse correlation to PhA values (p<0.001), a very good diagnostic capacity concerning malnourished patients (AUC=0.826, p<0.001) and its positive correlation to hospitalization duration (days) (p<0.001) suggests a strong predictive value. Moderate agreement and correlations were demonstrated between SMART and PYMS, STRONGkids and STAMP (p<0.001) with ROC curves for high risk categorization displaying Areas Under the Curve (AUC) 0.869, 0.830 and 0.813 respectively (p<0.001). Inter-observer agreement was moderate (k=0.474, p<0.001).

Conclusion: The proposed SMART is a simple and rapid tool that was found to be sensitive and accurate in malnutrition risk prediction. In its electronic form it could be part of the electronic medical record.

458  UTILITY OF UPPER GASTROINTESTINAL SERIES PRIOR TO GASTROSTOMY TUBE PLACEMENT. Catherine Larson-Nath1, Amy Wagner2, Praveen S. Goday1, 1Pediatric Gastroenterology and Nutrition, Medical College of Wisconsin, Milwaukee, WI; 2Pediatric Surgery, Children's Hospital of Wisconsin, Milwaukee, WI

Objective: Performing Upper Gastrointestinal fluoroscopy (UGI) prior to gastrostomy tube placement to assess for intestinal malrotation is the standard of care at many institutions. We hypothesized that in children undergoing gastrostomy tube placement, midgut rotational anomalies are more common in children with anomalies of other organ systems, chromosomal abnormalities or genetic syndromes than in children without such conditions.

Methods: A preliminary retrospective chart review of all initial gastrostomy tubes (PEG and surgical) placed in 2011 and 2012 at a large academic children's hospital was undertaken. UGI results and other major anomalies were analyzed. Exclusion factors were the diagnosis of gastroschisis, omphalocele, and congenital diaphragmatic hernia as by definition these children have malrotation.

Results: Over the study period 393 patients met our study criteria. The average age at tube placement was 2.7y (median 184 d, range 1 d-25 y). Of those 23 did not have an UGI or results from an UGI. A total of 14 episodes of malrotation were found (4%). All of these children had other major anomalies. The overall rate of malrotation in children with other anomalies was 5.2%. The associated anomalies in children with malrotation included: Neurological (71%), Cardiac (57%), Gastrointestinal (21%), Chromosomal (14%), Renal (7%),
Asplenia (7%), Cleft palate (7%), and Cystic fibrosis (7%). Five children with malrotation had more than one system affected by an anomaly. Of the children without malrotation 100 had no associated anomaly (28%).

Conclusion: Malrotation is more common in children with other major anomalies needing gastrostomy tubes than those without other major anomalies. Overall there is a low incidence of asymptomatic malrotation in children without other anomalies. Our findings question the need for routine UGI prior to PEG placement in children without other major anomalies.

459 THE ASSOCIATION OF DIET AND EXERCISE WITH BODY COMPOSITION IN PEDIATRIC CROHN'S DISEASE.

BACKGROUND: Pediatric Crohn's disease (CD) often presents with lean mass (LM) and fat mass (FM) deficits. With treatment, weight and FM improve but LM deficits persist. This study assesses associations of diet and physical activity with LM and FM over 24 months.

METHODS: Children and adolescents, ages 8-21 years, with >6 months since CD diagnosis and a bone mineral density <25th percentile for age were eligible. At baseline, 6, 12, and 24 months, leg LM (excluding bone) and whole body FM were assessed using DXA. Race and sex-specific z-scores for LM and FM were generated relative to age, and then adjusted for leg-length and height z-scores respectively (LM-Z, FM-Z) to account for differences in body size and maturation. At each visit, anthropometry, Tanner stage, disease activity (PCDAI), and medications were assessed. In the week after each visit, three-24 hour dietary recalls were obtained. For each subject, estimated energy requirement (EER) was calculated, and percent intake (%EER) assigned based on the dietary recalls. Physical activity was assessed using RT3 tri-axial accelerometers worn for 1-week intervals quarterly. The mean time (minutes/day) of moderate-to-vigorous physical activity (MVPA) was computed for each subject. Longitudinal data analysis was performed using generalized estimating equations (GEE) to evaluate determinants of LM-Z and FM-Z over time. Within and across subject effects were assessed for time-varying covariates.

RESULTS: A total of 138 subjects (48% male) enrolled with a mean +/- SD age of 14.2 +/- 2.8 and median (range) disease duration of 2.7 (0.5-11.8) yr. Median (range) PCDAI at enrollment was 10 (0-45) and 13% were treated with glucocorticoids at enrollment. At baseline, children had mean +/- SD LM-Z of -1.01 +/- 0.97 and height-Z (HAZ) of -0.76 +/- 1.0. Significant increases in both LM-Z and HAZ were seen over 24 months, but deficits still persisted with values of -0.79 +/- 1.02 and -0.49 +/- 0.99, respectively. FM-Z at baseline was 0.29 +/- 1.02 and did not change significantly over 24 months. A multivariate model for LM-Z demonstrated a positive association with MVPA, with the highest active quartile having a LM-Z 0.43 (P=0.01) greater than the lowest active quartile. This lean mass model demonstrated children with moderate-to-severe disease to have a -0.53 (p<0.005) lesser LM-Z compared with those having inactive disease. FM-Z was not significantly associated with MVPA, disease activity, or steroid exposure. We found both LM-Z and FM-Z to have significant negative associations with %EER(p=0.005 and p<0.005, respectively). A model with %EER as the outcome showed greater %EER to be significantly associated with NG-tube feeds (p<0.005), low height (p<0.005), and low FM-Z (p<0.005).

CONCLUSION: In pediatric CD, greater physical activity was associated with greater LM and was not associated with FM. Greater disease activity was associated with lower LM. We hypothesize that the association of higher %EER with lower LM-Z and FM-Z reflects the needs for supplementation and greater caloric drive in children with poor nutrition.

460 DEFICIENCIES IN CORTICAL AND CANCELLOUS BONE MINERAL DENSITY BY QUANTITATIVE CT IN LACTASE DEFICIENT PEDIATRIC CELIAC DISEASE.
Malinda Lin, Michelle Pietzak, Pediatrics, Childrens Hospital Los Angeles, Los Angeles, CA; Pediatrics, Keck School of Medicine at the University of Southern California, Los Angeles, CA

Background: Low bone mineral density (BMD) is a common complication of untreated celiac disease (CD). Factors such as malabsorption, inflammation, and inadequate intake of calcium and vitamin D contribute to the development of osteopenia. However, it is not known if children who are identified as lactase deficient, or on a lactose free diet, are at higher risk for osteopenia.

Objective: To evaluate the impact of hypolactasia and lactose free diet (LFD) on bone mineral density (BMD) in newly diagnosed pediatric CD.

Methods: We measured cortical and cancellous BMD using quantitative computed tomography (QCT) in children with biopsy proven CD. Cortical density was measured at mid-shaft of the femur. Cancellous density was measured at L1-L3 vertebrae. QCT was performed within one month to six years after diagnosis, with one child having QCT immediately prior to biopsy. Assays for disaccharidase levels from initial biopsies were sent to Joli Diagnostics. Serum calcium, 25OH vitamin D, and parathyroid hormone (PTH) were measured. Retrospective chart review was performed to assess symptoms of lactase deficiency and dietary lactose restriction.

Results: Twenty children and adolescents were included with the following characteristics: age 21 months to 19 years at diagnosis; 70% female; 15 Caucasians, 4 Latinos, 1 Asian. 90% were lactase deficient. 13 children had either low cancellous or low cortical BMD; 6 had low measures of both. Higher Marsh grade correlated with more profound hypolactasia. While all children with low cancellous BMD were lactase deficient, only 80% of children with low cortical BMD were lactase deficient. Symptoms consistent with lactose intolerance were reported in 50% of the cohort. Among lactase deficient children, all those on LFD had at least one low BMD measurement; whereas, 50% of children who did not restrict lactose still had low BMD. Only one child with low BMD measurements had high PTH. Serum calcium, 25OH vitamin D and PTH levels were normal in the remainder of the cohort.

Conclusions: In our cohort, lactase deficiency was present in 90% of children, although half denied symptoms of lactose intolerance. LFD was associated with low BMD. However, we were surprised that in children with lactase deficiency, who continued to ingestion lactose, still often had low BMD. Often it is difficult to differentiate symptoms of lactose intolerance from gluten ingestion. It is known that serum calcium, PTH and 25 OH vitamin D levels are poor non-invasive measures of BMD, and this was likewise validated by our cohort. Although it is controversial to screen for low BMD in pediatric CD, we believe it important to obtain lactase levels and BMD measurements to evaluate and treat for osteopenia early in pediatric CD.
461 NATURAL HISTORY OF CONJUGATED BILIRUBIN TRAJECTORY IN NEONATES FOLLOWING PARENTERAL NUTRITION CESSION. Nisha Mangalat¹, Cynthia Bell¹, April Graves², Essam Imseis², ¹Pediatrics, Saint Louis University, Saint Louis, MO; ²Pediatrics, The University of Texas Medical School at Houston, Houston, TX; Clinical Pharmacy, Memorial Hermann-Texas Medical Center, Houston, TX

BACKGROUND: There is little published data regarding the rate of bilirubin clearance in newborns following total parenteral nutrition (TPN) cessation, particularly in the neonatal intensive care unit (NICU) population without intestinal failure. AIM: The primary aim of this retrospective chart review was to determine the duration and severity of bilirubin elevation in neonates without intestinal failure. Secondary aims were to determine factors that would influence the duration and severity of this biochemical elevation. METHODS: The authors conducted a retrospective chart review of all infants receiving TPN for ≥ 21 days and with elevated conjugated bilirubin (CB) ≥ 3mg/dL upon TPN cessation in a tertiary care NICU from January 1, 2008 to December 1, 2010. Patients with known causes of liver disease or without laboratory values at least four weeks after PN cessation were excluded. Time to maximum conjugated bilirubin post TPN cessation and normalization were the primary outcomes. Secondary factors including number/timing of sepsis events, ethnicity, and ursodiol use were also evaluated. RESULTS: A total of 341 neonates receiving TPN for ≥ 21 days were screened for inclusion. Of these, 43 met inclusion criteria. The majority of patients had increased CB post TPN cessation ("up" group; 27/43, 63%) with max CB reached 13 days (SD ± 10.3) after TPN cessation. The majority of the cohort achieved normalization of the bilirubin prior to discharge (28/43, 65%). There was no difference in rate of normalization (p=0.342) between the "up" group (59%) and the group of patients whose bilirubin trended downward following PN cessation ("down" group, 75%). There were no differences between the two groups with respect to gestational age at birth, birth weight, number of sepsis events, gram negative sepsis events, or intestinal resection. Only 30% of Hispanic patients had increased CB post TPN cessation compared to the majority (71%) of non-Hispanic patients. The maximum conjugated bilirubin (maxCB) of those that had complete normalization was significantly lower value than the maxCB of those that did not normalize (p=0.016). CONCLUSIONS: The majority of infants experience a rise in serum conjugated bilirubin following TPN cessation that can last for weeks, but bilirubin generally normalizes with time in the majority of infants. The precise mechanism of TPN associated liver disease, and reasons for increase in CB post TPN cessation warrant further investigation.

462 GASTRIC EMPTYING AND CHILDREN WITH POOR APPETITE: IMPORTANCE OF THE 15 AND 30 MINUTES VALUES DURING THE RADIONUCLIDE STUDY. Maria Marano¹, Maria Ramsay², Ana Sant'Anna², ¹Pediatrics, Division of Gastroenterology and nutrition, Montreal Children's Hospital, Montreal, QC, Canada; ²Feeding Disorders Program, Montreal Children's Hospital, Montreal, QC, Canada

Background: Assessment of gastric emptying by performing a milk scan is an integral part of the investigation of children with poor appetite. Normal values of gastric emptying for the 1h and 2h milk scan transit times have been reported and being used as a guide to determine the presence of delayed gastric emptying. However, this is not the case for the 15, 30 and 45min transit times. Given children with poor appetite manifest with a prolonged feeding time and consequently start digesting the radiolabelled meal prior to the set time zero, we believe gastric emptying values obtained at 15 and 30min are of more importance in this subset of population.

Aims: The aims of the study were: 1) to describe the gastric emptying values obtained at 15 and 30 min in a poor appetite population, given their abnormal meal time pattern; and 2) to compare the gastric emptying rate among patients with poor appetite alone vs those presenting with failure to thrive.

Methods: This study consists of a chart review of all patients followed in the Feeding Disorders Clinic of the Montreal Children's Hospital from August 2009 to July 2011 having performed a milk scan. Forty patients were included. Patients were divided into two groups: group I, 0-2 years old (22 patients); and group II, ≥ 2 years old (18 patients). Each group was then divided into two subgroups: a) poor appetite only group and b) poor appetite + failure to thrive group. For each subject, results of the milk scan including gastric emptying (% emptied) at 0, 15, 30 and 45min as well as 1h and 2h were determined. Demographics of the patients were reviewed, as well as size of radiolabelled meal, rate of ingestion and medications at time of exam. A statistical analysis for each transit time was then performed for each subgroup.

Results: (Table1). The comparison of gastric emptying time between the poor appetite only group and the poor appetite + failure to thrive group < 2 years old was statistically significant (p < 0.05) at the 30 and 45min transit time and milder statistical correlation at 60min. However, once at 2h, this comparison among the two subgroups is no longer seen. As for the group ≥ 2 years old, differences showed no significant differences among the two subgroups.

Conclusion: The relation between the severity of poor appetite and delay in gastric emptying cannot be ignored for the group < 2 years old. Our results support a worse gastric emptying rate in children with poor appetite + failure to thrive than poor appetite alone at earlier time frames which then slowly reach equal rates at 2h. This is an important result to correlate with the physiology of a meal, which should not last more than 30min. Further studies are needed to evaluate better these patients and further optimize these milk scan time points for routine use.

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<th>Ia</th>
<th>Ib</th>
<th>Ila</th>
<th>(Q1,Q3)</th>
<th>(Q1,Q3)</th>
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<tbody>
<tr>
<td>Gastric emptying (%) at 15 min</td>
<td>27 (22,32)</td>
<td>13 (6,22)</td>
<td>17.5 (15,5,22.5)</td>
<td>33.5 (14.5,52.25)</td>
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<td>Gastric emptying (%) at 30 min</td>
<td>36 (28,44)</td>
<td>22 (9.5,23)</td>
<td>21 (15.75,30.5)</td>
<td>35.5 (17.25,55.5)</td>
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<td>Gastric emptying (%) at 45 min</td>
<td>49 (36,63)</td>
<td>25 (16,33)</td>
<td>27.5 (18.75,32.5)</td>
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<td>55 (37,79)</td>
<td>32 (25,36)</td>
<td>30.5 (22.25,43.75)</td>
<td>40.5 (21.5,57.5)</td>
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<td>Gastric emptying (%) at 120 min</td>
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<td>87 (58.25,95.75)</td>
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463 EXPERIENCE WITH ESTABLISHING MULTICENTER OFFICE BASED CLINICAL RESEARCH: BARRIERS TO IMPLEMENTATION OF THE CPMI STUDY. Sudipta Misra1, Sari Acra2, Ian Leibowitz2, Neil Saha1, 1Pediatrics, Brody School of Medicine, Greenville, NC; 2Pediatrics, Vanderbilt School of Medicine, Nashville, TN; 1Pediatrics, Inova Fairfax Hospital for Children, Fairfax, VA; 2San Juan Bautista School of Medicine, San Juan

Background: Multicenter office based studies face multiple barriers which have not yet been documented. We share our experience with establishing the CPMI study though the NASPGHAN Research Committee and Practitioner's Forum.

Methods: In 2010, a core group was formed to explore the idea of multicenter office based clinical research. The group decided to 1. Encourage clinicians in private practice to participate. 2. Keep the study simple to attract minimal regulatory review. 3. Help the participants with regulatory paperwork by providing a model protocol, consent form and support by phone and e mail. 4. Use internet based Redcap database for data collection and analysis. Suggestions on research topics were sought by presentation at the conference, survey at the NASPGHAN website and request on the bulletin board. The likely participants chose cow's milk protein Intolerance (CMPI) as the research topic based on clinical relevance, availability of subjects and minimal time commitment on the part of the participants. A protocol was discussed among the participants, reviewed and approved by the leadership. Each center was provided with the documents. In June 2013, a follow up survey was sent to the participants regarding their experience with IRBs and the process. The study was endorsed by NASPGHAN but no funding was available for the project.

Results: In June 2012, 103 centers had expressed interest in the study. By November 2012, 55 North American and 6 international participants had confirmed participation. None of the international centers followed through with regulatory paperwork. Overall, common reasons cited for dropping off were "lack of time" (40%), "priority commitment" (40%) and "inability to do IRB paperwork" (20%). By June 2013, 27 centers had officially indicated involvement in the study: 17 were IRB approved (with 7 of them having started enrollment), while 10 were still working on their IRB approval. 4 participants were not from academic institutions. The time required for IRB approval was between 2 weeks and >6 months, with an average of 8.1 weeks. Most (65%) of the centers were approved within 8 weeks, while about a third had to wait/were waiting for >6 months. Number of queries and resubmissions ranged from 0-6 (mean 1.7) and 0-9 (mean 2.5) respectively. Non-academic centers appeared to have slightly faster IRB approvals than academics (mean 7 weeks vs. 8.4 weeks). Of those centers experiencing delays in IRB approval, 10% cited the need for greater support by study coordinators, while 90% attributed the delay to local IRBs.

Conclusion: - There is significant interest among private and academic clinicians to engage in clinical research. However, lack of time, aversion to regulatory procedures, lack of funding and resources and wide and unpredictable variations in responses of the individual IRBs were major barriers to greater participation in this multicenter office based study. While this study presents a model that can be used for office based multi-center clinical research, addressing these barriers can lead to wider participation.

Acknowledgement: CPMI research participants.

464* WEANLING UNDERNUTRITION PRODUCES CHRONIC GROWTH FAILURE IN MALE BUT NOT FEMALE MICE AND REVEALS SEX DIFFERENCES IN MICROBIOME AND GUT GENOMIC RESPONSES. Sean R. Moore, Elizabeth Maier, Yael Haberman, Lee A. Denson, Pediatrics -- Gastroenterology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background & Aims: Early weaning of infants in low- and middle-income countries to diets deficient in fat, protein, or key micronutrients contributes to a vicious cycle of undernutrition and enteric infections, with long-term adverse effects on growth and neurodevelopment. A number of clinical studies suggest male children are more susceptible to this cycle, therefore we examined the influence of gender on intestinal and systemic responses to undernutrition in weanling mice. Methods: C57BL/6 dams with 10-day-old pups were randomized to ad lib access to a standard purified diet (65% carbohydrate, 20% protein, and 15% fat) vs. an isocaloric, multideficient regional basic diet (RBD, 88% carbohydrate, 7% protein, and 5% fat). On day of life 21, suckling pups were weaned to their dams' diet and segregated by sex. Upon sacrifice at 6 weeks of age, we harvested jejunal segments for RNA-seq analysis and ELISA quantification of claudins and cytokines, mesenteric lymph nodes for bacterial culture, stool for PCR analysis of microbiota, and serum for ELISA quantification of LPS-binding protein (LBP). Results: Pups of RBD dams failed to thrive compared to pups of control dams. Upon weaning, no sex differences in weight were apparent within RBD or control groups, however by 6 weeks of age, female RBD mice had achieved parity with female controls, while male RBD mice remained 25% underweight relative to control males (P<.001). RBD mice showed a 5-fold increase in bacterial translocation (P<.05) vs. controls, with a 3-fold increase in RBD males vs. RBD females (P<.05). RBD mice further showed a 1.4-fold increase in serum LBP, together with increased IL-6 and decreased claudin-3 and claudin-15 in the jejenum (P<.05). Interestingly, increased intestinal IL-1b and IL-17 levels in female RBD mice were associated with decreased undernutrition. Decreases in fecal Firmicutes and Acinetobacter in RBD mice were more pronounced in males. RNA-seq of the jejenum (n=3 mice per group) revealed 361 transcripts differentially expressed >1.5-fold between male vs. female control mice, 1763 between RBD vs. control mice, and a remarkable 5096 between RBD males vs. RBD females. Conclusions: Adverse effects of weanling undernutrition on mouse growth, intestinal barrier function, and fecal microbiota are more severe in males. Further studies are needed to determine the extent to which a coordinated transcriptional response to undernutrition in the female gut promotes intestinal homeostasis in the setting of nutritional scarcity.

465 CLINICAL PHARMACIST RECONCILIATION OF PRESCRIBED AND COMMERCIALY COMPOUNDED HOME PARENTERAL NUTRITION SOLUTIONS IN A NATIONAL COHORT. Margaret Murphy, Kathleen M. Gura, Meghan K. Dalton, Casey B. Walf, Brittany Tellier, Sharon Collier, Christopher Duggan, Jenifer Lighthall, Bram Raphael, Pharmacy, Boston Children's Hospital, Boston, MA; 7Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA

Background: Parenteral nutrition (PN), a high-risk therapy composed of 10-15 active ingredients, is increasingly being prescribed for home use. Multiple commercial vendors are available nationally and routinely accept prescriptions to compound home PN using a variety of products.

Aim: To compare PN prescriptions and the ingredients of actual compounded solutions delivered to patients' homes.
Methods: Boston Children's Hospital PN pharmacists prospectively reconciled compounding records with electronic Home PN prescriptions during all routine ambulatory encounters in our Home PN clinic from 1/7/2013 to 4/29/2013. Discrepancies were defined as any difference between the gold-standard Home PN prescription and the compounded solution. Pharmacists used the Medication Error Reduction Plan (MERP) to code frequencies, types and causes of discrepancies between prescribed and compounded solutions. Results: Solutions prepared by 14 different home infusion companies for 89 unique patients residing in 14 states (CA, CT, LA, MA, NV, NY, RI, NH, NJ, PA, NC, MO, WI, MN) from a total of 101/117 (86%) ambulatory encounters were reviewed. 46% (46/101) of all prescriptions involved at least 1 discrepancy, with a total of 60 discrepancies identified, affecting 40% (34/89) of patients. There was at least 1 discrepancy in solutions originating from 71% (10/14) of home infusion companies. The most common discrepancies were amino acid brand substitution (n=25) and incorrect anion balance (n=15). Absence of selenium in solution was the most common error of omission (n=12). 62% (37/60) of discrepancies were Level C MERP errors (ie. reached patient but did not cause harm), and 38% (23/60) were Level D (ie. reached patient and required monitoring and/or interventions to preclude harm). Conclusions: We found an alarmingly high rate of discrepancies between Home PN prescriptions and commercially prepared solutions in a national cohort. Participation of clinical pharmacists in ambulatory Home PN encounters may be critical for reconciling prescriptions. While home infusion companies provide an indispensable function, errors with potential for harm may be more common than previously appreciated.

466 PLANT STEROL ACCUMULATION IN NEONATES RECEIVING PARENTERAL NUTRITION. T. Hang Nghiem-Rao1, Alisha Mavis1, Elizabeth M. Polzin2, Mary F. Firary3, Pippa Simpson1, Shailendra B. Patel3, 4, 1Pediatrics, Medical College of Wisconsin, Milwaukee, WI; 2Clinical Nutrition, Children's Hospital of Wisconsin, Milwaukee, WI; 3Pharmacy, Children's Hospital of Wisconsin, Milwaukee, WI; 4Quantitative Health Sciences, Medical College of Wisconsin, Milwaukee, WI; 5Medicine, Medical College of Wisconsin, Milwaukee, WI; 6Clement J. Zablocki Veterans Medical Center, Milwaukee, WI

Background: Parenteral nutrition (PN) is essential for the survival of premature and critically ill newborn infants; however prolonged exposure can lead to potentially devastating PN-associated liver disease (PNALD). Plant-derived sterols in Intralipid (IL) are believed to contribute to liver injury, which may be worsened by hepatic immaturity. Studies describing the kinetics of plant sterol accumulation during IL infusion in infants are lacking.

Objectives: To determine the kinetics of plasma plant sterol concentrations in neonates receiving IL.

Design/Methods: Forty-three infants with anticipated need for PN of at least 5 days, and 9 control infants without PN exposure were enrolled in a prospective pilot study. Serial measurements of the plant sterols stigmasterol, campesterol, and sitosterol were performed at initiation, during, and after discontinuation of PN. Clinical data were abstracted from the medical record and sterol levels were measured by GC/MS.

Results: Five patients were eliminated based on exclusion criteria, leaving 38 IL-exposed and 9 control infants eligible for data analysis. During their hospitalization, IL-exposed infants had higher median sitosterol (1.01 mg/dL vs 0.01 mg/dL, p<0.001) and campesterol (0.54 mg/dL vs 0.12 mg/dL, p=0.002) levels and reached higher maximum sitosterol (2.61 mg/dL vs 0.01 mg/dL, p<0.001) and campesterol (1.60 mg/dL vs 0.34 mg/dL, p=0.003) levels than controls. Accumulation of stigmasterol was not affected by PN-exposure. Among those who received IL, half underwent a GI surgical procedure. In subgroup analysis of IL-exposed infants, maximum sitosterol level was similar for surgical infants and non-surgical infants (3 mg/dL vs 2.29 mg/dL, respectively, p=0.16), however, the time to reach maximum sitosterol was longer for the surgical group (13 days vs 5 days, respectively, p=0.01). Higher maximum conjugated bilirubin levels were seen in IL-exposed infants who underwent surgery compared than those who did not (0.7 mg/dL vs 0 mg/dL, respectively, p=0.003). Conclusions: Plant sterols accumulate in neonates during IL infusions. Our data suggests that time to reach maximum sitosterol is important in the pathogenesis of PNALD.

467 GROWTH AND FEEDING TUBE OUTCOMES IN SURVIVORS OF CONGENITAL DIAPHRAGMATIC HERNIA IN A LARGE ACADEMIC CENTER. Anne Pierog, Joshua Kriger, Mengfei Wu, Ali A. Mencin, Columbia University, New York, NY

Objective: This study's purpose was to review our center's experiences with feeding and growth outcomes in children with congenital diaphragmatic hernia (CDH).

Study Design: We conducted a retrospective review of infants with CDH treated in our center from January 1, 2007 to June 30, 2012. This is the largest study of CDH infants with follow-up to at least one year that examines feeding and growing disorders, and the only study which takes into consideration the role of pulmonary hypertension (PPHN), which was graded by one expert cardiologist's echocardiogram readings. Chi-squared, logistic regression and Fisher's exact tests were used for statistical analysis.

Results: Our NICU treated 93 infants with CDH during this time. 89% survived to at least one year of age. 62/83 (75%) were followed to at least one year of age. 31 (50%) were failure to thrive (FTT defined as <5th percentile for weight) at one year and 13 (21%) required tube feedings at one year. 21 (22.6%) required extracorporeal membrane oxygenation (ECMO), and in those who survived to one year (n=18), there was an increase in the need for continued tube feedings compared to those that did not receive ECMO (OR=13.12, p=0.0001). There was no difference in FTT between ECMO and non-ECMO groups (OR=2.3480, p=0.1985). 63.7% of all CDH patients had some degree of PPHN diagnosed by echocardiogram at one and/or three months of life. There was an increase in tube feedings at one year of age in the patients with moderate or severe PPHN at three months compared to those with no or mild PPHN at three months (OR=40.0, p=0.0022). There was no increase in FTT between these two groups (OR=0.90, p=0.9185). Although only a minority of patients (n=20) underwent pH probe testing, those with reflux (n=10) were not at increased risk for FTT (OR=1.01, p=0.2509) or tube feedings at one year of age (OR=1.00, p=0.8327).

Conclusions: Our data shows the importance of counseling families of CDH infants prior to NICU discharge about the increased risk of requiring tube feedings if ECMO was required or if moderate or severe PPHN was seen on a post-natal echocardiogram. Targeting babies with these risk factors for more aggressive and earlier nutritional interventions may prevent growth issues in the future.
468 NUTRITION EFFECTS OF APPETITE MANIPULATION IN CHILDREN WITH FEEDING DISORDER ADMITTED TO A COMPREHENSIVE INPATIENT FEEDING PROGRAM. Alyssa Pollow1, Catherine Karls1, Mary Witzlib2, Michelle Stoeher2, Richard Noel1, Alan Silverman2,1, 1Childrens Hospital of Wisconsin, Milwaukee, WI; 2Pediatrics, Medical College of Wisconsin, Milwaukee, WI

Limited published data describe the effects of appetite manipulation to wean children from gastrostomy tube (GT) feeding dependence. This study presents data relating to nutritional outcomes observed over the course of care for medically complex GT feeding dependent patients who completed an inpatient treatment protocol.

Methods: This retrospective study assessed a clinical cohort of children diagnosed with a feeding disorder, GT feeding dependence (greater than 1-year), and an inability to maintain acceptable growth via oral feeding from 2005-2012. These patients had all tube feedings discontinued and had three therapeutic meals each day to promote oral feeding. Due to concerns of acute nutrition and medical instability, patients were admitted to the inpatient unit of the hospital for medical monitoring. Data were collected on age, length of stay, past medical history, daily weight, oral calorie intake, oral fluid intake, days requiring supplementation either by rehydration solution, tube feeding formula or parenteral IV fluids, urine ketones, urine specific gravities and fasting blood glucose.

Results: 127 children ages 1-13 years (M=4.8; SD=2.5) were hospitalized for a duration of 2 to 21 days (M=10.1; SD=2.4). 58% of children were completely weaned from GT use by discharge and the remaining children all had some degree of tube use reduction. While hospitalized 55% of children had measurable ketones (M=1.3 days; SD=1.7), 58% had concentrated urine gravity (M=1.3 days; SD=1.7), and 12% experienced low blood sugars (M=2.0; SD=6.3). To prevent or treat acute nutrition problems 85% of children were supplemented with Enfalyte for hydration (M=6.3 days; SD=4.7), 17% were given formula supplementation (M=0.31 days; SD=1.3) and 5% received IV fluids (M=0.1 days; SD=0.6). Periods of nutrition instability typically occurred during the first 3 days of the hospital admission.

Conclusions: Patients undergoing appetite manipulation can be rapidly weaned from GT dependence. However, children may experience periods of nutrition instability, especially during the first few days of treatment. The inpatient facility was able to offer appropriate and effective medical support during these events. No predictors of medically instability were identified necessitating medical monitoring of all patients undergoing appetite manipulation.

469 PEDIATRIC HOME PARENTERAL NUTRITION PATIENTS WITH INTRAVENOUS LIPID RESTRICTION AT RISK FOR GLUCOSURIA. Meghan K. Dalton1, Casey B. Wall1, Brittany Tellier1, Sharon Collier1, Kathleen M. Gara2, Christopher Duggan1, Bram Raphael2, 1Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital Boston, Boston, MA; 2Pharmacy, Boston Children's Hospital, Boston, MA

Background: Using the hepatoprotective strategy of intravenous (IV) lipid restriction, patients on cycled home parenteral nutrition (HPN) may be exposed to glucose infusion rates (GIR) that exceed glucose oxidation rates.

Aim: To determine the frequency of glucosuria in HPN patients.

Methods: From 10/5/2011 to 5/2/2013, patients followed at Boston Children's Hospital Home PN program collected urinalysis for glucose during nocturnal infusion or first morning void. Inclusion criteria included GIR >20 mg/kg/min or clinical suspicion of PN dextrose intolerance (e.g., polyuria, polydipsia, altered mental status). Exclusion criteria included inability to collect urine specimen or lack of follow-up. Continuous outcomes expressed as median (IQR), unless otherwise mentioned.

Results: 59 HPN patients (short bowel syndrome n=39) submitted urine specimens. Age at first screening was 4.4 (3-7) years. IV lipid dose was 0.9 (0.8-1) grams/kg/day (Intralipid 60%, Omegaven 37%, no IV lipid 3%). PN infusion cycle was 12 (range 9-19) hours. Glucosuria occurred in 22% (13/59) patients, all of whom had GIR >20. 5 patients underwent alteration in PN cycling, usually increasing infusion time. The remainder only had glucosuria associated with acute stress (infection, post-operatively), which resolved when clinically stable. The mean (SD) GIR among patients with glucosuria 24 (8) vs. those without glucosuria 23 (8) (p=0.9). The presence of glucosuria was not associated with age, weight, weight Z-score, height Z-score, PN infusion time, PN frequency, PN energy, PN protein content, or IV lipid dose. GIR was significantly associated with PN energy intake (r=0.8, p<0.05).

Conclusion: Nearly one quarter of children receiving cycled HPN and IV lipid restriction have evidence of glucosuria. Appropriate monitoring of PN glucose intolerance is critical to identifying these patients.

470 A RETROSPECTIVE REVIEW OF NASOGASTRIC AND GASTROSTOMY TUBE PRACTICES AT A TERTIARY PEDIATRIC HOSPITAL. Amanda Ricciuto, Robert J. Baird, Ana Sant'Anna, McGill University, Montreal, QC, Canada

Background: Nasogastric (NG) and gastrostomy (GT) tubes are common methods for administering enteral nutrition support (ENS) to children with feeding difficulties. Despite published recommendations about the timing of GT insertion, there is little data clarifying best practices and differences in outcomes between both modalities. At our institution, (Montreal Children's Hospital; MCH), decisions regarding the route of ENS are non-standardized, with many patients on prolonged NG feeding. This study aims to characterize ENS practices at the MCH and to compare outcomes between prolonged NG and GT use. We hypothesize that earlier GT improves patient outcomes, specifically the development of oral feeding difficulties.

Methods: We performed a retrospective chart review of all pediatric patients (0-18 years) commencing long-term (≥3 months) nasogastric or gastrostomy feeds over a 5-year period (Jan 2007-Dec 2011) at the MCH, with follow-up until May 2013. Data was included for completed and active patients as appropriate. Variables recorded included patient demographics, diagnosis, occupational therapy assessment, baseline anthropometric parameters and patient/caregiver thoughts about starting ENS where available. Outcomes assessed included anthropometric parameters yearly until ENS completion or end of follow-up, duration of ENS and ENS-related complications, including user dissatisfaction, particularly if resulting in ENS discontinuation or a change in ENS modality. Complications were expressed as number of hospital visits per 1000 NG or GT days, and comparative statistics were calculated using the Fisher's exact test or student-t test as appropriate, with significance defined as p<0.05.
Results: 166 patients were identified. Of these, 49 were on NG only, 28 on GT only and 89 on NG followed by GT. The median number of days on NG feeds was 237 (range 0 to 1455 days). The majority of patients (84%) were assessed by occupational therapy. Food refusal was documented in 65 patients (39%); the incidence was 0.13 in those patients on NG ≤90 days and 0.5 in those on NG >90 days (RR 3.88, p<0.0001). Minor complications occurred in 75% of GT users (granulation tissue, tube displacement, leak) and 40% of NG users (predominantly tube displacement). Complications requiring hospital visits averaged 2.3 per 1000 GT days and 0.94 per 1000 NG days, with 13 episodes of aspiration pneumonia in both groups. The most common major GT complications were gastrocutaneous fistula and cellulitis, with 3 cases of gastric perforation. Although twice as many families expressed opposition to starting GT compared to NG (n=11, 9.4% vs. n=6, 4%), far more NG than GT users discontinued ENS or opted for the alternate feeding method due to negative experiences (11.6% vs. 1%).

Conclusion: These findings confirm that prolonged NG feeding is a common occurrence at our institution and that it is associated with the development of food refusal. A change in practice toward earlier GT may thus be warranted. Sufficient effort should be devoted to addressing patient or parental concerns regarding GT as this appears to be at least one of the barriers to early placement.

471 NASOGASTRIC TUBE FEEDING AT HOME: ANALYZING OUTCOMES IN A PEDIATRIC POPULATION. Danya Rosen, Rachael Schneider, Ruijun Bao, Patrice Burke, Clare Ceballos, Kathy Hoffstadter-Thal, Keith Benkov, Department of Pediatric Gastroenterology, Mount Sinai Medical Center, New York, NY

Home enteral nutrition (HEN) is often regarded as a safe and effective method to provide nutrition to children with chronic diseases. Advantages of HEN include shorter hospitalizations, lower cost, and decreased risk of secondary malnutrition-associated complications. There is limited pediatric data with regards to follow up and growth status after discharge to assess whether HEN is successful long-term. The purpose of this study was to conduct a retrospective chart review of children discharged on nasogastric (NG) feeds and to determine if there was adequate follow-up and an impact on growth. From January 2010 through December 2012 a total of 90 patients were enrolled and 20 were randomly selected for initial analysis. Patients were grouped by diagnosis, formula type and method of home feeding (bolus and/or continuous). We analyzed height and weight at time of discharge, 6 to 12 weeks after discharge and at time of NG feed discontinuation (if applicable). The median age of the population was 2.38 years with a range of 6 months to 18 years. Of the initial 20 patients analyzed, 65% (n=13) had an underlying diagnosis of congenital heart disease, 10% (n=2) had inflammatory bowel disease, 15% (n=3) had liver disease, 5% (n=1) had metabolic disease and 5% (n=1) had neurologic impairment. Fifty percent (n=10) were discharged on expressed breast milk or a standard infant formula, 15% (n=3) on a polymeric formula, 10% (n=2) on an amino acid formula, 10% (n=2) on a hydrolyzed protein formula, 5% (n=1) on a metabolic formula, and 10% (n=2) on other formulas. Seventy percent (n=14) were discharged on a combination of bolus and continuous feeds, 20% (n=4) on only continuous feeds and 10% (n=2) on only bolus feeds. All patients received NG teaching by a GI advanced practice nurse prior to discharge and all but one patient had visits from a homecare nurse. Upon review of feeding status at most recent follow up visit, 55% (n=11) had discontinued NG feeds. Of those, 8 had successfully completed treatment and were able to take full PO feeds, 2 patient's parents discontinued NG feeds on their own, and one patient was unable to maintain the tube in place. Twenty percent (n=4) continued on NG feeds, 5% (n=1) had a gastrostomy tube placed, 10% (n=2) were lost to follow up, and 10% (n=2) died after feeds had been discontinued. Z-scores were calculated from time of discharge to time of NG tube discontinuation for 14 out of the 20 patients, as 4 patients continued on NG feeds and 2 patients were lost to follow up. The average length of follow-up from hospital discharge to discontinuation of NG feeds was 7.2 months with a median of 4 months. During this time the average weight Z-score of the 14 patients improved from -3.1 (±0.3) to -2.5 (±0.3) and the average height Z-score improved from -2.1 (±0.4) to -1.3 (±0.3). By examining the data and identifying trends after discharge, we hope to provide valuable follow-up information that will serve as a quality improvement measure across the multiple departments that care for children with chronic illness.

472 RISK FACTORS FOR CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTIONS IN CHILDREN WITH INTESTINAL FAILURE. Catherine M. Sampert¹, Gregory J. Stoddard², M. Kyle Jensen¹, W. D. Jackson¹, ¹Pediatric Gastroenterology, Hepatology, and Nutrition, University of Utah, Salt Lake City, UT; ²Internal Medicine, University of Utah, Salt Lake City, UT

Importance: Central line associated bloodstream infections (CLABSI) are the greatest source of morbidity and mortality for children with intestinal failure (IF), yet limited data exist regarding which factors contribute most to CLABSI in these children.

Objective: To determine which of the following risk factors are most predictive of CLABSI: absent ileum, small bowel length <40cm, patient and catheter age, and >18 hours of parenteral nutrition daily. Secondary outcomes included PICC and antibiotic lock therapy (ALT).

Design: Retrospective cohort study.

Setting: Ambulatory and hospitalized patients at a tertiary pediatric medical center between January 1, 2005 and June 30, 2012. Participants: 157 patients were identified using ICD-9 codes associated with IF: 48 met inclusion criteria after chart review and comprised the study cohort.

Exposures: Included absent ileum, catheter age of ≥7 days, small bowel length <40 centimeters, patient age <90 days, >18 hours of parenteral nutrition (PN) daily, type of central venous catheter (CVC) and ALT.

Main Outcome Measure: Rate of CLABSI per 1,000 catheter days.

Results: We identified 357 CLABSI over 22,269 line-days in 48 patients, or 16 CLABSI per 1,000 catheter days. Median age at time of CLABSI was 1.18 years (IQR: 0.61-2.80 years), with 294 (82%) occurring in children with short bowel syndrome. Univariate analysis demonstrated that <40 centimeters of small bowel had the highest risk ratio (RR) of 2.83 (95% CI: 1.37,5.85), age <90 days a RR of 2.01 (95% CI: 1.28,3.17), absent ileum a RR of 2.10 (95% CI: 1.35, 3.29), and >18 hours of daily parenteral nutrition a RR of 1.72 (95% CI: 1.11, 2.67). Unexpectedly, catheter age ≥7 days had a low RR of 0.06 (95% CI: 0.04, 0.09). PICCs were the greatest modifiable risk factor, with a RR of 2.19 (95% CI: 1.65, 2.89) and ALT was the most protective factor with a RR of 0.47 (95% CI: 0.20, 1.12). Multivariate analysis confirmed these trends.
Conclusions and relevance: Our results identify significant risk factors for CLABSI in children with IF and quantify the impact of each variable. These findings offer a foundation for evidence-based interventions directed at the most significant, modifiable risk factors.

Table 1: CLABSI Characteristics

<table>
<thead>
<tr>
<th>Male (%)</th>
<th>204 (57)</th>
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<tr>
<td>Short bowel syndrome (%)</td>
<td>294 (82)</td>
</tr>
<tr>
<td>CIPO (%)</td>
<td>53 (15)</td>
</tr>
<tr>
<td>Median age (IQR)</td>
<td>1.18 years (0.61-2.80 years)</td>
</tr>
<tr>
<td>Total patients</td>
<td>48</td>
</tr>
<tr>
<td>Total CLABSI</td>
<td>357</td>
</tr>
<tr>
<td>Total Linedays</td>
<td>22,269</td>
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<tr>
<td>Mean CLABSI/1000 catheter days</td>
<td>16</td>
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</tbody>
</table>

CLABSI = central line associated blood stream infection, % = frequency with percentage, CIPO = chronic intestinal pseudo-obstruction, IQR = interquartile range

473 CAN GROWTH OF INFANTS WITH PNALD BE OPTIMIZED IN THE ERA OF LIPID RESTRICTED PN THERAPY? Timothio Sentongo¹, Stacy Kahn¹, Melanie Purser¹, Dana Weinstein¹, Ellen Newton¹, Kristin Wroblewski¹, Hillary Jericho¹, Ranjana Gohkale¹, Stefano Guandalini³, ¹Pediatrics, University of Chicago, Chicago, IL; ³Biostatistics, University of Chicago, Chicago, IL

Background: Restricting the dose of Soy-intralipids (SL) during Parenteral Nutrition (PN) therapy is now a widely accepted practice for prevention and management of PN associated liver disease (PNALD). However, there are currently no consistent criteria or standard approach for implementing SL restriction. Intralipids are important for providing calories and essential fatty acids during nutrition support. The objective of this study was to examine the growth outcomes in infants with PN dependency and PNALD managed using a consistent approach for implementing SL restriction.

Methods: All infants prescribed PN therapy between 7/2010 - 6/2011 enrolled. Infants were advanced to standard dose (2.5 - 3.0 g/kg/d) consistent approach of Stepwise SL Restriction (SSLR).

Results: Of 348 infants started on PN, 266 (76%) were weaned off in <3 weeks. Of the 82 infants who received PN for ≥3-weeks, 38 (14%) developed PNALD that was managed by SSLR. Infants who developed PNALD tended to have lower birth WAZ and LAZ scores compared those without PNALD (median/range): WAZ, -0.65 (-3.17, 2.00) vs. -0.14 (-1.91, 2.28), p = 0.068; LAZ -0.38 (-3.17, -2.00) vs. -0.20 (-2.48, 2.55), p = 0.06; higher prevalence of gastrointestinal problems: 39% vs. 20%, p = 0.059, and; longer duration of hospital stay: 17.5 weeks (3.0, 54.0) vs. 8.7 weeks (2.9, 33.6), p <0.001. However, growth outcomes at discharge in infants with PNALD managed using the SSLR approach did not differ from infants without PNALD who received standard dose SL: WAZ, -0.78 (-4.53, 3.22) vs. -0.77 (-3.64, 1.48), p = 0.68; LAZ, -1.68 (-6.91, 4.86) vs. -1.28 (-5.46, 1.36), p = 0.513; HCZ, -0.84 (-3.83, 1.30) vs. -0.51 (-4.16, 4.42), p = 0.153.

Conclusion: In this sample of infants who received PN therapy, only infants who developed PNALD were managed with SSLR. The growth outcomes in infants managed with this approach of SSLR did not differ from infants without PNALD who received standard dose SL. Future studies are needed to examine neurodevelopmental outcomes in infants managed with SSLR.

474 HEALTH BENEFITS AND TOLERANCE OF DIETARY FIBER SUPPLEMENTS IN CHILDREN. Sabeen A. Syed, Riad Rahhal, Warren P. Bishop, Pediatrics, University of Iowa, Iowa City, IA

BACKGROUND: Children in the US eat, on average, about half of the dietary fiber recommended by the USDA. Low fiber intake in this population may be associated with constipation and obesity.

HYPOTHESIS: Fiber supplementation will result in softer, more frequent stools, reduce obesity, improve QOL, and be well-tolerated.

METHODS: This was a prospective double-blind, placebo-controlled 4-month long study, funded by the General Mills Bell Institute of Nutrition, of 100 elementary school children 5-12 years old. All subjects received a rice-based snack bar twice daily at the school and at home on weekends/holidays. Children were randomized to soluble corn fiber-supplemented (5 g per bar, 10 g per day) or unsupplemented groups. Snack bars were indistinguishable in taste and texture between groups, and labeling did not reveal fiber content.

During the prestudy period, baseline characteristics (BMI, defecation patterns and QOL scores and a 3-day diet diary was obtained. Subjects were given two bars per day, with compliance monitored by the before and after school program. Families completed a weekly online diary via internet link on RedCap. At the end of the study, all characteristics of interest were reassessed, an exit questionnaire was administered, and analysis was performed.

RESULTS: At baseline, both groups were comparable in age, weight, height, BMI, quality of life scores, frequency and consistency of bowel movements, symptoms of abdominal pain, and frequency of fecal soiling. This middle-class population exhibited higher baseline
fiber intake (around 14 g per day) than previously reported in U.S. children (8 g per day). Compliance with study requirements was excellent in both groups (> 85%). Most children who dropped out stated that they had become tired of eating the snack bars. At the end of the study, no statistical differences were noted in weight, height, BMI, QOL scores, abdominal pain, or soiling episodes at the time points of interest. However, there was a statistically significant difference in stool consistency between the two groups. Compared to the placebo group, more subjects in the fiber group who began the study with harder stools (Bristol type 1-2) developed softer stools (Bristol type 3-5) as the study progressed. Stools were also more frequent in the fiber group. Although more subjects in the fiber group reported gassiness and belching compared to the placebo group (40% versus 10% for flatulence, P < 0.001; 16% versus 0% for eructation P 0.01), none dropped out of the study because of these symptoms. Most parents were able to guess to which group their child had been randomized, based on stool characteristics and presence or absence of increased gas.

Conclusion: Soluble fiber supplementation resulted in softer, more frequent stools but did not change BMI or the QOL index. Although increased flatulence and eructation was reported with fiber supplementation, it was well-tolerated.

**RESULTS OF EXIT QUESTIONNAIRE**

<table>
<thead>
<tr>
<th></th>
<th>Fiber</th>
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<th>p-value</th>
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<tbody>
<tr>
<td>Softer stools</td>
<td>29/49</td>
<td>7/47</td>
<td>&lt;.001</td>
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<tr>
<td>More frequent stools</td>
<td>25/49</td>
<td>10/47</td>
<td>.025</td>
</tr>
<tr>
<td>Guessed child took fiber</td>
<td>40/49</td>
<td>10/47</td>
<td>&lt;.001</td>
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</table>

**475 CORRELATION BETWEEN ADIPOSITY MEASURED BY BIOIMPEDANCE ANALYSIS AND SERUM INFLAMMATORY BIOMARKERS (CRP AND TNF-α) IN SCHOOLCHILDREN.** Carmen A. Sánchez-Ramirez, Fatima López-Alcaraz, Mariela del Toro Equihua, Mariana Orta-Duarte, Yunue Flores-Ruelas, Facultad de Medicina, Universidad de Colima, Colima, Mexico

Aim. To correlate adiposity using bioimpedance analysis, body mass index, waist circumference, triceps skin fold and subscapular skin fold with the serum concentrations of C-reactive protein and tumor necrosis factor alpha in schoolchildren.

Patients and Methods. Design: cross sectional. Data were collected from 74 schoolchildren randomly selected in a local primary school in the city of Colima, Mexico. The mean age was 9.4 years (1.5, SD); thirty-three (44.6%) children were girls. The adiposity (percentage of fat mass) was measured using bioimpedance analysis and anthropometric measurements. Serum C-reactive protein and tumor necrosis factor alpha were determined with enzyme-linked immunosorbance assay. The association between adiposity and serum inflammatory biomarkers was assessed with a Pearson's correlation.

Results. Significant correlations were identified between serum levels of C-reactive protein with the adiposity determined by bioimpedance analysis (r=0.358, p=0.002); body mass index (r=0.307, p=0.008); triceps skinfold (r=0.293, p=0.011); and subscapular skinfold (r=0.316, p=0.006). No correlation was found between adiposity and serum tumor necrosis factor alpha.

Conclusion. Subclinical inflammation manifested by higher serum levels of C-reactive protein was identified in schoolchildren with higher percentage of fat mass determined by bioimpedance analysis and other anthropometric measurements.

**476 USE OF ORAL NUTRITION SUPPLEMENTS REDUCES LENGTH OF STAY AND EPISODE COST IN HOSPITALIZED PEDIATRIC PATIENTS AGED 2 TO 8.** Jacqueline Vanderpuye-Orgle1, Maria Mascarenhas2, Darius N. Lakdawalla3, Chris LaVallee1, Mark Linthicum1, Julia Thornton Snider1, Precision Health Economics, Los Angeles, CA; 2The Children’s Hospital of Philadelphia, Philadelphia, PA; 3University of Southern California, Los Angeles, CA

Objectives: To assess the effect of oral nutritional supplement (ONS) use on inpatient length of stay and episode cost in pediatric patients.


Methods: Analyses were conducted using the Premier Perspectives Database, which contained data on 557,348 pediatric inpatient episodes of any primary diagnosis involving patients aged 2-8 years. A matched sample of ONS and non-ONS episodes was created, using propensity score matching. To eliminate bias from confounding, instrumental variables regression analysis was performed to quantify the effect of ONS use on length of stay and episode cost.

Results: Within the database, 1.09% of 557,348 pediatric inpatient episodes (ages 2-8 years) involved ONS use. Based on a matched sample of 11,031 episodes, ONS patients had a shorter length of stay by 1.39 days (95% confidence interval [CI] 0.11 to 2.67), from 7.68 to 6.28 days (18.1% decline). In the same matched sample, ONS patients had a decreased episode cost of $1146 (95% CI -$1433 to -$859), from $17,642 to $16,495 (6.5% decline).

Conclusions: Use of ONS decreases length of stay and episode cost in the pediatric inpatient population. Thus, the use of ONS in hospitalized pediatric patients may provide a cost-effective, evidence-based solution in the evolving healthcare environment.

**477 VITAMIN B12 DEFICIENCY IN CHILDREN WITH INTESTINAL RESECTIONS IN INFANCY.** Juliana Vaughan1, Timothy Sentongo2, Cassandra Sova1, Praveen S. Goday4, 1University of Arkansas for Medical Sciences, Little Rock, AR; 2The University of Chicago, Chicago, IL; 3Children's Hospital of Wisconsin, Milwaukee, WI; 4Medical College of Wisconsin, Milwaukee, WI

Background: Vitamin B12 deficiency may present with neurological symptoms before onset of anemia. Deficiency of vitamin B12 is confirmed by detecting low serum B12 in association with increased serum methylmalonic acid (MMA) levels that improve following appropriate therapy.

Hypothesis: In children, vitamin B12 deficiency after intestinal resection is diagnosed by a combination of a low serum vitamin B12 and an
elevated serum MMA.

Aims:
1. To describe the clinical characteristics of children with vitamin B12 deficiency after intestinal resection in the first 2 years of life
2. To determine the sensitivity and specificity of various levels of vitamin B12 at predicting MMA levels

Methods: Retrospective multicenter study of children with significant intestinal resections in the first 2 years of life. Vitamin B12 deficiency was defined as an elevated MMA level that either decreased by 50% or normalized with parenteral vitamin B12. We also studied all children with intestinal resections who had simultaneous vitamin B12 and MMA levels documented.

Results: We identified 14 children with B12 deficiency (male=7). Median age at diagnosis was 34 months (range 11-175). Patients were on parenteral nutrition (PN) for a median of 8.5 months (range 1-56) and were diagnosed with B12 deficiency a median of 14 months (range 3-114) after PN cessation. One patient remains on PN. Of the 12 children where the extent of resection was available, 8 had no ileum. Only 4/14 children had their ileocecal valve (status unknown in 1 child). None of the children had concomitant gastric resections or concerns for pancreatic insufficiency. None of the children had anemia and one child presented with ataxia which improved with therapy. Median B12 and MMA levels at diagnosis were 299 pg/ml, (IQR 108.75) and 1537.5 nmol/l, (IQR 954.25) respectively and improved to 730.5 (IQR 403.75) and 440 (IQR 352.5) respectively after parenteral B12 therapy.

The sensitivity and specificity of B12 levels at predicting MMA levels of more than 400 and 1000 nmol/l are shown in the table. Conclusions: Vitamin B12 deficiency in children in which partial and complete ileal resections usually occurs after cessation of PN and biochemical parameters improve with therapy. The median duration to diagnosis of B12 deficiency in this sample of children was 14 months after discontinuation of PN. While a vitamin B12 level <200 pg/ml is extremely specific for predicting high MMA levels, levels between 200 and 400 have moderate sensitivity and specificity at predicting these levels. We suggest that patients at risk for vitamin B12 deficiency be monitored using a combination of vitamin B12 and MMA levels.

Sensitivity and specificity of vitamin B12 levels in predicting MMA levels

<table>
<thead>
<tr>
<th>Vitamin B12 &lt;200 at predicting MMA&gt;400</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Vitamin B12 &lt;400 at predicting MMA&gt;400</td>
<td>69.2%</td>
<td>85.9%</td>
</tr>
<tr>
<td>Vitamin B12 &lt;200 at predicting MMA&gt;1000</td>
<td>31.6%</td>
<td>100%</td>
</tr>
<tr>
<td>Vitamin B12 &lt;400 at predicting MMA&gt;1000</td>
<td>84.2%</td>
<td>70%</td>
</tr>
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</table>

MMA: Methylmalonic acid, nmol/l; Vitamin B12, pg/ml
THE ROLE OF FOLATE RECEPTOR AUTOANTIBODIES IN PRETERM BIRTH. Hanh D. Vo, Agnes Perenyi, Jeffrey M. Sequeira, Steven M. Schwarz, Edward V. Quadros, Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY; Medicine, SUNY Downstate Medical Center, Brooklyn, NY

Background: Folate deficiency has been associated with adverse pregnancy outcome and fetal developmental anomalies. Prior publications have shown that an autoantibody (FRAb) directed against folate receptor (FR) α is implicated in subfertility and neural tube defects in the fetus. The aims of this pilot study were to measure the prevalence of FRAbs in pregnant women who gave birth prematurely, and to compare it with that of the general population.

Methods: We conducted a prospective study by documenting clinical variables of mother-infant pairs, and determining blocking and binding FRAbs in mother's blood and cord blood. Infants with gestational age (GA) ≤ 32 weeks and/or birth weight ≤ 1,500 g were included. Mothers with known or suspected immune disorders and their infants were excluded. Blocking FRAbs were measured by the blocking of radiolabeled folate binding to a known amount of purified FRα from human milk. Binding IgG FRAbs were quantified by an ELISA-based assay.

Results: Thirty-three pregnant women's blood was analyzed for FRAbs along with their 15 premature infants' cord blood (2 women with twin pregnancy). All but one mother gave birth via C-section; three women (23%) had a history of preterm birth; and 10 women (77%) went into preterm labor in the current pregnancy. Mean GA was 28.4 ± 2.6 weeks (range: 24-31.6 weeks). Mean birth weight was 1,112 ± 362 g (range: 650-1,760 g). Binding FRAbs were detected in 8/13 mothers and in 3/15 infants. Blocking FRAbs were positive in 1/12 mothers and in 6/8 of the cord blood samples. Overall, FRAbs were found in 69% of the mother's blood and in 75% of the cord blood samples.

Mean binding and blocking FRAb titers (pmoles/ml) were 0.36 ± 0.16 and 0.33 in the mothers, and 0.43 ± 0.16 and 0.57 ± 0.35 in the cord blood, respectively.

Conclusions: The prevalence of maternal FRAb autoimmunity (69%) in this study was found to be much higher than in the US population (10-15%). Our preliminary data suggested that FRAb autoimmunity might be a contributing factor to poor pregnancy outcome, i.e. premature labor, which could be prevented with appropriate testing and therapeutic intervention. We plan to investigate further the possible mechanism of maternal and fetal sensitization resulting in FRAb production and its possible clinical correlates.

Genetic Licensing Uncovers a Role for NK Cells in Immune Colitis by Co-Activation of CD4+ T Cells. Susy Yusung, Lin Lin, Jonathan Braun, Pediatric Gastroenterology, UCLA, Los Angeles, CA; Department of Molecular and Medical Pharmacology, UCLA David Geffen School of Medicine, Los Angeles, CA; Department of Pathology and Laboratory Medicine, UCLA David Geffen School of Medicine, Los Angeles, CA

Natural Killer(NK) cells are members of the innate immune system mainly known for their cytolytic abilities. They are divided into distinct subsets comprised of licensed and unlicensed NK cells. NK cells are programmed at a genetic level to express discriminating Killer Immunoglobulin Receptors (or KIRs) in humans and Ly49 receptors in mice. The engagement of these receptors by its cognate HLA ligand induces differentiation of NK cells into a licensed subset which has functional properties distinct from the unlicensed types. In humans, evidence suggests that genetic licensing is a risk factor for Crohn's disease and recent work (L Lin et al) uncovered diverse cytokine production states programmed by genetic licensing. However, limited and discrepant studies exist on the relationship of NK cells to immune mediated colitis. To biologically test this genetic association, this study investigates the interaction between licensed NK cells and CD4+ T cells which are well known mediators of inflammation in mouse colitis models. Here we show that licensed NK cells from C57/BL6 mice augment CD4+ T cell proliferation ex vivo. Multiplex cytokine analysis of licensed NK cell media also demonstrate higher levels of Interleukin-6(IL-6), Interferon-gamma(IFNg), and Tumor necrosis factor-alpha(TNFα) production compared to unlicensed NK cells. This cytokine profile mirrors the cytokine secretion profile of licensed human NK subsets. In contrast to licensed human NK cells however, transwell studies showed that licensed NK cell stimulation of CD4+ T cells occurred in a synaptic contact dependent manner. Antibody blockade of candidate receptor-ligand interactions (OX40-OX40L, CD28-CD86, CD28-CD80) between NK and CD4+T cells diminished the stimulatory effect of NK cells. In conclusion, augmentation of CD4+T cells by licensed NK cells is mediated by soluble cytokines and contact dependent manner in the mouse model, which is different from the solely cytokine mediated stimulation seen in humans.

Cell-Mediated Immunity in Infants Vertically Exposed to Hepatitis C Virus. Ryan Cox, Bomi Omikuinle, Christopher Walker, Jonathan Honegger, Gastroenterology, Hepatology, and Nutrition, Nationwide Children's Hospital and the Department of Pediatrics, The Ohio State University, Columbus, OH; Infectious Diseases, Nationwide Children's Hospital and the Department of Pediatrics, The Ohio State University, Columbus, OH; Center for Vaccines and Immunity, The Research Institute at Nationwide Children's Hospital, Columbus, OH

BACKGROUND: While vertical transmission is the leading cause of hepatitis C virus (HCV) infection in children, only 4-7% of vertically-exposed infants are infected. Multiple maternal and obstetric risk factors play a role in HCV vertical transmission including high maternal HCV viral load, maternal HIV, fetal scalp electrodes, and prolonged rupture of membranes. Given the overall low transmission rate however, we suspected that fetal and/or infant cellular immunity may provide a protective role. HCV-specific T-cell responses are important for clearance of acute HCV in adults, and these virus-specific responses have also been detected in seronegative,
aviremic individuals with occupational, sexual, or household contact with HCV (including older children born to HCV-infected mothers). No published studies have addressed whether these potentially protective HCV-specific T-cells are detectable in the first year of life following vertical exposure.

OBJECTIVE: To determine the presence of HCV-specific T-cell responses in infants vertically exposed to HCV.

DESIGN/METHODS: We prospectively enrolled HCV-RNA positive and negative pregnant women and their infants from a high risk obstetrics clinic, and infant blood was evaluated for HCV-RNA and HCV-specific T-cell immunity. Antigen-specific T-cell responses were measured by IFN-γ ELISpot assay and upregulation of extracellular activation markers (CD25, CD69, and CD134) on flow-cytometry using peripheral blood mononuclear cells (PBMCs) stimulated with genotype-matched HCV peptides pools.

RESULTS: Fourteen children born to HCV genotype 1 or 3 infected mothers were tested by IFN-γ ELISpot assay in the first 3-6 months of life. HCV-specific responses were detected in 0 of 12 HCV-RNA negative children and 1 of 2 HCV-RNA positive infants. To investigate the possibility that the HCV-RNA negative children had HCV-specific T-cell responses that lacked capacity to produce IFN-γ, antigen-specific activation marker upregulation was compared in 19 HCV-RNA negative infants born to HCV infected mothers and 7 infants born to uninfected mothers. Overall we did not detect significant differences in upregulation of CD25, CD69, or CD134 on CD4+ or CD8+ T-cells exposed to HCV peptides from infants vertically exposed to HCV versus those who were not exposed.

CONCLUSIONS: HCV-specific T-cell responses were detected in 1 of 2 HCV-infected infants in the first 6 months of life but not in uninfected, vertically-exposed infants using sensitive IFN-γ ELISpot and surface marker assays. These findings suggest that infant T-cell immunity may not contribute to defense against vertical transmission of HCV and that other cellular or humoral mechanisms of protection warrant investigation.

483 THE DISTRIBUTION OF HAPTOGLOBIN GENOTYPES IN AUTOIMMUNE AND INFLAMMATORY DISORDERS.

Craig Sturgeon1,2, Anna Sapone3, Debora Angrisani1, Amalia Cirillo1, Laura De Magistris3, Alessio Fasano1,1 Pediatrics, Massachusetts General Hospital, Charlestown, MA; 2Graduate School in Life Sciences, University of Maryland, Baltimore, Baltimore, MD; 3Experimental Medicine, Second University of Naples, Naples, Italy

Intestinal permeability has recently been implicated in many inflammatory disorders including celiac disease, type-1 diabetes, autism, inflammatory bowel disease, and asthma. Zonulin is a major regulator of intestinal permeability and is overexpressed in celiac disease and diabetes. We have described zonulin to be the precursor to haptoglobin 2 (pHP2). Prior to our identification of zonulin as pHP2, haptoglobin genotypes have been shown to be associated with many disorders. We therefore explored the distribution of haptoglobin genotypes in inflammatory disorders. We genotyped a total of 224 celiacs, 138 T1D, 50 Sjogrens and 41 autistic patients. We compared these results to previously published controls. The controls had a genotype distribution of 16.5% HP1-1, 48.3% HP2-1 and 35.0 % HP2-2. The genotype distribution for celiacs is 13.4 % HP1-1, 42.0% HP2-1, and 44.6% HP2-2. The genotype distribution for diabetics is 20.3% HP1-1 49.3% HP2-1, 30.4% HP2-2. The genotype distribution for Sjogren's disease is 18.0% Hp1-1, 46.0% HP2-1, and 36.0% HP2-2. The genotype distribution for Autism is 9.8% HP1-1, 56.1% HP2-1, and 34.1% HP2-2. Only the genotype distribution for celiac disease reached statistical significance (p<0.01). There was no difference for T1D or Sjogrens disease patients. While the distribution for autism did not reach statistical significance there is still a shift of genotypes away from HP1-1. Combined these data show that both celiac disease and autism show a shift away from the HP1-1 genotype, while only celiac disease shifts toward HP2-2. Both T1D and Sjogren's patients show similar distributions to controls.

484 RESPONSE TO HEPATITIS B VACCINATION IN THE AMERICAN FAMILY CHILDREN'S HOSPITAL CELIAC POPULATION. Matthew D. Egberg2, Dorota Walkiewicz2, Jens Eckhoff5, Pediatrics, University of Wisconsin, Madison, WI; 2Pediatric Gastroenterology and Nutrition, Children's Hospital Boston, Boston, MA

Background: Studies of adult patients with Celiac Disease (CD) have shown insufficient protective antibody titers to Hepatitis B (HB) following the primary vaccination series. The non-response rate in the general healthy population ranges from 5-10%. A gap exists in the literature in regards to pediatric CD populations and the response to vaccination.

Objective: The purpose of this study is to identify pediatric CD patients at the American Family Children's Hospital, Madison, WI who received the primary HB vaccination series to HB and investigate their immunologic response to HB vaccination.

Design/Methods: Chart review (electronic and paper) was used to identify AFCH Celiac patients (biopsy changes and positive serology for celiac disease) and those who received the primary HB vaccination series. Patients were then compared to patients who did not receive the HB vaccination series for antibody titers to HB. Results were compared using t tests.

Results: 54 patients had titers drawn and 53 results were available for analysis. 46% of respondents were male and the mean age of patients was 9.6 years (SD 4.9). 52% had additional co-morbidities. Of the 53 patients analyzed, 31 (58.4%) did not meet the titer threshold for "protective" antibody titers. The mean time between completion of HB vaccination and diagnosis of CD was 8.1 years (SD 3.8) and 10.5 years (SD 4.4) for responders and non-responders respectively (p= 0.0607). Time between completion of vaccine series and diagnosis of CD was identified as a statistically significant predictor of response to the vaccine with an odds ratio of 0.69 (p= 0.0214), after adjusting for age and comorbidities.

Conclusions: The pediatric CD population at AFCH shows a high rate of response failure to the primary HB vaccination series. There is indication that time between completion of HB vaccination and diagnosis of CD is an independent predictor for response.
Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease in the adult and pediatric population. NAFLD has significant public health implications as it has multiple associated co-morbidities including obesity, hypertension, type 2 diabetes, and cardiovascular disease, all of which increase the risk of premature death. NAFLD denotes a histological spectrum of disease ranging from macrovesicular steatosis, to steatohepatitis with inflammation, to fibrosis. NAFLD is a complex disease that has 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 IPS-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. 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.

**IMAGING MUCOSAL SURFACES WITH MICRO-OPTICAL COHERENCE TOMOGRAPHY.** Mark E. Kusek1,2, Kengyeh K. Chu1, Linbo Liu1, Eric Wildstrander1, Gregory Dierksen1, Wayne G. Shreffler2, Guillermo J. Tearney3, Bryan P. Hurley2
1Pediatric Gastroenterology, Massachusetts General Hospital for Children, Boston, MA; 2Mucosal Immunology Lab, Massachusetts General Hospital for Children, Charlestown, MA; 3Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA; Center for Immunology and Inflammatory Diseases, Massachusetts General Hospital for Children, Boston, MA

Paramount to effective host defense is the mobilization of neutrophils from the vasculature through extracellular matrix and across epithelial barriers in response to pathogens capable of infecting various mucosal surfaces. Although this influx of inflammatory cells is necessary for resolution of infection, it also brings deleterious consequences by mediating nonspecific tissue damage. An in vitro model of intestinal epithelial cells grown on permeable Transwell filters has been previously developed and is widely employed to elucidate key features of host-pathogen interactions as well as neutrophil trans-epithelial migration. Leveraging a novel imaging tool called micro-Optical Coherence Tomography (μOCT), we sought to explore key pathological events occurring at mucosal surfaces modeled using the in vitro Transwell system. The imaging technique, μOCT, enables visualization using near-infrared light of living biological tissues at a cellular level without need for sample fixing or staining. μOCT also supports 3D reconstruction of imaging targets as well as the ability to observe changes occurring within a fixed area of the target over a defined period of time. Results indicate that μOCT is capable of revealing clearly resolvable images of the polarized epithelial monolayer grown on the Transwell filter. Further, treatment of the monolayer with EDTA results in a loss in polarity and barrier integrity that is perceivable upon imaging with μOCT. The dynamic process of neutrophil trans-epithelial migration in response to a gradient of the chemo-attractant fMLP is observed using μOCT, whereby neutrophils are distinguishable from epithelial cells and migrate in clusters across the epithelial barrier. Investigation of mucosal surfaces with μOCT provides a new visual perspective that will likely lead to novel insight unveiling key mechanistic features of the complex interactions between inflammatory cells, epithelial cells, and pathogens. A better understanding of these mechanisms facilitated by further exploration using μOCT will assist in the development of novel therapeutics to reduce the detrimental effects of infection with pathogens and mucosal inflammation.

**ROLE OF THE VOPE EFFECTOR PROTEIN IN V. CHOLEREA TYPE THREE SECRETION SYSTEM MEDIATED PATHOGENESIS.** Vibha Sood1, Kelly A. Miller1, Michelle Dziejman1, 1Division of Pediatric Gastroenterology and Nutrition, Golisano Children's Hospital,University of Rochester Medical Center, Rochester, NY; 2Department of Microbiology and Immunology, School of Medicine and Dentistry,University of Rochester, Rochester, NY

*Vibrio cholerae* is a Gram-negative bacterium that can cause the life threatening diarrheal disease, cholera, typically when ingested via contaminated water sources. Bacteria are found in marine environments worldwide, but endemic disease is restricted mainly to Southeast Asia, Africa, South America, and countries where infrastructure has been disrupted by environmental disaster, war or overcrowding. As a species, *V. cholerae* is very diverse in its genetic content and pathogenic potential. Strains can be classified based on the structure of the variable somatic O-antigen, and more than 250 serogroups have been identified to date. Although only O1 and O139 serogroup strains cause pandemic and epidemic disease, strains of other serogroups, referred as non-O1/non-O139 serogroup strains, are associated with sporadic disease globally and have recently been documented as causing limited outbreaks. A subset of pathogenic non-O1/non-O139 serogroup strains cause disease using Type 3 Secretion System (T3SS)-mediated mechanisms, instead of the classical virulence factors (e.g. cholera toxin) present in epidemic strains. The T3SS is encoded on a ~48 kb genomic pathogenicity island that includes the genes for the secretion apparatus, effector proteins that are translocated from the bacteria into the mammalian host cell, and two transmembrane transcriptional regulators, VtrRα and VtrRβ. Our studies use a clinically isolated, T3SS-positive O39 serogroup strain named AM-19226, which encodes 12 effector proteins. We are interested in understanding how the effector proteins function to promote host colonization as well as to cause diarrheal disease, presumably by disrupting intestinal cell homeostasis. In other bacterial pathogens, effector proteins can function individually or cooperatively, and have various roles in both promoting disease and in stabilizing some cellular functions to ensure a productive infection. Although most effector proteins do not share amino acid similarity with known proteins, the *V. cholerae*...
VopE protein encodes a Rho GTPase domain motif that is also present in effector proteins from other bacterial species, such as the *Yersinia pseudotuberculosis* effector YopE. We hypothesize that VopE functions to modulate host cell signaling by interacting with eukaryotic Rho proteins. To begin to understand the role of VopE in *V. cholerae* pathogenesis, we determined whether VopE is necessary for colonization in vivo using an infant mouse model, and evaluated whether VopE is important for bile-dependent cytotoxicity in vitro in a Caco2-BBE mammalian cell culture model. The results indicate that VopE does not play a significant role in colonization or cytotoxicity in either model. We therefore predict that VopE performs a redundant function or functions to moderate cell signaling disrupted by other effectors during infection.

488*  THE ROLE OF THE INTESTINAL STEM CELL NICHE IN REGULATING THE EPITHELIAL RESPONSE TO CHEMOTHERAPEUTIC INJURY. Kristen Seiler, Richard von Furstenberg, Michele Bresler, Susan Henning, UNC Chapel Hill, Cary, NC

Background: The chemotherapeutic agent doxorubicin causes intestinal stem cell (ISC) death with subsequent crypt degeneration, followed by robust ISC proliferation to regenerate the intestinal epithelium. A growing body of work implicates the ISC niche in regulating ISC behavior. However, the cellular and molecular factors responsible for eliciting ISC responses remain poorly characterized.

Hypothesis: Following damage from doxorubicin, ISCs are dependent on niche signals to induce a regenerative epithelial response.

Methods: Mice were dosed with doxorubicin at 15 mg/kg and sacrificed at 0 (no treatment), 2, 4, 6, and 8 days after treatment. Jejunal specimens were harvested for histology and crypt culture. A separate group of animals was injected with EdU prior to sacrifice for analysis of ISC proliferation by flow cytometry using CD24 antibodies as described by von Furstenberg et al. 2011. Crypts were cultured in a Matrigel-based system employing R-spondin and Y compound which supports development into enteroids with minimal budding. Co-culture of untreated crypts with epithelial-depleted jejunal tissue (EDJT) was used to assess proliferation signals from the ISC niche. The primary outcome was the number of buds per enteroid following 7 days in culture. Results: By histology, maximum crypt depth occurred at 6 days after doxorubicin, whereas crypt fission was significantly increased by day 8 after doxorubicin. This suggested that regenerative signals were likely elevated prior to day 6, leading us to investigate proliferative niche signals and ISC activity at day 4 after doxorubicin. Flow data confirmed increased ISC proliferation 4 days after doxorubicin: 19.5% of CD24lo cells were EdU positive in controls vs. 35.5%, 4 days after doxorubicin. In culture, there was no apparent difference in the endogenous proliferative activity of crypts harvested from doxorubicin-treated vs. control mice, suggesting that proliferative signals were not maintained in the absence of niche stimuli. However, the addition of EDJT collected from mice 4 days after doxorubicin resulted in a significantly increased average bud number per enteroid [control crypts with 1.63 ± 0.36 buds (n=6) vs. 5.16 ± 2.11 buds of control crypts plus EDJT from mice 4 days after doxorubicin (n=3)]. Conclusions and Future Directions: These data suggest a critical role of the intestinal niche in regulating the proliferative response of the ISC following epithelial damage. Transcriptome analysis of EDJT with confirmatory staining will lend insight to the cellular and molecular factors regulating this response. Identified proliferative factors will be explored further in our crypt culture model.

This work was supported by the National Institutes of Health Grants T32-DK007773, P30-DK034987, and U01-DK085547. The latter grant is part of the Intestinal Stem Cell Consortium, a collaborative research project funded by the National Institute of Diabetes and Digestive Kidney Diseases and the National Institute of Allergy and Infectious Diseases.

Research Session V: Intestinal Disorders

489  A CYTOKINE SIGNATURE FROM ESOPHAGEAL MUCOSA DIFFERENTIATES EOSINOPHILIC ESOPHAGITIS FROM GASTROESOPHAGEAL REFLUX DISEASE. Wael N. Sayej1, Antoine Menoret1, Marina Fernandez1, Francisco Sylvester1,2, Zhu Wang1, Jeffrey Hyams1, Tony Vella1,2, 1Digestive Diseases, Hepatology and Nutrition Center, Connecticut Children’s Medical Center, Hartford, CT; 2Immunology, University of Connecticut Health Center, Farmington, CT

Background: Eosinophilic esophagitis (EoE) is characterized by infiltration of eosinophils into the esophageal mucosa in the absence of acid reflux (GER). However, it is challenging to differentiate between EoE and GER in individual patients due to the overlap in clinical features in the two conditions.

Hypothesis: Esophageal mucosa from patients with EoE will demonstrate a distinct cytokine profile from children with GER.

Methods: We enrolled 44 patients: 12 with EoE, 14 EoE in remission (13 with diet restriction alone), 13 controls and 5 with GERD. We collected 5 endoscopic esophageal biopsies from each patient. We then phenotyped lymphocytes (TCR-αβ, γδ, CD3, CD4, and CD8) from 4 collagenase/dispase-digested biopsies and measured their cytokine potential (TNF-α and IFN-γ) by flow cytometry. Another biopsy (10 EoE, 5 EoE in Remission, 5 Control, 5 GERD) was placed in cell culture medium in a 5% CO2 atmosphere at 37 °C for 72 hours. Cytokines in the culture supernatant were measured by multiplex cytokine array (Myriad RBM™).

Results: There was no difference in the CD3+ TCRαβ+ CD8+/CD4+ ratio between the 4 study groups. CD3+ cells had greater IFN-γ production potential in EoE (21.89 %, n =10) and controls (24.08 ± %, n =5) compared to the EoE-remission (9.25 %, n =5), p<0.05. Specifically, there was a significant difference in CD8+ IFN-γ potential compared to CD4+ T cells (33.64% vs. 11.81%), p<0.01. When comparing the groups, 40.4% of CD8+ T cells in the EoE group and 41.1% of the controls produced significantly higher amounts of IFN-γ than the EoE-remission group (19%), p<0.01. There was a significant difference in TNF-α production by CD8+ T cells compared to CD4+ T cells. In the CD3− lymphocytes, however, there was a significantly higher potential for IFN-γ production in the EoE group compared to those in remission and controls raising a possible role for other non-T cell lymphocytes. Lastly, culture supernatants taken from explant esophageal tissue demonstrate the presence of a cytokine profile that reliably distinguished EoE from the other study groups. Unsupervised principle component analysis and cluster analysis based on these cytokines showed distinct grouping of EoE patients from other cases. The cytokines include IL-6, IL-8, IL-10, Macrophage Inflammatory Protein 1 beta (MIP-1b), Monocyte Chemotactic Protein 1 (MCP-1), Intercellular Adhesion Molecule-1 (ICAM-1), and Tumor necrosis factor alpha.

Summary: Our results suggest a previously unappreciated role for CD8+ T Lymphocytes and a distinct mucosal cytokine mucosal
network that may differentiate EoE from GERD. Since endoscopic biopsies largely sample the esophageal epithelial layer, our results suggest that esophageal epithelial cells may have immune effector functions in EoE. Our results also indicate that macrophages and possibly dendritic cells play a role in the inflammatory cascade that leads to eosinophilic esophagitis.

**490 ALGESIA DURING PEDIATRIC COLONOSCOPY: A DOUBLE-BLIND RANDOMIZED CONTROLLED STUDY COMPARING TWO PROTOCOLS FOR PROCEDURAL SEDATION USING COMPLEMENT OF KETAMINE VERSUS PLACEBO.**

Celine Halb1, Kelly Grzywacz2, Patricia Perrault3, Valerie Marchand4, Colette Deslandres1, Prevost Jantchou1, Edith Villeneuve5, Denise Herzog1, Christophe Faure1, 1Division of Pediatric Gastroenterology, Department of Pediatrics, CHU Ste-Justine, Montreal, QC, Canada; 2Department of Pediatric Anesthesiology, CHU Ste-Justine, Montreal, QC, Canada

The aim of this study was to compare the pain and discomfort during colonoscopy in patients receiving our standard protocol of IV midazolam and IV meperidine with the addition of IV ketamine or placebo. Patients and Methods: We performed a double-blind, randomized controlled and IRB approved trial. Patients > 10 years of age, undergoing a colonoscopy were included. The protocol for sedation consisted of midazolam 0.1 mg/kg IV and meperidine 1mg/kg IV, and a placebo in the first group (Group A) or IV ketamine 0.5mg/kg in the second group (Group B). Two rescue doses of meperidine were permitted during colonoscopy. Presence of pain and discomfort during colonoscopy and adverse reactions including hypoxemia, bradycardia, hypertension, hypotension, hallucinations, vomiting and nystagmus were recorded. Results: Eighty-nine children (53 girls, median age 15.5 years, range 10 - 18.4) were included. There was no difference in demographics (age, sex ratio, weight and indication for colonoscopy) between the 2 groups. Results (number; %) are reported in Table 1. Conclusion: Although adverse events occurred more frequently with ketamine, severe adverse reactions including hypoxemia, bradycardia and desaturation were similar between the 2 groups. Administration of IV ketamine in addition to midazolam and meperidine is safe and decreases pain and discomfort during colonoscopy.

Table 1

<table>
<thead>
<tr>
<th>Pain/discomfort during endoscopy</th>
<th>Group A (n=46)</th>
<th>Group B (n=43)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rescue during endoscopy</td>
<td>26 (57%)</td>
<td>15 (35%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>All adverse events</td>
<td>22 (48%)</td>
<td>6 (14%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe adverse reaction only (Hypotension, bradycardia, desaturation)</td>
<td>17 (37%)</td>
<td>29 (67%)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**491 ESOPHAGEAL EPITHELIAL CELLS ACQUIRE FUNCTIONAL CHARACTERISTICS OF ACTIVATED MYOFIBROBLASTS FOLLOWING THE DEVELOPMENT OF EPITHELIAL TO MESENCHYMAL TRANSITION.**

Amanda Muir, Sarit Toltzis, Mei-Lun Wang, Children's Hospital of Philadelphia, Philadelphia, PA

Background and Aims: Eosinophilic esophagitis (EoE) is an allergic inflammatory disease characterized by esophageal infiltration of eosinophils. The most devastating side effect of EoE is the scarring and fibrosis that lead to dysphagia and food impaction. Consistent with the reports of others, we have recently shown that in EoE, esophageal epithelial cells can undergo epithelial to mesenchymal transition (EMT), acquiring features of activated myofibroblasts. In our model, we proposed that cross-talk between esophageal epithelial cells and fibroblasts lead to epithelial transdifferentiation under the influence of fibroblast-derived cytokines including TNFα, and IL1β. Whether epithelial cells exposed to a profibrotic cytokine milieu can also acquire the functional characteristics of activated myofibroblasts, including cell migration and ECM deposition, is highly relevant to our understanding and treatment of EoE associated fibrogenesis. In the current study, we investigated cell mobility and extracellular matrix production of epithelial cells that have undergone EMT. Methods and Results: Stimulation of human non-transformed immortalized esophageal epithelial cells (EPC2-hTERT) with known profibrotic cytokines TNFα, TGFβ, and IL1β for three weeks led to acquisition of mesenchymal αSMA and loss of epithelial e-cadherin expression, along with changes in cell morphology consistent with EMT. To evaluate migration, we performed an in vitro scratch test followed by live cell imaging using Nikon Eclipse Ti-U movie-making technology. Interestingly, the unstimulated injured cells that had not undergone EMT, did not migrate over a 24 hour time period. However, cells stimulated with the pro-fibrotic cytokines became mobile and elongated and were able to traverse the wound. Co-culture with budesonide and profibrotic cytokines restored cell morphology and prevented cell mobility. We next examined the extracellular matrix production of epithelial cells that have undergone EMT. Compared to unstimulated controls, esophageal epithelial cells which had undergone EMT exhibited a 75-fold induction of type 1 collagen. Conclusions: Esophageal epithelial cells that have undergone EMT acquire functional characteristics of activated myofibroblasts including the ability to express components of the ECM. Pro-fibrotic cytokine-induced changes in cell mobility and alterations in cell morphology can be reversed by budesonide in vitro.

**NASPGHAN Endoscopy Prize**

**492 ENDOTRACHEAL INTUBATION VERSUS LARYNGEAL MASK AIRWAY FOR ESOPHAGOGASTRODUODENOSCOPY IN CHILDREN; A PROSPECTIVE, RANDOMIZED, CONTROLLED TRIAL.**

Michael A. Acquaviva, Nicole D. Horn, Sandeep K. Gupta, Indiana University School of Medicine, Indianapolis, IN

**INTRODUCTION:** Increasing numbers of pediatric endoscopies are being performed under general anesthesia (GA). While safe and effective, endotracheal tube (ETT) in children for EGD can result in delayed awakening and slow room turnover, particularly when intravenous medications are required for intubation. Laryngeal mask airway (LMA) is an alternative to intubation and permits removal before full awakening.
AIM: To prospectively examine the safety and efficacy of LMA compared to ETT for children undergoing elective EGD.

METHODS: ASA I-III patients were randomly assigned in this prospective study in a major children's hospital to receive LMA (Group LMA) or ETT (Group ETT) for airway management during EGD. All participants were pre-medicated with midazolam 0.5mg/kg (up to 15mg) 15-30 minutes prior to transfer to operating room (OR). Airway device placement occurred after induction with 8% sevoflurane and 100% oxygen, placement of an intravenous catheter, and intravenous lidocaine 2mg/kg up to 100mg. Data collected included various parameters (for example time from induction of anesthesia to placement of the airway device; time from end of procedure to arrival in postoperative acute care unit (PACU); time spent in PACU; overall time from arrival in the OR and end of procedure to discharge home; vomiting after the procedure; nausea requiring medicine after the procedure; lowest oxygen saturation level during or after the procedure; highest concentration of sevoflurane during the procedure; highest pain level after the procedure; amount of pain medicine given; adverse events; and satisfaction level of the doctor doing the EGD).

RESULTS: 84 children ages 3-17 years were prospectively enrolled and randomized to LMA or ETT (42 patients in each group; 20 males in each group; mean age 10.4 and 10.1 years Group LMA and ETT respectively). Group ETT had significantly longer time from OR arrival to airway placement, OR arrival time to hospital discharge, airway placement to hospital discharge, and end of procedure to discharge. Specifically and of clinical import, the time from end of procedure to PACU was lower in Group LMA compared to the Group ETT (4.4 min vs. 9.2 min; p value <0.00001) and post-procedure hospital stay was shorter in Group LMA compared to Group ETT (completion of procedure to discharge home time of 64.4 min vs. 79.3 min; p value 0.0238).

CONCLUSIONS: LMA appears to be a safe alternative to ETT for otherwise healthy children undergoing routine EGD. Benefits to using LMA are decreased incidence of vomiting and overall decreased time spent in the hospital. This will allow more efficient use of operating room/endoscopy suite resources while providing safe and appropriate care. This prospective, randomized clinical study also addresses several questions posted recently on-line on the Pediatric GI bulletin board on use of LMA in pediatric endoscopies.

Research Session VI – Clinical and Translational Research in Inflammatory Bowel Disease

493 TRANSCRIPTIONAL PROFILING OF PERIPHERAL BLOOD MONONUCLEAR CELLS IDENTIFIES GENES AND GENE PATHWAYS ASSOCIATED WITH PEDIATRIC IBD AND THAT DIFFERENTIATE CROHN'S DISEASE AND ULCERATIVE COLITIS. Jess L. Kaplan1, Manoj K. Bhasin2, Christopher J. Moran1, Marie G. Joseph3, Mara Storto1, Tovia A. Libermann1, Harland Winter1, 1Division of Pediatric Gastroenterology, MassGeneral Hospital for Children, Boston, MA; 2Interdisciplinary Medicine and Biotechnology, Beth Israel Deaconess Medical Center, Boston, MA; 3BIDMC Genomics, Proteomics, Bioinformatics and Systems Biology Center, Beth Israel Deaconess Medical Center, Boston, MA

BACKGROUND & AIMS: The pathogenesis of inflammatory bowel disease (IBD) is thought to result from an exaggerated and inappropriate mucosal immune response to luminal/environmental triggers in genetically susceptible hosts. Transcriptional profiling of intestinal mucosa has revealed novel etiologic pathways and disease biomarkers in IBD, but identifying transcriptional factors from circulating peripheral blood mononuclear cells (PBMCs) may serve as surrogate biomarkers for IBD-induced gene expression in cells that are more accessible than gastrointestinal mucosa. We evaluated the transcriptional profile of PBMCs in children with and without Crohn's Disease (CD) and Ulcerative Colitis (UC) using genome wide microarray analysis.

METHODS: Transcriptional profiling using Affymetrix Gene Chip HT HG-U133+ PM Array Plates, containing more than 47,000 transcripts, was performed on RNAs isolated from PBMCs of 47 patients (14 with CD, 7 with UC, 11 without gastrointestinal inflammation [NI-CTL] and 12 with non-IBD gastrointestinal inflammation [I-CTL]). Data analysis for identifying IBD affected genes was performed on individual genes using unpaired univariate t-tests (significant if p < 0.01) and on biologically related gene sets using Gene Set Enrichment Analysis (GSEA) which can detect more subtle expression differences between groups. Pathways of the differentially expressed genes/gene sets were assessed with Ingenuity Pathways Analysis.

RESULTS: 141 transcripts were up-regulated and 21 down-regulated in IBD patients (CD + UC) compared to non-IBD patients (I-CTL + NI-CTL). Comparison of CD and NI-CTL patients yielded 216 up-regulated transcripts and 114 down-regulated transcripts; whereas, comparison of CD and I-CTL patients yielded 109 and 18 up and down-regulated transcripts, respectively. These data suggest distinct gene expression profiles in CD compared to other GI inflammatory disorders. When CD patients were compared to UC patients, 63 transcripts emerge as differentially expressed and overlap with UC and CD-specific genes was noted in 28 and 16 of these genes when compared to controls (I-CTL + NI-CTL). Up-regulated genes in CD and UC included those highly expressed in neutrophils, mast cells and eosinophils, while NK cell and regulatory T-cell associated genes were down-regulated. The genes with highest expression in both CD and UC were neutrophil specific markers. Genes specifically expressed in CD compared to UC and controls included inflammasome markers and genes involved in pathogen recognition and the activation of innate immunity. A three gene predictor model (kNN-C) showed 71.4% sensitivity and 82.6% specificity for IBD.

CONCLUSION: Transcriptomic analysis of PBMCs shows distinct changes in gene expression that may help differentiate CD and UC and separate IBD from both non-inflamed controls and those with non-IBD inflammatory GI conditions. Further investigation may reveal non-invasive disease biomarkers and novel pathogenic pathways that could result in innovative therapies.

This work was supported by the Pediatric IBD Foundation

494 ENDOSCOPIC TREATMENT OF IBD-RELATED STRICTURES IN PEDIATRIC PATIENTS. Roberto Gugig, UCSF, Visalia, CA

Crohn's disease (CD) is a chronic unremitting immune-mediated inflammation involving the whole GI tract and occurring in the pediatric age group with an incidence of 5 to 6/100,000 per year in Western countries. The course of pediatric CD is commonly complicated by strictures in around 30% of patients on long-term follow-up. These often require intestinal resection or strictureplasty. Unfortunately, strictures tend to recur after resection and can lead to repeated surgical interventions, increasing morbidity and mortality. Recently,
endoscopic balloon dilation (EBD) plus intramural corticosteroid (CS) injection has become an attractive conservative therapy in adults. We evaluated the prospective use of endoscopic balloon dilation (EBD) plus intramural CS injection (four-quadrant triamcinolone 40mg/ml in 0.5 to 1 ml aliquots) in 9 patients (6 male, median age 14.5 years; range 9 to 17.5 years) with IBD-related strictures. Strictures located in esophagus (1), antrum (1), right colon (2), ileum (6). Strictures were inflammatory, < 4 cm in length, not post-surgical. 9 patients underwent 12 dilations, 3/9 (33%) required repeat dilations (1 antral stricture, 2 ileal strictures), Technical success as defined by the ability of the scope to traverse the stricture post-dilation and improvement of symptoms was achieved in all patients (100%), long-term success defined as symptom free > 1 year was achieved in 6/9 (66%). None of the patients required surgery and no perforations seen.

In a select group of pediatric patients with CD and strictures, endoscopic management including balloon dilation plus intramural CS injection is an effective, non-invasive strategy and reduces the need for surgical interventions.

**495 EARLY RESPONSE TO TREATMENT WITH ADALIMUMAB IN CHILDREN WITH MODERATELY TO SEVERELY ACTIVE CROHN’S DISEASE: RESULTS FROM IMAGINE 1.**

Joel Rosh1, Jaroslaw Kierkus1, Wallace Crandall2, Jeffrey Hyams3, James Markowitz4, Robert Baldassano5, Andreas Lazar6, Yaqin Wang2, Samantha Eichner2, Roopal B. Thakkar2, 1Children’s Mem Health Inst, Warsaw, Poland; 2Nationwide Children’s Hospital, Columbus, OH; 3CT Children’s Medical Center, Hartford, CT; 4Goryeb Children’s Hospital/Atlantic Health, Morristown, NJ; 5Cohen Children’s Medical Center of NY, New Hyde Park, NY; 6Children’s Hospital of Philadelphia, Philadelphia, PA; 7AbbVie Deutschland, Ludwigshafen, Germany; 8AbbVie Inc, North Chicago, IL

Objective: To evaluate adalimumab (ADA) efficacy at week (wk) 4 in pediatric patients (pts) with moderately to severely active Crohn’s disease (CD) enrolled in the randomized clinical trial IMAGINE 1.

Methods: Pts aged 6-17 yrs with baseline (BL) PCDAI >30 and CD resistant or intolerant to conventional therapy, including infliximab (IFX), received open-label induction of ADA at wks 0/2 as per body weight (≥40kg, 160/80mg; <40kg, 80/40mg). Proportion of pts in clinical remission (PCDAI≤10) and response (PCDAI decrease ≥15 points from BL), along with median change in C-reactive protein (CRP) levels from BL were measured at wk 4. Non-responder imputation (NRI) was used for missing data. Safety data were reported previously.

Results: At wk 4, 155 (81%) pts responded to induction and 52 (27%) were in clinical remission. Remission and response rates were comparable between the induction dose groups (Table). A numerically higher proportion of IFX-naïve pts achieved remission at wk 4 than IFX-experienced pts (Table), but the differences were not statistically significant. Comparable decreases in median CRP levels occurred in both groups at wk 4 (P=.097).

Conclusion: ADA induced clinical remission and response in children with moderately to severely active CD as early as wk 4. The early clinical benefits were comparable for both induction doses, with a trend towards greater benefits observed in anti-TNF naïve patients. Reference: 1. Hyams JS, et al. 2012. Gastroenterology; 143:365.

Efficacy at wk 4 in ADA-treated pts in IMAGINE1 (NRI)

<table>
<thead>
<tr>
<th></th>
<th>ADA 160mg/80mg N=123</th>
<th>ADA 80mg/40mg, N=69</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline PCDAI score, mean</td>
<td>40</td>
<td>42.6</td>
<td>NA</td>
</tr>
<tr>
<td>Remission, n/N (%)</td>
<td>36/123 (29)</td>
<td>16/69 (23)</td>
<td>0.36</td>
</tr>
<tr>
<td>IFX-naive</td>
<td>22/65 (34)</td>
<td>12/42 (29)</td>
<td>0.57</td>
</tr>
<tr>
<td>IFX-experienced</td>
<td>14/58 (24)</td>
<td>4/27 (15)</td>
<td>0.33</td>
</tr>
<tr>
<td>Response (n/N%)</td>
<td>97/123 (79)</td>
<td>58/69 (84)</td>
<td>0.38</td>
</tr>
<tr>
<td>IFX-naive</td>
<td>56/65 (86)**</td>
<td>35/42 (83)</td>
<td>0.69</td>
</tr>
<tr>
<td>IFX-experienced</td>
<td>41/58 (71)</td>
<td>23/27 (85)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

NA: Not applicable. *Chi-square test comparison between dose groups. **P<0.05 for IFX-naïve vs IFX-experienced comparison; P>0.05 for all other IFX-naïve vs IFX-experienced comparisons

**Research Session VII – Disorders of Intestinal Development or Motility**

**William F Balistreri Prize**

**496 ACID SUPPRESSION CHANGES THE DIVERSITY AND ABUNDANCE OF GASTRIC AND LUNG MICROBIOTA.**

Rachel L. Rosen1, Janine Amirault1, Doyle Ward1, Lan Hu1, Umakanth Khatwa1, Samuel Nurko1, 1Children’s Hospital Boston, Boston, MA; 2Center for Computational Cancer Biology, Dana Farber Cancer Institute, Boston, MA; 3The Broad Institute, Cambridge, MA

Background: Acid suppression is associated with an increase risk of pneumonia and upper respiratory infections. The mechanism behind the increase risk is not known but it may be related to gastric bacterial overgrowth with resultant upstream effects on lung microbiota. It is the goal of this study to determine, using 16S sequencing, if: (1) patients taking acid suppression have an increased diversity or abundance of gastric bacteria; (2) patients taking acid suppression have an increased diversity or abundance of lung bacteria; and (3) if there is a relationship between gastroesophageal reflux burden and lung microbiota.

Methods: We prospectively recruited 99 patients, 51 on and 48 off acid suppression therapy, between the ages of 1 -18 years who were undergoing simultaneous bronchoscopy and endoscopy for the evaluation of cough. Gastric fluid and bronchoscopy fluid (BAL) were collected. DNA was isolated from the samples and then samples were run using previously reported sequencing methods. A subgroup of
Neurogastroenterology and Motility Prize - Clinical

497 EFFECT OF PROPOFOL ON INTERNAL ANAL SPHINCTER PRESSURE DURING ARM. Khoa Tran1, Brad Kuo2, Audrius Zibiatis2, Somalatha Bhattacharya2, Charles Cote2, Jaime Belkind-Gerson1, 1Pediatric GI, MGH, Burlington, MA; 2Pediatric Anesthesia, MGH, Burlington, MA; 4Gastroenterology, MGH, Boston, MA

Background and Aim: An anorectal manometry (ARM) is a common test in the evaluation of outlet obstruction in constipation. In children under 6 yo, anesthesia is often used for patient comfort and compliance. The choice of anesthesia for ARM varies from center to center and includes the use of ketamine, inhalation agents, and propofol. With the increased use of propofol, our aim is to determine the effect of propofol on resting internal anal sphincter (IAS) pressure while performing an ARM under general anesthesia.

Methods: Prospective cohort of chronically constipated children ages 2-6 yo underwent water perfusion ARM per standard protocol with sevoflurane as the induction inhalational agent. At completion of ARM, 1 mg/kg propofol bolus was administered by the anesthesiologist to reduce likelihood of delirium from anesthesia. The manometry catheter was kept in place with continuous measurement of the IAS up to a maximum of 5 min. Outcome measures included: 1) Initial pre-propofol resting baseline IAS, 2) Post-propofol IAS nadir pressure, 3) Post-propofol IAS baseline pressure. 4) Time to reach post-propofol nadir and 5) new IAS baseline pressure. Statistical analysis utilized paired t-tests.

Results: 20 subjects (14M, 6F), ages 2-6 yo (mean: 4.2 yo) were enrolled. Mean resting IAS pressure was 51.5 ± 15.3 mmHg. After IV propofol bolus, the resting IAS pressure showed a significant decrease in 19/20 patients to a mean nadir of 21.7 ±10.5 mmHg, which was significantly lower (p<0.005) compared to mean resting IAS pressure. The average reduction in IAS pressure was 58% (29.9 ± 13.8 mmHg). The new post-propofol IAS resting pressure was 47.0 ± 12.4 mmHg which was significantly lower compared to pre-propofol IAS pressure(p<0.0001). Mean time for IAS to reach nadir was 42 seconds while average time for IAS to recover and establish new baseline was 170 seconds.

Conclusions: In children < 6 yo undergoing ARM under general anesthesia, an IV propofol bolus leads to a significant decrease in the IAS pressure. This effect is transient and the IAS returns to a new post-propofol baseline pressure which is significantly lower than the initial pre-propofol baseline IAS. Propofol should be used with caution as an anesthetic in young children undergoing anorectal manometry given the potential for confounding measurements. The one patient who did not show response to propofol had undergone rectal injection of botulinum toxin 3 months prior. This finding suggests the patient may have been at maximal IAS relaxation at baseline or that the mechanism of IAS relaxation by propofol is mediated by pathways that can be inhibited by botulinum toxin.

Neurogastroenterology and Motility Prize – Basic Science

498 INFLUENCE OF INTESTINAL MICROBIOTA ON THE POSTNATAL DEVELOPMENT OF DOPAMINERGIC ENTERIC NEURONS. Kal A. Mungovan1,2, Rajka Borojevic1,2, Elyanne Ratcliffe1,2, 1Pediatrics, McMaster University, Hamilton, ON, Canada; 2Farncombe Family Digestive Health Research Institute, McMaster University, Hamilton, ON, Canada

Colonization of the gastrointestinal (GI) tract begins at birth and proceeds rapidly in early life. During this postnatal period, the enteric nervous system (ENS) continues to undergo significant morphological and functional changes. Observations in early postnatal germ-free (GF) mice have demonstrated a structurally and functionally normal ENS, raising the possibility that intestinal microbiota are necessary for the normal development of enteric innervation. Enteric neurons are "born" at different stages of development, with some populations, such as dopaminergic neurons, characterized as "late-born" neurons. We tested the hypothesis that postnatal exposure to intestinal microbiota can influence the development of "late-born" dopaminergic neurons.

The ENS of specific pathogen-free (SPF) and GF NIH Swiss mice were examined in whole-mount preparations of small and large intestine at three time-points: postnatal day 1, day 7, and day 28. Enteric neurons and dopaminergic neurons were visualized using double-label immunohistochemistry with antibodies to Human Neuronal Protein C/D (HuC/D) and tyrosine hydroxylase (TH), respectively. The proportion of TH-positive cell bodies per total number of HuC/D-positive neurons was quantified in each sample and expressed per 1000 neurons.

At postnatal day 1, the proportion of TH-positive neurons did not differ significantly between GF and SPF mice in any region of the intestine examined. By postnatal day 7, however, the ileums of GF mice had a significantly lower proportion of TH-positive neurons than...
did those of SPF mice (18 vs. 3; p=0.03). This difference persisted until postnatal day 28 (40 vs. 4; p=0.01). No differences were seen between the SPF and GF duodenum, jejunum and colon at all time points. These findings are consistent with the idea that enteric microbiota can influence the development of “late-born” neuronal populations. The reduced proportion of dopaminergic neurons in the ileum of GF mice at one week and four weeks of age may contribute to the previously described altered motility patterns in postnatal GF mice. Further studies are needed to elucidate the mechanisms by which intestinal microbiota interact with developing enteric neurons.

499 INCREASED ENTERIC NEUROGENESIS BY STIMULATION OF 5-HT4 SIGNALING. Jaime Belkind-Gerson1,2, Ryo Hotta2, Sarah A. Miller2, Allan M. Goldstein2, 1Pediatric Neurogastrology, Massachusetts General Hospital, Boston, MA; 2Pediatric Surgery, Massachusetts General Hospital, Boston, MA

Introduction: The enteric nervous system (ENS) coordinates essential intestinal functions including peristalsis, sensation, absorption, secretion, immunity and blood flow. Throughout life, the ENS is subject to injury from inflammation, toxins, infection, metabolic disorders and aging, all of which can contribute to sensory and/or motor diseases of the gut. The resulting enteric neuropathies are highly prevalent and lead to significant morbidity and health care expenditure. Replacing abnormal or injured neurons through neural stem cell transplantation or with endogenous neurogenesis would offer a novel approach to treating these conditions.

Methods: We have previously shown that Neurospheres can be isolated from muscularis and mucosa/submucosa, which differentiate into neuronal, glial, and mesenchymal lineages in vitro. In hopes of augmenting the neuronal population upon differentiation, dissociated neurospheres were cultured for 7 days in media containing low (100 nM) or high (500 nM) 5HT4 receptor agonist RS67506. Neuronal differentiation was determined by immunohistochemical detection to the pan-neuronal marker, Tuj1. Additionally, Intestinal muscle strips containing the endogenous myenteric ganglia were then cultured with the 5HT4 receptor agonist alone (500 nM) or with the 5HT4 receptor antagonist GR125487 (500 nM). Neurogenesis was identified through immunostains for mitosis (Phospho-Histone H3) in neuronal progenitors (Hu C/D).

Results: Exposure of dissociated cells to the 5HT4 agonist resulted in an increase in the number of Edu+ neuronal precursors. The percentage of neurons in culture increased with the dose of 5HT4 agonist added (*p<0.05). In the ex vivo model, intestinal muscle strips containing the endogenous myenteric ganglia were cultured with the 5HT4 agonist. Neurogenesis was again noted to increase significantly, and could be blocked by the addition of a 5HT4 antagonist (*p<0.05).

Conclusions: 5HT4 signalling promotes neurogenesis in both dissociated neurosphere cultures and in explanted myenteric plexus preparations.