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Annual Meeting
October 20–23, 2011
Orlando, FL

POSTER SESSION I
Thursday, October 20, 2011
5:00pm – 7:00pm

INTESTINE/COLON/IBD

1 EFFECTS OF TOP-DOWN THERAPY IN PEDIATRIC PATIENTS WITH CROHN’S DISEASE. Aliza Solomon, Melissa Rose, Claire Zar-Kessler, Pediatrics, NYUH-Weill Cornell, New York, NY
Objectives: Conventional treatment of pediatric patients with moderate to severe disease has used a step-up approach, involving initiation of therapy with corticosteroids and/or aminosalicylates. In the top-down treatment paradigm, biologic agents are offered in early onset disease. Our aim is to show that pediatric patients with early IBD experience a faster and longer-lasting remission with less morbidity when employing a top-down approach to therapy in comparison to patients using a step-up approach to treatment.

Patients and Methods: A preliminary retrospective analysis was conducted of 34 pediatric patients ages 4-18 with Crohn’s disease diagnosed between 7/2005 and 3/2010 who were treated with anti-TNF agents or immunomodulators. Patient demographics, treatment course and outcomes were reviewed. These patients were divided into two groups based on time from diagnosis to initiation of anti-TNF or immunomodulator therapy.

Results: Among the 34 patients, 12 patients (35%) were treated in a top-down manner.

Conclusions: Though it was expected that pediatric patients with early IBD experience a faster and remission with fewer side effects such as hospitalization and surgery when employing a top-down approach to therapy, there was no statistically significant difference in outcomes with top down versus bottom up therapy.

2* ILEAL POUCH-ANAL ANASTOMOSIS IN A LARGE COHORT OF PEDIATRIC PATIENTS WITH ULCERATIVE COLITIS: LONG-TERM OUTCOME FROM A SINGLE CENTER EXPERIENCE. Angela Shannon, Mark Kay, Steven Blanchard, Richard Wyllie, Mahajan, William Worley, Jenna Bena, Ira Laverty, Vincent Fazio, Cleveland Clinic, Cleveland, OH
Many pediatric patients with ulcerative colitis (UC) will require surgery, frequently ileal pouch-anal anastomosis (IPAA). These patients tend to develop complications over time, including change in diagnosis to Crohn disease. Our aim was to determine the long-term incidence of complications in a large cohort of pediatric patients who underwent IPAA at our institution.

Methods: Pediatric patients who underwent IPAA for UC were contacted to determine pouch history, complications, medication use and quality of life. The study was IRB approved. Patients were part of a previous cohort in which pouch outcome was evaluated at 2 and 5 years postoperatively.

Results: Data was obtained from 45 patients out of 157 comprising a previous cohort evaluating pouch outcome. Median age at diagnosis was 15y (11-17y). Median age at surgery was 18y (15-20y). Median duration of follow-up was 29y (19-22y). Reported complications were pouchitis-29%, strictures-16%, fistulae-27%, obstruction-16%, and change of diagnosis to Crohn disease-11%. 33% reported no complications. 13% had pouch failure defined as the pouch being taken down. Crohn disease was the most frequent complication in those with pouch failure, occurring in 50% of this group. In those with children (62%), 33% reported problems conceiving; 47% of women had pregnancy complications. There was no report of cancer identified in any pouch. 76% reported that they were very satisfied after IPAA at 20 years follow-up vs 94% at 2 years follow-up.

Conclusion: To our knowledge, our study represents the largest and longest term follow-up of pediatric patients undergoing IPAA. IPAA remains an excellent option for pediatric patients with UC, and a majority of patients report high satisfaction. Change in diagnosis to Crohn disease is a risk factor for pouch failure. Development of fistula and/or obstruction tends to be associated with a change in diagnosis to Crohn disease. Pediatric patients and their families should be informed of these issues prior to undergoing IPAA.
**3** NON-INVASIVE MAPPING OF THE GUT MICROBIOTA AS A SCREENING METHOD FOR IBD IN CHILDREN AND YOUNG ADULTS. Eli Papa1, Michael Docktor2, Joshua Korzenik2, Doyle Ward3, Dirk Gevers4, Jay Ingram1, Christopher Smillie1, Georgia Giannoukos5, Diana Tabb6, Dawn Ciuilla7, Ramnik Xavier3, Eric Alm3, Athos Bousvaros1,7, Children’s Hospital Boston, Boston, MA; 2MIT, Boston, MA; 3Broad Institute, Boston, MA; 4Massachusetts General Hospital, Boston, MA

Background & Aims: Pediatric Inflammatory bowel disease (IBD) may be challenging to diagnose because of non-specific symptoms. Delay in the diagnosis of pediatric IBD may lead to inappropriate treatment plans and poor patient outcomes. To address this issue, we demonstrate the use of 16S rRNA sequencing of fecal samples and new analytical methods to create a sensitive and specific screening test for IBD. Methods: We applied machine learning analysis to 16S sequencing data obtained from: i) published surveys of microbiota diversity in IBD and ii) fecal samples obtained from a group of 91 children and young adults receiving care in the gastroenterology program of Children’s Hospital (Boston, USA). Results: Our method is accurate in distinguishing control and active IBD patients, with an area under the receiver-operating-characteristic curve (AUC) of 0.903, and translates across data sets with vastly different sampling and sequencing methods. Our method can identify key taxa associated with disease states and distinguish Crohn’s disease and ulcerative colitis patients with reasonable accuracy. Blind validation with an additional data set of 83 patients showed 85% agreement with the model predictions. Conclusions: These results demonstrate the feasibility of microbiome-based diagnostics in the screening of IBD. While not replacing endoscopy and histological examination as diagnostic tools, we propose that classification based on microbial diversity can be an effective complementary technique to aid in screening of IBD, particularly in early-stage pediatric patients.

**4** LYMPHOMA RISK IN CHILDREN WITH IBD. Lori Ashworth1, Paul Mitchell1, Amy Billett1, Federica Nuti2, Athos Bousvaros3,7, Children’s Hospital Boston, Boston, MA; 2Sapienza University Hospital, Rome, Italy

BACKGROUND: Prior studies suggest an increased risk of lymphoma in adults with inflammatory bowel disease. Cases of lymphoma have also been reported in children with IBD. However, the precise risk of lymphoma in relation to drug exposure has not been ascertained in children. METHODS: We conducted a single center, retrospective study of 1374 children and young adults with IBD followed at our center between 1980 and 2008. Charts were reviewed to determine whether lymphoma developed while they were receiving their clinical care at our institution, and the duration of exposure to various IBD medications. RESULTS: Of 1374 patients (741 male; age at diagnosis 12.1±4.0y; 791 CD, 535 UC, 48 IBD unclassified), we identified two patients who developed lymphoma (one Hodgkin, one anaplastic large cell), in 6,624 patient-years of follow-up (mean duration follow-up 4.8 years per patient). Both patients were males (ages 12 and 18 years at time of lymphoma onset), and were receiving thiopurines but had not yet received biologics at the time of their cancer diagnosis. They were both treated with chemotherapy, and are alive without disease 32+ and 76+ months since diagnosis. The ratio of lymphoma to patient years of exposure for various medication classes is summarized in the table. Using the SEER database, we estimated the absolute incidence rate of lymphoma for patients receiving thiopurines was 4.66 per 10,000 patient-years compared to the expected rate in SEER of 0.58 per 10,000 patient-years, with a standardized incidence ratio (SIR) of 7.78 (95% CI 0.77-43.45). CONCLUSION: The overall risk of lymphoma in children with IBD is low. However, this study suggests an increase in risk in the subset of children receiving thiopurines, comparable to that reported in studies of adults.

<table>
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<th>Medication</th>
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<th>Person years observed</th>
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<td>0</td>
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<td>1811</td>
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<td>0</td>
<td>303</td>
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**5** PATTERNS OF NON-ADHERENCE TO MEDICATIONS IN PEDIATRIC PATIENTS WITH IBD. Christopher Hayes, Sarah Hagan, Deborah Lobato, Neal LeLeiko, Brown/Hasbro Children’s Hospital, Providence, RI

Background: Treatment of IBD aims to decrease the frequency and severity of flare-ups through close adherence to a regimen of daily anti-inflammatory medications (5-aminosalicylic acid) and immunomodulators (6-mercaptopurine). Previous work has focused on rates and predictors of non-adherence in patients as if each patient has an individualized rate of their own. Our studies have found an average adherence rate of 50% with almost one-third of patients taking less than one third of their prescribed medications. Our work also suggests that, while pediatric IBD patients on average open their pill bottles approximately 50% of the time prescribed, there is also great variability within the same patient. Goals: The aim of this report is to look at how adherence varies within the same patient over time, describe clinical factors that may impact adherence rates, and to suggest potential areas for further study. Methods: Adherence was measured over 6 months via bottles fitted with electronic track caps containing microchips which monitor how often patients open their medication bottles. Additional data were abstracted from the medical records including medication changes, symptoms, laboratory results, surgeries, hospitalizations, and PGA scores.
Results: We found many different patterns of adherence to medications. In individual patients, adherence varied from 0% to 60% over 4-6 week intervals. In some patients, adherence variability appeared to reflect clinical events. For example, periods of non-adherence may precede escalation of medical therapy, hospitalization, and steroid courses.

Conclusions: Measures of adherence using electronic monitoring devices demonstrate that over a six-month interval, actual adherence rates may vary greatly within the same patient. Given the variability of adherence, physicians may draw incorrect conclusions about medication effectiveness. Our data suggests that periods of non-adherence may precede escalation of medical therapy, hospitalization, and steroid courses. These escalations and adverse events may be avoided with improved methods to encourage adherence.

6  **VSIG4/Z39Ig, AN INHIBITORY B7 SUPERFAMILY MEMBER, IS DOWN-REGULATED IN INTESTINAL MUCOSA IN IBD.** Clifton S. Huang, Oscar Medina, Duke Geem, Wooki Kim, Subra Kagathasan, Tim Denning, Pediatric Gastroenterology, Hepatology and Nutrition, Emory University, Atlanta, GA

Pathogenic T cells play an important role in initiating chronic intestinal inflammation in IBD. Differentiation of naïve T cells into pathogenic effectors is influenced by APCs expressing co-stimulatory molecule ligands. VSIG4 (in mice)/Z39Ig (in human) is an Ig domain-containing B7 superfamily member that is primarily expressed by tissue macrophages (Mo). VSIG4/Z39Ig is down regulated upon activation and acts as a negative regulator of T cell responses. Neutralization of VSIG4/Z39Ig reduces the induction of T cell responses in vivo and inhibits the production of Th cell-dependent IgG response, however little is known about its role during intestinal inflammation. We investigated the expression of VSIG4/Z39Ig in the murine and human intestine. Gene array profiling of FACS-sorted, lamina propria (LP) Mo from colons of healthy or colitic mice revealed VSIG4 as the single most repressed gene (16-fold) during inflammation. These data were confirmed using quantitative real-time PCR which demonstrated a 30-fold decrease in VSIG4 mRNA in Mo isolated from colitic mice when compared to healthy mice. Using real-time PCR we confirmed that Z39Ig is preferentially expressed in intestinal biopsies obtained from normal compared to Crohn's Disease or Ulcerative Colitis biopsies. Using 10-color FACS, we investigated Z39Ig protein expression on isolated LP cells obtained from intestinal biopsies in normal & IBD patients. A 65% increase in Z39Ig surface expression on LP Mo (CD11b+CD11c+) was seen in normal biopsies as compared to inflamed biopsies. The presence of high-level Z39Ig expression on intestinal Mo in healthy patients suggests that this protein is important for maintaining T cell hyporesponsiveness towards commensal bacteria. In IBD however, loss of Z39Ig on resident or infiltrating macrophages may promote pathogenic T cell differentiation that contributes to disease progression. Investigating the role of VSIG4/Z39Ig in maintaining mucosal homeostasis may provide insight into exploiting this inhibitory pathway in the treatment of IBD.

7  **ANALYSIS OF CURRENT TREATMENTS USED IN CLINICAL PRACTICE IN A PEDIATRIC SUMMER CAMP POPULATION FOR CHILDREN WITH IBD.** Danya J. Rosen, Kathy Hoffstader-Thal, Ruijun Bao, Juli Tomaino, Clare Ceballos, Keith Benkov, Pediatrics, Mount Sinai Medical Center, New York, NY

Many treatment options exist for children with IBD, yet the lack of clinical guidelines for management has lead to great variation in care. The purpose of this project was to evaluate current treatment modalities in children from the Northeast US who applied to the 2010 session of Camp Oasis, a CCFA-sponsored camp for children ages 8-17 with medically stable IBD. Patient demographics, medical history, and current medications were entered into the camp database. The subjects were de-identified and divided into two groups; Crohn’s disease (CD) or ulcerative colitis/indeterminate colitis (UC/IC). Chi-square test, Fisher’s exact test and Wilcoxon rank sum test were applied for univariate analysis using SPSS 19. 164 applicants were included, 121 (74%) with CD and 43 (26%) with UC/IC. There were no significant differences between the two groups with respect to median age at the time of camp, median age at diagnosis, or median length of illness. Of the 121 applicants with CD, 13 (10.7%) were on an antibiotic, 56 (44.3%) were on a 5-ASA, and 10 (8.3%) were on corticosteroids. 57 (47.1%) were on immunomodulators (thiopurines or methotrexate), 44 (36.4%) were on a biologic agent, and 6 (5%) were on both. Of the 43 subjects with UC/IC, 19 (44%) were on a 5-ASA as monotherapy, 2 (4.7%) were on corticosteroids, 13 (30.2%) were on an immunomodulator, and 4 (9.3%) were on a biologic agent. We concluded that variation in treatment was observed among this camp population. Immunomodulators are still common therapy in CD (42.1%) though biologics have become almost as common (36.4%). Few CD subjects were on both an immunomodulator and a biologic agent (6%). Many subjects with UC were on a 5-ASA as monotherapy, and the use of biologics for UC is increasing (9.3%). The use of corticosteroids was limited in both groups (8.3% in CD, 4.7% in UC/IC). Identifying current treatment patterns may lead to a better understanding of therapy and the establishment of clinical guidelines to standardize the treatment of pediatric IBD.

8*  **TNFα STIMULATION OF MIR106A CAUSES DEFECTIVE REGULATORY T CELL FUNCTION EXACERBATING CHRONIC INTESTINAL INFLAMMATION.** Colm B. Collins3,2, Ping-Yao Zeng1,2, Kayla Pound1,2, Edwin F. deZoeten1,2. 1Digestive Health Institute, Children's Hospital Colorado, Aurora, CO; 2Mucosal Inflammation Program, The University of Colorado Denver, Aurora, CO

Inflammatory Bowel Disease (IBD) is thought, in part, to reflect a failure of the enteral immune system to regulate itself, resulting in uncontrolled inflammation. Regulatory T cells (Tregs) mediate suppression of this overactive immune response, thus a better understanding of Treg function may provide targets for future therapy. Using a TNFα-driven model of ileitis (TNFAARE) that recapitulates many features of Crohn’s disease, we assessed changes in frequency and function of Tregs within the inflamed ileum by flow cytometry and RT-PCR. Next we assessed the effect of TNFα blockade on disease severity, Treg frequency and IL-10 production by those cells from the inflamed ilea of TNFAARE mice. Tregs accumulated in inflamed ilea, however, production of the anti-inflammatory cytokine, IL-10, by Tregs from inflamed mice was significantly depressed. This effect was independent of changes in IL-10 mRNA, suggesting involvement of a post-transcriptional regulatory mechanism. Furthermore, Tregs from TNFAARE mice had decreased function, which may be critical to the chronic nature of ileitis in these
mice. Anti-TNF therapy attenuated inflammation in TNFΔARE mice, restored function to the Tregs and improved IL-10 production both in vitro and in vivo, implicating TNF as a mediator in the depression of IL-10 production. Finally, we noted that Tregs from the TNFΔARE mice express high levels of the microRNA mir106a, previously shown to inhibit the production of IL-10, suggesting a possible mechanism for TNF effects on Tregs. Anti-TNF therapy resulted in decreased mir106a expression and increased IL-10 production. Inhibition of mir106a by lentiviral transduction of cells with an anti-mir106a resulted in significantly increased IL-10 secretion. These results provide new insight into the role of TNF as a cause of chronic inflammation and provide novel targets to improve Treg function.

9 A 20-YEAR MEXICAN EXPERIENCE IN PEDIATRIC INFLAMMATORY BOWEL DISEASE. Elisa Gaona, Liliana Worona, Hospital Infantil de México Federico Gómez, México, Mexico

Background: Few studies have been published about epidemiology of childhood-onset inflammatory bowel disease (IBD) in Latin America. An early trend in the incidence of pediatric IBD and an increasing frequency has been noticed in our center similarly to reports worldwide.

Methods: Data were collected from medical records at Hospital Infantil de México Federico Gómez from 1990 to 2010.

Results: A total of 32 patients with IBD were diagnosed during the 20-year period; ulcerative colitis (UC):24, Crohn’s disease (CD):4, indeterminate colitis (IC):3. The average number of diagnosed cases increased from two per-year in the period 1990-2007 to five per-year in 2008-2010. The median age at diagnosis was 7.8-years-old. The youngest patient had IC and was 4-months-old at time of diagnosis. 35% patients received azathioprine (AZA) at induction. Thirty-day outcomes: complete remission (CR) UC 13(54%), CD 1(25%), IC 2 (67%); partial remission (PRS) CD 2 (50%) and no response (NR) UC 11(46%), CD 1(25%), IC 1 (33%). One-year outcomes: prolonged response (PR) UC 15(62%), CD 1 (25%), IC 1(33%); corticosteroid dependence UC 7(29%), CD 3(75%) and corticosteroid resistance UC 2(8%), IC 1 (33%). Only 37% UC patients who received AZA initially needed an extra cycle of PDN vs 71% who didn’t receive it. Histological one-year follow-up was measured in UC 12(50%), CD 4(100%) and IC 1(33%). Histological partial response: UC 4 with PR and 3 with NR; CD 1 with PR. No histological changes: UC 2 with PR and 3 with NR; CD 1 with PR, 2 with PRS and 1 with NR; IC 1 with PR.

Conclusions: It seems that frequency of IBD in Mexican pediatric population has increased in the last 5-years with younger patients detected. UC was more frequent than other forms of IBD, just as observed in Hispanic pediatric population. It appears that patients with UC who received AZA with PDN at induction had better outcomes than those who didn’t. Histological activity can persist even in patients with prolonged clinical remission. More studies are needed to assess the importance of re-induction treatment for those patients and to establish the most effective therapeutic approach.

10 GROWTH IN EARLY VERSUS LATE ONSET PEDIATRIC INFLAMMATORY BOWEL DISEASE. Elizabeth A. Garnett, Yvette K. Wild, Deepal H. Dalal, Melvin B. Heyman, Pediatrics, University of California, San Francisco, CA

Background: Pediatric patients with Inflammatory Bowel Disease (IBD) are commonly affected by growth delay.

Aim: To test the hypothesis that patients with early onset have more problems with growth than later onset IBD and to determine the relationship of symptoms and growth at diagnosis.

Methods: Cross-sectional study by chart review of patients at UCSF Pediatric IBD Clinic from 1999 to 2011. Children 2-18 years of age at IBD diagnosis and with more than 6 months of follow-up were included. Early onset was defined as IBD diagnosis before 8 years of age. BMI and height Z-scores were calculated. Statistical analyses included t-test and chi-square test. Data are listed for early and late onset groups respectively and are mean±SD.

Results: 200 patient charts (29 early onset) were reviewed (follow-up 5.7±4.4 years (yrs) early and 4.8±2.8yrs late onset, p=0.14). Mean time from symptom onset to diagnosis did not differ between groups (p=0.99). Age at IBD diagnosis was 4.4±1.5yrs and 12.9±2.7yrs. Height Z-score at diagnosis (-0.21±1.0 and -0.22±1.2, p=0.97) and final visit (-0.30±1.0 and -0.24±1.2, p=0.79), and change in height Z-score during follow-up (-0.09±0.98 and -0.02±0.83, p=0.67) did not differ between groups. BMI Z-scores at diagnosis differed between groups (0.46±0.21 and -0.14±0.08, p=0.01). However, the change in BMI Z-score from diagnosis to follow-up visit was not different (0.09±0.17 and 0.22±0.07, p=0.51). Final visit BMI Z-scores remained different between groups (0.55±0.16 and 0.08±0.08, p=0.02). No relationship was found between BMI Z-score and other presenting symptoms including diarrhea, bloody stool, abdominal pain, or joint problems.

Conclusion: Patients with early onset IBD present with higher BMI Z-scores than patients with later onset IBD. The growth pattern differences do not appear to be overcome in long-term follow up of these patients, suggesting that patients presenting at an older age are more prone to persistent BMI (weight) deficiency compared with early onset IBD.

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11 MTG16 INVOLVEMENT IN COLITIS ASSOCIATED CARCINOMA. Elizabeth M. McDonough1, Caitlyn W. Barrett1, Amber M. Burch2, Choksi A. Yash1, Scott W. Hiebert3, Christopher S. Williams2,4 1Pediatrics, Vanderbilt University Medical Center, Nashville, TN; 2Medicine, Vanderbilt University Medical Center, Nashville, TN; 3Biochemistry, Vanderbilt University Medical Center, Nashville, TN; 4Cancer Biology, Vanderbilt University Medical Center, Nashville, TN

MTGR1, MTG8 and MTG16 are members of the myeloid translocation gene (MTG) family, originally identified in the 8:21 translocation in acute myeloid leukemia. The MTGs function as transcriptional co-repressors, participate in developmental and epithelial wound healing and repair processes and, therefore, likely play a role in the way the gut responds to injury. Previous studies from our group have demonstrated that Mtg1 and Mtg16 participate in intestinal injury response programs. Additionally, Mgr1-/- has been linked as a tumor modifier in murine colitis associated carcinoma. We postulated that Mtg16 may also contribute to tumor formation after intestinal injury. To test this hypothesis, age and sex-matched wild-type and Mtg16-/C57BL6 mice were treated with azoxymethane (AOM), functioning as a tumor initiator, followed by repeated cycles of colonic injury using dextran sodium sulfate (DSS). Weights, stool scores, and mortality rates were measured during each day of
treatment. At the end of the second round of DSS, colonoscopies were performed to evaluate tumor burden. Colons were then extracted and examined for injury and tumor burden. Mtg16/-/ mice showed worsening colitis in response to AOM/DSS when compared to wild type mice with more severe weight loss, stool scores and overall mortality, 75% vs. 95%, respectively. Additionally, Mtg16/-/ mice had increased tumor multiplicity (1.22 vs. 14.53, p<0.001) and increased tumor burden compared to the wild type mice (4.83mm2 vs. 1.71mm2, p<0.001).

Mtg16 is an important modulator of colitis and tumor development in the AOM/DSS model of inflammatory carcinogenesis. This represents the first observation linking Mtg16 to colonic wound healing and carcinogenesis, suggesting that Mtg16 functions as a tumor suppressor in epithelial malignancy.

12 TPMT SCREENING AND VARIABILITY AMONG INNER CITY RACIALLY DIVERSE PEDIATRIC IBD POPULATION. Gitti Tomer, Inna Novak, Russell Cameron, Debra Pan, Anthony Lozizides, John Thompson, Yolanda Rivas, Pediatric Gastroenterology and Nutrition, Children’s Hospital at Montefiore, Bronx, NY

Background: Pediatric Inflammatory Bowel Disease (IBD) Guidelines recommend checking thiopurine S-methyltransferase (TPMT) genotype or phenotype before starting 6-Mercaptopurine (6-MP), an immunomodulator commonly used to treat IBD. Checking TPMT before 6-MP therapy can prevent life-threatening toxicity. Objective: To examine the utilization of TPMT status and epidemiology of TPMT genotype or phenotype in pediatric IBD patients. Methods: A retrospective study of patients who were followed in the Division of Pediatric Gastroenterology from 1/09 through 6/10 was performed. Patient demographic, clinical and TPMT data were analyzed. Results: Eighty-six pediatric IBD patients were studied. 76% were treated with 6-MP. Fifty-three had a diagnosis of Crohn’s Disease (CD), 8 ulcerative colitis (UC) and 4 IBD- undefined, the mean age was 12. Of the patients treated with 6-MP 78% were male and 22% female. In contrast among patients that did not receive 6-MP 71% were female and 29% male (p=0.0001), suggesting a more severe disease in males. 41% were black, 21.5% multiracial, 3.7% Asian, 12.3% Caucasian and 21.5% declined to report racial status. 97% had their TPMT genotype or phenotype tested showing strong adherence to the guidelines. 49% had both phenotype and genotype and of them 6 (19%) had discrepant results with normal genotype but intermediate enzyme levels. Overall, of 44 patients that had enzyme levels measured, 12 (27%) had intermediate levels, of which 10 were Black, 1 multiracial and 1 subject declined to report racial status. Conclusions: 1. All the physicians at CHAM follow guidelines for TPMT testing prior to 6-MP therapy. 2. Significantly more males were on 6-MP suggesting a more aggressive disease in males in our population. 3. We observed a very high prevalence of intermediate TPMT enzyme levels in Black population with frequent discrepancy with TPMT genotype, suggesting that different genotypes may exist in Black patients. 4. We recommend testing enzyme levels with or without genotype in Black patients.

13 BIOMARKERS AT DIAGNOSIS IN A RACIALLY DIVERSE PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD) POPULATION. Gitti Tomer, Yolanda Rivas, John Thompson, Pediatric Gastroenterology and Nutrition, Children’s Hospital at Montefiore, Bronx, NY

Background: IBD is increasingly recognized in diverse ethnic populations. In the United States, IBD among minority populations has not been thoroughly studied and there are scarce data regarding disease presentation and laboratory values. Objective: To determine biomarkers characteristics of a newly diagnosed diverse pediatric IBD population. Methods: A retrospective chart review of patients with IBD who are followed in pediatric Gastroenterology center. Biomarkers at diagnosis were recorded, including hemoglobin, platelet count, albumin, sedimentation rate (ESR) and C-reactive protein (CRP). Results: Of a total of 86 patients with IBD, 11 were excluded (8 diagnosed elsewhere and 3 had sickle cell disease). Seventy five patients were studied. 58 with Crohn’s disease (CD), 15 with ulcerative colitis (UC) and 2 IBD unclassified. The mean time to diagnosis was 25 weeks. The mean age was 12.7; 69% were male. Thirty two percent were Black, 19% Caucasian, 4% Asian, 27% multiracial and 19% declined reporting racial status. Among CD patients, 66% had ileocolonic disease and 57% had upper tract disease; 22% had penetrating disease and 16% had strictureing disease. Seventy two percent of CD patients and 75% of UC patients had elevated sedimentation rate; 77% of CD patients but only 33% of UC patients had elevated CRP. Among 48 IBD patients that had both CRP and ESR done, 23% had normal CRP but elevated ESR; 12.5% had normal ESR but elevated CRP. Altogether there was discrepancy between ESR and CRP in 35.5% of patients. Platelets were elevated in 44% of patients. Low albumin was seen in 36% of patients and anemia was seen in 65% of patients. Normal values of ESR, CRP, albumin, Platelets, and Hemoglobin were seen only in 8% of patients. Conclusion: Due to the discrepancy between the different biomarkers of disease activity, we recommend screening laboratory tests to include CBC, albumin, ESR, and CRP as it increases the yield of abnormal results, alerts physicians to the possibility of inflammatory bowel disease diagnosis and may prevent delay in diagnosis.

14 OBESITY AMONG DIVERSE INNER CITY PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD) POPULATION. Russell Cameron, John Thompson, Gitti Tomer, Pediatric Gastroenterology and Nutrition, Children’s Hospital at Montefiore, Bronx, NY

Background: National statistics of body mass index (BMI) of children and adolescents show that 31.7% are overweight/obese. Data from New York City and the Bronx show a prevalence of 38-47%. Studies have shown that 10-30% of pediatric IBD patients are overweight or obese. Objective: To study BMI of diverse pediatric IBD patients at presentation. Methods: A retrospective study of IBD children followed at our center. Patient demographics, clinical information, and anthropometrics were analyzed. Results: Of a total of 86 IBD patients 19 were excluded for comorbid conditions, incomplete data, or age < 2 years. Sixty-seven patients were studied; 79% with Crohn’s Disease (CD) and 21% with Ulcerative Colitis (UC). The mean age at diagnosis of IBD was 13.26 years; 30% were black, 18% Caucasian, 4% Asian, 28% multiracial and 18% declined reporting racial status. The prevalence of overweight/obesity among patients with IBD was 15%. Only 9% of CD patients and none of UC patients had a low BMI (< 5%). Overall 78% of children with CD and UC had a BMI in the normal range; 47% of CD patients had BMI > 50% and 64% of UC patients had BMI >50%. The mean duration of symptoms prior to diagnosis for all patients was
22.7 weeks and was not significantly different among patients with BMI>85%, >5%BMI<85%, BMI <5%; the duration of symptoms was also not different between racial groups. The male to female ratio was not different in the obese vs. normal/low weight patient. CD patients had longer time to diagnosis than those with UC (25.9 vs. 11.1 weeks, p=.001). Among CD patients with BMI>85%, >5%BMI<85%, and BMI <5%, there was no difference in disease location and phenotype. Conclusions: 1. In our diverse inner city pediatric IBD patients, prevalence of BMI<5% was lower as compared to that reported in the literature. 2. Most of newly diagnosed children with IBD had BMI in the normal range and obese category. 3. In our pediatric IBD patient population obesity was not associated with longer duration to diagnosis or any unique demographic or clinical characteristics.

15 A 3-MARKER HAPLOTYPE IN IRF5 IS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE IN A NORTH AMERICAN COHORT. Grace Gathungu1, Clarence K. Zhang2, Judy H. Cho2 1Pediatrics, Division of Pediatric Gastroenterology, Stony Brook Medical Center, Stony Brook, NY; 2Internal Medicine, Section of Digestive Diseases, Yale University, New Haven, CT

Introduction: The IRF5 gene is located on human chromosome 7q32. It is associated with multiple Immune Mediated Inflammatory Disorders. IRF5 regulates pro-inflammatory cytokines and Type I Interferons. We further investigate the role of IRF5 polymorphisms in a cohort of Inflammatory Bowel Disease patients from a North American IBD Consortium.

Methods: We genotyped six single nucleotide polymorphisms (SNPs) and a 5-bp (CGGGG) insertion-deletion of the IRF5 gene in two populations, a case-control cohort with 3600 cases, and a family cohort with 600 Trio and Tetrads families. In addition, cytokine expression was measured in primary lymphocytes after TLR9 stimulation.

Results: In a combined analysis, 3-marker haplotypes containing the CGGGG 5-base pair insertion/deletion polymorphism, the rs7808907 and rs4728142 SNPs are strongly associated with IBD protection (p=3.43E-14, p=6.54E-10) (European ancestry); and p=1.6E-11, p=0.01, p=0.011 (Jewish ancestry) and IBD risk p=0.046 (European ancestry) and p=0.006 (Jewish ancestry). IRF5 polymorphisms were risk factors for both Crohn’s and Ulcerative colitis. IL-12p70 cytokine expression was increased (p=0.05) in PBMCs with two alleles of the risk variant for the CGGGG indel.

Conclusions: IRF5 gene polymorphisms contribute to the risk profile for both Crohn’s and Ulcerative colitis along with ancestry, appendectomy and smoking. IRF5 may further predispose to Multiple Immune Mediated Inflammatory Disorders by altered apoptosis and increased expression of pro-inflammatory cytokines.

Table 1: IRF5 gene significant 3-marker* haplotype association

<table>
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<tr>
<th>All European ancestry haplotype</th>
<th>Haplotype Frequency</th>
<th>OR (95% C.I.)</th>
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<tr>
<td></td>
<td>IBD Cases</td>
<td>Controls</td>
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<tr>
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<tr>
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<tr>
<td>A-G-C</td>
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*Risk alleles: A for rs4728142 (A/G), insertion for CGGGG Indel, C for rs7808907(C/T); Indel: insertion/deletion.

16 HEALTH-RELATED QUALITY OF LIFE IN PAEDIATRIC ULCERATIVE COLITIS PATIENTS ON CONVENTIONAL MEDICAL TREATMENT COMPARED TO THOSE AFTER RESTORATIVE PROCTOCOLECTOMY. Bushra A. Malik1, Kristen Gibbons1, Don Spady1, Gordon Lees2, Anthony Otley3, Hien Q. Huynh1 1Pediatrics, University of Alberta, Edmonton, AB, Canada; 2Surgery, University of Alberta, Edmonton, AB, Canada; 3Pediatrics, Dalhousie University, Halifax, NS, Canada

Background: Health related quality of life (HRQL) in not well studied in proctocolectomy patients with pediatric onset of UC. We aimed to (1) determine the factors that influence HRQL; (2) compare the HRQL of proctocolectomy patients with those treated with conventional therapy.

Methods: Chart review was done on patients diagnosed with pediatric onset of UC (<18) at the Stollery Children’s Hospital. HRQL was evaluated in 88 patients using two disease and age specific questionnaires; IMPACT-III (<18) and inflammatory bowel disease questionnaire (IBDQ); ≥18). Demographics, disease characteristics, disease index (PUCAI), EuroQoL (EQ)-5D index and the visual analog scale (VAS) were collected and analyzed from all patients.

Results: Sixty five patients completed the IMPACT-III (74%) and twenty three patients completed the IBDQ (26%). Twenty surgical patients (31%) responded (mean IMPACT-III score= 148.9±12.7; PUCAI= 18.3±10.5; EQ-5D-5TM-VAS= 84±11.8). There was no significant difference in IMPACT III scores of surgical patients vs. medically treated patients (148.9±12.7 vs. 140.6±19.4, p=0.09). Patients with high IMPACT scores (>143 points) were most likely to be in remission (p = 0.05), they were less likely to be on medication (p < 0.05), have parent/guardian with postsecondary education (p = 0.01) and or did not report depression (p < 0.02). The IMPACT correlation with PUCAI (adjusted R2 = 0.33) and EQ-VAS (adjusted R2 = 0.45) was strong.

Conclusions: Restorative proctocolectomy is a viable option. Surgical patients reported to have a HRQL comparable to or better than the non-surgical patients. Depression, tiredness, parent/guardian education and drugs influence HRQL.
17  RUNX3 EXPRESSION IN INFLAMMATORY BOWEL DISEASE. Humaira Hashmi, Robert D. Baker, Razan Alkhour, Zha Lixin, Pediatric Gastroenterology, University at Buffalo, Buffalo, NY

Background: Inflammatory bowel diseases (IBD), comprised of crohn’s disease (CD) and ulcerative colitis (UC), are characterized by chronic relapsing inflammation of the gastrointestinal tract. Concordance rates in twins and siblings suggest that a genetic predisposition contributes to the pathogenesis of IBD. RUNX3 is involved in T-cell differentiation and functions as a tumor suppressor gene in gastric cancer. The RUNX proteins appear to have a potential role in autoimmune diseases, although very little is known about how these transcription factors are involved in these disorders. The gene encoding for RUNX3 resides on the chromosomal region 1p36, which has been found to be a susceptibility locus for IBD. Moreover, RUNX3 and TGFβ are down regulated in peripheral blood cells of CD patients, which might suggest involvement of this pathway in the human pathogenesis of IBD. The RUNX3 expression in intestine tissues was not studied, which is the subject of this report.

Methods: The RUNX3 gene expression in CD and UC was examined and compared to the normal control. Inflamed mucosa of CD and UC, as well as the normal mucosa of CD and UC were examined. Complementary DNA was prepared from intestinal biopsy specimens from CD, UC and normal control subjects. Quantitative real-time PCR analysis was performed to compare gene expression of RUNX3.

Results: RUNX3 is down regulated in CD as well in UC versus normal control. We have also seen difference in inflamed mucosa of the CD and UC versus normal mucosa of the same patients. The P value of the normal control versus CD is 0.0054 and for the normal versus UC is 0.0054.

Conclusion: We conclude that drastic decrease of the RUNX3 expression in diseased tissue suggest an important role in the pathogenesis of IBD and tumorgenesis of IBD patients.

RUNX3 expression

<table>
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<tr>
<th>Site</th>
<th>Normal</th>
<th>CD</th>
<th>UC</th>
<th>Normal vs CD P value</th>
<th>Normal vs UC P value</th>
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<td>2.4</td>
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<td>1.7</td>
<td>1.2</td>
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18  THE EFFICACY AND SAFETY OF CONCOMITANT THERAPY WITH METHOTREXATE AND ANTI-TNFα IN PEDIATRIC PATIENTS WITH REFRACTORY CROHN’S COLITIS: A CASE SERIES. Imad Absah, William A. Faubion, Pediatric Gastroenterology and Nutrition, Mayo Clinic, Rochester, MN

Background: Crohn’s colitis refractory to anti-TNFα therapy is commonly seen in tertiary care centers for pediatric inflammatory bowel disease (IBD). We report our experience in managing pediatric refractory Crohn’s colitis with concomitant use of methotrexate and anti-TNFα therapy.

Methods: We reviewed records from 2007 to 2010 at the Mayo Clinic pediatric IBD center. We included all patients with CD failing anti-TNFα therapy who then received concomitant methotrexate. The primary end point was clinical remission, defined as inactive disease in accordance with the physician global assessment (PGA). The secondary end point was last day of follow-up.

Results: Fourteen patients with CD received concomitant methotrexate and anti-TNFα treatment (age, mean [range], 15.7 [6-20] years; SD, 3.4 years). Mean age at diagnosis was 12.5 years (range, 3-17 years; SD, 3.83 years). The male to female ratio was 10:4. All patients had moderate to severe disease activity through PGA and had predominately Crohn’s colitis. Twelve patients had failed thiopurine treatment (85.7%). Seven patients (50%) were in clinical remission within an average of 6 weeks post methotrexate induction. Five patients (35.7%) experienced adverse events, including nausea and headache that resolved with cessation of methotrexate therapy. Clostridium difficile colitis was documented in 4 patients (28.6%).

Conclusions: Concomitant use of methotrexate and anti-TNFα therapy is a safe, viable option for children with refractory Crohn colitis before they are referred to surgery. Prospective controlled trials are indicated to determine efficacy and long-term results of concomitant therapy in pediatric Crohn colitis.

Keywords: adverse effects; tumor necrosis factor; Crohn disease; inflammatory bowel diseases; methotrexate

19* RISING IN-HOSPITAL POST-COLECTOMY COMPLICATIONS RATES IN CHILDREN WITH ULCERATIVE COLITIS DESPITE CONSTANT COLECTOMY RATES IN THE UNITED STATES BETWEEN 1997 AND 2006. Ing Shian Soon1,2, Jennifer deBruyn1, James Hubbard1, Iwona Wrobel1, David Sigal1, Reg Sauve1,2, Gilaad Kaplan1,2,3 Pediatrics, University of Calgary, Calgary, AB, Canada; 1Medicine, University of Calgary, Calgary, AB, Canada; 2Community Health Sciences, University of Calgary, Calgary, AB, Canada; 3Surgery, University of Calgary, Calgary, AB, Canada

BACKGROUND: In children with ulcerative colitis (UC), data on temporal colectomy trends and in-hospital post-colectomy complications is limited. Thus, we evaluated the United States (US) nationwide population-based trends in colectomy rates and post-colectomy complications in children with UC.

METHODS: We identified all admissions for children (≤18 years) with a diagnosis code of UC (ICD-9: 556.X) and a procedure code of colectomy (ICD-9: 45.8 and 45.7) in the Healthcare Cost and Utilization Project Kids’ Inpatient Database for 1997, 2000, 2003, and 2006. The incidence of colectomies for pediatric UC was calculated by dividing the annual total number of colectomies by the U.S. Census population. Poisson regression analysis was performed to evaluate the change in rate of
colostomy and postoperative complications over time.

RESULTS: During the four study years, 648 children with UC underwent colectomy. The annual overall colectomy rate was 0.40 per 100,000 person-years, which was stable throughout the study period (p>0.05). Postoperative complications were experienced in 24% of children. Postoperative complication rates increased significantly by an annual rate of 5.9% from 1997 to 2006 (p<0.05). Patients with postoperative complications had significantly longer lengths of stay (5.8 vs 8.6 days; p< 0.0001) and higher total hospital charges ($51,924 vs $73,306; p<0.0001) compared to those without complication.

CONCLUSION: Colectomy rates across the US in children with UC have remained constant between 1997 and 2006; however, in-hospital postoperative complication rates have increased.

20 NATURAL KILLER T CELLS (NKT) BEARING THE IL-13Rα2 ARE CYTOTOXIC FOR EPITHELIAL CELLS AND MEDIATE THE PATHOGENESIS OF HUMAN AND EXPERIMENTAL ULCERATIVE COLITIS (UC). Ivan J. Fuss1, Bharat Joshi2, Zhiqiong Yang1, Heba Degheidy2, Raj K. Puri1, Warren Strober, 1Mucosal Immunity Section, NIH, Bethesda, MD; 2Division of Cellular and Gene Therapies, CBER FDA, Bethesda, MD

In prior studies, we showed that oxazolone colitis (Oxa), a murine colitis model that has features of UC, is driven by NKT cells which secrete increased amounts of IL-13. In human studies, we showed that UC LPMC also produce significant amounts of IL-13 arising from NKT cells. Moreover, these NKT cells were directly cytotoxic for HT-29 epithelial cells, thus establishing their possible mechanism of injury in UC. Recently it has been demonstrated that IL-13Rα2 can function as a signaling receptor for IL-13. In the present studies we determined the relationship of cells bearing this receptor to the occurrence of inflammation.

Results: In initial flow cytometric studies we found that peripheral blood T cell populations of UC patients contained a higher percentage of cells that bear both CD161 (NKT) and IL-13Rα2 markers as compared to Crohn’s disease or normal control cell populations. This correlated with the presence of large numbers of CD161+ LP cells expressing IL-13Rα2 in LP cell populations of UC patients as compared to CD or normal control patients. In further studies we demonstrated that depletion of IL-13Rα2 cells from UC patient LP population with a cytotoxic agent, mutated IL-13 coupled to pseudomonas exotoxin, that binds specifically to IL-13Rα2-bearing cells led to: 1) loss of CD4+ cells producing IL-13 and 2) reduced cytotoxicity of CD4+ T cells for HT-29 targets. Finally, to examine the pathogenicity of the IL-13Rα2 bearing cells we treated mice with oxazolone colitis with the IL-13 pseudomonas exotoxin and found that such treatment led to both amelioration of intestinal inflammation and decreased IL-13 secretion. Conclusion: These studies show that UC is characterized by large numbers of IL-13Rα2-bearing, CD4+ NKT cells that produce IL-13 and manifest cytotoxicity for epithelial cells. Taken with data that such cells mediate oxazolone colitis, these studies suggest the IL-13Rα2 cells direct the pathogenesis of UC.

21 RESPONSE TO HEPATITIS B VACCINE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE RECEIVING INFlixIMAB. J. Moses, N. Alikhoui, A. Shannon, K. Raig, R. Lopez, L. Danziger-Isakov, A. Feldstein, N. Zein, R. Wylle, C. Carter-Kent, The Cleveland Clinic, Cleveland, OH

Infliximab has revolutionized the treatment of pediatric Crohn’s disease (CD); however, this medication is a potent immunosuppressant that may compromise response to immunizations. The aim of this study was to evaluate the immunoegenicity of the hepatitis B virus (HBV) vaccine in children with CD treated with infliximab.

Methods: This was a prospective single-center study. Our cohort consisted of children and adolescents with CD who were diagnosed between the ages of 5 and 18 years. We screened 102 pediatric patients on infliximab for hepatitis B immunity and we were able to identify patients who were not immunized. Eight out of these 13 patients completed HBV immunization series at 0, 1, and 6 months with the recombinant HBV vaccine (Recombivax). Serum samples were collected four weeks after completing the series to assess for seroconversion (the presence of protective antibodies defined as anti-HBs level ≥10 mIU/mL).

Results: The mean age at diagnosis was 13.5 ± 2.3 years and at time of first HBV vaccine dose was 19.6 ± 2.4 years. All patients were Caucasian and 75% were male. The majority of patients had ileocolonic disease (75%). None of the patients were positive for HBV surface antigen or core antibody. Only 50% of the patients achieved seroconversion after HBV vaccination. Non-responders tended to be older at time of first vaccine dose. None of the patients were receiving prednisone at the time of HBV immunization and 4 patients were on concurrent immunomodulators. There were no serious adverse events related to HBV vaccine during the study.

Conclusion: Treatment with infliximab for pediatric CD patients may decrease their response to HBV vaccine with only half of our cohort developing protective levels of anti-HBs. HBV vaccine appears safe when given during infliximab therapy with no serious adverse events noted during the study. Efforts should be made to screen for HBV immunity at the time of CD diagnosis and immunization should be considered for non-immune patients.

22 EFFICACY OF INDUCTION THERAPY WITH INFlixIMAB IN POLISH CHILDREN WITH CROHN DISEASE. Jaroslaw Kierkus, Maciej Dadalski, Grzegorz Oracz, Agnieszka Wegner, Monika Gorczewska, Jozef Ryzko, Dep. of Gastroenterology, Hepatology and Immunology, The Children's Memorial Health Institute, Warsaw, Poland

Background: There is so far lack of satisfactory data about infliximab therapy in children with CD from Eastern and Medium Europe.

Aim: The aim of this study was to assess clinical efficacy of induction and maintenance therapy with infliximab in Polish children with CD.

Methods: 66 CD children (PCDAI >30) with history of immunomodulation therapy (48 with AZA, 21 with Mtx) were involved to study. Pts received infliximab (5 mg/kg) in three repeated infusions at 0, 2, 6 weeks and next one year therapy every 8 weeks. Clinical evaluations were performed at baseline, week 10 and week 52. SES-CD was calculated for colonoscopies performed before treatment week 10 and week 52.

Results: Induction: 22 (33%) pts has reached clinical remission (PCDAI score≤ 10), 26 (39%) clinical response (PCDAI decrease...
were 44 youth with IBD and 23 healthy children (ages 11-18, M=14.83). Children completed a project-developed survey and control colonoscopy. 15 out of 66 patient had score 0 in control endoscopy vs. 2 out of 66 in initial one p<0.05. We have not found significant changes in SES-CD at week 10 and week 52.

Conclusions: 1. Induction therapy with infliximab is clinically efficient in 72% of Polish children with CD. 2. Therapy with infliximab improves nutritional status of these patients. 3. Maintenance therapy with infliximab increases the remission percentage in children with CD and prevents CD flare. 4. Biological therapy with infliximab is effective to achieve mucosal healing in paediatric patients with CD.

23 A COMPARISON OF THE PREVALENCE OF INFLAMMATORY BOWEL DISEASE AMONGST ETHNICITIES IN A SOUTHWESTERN PEDIATRIC GASTROENTEROLOGY PRACTICE. Jennifer Adair, David Gremse, Rebecca Scherr, Pediatrics, University of Nevada School of Medicine, Las Vegas, NV

Purpose: Inflammatory bowel diseases (IBD) affects approximately 2 million Americans. While it has been historically thought to be a disease affecting Caucasians it is now apparent that other ethnic groups are also affected. The Hispanic population is increasing in the United States therefore this study was done to determine the prevalence of IBD among ethnicities in a southwestern pediatric gastroenterology clinic.

Methods: We performed a retrospective record analysis of patients between the ages of 1 and 18 years old who were seen at a pediatric gastroenterology center in Las Vegas during the years 2003-2010. All patients seen by this practice were separated by race/ethnicity including African American, Caucasian, Hispanic, Asian/other or unknown. All patients’ charts with the diagnosis of Crohn disease, ulcerative colitis, proctitis, nonspecific colitis, IBD, or colitis were evaluated for radiographic, endoscopic, histologic and clinical course consistent with the diagnosis of IBD. The diagnosis was confirmed by the patient’s gastroenterologist.

Prevalence of IBD within each race was determined. Statistical significance was calculated using two sample t-test.

Results: 1424 patients (IBD and controls) were included in the study. The race/ethnicity distribution was 11.6% African American, 42.8% Caucasian, 39.2% Hispanic, 3.2% Asian/other, 3.2% unknown. Forty-three of the 1424 patients were diagnosed with IBD. Twenty-nine had Crohn disease and 14 ulcerative colitis. Of these 8 were Hispanic, 8 African American, and 27 Caucasian. The prevalence of IBD between Caucasians and African Americans was not statistically significant p=0.82. However, the prevalence of IBD was significantly higher in each of these races compared to Hispanics p<0.01.

Conclusion: Compared to Caucasians and African Americans, Hispanics have decreased prevalence of IBD among pediatric patients. Although genetics contribute to the development of IBD, the role of environmental and dietary factors cannot be overlooked.

24 RISING HOSPITALIZATION RATES FOR PEDIATRIC INFLAMMATORY BOWEL DISEASES IN THE UNITED STATES (1997-2006). Jennifer deBruyn2, Ing Shian Soon1,3, James Hubbard1, Iwona Wrobel2, Gilad G. Kaplan2,3,1
1Pediatrics, University of Calgary, Calgary, AB, Canada; 2Medicine, University of Calgary, Calgary, AB, Canada; 3Community Health Sciences, University of Calgary, Calgary, AB, Canada

BACKGROUND: The global incidence and prevalence of pediatric Crohn’s disease (CD) and ulcerative colitis (UC) are rising. Yet data is limited on time trends in pediatric CD and UC hospitalization and surgical rates. Thus we evaluated the United States (US) nationwide population-based trends in hospitalization and surgical rates in children with CD and UC.

METHODS: We identified all admissions for children ≤18 years old with a primary diagnosis of CD (ICD-9: 555.X) or UC (ICD-9: 556.X) in the Healthcare Cost and Utilization Project Kids’ Inpatient Database for 1997, 2000, 2003, and 2006. The yearly incidences of hospitalization and surgery were obtained using the US Census population. We also obtained trends in hospital resource utilization (length of stay, total hospital charges). Poisson regression analysis was used to evaluate temporal changes in incidence of hospitalization and surgeries, and hospital resource utilization.

RESULTS: There were 8,928 and 5,383 hospitalizations for CD and UC, respectively. The yearly hospitalization rates were 5.3 and 3.2 per 100,000 persons for CD and UC, respectively, with significant increases over time for CD (3.7% 95% confidence interval [CI] 3.2-4.1%) and UC (4.7% 95% CI 4.0-5.3%). For CD, there were significant temporal increases in total hospital days (6.4% P=0.03) and total hospital charges (11.3% P=0.01); however mean length of stay and mean charge per patient remained stable. For UC, there were significant time trends in total hospital days (7.8% P=0.01), mean length of stay per patient (-1.4% P=0.01), and total charges (7.8% P=0.02); however mean charge per patient remained stable. The yearly surgical rates were 0.89 and 0.45 per 100,000 persons for CD and UC, respectively, remaining stable over time.

CONCLUSION: In concordance with rising incidence and prevalence of pediatric CD and UC, US hospitalization rates along with total hospital resource utilization for children with CD and UC rose from 1997 to 2006.

25 SOCIALLY INTERACTIVE TECHNOLOGY USAGE IN PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD), Jessica Ruff1, C. M. Ross2, L. M. Mackner1, K. Vannatta1, W. V. Crandall2, ‘Biobehavioral Health, Nationwide Children’s Hospital, Columbus, OH; 2Gastroenterology/Nutrition, Nationwide Children’s Hospital, Columbus, OH

Youth with IBD have significant social difficulty compared to healthy peers. Social networking sites (SNS) and text messaging (short message service; SMS) have become more popular, but it is unknown if their social difficulty extends to these arenas. The purpose of this study is to examine the use of social technology in youth with IBD compared to healthy children. Participants were 44 youth with IBD and 23 healthy children (ages 11-18, M=14.83). Children completed a project-developed survey and
displayed information from their SNS and SMS websites on study netbooks for objective data collection. Recruitment is ongoing. Preliminary data suggest that those with IBD spend less time on the internet (M=10.8 hrs, s.d.=14.1) and SMS (M=8.8 hrs, s.d.=13.6) per week compared to their healthy peers (M=13.0 hrs, s.d.=12.7 and M=10.8 hrs, s.d.=12.5 respectively). Fifty-one percent of youth with IBD reported feeling that they use SNS less than their peers, compared to only 36% of healthy comparisons. They have fewer Facebook friends (M=274, s.d.=213) vs. M=300, s.d.=163) and send fewer texts per billing cycle (Mdn=23.6, s.d.=139.1 vs. Mdn=65.1, s.d.=96.2) Youth with IBD used SNS less often than healthy to keep in touch with friends (58% vs. 78%), look at friends’ profiles (49% vs. 61%), or coordinate plans (25% vs. 57%, p=.037). Similarly in SMS usage, youth with IBD less often coordinate plans (74% vs. 90%) or send greetings (65% vs. 84%) compared to healthy youth. Interestingly, healthy children do not use SNS as often as those with IBD to meet new friends (6 vs. 17%). They were also more likely to use SNS sites when not feeling well than peers (31% vs. 17%, p=.047). There were no differences in the rates of online peer victimization (range 3-11% for both). The social difficulty youth with IBD experience may include their use of social technology. Given the importance of this technology in youth culture, interventions aimed at improving social functioning should include SNS and SMS usage.

26 CHARACTERISTICS OF PEDIATRIC IBD IN TEXAS. Kalpesh Thakkar¹, Ashish Patel², Carolyn Thibodeaux¹, George Ferry¹, ¹Baylor, Houston, TX; ²UT Southwestern, Dallas, TX

Background: There is little information regarding the characteristics of newly diagnosed IBD in children residing in the USA. Additionally, the frequency and presentation of pediatric onset IBD in minority populations has not been well studied. Methods: We conducted a prospective study to assess the characteristics and ethnic/racial variations of pediatric IBD (0-15 years) with questionnaire-based data collection at 10 pediatric facilities in Texas between Jan 2009 and Oct 2010. We included all children with new diagnosis of IBD at each center and collected clinical characteristics for each patient enrolled in the study. We compared racial groups with respect to presenting symptoms, blood work (hemoglobin, albumin, ESR, CRP), gender, age, IBD type and initial therapy. Results: We enrolled 150 children with newly diagnosed IBD (mean age 11.3; SD 2.8) including 82 (54.7%) female patients and 86 (57.3%) patients with Crohn’s disease (CD), 58 (38.7%) with Ulcerative Colitis, and 6 (4%) with Indeterminate Colitis. Race was described as “White/Caucasian” (90, 60%), followed by “Black/African-American” (28, 18.7%), “Hispanic” (23, 15%) and “Asian” (5, 3.3%). A family history of IBD was reported in 38 (25.3%) patients. 76 (50.7%) of patients presented with weight loss, 25 (16.7%) with arthritis/arthritis, and 83 (55.3%) had gastrointestinal bleeding. Initial therapy included corticosteroids in 84 (56%), 5ASA products in 80 (53%), infliximab in 23 (15%), 6-mercaptopurine in 19 (13%), and azathioprine in 21 (14%) children. The prevalence of anemia, hypoalbuminemia, elevated CRP was not associated with race. Elevated ESR was associated with new-onset IBD in African American children (0.03). White/Caucasian patients did have a significantly higher rate of CD than other races (p=0.04). No association was found between IBD type and minority groups. Conclusions: Our findings suggest that approximately 40% of pediatric IBD occurs in minority populations. White/Caucasian patients are more likely to have CD than other racial groups. ESR may have additional utility in African-American children presenting with IBD symptoms.

27 PATHOLOGICAL FINDING AT DIAGNOSIS: AS A PREDICTOR OF STEROID DEPENDENT / RESISTANT ULCERATIVE COLITIS IN CHILDREN. Katsuhiro Arata¹, Tadahiro Yanagi¹,², Natsuko Nakano¹, Hirohata Shimizu¹, Atsuko Nakazawa¹,², Div. of Gastroenterology, National Center for Child Health and Development, Setagaya, Japan; ²Dept. of Pathology, National Center for Child Health and Development, Setagaya, Japan; ³Dept. of Pediatrics, Keio University, Shinjuku, Japan

The prevalence of ulcerative colitis (UC) in children is getting higher worldwide. Approximately 30-40% of children with UC are steroid dependent or resistant, and require second-line therapy such as leukocyteapheresis, cyclosporin, tacrolimus or infliximab. Some children even require colectomy. Prolonged use of steroid or second therapy is important for the better outcome. Methods: This is a retrospective chart review of 35 children with UC followed at National Center for Child Health and Development, Japan for more than 6 months between 2003 and 2010. Cases with primary sclerosing cholangitis, infantile onset, or incomplete initial data were excluded. Patients were divided into two groups; first line treatment responsive group (group A) and steroid dependent / resistant group (group B). Possible predictors of steroid dependence / resistance were compared between group A and B. In order to assess the effect of pathological finding, UC-S score, know as a predictor of adult with UC who ultimately required surgery, were used as a possible predictor of steroid dependence / resistance in children with UC. Results: 20 children were enrolled for this study. Among them, 9 children were steroid dependent / resistant (group B). There were no significant difference between two groups in sex, age at onset, age at diagnosis, duration between disease onset and diagnosis, extent of disease, CRP at diagnosis, as well as Mats classification. PUCAI was significantly higher in group B (median (range): 40(25~50) vs 60(40~80), p<0.001). UC-S score was significantly higher in group B (2.0(3.7~6.1) vs 4.0(2.0~8.4), p<0.05). Conclusions: Besides PUCAI score, UC-S score may be useful in predicting the steroid dependent / resistant children with UC.

28 OUTCOME AFTER INFliximab TREATMENT IN PEDIATRIC ULCERATIVE COLITIS. Kimberly Isola, Kathy Hoffstadter-Thal, Juli Tomaino, Clare Ceballos, Kevin Bao, Nanci Pittman, Keith Breglio, Keith Benkov, Pediatric GI, Mount Sinai, New York, NY

Background: Medical treatment is limited for corticosteroid dependant/refractory ulcerative colitis (UC). Infliximab has been efficacious in short-term management of UC in the adult population. Long-term data in pediatrics is lacking: with two studies, 52 and 22 subjects, demonstrating short-term success. Aims: Determine clinical and surgical outcomes after infliximab in pediatric UC.
Methods: The Mount Sinai Children’s IBD database, containing over 1600 records, was used to identify patients with UC who received at least one infliximab infusion. Clinical and surgical data for three years post infliximab initiation was reviewed, and colectomy and corticosteroid free remission rates determined.

Results: Twenty-seven UC patients who received infliximab were identified. Forty-four percent were females. Seventy-five percent had pancolitis on diagnostic colonoscopy. Mean age at first infliximab infusion was 12.1 years (2-20). Median time from diagnosis to infliximab was 11 months (IQR 2-16.5). Median number of doses was 3 (IQR 2-5). Eighteen percent of patients required dose escalation from 5mg/kg/dose. Ninety percent received their first infliximab infusion as an inpatient. Sixty-two percent were steroid refractory while 38% were steroid dependent. Previous treatments included corticosteroids (100%), immunomodulators (77%), 5-aminosalicylates (96%), and cyclosporine (11%). Colectomy rates were 19%, 33%, 57%, 75% at 6mo, 12mo, 24mo, and 36mo respectively. Median time from infliximab to surgery was 16 months (IQR 4-22). Corticosteroid free remission at those times was 25%, 21%, 20% and 0%.

Discussion: In this pediatric UC population who received infliximab, 75% had colectomy within 3 years post infliximab. Only 20% achieved steroid free remission at 24 months and 0% at 36 months.

29  CAN PROVIDER AWARENESS ALONE IMPROVE TRANSITION READINESS SKILLS IN PATIENTS WITH IBD? Laurie Fishman1, Sonja Ziniel2, Max Adrichem3, Janis Arnold1, 1Inflammatory Bowel Disease Center, Childrens Hospital Boston, Boston, MA; 2Clinical Research Program, Childrens Hospital, Boston, MA; 3University of Amsterdam, Amsterdam, Netherlands

Introduction: There is increased recognition of the need for gradual assumption of responsibility by adolescent patients with chronic health conditions. Self-management skills are needed for successful transfer to adult health care but the ideal transition process is still debated. Pediatric providers play a pivotal role in this process.

Objective: To evaluate if informal education of pediatric providers regarding transition improves IBD patient self-management skills.

Methods: Consecutive IBD patients over age 10 who presented to the outpatient setting were administered a survey regarding self-management behaviors in 2008 and in 2011. There was 28% overlap of patients. In the intervening time, several conferences on transition were presented to the providers.

Results: Cohorts demographics were similar. For 2008, N=294 (82% response rate) while 2011, N=121 (89% response rate). About half were male (50% vs. 42%) and most had Crohn’s (68% vs. 66%). The mean age was around 16 years (16.7 vs. 16.2). For the 16-18 year old patients, the increase in responsibility was not significant. Contacting the provider between visits increased from 12% to 13% (ns), calling in refills increased from 13% to 22% (ns), and asking questions during the visit changed from 14% to 22% (ns). Scheduling appointments dipped from 9% to 7% (ns).

For patients 19 years and older, there was a more dramatic rise in self-management skills. Contacting the provider changed from 46% in 2008 to 66% in 2011 (p= 0.06). Calling in refills rose from 58% to 73% (ns), and scheduling appointments from 48% to 72% (p= 0.02). Asking questions during the visit increased from 48% to 77% (p= 0.001).

Conclusion: Increasing awareness around transition readiness for pediatric providers had a positive effect on IBD patient self-management skills. However, to increase skills further, particularly in the younger age groups, a structured transition program may be needed.

30* THE EFFECT OF IMMUNOMODULATORY THERAPIES ON SURGICAL INDICATION IN CHILDREN WITH CROHN DISEASE. Lori A. Zimmerman1, Robert Shamberger2, Bradley Linden2, Clarissa Valim1, Athos Bousvaros1,1Gastroenterology, Children's Hospital Boston, Boston, MA; 2Surgery, Children's Hospital Boston, Boston, MA

Background: A significant number of children diagnosed with Crohn disease (CD) in childhood will require bowel resection during the childhood years. While prior studies have attempted to identify risk factors for surgery and postoperative recurrence, the effects of immunomodulatory therapies (6-mercaptopurine and azathioprine) on the indications for surgery have not been well characterized.

Methods: We reviewed a series of 91 consecutive children with CD that underwent bowel resection between 1979 and 2005 at Children's Hospital Boston. Patients were included if they underwent a resection of small bowel or colon with immediate or subsequent reanastomosis, and were followed for at least 6 months. Patients with only perianal surgery, or who underwent colectomy with permanent ostomy were excluded. A perforating complication was defined as an abdominal abscess or internal fistula. The primary outcome of the study was postoperative indication for surgery (perforating complication vs. other indication). Covariates examined included age, sex, disease location, disease behavior, and preoperative medications.

Results: Of the 50 patients who received immunomodulatory therapy prior to surgery, 11 patients (22%) required surgery for a perforating complication, while 39 patients (78%) required surgery for strictures or medically refractory disease. In contrast, of the 40 patients who did not receive immunomodulatory therapy preoperatively, 18 patients (45%) developed a perforating complication, and 22 (55%) were operated on for refractory disease. The patients receiving preoperative immunomodulatory therapy had a significantly lower rate of operation for perforating complications (22% vs. 45%), p<0.05. Aside from preoperative immunomodulator therapy, we did not identify any other significant risk factor for abscess or fistula formation.

Conclusion: Of children with Crohn disease who require surgery, use of immunomodulators is associated with reduced likelihood of an abdominal abscess or fistula.
31 INCIDENCE OF IBD IN ICELANDIC CHILDREN 1950-2010: NATIONWIDE POPULATION BASED STUDY. Ulfiur Agnarsson, Sigurdur Bjornsson, Luther Sigurdsson, Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison, WI Aim: Describing the changes in incidence of IBD in Iceland. Material and methods: All IBD patients < 16 years of age diagnosed in Iceland 1950-2010 were included. From 1950-1989 patients were identified retrospectively reviewing charts and pathological specimens. Since 1990 we prospectively obtained data on IBD patients. Only patients fulfilling Lennard-Jones1 criteria for Ulcerative colitis (UC) and Crohn’s disease (CD) were included. Colitis not clearly UC or CD was called indeterminate colitis (IC). Results: 110 children were diagnosed to have IBD, 61 with UC, 44 CD and 5 were indeterminate. The median age of children was 13.7+/−2.6 years; there were 70 boys and the sex distribution varied decade to decade (M:F 1.6:1 to 5:1). Twenty percent of both patients with UC and Crohn’s disease had a family history of IBD. From 1951 until 2000 there was a dramatic increase in the incidence of IBD from 1.2 per 100,000 children < 16 years of age to 5.6 per 100,000; however, in the last decade (2000-2010) the incidence stabilized at 5 per 100,000. Right sided disease became more prominent in last 3 decades. Conclusion: In this population-based pediatric cohort that included all children in one country over 6 decades, a dramatic increase in the incidence of IBD was observed during the last 30 years. These findings are similar to the few other studies available in children however the stabilization of incidence in the last decade is a new finding.

1 Lennard-Jones JE Scand J Gastroenterol 1989, 24(suppl 170), 2-6

Incidence of IBD per 100,000 children < 16 years in Iceland

<table>
<thead>
<tr>
<th>Year</th>
<th>IBD</th>
<th>UC</th>
<th>CD</th>
<th>IC</th>
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<tr>
<td>1951-1960</td>
<td>1.2</td>
<td>1.1</td>
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</tr>
<tr>
<td>1961-1970</td>
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<td>0.7</td>
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<td></td>
</tr>
<tr>
<td>1981-1990</td>
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<td>2000-2010</td>
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<tr>
<td>p-value (trend)</td>
<td>0.022</td>
<td>0.065</td>
<td>0.014</td>
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</table>

32 INCIDENCE OF PEDIATRIC INFLAMMATORY BOWEL DISEASE IN THE MARITIME PROVINCES OF CANADA. Mohsin Rashid, Anthony Otley, Gamal Mahdi, Heather Lomas, Dalhousie University, Halifax, NS, Canada Background: Inflammatory bowel disease (IBD) in children has been reported from around the world with varying epidemiological results. The IWK Health Center in Halifax, Nova Scotia is the only tertiary care, university-affiliated pediatric hospital providing care to the children of the three Canadian Maritime provinces of Nova Scotia, New Brunswick and Prince Edward Island. It is the only facility offering services in pediatric gastroenterology thus providing a unique opportunity to capture data prospectively on all new cases of IBD in children in this region.

Objective: To investigate the incidence of IBD in children in the Canadian Maritime provinces.

Methods: All patients 0-16 yrs of age diagnosed with IBD [Crohn’s disease (CD) and ulcerative colitis (UC)] at Division of Gastroenterology, IWK Health Center from 2006-2010 were studied. Population figures for each province were obtained from the Canadian Socio-economic Information Management System (CANSIM) database of Statistics Canada. Data is expressed as mean per 100,000 pediatric population.

Results: Total cases with IBD were 174 (CD101, UC73), 60% males, mean age 11.4(±3.3) yrs, range 1-16. The cumulative incidence per 100,000 for all three provinces are shown in the Table below. In the last five years, the incidence of all IBD has almost doubled and that of UC up 2.8 times. Nova Scotia and New Brunswick have seen a significant increase both in CD and UC. In 2010, the incidence of IBD in children in Nova Scotia was 15.4 (CD7.4, UC8.0) one of the highest reported from anywhere and in New Brunswick 13.7 (CD8.4, UC5.3).

Conclusions: The incidence of IBD in children in the Maritime region of Canada has increased significantly, the cause remaining unclear. Nova Scotia has the highest reported rate of IBD in pediatric population. This offers an opportunity to study the genetic and environmental factors that may play a role in the etiology of this disorder.

<table>
<thead>
<tr>
<th>Year</th>
<th>2006</th>
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<tr>
<td>All IBD</td>
<td>7.3</td>
<td>11.7</td>
<td>9.7</td>
<td>10.4</td>
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<td>8.4</td>
<td>4.9</td>
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<td>7.2</td>
</tr>
<tr>
<td>UC</td>
<td>2.3</td>
<td>3.3</td>
<td>4.8</td>
<td>5.2</td>
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</table>
33 OUTCOMES OF ADULT PATIENTS WITH CROHNS DISEASE CARED FOR BY A PEDIATRIC GASTROENTEROLOGIST. Olga Leykikhman, Mayar D. Srivastava, Medicine and Pediatrics, State University of New York at Buffalo, Williamsville, NY

Background: Crohn’s disease (CD) is an incurable inflammatory bowel disease of adults and children affecting physical and emotional health and social function. It is recommended that young adults with childhood onset CD transition to adult gastroenterology (GI). Limitations to transition include data transfer, patient reluctance, insurance coverage, and paucity of data on cost and outcome. Yet, some pediatric GI's look after adults, and some adult GI's care for children at tertiary centers and in practice. We analyzed the outcomes of adult onset CD patients in a private pediatric GI practice. The primary aim was to determine disease control. Methods: Twenty-five (n=25) adult onset Crohn's disease patients were identified by billing codes 555.0, 555.1, and 555.2. All were included for study by retrospective chart review. CDAI at last visit was calculated. Current treatments, complications, and marital and work status were recorded. Results: There were 13 females (ave age 35) and 12 males (ave age 45) in the study with average age at diagnosis 25 and 33 years; and average duration of disease of 10 and 12 years respectively. Average time in the practice was 28 months. CDAI at last visit ranged from 3.8 to 412 with average 110. The one outlier had been diagnosed with metastatic neuroendocrine tumor. Patients in the practice 12 months or longer (n=16) had average CDAI of 96, while those cared for less than 12 months (n=9) has average CDAI of 135. Six of 25 had had surgery at some point in their disease course, 12 of 25 had suffered complications, increasing with disease duration. 63% were on a TNF-inhibitor, 28% on antidepressants, 0% on narcotics; 72% were married and 76% employed full-time. Conclusions: In general, these adult patients were in good control and had good social function, despite being highly complex and having a complicated past disease course. A majority were being managed using potent TNF inhibitors. Pediatric GI's treating adult patients can have excellent outcomes and larger studies are needed.

34 THE EFFICACY OF INFlixIMAB THERAPY ON GROWTH PARAMETERS IN PEDIATRIC CROHN’S DISEASE. Raghu U. Varier, Julie A. Bass, Julia Bracken, Amanda A. Drews, William San Pablo, Craig A. Friesen, Children's Mercy Hospital, Kansas City, MO

Background: Growth monitoring is a key priority in the management of pediatric inflammatory bowel disease (IBD). Studies of infliximab, a commonly used therapeutic agent for Crohn’s Disease (CD), have produced conflicting results regarding the drug’s impact on growth parameters in children with CD. We hypothesized that height, weight, and body mass index (BMI) of pediatric CD patients treated with infliximab would improve from 18 months pre-therapy to 18 months post-therapy. Methods: A single-center retrospective chart review was conducted for 160 patients (48% males) with CD, ages 2-18 years old, treated with infliximab between January 1998 and May 2009. Demographic data, height, weight, BMI and corresponding z-scores, were recorded. Paired samples t-tests were performed to compare z-scores from initiation of infliximab to 18 months post-therapy. Piecewise linear regression was performed to compare the slope of growth velocities before and after treatment. Results: Significant increases in weight (p=0.003) and BMI (p=0.004) z-scores were observed from infliximab initiation to 18 months post-therapy (n=42). There was no significant increase in height z-score during this same time period. Piecewise linear regression, performed separately for height, weight, and BMI z-scores (n=160), revealed no significant differences in growth velocity before vs. after therapy. Conclusions: Significant improvement in weight and BMI z-scores of pediatric CD patients after completion of 18 months of infliximab therapy was observed in this study. However, piecewise linear regression failed to detect a significant change in the slope of growth parameters before vs. after therapy. Factors that may have influenced our findings, but were not analyzed, include disease severity, nutritional status, steroid therapy, and Sexual Maturity Rating. This study is limited by its retrospective nature, small sample size and the multi-dimensional nature of growth failure in this group. Further prospective study of infliximab’s effect on growth in children is needed.

35 PARAOXONASE GENE EXPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Razan H. Alkhouri, Susan Baker, Humaira Hashmi, Robert Baker, Wensheng Liu, Daniel Geifman, Lixin Zhu, Digestive Disease and Nutrition Center, SUNY at Buffalo, Buffalo, NY

Background: The etiology and pathogenesis of Inflammatory Bowel Disease (IBD) remains unclear, but the theories suggest that it is multifactorial and results from a complex interplay between genetic predisposition, immune dysregulation, and environmental factors. That includes oxidative stress and improper handling of bacteria by the gut mucosa. The Paraoxonase (PON) 1, 2 and 3 genes and proteins are expressed in the human intestine. All three genes are located on chromosome 7 in humans and have a role in preventing oxidative stress, fighting inflammation, and acting as bacterial quorum quenching by their lactonase activity. The aim of this study is to evaluate the expression of PON 1, 2, and 3 genes in mucosal biopsies of pediatric patients with Crohns disease (CD), Ulcerative colitis (UC), as compared to normal tissue from healthy individuals. Methods: 15 pediatric patients ages 5-18 were included in the study (8 females, 7 males), 5 patients had CD, 5 with UC and 5 healthy individuals. We obtained biopsies for each patient from the terminal ileum (TI), and sigmoid colon (SC). PON 1, 2, and 3 gene expressions were determined by quantitative real time PCR. Results: The PON 1, 2, and 3 gene expression is found to be decreased in the intestinal mucosa of patients with IBD when compared to healthy individuals. PON2 expression was decreased by about 90 % in the TI and SC of CD and UC when compared to healthy individuals (p value < 0.05). PON3 expression was decreased by 99% in TI and SC of both UC and CD as compared to control (p value < 0.05). PON 1 expression was decreased by about 60% in the TI and SC of IBD patients (p value = 0.1).
36 USE OF CERTOLIZUMAB PEGOL IN CHILDREN AND ADOLESCENTS WITH MODERATE TO SEVERE
ACTIVE CROHN’S DISEASE: PHARMACOKINETICS OVER 6 WEEKS IN THE NURTURE STUDY. Sunny
Hussain¹, Brian Feagan², Ahmed Samad¹, Sylviane Forget³, David Sen¹, Brigitte Lacroix⁴. ¹WK Pediatric Specialists, Shreveport, LA; ²Robarts Research Institute, University of Western Ontario, London, ON, Canada; ³UCB, Raleigh, NC; ⁴Montreal Children's Hospital, McGill University Health Center, Montreal, QC, Canada; ⁵UCB SA, Braine l'Alleud, Belgium

Purpose: NURTURE is an ongoing, open-label, multicenter study evaluating the safety, efficacy, pharmacokinetics (PK), and immunogenicity of certolizumab pegol (CZP) in pediatric patients, aged 6-17 years, with active Crohn’s disease (CD). An interim PK analysis of CZP from baseline to Wk 6 is presented.

Methods: Prior to entry into a 52-wk maintenance period, patients were induced with CZP, given subcutaneously every 2 wks for 3 administrations (Wk 0, 2, and 4) at a dose determined by body weight (BW): 400 mg, ≥40 kg; 200 mg, 20 to <40 kg. Plasma CZP concentrations were analyzed by BW and age group. Data analysis for the first 14 pediatric patients completing the induction period are presented.

Results: The geometric mean plasma CZP (gmCZP) concentration for the total pediatric population at Wk 6 (25.9 μg/mL; 95% CI 17.6-38.0) was similar to that in adults (27.2 μg/mL; 95% CI 24.6-30.0 μg/mL). Compared with adults, the gmCZP at Wk 6 was slightly lower in the 12-17 year age group and higher in the 6-11 year age group (Table).

Conclusion: Interim analysis of a pediatric population aged 6-17 years with moderate to severe active CD suggests that overall plasma CZP concentrations during the 6-wk induction period are similar to those observed in adults when BW is taken into account. The disparity between age groups may be explained by the high proportion of patients in both groups with BWs close to the cut-off for dose elevation.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Wk 0</th>
<th>Wk 1</th>
<th>Wk 4</th>
<th>Wk 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 6-11 years (n=4)</td>
<td>1.1 (0.02-62.1)</td>
<td>61.5 (50.7-74.7)</td>
<td>47.6 (36.8-61.6)</td>
<td>50.7 (40.3-63.8)</td>
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<td>12-17 years (n=10)</td>
<td>0.4 (0.2-0.6)</td>
<td>22.4 (14.0-35.7)</td>
<td>19.6 (14.1-27.2)</td>
<td>19.8 (13.0-30.3)</td>
</tr>
<tr>
<td>BW &lt;40 kg (n=4)</td>
<td>1.1 (0.02-63.6)</td>
<td>18.0 (2.8-115.3)</td>
<td>18.3 (5.4-61.7)</td>
<td>24.1 (8.2-70.3)</td>
</tr>
<tr>
<td>≥40 kg (n=10)</td>
<td>0.4 (0.2-0.6)</td>
<td>36.6 (27.9-47.9)</td>
<td>28.7 (20.6-39.9)</td>
<td>26.7 (16.2-43.9)</td>
</tr>
<tr>
<td>Overall (n=14)</td>
<td>0.5 (0.2-1.2)</td>
<td>29.9 (19.7-45.4)</td>
<td>25.2 (18.1-35.1)</td>
<td>25.9 (17.6-38.0)</td>
</tr>
</tbody>
</table>

37 MASTOCYTIC COLITIS: AN EMERGING DIAGNOSIS IN THE CHILD WITH CHRONIC ABDOMINAL
PAIN, CONSTIPATION AND/OR DIARRHEA. Sussana Attia, Adam Raskowski, Shaisa Safder, Tejas Mehta. Pediatric Gastroenterology, Arnold Palmer Hospital for Children, Orlando, FL

Context: Mastocytic colitis is an infrequently discussed cause of chronic abdominal pain with constipation or diarrhea. A literature review of Pubmed for all years available reveals only 4 studies which discuss mastocytic colitis. None includes children (0-21 years).

Objectives: To elucidate current understanding of mastocytic colitis and its manifestation in children & to present two cases of histology-proven mastocytic colitis.

Case Presentations: TN is a 9 year old female with chronic alternating diarrhea & constipation with abdominal pain with no improvement from miralax, amitriptyline, or hyoscymamine. Colonoscopy revealed acute colitis in the cecum, ascending, and transverse colon. She was treated with metronidazole therapy without improvement. Subsequent tryptase staining of the sigmoid colon showed 24 mast cells per high power field. She was started on cromolyn and rantidine with resolution of her symptoms. BZ is a 16 year old female with chronic diarrhea and abdominal pain. Colonoscopy and EGD revealed chronic gastritis and focal acute sigmoid colitis. She received metronidazole therapy with improvement, however her symptoms returned. Repeat colonoscopy and EGD were normal but tryptase staining revealed 24 to 26 mastocytes per high power field and no evidence for IBD. She had little improvement with cromolyn but had remarkable improvement with budesonide.

Conclusions: Mastocytic colitis should be considered in cases of chronic abdominal pain with constipation or diarrhea in the absence of evidence for inflammatory conditions or response to treatment for irritable bowel syndrome. Diagnosis requires tryptase mucosal staining and is not apparent on routine pathologic or histologic examination. Findings of >20 mastocytes per high power field with tryptase staining is diagnostic of mastocytic colitis & may be treated with anti-mastocytic agents such as histamine antagonists or mast cell stabilizers.

Future Directions: More research is needed into the pathophysiology, prevalence, and management of mastocytic colitis in children.
38 CHRONIC GRANULOMATOUS DISEASE AND IBD: WHERE DOES THE OVERLAP END? Suzanna Attia, Reinaldo Figueroa, Shaista Safder, Pediatric Gastroenterology, Arnold Palmer Children’s Hospital, Orlando, FL

Context: Chronic Granulomatous Disease (CGD) is an X linked or autosomal recessive defect in neutrophil oxidative function. It is characterized by unusual and severe infection and often presents with symptoms and pathologic changes consistent with IBD. Routine immunosuppressive therapy in patients with IBD and undiagnosed CGD may result in fatal infection with catalase positive pathogens or fungi.

Objectives: To review the clinical and pathologic overlap between CGD colitis and IBD. To present a case of CGD presenting as ulcerative colitis.

Case Review: RC is a 17 year old Italian-American male with a history of neonatal milk protein allergy, rectal prolapse, Bartonella henselae, and an infected lymph node who presented with recurrent abdominal pain, diarrhea, hematochezia, and intermittent mouth ulcers. He has no family history of immune deficiency. Laboratory work revealed anemia and elevated ESR and CRP with low IgA. Endoscopy and colonoscopy showed active chronic H pylori negative gastritis and active chronic colitis of the descending colon, sigmoid, and rectum consistent with ulcerative colitis. PPD was placed and negative. He was started on Lialda, omeprazole, and prednisone with resolution of his symptoms. One month later, he was admitted to our hospital with extensive bilateral pneumonia. Sputum culture was suspicious for Nocardia but revealed Tsukamurella. Oxidative burst testing showed little to no neutrophil activity, and he was diagnosed with CGD. Bactrim and itraconazole prophylaxis were begun immediately. Prednisone therapy was weaned. He was referred to Immunology and began interferon gamma-1b.

Conclusions: Early testing for and recognition of CGD can prevent potentially fatal infection on immunosuppressive therapy for IBD. CGD enteritis may present with symptoms and pathologic changes consistent with Crohn’s disease or ulcerative colitis. Frequent or overwhelming infection with catalase positive organisms or fungi should prompt testing for CGD.

Future directions: More research into the pathologic overlap between CGD and IBD is needed.

39 VITAMIN D DEFICIENCY AND ABNORMAL BONE DENSITY IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Vesta Salehi1, Lesley Small1, Mabel Yau1, Robbyn Sockolow1, Pediatrics, New York Presbyterian Hospital, New York, NY; 2Pediatric Gastroenterology, Weill Cornell Medical College, New York, NY; 3Pediatric Endocrinology, Weill Cornell Medical College, New York, NY

Background and Aims: Previous studies have identified a relationship between vitamin D deficiency and inflammatory bowel disease. We proposed to identify the number of patients with IBD seen in our practice who had vitamin D deficiency. We also correlated the vitamin D levels with the findings on DEXA scan in these patients. We further assessed the clinical status of these patients with use of PCDAI for Crohns and PUCAI in ulcerative colitis.

Methods: This was a retrospective chart review of 120 patients seen in our outpatient practice with a diagnosis of Inflammatory Bowel Disease (Crohn’s, Ulcerative Colitis, or Indeterminate Colitis). Demographic data was gathered including patient’s age at time of diagnosis, age at measurement of vitamin D level, diagnosis, extent of disease, medications used, and DEXA scan Z-score of Lumbar spine if results were available.

Results: Of the 110 patients studied 63.6% were found to be Vitamin D deficient. 64% of the Vitamin D deficient patients were prescribed Vitamin D supplementation. Of the Vitamin D deficient patients 87% got DEXA scans. Of the patients who were Vitamin D deficient who got DEXA scans 42.6% were abnormal. Of the patients with evidence of osteopenia on DEXA scan, a repeat DEXA scan was obtained which showed improvement after being started on vitamin D supplementation with normalization of vitamin D levels. Serum vitamin D concentration was positively correlated with disease activity based on PCDAI and PUCAI. There was also a correlation between use of corticosteroids and vitamin D deficiency.

Conclusion: Identifying and treating vitamin D deficiency in pediatric patients with IBD is critical to their bone health. Vitamin D status needs to be assessed more closely in patients who have more aggressive disease.

40 CHILDHOOD-ONSET INFLAMMATORY BOWEL DISEASE IN SAUDI ARABS: IS IT DIFFERENT FROM THE WEST? Mohammad El Mouzan1, Mohammad Al Mofarreh2, Asaad Assiri3, Yassin Hamid3, 1Pediatrics, King Saud University, Riyadh, Saudi Arabia; 2Al Mofarreh Polyclinic, Riyadh, Saudi Arabia

Background: Inflammatory bowel disease (IBD) occurs with variable frequency in different ethnic groups. The objective of this report is to define the characteristics of IBD in Saudi Arab children, a well-defined ethnic population

Material and methods: this is a retrospective review of the medical record of children below 18 years of age with confirmed diagnosis of IBD in two medical centers in Riyadh. The charts were reviewed for age of onset, age of first physician consultation, age at final diagnosis, gender and presenting clinical and laboratory findings. An estimated incidence and time trend were calculated for the greater Riyadh region.

Results: there were 218 children diagnosed with IBD over 19 years period (1993 to 2010). However only 181 medical records were available for analysis. There were 52 children (29%) with ulcerative colitis (UC) and 129 (71%) with Crohn disease (CD) indicating predominance of male gender and CD. However UC was more common in girls and children below 8 years of age. All were Saudi Arabs. The incidence of CD is increasing over the last 10 years while that of UC remained unchanged. The mean age at onset, presentation and final diagnosis were 13.7,14.9, and 15 years respectively indicating a significant delay in consulting physicians. Family history was positive in 14.8%. Abdominal pain was the commonest presenting feature occurring in 91% and 88% of the children with CD and UC respectively. The commonest presenting laboratory findings were low hemoglobin, high ESR and high platelets in 79%, 65% and 50% respectively in UC patients compared to 40%, 52% and 37% respectively, indicating significant lower finding in CD patients. The commonest phenotype of CD at presentation was inflammatory in 56% of the children.

Conclusions: This report demonstrates characteristics of IBD in Saudi Arab ethnic population similar to descriptions from other countries, suggesting similar lines of research of the etiology of IBD.
41 OX40 IS IMPLICATED IN T CELL PROLIFERATION AND INFLAMMATORY BOWEL DISEASE. Zili Zhang1, Wenwei Zhong1, Andrew Weinberg2, James T. Rosenbaum1, 1Pediatrics, Oregon Health & Science University, Portland, OR; 2Providence Portland Medical Center, Portland, OR

T cells play an important role in inflammatory bowel disease (IBD), and activated T cells express co-stimulatory molecule OX40. Although OX40 enhances T cell proliferation and function, it is unclear if OX40 is implicated in the pathogenesis of IBD. In this study, we showed a robust infiltration of lymphocytes in the intestinal mucosa of IBD patients, and these cells strongly expressed OX40. Next, we characterized the role of OX40 in a murine colitis model. The treatment of OX40-specific activating antibody accelerated dextran sulfate sodium (DSS)-induced colitis. In addition, activation of OX40 substantially increased the lymphocyte population in the lamina propria. To further explore the mechanism of OX40-mediated T cell expansion, we demonstrated that the OX40 activating antibody significantly augmented antigen-induced production of interleukin (IL)-21, a common γ cytokine critical for the proliferation of multiple T cell subsets. In addition, proliferating CD4+ cells expressed a higher level of OX40 and IL-21R than quiescent lymphocytes. This result suggests that OX40+ cells are in a proliferating state and readily respond to IL-21. Thus, these data reveal a pathogenic role of OX40 in IBD. Furthermore, OX40 exaggerates intestinal inflammation in part by the expansion of activated lymphocytes.

NUTRITION/ NUTRITION SUPPORT

59 ENTERAL NUTRITION SUPPORT WITH ZINC SUPPLEMENTATION IMPROVES WEIGHT GAIN IN THE HIGH RISK NEONATE. Ala K. Shaikhkhalil1, Jennifer Curtis2, Teresa D. Puthoff3, Christina J. Valentine3, 1Division of Gastroenterology, Hepatology, and Nutrition, Nationwide Children's Hospital/ The Ohio State University, Columbus, OH; 2Section of Neonatology, Nationwide Children’s Hospital/ The Ohio State University, Columbus, OH; 3Department of Pharmacy Services, Nationwide Children’s Hospital, Columbus, OH

Background: Postnatal growth failure affects the majority of extremely low birth weight (ELBW). ELBW infants are at increased risk of zinc deficiency due to lower stores and increased losses. Zinc deficiency could be contributing to poor growth in this population.

Methods: Retrospective chart review of thirteen ELBW infants who received zinc supplementation in the neonatal intensive care unit (NICU) between September 2008 and August 2010. We recorded the following: gestational age, birth weight, serum alkaline phosphatase and weekly weight gain (grams) before and after zinc supplementation. The rate of weight gain and changes in serum alkaline phosphatase before and after zinc supplementation were compared (paired t-test).

Results: Mean gestational age was 24.4 weeks, mean birth weight 658 grams. Zinc acetate was begun at a mean postnatal age of 33 weeks (range 29.3-36.1) at doses of 1 mg twice daily (54% of infants) or 1 mg three times daily (46% of infants). Twelve infants (92%) received fortified human milk. There was a statistically significant increase in the rate of weight gain after zinc supplementation from a mean of 67 grams/week to a mean of 138 gram/week (p= 0.0013). The change in serum alkaline phosphatase was not statistically significant.

Conclusions: Nutrition support with zinc supplementation could be a tangible way to improve weight gain in ELBW infants. Alkaline phosphatase may not be a sensitive marker for zinc status in this population. Further investigation is warranted to study the effect of zinc supplementation in ELBW infants and identify biological markers to help diagnose subclinical zinc deficiency.

60 NUTRITIONAL STATUS OF CHILDREN/ADOLESCENTS WITH CYSTIC FIBROSIS LIVER DISEASE (CFLD).

Alexandra Vasilescu, Peter Mogayzel, Kathryn Carson, Kathleen Schwarz, Johns Hopkins University, Baltimore, MD

CFLD has become an important cause of morbidity/mortality in CF patients and nutritional status is a strong predictor. In our study we tested the hypothesis that nutritional status would be impaired not only in patients with CFLD, but also in patients with elevated ALT not labeled as CFLD. Methods: Retrospective CF database review from one time clinic visit of 0-25yo CF patients from 07/07 to 07/10. Data included demographics, BMI z-score, chronic abx use, PFTs, CFRD (CF related diabetes), fat-soluble vitamin status, albumin, AST, ALT, bilirubin, platelets and APRI (AST: platelet ratio index). Used as indicator of hepatic fibrosis in chronic hepatitis (diagnosis <0.5 nmol fibrosis, >1.5 advanced fibrosis). The four patient groups were: established CFLD (HSM on physical exam, thrombocytopenia, evidence of cirrhosis on CT/U/S or liver bx); mild CFLD (no evidence of established CFLD, but labeled as CFLD by CF physician, started Ursodiol); CFPD (CF pulmonary disease, FEV1 < 50% without CFLD); Control CF (without CFLD or CFPD). The entire CF population was classified into normal ALT values (as defined by age/gender), mild ALT elevation (1.1-1.4 x upper limit of normal/ULN) or moderate ALT elevation (1.5 xULN). Results: 188 children, 95 female and 93 male (Caucasian 88%, AA 10%, mixed race 2%) were included in the study. The BMI z-scores are lower in established CFLD patients, but worse in CFPD patients. The APRI score was significantly elevated in the established CFLD group when compared to the other three groups. In the ALT analysis, 126 had normal ALT values, 25 had mild ALT elevation and 37 had moderate ALT elevation. There is no correlation in this population on regression analysis of ALT values with BMI z-scores. Conclusion: Established CFLD patients have poor nutritional status (low BMI z-score), but it is even lower in CFPD patients. BMI z-score of patients with mild CFLD is similar to that of control CF patients. APRI score is significantly elevated in patients with established CFLD, suggesting an inexpensive, readily available marker of liver fibrosis.
61 ASSOCIATION OF ADIPOSY WITH SOCIO-DEMOGRAPHIC FACTORS, DIET AND PHYSICAL ACTIVITY IN PRESCHOOLERS. Alfredo Larrosa-Haro, Rocio M. Macias-Rosas, Elizabeth Lizarraga-Corona, Larissa Velasco-Ruiz, Juan R. Vallarta-Robledo, Edgar M. Vásquez-Garibay, Enrique Romero-Velarde, Laura L. Salazar-Preciado, Clio Chávez-Palencia, Ana K. Ramírez-Anguiano, Maria E. Cámaras-López, Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; Departamento de Clínicas de la Reproducción Humana, Crecimiento y Desarrollo Infantil, Universidad de Guadalajara, Guadalajara, Mexico; Unidad de Investigación Médica, UMAE Hospital de Pediatría, CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico

Aims: To evaluate the association of adiposity with socio-demographic factors, diet and physical activity in preschoolers.

Methods and patients: This cross-sectional study was carried out in 89 children 3-6 years-old in a random sample of a nursery school. Independent variables: Socio-demographic variables were evaluated with a validated survey. Diet was evaluated with two-day 24-hour recalls and a diet-habit questionnaire. Physical activity was estimated with an ad hoc questionnaire evaluating spontaneous activity during school recess and at home, way of transportation to school and to other activities, sedentary and sport activities. Podometry was performed at the school recess. Dependent variable: Adiposity was estimated by anthropometric indicators and bioelectrical impedance.

Results: Mean age was 60.44 ± 8 months; 48 (53.9%) were females. Adiposity increased gradually with age and it was higher in girls. Mean weight, triceps skinfold and arm fat area was higher in children whose mothers were >32 years-old. Weight was higher in children from nuclear families. Correlations of the calorific intake with adiposity indicators were not significant; however, carbohydrate intake showed a positive correlation with body fat percentage. Dietary habits showed no association with the adiposity indicators graded to 1 and 2 SD. Walking time had a negative significant correlation with body fat percentage; otherwise, physical activity variables showed no significant associations or correlations.

Conclusions: Association of the independent variables with adiposity was scanty with a few exceptions as mother’s age, children’s age, gender, carbohydrate intake and walking habits.

62 ARM ANTHROPOMETRIC INDICATORS VERSUS WEIGHT FOR HEIGHT IN CHILDREN. Alfredo Larrosa-Haro, Rocio M. Macias-Rosas, Elizabeth Lizarraga-Corona, Larissa Velasco-Ruiz, Juan R. Vallarta-Robledo, Edgar M. Vásquez-Garibay, Enrique Romero-Velarde, Laura L. Salazar-Preciado, Clio Chávez-Palencia, Ana K. Ramírez-Anguiano, Maria E. Cámaras-López, Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; Departamento de Clínicas de la Reproducción Humana, Crecimiento y Desarrollo Infantil, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; Servicio de Gastroenterología y Nutrición, UMAE Hospital de Pediatría CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico

Objective: To evaluate the correlation of arm anthropometrical indicators with weight for height (W/H) and to compare them in the identification of malnutrition.

Methodology: This cross-sectional study included 1366 infants, children and adolescents, 615 hospitalized or seen as outpatients in a referral pediatric hospital and 751 students of preschool and elementary schools. The anthropometrical measurements and indicators were height, weight, weight/height (W/H), upper arm circumference (UAC), triceps skinfold (TSF) and arm areas. Z-scores normality limits were -2 to +2SD; cases with z-score < -2SD were considered undernourished. Samm’s tables were used for infants <24 months and Frisano’s tables for children and adolescents. Data were analyzed with linear correlations and chi2.

Results: All correlations of W/H with arm indicators were significant (p<0.001). The “r” values were: UAC 0.728, TSF 0.669, arm muscle area 0.525, total arm area 0.733, arm fat area 0.719 and arm fat index 0.561. No differences were observed in the identification of cases < -2SD of W/H with indicators of adiposity (Fat arm area p=0.9, TSF p=0.3 and arm fat index p=0.24).

MUAC and total arm area identified more cases < -2SD than W/H (p<0.001 and p=0.005 respectively). Arm muscle area versus W/H showed no differences.

Conclusion: The strong and significant correlations between arm indicators and W/H support the value of the former in the diagnosis of the nutritional status. Adiposity arm indicators seem better tools to estimate acute malnutrition. Arm muscle indicators seem related to chronic malnutrition.

63 REDUCED STARCH DIGESTION IN CONGENITAL SUCRASE-ISOMALTASE DEFICIENCY (CSID)

PATIENTS. Antone R. Opekun, Bruno Chumpitazi, Claudia C. Robayo-Villa, Maricela Diaz-Sotomayor, Roberto Quezada-Calvillo, Buford L. Nichols, Pediatrics-Nutrition, Baylor College of Medicine, Houston, TX; Pediatrics-Gastroenterology, Baylor College of Medicine, Houston, TX; CIEP-Facultad de Ciencias Químicas, Universidad Autonoma de San Luis Potosi, San Luis Potosi, Mexico

Sucrase-isomaltase (SI) enzyme complex accounts for 80% of in vitro mucosal starch digesting activity (2007). It is unknown whether the dominant role of SI on starch digestion is clinically and nutritionally important. Because it is believed that some CSID patients have starch as well as sucrose intolerance we investigated 11 children with CSID previously documented by duodenal biopsy assays and sucrose BT (2009). Hypothesis: Deficiency of sucrase activity will reduce the efficiency of starch digestion. Methods: UL 13C-glucose, 13C-sucrose, and 13C-starch (20mg, Isotec, Miamisburg, OH) were given orally. After the 13C-load, breath samples were collected every 15 min for 120 min. Breath 13C enrichments were measured with an infrared spectrophotometer (POConverter, Otsuka Electronics, Tokyo, Japan) and expressed as % coefficient of DOB 13CO2 of M 30-90 min sucrose or starch / glucose oxidation (CGO %). Control subjects (6) had normal duodenal enzyme activities. Results: Sucrase activity of controls was 44.8 ± 11.4 vs. CSID (11) 2.1 ± 2.8, P= 0.000. Maltase activity of controls was 139.6 ± 21.8 vs. CSID (9) 41.3 ± 26.2, P= 0.000. Sucrose BT CGO% of controls was 137.7 ± 24.6 vs. CSID (11) 29.6 ± 24.2, P= 0.000. Starch BT CGO% of controls was 91.1 ± 25.8 vs. CSID (11) 19.4 ± 10.6, P=0.001. The regression of starch BT= 6.528 + 0.5638 sucrose BT R2-Sq = 68.8%, P= 0.000. We tested the Sucränd (QOL Medical, Mooresville, NC) enzyme supplement used for treatment of CSID for in
vitro starch digestion and found it inactive. Conclusions: We document that all the CSID patients have poor starch digestion. Our hypothesis that deficiency of SI reduces the digestibility of starch is confirmed. SI accounts for 80% of mucosal starch digestion but duodenal biopsy maltase assays are not an accurate measurement of starch digestion because the assay includes other activities.

64 A TEN-YEAR EXPERIENCE WITH THE TREATMENT OF PEDIATRIC ULTRASHORT BOWEL SYNDROME. Benjamin J. Infantino, David F. Mercer, Brandy D. Hobson, Ryan T. Fischer, Brandy K. Gerhardt, Stephen C. Raynor, Jean F. Botha, Wendy J. Grant, Alan N. Langnas, Rubèn E. Quiros-Tejeira, University of Nebraska Medical Center, Omaha, NE.

Introduction: Ultrashort small bowel (USSB) syndrome represents a disorder associated with significant morbidity and mortality, with frequent referral for transplantation and reduced attempts at medical management. Programs dedicated to both transplantation and intestinal rehabilitation have greatly improved the prognosis for all children with short bowel syndrome. We have reviewed our program’s ability to aid USSB children.

Aim: To investigate treatment outcomes of pediatric USSB syndrome patients at a transplant/intestinal rehabilitation center.

Methods: A series of 28 children with USSB (<20 cm of small bowel) referred to our center over the past 10 years was identified and their records were reviewed. Descriptive statistics were formulated and univariate analysis was performed on the data.

Results: Of 28 patients identified, 27 (96%) survived. Over half (56%) are no longer dependent on TPN. Significant improvements in mean height and weight Z-scores, AST, ALT, TPN kcal/kg, and total bilirubin levels (all p<0.03) were observed in all survivors. The non-adapted group contained significantly more patients with gastroschisis, whereas the adapted group had nearly double the mean time enrolled in the program (45.2 vs. 25.6 months, p<0.02). An intact colon and ileocecal valve were found to be present more often in adapted patients, just at the level of significance (p=0.05). Six (40%) of the adapted patients did not have an ileocecal valve and intact colon.

Conclusions: Enrollment in a transplant/intestinal rehabilitation program for children with USSB provides an excellent probability of survival. In less than 4 years of time enrolled, over half of pediatric USSB patients are capable of achieving intestinal adaptation. Gastroschisis appears to be a poor prognostic factor for rehabilitation. The USSB population as a whole can attain reduced parental nutrition dependence, improvement of parental nutrition-associated liver disease, and enhanced growth.

65 COMPOUND HETEROZYGOTIC INHERITANCE VARIED IN 3 SIBLINGS WITH CONGENITAL SUCRASE-ISOMALTASE DEFICIENCY (CSID). Bruno P. Chumpitazi1, Claudia C. Robayo-Villa1, Antone R. Opekun2, Mark A. Gilger2, Bianca Haase1, Toso Leeb3, Hassan Naim4, Buford L. Nichols2,3, Pediatrics-Nutrition, Baylor College of Medicine, Houston, TX; 2Pediatrics-Gastroenterology, Baylor College of Medicine, Houston, TX; 3Institute of Genetics, University of Bern, Bern, Switzerland; 4Physiological Chemistry, University of Veterinary Medicine, Hannover, Germany.

Sucrase-isomaltase (SI) is an enzyme complex with 2 activities, sucrase (SUC) and isomaltase (IM) that serves as a catalyst for the cleavage of sugar and starch. A 2001 report identified compound heterozygous mutations (CHM) at V577G (IM) and G1073D (SUC). Cellular studies have documented that V577G (IM) and G1073D (SUC) mutations inhibit exiting from the ER; the SUC mutation blocks its chaperone function for IM. Objective: Determine mode of inheritance in a family with CHM-CSID.

Methods: Study of 3 siblings with CSID diagnosed by duodenal enzyme assays and 22 kindred by sucrose breath testing (SBT) and genomic SI sequencing. UL 13C glucose and 13C sucrose oxidation (CGO %). Controls were 16 kindred without mutations. DNA was isolated from blood and all exons of SI were amplified by PCR and directly sequenced. Results: The 3 siblings, father and paternal grandmother had deficient digestion (< 98 CGO %) by SBT. Sequencing of SI revealed single mutations. The novel maternal mutation G1476A of SUC appears to act as dominant negative suppressing sucrase digestion in the youngest child lacking the familial V577G IM mutation.

Enzyme activities and BTs of 3 Siblings with CSID.

<table>
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<th>Lactase</th>
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<th>Malatase</th>
<th>Palatinase</th>
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66 CHANGES IN NUTRITIONAL STATUS OF CHILDREN HOSPITALIZED AT A 3TH LEVEL INSTITUTION. Ericka M. Barrios, Roberto C. Bustamante, Jaime R. Mayans, Flora Z. Mondragón, José C. León, Margarita G. Campos, Pediatric Gastroenterology and Nutrition, Instituto Nacional de Pediatría, México, Mexico.

Background: Undernutrition prevalence in hospitalized children rates between 30-55%. Therefore, the importance of performing nutritional assessments including: anthropometric, dietetic, clinical and biochemical parameters.

Aim: To determine some parameters related to nutritional status in hospitalized children in order to perform an opportune
interventions.
Method: Children less than 5 years, hospitalized at the INP for more than six days were included. Nutritional assessments were done at entrance (1) and discharge (2) considering: weight for height (W/H), height for age (H/A), middle arm circumference (MAC), tricipital skinfold (TSF), physical exam, protein and energy consumption and biochemical parameters.
Results: 50 patients were evaluated; 58% were male. 60% of patients increase weight nevertheless, weight for height by z score do not improve. MAC and TSF decreased during hospitalization. Transferrin and albumin increased during hospitalization, 70% and 92% respectively. Comparing well nourished versus undernourished children, those with an adequate nutritional status consumed more energy than undernourished, who consumed more protein; both results statistical significant (p=0.035, p=0.005 respectively).
Conclusions: There is a high prevalence of undernutrition, similar to reports by other authors. Weight gain and increase in transferrin and prealbumin levels do not impact body composition. Undernourished children consumed less energy and more protein than expected. Dietetic support should be improved.

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<td>Hospitalization (days)</td>
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<td>62</td>
<td>60</td>
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**67 ANTOPOMETRIC MEASUREMENTS AND ITS RELATIONSHIP WITH BIOCHEMICAL MARKERS IN METABOLIC SYNDROME.** Ericka M. Barrios, Pediatric Gastroenterology and Nutrition, Instituto Nacional de Pediatría, México, Mexico

**BACKGROUND:** It has been found significant relationship between metabolic syndrome in children and adolescents and antopometric measurements.

**OBJECTIVE:** To know the frequency of overweight and obesity according to body mass index and fat percentage in school aged children. To correlate the nutritional status with biochemical markers of metabolic syndrome and other biochemical markers of obesity.

**METHOD:** In a randomized elected elementary school, we took blood samples from school aged children to determine: glucose and insulin level, lipid profile and hepatic enzymes. We determined the degree of insulin resistance by HOMA index and obtained the following measurements: body mass index (BMI), bioelectrical impedance percentage (BIE), four measurements of skinfold, waist, and waist/height index. The total of patients were divided according with their nutritional status: malnourished, with or without overweight, or with obesity.

**RESULTS:** 255 children, between 7 - 13.4 years old, male and female. According to BMI: there was obesity in 20.4% and overweight in 20.8%. According to fat percentage measured by BIE: there was obesity in 29.2% and overweight in 18.7%. The most common marker of metabolic syndrome was the low level of HDL cholesterol in 48.3% of the total sample. In 98.4% the blood glucose level was normal, but in 17.2% the HOMA index was high. As for the correlation of nutritional status with the biochemical markers, all showed statistically significant differences, except blood glucose level.

**CONCLUSIONS:** Blood glucose level is a biochemical marker included in metabolic syndrome criteria; nevertheless, in this study we observed that although the high frequency of overweight and obesity in our population, most of the sample did not present with alterations of blood glucose level and 17.2% presented with insulin resistance, that can lead to metabolic syndrome or diabetes mellitus type 2. These findings suggest that it should be taken into account the insulin resistance as an initial evaluation in these patients.

**68 A PROSPECTIVE STUDY ON THE NUTRITIONAL ZINC STATUS OF IRON-DEFICIENT INFANTS UNDER TWO YEARS OF AGE IN KOREA.** Ju Young Chang1,2, Jeong Su Park1, Sue Shin1,2, Hye Ran Yang2, Jae Sung Ko2, Jeong Kee Seo2, 1Pediatrics, Seoul Metropolitan Government Seoul National University Boramae Medical Center., Seoul, Republic of Korea; 2Pediatrics, Seoul National University College of Medicine, Seoul, Republic of Korea; 3Laboratory Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

It has been reported that iron deficiency (ID) can be accompanied by zinc deficiency (ZD), but infant-based studies are rare. By measuring serum and hair zinc concentrations in iron-deficient infants, the correlation between ID and ZD, and dietary risk factors associated with ZD were evaluated. Infants less than 2 years of age were recruited from an outpatient clinic. Dietary information was collected using questionnaires. Hemoglobin, serum iron/total iron-binding capacity, serum ferritin, zinc concentrations and zinc content of hair were measured. Among 108 infants analyzed, 72 (66.7%) exhibited ID. Serum ZD was observed in 13 (26%) of 50 iron-deficient infants and 3 (10%) of 30 control infants. The serum zinc concentration (median [interquartile range]) in iron-deficient infants (78.0 μg/dL [68.8-85.8]) was less than that in the control group (86.5 μg/dL [77.8-
profiles in children with nonalcoholic fatty liver disease (NAFLD) and insulin resistance (IR). Aim: We explored the relationship between fructose (FRU) consumption, serum uric acid (UA), and metabolic complications in children.

A major determinant of the rise in obesity and metabolic syndrome (MS) among children is increased fructose (FRU) consumption. In adults, increased FRU consumption is associated with hepatic fibrosis, hyperuricemia, and complications of insulin resistance (IR). Aims: We explored the relationship between FRU consumption, serum uric acid (UA), and metabolic profiles in children with nonalcoholic fatty liver disease (NAFLD). Methods: We studied 347 children, ages 2-17, from the Department of Pediatrics, Division of Pediatric Gastroenterology, Nutrition & Liver Diseases, Hasbro Children's/Rhode Island Hospital, Alpert Medical School of Brown University, Providence, RI; Department of Psychiatry, Division of Child Psychology, Hasbro Children's/Rhode Island Hospital, Alpert Medical School of Brown University, Providence, RI.

Introduction: Neonates requiring intravenous nutrient support or total parenteral nutrition (TPN) are exposed to an increased oxidative stress, which could impair their development. The influence of TPN on redox balance in older children remains unknown. We evaluated metabolic and physiological markers of oxidative stress in children receiving long term TPN.

Methods: Data from 7 children aged 50 months [17.5-137] on TPN for a median of 24 months [9-50] were compared to 16 children in a control group aged 39 months [14-138]. Oxidative stress was assessed with urinary hydroperoxide and isoprostanes (urinary and plasmatic). The markers of antioxidant defense were total glutathione (GSH) in erythrocytes and ascorbate (in urine and in erythrocytes). Ascorbate intake among the TPN group was noted. Correlations between the different markers were evaluated.

Results: In the TPN group, urinary hydroperoxide was significantly higher than in the control group (0.24 ± 0.10 µmol/mg creatinin versus 0.06 ± 0.01; p<0.05). Plasmatic and urinary isoprostanes were also higher in children receiving TPN (p<0.0002). GSH stock in erythrocytes was significantly lower in the TPN group: 3.2 ± 0.4 nmols of GSH/mg of proteins versus 5.7 ± 0.5 (p<0.005). In erythrocytes and in urine, ascorbate levels were not lower; rather they were significantly higher in the TPN group: 84 ± 6 versus 60 ± 7 µM in erythrocytes, p<0.05 and 6.7 ± 2.4 versus 1.1 ± 0.3 µmol/mmol of creatinin in the urine, p<0.005. In TPN patients, ascorbate content in erythrocytes was correlated neither to ascorbate intake nor to urinary ascorbate. However, ascorbate intake was significantly correlated to urinary excretion (r² = 0.9, p<0.01).

Conclusion: Children receiving long term TPN have increased oxidative stress and decreased total GSH. Ascorbate levels are not decreased in these patients and are even sufficient to allow high excretion. However, these levels of vitamin C do not neutralize the increased oxidative stress. Further studies are needed to understand mechanisms and consequences of oxidative stress in these patients.

70 HOW COMMON IS STUNTING AND UNDERWEIGHT IN A POPULATION OF CHILDREN WITH FEEDING DISORDERS? Katja K. Kovacic1, Sarah Hagin2, Carolina S. Cerezo1, 1Department of Pediatrics, Division of Pediatric Gastroenterology, Nutrition & Liver Diseases, Hasbro Children's/Rhode Island Hospital, Alpert Medical School of Brown University, Providence, RI; 2Department of Psychiatry, Division of Child Psychology, Hasbro Children's/Rhode Island Hospital, Alpert Medical School of Brown University, Providence, RI.

Background: Childhood feeding problems are common, and may result in growth faltering. Few studies have described growth patterns in children with feeding disorders.

Objectives: We aimed to determine the prevalence of stunting and underweight (skinny) in a population of children with feeding disorders and to identify factors associated with stunting and underweight.

Methods: Medical records of 273 children referred to an outpatient feeding program were analyzed. Demographic and anthropometric data were collected at two time points. Birth weight, gestational age, and number of co-morbid conditions were obtained. Z-scores were calculated from standardized CDC height and weight percentiles. A Z-score of less than -2 standard deviations (SD) for weight and height satisfies the criteria for skinny and or stunted. Children were classified as skinny, stunted, both or neither.

Results: At presentation, 39.9%, 24.7% and 20.4% were classified as skinny, stunted and both respectively. At 6-12 months prior to evaluation, 41.2% were skinny, 29.3% were stunted and 24.2 were both skinny and stunted.54.3% of skinny children and 60.3% of stunted children were born preterm while close to 43% of skinny children and 53.6% of stunted children had low birth weights. In children that were both skinny and stunted, 58% were preterm and 52.2 had low birth weights.

Conclusion: There was a high prevalence of underweight and stunting in this population. Prematurity and low birth weights appear to be common factors in both groups. Results of this study give further insight into the growth patterns of children with feeding problems. Prompt diagnosis and early intervention should prevent and correct nutritional and growth complications.
NASH Clinical Research Network. FRU consumption was reported based on servings/week of Kool-Aid, fruit juices, and non-diet soda. The association of high FRU consumption (≥7 servings/week) with metabolic parameters was analyzed using regression models. Results: A significant interaction was found between FRU consumption and pubertal stage (p=0.04). Specifically, no effect of FRU consumption on serum UA in pre-pubertal children but an increase in serum UA in post-pubertal children (p<0.03) was noted. High FRU consumption was also associated with decreased serum glucose (p<0.02) and increased serum insulin and HOMA-IR (p<0.03 and p<0.05, respectively) after controlling for confounding factors. In the entire cohort, the influence of FRU on IR was noted irrespective of pubertal stage. Post-pubertal children with hyperuricemia (serum UA > 5.5 mg/dL) had lower HDL levels (p<0.0001) and higher insulin and HOMA-IR levels (p<0.02 for both). Conclusion: In children with NAFLD, FRU consumption is associated with worse IR, and in post-pubertal children is strongly associated with higher UA levels. The clinical significance of hyperuricemia in the severity of NAFLD and MS in children requires further investigation.

**72. EVALUATION OF ETHANOL LOCK THERAPY IN PEDIATRIC PATIENTS ON LONG TERM PARENTERAL NUTRITION.** Kevin P. Pieroni, Colleen Nespor, Marissa Ng, William Berquist, John Kerner, Pediatric Gastroenterology, Stanford University, Palo Alto, CA; Jamie Westcott, Pediatric Home Pharmacy, Lucile Packard Children's Hospital at Stanford, Palo Alto, CA

Background: Pediatric home parenteral nutrition (PN) patients present a unique challenge with risks of catheter related blood stream infections (CRBSI), sometimes requiring subsequent catheter removal. These children use PN as their primary nutrition source via a central venous catheter (CVC). Recurrent infections can lead to line removal and potential loss of venous access in the future. Previous small studies have shown that ethanol lock therapy (ELT) can potentially decrease CRBSI.

Objective: Demonstrate that weekly ELT decreases CRBSI in long-term home PN patients and decreases line removal due to infections.

Methods: Starting August 2007, patients receiving PN with a history of previous CRBSI were started on ELT. One to two milliliters of 70% ethanol solution was instilled into the CVC for two hours weekly. The solution was then withdrawn, and the CVC was flushed with normal saline and heparin. Once followed by our home pharmacy, episodes of CRBSI and catheter removal due to infection were documented in patients prior to and after ELT.

Results: Thirteen patients were followed for an average of 537 days after ELT was initiated. Patients had short bowel syndrome secondary to gastroschisis, necrotizing enterocolitis, intestinal atresia, long segment Hirschsprung’s disease, or a previous surgical complication. These patients were found to average 14 CRBSI per 1000 days and 1.5 catheter removals prior to starting ELT. After ELT, there were only 2.8 CRBSI per 1000 days (p < 0.001) and 0.3 catheter removals with 9 patients not requiring any further line removals.

Conclusion: Our group showed an 80% reduction in CRBSI and catheter removal due to infection after ELT. In our patient population, weekly ELT for 2 hours is an effective technique to reduce CRBSI and catheter removal in long-term home PN patients. This significant decrease in infection and catheter removal can decrease mortality secondary to sepsis, worsening liver function, and loss of permanent vascular access sites.

**73. EFFECTS ON THE INTESTINAL MICROBIOME OF EXCLUSIVELY BREASTFED INFANTS (EBFI) ON 3 COMPLEMENTARY FEEDING REGIMES WITH DIFFERENT IRON (FE) EXPOSURE.** Laurie Sherlo, Dan Frank, Charles Robertson, Jamie Westcott, Diana Culbertson, Leah Feazel, Nancy Krebs, Pediatrics, UC Denver, Aurora, CO; Charles Robertson, Jamie Westcott, Diana Culbertson, Leah Feazel, Nancy Krebs, Pediatrics, UC Denver, Aurora, CO; Molecular Biology, UC Boulder, Boulder, CO

Background: Many factors are known to influence infants’ transformation of the enteric microbiome from sterility to an adult-like colonization. No studies to date have considered the effect of different complementary foods (CF). For example, the low bioavailability electrolytic Fe in infant cereals results in high Fe exposure for gut organisms, which may alter the balance of microbiota in the developing intestine.

Objective: To compare the development and composition of the enteric microbiome among groups of healthy BFI on different CF regimens, specifically providing a range of unabsorbed iron.

Methods: 42 healthy EBF1 were randomized to 1 of 3 CF regimens initiated at 6 mo: Fe-fortified infant cereal (IFC), Fe+Zn-fortified cereal (IZFC), or meat (M). Infants were allowed ad lib other foods with low amounts of Zn and Fe. All infants continued breastfeeding and received no formula during the study. Stool samples were obtained monthly from 14 infants from 5-9 months of age (n = 4 IFC; 6 IZFC, 4 M). Dietary Fe was determined by monthly 3 d diet records. Bacterial profiles were analyzed by broad-range PCR of 16S rRNA genes and phylogenetic sequence analysis. Results: At 9 mo, mean Fe intake was 13 vs 3.7 mg/d for IFC+IZFC vs M respectively. Preliminary analysis of sequence data identified the longitudinal development of several phylum-level differences in intestinal microbiota by feeding group, specifically in abundances of Firmicutes and Bacteroidetes. Differences are also evident in specific families, including Enterobacteriaceae and Bifidobacteriales. More species diversity was observed in the infants from the M group than either of the Fe-fortified groups. Conclusions: This longitudinal study indicates that the composition of CF, including Fe exposure, influences the development of the infant enteric microbiota.

Support: NIH: T32DK007658-20S, K24DK083772, 1R21HG005964-01and The Beef Checkoff, NCBA
74 25(OH)D3, METABOLIC SYNDROME, AND SUBCLINICAL ATHEROSCLEROSIS: A PROSPECTIVE STUDY IN CAUCASIAN CHILDREN AND ADOLESCENTS.
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Rome, Italy
Objectives: Evidence of the association between vitamin D and cardiovascular (CV) risk factors in the young is limited. We therefore assessed: 1) the relationships between circulating 25-hydroxyvitamin D3 [25(OH)D3] and metabolic syndrome (MetS), its components, and early atherosclerotic changes in 452 (304 overweight/obese, 148 healthy, normal weight) Caucasian children; 2) the effects of weight reduction on 25(OH)D3 concentrations and CV risk factors.
Methods: We determined serum 25(OH)D3 concentrations in relation to MetS, its components [central obesity, hypertension, low HDL cholesterol, hypertriglyceridemia, glucose impairment and/or insulin resistance], as well as to impairment of flow-mediated vasodilatation (FMD) and increased carotid intima-media thickness (cIMT) - two markers of subclinical atherosclerosis. Results: The prevalence of MetS decreased progressively and significantly across increasing serum 25(OH)D3 tertiles. Central obesity, hypertension, hypertriglyceridemia, low HDL cholesterol, IR, and MetS were all associated with an increased odds of being 25(OH)D3 deficient (lowest vs highest tertile), after adjustment for age, sex, and Tanner stage. After additional adjustment for SD score (SDS)-BMI, hypertension and MetS remained significantly associated with low vitamin D status. No correlation was found between 25(OH)D3 concentrations and either FMD or cIMT. In a stepwise regression model including age, sex, SDS-BMI, and all individual components of MetS, low 25(OH)D3 level was significantly associated with hypertension and SDS-BMI. Reduction of weight in children led to a significant increase in 25(OH)D3 concentrations, and improvement in clinical and metabolic parameters.
Conclusions: In Caucasian children, vitamin D deficiency is inversely related to MetS, the degree of total adiposity, and hypertension.

Background: Choline deficiency is described in patients with CF. LYM-X-SORB™ is a novel choline containing organized lipid matrix. The effect of choline supplements on muscle lipid & choline content in CF is unknown. Objective: To describe muscle choline & fat content using MRS of calf muscle in subjects with CF, before & after 12-month daily supplements with LYM-X-SORB™, compared to healthy matched controls. Methods: Subjects with CF & PI took part in a double-blind randomized placebo-controlled supplementation trial of LYM-X-SORB™. Choline content was higher in LYM-X-SORB™ (591-887 mg/d) v. placebo (78-117 mg/d). Fasting MRS scans (1.5T Siemens Avanto Whole Body Scanner) were obtained in subjects with CF at baseline & 12-month, & in healthy subjects on 1 occasion. Muscle Proton MRI/Spectroscopy (Siemens Extremity coil) using Chemical Shift Imaging (TR=1.7s, TE=30ms, spectral width=1KHz; 4 averages) with/without water suppression was obtained from regions in the soleus muscle. Percent muscle choline (MC%), intra- (IMF%) & extra-myocellular (EMF%) fat content were determined. Height (HAZ), weight (WAZ), & BMI (BMIZ) Z scores were calculated. Results: Compared to controls (n=10; 7 male, 14.0±3.0 y), subjects with CF (n=14; 10 male, 12.9±1.5 y) had significantly lower MC% at baseline (0.09±0.02 v. 0.12±0.03%, p=0.001), but similar IMF% & EMF%. Group, age & WAZ predicted MC% at baseline (F=9.1, R²=0.59, p=0.001). After 12 months, MC% significantly increased (p=0.03) in subjects with CF on LYM-X-SORB™ (n=8, 0.12±0.04%), but not on placebo (n=6, 0.09±0.02%). Age & HAZ predicted MC% at 12 months (F=6.1, R²=0.47, p=0.003). IMF% was higher in subjects with CF compared to controls at 12 months (2.2±1.1 v. 1.0±0.6%, p=0.01). Conclusion: Muscle choline content was 1) lower in baseline CF subjects compared to controls; 2) increased after 12 months of LYM-X-SORB™ supplements in CF subjects; 3) was associated with better growth status. Daily choline supplements can improve choline status.

76 SUCCESSFUL GASTROSTOMY FEED WEANING PROGRAM USING AN INTENSIVE MULTIDISCIPLINARY TEAM APPROACH. Mitchell Katz, Jessica Brown, Cindy Kim, CHOC Children’s Hospital, Orange, CA
Introduction: The Feeding Program at CHOC Children’s Hospital utilizes a multidisciplinary team approach for the treatment of children with complex feeding problems. The purpose of this study was to evaluate the effectiveness of this intensive inpatient model for gastrostomy tube (GT) feed weaning. This unique program includes specialists from gastroenterology, speech therapy, occupational therapy, psychology, social work, and nutrition. Methods: Twenty-one GT dependent children, ages 4.27 (±1.6) years, were admitted to the inpatient feeding program (length of stay 19 days) from 2009 to 2011. Administered GT calories were decreased on admit by an average of 72% from home regimen. Caloric goals were estimated by a dietitian based on previous home regimen or recommended dietary allowance for actual or ideal body weight (IBW). Patients were offered 3 meals and 2-3 snacks per day. Patients received 3 intensive feeding therapy sessions per day (Mon-Fri) along with psychosocial support, nutrition guidance, and behavioral therapy. Daily calorie counts and weights were recorded.
Statistical Methods: Data was analyzed using Paired Samples T-Tests. Results: Prior to admission, patients received 76% (±22) of goal calories enterally. Average caloric intake by mouth as a percentage of goal increased over the course of weeks 1, 2, and 3 (60%, 77%, and 85% respectively), with a statistically significant increase between week 1 and 3 (p=0.001). At discharge, 86% had discontinued GT feedings with 53% (±24) of oral intake coming from nutritional supplements. Fourteen percent were discharged on nighttime GT feeds, receiving 15-38% of goal calories. Average percent weight change during admission was 0.8% (±4). Average percent IBW at admission was 95% (±7) and 95% (±9) at discharge. At three months follow up, 16 of 19
remained successfully off of GT feedings. Conclusions: Children who are GT dependent can be successfully weaned off of GT feedings during a three week intensive admission using a multidisciplinary feeding model.

77 DOES EARLY INFANCY WEIGHT GAIN INCREASE THE RISK FOR CHILDHOOD OBESITY? : A SYSTEMATIC REVIEW AND META-ANALYSIS, Nidhi Rawal, Benjamin Caballero, International Health and Nutrition, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Objectives: To systematically review and perform a meta-analysis of the literature reporting association between rapid weight gain in infancy and childhood risk for obesity.

Methods: PubMed and EMBASE databases were searched for studies that reported the estimates of risk for being obese as a function of early childhood risk factors. Articles underwent title-abstract screening, full text review and qualitative assessment. Heterogeneity was first assessed qualitatively, then quantitatively using I2 statistic and chi square test of heterogeneity.

Results: We included 6 studies reporting data in terms of Odds Ratios, for the risk of obesity in healthy children who had rapid weight gain in their infancy. We grouped the studies into two subgroups, based on the definition of exposure. The pooled odds ratio for the association between rapid weight gain in early infancy (0-2 years) and risk for childhood obesity was 1.44 (95% CI 1.28-1.61, P<0.0001) with high statistical significance and low statistical heterogeneity (I2 = 36%, P<0.17). Odds ratio continued to be significantly positive, regardless of the definition for “rapid weight gain” (Subgroup 1: OR = 1.62, 95%CI 1.08, 2.43; P value for overall effect=0.02, I2 = 51%; Subgroup 2: OR = 1.39, 95% CI 1.33,1.44; P value < 0.00001).

Conclusions: This review and meta-analysis provide strong evidence that rapid weight gain in early infancy (0-2 years) increases the odds for childhood obesity (2-17 years) by at least 40%. Hence, there is a 60% probability that a healthy infant with rapid weight gain will be obese in his/her childhood years. On the basis of qualitative assessment performed in this review, we concur with the earlier reviews and propose that rate of weight gain in infancy is an important determinant and infancy is a critical period for development of childhood obesity. This information can have significant impact on public health recommendations, obesity prevention programs, government funding and formulation of new approaches to prevent obesity.

78 ASTRINGENT DIET IN CHILDREN WITH ACUTE GASTROENTERITIS: DOES IT MAKE A DIFFERENCE? Rafael Guerrero-Lozano1, Nubia Farías2, Ángelica Losada3,4, 1Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia; 2Hospital de la Misericordia, Bogotá, Colombia

Introduction: It is often observed that changes in the diet are indicated in the treatment of children with acute gastroenteritis (AG). The information regarding the usefulness of the so called astringent diet (AD) is scarce.

Aim: To determine whether the use of a modified astringent diet in children with AG, managed as outpatients, reduces the duration of disease, when compared with that in children who receive their normal diet.

Methods: This was a randomized controlled clinical trial with children between 6 and 48 months of age who had already started solid foods and who consulted due to AG. After hydration (oral or parenteral), the experimental group received AD, based on poultry and lean meats, rice, guava, apple and pear, while children in the control group were indicated to consume their usual diet (ND). The primary endpoint was duration of diarrhoea (days) after the introduction of the diet.

Results: 84 (53.6% male) children, aged 17.8 ± 10.2 months, were included; 48 were assigned to ND and 36 to AD. Three fourths (75.7%) were eutrophic. Eighty one percent received oral rehydration and 69% were well hydrated at the time of consultation. With the exception of 2, all received lactose (milk or formula). Osmotic diarrhoea accounted for 82.1%. The duration of diarrhoea on admission had been 2.8 ± 1.6 days and the number of stools reported the day before admission 6.6 ± 3.0. Good compliance with feeding was recorded in 89.4%. Treatment failure was present in 19.1%, with no difference between groups.

The whole duration of diarrhoea was 5.1 ± 2.9 vs. 4.8 ± 2.6 days and duration after refeeding was 2.5 ± 2.3 vs. 2.0 ± 1.9 days for AD and ND, respectively (p = NS).

Con: The results of this study indicate that there is no therapeutic benefit in the use of a modified astringent diet in the management of children with acute gastroenteritis.

79 LEPTIN AND METABOLIC SYNDROME IN PAEDIATRIC PATIENTS WITH DOWN'S SYNDROME. Ana Clavijo, Rafael Guerrero-Lozano, Angela Camacho, Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia

Introduction: Interest in the relationship between metabolic syndrome and Down's syndrome in children is recent. This population is known to have up to 4 times greater risk of obesity; however, it has not been established if hypertension and hyperinsulinism occur more frequently.

Aims: To compare serum leptin levels and the frequency of metabolic syndrome in obese children with and without Down's syndrome.

Methods: Case (obese patients with Down's syndrome) and controls (obese patients) study with participants aged 2-17 years.

Fasting levels were obtained for leptin, HDL-cholesterol, triglycerides, insulin and glucose. An average of two blood pressure measurements was registered. Statistical analysis was performed with SPSS 17.0 and STATA 10.1. The Mann Whitney U test was used for nonparametric variables.

Results: 22 (66.7% girls) cases and 18 (54.5% girls) controls, aged 12 ± 3.9 and 11. 3 ± 2.5 years, BMI 25.6 ± 4.5 and 24.8 ± 4.6 kg/m2, respectively, were included. Leptin levels in cases were 15 ± 7.6 ng/ml as opposed to 9.4 ± 5.4 in controls (p = 0.001). Levels were not related to the frequency of metabolic syndrome that showed no significant difference between groups.

Conclusion: Obese children with Down's syndrome have higher serum leptin levels when compared to their peers without such chromosomal defect; the difference is not related to the frequency of metabolic syndrome in the study groups.

E23
80 QUALITY OF LIFE CHANGES FOLLOWING AN INTENSIVE FEEDING PROGRAM. Robyn F. Robinson, Mitchell H. Katz, PSF GI, CHOC Children’s Hospital, Orange, CA

Objective: To determine how resolution of feeding problems through participation in a multidisciplinary intensive feeding program affects quality of life. Participants in the program are medically-stable children with complex feeding problems dependent on gastrostomy tube feedings or at risk of gastrostomy tube placement.

Methods: Parents of 10 children between 2-6 years of age completed a parent-proxy quality of life tool (ITQOL® HealthActCHQ Inc.) 1-3 days before admission to a 19 day intensive, inpatient feeding program in 2009-2010 and then three months following discharge. This tool is a 103 item questionnaire that assesses physical and psychosocial domains of quality of life and the impact of the child’s health on parents.

Scores were compared with questionnaires completed four months apart by parents of 10 children of similar age, gender, gestational age and history of gastroesophageal reflux, during the same time period, on a waiting list for the inpatient feeding program.

Statistical Methods: Total ITQOL scores between groups were compared with a Mann-Whitney U test.

Results: Statistically significant changes between control and experimental group scores were seen in two of the nine domains evaluated by the ITQOL. Parental worry about the child’s health (p = .043) and parent’s perception of their child’s health (p = .005) were improved three months following the feeding program compared to controls. Two additional domains trended towards improved quality of life in the experimental group but did not reach statistical significance. These included parent personal time limitations (p = .075) and frequency of negative behaviors (p = .099).

Conclusion: Resolution of feeding problems following an intensive inpatient program led to significant improvements in quality of life. At three months follow up, parents of participants, compared to controls reported significant improvement in two quality of life domains, parental worry and perception of their child’s health. Parent personal time limitations and frequency of negative behaviors trended towards improved quality of life but did not reach statistical significance.

81 PICCING THE RIGHT CATHETER. Russell J. Merritt1, Li Hong2, Pui Yuk Yan1, Choo Phee Wee1, Kim Rinauro3, Phillip Stanley4, Tracy Griksethe1, 1Department of Pediatric Gastroenterology, Hepatology and Nutrition, Children’s Hospital Los Angeles, Los Angeles, CA; 2Department of Clinical Nutrition, Shanghai Children’s Medical Center, Shanghai Jiaotong University School of Medicine, Shanghai, China; 3Department of Pediatric, Children’s Hospital Los Angeles, Los Angeles, CA

Infants and children with severe, chronic intestinal failure require intravenous access for parenteral nutrition. Intravenous catheter options include percutaneously inserted central catheters (PICC) and surgically tunneled catheters (Bro). We retrospectively compared adverse events from PICC and Bro in 25 children (15 females, 10 males) aged 3 months to 19 years in a pediatric home parenteral nutrition program over a 30-month time period. During this interval, we collected data on 52 PICC and 28 Bro including 3755 PICC and 5311 Bro days. There were 79 adverse events out of a total of 102 recorded events, which were characterized as mechanical, metabolic or infectious and tabulated per 1000 catheter days. There were no adverse events in 6 patients. In total, 23 catheters were censored at the end of study. The data suggested that PICC has a higher adverse event rate than Bro (p <0.0001). There were more mechanical complications in PICC with incidence rate of 7.46 per 1000 catheter days compared to Bro with incidence rate of 1.13 per 1000 catheter days (p <0.0001). There was no difference in metabolic complications between the groups. Presumed catheter infections expressed per 1000 catheter days (positive blood culture drawn through the catheter) were higher in PICC with incidence rate of 6.39 vs. 3.77 in Bro (p=0.0824). When selecting the most appropriate catheter, the potential for complications requiring therapy, including hospitalization, as well as vein-sparing considerations, need to be factored into the decision.

82 ETHANOL LOCK THERAPY REDUCES CENTRAL VENOUS CATHETER-ASSOCIATED INFECTIONS IN CHILDREN WITH INTESTINAL FAILURE. Ryan Fischer, Hannah Sneller, Ruben Quiroa-Tejetea, Kari Simonsen, Raynor Stephen, David Mercer, University of Nebraska Medical Center, Omaha, NE

Purpose: Central venous catheter (CVC)-associated infections represent a significant cause of morbidity and mortality in children with intestinal failure (IF) and parental nutrition (PN) dependence. Lock therapy with ethanol may prevent such infectious complications. We present our institution’s experience with the use of ethanol locks in a pediatric IF population.

Methods: In a retrospective analysis of 49 patients (23 male; 46%), we evaluated the rate of CVC-associated infections per 1000 days for patients with or without ethanol locks per 1000 catheter days (p <0.0001). There was no difference in metabolic complications between the groups. Presumed catheter infections expressed per 1000 catheter days (positive blood culture drawn through the catheter) were higher in PICC with incidence rate of 6.39 vs. 3.77 in Bro (p=0.0824). When selecting the most appropriate catheter, the potential for complications requiring therapy, including hospitalization, as well as vein-sparing considerations, need to be factored into the decision.

Results: The mean duration of ethanol lock therapy was 254 +/- 160 days. Pre-ethanol lock therapy, the CVC-associated infection rate per 1,000 CVC days was 8.8. On ethanol lock therapy, the CVC-associated infection rate was 3.4. Dwell times longer than 2 hours were associated with 2.1 infections per 1000 CVC days. Overall, the use of ethanol locks was associated with a 62% reduction in infection rates (p < 0.01). On ethanol lock therapy, the percentage of infections caused by gram-negative rods decreased from 47% to 31%, and the percentage of infections caused by yeast decreased from 18% to 6%. However, the percentage of CVC-associated infections attributed to gram-positive cocci increased from 32% to 51%.

Conclusion: Ethanol lock therapy reduces the rate of CVC-associated infections in children with IF. Longer dwell times may increase efficacy. Interestingly, the incidence of infections attributable to gram-positive cocci may increase. However this is offset by decreased incidence of infections caused by gram-negatives and yeast.
83  VITAMIN D INSUFFICIENCY COMMON IN PEDIATRIC PATIENTS WITH INTESTINAL FAILURE, REGARDLESS OF INTESTINAL ANATOMY. Ryan Fischer, Marisa Fisher, Brandy Hobson, Ruben Quirros-Tejeira, Stephen Raynor, David Mercer, University of Nebraska Medical Center, Omaha, NE

Purpose: Patients with short bowel syndrome (SBS) and/or intestinal failure (IF) are at high risk of vitamin D insufficiency or deficiency secondary to malabsorption and the impaired ability to absorb nutrients enterally. We sought to analyze a population of patients followed in a pediatric intestinal rehabilitation program for the prevalence of vitamin D deficiency or insufficiency.

Methods: The charts of 22 children were retrospectively reviewed in our intestinal rehabilitation program to collect evidence of vitamin D insufficiency (serum levels of ≤30 ng/ml) and deficiency (≤10 ng/ml). Data collected included the patients’ underlying etiology of SBS/IF, estimated small bowel length, presence or absence of ileocecal valve, colonic anatomy, and serial vitamin D measurements, when available. We used unpaired T-tests or single factor ANOVA to compare mean vitamin D levels among patient groups.

Results: The majority of patients in our program had evidence of vitamin D insufficiency or deficiency. Of 22 patients, 19 (86%) had one or more serum levels of ≤30 ng/ml. Three patients (13%) had at least one serum level of ≤10 ng/ml. For 9 patients, the mean of serial vitamin D levels was ≤30 ng/ml (40%). The etiology of the SBS/IF, and (for patients with IF due to SBS) small bowel length, colonic anatomy, and the presence of the ileocecal valve were not significantly associated with mean vitamin D levels (p values of 0.3, 0.2, 0.3, and 0.4, respectively).

Conclusion: Vitamin D insufficiency is common in children with SBS/IF. Considering the importance of vitamin D to numerous biologic pathways, inadequate vitamin D may adversely impact the health of children with SBS/IF. While the specific etiologies of SBS/IF and intestinal anatomy do not seem to be significantly associated with vitamin D levels, SBS/IF itself puts children at risk for vitamin D deficiency and its consequences.

84  FATP2 KNOCK-OUT MICE ARE PROTECTED FROM DIET INDUCED HYPERGLYCEMIA INDEPENDENT OF WEIGHT GAIN AND HEPATIC STEATOSIS

Samir Sofitc°, Michelle Kirby1, Rohit Kohli1, 1Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 2Pediatrics, Riley Hospital for Children, Indianapolis, IN

Non-alcoholic Fatty Liver Disease (NAFLD) correlates strongly with obesity, hyperinsulinemia and type 2 diabetes. Murine models of high-fat diet (HFD) induced hepatic steatosis take 8-12 weeks to develop and invariably acquire concomitant hyperglycemia and hyperinsulinemia. Increased dietary free fatty acid flux to the liver is postulated to induce insulin resistance. We recently reported that insulin concentration mediates hepatic steatosis via Insulin Receptor Substrate dependent up-regulation of Fatty Acid Transport Proteins (FATPs). Therefore, we hypothesize that mice lacking relatively liver specific fatty acid transporter (FATP-2 KO) would uptake less FFA in the liver and be protected from HFD associated hyperglycemia. Methods: Adult, 6-8 week old, male, FATP-2 KO mice were placed either on a high-fat diet (60% kcal from fat) or Chow diet for twelve weeks. Food intake and body weights were measured weekly. Results: Chow fed mice consumed 9.9 kcal/day, comparable to HFD-fed mice, which consumed 10.1 kcal/day. After 12 weeks, HFD-fed mice gained significantly more weight than chow-fed controls (39.3±1.68 vs. 32.9±0.46g; p=0.01). Furthermore, HFD-fed mice developed significant steatosis, compared to chow controls, as quantified by hepatocyte triglyceride content (80.5±7.2 vs. 453.6±58.4 mg/dL per 100mg liver; p=0.003). In spite of being on HFD for 12 weeks, gaining more weight and developing significant steatosis, fasting blood glucose of HFD-fed mice were not statistically different from chow-fed controls (119.8±3.3 vs. 131.8±4.2g/dL). Conclusion: In summary, knock-out of liver specific FATP-2 transporter resulted in protection from diet induced hyperglycermia, while it had no effect on weight gain and hepatic steatosis.

85  DEVELOPMENT OF GROWTH CENTILE CHARTS (ANTHROPOMETRIC MEASUREMENT OF PAKISTANI PEDIATRIC POPULATION).

Sina Azizi1, Wajeeha Noor-Ul-Ain2, Rukhsana Majid1, Amanullah Khan3, Ifitikar Qayum1, Intisar Ahmed4, Kehkashah Hosain5, 1Pediatrics, DUHS, Karachi, Pakistan; 2Community medicine, Bolan Medical College, Quetta, Pakistan; 3 equivalence, Fatima Memorial College, Lahore, Pakistan; 4Medical research, Rehman Medical College, Peshawar, Pakistan; 5Medical education, CPSP, Karachi, Pakistan; 6Nutrition, SIUT, Karachi, Pakistan

Objective:
1. To measure Height and Weight of Pakistani school children (of different socio-economic and cultural background) 3-16y.
2. To develop growth centile charts, based on the above measurement.
3. To document obesity and stunting in Pakistani Pediatric population, based on the above measurement.

Methods: Cross-sectional study. Multistage stratified sampling. Nationwide project of Higher Education Commission (HEC, Ref no: 20-441/R&D/2008).Study conducted yr 2006-2009. Children studying in private and government schools of four provinces of Pakistan were included. Prior to starting the study permission from the principal of school and parents was taken.

Total 12900 children with normal birth weight, complete immunization, no history of chronic infection 3-16 yr were included. Height (cms), weight (kg), BMI (kg/m2), 24 hour diet recall was obtained. All socioeconomic groups were included. Food records of the children were subjected to USDA food exchange list. Forms were used as inputs to generate tables for Statistical Package for social sciences -SPSS, Window 13.0.
Results: Table shows mean height, weight, BMI (z score) of 12900 Pakistani children. Related with CDC charts height and weight in the three groups >3-5y, >5-10y, >10-16y were at 10-25 centile. Few children based on their BMI were obese. Stunting in children >5-10 yrs was present in both genders.

Conclusion: Overall, the prevalence of stunting was less than 24 % and height and weight was 10-25 centile of the CDC charts. Z score (cut off 1.96) in Pakistani school children 3-16 years of age for height, weight and their BMI N=12900

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86 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBES PRIOR TO BONE MARROW TRANSPLANTATION: REVIEW OF CURRENT PRACTICE AT A SINGLE CENTER
Sunpreet Kaur, Keith Benkov, Clare Ceballos, Kathy Hoffstutder-Thal, Pediatric Gastroenterology, Mount Sinai School of Medicine, New York, NY

Introduction: BMT is an important treatment/cure for many diseases. The risks of developing GVHD and mucositis are increased after BMT. The underlying disease along with side effects of chemotherapy predisposes patients to malnutrition. It has been shown in previous literature that enteral feeding is the preferred method of nutrition for BMT patients. NG tubes are currently employed at many centers for enteral feeding in BMT patients, but carry infectious risks and other side effects. A more recent approach employed at our center is placement of a PEG tube prior to BMT. This study sought to establish the safety and complications of PEG placement prior to BMT.

Methods: A retrospective chart review of 11 children who received a PEG prior to BMT at Mount Sinai Medical Center from 2007 to 2010 was queried for the incidence of complications related to the PEG. We compared this to the incidence of complications in 30 children who had PEG tube placement from 2007-2010 at our institution and did not have a BMT.

Results: A total of 12 children received a PEG prior to BMT; 11 patients received BMT at MSIH, 1 patient went to an outside institution for a BMT and was excluded from the study. Of the 11 patients, 4 (36%) had a significant complication related to PEG requiring IV antibiotics and 3 of those required PEG removal. 2 of the 4 patients who developed a major complication related to PEG during BMT course were neutropenic (ANC<1000) at the time of PEG placement. Of the 30 subjects who had PEGs and did not have BMT, 1 (3%) had a complication with cellulitis requiring enteral antibiotics.

Conclusions: The incidence of complication in BMT patients vs. non BMT patients was significant, with p value of 0.01. The remaining patient characteristics were not significantly different between the two groups. 2 of the 4 patients who developed complications were neutropenic at time of PEG placement. Our findings support that ANC should be considered prior to placement of PEG as neutropenic patients are more prone to infections.

87 PRE-EMPTIVE RESTRICTION OF INTRALIPIDS DOSE IS NOT NECESSARY FOR MANAGEMENT OF PNALD. Timothy Sentongo, Ellen Newton, Dana Weinstein, Melanie Purser, Ranjana Gokhale, Stefano Guandalini, University of Chicago, Chicago, IL

Background: Recent incrimination of Soy-based intralipids in progression of Parenteral Nutrition Associated liver disease (PNALD) has prompted the practice of pre-emptive reduction in initial dose of Soy lipids or use of fish oil-based intralipids. This study demonstrates the efficacy of liberal Soy-based intralipids with close monitoring and individualized dose adjustment to manage PNALD.

Methods: Review of Nutrition Support Practice in NICU infants during 7/09 to 6/10. 520 infants received PN therapy; 129 (25%) were randomly sampled. PN was initiated by day 2 of life (DOL) and advanced to goal of 150 mL/kg/d; 90 - 100 kcal/kg/d; Protein 3-4 g/kg/d and intralipids 3 g/kg/d by DOL 7-10. PN volume was reduced while advancing enteral feeds. At onset of PNALD (direct bilirubin >1.5 mg/dL, x >7 d) the lipid dose was gradually reduced by 0.5 - 1.0 g/kg/d/week to minimum of 1 g/kg/d x 3/week depending on severity of PNALD and maintenance of weight gain. Prevalence of PNALD, risk factors, time to onset and reversal of PNALD were examined.

Results: 129 infants (49% female), birth weight (median; range) 1557 g (425 - 4085 g), gestation age 31 weeks (23 - 41). The most frequent co-morbidity was severe pulmonary disease (76%) followed by cardiac 21% and gastrointestinal disorders (11%). The duration of PN was 16-d (1 - 322), 22 infants (16%) developed PNALD, with 33-days as the median duration of PN to onset of PNALD. The median duration of PN in infants that developed PNALD vs. no PNALD was 51 d, p <0.01. There was a significant association between resolution of PNALD and reduction of intralipids dose p = 0.026. Average weight gain was 12 g/d. Resolution of PNALD occurred in 100% of infants regardless of birth weight, degree of prematurity or presence of GI disease.

Conclusion: Duration of PN therapy was the most consistent risk for onset of PNALD, while reduction in lipids was significantly associated with resolution of PNALD. Time to onset of PNALD was variable and thus did not support the practice of pre-emptive restriction of lipid dose.
88 OBESITY DOES NOT INFLUENCE MORTALITY AND MORBIDITY IN CRITICALLY ILL CHILDREN.  
Vi Lier Goh1, Martin K. Wakeham2, Theresa A. Mikhailov3, Praveen S. Goday4, 1Pediatric Gastroenterology and Nutrition, Medical College of Wisconsin, Milwaukee, WI; 2Pediatric Critical Care, Medical College of Wisconsin, Milwaukee, WI  
Aim: To evaluate the effect of obesity on mortality and length of mechanical ventilation in critically ill children  
Methods: Retrospective cohort study in 2-18 year-olds, admitted to the PICU at the Children’s Hospital of Wisconsin from 2005-2009 who required invasive ventilation. Weight z-score was used to categorize subjects as normal (-1.89 to 1.04), obese (1.65 to 2.33), and severely obese (>2.33). Malnourished and overweight patients were excluded. Age, gender, admission type, Pediatric Index of Mortality 2 score, operative status, trauma status, admission Pediatric Outcome Performance Category (POPC), and diagnosis categories were also collected via the Virtual PICU System (VPS database). Patients with missing height on admission were analyzed as a sub-group. The outcomes were ventilator-free days (VFD) (i.e., days alive and breathing unassisted within 28 days after admission) and mortality.  
Results: A total of 901 patients were included in the study with 759 normal, 78 obese, and 64 severely obese. Obesity (adjusted OR 0.80, 95%CI 0.38-1.67) and severe obesity (adjusted OR 1.002, 95%CI 0.46-2.20) were not associated with mortality. Mortality was higher in patients with no height available (OR 3.77, 95%CI 2.39-5.95). There was no difference in mortality between the normal, obese, and severely obese within this group. Patients with VFD=0 were analyzed separately due to the skewed distribution of the results. There were 117 patients with VFD=0 with 83.8% normal, 8.6% obese, and 7.7% severely obese. VFD was similar between the normal (median=26.9), obese (median=27.1), and severely obese (median=26.2) group (p=0.63) in patients with VFD>0.  
Conclusions: Patients with missing height have higher mortality, which may be due to the higher severity of illness. There is no difference in mortality and ventilator-free days between obese, severely obese, and children of normal weight, irrespective of recorded height. These data need to be confirmed by larger prospective studies.  
89 A LONGITUDINAL EVALUATION OF THE GROWTH OUTCOMES AFTER HOSPITALIZATION OF VERY LOW BIRTH WEIGHT PRETERM INFANTS. Toméu E. Larios del Toro1, Edgar M. Vásquez-Garibay2, Alejandro González-Ojeda1, Juan M. Ramírez-Valdivia2, Rogelio Troyo-Sanromán1, Guadalupe Carmona-Gómez1, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2Servicio de Neonatología, Hospital Civil de Guadalajara Dr. Juan I. Menchaca, Guadalajara, Mexico; 3Unidad de Investigación en Epidemiología Clínica, Centro Médico Nacional de Occidente. Instituto Mexicano del Seguro Social, Guadalajara, Mexico  
Aim: To demonstrate that hospitalization in a neonatal intensive care unit (NICU) may have an unfavorable impact on anthropometrical indicators of preterm infants ≤1500g.  
Methods: In a prospective study, 114 very low birth weight (VLBW) preterm infants (≤ 1500g) of both sexes, with normal and/or low weight for gestational age were included. At the start, weight, length, mid-upper arm, thigh and cephalic circumferences (MUAC, TC, CC respectively) were measured. Weight/age (W/A), length/age (L/A) and weight/length (W/L) (+ z-score) indices were calculated. Measurements were taken at inclusion, 7, 15 and 30 days of hospitalization. Chi square, ANOVA and repeated measures test among those indicators were estimated.  
Results: 13 cases (14%) were excluded due to death soon after the first determinations were made. Nine (8.9%) died during the study, 12 (11.9%) were discharged because their health improved and 80 (79.2%) completed the study. Z-score of W/A decreased from initial vs. 2nd, 3rd and 4th weeks (p < 0.001). L/A decreased between 1st vs. 2nd, 3rd vs. 4th (< 0.01), 1st vs. 3rd, 1st vs. 4th , 2nd vs. 4th (p < 0.001). MUAC also decreased between 1st vs. 2nd, 1st vs. 3rd, 1st vs. 4th and 2nd vs. 4th weeks (p < 0.01).  
Conclusion: Hospitalization in the NICU had an unfavorable effect on the anthropometrical indicators. L/A and MUAC were the most useful indicators for detecting changes and deficits over this short period of time.  
90 CHOICE OF ELEMENTAL VS POLYMERIC FORMULA FOR NEONATAL SHORT BOWEL SYNDROME: STUDIES IN PIGLETS. Zheng Hua1, Justine Turner1, Patrick Nation1, Pamela Wizzard2, Diana Mayer1, Ronald Ball1, Paul Pencharz2, David Sigaret1, Paul W. W. Ho1, 1University of Alberta, Edmonton, AB, Canada; 2University of Toronto, Toronto, ON, Canada; 3University of Calgary, Calgary, AB, Canada  
Introduction: Recovery from short bowel syndrome (SBS) requires intestinal adaptation, dependent on enteral nutrition and peptides, like glucagon-like peptide-2 (GLP-2). In clinical practice, elemental formula is often used to feed neonates with SBS. Animal studies suggest polymeric formula is better for adaptation. We compared elemental to polymeric formula in SBS piglets.  
Methods: 48 piglets were assigned to: 75% mid-intestinal resection with jejunoileal anastomosis (JI); 75% distal-intestinal resection with jejunoileal Anastomosis (JI); or sham with no resection. Postoperatively piglets were initially on parenteral nutrition (PN), tapered as enteral nutrition increased. Within groups, piglets were randomized to iso-caloric/iso-nitrogenous elemental (amino acid) or polymeric (intact protein) formula. Data collection included fat absorption, plasma GLP-2 and jejunal histology at 14 days.  
Results: PN duration was shorter for JI versus JC SBS piglets (10.2±2.7 vs. 12.8±1.6 days, p<0.01). JI piglets had longer villi (7.2±1.7 vs. 5.3±1.0 x 10-1mm, p<0.01), deeper crypts (2.0±0.3 vs. 1.7±0.3 x 10-1mm, p<0.01) and higher plasma GLP-2 (73±33.9 vs. 28.4±21.0 pM, p<0.001). Within all groups, weight gain, fat absorption and adaptation did not differ by formula. In JC piglets polymeric formula was associated with a longer duration of PN (13.8±0.5 vs. 12.0±1.8 days; p<0.05) and diarrhea (12.3±12 vs. 9.9±2.4 days; p<0.05). In JC piglets polymeric formula was associated with higher plasma GLP-2 (40.3±20.7 vs. 19.1±16.8 pM; p<0.05).  
Conclusions: SBS piglets without ileum have limited adaptation, longer duration of PN dependence and less tolerance of polymeric formula. Although polymeric formula did stimulate GLP-2 production, presumably from the colon, an overall benefit over elemental formula on gut adaptation was not observed.
HEPATOBLIARY/TRANSPLANT

99 SERUM BIOMARKERS OF NONALCOHOLIC STEATOHEPATITIS IN MORBIDLY OBESE ADOLESCENTS. Abbey Fingere1, Joel E. Lavine2, Ilene Fennoy3, Jeffrey Zitsman1,2, Surgery, Columbia University Medical Center, New York, NY; 3 Pediatric Gastroenterology, Hepatology, and Nutrition, Columbia University Medical Center, New York, NY; 4 Pediatric Endocrinology, Columbia University Medical Center, New York, NY; 4 Pediatric Surgery, Columbia University Medical Center, New York, NY

Background: Nonalcoholic fatty liver disease is a spectrum of pathology from benign simple steatosis (SS) to nonalcoholic steatohepatitis (NASH). The current gold standard for the diagnosis of NASH is a liver biopsy. Objectives: To determine serum biomarkers associated with the severity of NAFLD in morbidly obese adolescents.

Materials and Methods: Eleven adolescents undergoing laparoscopic bariatric surgery for morbid obesity who also had transaminisats or ultrasound findings of hepatomegaly or echogenicity were included. Liver biopsy specimens were reviewed to determine a NAFLD activity score (NAS). Simple steatosis was defined by NAS<5, NASH by NAS≥5. Patient characteristics were compared including age, BMI, BMI z-score, transaminases, total cholesterol, hemoglobin A1c, C-reactive protein, and hepatomegaly or echogenicity. Serum cytokeratin 18 fragments, adiponectin and leptin were measured using enzyme-linked immunosorbent assays. Statistical analysis was performed with Mann-Whitney U test and Fisher’s exact using SAS software.

Results: Three patients had NASH with NAS≥5, the remaining eight had NAS<5. No difference was found with regard to age, gender, BMI, BMI z-score, total cholesterol, hemoglobin A1c, hepatomegaly, echogenicity, serum C-reactive protein, adiponectin or leptin. In the NAS group, four serum biomarkers were significantly higher than the SS group: serum cytokeratin 18 M30 fragments (mean 270.4 U/l vs 78.0), M65 fragments (mean 712.6 U/l vs 247.7), alanine aminotransferase (mean 89.0 U/l vs 22.0) and aspartate aminotransferase (mean 57.7 U/l vs 21.9).

Conclusions: Cytokeratin 18 represents a potential non-invasive biomarker to determine the severity of NAFLD in morbidly obese adolescents. Additional testing of this study population is required to validate these findings and determine appropriate cutoff values.

100 INFLAMMATORY AND OXIDATIVE STRESS BIOMARKERS OF CARDIOVASCULAR RISK ARE INCREASED IN CHILDREN WITH OBESITY AND FATTY LIVER. Angela Shannon, R. Schlanger, N. Alkhouri, M. Karafa, L. Cho, S. Hazen, C. Carter-Kent, A. Feldstein, Cleveland Clinic, Cleveland, OH

Obesity and fatty liver in children have been recognized as potential risk factors for cardiovascular disease (CVD); however, little is known regarding the prevalence and significance of inflammatory/oxidative stress biomarkers of CVD risk in children. Myeloperoxidase (MPO) and high-sensitive C-reactive protein (hsCRP) are associated with cardiovascular disease (CVD) in adults.

The aim of this study was to investigate the association between MPO and hsCRP with obesity and fatty liver in children.

Methods: Data was collected prospectively in children attending the Pediatric Preventive Cardiology and Metabolic Clinic at Cleveland Clinic and included demographic, anthropometric and laboratory data (fasting serum insulin, fasting lipid panel, liver function tests, serum MPO and hsCRP). The cohort was divided into different groups based on gender, age and BMI. Results: 151 patients were included for analysis. Mean age was 12.8±3.4. 55% were males; 51% were Caucasian. Mean BMI for the entire cohort was 34.1±7.9, for overweight patients 25.5±2.4, for obese patients 30.6±3.7 and for morbidly obese patients 37.2±8.5. MPO tended to be higher in males and in younger patients. MPO levels were markedly elevated in obese patients compared to overweight patients (432±200 vs 182±90, P<0.023), and even more so in morbidly obese compared to overweight patients (445±165 vs 182±90, P<0.004). MPO and hsCRP levels had a significant positive correlation with BMI%ile (rho 0.42 and 0.47, respectively, p<0.001). In patients with hepatic steatosis, there was a stronger correlation between MPO and hsCRP levels and BMI compared to patients without hepatic steatosis (rho 0.65, 0.56 vs 0.46, 0.41, respectively). Conclusion: This is the first pediatric study evaluating the association between obesity and MPO. MPO and hsCRP are correlated with increasing BMI and this correlation is strengthened in the presence of hepatic steatosis. These biomarkers may become useful tools to identify obese children that are at increased risk of CVD, allowing for early intervention.

101 IMPORTANCE OF HBV DNA CONFIRMATION IN POSITIVELY SCREENED CHILDREN WITH HEMATOLOGIC OR ONCOLOGIC CONDITIONS. David Ahamba, Mahjabeen Khan, Stephanie Howe, Lekshmi Pillai, Daniel Leung, Pediatric Gastroenterology, Hepatology, and Nutrition, Baylor College of Medicine, Houston, TX

Background: Hepatitis B virus reactivation (HBVR) is a well described complication in cancer patients who receive chemotherapy. Active surveillance of HBV at a children’s hospital revealed a significant number of children with oncologenic or hematologic conditions with Hep B core Ab. These children often require immunosuppressive therapy, underscoring the importance of knowing HBV status. Aims: 1) To characterize the oncologenic and hematologic conditions in children with positive HBV screen 2) To investigate current practices among oncologists given positive HBV screening among children (ages 0-17) at a quaternary children’s hospital.

Methods: A retrospective analysis of hospital-affiliated patients (0-17 yrs) who tested positive on HBV screening from 1999-2009.

Results: 131/473 children (28%) who screened positive for HBV carried an oncologic or hematologic diagnosis. Leukemia, anemia, and thrombocytopenia comprised 31%, 27% and 25% of cases. 90% tested core Ab+, 8% tested surface Ag+, and 2% tested positive for both. Up to 50% demonstrated ALT elevation (>45 U/L). Only 17% of positively screened children received confirmatory HBV DNA testing. 25% and 12.5% of children with leukemia and anemia who had DNA testing were confirmed to have HBV. 19% of patients with HBV DNA testing were confirmed to have true disease. All were previously immunized for HBV.
Conclusions: Children with oncologic or hematologic conditions may have a higher risk of testing positive for Hep B core Ab. Whether these represent false positives or a true diagnosis needs to be confirmed. <20% of positively screened children received HBV DNA testing despite elevated ALT. The number of true HBV cases in this vulnerable group is likely underreported. Children requiring immunosuppression are at high risk of HBVR despite prior immunization. Greater education regarding these risks is needed and guidelines for managing positive HBV screening in children with malignant conditions are necessary.

102 HEPATIC FUNCTION RESERVE ASSESSMENT WITH 13C-METHACETIN BREATH TEST IN CHILDREN WITH CHRONIC LIVER DISEASE. Elisa Gaona1, Segundo Moran-Villota1, 1Hospital Infantil de México Federico Gómez, México, Mexico; 2Centro Médico Nacional Siglo XXI, México, Mexico

Background. 13C methacetin breath test (13C-MBT) measures methacetin oxidation dependent on cytochrome P450's activity. In adults it's used to assess the hepatic function reserve and as a cirrhosis predictor (sensitivity 92.6%, specificity 94%). Nevertheless, there is no information about its use in pediatric population.

Objective. Compare hepatic reserve in children with chronic liver disease and healthy controls using 13C-MBT.

Methods and Materials. We included 18 patients (7.7±4.5 years-old) with chronic liver disease (biliary atresia n=6, glucagonemia n=4, criptogenic hepatitis n=4, autoimmune hepatitis n=2, Alagille syndrome n=2) and 19 healthy controls (10.4±7.8 years-old) with normal biochemical hepatic function. Every child had a clinical evaluation, 13C-MBT and a venous blood sample for hepatic function tests.

Results. The percentage of oxidated methacetin dose (%doxi) in children with chronic liver disease was significantly less (p<0.05) than healthy controls at 10, 15, 20 and 30 minutes, respectively (%doxi 10 min=0.56±0.64 vs 1.18±0.64; %doxi 15 min=1.02±1.02 vs 2.07±1.09; %doxi 20 min= 1.79±1.5 vs 3.5±1.71; %doxi 30 min= 3.64±2.56 vs 6.60±2.82).

Conclusion. The results support the potential of 13C-MBT to assess hepatic function reserve in children.

103 TACROLIMUS IS EFFECTIVE FOR “DIFFICULT-TO-TREAT” AUTOIMMUNE HEPATITIS IN CHILDREN. Genie L. Beasley, Regina P. González-Peralta, Allah Haafiz, Pediatrics, Division of Pediatric Gastroenterology, Hepatology and Nutrition, University of Florida, Gainesville, FL

Background: Autoimmune hepatitis (AIH) is a chronic progressive liver disease. Corticosteroids alone or with azathioprine (AZA) are the mainstay of treatment but a proportion of patients with AIH do not respond to this conventional therapy. Calcineurin inhibitors have been effectively used in this setting in adults but little is known about this treatment in children.

Aim: To assess efficacy of Tacrolimus (Tac) in a group of children with AIH and poor response to conventional therapy.

Methods: We reviewed charts of children with AIH and analyzed clinical and biochemical parameters of those treated with Tac.

Biochemical parameters at the time of initiating Tac were compared to similar tests performed at 3, 6, 12, and 24 months afterwards. The data were analyzed by GraphPad Instat using a p value ≤0.05 as statistically significant.

Results: Between 1999 and 2011, six patients (4 females) were treated with Tac. Mean age (years ±SEM) at AIH diagnosis and at switch to Tac therapy was 13 ± 1.5 and 14.6 ± 1.6, respectively. Four of the six patients were started on Tac because of persistent biochemical abnormalities despite combination therapy with steroids and AZA. Two patients presented with acute and severe AIH that did not respond to high-dose corticosteroids. Mean ALT (IU/L) were significantly lower after 3 months of Tac therapy (264 ± 85 vs. 82 ± 19; p ≤0.05) and this trend persisted through two years of treatment. There was a decline in bilirubin level (mg/dl) during Tac therapy, although it did not reach statistical significance. Tac therapy allowed for significant decrease in mean prednisone dose (mg) from 29 ± 7 to 11 ± 3 at 2 years of therapy (p ≤0.05). Mean trough Tac levels (µg/L) were 5 ± 0.5, 6 ± 2; 6 ± 1; and 6 ± 3 at 12, 15, and 24 months, respectively. Hematological and renal functions remained stable during Tac therapy.

Conclusion: Tac may be effectively used to manage ‘difficult-to-treat’ children with AIH. Optimal timing and indications for Tac therapy in this group remains to be determined.

104 SIROLIMUS AS RESCUE THERAPY IN REFRACTORY PEDIATRIC AUTOIMMUNE HEPATITIS. Jacob Kaurowski, Hector Melin-Aldana, Cindy Riazzi, Therese Hess, Lee Bass, Estella M. Alonso, Peter F. Whittington, Udeme D. Ekonog, Children's Memorial Hospital, Chicago, IL

Background: Refractory autoimmune hepatitis is reported to occur in about seven to ten percent of adult and pediatric patients with autoimmune hepatitis (AIH), with about ten to fifteen percent of patients failing to improve and progressing to liver transplantation. A defect in immunoregulation affecting regulatory T cells has been demonstrated in AIH, and sirolimus has been shown to selectively expand regulatory T cells in vitro. We therefore hypothesized that sirolimus would be successful as rescue therapy for refractory AIH. Objective: this is a retrospective case series describing the use of sirolimus as rescue therapy for refractory AIH. Methods: we queried our medical records for all patients with a diagnosis of AIH who were receiving or had received treatment with sirolimus between January 1998 and June 2010. We defined success as liver enzymes ≤2X ULN with histological resolution of inflammation. Target sirolimus level was 4-8 ng/ml for all patients. Results: five patients were identified (Table 1). Three patients achieved biochemical remission on sirolimus with an average time to remission of 4.7 ± 2.3
months. Responders showed a significant reduction in liver enzymes compared to non-responders \( (p=0.02) \). Histologic inflammation improved by two grades (Batts and Ludwig system) and all three biochemical responders tolerated significant reduction of their prednisone dose compared to non-responders \( (p=0.01) \). Conclusion: Sirolimus might prove to be successful in inducing remission in refractory AIH. Whether remission is associated with a significant improvement in fibrosis remains to be seen.

### TABLE 1: demographics, autoantibody titers and protein levels at diagnosis

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age at Diagnosis (years)</th>
<th>Sex</th>
<th>Anti-nuclear antibody titer</th>
<th>Anti-smooth muscle antibody titer</th>
<th>Anti-liver kidney microsomal antibody titer</th>
<th>Total Protein g/dL</th>
<th>Albumin g/dL</th>
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<tr>
<td>1</td>
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<td>1:1280</td>
<td>*</td>
<td>6.9</td>
<td>2.0</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>F</td>
<td>&lt;1:80</td>
<td>1:1280</td>
<td>&lt;1:40</td>
<td>8.7</td>
<td>2.4</td>
</tr>
<tr>
<td>4</td>
<td>0.5</td>
<td>M</td>
<td>&lt;1:80</td>
<td>&lt;1:80</td>
<td>&lt;1:40</td>
<td>5.3</td>
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<td>1:640</td>
<td>&lt;1:40</td>
<td>8.3</td>
<td>3.6</td>
</tr>
</tbody>
</table>

*Not Available

### 105 CHILDHOOD OBESITY AND CORRELATES OF NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN AN URBAN CLINIC POPULATION.

Khyati Mehta\(^1\), R. McEachern\(^1\), E. Neimark\(^1\), N. LeLeiko\(^1\), J. Wands\(^2\), S. DeLaMonte\(^2\), \(^1\)Pediatric Gastroenterology, Hasbro Children's Hospital, Brown U, Providence, RI; \(^2\)Medicine, Alpert Medical School- Brown U, Providence, RI

Background: Obesity continues to grow as a major public health problem in the US, with now more than 60% of adults and 30% of children classified as overweight or obese. The problem in children is worrisome due to the alarming rates of T2DM & NAFLD, increasing risks of hepatocellular carcinoma, premature cardiovascular & cerebrovascular disease, osteoarthritis & shortened lifespan.

Aims: This survey was designed to identify risk factors for developing NAFLD in a population of obese children, looking forward towards increasing the use of non-invasive tools for early diagnosis & patient feedback.

Methods: We conducted a retrospective electronic chart review of children regularly monitored in the Rhode Island Hospital obesity clinic. Subjects with T2DM were excluded. Data were analyzed using descriptive, frequency & correlational statistics.

Results: 75 subjects (52% female) were included in the study. Ages ranged from 4 to 18 years (mean±SD:13.1 ± 2.7 yrs).96% were morbidly obese, BMI was 34.9±6.1 & waist circumference was 96.1±13.1 cm. 34.7% had dyslipidemia (HDLL: 39.7 ± 10.0;LDL 96.7 ± 28.5), 80% had peripheral insulin resistance & 16% were diagnosed with NAFLD based on ultrasound & elevated LFTs. BMIs in both mothers (34.7 ± 17.1) & fathers (35.9 ± 14.9) were similarly elevated, categorizing them as morbidly obese. Moreover, obese females had significantly worse academic performance than males. Regression analysis demonstrated a significant correlation between BMI & school grade/age \( (P<0.0001) \) and an inverse correlation between BMI & activity index \( (P=0.034) \). Children with NAFLD had significantly lower mean BMIs \( (P=0.003) \) but consumed more junk food \( (P=0.03) \). Other parameters, e.g. activity index & TV frequency showed trends only with respect to NAFLD, probably due to insufficient power of the study.

Conclusions: Since BMI increases with age/school grade, early intervention is urgently needed with respect to increasing activity & curbing junk food consumption.

### 106* MODELING LIVER DISEASE OUTCOME IN ALAGILLE SYNDROME (ALGS).

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Liver disease in ALGS manifests with cholestasis that can improve around 5 yrs age, though 20% progress requiring liver transplant(LT). Aim:To identify parameters present in the first 5 yrs of life, that predict ALGS liver disease outcome.

Serial data were collected from 0-5yrs from 6 centers. Patients were stratified into mild (M) or severe(S) hepatic outcomes based on data at the oldest age. M outcome was defined as biochemical abnormalities/minimal symptoms; S was liver disease with a complication or requiring biliary diversion/LT. We performed univariate analysis of risk factors, logistic regression modeling to predict S outcome, receiver operating characteristic (ROC) curves to quantify predictive ability of the models, mixed model analyses for laboratory data & recursive partitioning to determine classification thresholds.

Data were available on 101 ALGS patients (M=51,S=50; mean follow-up age 13yrs). Univariate analysis revealed: fibrosis on biopsy \( (p=0.034) \), xanthomas \( (p=0.007) \) & posterior embroytoxon (PE) \( (p=0.017) \) were associated with S. Combining the ROC of these 3 to quantify the predictive ability of S, the ROC was 80% \( (CI 67-93) \). From mixed model analyses total bilirubin (TB, \( p=0.001) \) & cholesterol (p=0.002) were associated with outcome. Graphical analysis of serial data revealed TB falls between 1-2yrs in the M group. Recursive partitioning revealed a threshold of 3.8mg/dL that differentiated between M & S.

Conclusions: Combined presence of hepatic fibrosis, xanthomas & PE in the first 5 yrs is predictive of S. This supports the role of liver biopsy for ALGS prognosis. TB>3.8mg/dL between ages 1-2 yrs also predicts S. These are clinically applicable tools that will aid in ALGS management.
107 FREQUENCY OF HIV, HEPATITIS B AND C IN GARBAGE COLLECTING PERSONS COMMUNITY (BASTI). Mohammad Uzair Abdul Rauf1,2, Muhammad Danish Saleem3, Muhammad Osama Anwer1,2, Gulraiz Ahmed1,2, Sina Aziz2,1
1 Dow Medical College, DUHS, Karachi, Pakistan; 2 Pediatrics, DUHS, Karachi, Pakistan

Objective: To study the frequency of HIV, Hepatitis B (HBV) and Hepatitis C (HCV) and risk factors in garbage collecting persons basti.

Methods: A cross sectional (ongoing) study was performed in low socio economic garbage collecting persons’ (majority afghan refugees) basti. The study involved targeting garbage collectors primarily children, who were professional garbage collectors.

Written consent was taken from each respondent for participation in the study. After performing pre test counseling a questionnaire was completed of the respondents and 5cc of blood was drawn for HIV, HBV and HCV test. HIV test was performed by ELISA technique, while HBV and HCV test by ICT method and those found positive were run on ELISA.

Results: A total of 81 males agreed to participate in the study out of which 60 were <25 years (mean±SD 17±4, range 9-25yr) while 21 were >25 years (mean±SD 39±9, range 26-48yr) of age. Percentage of Afghans, Pakhtoon, Punjabi, urdu and Baloch speaking were 58, 22, 14, 4 and 2 percent respectively. About 54% were illiterate, 17% could read and write, 24% received primary education and 5% had attended secondary school. A total of 46 respondents agreed to give blood for the diagnosis of all three tests, 21 agreed to get pricked for the required tests and 14 agreed to complete the questionnaire. None of them were found to be positive for HIV, while 10 (21.2%) individuals were HBV positive in age limit <25yr and 2 (10%) in the age group >25 yrs. Two HCV positive cases were seen one in the age group ≤25 yrs and one >25 yrs. Two individuals were co infected with HBV and HCV, one in each age group of ≤25 and <25 yr.

Conclusion: The results show frequency of HBV (18%). Daily habits/practices of these young children and their families suggest that these diseases would continue to grip them if immediate preventive measures are not taken. Proper counseling to improve hygiene/practices and prevention of child labor will, reduce incidence of life threatening diseases.

1 Pediatrics, CHOP, Philadelphia, PA; 2 Infectious Diseases, CHOP, Philadelphia, PA

Background: Biliary atresia (BA) is a neonatal liver disease of unknown etiology that leads to the fibro-inflammatory destruction of extrahepatic bile ducts, resulting in cholestasis. BA patients typically present with acholic stools within the first 4 to 8 weeks of life, and if untreated, will die by 24 months. No medical therapy exists, and biliary atresia is the leading indication for pediatric liver transplantation worldwide.

MicroRNAs are a class of short (18-23 nucleotide), non-coding RNA molecules, which act as negative regulators of the mRNA stability and protein expression of target genes. We have profiled miRNA transcript levels in the experimental mouse BA model at 3, 8 and 14 days post infection. Here we focus in particular on the miR-29b/29a cluster, which is up-regulated 3-fold in RRV infected liver, and present the first delineation of the full set of hepatic genes regulated by miR-29.

Methods: To address the role of miR-29 in experimental BA, we first performed gene expression microarray analysis on liver isolated from adult BALB/c mice injected with miR-29a or control antisense inhibitors. We identified 104 up- and 70 down-regulated transcripts altered ≥ 50% at an FDR of 10%. We validated the array, and performed pathways analysis. Using the same antisense strategy in the context of experimental BA, we assessed therapeutic intervention by serology, histology and target gene expression.

Results: Our data is supported by the presence of known direct targets including Dnmt3a and collagen genes among the up-regulated transcripts, and gene set analysis confirms significant enrichment for in silico-predicted miR-29 targets. Pathways (DAVID) analysis indicates that miR-29 represses ECM structural components and remodeling factors. While miR-29 antisense affected target genes in adult liver, these were unaffected in neonates, regardless of the dosage, dosing regimen, or antisense chemistry, suggesting that genetic models will be necessary to address miRNA function during the neonatal period.

109* PORTAL VENOUS FLOW ABNORMALITIES ARE PRESENT AND ARE ACCENTUATED AFTER ISCHEMIA REPERFUSION INJURY OF A STEATOTIC LIVER.
Nitika A. Gupta1, Vasantha L. Kolachala1, Rong Jiang2, Carlos Abramowski2, Stuart Knechtle3, Allan Kirk1, 1 Department of Pediatrics, Emory University School of Medicine, Atlanta, GA; 2 Department of Pathology, Emory University School of Medicine, Atlanta, GA; 3 Department of Surgery, Emory University School of Medicine, Atlanta, GA

Background: Ischemic insults to a fatty liver lead to extensive hepatocellular damage. This is becoming a burgeoning problem in the ratio in the mice with fatty liver (3.6 ± 0.21) as compared to the lean mice (2.4 ± 0.38) which was significant ; p<0.01. The resistive index was significantly higher in mice with fatty liver as compared to lean, post IRI (0.70 ± 0.01 vs 0.49 ± 0.03; p<0.0001) as well as prior to IRI (0.64 ± 0.03 vs 0.50 ± 0.02; p<0.02). Pulsatility index (PI) showed a similar trend. There was also a 5.4 fold increase in reversibility of portal blood flow as compared 1.7 fold in lean. On H&E staining, mice fed a HFD had...
narrowing of the sinusoidal space and showed a significant increase in serum ALT levels compared to lean mice. Conclusion: Our study shows that portal venous blood flow abnormalities are present and are further accentuated in mice with fatty liver after IRI. We postulate that these blood flow abnormalities contribute to the increasing hepatocellular damage which is seen after IRI in a steatotic liver.

110 IMPACT OF OBESITY ON PEDIATRIC CHOLECYSTECTOMY. Nitin Gupta1, Edmund Kessler2, Aliza Solomon1, 1Pediatric Gastroenterology, Weill Cornell Medical Center, New York, NY; 2Pediatric Surgery, Weill Cornell Medical Center, New York, NY

Background: The prevalence of cholecystectomies in children is on the rise. The impact of obesity on gallbladder disease and surgical outcomes in adults is well documented; however, there is minimal data in the pediatric population. Obesity appears to be a risk factor in pediatric gallbladder disease leading to a parallel increase in cholecystectomies.

Methods: A retrospective chart review was performed on patients who underwent cholecystectomies between the years 2005-2010. Data collected included age, sex, height, weight, Body Mass Index (BMI) percentiles, past medical history, indications, prior imaging, length of stay, complications, comorbidities and type of surgery.

Results: Preliminary results of 58 records were reviewed. The mean age of patients was 17.8 years (range 8-21) and 82.8% were female. There were 26 in the normal weight (NW) group and 32 in the overweight (OW) (BMI >85%) group. 55% of the surgeries were performed on the OW group. The mean number of cholecystectomies was 11 per year and there was no increased incidence of cholecystectomy across 5 years. The indication for cholecystectomy did not differ between the groups. The length of stay for acute surgery was longer amongst the NW group with 3.2 days (range 1-13) compared to 2.5 days (range 1-9) for the OW group. More patients in NW group had associated comorbidities that contributed to hospital stay such as sickle cell disease, renal disease and congenital heart defects. The mean operative time was 132.9 minutes (range 79-213) in the NW group and 154.8 minutes (range 96-249) in the OW group.

Conclusion: Although many pediatric patients undergoing cholecystectomy are obese, obesity may not necessarily be directly linked with an increased prevalence of surgery. Obesity did impact the mean length of surgery and further studies are needed to examine this data for causal relationship.

111 HEALTH RELATED QUALITY OF LIFE IN CHILDREN WITH AUTOIMMUNE LIVER DISEASE. Reema Gulati, Kaddakal Radhakrishnan, Vera Hupertz, Naim Alkhouri, Ariel Feldstein, Cleveland Clinic, Cleveland, OH

Background: Health related quality of life (HRQOL), a pivotal outcome indicator of health care interventions, has not been evaluated to date in children with autoimmune liver disease (AILD). Aim: To determine the HRQOL in children with Autoimmune Hepatitis (AIH) and Primary Sclerosing Cholangitis (PSC), and identify specific prognostic factors affecting it.

Methods: The Pediatric Quality Of Life Inventory (PedsQL 4.0), generic core scale, was used to collect HRQOL data on children with AILD, at Cleveland Clinic. Specific liver disease related questions were added. Results: Survey responses were received from 20/40 patients. The mean age of the patients was 11.6 yrs, they were predominantly Caucasians (78%), with a F:M ratio of 1.3:1, and had AILD for an average of 4.6 years, with AIH in 40%, PSC in 45% and overlap syndrome in 15% of the patients.

Advanced liver disease was present in 73% patients. The mean overall health summary scores for the group per child and parent reports were 71.6 and 71.3 respectively, which were significantly lower than healthy controls: 83.9 and 82.3 (p=0.002), and similar to other chronic pediatric disorders. Experiencing frequent liver related symptoms was associated with impaired physical and school functioning by child (p=0.034 and 0.047) and parent reports (p=0.018). Overall, abdominal pain, fatigue and psychological symptoms were found to adversely affect HRQOL. Although advanced disease per se didn’t seem to effect HRQOL, having any complication impaired social functioning per child report (p=0.018), as also presence of ascites, per parent report (p=0.036). There were no differences in QOL scores in children with AIH vs. PSC vs Overlap syndrome. Conclusion: This is the first study to date, showing that AILD in children significantly affects HRQOL, especially when they are frequently having symptoms related specifically to liver disease. The study also showed good concordance between children and their parent’s perception of their HRQOL. These findings need to be validated in larger, multicentre studies and will help practitioners focus their efforts in counseling patients and optimizing care.

112 INTESTINAL ALLOGRAFT REJECTION CHARACTERIZED BY ELEVATIONS IN TUMOR NECROSIS FACTOR-ALPHA LEVELS. Ryan Fischer, Alexandra Moustakes, Geoff Talmon, David Mercer, Ruben Quiros-Tejeira, Alan Langnas, Nora Sarvetnick, University of Nebraska Medical Center, Omaha, NE

Purpose: Tumor necrosis factor-alpha (TNF-α) is a cytokine released during tissue injury and inflammation to regulate the immune response. Dysregulation of the production and function of TNF-α and its receptors (TNFR1 and TNFR2) is implicated in the pathogenesis of autoimmune disorders, and in the rejection of cardiac, kidney and liver allografts. However, the roles of TNF-α and its receptors in small intestine allograft rejection are ill-defined.

Methods: Plasma samples were obtained from patients following isolated intestinal or combined liver, pancreas and intestinal allografts under an IRB-approved protocol. Plasma levels of TNF-α and the soluble forms of TNFR1 and TNFR2 were quantified by ELISA and compared with the histologic presence or absence of allograft rejection. We also performed immunohistochemical staining for TNF-α, TNFR1 and TNFR2 in tissue samples with and without rejection.

Results: Nine patients without symptoms of rejection undergoing surveillance endoscopy had a mean plasma TNF-α level of 9.2 pg/ml, compared with 11 patients with histologic confirmation of rejection who had a mean TNF-α level of 30.7 pg/ml (p = 0.04). Mean soluble TNFR1 and TNFR2 were also elevated in patients with rejection, and trended toward statistical significance, with p-values of 0.14 and 0.07 respectively. Tissue from rejection biopsies stained strongly for TNF-α and TNFR1. TNFR2 staining appeared strongest on infiltrating lymphocytes.
Conclusion: Our findings show an elevation in plasma and tissue TNF-α in intestinal allograft recipients with histologic evidence of rejection. Elevations of plasma and tissue TNFR1 and TNFR2 are also present in rejection. Such information may help define the role of TNF-family cytokines in intestinal allograft rejection, and may help to select patients with rejection that could respond to currently available anti-TNF-α therapy.

113 IMPACT OF PARAOXONASE 1 (PON1) IN PEDIATRIC NON-ALCOHOLIC STEATOHEPATITIS. Sonal Desai1, S. Baker2, W. Liu1, R. Kozieleski2, R. Browne2, R. Patel1, R. Baker1, L. Zhu1, 1Pediatric Gastroenterology, SUNY at Buffalo, Buffalo, NY; 2Pathology, SUNY at Buffalo, Buffalo, NY; 3Biochemistry, SUNY at Buffalo, Buffalo, NY
An increasing number of children are being diagnosed with non-alcoholic fatty liver disease (NAFLD) and pediatric (type 2) non-alcoholic steatohepatitis (NASH). A common finding in NASH patients is increased levels of free fatty acids (FFA). Peroxidation of FFA by reactive oxygen species (ROS) has been shown to cause damage intracellularly. Studies have demonstrated that oxidative stress, which produces ROS, is a critical player in the pathogenesis of NASH. Human serum PON1 is an enzyme synthesized in the liver and bound exclusively to High Density Lipoproteins (HDL) in the blood. PON1 functions as an antioxidant preventing the oxidation of HDL. Studies in adults have shown comparable activity of PON1 in both liver and serum, thus making it a potential biomarker for evaluating liver disease. Currently the relationships between PON1 and type 2 NASH are unknown. This study focuses on the activity and gene expression of PON1 in type 2 NASH.

Methods/Results: NASH was diagnosed according to Kleiner’s criteria. Data mining on NASH microarray database [1] showed a difference in the relative expression of PON1 among insulin resistant (1.77x) and non insulin resistant (2.24x) pediatric NASH patients compared to normal controls (NC). Additional quantitative analysis of the PON1 expression in liver tissue of NASH (n=18) and NC (n=4) with GAPDH as the housekeeping gene was performed with real time PCR. PON1 mRNA expression level was found to be 8.18 times that of the NC (p<0.005).

Conclusion: The increase in the expression of PON1 in pediatric NASH livers suggests a shift in the balance between antioxidants and oxidative stress. Adult NASH studies show a decreased level of PON1 activity in serum with type 1 NASH. Our findings suggest that the hepatic damage involved in type 2 NASH is not as extensive compared to the hepatic damage noted in type 1 NASH. Additional studies are warranted.

114 A SINGLE INSTITUTE’S SIX YEAR EXPERIENCE WITH TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS) IN THE PEDIATRIC PATIENT POPULATION. Namita Singh1, Simon Horslen1, Jack Vo2, Andre Dick, 1Gastroenterology, Seattle Children’s Hospital, Seattle, WA; 2Interventional Radiology, Seattle Children’s Hospital, Seattle, WA
Introduction: TIPS is successful in reducing portal hypertension (PHTN) and has been widely studied in adults. Data is lacking in the pediatric population, with experience largely based on case reports. TIPS may be an appropriate intervention for some pediatric patients, after extensive evaluation using a multidisciplinary approach.

Objective: In a center with a long experience of endoscopic and surgical interventions for children with PHTN, we discuss our experience with TIPS.

Methods: From 2005 to 2011, 11 patients, ranging from 17 months to 20 years of age, underwent TIPS. Primary causes of liver disease were biliary atresia, cystic fibrosis, autoimmune hepatitis, sclerosing cholangitis, congenital hepatic fibrosis and veno-occlusive disease. Indications for TIPS were gastric varices(2), esophageal varices with bleeding despite endoscopic management(2), uncontrolled acute variceal bleeding(1), splenic artery aneurysm(1), bleeding from portal hypertensive gastropathy(1), massive splenomegaly(1), intractable ascites(1), and portal/mesenteric thrombosis(2). Multidisciplinary evaluation preceded the decision to proceed to TIPS.

Results: Post-TIPS, all patients received ultrasound imaging to assess shunt patency. No patient had further GI bleeding, and all had decreased splenomegaly. One patient required shunt revisions secondary to stenosis; all other non-transplanted patients have remained with shunt patency. In two patients concern arose for shunt dysfunction, which was unsubstantiated upon further imaging. Two patients received liver transplantation following TIPS. There has been no evidence of encephalopathy.

Conclusion: By careful assessment of a patient’s clinical history and hepatic vascular anatomy, individualized treatment plans may be produced. Our experience with TIPS, in even young patients, has shown it to be an effective procedure in managing sequelae of PHTN in selected pediatric patients.

PANCREAS/CYSTIC FIBROSIS

130 SERUM AMINO ACID PROFILES IN CHILDREN WITH CF RECEIVING SUPPLEMENTAL CALORIES, FAT AND CHOLINE. Asim Maqbool1, J. Schall1, M. Mascarenhas1, M. Bennett1, N. Latham1, T. Wooden1, K. Dougherty1, V. Stallings1, 1GI, Hepatology & Nutrition, The Children’s Hospital of Philadelphia, Philadelphia, PA; 2Pathology & Laboratory Medicine, The Children’s Hospital of Philadelphia, Philadelphia, PA
Background: Children with CF are at risk for essential fatty acid & choline deficiency. Standard LFTs are used to follow liver disease, but do not provide a complete picture of hepatic protein metabolic status. The effects of supplemental calories, fat & choline on serum amino acid (AA) profiles in CF are not known. Objectives: To describe changes in AA profiles in children with CF & PI receiving 18 mo. of daily supplementation with LYM-X-SORB™ (LXS), an organized lipid matrix with choline and fatty acids v. a placebo with similar calorie & fat content, but 1/8th the choline. Methods: Subjects with CF & PI participated in a double-blinded RCT of LXS v placebo. Fasting branched chain (BCAA), aromatic (AAA) AA acids, LFTs & total protein(TP) were obtained at baseline, 3, 12 & 18 mo. Results: 49 subjects (20F,10.7±2.7y) completed 18 mo. of daily supplementation with LXS (n=22,10F) or placebo (n=27,10F). Combined group results are in the Table, as there were no differences between the 2 groups at baseline or over time. Compared to baseline, BCAA were significantly lower at 18 mo.; AAA were lower at both 12 &
18 mo. BCAA:AAA was higher at 12 mo. TP was higher at 18 mos. Other LFTs did not change over time or vary by group.

Conclusions: Supplementation with extra calories & fat for 18 mo. decreased serum AAA and improved BCAA:AAA in subjects with CF, suggesting improved hepatic protein metabolism. The additional choline did not result in further changes to the AA profile. Supported by NIDDK (R44DK060302), CTRC (UL1RR024134), the CHOP Nutrition Center and Avanti Polar Lipids, Inc.

Group Serum Amino Acid Profiles, μmol/L (n=49)

<table>
<thead>
<tr>
<th></th>
<th>baseline</th>
<th>3 mos.</th>
<th>12 mos.</th>
<th>18 mos.</th>
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<tbody>
<tr>
<td>BCAA</td>
<td>411±67</td>
<td>407±71</td>
<td>407±73</td>
<td>372±63‡</td>
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<tr>
<td>AAA</td>
<td>124±21</td>
<td>131±25</td>
<td>116±23†</td>
<td>110±23‡</td>
</tr>
<tr>
<td>BCAA:AAA</td>
<td>3.4±0.06</td>
<td>3.2±0.05†</td>
<td>3.6±0.07†</td>
<td>3.5±0.07</td>
</tr>
<tr>
<td>total protein, g/dL</td>
<td>7.2±0.7</td>
<td>7.3±0.7</td>
<td>7.4±0.6</td>
<td>7.4±0.6†</td>
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sig. different from baseline; ‡p<0.05; †p<0.01

131 NUTRITIONAL OUTCOMES FOLLOWING GASTROSTOMY IN CHILDREN WITH CYSTIC FIBROSIS.
Gia M. Bradley1, Kathryn A. Carson2, Amanda R. Leonard1, Peter J. Mogayzel1, Maria Oliva-Hemker1, 1Department of Pediatrics, Johns Hopkins University, Baltimore, MD; 2Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

In 2005 the CF Foundation recommended that children 2-20 yrs have BMI≥50%ile for age due to the association with improved pulmonary function and survival. Data also suggest that a faster rate of weight gain over 2 yrs may lead to better lung function.

Aim: To evaluate if children with CF and BMI<50% who receive gastrostomies (GTs) will reach BMI≥50% more quickly than those who do not.

Methods: We performed a retrospective cohort study of 20 CF children 2-20 yrs with GTs placed between Jan 2005 and Apr 2010. Each case was pair-matched using age, sex, pancreatic status, BMI and FEV1 with a child who did not have a GT. Outcome data included nutritional status and PFTs at 6 mo and 1 yr and time to BMI≥50%. Within-group changes were assessed by paired t-tests; groups were compared with McNemar’s test, two-sample t-tests and Kaplan-Meier survival analysis.

Results: Each group had 8 males and 12 females with pancreatic insufficiency. At the match, mean (±SD) age was 9.0±4.4 yrs for cases and 9.1±4.7 yrs for controls (p=0.54). Cases had a mean BMI Z-score of -1.19±0.60; controls had a value of -1.10±0.50 (p=0.10). Mean FEV1 % predicted for cases was 76.4±19.5% and for controls was 75.7±19.0% (p=0.90). One case had a surgical GT; the rest had percutaneous endoscopic GTs. Controls received oral supplements, appetite stimulants or no additional nutritional intervention. Cases had a significant 6-mo increase in mean BMI Z-score to -0.29±0.84 compared to -1.02±0.67 for controls (p<0.001). At 1 yr, the mean BMI Z-scores were less different at -0.41±0.76 for cases and -0.71±0.51 for controls (p=0.07). Both groups had stable lung function. Probability of reaching BMI≥50% at 6 mo was 36% for cases and 5% for controls; at 1 yr, it improved to 40% and 18% respectively. Conclusion: Our study suggests that children with CF who receive GTs achieve BMI≥50% more quickly than those who did not. Future studies should investigate the longer-term impact of GTs on growth and lung function.

132 CHRONIC PANCREATITIS WITH AUTOIMMUNE ORIGIN IN CHILDREN. Grzegorz Oracz, Bozena Cakrowska, Jaroslaw Kierkus, Maciej Dadalski, Jozef Ryzko, Jerzy Socha, Dep. of Gastroenterology, Hepatology and Immunology, The Children's Memorial Health Institute, Warsaw, Poland

Background: In the last decade we can observe gradual increase of autoimmune diseases. The reported paediatric experience with chronic pancreatitis (CP) is small and little is known about the role of autoimmune chronic pancreatitis (AICP).

Aim: The aim of the study was to assess the frequency of autoimmune markers in children with CP.

Patients and Methods: During 2000 to 2010, we hospitalized 66 children with CP (35 boys and 31 girls; age 2-18 years, mean age: 9.1 years). Clinical data were recorded and analyzed. Gammaglobulins, IgG4, autoantibodies (ANA, ASMA, AMA, APCA, LKM and AHA) were measured in all children.

Results: Autoimmune disease was present in 5 patients (7.6%): ulcerative colitis in 2 patients, PSC, dermatomiositis and panniculitis in 1 patient each. Hypergammaglobulinemia (>16g/l) was present in 14 cases. An increase of IgG4 level was present in 5 children. Autoantibodies were present in 38 children (57.6%). ANAs (>1/80e) were present in 18 patients with CP (in 6 pts >1/640e). ASMAs (>1/80e) were present in 21 children. APCRAs, AMAs, AHAs and LKM were absent in all patients. Combining clinical and biochemical autoimmune parameters, 41 patients (62.1%) had at least 1 autoimmune marker of the disease. In 20 patients (27.4%) with CP and autoimmune stigmata other known causative factors of CP were present. In 16 patients we found gene mutations predisposing to CP. There was no difference in the severity of the disease and clinical course between children with autoimmune stigmata and patients without autoimmune markers. 3 patients were treated with steroids with good clinical response.

Conclusions: In children with CP, similarly to adults, there is a high frequency of clinical and biochemical markers of autoimmunity. Number of CP with autoimmune origin in children is greatly underreported.

133* USE OF COMPUTER VISION TECHNOLOGY TO INTERPRET CLINICAL PAIN IN CHILDREN.
Jeanie Huang1, Gwen Littlewort2, Marian Barlett2, 1Pediatrics, University of California, San Diego (UCSD), San Diego, CA; 2Institute for Neural Computation, UCSD, La Jolla, CA

Background: Pain assessment in children is difficult owing to developmental and cognitive barriers and reliance on proxy measures (parent report). Information exists in the face for assessing pain; however, person-observers inadequately evaluate pain
in facial expressions. Computer vision techniques for automatic estimation of pain from facial expressions have now been demonstrated.

Methods: Four children (2 males, 2 females, 11-14 years) hospitalized for acute pancreatitis underwent multiple pain assessments with video recordings. At each session, subjects were video recorded during a rest period (no stimulus) and during a pain stimulus (abdominal exam), and subjects reported their pain level on a scale of 0-10. Representative video segments during the rest period and at the pain stimulus were passed through the Computer Expression Recognition Toolbox, a computer vision system for measuring facial expressions in real time. Nine facial actions associated with pain (PFA) were analyzed in comparison to self-reports of pain (SRP) within subject and between subjects. The 9 PFA measures were combined in a multiple regression model to jointly predict SRP. Cross-validation was employed to estimate model performance on data not used to estimate model parameters.

Results: Within-subject analysis demonstrated significant correlations \( r=0.77-0.97 \) between 6 of the 9 PFA and SRP. Analysis across subjects revealed significant correlations between 4 of the 9 PFA and SRP respectively for eye closure \( r=0.79, p<0.001 \), orbit tightening \( r=0.60, p<0.01 \), levator action \( r=0.56, p<0.01 \), and eyelid tightening \( r=0.34, p<0.05 \) respectively. In the regression model, the correlation between PFA and SRP was 0.71 (RMSE=2.6).

Conclusions: There is notable promise for use of computer vision technology to automatically assess pain severity in children. Further evaluation and study is required to determine whether such technology may be effectively used in the clinical setting for real time assessment of pain.

134 PANCREATIC DAMAGE IN A CYSTIC FIBROSIS PIG MODEL INVOLVES THE ACTIVATION OF PROINFLAMMATORY PATHWAYS. Matsam Abu el hajia1, Shyam Ramachandran2, David Meyerholz2, Marwa Abu-El-Hajia1, Michelle Griffin1, Radhamma Giriyappa1, Michael J. Welsh1, Paul McCray1, Aliye Uc2, 1Pediatrics, Uni of Iowa Hospitals and Clinics, Iowa City, IA; 2Pathology, Uni of Iowa Hospitals and Clinics, Iowa City, IA; 3Internal medicine, Uni of Iowa Hospitals and Clinics, Iowa City, IA

Background: Pancreatic disease in cystic fibrosis (CF) progresses over time to complete destruction of the organ. Mechanisms leading to pancreatic damage are not well understood. Hypothesis: Proinflammatory pathways are involved in the destruction of the pancreas in CF. Methods: We used microarray gene expression profiling to explore the differences between CF and non-CF pig pancreata of newborn and 90-day-old fetal pigs. Results were validated using qRT-PCR and immunohistochemistry (IHC).

Results: Microarray gene expression profiling of the newborn and CF fetal pig pancreas showed significant upregulation of proinflammatory, complement cascade and profibrotic pathways compared to non-CF. IL-8 and NFXB expression (qRT-PCR) were increased in the CF pig pancreas (48 and 1.5 fold increase in the fetus, \( p<0.001 \) and 0.05 respectively; 30 and 5 fold increase in the newborn, \( p<0.001 \)). Complement 3 (C3), C1Qb and complement factor B (CFB) were also upregulated in the CF pig pancreas (12, 8 and 12 fold increase in the fetus; 26, 31, 12 fold increase in the newborn, \( p<0.001 \)). Apoptotic cells were detected in the CF pig fetal and newborn pancreas (caspase-3, IHC). Involvement of the profibrotic pathways was demonstrated in fetal and newborn CF pig pancreas (alpha smooth muscle actin, IHC) and transforming growth factor beta1 (TGFβ1, qRT-PCR, 4 fold increase in the fetus, 9 fold increase in the newborn, \( p<0.001 \)). Duct cell proliferation (Ki-67, IHC) and mucous cell metaplasia (histology) were more readily detected in newborn pigs than fetuses with CF. Conclusions: Our findings suggest that pancreatic destruction in CF results from the activation of inflammatory pathways. Tissue remodeling and proliferation follow the destructive process. Manipulation of these pathways may alter the course of pancreatic disease in CF.

135 CLINICAL CHARACTERISTICS OF CHILDREN WITH RECURRENT ACUTE (RAP) OR CHRONIC PANCREATITIS (CP) WITH AND WITHOUT IDENTIFIED GENETIC MUTATIONS. Padade M. Vue1,2, Michael R. Narkewicz3,2, Peter DeWitt4, 1Pediatric GI, University of Colorado SOM, Aurora, CO; 2Pediatric GI, Children’s Hospital Colorado, Aurora, CO; 3Public Health, University of Colorado, Aurora, CO

Background: RAP and CP are rare in children. Among the various causes, mutations in cationic trypsinogen serine protease 1 (PRSS1), CFTR, and serine protease inhibitor Kazal type 1 (SPINK1) are potential etiologies.

Objectives: Describe the clinical features and outcomes of pediatric patients with RAP or CP who have mutations in PRSS1, CFTR and SPINK1 compared to those without mutations.

Patients and Methods: Retrospective chart review of all patients with RAP and CP from 1994 to 2011 who had testing for PRSS1, CFTR and SPINK1. We characterized clinical features and outcomes. Statistics: Comparisons between categorical values by Fisher’s exact test. Poisson regression, Polytomous Logistic regression or the Wald test for more complex analyses. Significance was a \( p<0.05 \).

Results: 26 subjects (12 male (46%), 10 Hispanic, 16 Caucasian) had RAP or CP and had testing. 11 (42%) had RAP and 15 (58%) patients had CP. 16 (62%) had at least one mutation (PRSS1 (4, 15.4%), CFTR (10, 38.5%) and SPINK1 (2, 7.7%)) and 10 (38%) had no mutation. Those with mutations were younger (mean age 6.9 ± 4.3 years) compared to those without mutations (12.3 ± 4.5 years, \( p = 0.009 \)). Children without mutations had a shorter time to intervention (ERCP or surgery). There were no significant differences in clinical symptoms, response to treatments, imaging abnormalities, or outcome. There was a trend to a positive family history in those with mutations. Patients without mutations underwent early ERCP and were less likely to be on antioxidants.

Conclusions: In a cohort of pediatric patients with RAP and CP, mutations in CFTR, SPINK1 or PRSS1 are present in about 2/3s. Patients with mutations were more likely to be younger and have a positive family history. Since clinical characteristics cannot reliably identify pediatric patients with mutations, all pediatric patients with RAP and CP without identified causes, should have testing for PRSS1, CFTR and SPINK1.
Fellow Research Award

143 JAG1 AND OSTEOGENESIS: CLINICAL IMPLICATIONS FOR ALAGILLE SYNDROME. Christina Bales1, Michael Dishowitz2, Erika Carr3, Lara Silvis4, Matthew Ryan5, Kurt Hankenson6, Kathleen Loomes4, 1 Div of GI, Hepatology & Nutr, Children’s Hosp of Philadelphia, Philadelphia, PA; 2 University of Pennsylvania School of Veterinary Medicine, Philadelphia, PA

Mutations in JAG1 cause Alagille Syndrome (AGS), which involves cholestasis and other congenital anomalies. Many AGS patients have skeletal abnormalities, including vertebral defects and pathologic fractures. Bone fragility is thought to result from cholestasis, leading physicians to consider liver transplantation for patients with severe fractures. An improved understanding of the relationship between JAG1 and skeletal fragility could alter the recommendations for transplant in these patients.

This study aimed to determine the effect of Jag1 mutation on skeletal development in two bone-specific conditional knockout mouse models. Jag1 was selectively ablated in the developing mouse skeleton by breeding Jag1-loxP mice with mice expressing Cre recombinase in osteoblasts (Jag1/Col2.3 model) and pre-osteoblasts (Jag1/Prx1 model). To evaluate differences in skeletogenesis, embryonic skeletons were stained with alizarin red and alcan blue and analyzed. To evaluate differences in bone ultrastructure and mineral density, micro-computed tomography (mCT) was performed on femurs from 8-week old mutant and control mice.

Skeletal stains of 17.5 dpc Jag1/Col2.3 embryos revealed butterfly vertebrae in 50% of the mutant mice (3/6) vs. none of the controls (0/9). In the mCT analysis, trabecular bone deficits were demonstrated in Jag1/Col2.3 male mice. Specifically, mutant mice had a decreased trabecular bone volume fraction (p = 0.01), number (p = 0.006), thickness (p = 0.04) and bone mineral density (p = 0.02). In contrast, significant cortical gains were demonstrated in Jag1/Prx1 mice. Mutant mice had an increased cortical bone volume fraction (p = 0.03), thickness (p < 0.01), and bone mineral content (p < 0.01).

Taken together, these results suggest that Jag1 plays a role in osteogenesis, which may have implications for the management of AGS patients with fragility fractures. Further studies are underway to explore the molecular mechanisms underlying these skeletal phenotypes.

Young Faculty Investigator Award

144 EPCAM DEFICIENT MICE SHOW SIGNIFICANT MORBIDITY AND PATHOLOGY RESEMBLING CONGENITAL TUFTING ENTEROPATHY. Mamata Sivagnanam, James Mueller, Carla Pena, Matthew McGeough, Hal Hoffman, Pediatrics, University of California, San Diego, San Diego, CA

Congenital tufting enteropathy (CTE) is an inherited intractable diarrhea of infancy presenting with chronic diarrhea. The diagnosis of CTE is made with the recognition of villous changes of the small intestinal epithelium including villous atrophy, crypt hyperplasia and focal epithelial tufts. We previously identified mutations in the gene for Epithelial Cell Adhesion molecule (EpCAM) in our CTE patients. mRNA from a subset of these patients has show splicing of exon 4. Additionally, significant decreases in protein levels of EpCAM have been seen by western blot and immunohistochemistry in intestinal tissue from CTE patients.

The objective of this project is to elucidate the role of EpCAM in intestinal development and function using in vivo model of intestinal epithelial cell function. We achieved this goal with a mutant EpCAM mouse model. Previous groups have shown EpCAM over-expressing mice or mice with absent expression. We have developed a novel mouse model with a deletion of exon 4 of EpCAM (as seen in some of our CTE patients). This is the first model to have decreased, but not absent, EpCAM expression. To confirm successful attenuation of EpCAM we have performed IHC to confirm decreased protein expression in mutant vs. wild-type mice. The mutant mice have shown significant morbidity and mortality. In most instances survival of the mutant mice is limited to 7 days or less. These mice are also noted to have have significant decreased weights as compared to their WT and HET littermates. Microscopic imaging of the small intestine and colon shows significant pathologic changes throughout the duodenum, jejunum and ileum in MUT mice. H&E staining reveals blunting of the intestinal villi, edema, crowding of enterocytes and tufted villi. HET and WT mice show normal histology. These findings are very similar to those in patients with CTE. This is the first murine model mimicking changes in EpCAM seen in CTE patients. This model will serve to further elucidate mechanism of CTE and potentially lead to improved therapeutic options.

CONCURRENT SESSION I – LIVER

10:30am – 12:00pm

145 SERUM MICRORNA IS A NOVEL BIOMARKER OF BILIARY ATRESIA. Adam M. Zahm, Nicholas J. Hand, Amber Horner, Joshua Friedman, Children’s Hospital of Philadelphia, Philadelphia, PA

Biliary atresia is a neonatal liver disease characterized by an inflammatory and fibrotic occlusion of the hepatic ductal system, culminating in cholestasis and jaundice. The only therapies are Kasai portoenteroscopy (KPE) and liver transplantation. Early diagnosis improves patient outcome following KPE. Diagnosing biliary atresia is a multi-step process involving serum biochemical testing, radionuclide scanning, liver biopsy, and intra-operative cholangiography. Novel biomarkers that facilitate an early diagnosis are likely to improve long-term patient outcome and reduce the need for transplantation.

MicroRNAs (miRNAs) are short nucleotides that decrease target mRNA stability and inhibit translation. Many disease states,
including liver fibrosis and inflammatory bowel disease, are associated with altered tissue miRNA expression profiles. Cell-free preparations of serum or plasma contain highly stable populations of miRNAs. Specific serum miRNA profiles have recently been associated with various conditions, including liver disease.

Here we describe a validation study using biliary atresia and cholestatic control serum samples (n=24 each) obtained from the Childhood Liver Disease Research and Education Network. TaqMan qRT-PCR was used to verify candidate BA-specific serum miRNAs. Of the 11 miRNAs chosen for validation, only miR-200b was significantly altered, with levels elevated over two-fold in the sera of biliary atresia subjects. The other members of the miR-200b-429 cluster, miR-200a and miR-429, were also significantly elevated in biliary atresia sera. Receiver operating characteristic (ROC) curves generated showed high area under the ROC curve (AUC) values, implying strong diagnostic potential. These observations overlap with results from an experimental mouse model of biliary atresia previously presented by our laboratory. These findings indicate that biliary atresia is associated with a distinct serum miRNA profile and indicate that serum miRNA should be explored as a non-invasive diagnostic biomarker for biliary atresia.

146 PERIPORTAL HEPATOCYTES RESPOND TO HIPPO SIGNALING. Dean Yimlamai1, Barry Evan1, Fernando Camargo2,3,1 Medicine, Children's Hospital Boston, Boston, MA; 2Stem Cell and Regenerative Biology, Harvard University, Cambridge, MA

Background: Liver growth and homeostasis is a carefully coordinated process. Liver injury initiates a set of processes that often restores the liver, although the specific details regarding activation of such a program is poorly understood. Recently, the Hippo Pathway was described as a means of regulating liver size. The Hippo Pathway is a conserved cascade of proteins, modulating the transcriptional transactivator Yap. Yap is primarily cytosolic when it is inactive, but translocates into the nucleus suppressing apoptosis and activating a cellular proliferation program. Prior studies in the liver modulating upstream Hippo signaling components commonly result in gradual liver growth. Cholangiocytes and hepatocytes both contribute to this overgrowth, but prior studies have not clearly delineated the contribution of either cell type to disease. In this study, we examine the effect of Hippo pathway activation by overexpressing Yap in hepatocytes in a time/spatially-restricted manner.

Results: Using a genetically modified Yap mouse model, transgene expression is induced by a combination of adenoviral cre recombinase and doxycycline administration. After administration of doxycycline, mouse liver to body weight ratios rapidly increased in size at 14 days (10.6%, n=2; control, 5.5%) and continued through 17 days (15.9%, n=2; control, 3.4 %) as compared to littermate controls not exposed to doxycycline. Liver histology shows massive proliferation as identified by Ki-67 staining, centered on perportal areas of the liver. To confirm this as a hepatocyte specific phenomenon, hepatocyte-specific adeno-associated Cre virus was given in a similar fashion followed by doxycycline administration. Similar perportal proliferation occurred suggesting these areas to be particularly sensitive to active Hippo signaling.

Summary: Periportal hepatocytes as compared to central venous hepatocytes are sensitive to Hippo pathway signal activation. Hepatocytes recently derived from liver stem cells may display increased sensitivity to Hippo pathway activation.

147 OMEGAVEN™ IN PEDIATRIC PNALD: FDA EXPERIENCE. John Troiani1, Nancy Snow1, Karyn Berry1, Kara Calkins1, Raluona Amarran1, Tara Varner1, Thomas Havranek4, John Kerner5, Simon Horslen1, William Walsh5, Andrew Mulberg5, 1FDA, Silver Spring, MD; 2Mattel Childrens Hospital, Los Angeles, CA; 3Palmetto Pedi Gastro, Columbia, SC; 4Cardinal Glennon Child Med Ctr, St. Louis, MO; 5Lucile Packard Childrens Hosp, Palo Alto, CA; 6Children Hospital, Seattle, WA; 7Monroe Carell Jr Childrens Hospital, Nashville, TN

Background: Omegaven™ is an I.V. fish oil lipid emulsion (omega-3 fatty acids) used to treat parenteral nutrition associated liver disease (PNALD). Although Omegaven™ is approved in Europe and Asia in adults as an adjunct to conventional lipid emulsions, it is not FDA-approved. In the U.S., it is available only through investigational new drug (IND) and emergency IND(eIND) applications in small cohorts and individual patients. Objective: To describe changes in direct bilirubin (dBili, mg/dL) before and after continuous Omegaven™ usage. Methods: 33 active INDs (9/1/04 to 3/31/10) provided 45 annual reports (ARs) for review. Most studies were at regional medical centers in patients ages 1-10 months. No eINDs were included. For ARs with individual patient data (6 active INDs), there were 46 patients with at least 2 direct bilirubin (dBili [mg/dL]) levels, whose data were pooled. Results: ARs were not received for all active INDs, and some reported only summary statistics. After a median Omegaven™ duration of 3 months (see table), mean dBili fell from 5.8 to 3.1 mg/dL (mean within-patient drop = 2.8 mg/dL). Overall, 63% of these 46 patients eventually achieved a dBili level <2.0. For safety, many ARs reported no adverse events. Deaths when reported were frequently sepsis-related (common in these patients). Conclusion: These data were uncontrolled, so the clinical importance of these results is not known. Multi-center controlled trials are needed to establish the effectiveness of Omegaven™ in pediatric PNALD.

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POSTER SESSION II
Friday, October 21, 2011
12:15pm – 2:15pm

CELLULAR/ MOLECULAR BIOLOGY

148 MEMBERS OF THE CORTICOTROPIN RELEASING HORMONE FAMILY OF NEUROPEPTIDES AND THEIR RECEPTORS ARE MEDIATORS OF INFLAMMATION IN ADIPOSE TISSUE DURING ACUTE COLITIS.
Christopher Finn1,2, Iordanis Karagiannidiss2, Charalabos Pothoulakis2,1Pediatric Gastroenterology, UCLA, Los Angeles, CA; 2Medicine - Inflammatory Bowel Disease Center, UCLA, Los Angeles, CA

Background and Aims: Whether adipose tissue is a participant or an innocent bystander in intestinal inflammation is still a matter of debate. Corticotropin releasing hormone (CRH), and its peptide family members the urocortins have been found to participate in intestinal inflammation. Recent evidence indicates that CRH receptors 1 and 2 are expressed by human adipocytes. Whether these ligands and receptors are modulated in the mesenteric fat during colitis has never been studied. Moreover, it is unknown if CRH signals adipocytes to release specific inflammatory cytokines. To test this hypothesis we examined expression of the CRH peptide family and their receptors at the mRNA levels in the mesenteric fat depots of mice during experimental colitis (TNBS). We also exposed human mesenteric preadipocytes in culture to CRH and measured changes in cytokine production at the mRNA and protein levels. Methods: Induction of acute colitis was performed in C57BL6 mice using a 48 hr exposure to TNBS. Mesenteric adipose tissue was harvested from the mice and mRNA was isolated for RT PCR. Human mesenteric preadipocytes were grown in culture and stimulated with CRH. Supernatant was collected for protein array and ELISA. From the cells, mRNA was isolated for use in RT PCR. Data were analyzed using a two tailed Mann Whitney test. Results: In the TNBS mouse model of acute colitis we found CRH, Unc2, and Unc2 were significantly increased by 112.9, 30.7, and 9.2 fold respectively. Protein array on CRH stimulated human mesenteric preadipocytes found elevations of TIMP-2 and Rantes (CCL5 gene product) and these elevations were confirmed by RT PCR. Conclusions: Adipose tissue is probably an active participant in colitis, we provide evidence that the CRH system modulates this inflammation. The elevation of TIMP-2 and Rantes in adipocyte supernatant suggests a mechanism.

149 ENTEROPATHOGENIC E. COLI AND S. FLEXNERI 2457T ADVERSELY AFFECT PARACELLULAR AND TRANSCELLULAR PERMEABILITY.
Jill Haper, Alessio Fasano, Mucosal Biology Research Center, University of Maryland School of Medicine, Baltimore, MD

EPEC and S. flexneri 2a cause a disproportionately high number of fatalities in children under the age of five. Several vaccine strains have been developed and tested but none has proven effective. Because vaccines against EPEC and S. flexneri are urgently needed, we are characterizing the pathogenic effects caused by wild type and potential vaccine strains of these pathogens in in vitro and ex vivo models. We used polarized T84 cells and Caco-2 cells to define the outcomes of infection. Strains 1204 and 1208 are derived from S. flexneri 2a strain 2457T; strain 1204 is a guanine auxotroph and 1208 is a mutant of 1204 lacking functional ShET1 and ShET2 enterotoxins as well as the mucinase pic. Although T84 and Caco-2 cells respond differently to the pathogens, the loss of ShET1 has a major impact on transepithelial electrical resistance (TEER), paracellular permeability, and cytokine and chemokine release after a three hour apical infection. Strain CVD206 is a mutant of EPEC 2348/69 lacking intimin, a necessary protein for the formation of attaching/effacing (A/E) lesions. A type three secretion system (T3SS) mutant of EPEC (EscN) was also tested. Inactivation of the T3SS of EPEC has a detrimental effect on the ability of EPEC to decrease TEER and increase paracellular permeability in T84 and Caco-2 cells, although the effects of CVD206 vary between the two cell lines. We reported in a previous study that EPEC 2457T increased short circuit current (i.e. transcellular secretory activity). Both the in vitro and ex vivo systems are effective means to study the mechanisms by which these pathogens change cellular permeability. Defining the proteins necessary for these effects will be essential to elucidating the mechanisms whereby these pathogens cause diarrhea and to developing effective vaccines against S. flexneri and EPEC.

150 DEFINING THE SECRETOGENIC PROTEINS OF S. FLEXNERI 2A IN AN EX VIVO MOUSE MODEL
Jill Haper1, Christina Faherty2, James Natario2, Alessio Fasano, Mucosal Biology Research Center, University of Maryland, School of Medicine, Baltimore, MD; 2University of Maryland, School of Medicine, Baltimore, MD; 3Center for Vaccine Development, University of Maryland, School of Medicine, Baltimore, MD

S. flexneri 2a is a major cause of infantile diarrhea in the developing world. As is the case with many diarrheal pathogens, S. flexneri 2a elaborates several toxins during the course of infection. We are currently defining the roles of these toxins, individually and in combination, in the induction of secretion in mouse tissues in the Ussing chamber system. Preliminary studies implicated both Shigella enterotoxin-1 (ShET1) and Shigella enterotoxin-2 (ShET2) as factors that increase short circuit current (Isc) in rabbit tissues in Ussing chambers. Several other known toxins are present in the genome including pic, SigA, and SepA that may influence secretion and the initiation of diarrhea. To characterize the changes in transcellular permeability and increased secretion we have developed a model in which toxin-containing supernatants are applied to mouse tissue in Ussing chambers. The change in short circuit current that occurs after the addition of supernatants is an indicator of the change in secretory activity of the tissue. Preliminary data implicates ShET1 and/or pic as major contributor(s) to secretion, as deletion of these genes greatly diminishes secretory activity. Removal of the virulence plasmid that encodes the type 3 secretion system (T3SS) as well as the T3SS effector ShET2 and the SPATE SepA decreases the short circuit current by 50% implicating factors encoded on this plasmid. Disruption of the type 3 secretion system (T3SS) also leads to a decrease in the short circuit current, although to a lesser
degree than removal of the entire plasmid, thereby specifically implicating at least one T3SS effector. Additional mutants are being generated and tested to identify a strain that is devoid of secretogenic activity. Defining the toxins that are responsible for increasing the secretory activity is crucial to elucidating the mechanism by which S. flexneri causes diarrhea.

151 THE ROLE OF RECIPROCAL REGULATION OF RETINOIC ACID AND ENDOTHELIN SIGNALING IN ENTERIC NEURAL PLEXUS MORPHOGENESIS, Jonathan M. Gisser1,2, Cheryl E. Gariepy3, Ting-Chung Suen1,4, Vadinvel Ganapathy1, Kim-Doan K. Nguyen1,2, Pediatrics, Division of Pediatric Gastroenterology, Georgia Health Sciences University, Augusta, GA; 2Biochemistry and Molecular Biology, Georgia Health Sciences University, Augusta, GA; 3The Center for Molecular and Human Genetics, The Research Institute at Nationwide Children's Hospital, Columbus, OH; 4The Department of Pediatrics, The Ohio State University, Columbus, OH

Background: Endothelin B receptor (EDNBR) signaling is critical for enteric nervous system (ENS) development. Although the EDNBR ligand, endothelin-3 (EDN3), inhibits neuronal differentiation, EDNBR-deficient ENS precursor cells (ENPCs) do not differentiate prematurely in vivo. This suggests that other factors modulate endothelin signaling. Since retinoic acid (RA) enhances the neuronal differentiation of ENPCs, we hypothesized that RA and EDNBR signaling interact to regulate ENPC differentiation. Methods: ENPCs, defined by P75 neurotrophin receptor expression, were immunomagnetically enriched from embryonic rat gut. Cells were then cultured for 14 days with RA and i) EDN3 (EDNBR agonist) or ii) BQ-788 (EDNBR antagonist). Neuronal and glial lineages were assessed by immunofluorescence microscopy, and expression of RA- and endothelin-related genes was quantified by RT-PCR. Results: RA in combination with the EDNBR antagonist induced the formation of an organized plexus punctuated by large neuron- and glia-containing ganglia interconnected by dense neurites. In contrast, cells cultured with RA and EDN3 differentiated but did not form an organized plexus. RA significantly upregulated the RNA expression of its own receptor (RARβ) and synthetic enzyme (RALDH2), and exogenous EDN3 suppressed this increase. RA also suppressed the expression of EDN3. Conclusions: We conclude that RA inhibits EDN3 expression while amplifying its own production and responsiveness, thereby creating a high RA/low EDN3 environment which favors differentiation and plexus formation. Conversely, adding EDN3 inhibits RA synthesis, creating a high EDN3/low RA environment which permits multilineage differentiation but inhibits plexus formation. Understanding the reciprocal relationship of EDNBR and RA signaling and its effects on ENPCs may yield critical insights for their therapeutic use in ENS deficits.

152 CHANGES IN ACTIN EXPRESSION INDUCED BY CHENODEOXYCHOLIC ACID IN ESOPHAGEAL EPITHELIAL CELLS, Ting-Chung Suen1, Vadinvel Ganapathy2, Kim-Doan K. Nguyen1, Pediatrics, Division of Pediatric Gastroenterology, Georgia Health Sciences University, Augusta, GA; 2Biochemistry and Molecular Biology, Georgia Health Sciences University, Augusta, GA

Background: Barrett’s esophagus (BE) is a pre-malignant condition that develops due to prolonged gastroesophageal reflux disease (GERD). Patients with GERD who develop BE have a higher prevalence of bile reflux. While studying the inflammatory response in HET-1A cells following bile acid exposure, we found that actin expression was affected by bile acids. AIMS: To assess how chenodeoxycholic acid (CDC) affects actin expression in esophageal epithelial cells. METHODS: HET-1A cells (normal human esophageal epithelial cells) were incubated with CDC 100-300 μM for up to 120 hrs at pH 7.4, then cell lysates and RNA were collected. Reverse transcription polymerase chain reaction (RT-PCR), real time RT-PCR, Western blot, and immunofluorescence microscopy (IF) were performed. Cell lines were also derived from HET-1A cells after at least 24 hr exposure to 300μM of CDC, where massive cell death occurred. The few surviving cells were allowed to grow in normal media without CDC, until a stable growing cell line was established, now designated as CD1. The same CDC kill-and-survive cycles were repeated on the CD1 line to obtain CD2, and successive generations. Actin expression may influence cell survival following CDC exposure. These findings suggest a potentially significant role of actin in the pathogenesis of BE.

153 P53 INDUCTION IN ESOPHAGEAL EPITHELIAL CELLS FOLLOWING EXPOSURE TO CHENODEOXYCHOLIC ACID, Ting-Chung Suen1, Vadinvel Ganapathy2, Kim-Doan K. Nguyen1, Pediatrics, Division of Pediatric Gastroenterology, GHSU, Augusta, GA; 2Biochemistry and Molecular Biology, GHSU, Augusta, GA

Background: Bile acids are implicated in the pathogenesis of Barrett’s esophagus (BE), a pre-malignant condition that develops due to prolonged gastroesophageal reflux disease (GERD). Point mutations of the p53 gene are detected during neoplastic progression of BE, and over-expression of p53 has been used to distinguish low-grade and high-grade dysplasia in BE. AIMS: To investigate the effect of chenodeoxycholic acid (CDC) on p53 expression in esophageal epithelial cells. METHODS: HET-1A cells (a normal human esophageal epithelial cell line) were incubated with various concentrations of CDC at pH 7.4. At various time points, both cell lysates and RNA were collected. Reverse transcription polymerase chain reaction (RT-PCR), real time RT-PCR, Western blot, and immunofluorescence microscopy (IF) were performed. Cell lines were also derived from HET-1A cells after at least 24 hrs exposure to 300μM of CDC, where massive cell death occurred. The few surviving cells were allowed to grow in normal media without CDC, until a stable growing cell line was established, now designated as CD1. The same CDC kill-and-survive cycles were repeated on the CD1 line to obtain CD2, and successive generations. The status of p53 in the CD series of cell lines was similarly studied. RESULTS: Exposure of HET-1A to CDC in normal pH media resulted in increased p53 expression, p53 induction was seen in CD1 and CD2 cells, and activated p53, as indicated by phosphorylation on Ser15, was observed to be persistent in CD3 and CD4 cells. CONCLUSIONS: Induction of p53 expression in HET-1A cells following CDC exposure is consistent with a response to cellular stress. The persistently activated p53 found in CD3 and CD4 cells is intriguing, as these cells were grown in the absence of CDC. Continuous development of the CD series of cell lines and...
their characterization will clarify the role of bile-acid induced transformation of esophageal squamous epithelial cells to Barrett’s epithelium.

154 POST-TRANSCRIPTIONAL CONTROLS IN GASTROINTESTINAL GENE EXPRESSION. Louis Ghanem1, Stephen Liebhaber2, 1The Children’s Hospital of Philadelphia, Philadelphia, PA; 2University of Pennsylvania, Philadelphia, PA

Post-transcriptional control of gene expression comprises a critical mechanism to modulate cell development and function in health and disease. While it is quite likely that these controls are important within the GI tract, this area has received minimal attention. Our laboratory studies the widely distributed RNA-binding proteins poly(C)-binding protein 1 (PCBP1) and poly(C)-binding protein 2 (PCBP2) and their effects upon nuclear transcript processing and cytoplasmic mRNA stability. Our studies have demonstrated that these proteins control and possibly coordinate multiple steps in expression of the human α-globin transcript in erythroid cells. As part of a broader exploration of PCBP1 and PCBP2 protein expression, we expanded our studies to the GI tract. We have demonstrated broad-based and abundant mucosal protein expression of both PCBP1 and PCBP2 throughout the murine GI tract including the esophagus, stomach, small and large intestines and pancreas. Within this landscape, our data revealed at least three unusual patterns of PCBP distribution: 1) compartmentalized expression in subsets of cells in the small bowel and gastric mucosa, 2) cytoplasmic to nuclear shifts during terminal differentiation along the crypt-to-villus axis, and 3) localized expression within the pancreatic islets. These findings uncover a remarkable and dynamic positioning of the PCBPs in the GI tract and suggest that these RNA-binding proteins may have selective and vital functions in gastrointestinal differentiation and physiology. Therefore, we hypothesize that PCBP1 and PCBP2 mediate important steps in post-transcriptional regulation of gene expression within the luminal GI tract and pancreas. We further propose that these controls coordinate the expression of multiple gene families according to the ‘RNA operon’ model. In our particular setting, this model predicts that coordinated expression of functionally related RNA transcripts containing C-rich elements is regulated by specific interactions with PCBP1 and PCBP2.

155 HELICOBACTER PYLORI-INDUCED IMPAIRMENT OF MUCOSAL BARRIER INTEGRITY: A HUMAN GASTRIC EPITHELIAL CELL MODEL. M. Fiorentino1, H. Ding2, T. Blanchard3, A. Fasano1, 1Mucosal Biology Research Center, University of Maryland, School of Medicine, Baltimore, MD; 2Department of Pediatrics, University of Maryland, School of Medicine, Baltimore, MD

Background: H. pylori infection is related to the development of diverse gastric pathologies, possibly by affecting epithelial junctional complexes that play critical roles in maintaining barrier function, cell polarity and intercellular adhesion. Using a gastric epithelial cell model, we have elucidated the effects of H. pylori infection on the epithelial barrier integrity.

Aim: To study the gastric mucosal biological effects triggered by wild-type H. pylori.

Methods: NCI-N87 gastric cell line was inoculated with wild-type H. pylori (strain 26695) to evaluate initial host-pathogen interactions and the effect of exposure and colonization of these strains on mucosal barrier function. Supernatants were collected for pro-inflammatory cytokines measurement.

Results: NCI-N87 cells are human gastric epithelial cells forming confluent monolayers and functional tight junctions. Co-culture with H. pylori caused a progressive decrease in TEER compared to uninfected control and filtered/heat killed bacteria treated monolayers. Cell viability was not altered by infection, suggesting that loss of barrier function was likely due to modulation of tight junctions. Immunohistochemistry on infected monolayers showed severe disruption with consequent mislocalization of ZO-1 and Claudin-1 proteins. Paracellular permeability assays showed a significantly increased net flux of FITC-labeled markers through the infected monolayer, showing that this increase in epithelial permeability can be accounted for a breakdown of the tight junction integrity.

Conclusion: NCI-N87 cell line provides an excellent and invaluable in vitro model to study the effects of H. pylori on the gastric mucosa barrier integrity. We have here determined that H. pylori dramatically alters gastric epithelial barrier function and that this impairment of barrier integrity occurs via modulation of tight junction cellular assembly and scaffolding.

156 INJECTION OF INTERFERON-GAMMA PROTEIN INTO DEVELOPING ZEBRAFISH LARVAE LEADS TO BILIARY DEFECTS. Shuang Cai, Megan M. Ross, Steven F. EauClaire, Randolph P. Matthews, Division of GI, Hepatology, and Nutrition, The Children’s Hospital of Philadelphia, Philadelphia, PA

Biliary atresia (BA) is a progressive fibro-inflammatory disorder of unclear etiology that occurs exclusively in infants. Others have demonstrated that interferon-gamma (IFNγ)-responsive genes are elevated in patients with BA, and that activation of IFNγ is critical for development of the mouse model of BA. We have demonstrated previously that patients with BA exhibit decreased DNA methylation of bile duct cells, and that inhibition of DNA methylation leads to elevation of IFNγ and to defects in biliary development in several zebrafish models. Here we report that DNA hypomethylation leads to a dramatic increase in expression of IFNγ pathway genes in zebrafish. Injection of IFNγ protein into developing zebrafish larvae produces defects similar to those observed after inhibition of DNA methylation, suggesting that activation of IFNγ is sufficient to produce defects in bile ducts in developing vertebrates. Notably, injection of IFNγ does not lead to the appearance of an inflammatory infiltrate. These results suggest that elevation of IFNγ negatively affects developing bile ducts, and our studies and others imply that this elevation may arise from multiple potential mechanisms. Our findings thus provide some insight into the pathogenesis of BA, suggesting that activation of IFNγ, arising from several potential etiologies, may be central.
157 A MUTATION IN THE INTS2 GENE LEADS TO SEVERE BILIARY DEFECTS IN ZEBRAFISH.
Steven F. EauClaire, Randolph P. Matthews, Division of GI, Hepatology, and Nutrition, The Children’s Hospital of Philadelphia, Philadelphia, PA
Genetic screens in zebrafish are a powerful tool to identify genes important in specific processes in an unbiased fashion. We have used the zebrafish to examine biliary development and disease, and have determined that the pathways and genes important in biliary development are well conserved between zebrafish and mammals. To screen for biliary mutants, we used the fluorescent reporter PED-6, which concentrates in the gallbladder in normal larvae. We found several families in which 25% of the larvae exhibited abnormal gallbladder PED-6 uptake. In one of these mutant families, rouen, we identified a mutation in the ints2 gene. Ints2 encodes a member of the integrator complex, an important component of RNA polymerase II that mediates the synthesis of small nuclear RNAs. The liver defects of rouen were striking, in that no biliary cells were evident and macrophages appeared to have taken up multiple cells. Little is known about cell-specific effects of the integrator complex, but here we demonstrate that genetic loss of an integrator complex gene leads to complete loss of biliary cells. These results identify a new gene family potentially important in biliary development and disease.

158 GLUTAMINE (GLN) AND ALANYL-GLUTAMINE (ALA-GLN) PROMOTE CRYPT EXPANSION, CRYPT-VILLOUS STRUCTURE, AND LG5+ STEM CELL ACTIVITY IN MOUSE SMALL INTESTINAL ORGANOIDS
Sean R. Moore, Jefferson Vallance, Noah F. Shroyer, Pediatrics, Gastroenterology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH
BACKGROUND & AIMS: Gln is a key fuel for the gastrointestinal (GI) epithelium, however its homeostatic mechanisms in the gut remain poorly understood. To test the hypothesis that GI stem cells (GISCs) regulate responses to Gln, we studied the effects of Gln and other non-essential amino acids in mouse small intestinal organoids.
METHODS: Jejunal crypts were harvested from wild type and Lgr5-EGFP mice and grown in culture using published methods (Sato et al. 2009 Nature 459:262-5). In Gln-supplemented media, organoids expanded to develop multiple crypt domains, with Lgr5-EGFP expressing GISCs. Organoids were then cultured in the presence or absence of iso-osmolar Gln, Ala-Gln, alanine, asparagine, glutamate, glutamine, glycine, or serine. In single- or double-crypt organoids, we measured new crypt formation. In multi-crypt organoids, we tested the effects of Gln deprivation on crypt morphology, Lgr5+ GISC activity, and epithelial proliferation (EdU incorporation) and apoptosis (cleaved caspase-3 expression).
RESULTS: In the presence of Gln or Ala-Gln, single- and double-crypt organoids exhibited a 2.6- to 3.1-fold increase in new crypts over 96 hours. In contrast, organoids cultured in other media showed a 1.1 to 2.0-fold crypt increase (p<0.001, 2-way RM ANOVA). In multi-crypt organoids, Gln deprivation led to reductions in proliferation and Lgr5, increased apoptosis, crypt atrophy, and eventual organoid collapse. Organoids maintained viable Lgr5+ GISCs for up to 7 days following Gln deprivation. Reintroduction of Gln or Ala-Gln increased Lgr5 expression at 24 hours and crypt recovery by 48 hours.
CONCLUSIONS: Gln and Ala-Gln support proliferation of Lgr5+ GISCs. The maintenance of Lgr5+ GISCs in the absence of proliferation, and the ability to stimulate crypt recovery after organoid collapse, suggest that Gln is an essential regulator of GISC activity. Further studies are needed to elucidate the mechanisms of these responses and their role in GI homeostasis.

159 CHARACTERIZATION OF HUMAN INTESTINAL STEM CELL (ISC) COMPARTMENT IN HEALTHY INDIVIDUALS AND CELIAC DISEASE PATIENTS. Stefania Senger, Alessio Fasano, Mucosal Biology Research Center, University of Maryland, School of Medicine, Baltimore, MD
Introduction: The epithelial lining of the intestine is characterized by its ability to continually turn over in a highly regulated fashion and rapidly renew itself after damage from injury. The intestinal epithelium is renewed by a population of intestinal stem/progenitor cells (ISCs), which give rise to all the intestinal epithelial cell lineages. Recent studies in mouse models support the hypothesis that the ISC compartment consists of two populations: the Lgr5+ stem cells, residing at the bottom of the crypts, representing the fast proliferating stem cells involved in maintaining the homeostasis of the intestinal epithelium and the label retaining stem cells (+4LRC), residing in position +4 of the crypts, representing a quiescent stem cell population that became active after injury or stress.
We aim to investigate the physiology of human intestinal stem cells and evaluate differences in the two stem cell compartments in normal and pathological conditions with particular regard to celiac disease (CD).
Results: Immunohistochemistry and immunofluorescence analysis of biopsies of healthy controls and patients affected by CD showed an increase in size of the Wnt responding, proliferating compartment (Transit Amplifying cells) We also assess alteration in Hedgehog, BMP4, Tgf-beta pathways, known to be involved in ISC activity.
Conclusions: Our preliminary data support the feasibility of generating an in vitro model system for intestinal epithelial diseases and support the hypothesis that the intestinal stem cell compartment homeostasis is altered in CD.

160 GENE ANALYSIS PROFILE OF INFLAMMATORY MEDIATORS AND ADHESIVE MOLECULES IN EOSINOPHILIC ESOPHAGITIS.
Solange M. Abdunour-Nakhoul, Nazih L. Nakhoul, Alexandra P. Eidelwein, Molly C. Hansen, Alex Gyftopoulos, Cathy Butcher, Noel Adams, Karen L. Brown, Youhanna Al-Tawil, Medicine, Tulane Medical School, New Orleans, LA; Pediatric Gastroenterology and Nutrition-GI for Kids, PLLC, East Tennessee Children’s Hospital, Knoxville, TN
Introduction: Eosinophilic esophagitis (EoE), a disease of allergic origin, causes eosinophil inflammation and does not respond to acid suppression therapy. Microscopic observation reveals massive eosinophil infiltration, remodeling of the epithelium and severe basal cells hyperplasia. Our aim is to investigate cellular & molecular factors involved in esophageal tissue damage and remodeling. Methods: We used real-time qPCR to study expression of two panels of genes in pinch biopsies obtained during routine endoscopy procedures in EoE & normal pediatric patients (NL). The first panel contains 84 genes involved in...
inflammatory response. The second contains 84 genes involved in extracellular matrix (ECM) structure, cell-to-cell communications & cell-matrix adhesion. We used cytokines & growth factors protein arrays and immunohistochemistry (IHC) to determine and localize specific proteins involved in the above pathways. Results: The inflammation gene array showed that eotaxin 3 & its receptor CCR3 are prominently upregulated (200 folds & 23 folds respectively). Interleukins (IL), IL13 & IL5 are upregulated by 10 & 4 folds respectively. In the ECM gene panel, CD44 & CD54, both hyaluronan binding molecules, & genes for ECM proteases (ADAMTS1 & MMP14) are upregulated significantly. Collagen genes (COL6A1 & COL15A1) are upregulated (3 folds), whereas COL14A1 is downregulated (2 folds). In EoE biopsies, a cytokine array showed an increase in epidermal & fibroblast growth factors and IHC experiments using an antibody to CD44 showed increase in staining. Conclusion: We have identified a number of novel genes whose expression is altered in EoE. Further investigating their role in inflammation and esophageal tissue damage could reveal the mechanisms of remodeling observed in the disease.

ESOPHAGUS/STOMACH

161 EOSINOPHILIC ESOPHAGITIS IN CHILDREN AND ADULTS: SAUDI EXPERIENCE. Abdulrahman A. Al-Hussaini1, Touqif Seaman2, Imad El Hag3, 1Pediatrics, King Fahad Medical City, Riyadh, Saudi Arabia; 2Medicine, King Saud Medical City, Riyadh, Saudi Arabia; 3Pathology, King Saud Medical City, Riyadh, Saudi Arabia.
Background: Despite the world wide distribution and reporting of eosinophilic esophagitis (EE) from different countries and ethnicities, however there are very rare reports from Arab countries. Whether the underreporting is due to true rarity of the disease or underrecognition remains to be determined.
Objective: To determine the clinical, laboratory, and endoscopic features of EE and response to therapy.
Methods: We identified patients diagnosed with EE in our centre from 2004 to 2011. EE was defined as esophageal mucosal infiltration with eosinophils count ≥ 20/HPF in biopsies obtained from distal, proximal, and midesophagus. Data were collected by retrospective chart review.
Results: Forty patients were diagnosed to have EE (32 males) with a median (range) age of 10.5 years (1-32 years). The presenting symptoms preceded the diagnosis of EE by median 12 months (2 - 72 months) and included: dysphagia (87.5%), weight loss (30%), meat impaction (25%), heart burn (20%), and vomiting (15%). Diagnosis of EE was made incidentally in 2 patients. Individual or family history of atopy was present in 95%. Peripheral blood eosinophilia was present in 50%. Esophageal endoscopic findings included: mucosal furrowing (95%), rings formation (37.5%), white specks (17.5%), linear ulcer (12.5%), stricture in 1 and normal appearance in 2 patients. Allergy testing (total IgE, RAST, skin prick test) was performed in 30%
Allergy testing guided dietary manipulation has been tried in 10 patients with complete response in 3 only. Thirty five patients received fluticasone inhaler (125 microgm/puff) 4 puffs twice a day for 2 months with complete response. Majority of patients experienced recurrence of symptoms of dysphagia in children and adults. Fluticasone inhaler is an effective therapeutic option, however symptoms tend to recur upon discontinuation of therapy.

162 CD3+CD69+ LYMPHO CYTES DISTIN GUISH EOSINOPHILIC ESOPHAGITIS FROM GERD. Ahmet Aybar1, Oral Alpan2, Thomas Blanchard1, Sergei P. Atamas3, Irina G. Lucinda1, 1Pediatrics, University of Maryland, Baltimore, MD; 2Section on Immunopathogenesis, O and O Alpan, Springfield, VA; 3Medicine, University of Maryland Medical Center, Baltimore, MD
Eosinophilic esophagitis (EoE) is an inflammatory disease of the esophagus characterized by mucosal eosinophilic infiltration. There is no universally accepted definition of EoE; all current definitions are histological, requiring mucosal eosinophilia above a certain threshold. The consensus diagnostic definition requires a combination of typical symptoms with finding of ≥ 15 eosinophils per high-powered field in maximally affected biopsy samples that were obtained while the patient was on maximal proton pump inhibitor therapy or with evidence of normal esophageal pH monitoring.
The presence of eosinophils in the esophagus, by itself, is not diagnostic of any particular etiology as it may also occur in real diseases or infections such as those caused by Candida species and herpes viruses. Our main objective was to find additional criteria that would allow for clearly separating EoE from GERD.
Fifty volunteers less than 21 years of age with established diagnoses of GERD (n = 16) or EoE (n = 22) were enrolled in this study. This cohort also included an age- and gender-matched control group (n = 12) in which patients who have undergone upper GI endoscopy mostly for abdominal pain and emesis and found to have normal esophageal histopathology. All specimens used were archived biopsy samples.
Biopsies were evaluated by immunohistochemistry for lymphocytic markers CD3, CD25, and CD69. There was a trend in higher presence of the early activation marker (CD25) in EoE, although this did not reach statistical significance when compared to GERD (p > 0.05). However, the presence of the very early activation marker (CD69) was strongly associated with the diagnosis of EoE (p < 0.01).
We postulate that CD69-positivity is an important diagnostic indicator in patients with esophageal mucosal eosinophilia, which increases diagnostic power of histological evaluation in such patients when a clear cut distinction is not present between GERD and EoE.
Compared to GERD cell lines, mRNA stability in EoE1 minimal increases in the GERD cell lines. The cytokine riboside (DRB). Resul...
expression and promoter transcriptional activity than in esophageal squamous cells from GERD patients. These observations suggest that the esophagus of EoE patients produces more eotaxin-3 in response to Th2 cytokine stimulation than that of GERD patients, and that these differences might underlie the degree of esophageal infiltration by eosinophils.

166 A NOVEL TEST FOR EOSINOPHILIC ESOPHAGITIS (EOE): THE ESOPHA GEAL STRING TEST (EST).

Glenn Furuta1,2, Amir F. Kagalwalla3, James Lee1, Sophie Fillon1,2, Wendy Moore1,2, Zhaoxing Pun1,2, Joanne Masterson1,2, Zachary Robinson2, Cheryl Frolkis2, Lindsay Hosford2, Shauna Schroeder1,2, Joe Raybai1,2, Sergei Ochkar1,2, Dan Atkins1,2, David Fleischer1,2, Katie Jacques4, Kelley Capocelli1,2, Brian Maybruck5, Caleb Kelley5, Steven J. Ackerman5,1

1Childrens Hospital Colorado, Aurora, CO; 2Pediatrics, Univ of Colorado School of Medicine, Aurora, CO; 3Pediatrics, National Jewish Health, Denver, CO; 4Biochemistry, Univ of Illinois Chicago, Chicago, IL; 5Biochemistry, Mayo Clinic Scottsdale, Phoenix, AZ; 6Pediatrics, Northwestern Univ; Children's Memorial Hospital, Chicago, IL; 7Pathology, Univ of Colorado School of Medicine, Aurora, CO

Background: We hypothesized that nylon strings from Enterotests™ could capture luminal mediators associated with EoE.

Methods: We measured eosinophil derived granule proteins (EDGPs) from EST samples and esophageal biopsy (EB) extracts obtained from children with active EoE, EoE in remission and controls with no inflammation. Eosinophil derived neurotoxin (EDN), eosinophil cationic protein (ECP) major basic protein (MBP1) and eosinophil peroxidase (EPX) were measured by ELISAs.

Results: ESTs and EBs were performed in 22 children (15 males, 11-17 years of age) with active EoE (n=6), EoE in remission (n=4), GERD (n=5) and normals (n=7). EDGPs measured in EST and EB samples correlated with peak eosinophils/hpf for MBP1 (EST: r=0.735, p<.001; EB r=0.808, p<.001), EDN (EST: r=0.758, p<.001; EB r=0.830, p<.001), ECP (EST: r=0.606, p<.01; EB r=0.908, p<.001). EST and EB EDGPs significantly correlated with mean eosinophils/HFP. EDGPs measured in EST vs. EB samples significantly correlated for MBP1 (r=0.621, p<.01) and ECP (r=0.436, p<.05). EDGP levels from EST samples were greater in active EoE compared to EoE in remission and normal controls (Active EoE vs. EoE remission vs. normal ng/ml respectively: EDN=3,372 vs. 803-p=0.109, vs. 577-p<.036; ECP=50,950 vs. 6,236-p=0.223, vs. 8,191-p=0.160; MBP1=16,029 vs. 6,304-p=0.111, vs. 5081-p<.036). EDGP levels in EST samples were greater in children with active EoE compared to GERD respectively, (EDN=3,372 vs. 964-p<.092; ECP=50,950 vs. 4,892-p=0.181; MBP1=16,029 vs. 2,237-p<.029).

Conclusions -ESTs can measure esophageal inflammation in children with EoE.

167 FAMILY FUNCTIONING AND PARENTAL DISTRESS IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS (EOE).

James P. Franciosi1, Kevin A. Hommel1, James W. Varni1, Alexandra Greenler1, J. P. Abonia1, Michael Eby1, Keith Marsolo1, Ron Bryson1, Sandeep K. Gupta1, Mary D. Klinnert1, Jonathan M. Spergel1, Glenn T. Furuta1, Marc E. Rothenberg1, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 2Texas A&M University, College Station, TX; 3Riley Hospital for Children, Indianapolis, IN; 4University of Colorado, Denver, CO; 5The Children's Hospital of Philadelphia, Philadelphia, PA; 6The Children’s Hospital, Denver, CO

Introduction: The aim of this study was to characterize the impact of pediatric EoE on family functioning and parental distress.

Methods: We conducted a multi-site internet based cohort study via the Registry for Eosinophilic Gastrointestinal Disorders (www.regid.org portal). Validated questionnaires administered included: the BSI-18 (parental psychologic distress), patient and parent proxy Pediatric EoE Symptom Severity (PEESS v2.0) metrics and PedsQL (Core, EoE Module, and Family Impact Module).

Results: 100 children (40 toddlers (T) age 2-4, 23 young children (YC) age 5-7, 19 children (C) age 8-12 and 18 teens (TE) age 13-18) and 97 parents (90.7% mothers) were enrolled. PedsQL Family Impact was significantly worse among T vs either TE or C (p<0.05), but not between T vs YC. Worse BSI-18 correlated with worse Family Impact scores (r=0.79, p<0.0001). Severe Family Impact scores correlated with parental PEESS v2.0 (r=0.51, p<0.0001), PedsQL parental EoE (r=0.51, p<0.0001), child EoE (r=0.38, p<0.005), parental Core (r=0.57, p<0.0001), child Core (r=0.57, p<0.0001), but not child PEESS v2.0 (r=0.1, p=0.5). PedsQL Family Impact total was significantly different across dietary subgroups and deteriorated with more severe dietary restrictions (no restrictions (n=6) mean 88.1 (range 75.0-98.6); elimination diet (n=47) mean 68.7 (range 30.5-93.8); and use of elemental formula (n=30) mean 51.0 (range 15.3-88.9), p<0.0001.

Conclusions: EoE Family distress is significantly worse in toddlers, is worse with more severe dietary restrictions, and family dysfunction related to EoE is concomitant with adverse parental psychological distress. These findings have substantial implications for EoE patients and those who care for them.

168 SUCCESSFUL DIETARY THERAPY FOR EOSINOPHILIC ESOPHAGITIS BASED ON SKIN PRICK AND ATOPY PATCH TESTING.

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Objectives: Skin prick tests (SPT) and atopy patch tests (APT) were first reported as a method to guide dietary elimination in patients with eosinophilic esophagitis (EoE) by Spergel et al. Yet, this method has not been widely adopted, in part because the data has yet to be replicated outside of his institution. We report our experience implementing a food elimination diet in children with EoE, guided by SPT and APT performed in a community setting.

Methods: Review of pediatric patients with EoE diagnosed between 2007 and 2011 who underwent elimination diet based on SPT and APT performed in one of two private allergy practices, followed by repeat biopsy. Patients with less than 15 eosinophils per most-involved microscopic high-powered field (Eos/HPF) on follow-up biopsy were considered to be responders, while those with 5 or fewer Eos/HPF were considered to be in remission.
Results: Of 62 patients (age 1 to 17 years) who underwent dietary therapy followed by biopsy, 43 (69%) were responders, with 36 (58%) achieving remission. The mean number of Eos/HPF among all responders dropped from 37 before diet to 3 after. The mean Eos/HPF among those in remission dropped from 34 before diet to 1 after. Excluding those in remission, responders still had a reduction in peak Eos/HPF of 77% from before to after diet. Mean Eos/HPF among non-responders dropped from 59 to 46. Conclusion: This is the 2nd largest cohort evaluating dietary therapy in children with EoE. It confirms the importance of food allergy in the pathogenesis of EoE and that allergy testing using SPT and APT is an effective method for identifying the responsible food antigens. We are the first to demonstrate SPT and APT can be performed accurately in a community setting and argue that directed dietary elimination should be more widely used for children with EoE.


Objective: Evaluate the safety of reslizumab in an ongoing open-label extension study of children and adolescents with EoE who had participated in a double-blind, placebo-controlled study. Methods: Patients with histological and clinical evidence of EoE were randomly assigned to infusions of reslizumab 1, 2, or 3 mg/kg or placebo every 4 wks for 12 wks. Patients who had not withdrawn because of a study drug-related adverse event were eligible for the open-label extension. All patients initially received 1 mg/kg reslizumab every 4 wks. At wk 8, doses could have been increased to 2 mg/kg at the investigator’s discretion or to 3 mg/kg with permission from the sponsor. We summarized adverse events that were recorded in the open-label extension as of 13 Jan 2011. Results: 190 patients entered the extension. 51 patients discontinued the study: adverse events (7), lack of efficacy (21), protocol deviations (3), lost to follow-up (5), and other reasons (15 patients). 100%, 81%, and 36% of patients received ≥1 infusion of 1, 2, and 3 mg/kg, respectively, while 44%, 59%, and 32% of patients received ≥2 infusions, and 4%, 9%, and 3% received ≥24 infusions. The most common adverse events were headache (24%), upper respiratory tract infection (18%), influenza (17%), and sinusitis (16%), most of which resolved. 20 patients had serious adverse events, none of which occurred in more than 2 patients. No serious adverse events were considered by the investigators to be related to study medication. Conclusion: Reslizumab was generally well tolerated in this open-label extension study of pediatric patients with EoE.

170 TOLL LIKE RECEPTOR-3 SIGNALING ENHANCES EOSINOPHIL ADHESION TO HUMAN ESOPHAGEAL EPITHELIAL CELLS IN VITRO. Prasanna Modayur Chandraomalueswaram, Diana M. Lim, Ish Mehta, Mei-Lun Wang

Division of GI and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA

Background and Aims: Eosinophilic esophagitis (EoE) is an allergic disease characterized by the infiltration of eosinophils into the esophageal epithelium. Very little is known about the mechanisms responsible for eosinophil-epithelial adhesion. Others have previously shown that epithelial ICAM-1 plays a role in epithelial-eosinophil interactions in other models of allergic disease, including asthma. We have shown that Toll-like receptor 3 (TLR3) is the most highly expressed and functional TLR in the esophageal epithelium, and that stimulation of the immortalized nontransformed human esophageal epithelial cell line EPC2-hTERT with the synthetic TLR3 ligand, poly(I:C), induces the expression of many pro-inflammatory cytokines and adhesion molecules relevant to eosinophils. In this study, we investigated the role of esophageal epithelial TLR3 signaling in eosinophil-epithelial adhesion in vitro. Results: Poly(I:C) stimulation of EPC2-hTERT cells led to inducible ICAM-1 expression, an effect which was partially suppressed in TLR3 siRNA transfected cells. To determine the role of TLR3 activation in mediating esophageal epithelial-eosinophil interactions, we generated a DN-TLR3 cell line in which the overexpressed TLR3 lacks the TIR-signaling domain. In vitro adhesion assays were used to investigate interactions between the DN-TLR3 cell lines and the HL-60 clone 15 eosinophil-like cell line. Esophageal epithelial poly(I:C) stimulation enhanced HL-60 eosinophil adhesion in vitro, compared to unstimulated epithelial controls. Activation of HL-60 eosinophils with GM-CSF, but not IL-5, enhanced eosinophil-epithelial adhesion. Importantly, poly(I:C)-mediated esophageal-epithelial adhesion was reduced in hTERT-ΔTIR-TLR3 cells compared to control cell lines. Conclusions: Our results suggest a role for esophageal epithelial TLR3 signaling in epithelial-eosinophil adhesion, which may have implications for the pathogenesis of EoE.

171 INCREASED CD3+ CELLS IN THE ESOPHAGEAL TISSUE OF EOSINOPHILIC ESOPHAGITIS. Minou Le-Carlsen, Scott Seki, Kenneth Cox, Kari Nadeau, Pediatrics, Stanford University Medical Center, Palo Alto, CA

Background and Aims: Eosinophilic esophagitis (EoE) is a gastrointestinal disorder that is increasing in incidence and prevalence. Several lines of evidence suggest an interplay between T cell and eosinophil populations in the pathogenesis of disease. The studies in human histopathology on endoscopic biopsies of the esophagus determining the relative extent of eosinophil and activated T cell infiltration have been limited. Therefore, we investigated the numbers of activated (CD69+) CD3+ T-cells associated with the presence of eosinophils (EG2+ cells) in the esophageal biopsies of patients with EoE and compared these findings with healthy controls. Methods: We evaluated the esophageal tissues of healthy controls (HC, n=3) and patients with eosinophilic esophagitis (EoE, n=5) via standard immunohistochemistry (IHC) techniques. Biopsies were co-stained with antibodies for CD3 (Vector Laboratories, Burlingame, CA) and EG2 (gift of Dr. Raggam Reinhard, Medical University of Graz, Austria). Stained cells were counted per high-power field (HPF, 400x) at 3 different sites with the mean count per HPF used. Statistical analysis was performed with GraphPad Prism software.
Findings: There was an increase in CD3+ T cells in patients with EoE versus healthy controls. The number of CD3+ cells was significantly higher in EoE patients (mean 15.8) versus HC (mean 7), (P=0.02). The number of CD3+/CD 69+ cells was also elevated in EoE patients in comparison to HC.

Conclusions: We demonstrate that the number of activated CD3+ T cells is higher in patients with EoE versus HC. Continuing studies are underway to analyze co expression of the IL-5 Receptor and CD69 in the T cells in EoE patients. This data provides further evidence that activated T cells could play an important role in the pathogenesis of EoE.

172 USEFULLNESS OF ALLERGY PATCH TESTING IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS
Eosinophilic esophagitis (EoE) is thought to be mediated by IgE and non-IgE dependent mechanisms. For that reason, skin prick testing (SPT, identifies IgE mediated food allergies) and allergy patch testing (APT, assesses delayed food hypersensitivity) have been used to identify foods that trigger EoE. The relative contribution of these different tests has not been examined. We examined the ability of APT to identify foods that cause EoE. During a 7-month period, patients diagnosed with EoE underwent APT. Dietary avoidance based on APT was recommended. Follow-up endoscopy was performed and 3 biopsies obtained from the middle and distal esophagus after at least 2 months of exclusion diet. We calculated the rate of successful dietary exclusion based on APT (less than 5 eosinophils/hpf on follow-up biopsies and symptoms resolved ) and compared ‘responders’ with ‘non-responders’. 43 new patients with EoE, were evaluated between June 2010 and Jan 2011: 4 had negative APT, 3 had technical problems with APT; 1 could not follow diet; 11 had other interventions (elemental diet, 5; medications, 3; several interventions, 3); 6 did not follow-up. The remaining 16 patients (12 male) were placed on an exclusion diet based on APT. Average age was 7.7 yrs (2.5-14.5 yrs). Patients had an average (SD) 6.4 (2.6), (range 2-11) foods positive on APT. The most common foods found were wheat (9), barley, beef, turkey (8), eggs (7). 6/16 patients (37.5%) responded to removal of foods. Responders were younger (mean, SD 5.2, 2.0 vs 9.3, 3.7 yrs; p=0.02) but had comparable number of food allergies (6.0.1.58 vs 7.0.24; p=.39). APT alone allows identification of offending foods in EoE in a minority of patients. The younger age of responders is consistent with the observation that younger children with EoE respond better to dietary interventions than adolescents and adults.

173 ESOPHAGEAL BARIUM TABLET IMPACTION: A NOVEL NON-INVASIVE DIAGNOSTIC TEST FOR EOSINOPHILIC ESOPHAGITIS. Peter Ngo1, Edward Lee1, Roy McCauley2, Donald Tracy3, Alejandro Flores4
1Ped. GI, Floating Hospital for Children at Tufts Medical Center, Boston, MA; 2Ped. Radiology, Floating Hospital for Children, Boston, MA; 3Radiology, Children’s Hospital Boston, Boston, MA
Eosinophilic Esophagitis (EoE) often presents with dysphagia or food impaction without anatomic abnormalities on fluoroscopic studies such as upper GI. Pill impactions have also been described in EoE in the absence of radiographic abnormalities. We hypothesized that use of a 13 mm dissolvable barium tablet following liquid contrast during fluoroscopic studies may improve detection of EoE. Methods: We reviewed the medical records of patients aged 7-25 years from 2005-2010 who had fluoroscopic studies including use of a barium tablet. Younger children often received a fraction of a tablet. Reports of barium tablet impaction or stasis (BTI) within the esophagus without fixed anatomic abnormality (i.e fundoplication, TEF, or stricture) were correlated with diagnosis of EoE. Results: 111 patients swallowed a barium tablet. 15 patients had BTI. 34 of the 111 patients had complete histologic and clinical data to confirm or disprove EoE. Among the 15 patients with BTI, 8 were diagnosed with EoE (4 prior, 4 subsequent to BTI), 4 were non-EoE and 3 had incomplete EoE evaluations. Among 96 patients without BTI, 2 had EoE, 20 were non-EoE, and the remaining 74 had incomplete EoE evaluations. Among the 34 patients with confirmed or disproved EoE, BTI was more frequent in patients with EoE 8/10 (80%) than non-EoE 4/24 (16.7%) p=0.0004. Sensitivity and specificity of BTI in identifying EoE were 80% and 83%, respectively. Among all patients, incidence of BTI in males: 26% (14/54) was significantly higher than in females: 2% (1/57), p=0.002. There were no complications with use of a barium tablet. Tablet stasis or impaction was transient and cleared during the study or on follow up. Conclusion: Use of a barium tablet in young patients is a safe fluoroscopic technique. BTI is strongly associated with both EoE and male gender. To confirm safety and efficacy of this technique, we are conducting a prospective study of barium tablet use in young patient.

174 CORRELATION AMONG CLINICAL SYMPTOMS, ENDOSCOPIC FINDINGS, AND HISTOPATHOLOGIC FINDINGS IN PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS. Ricardo Arbizu, Karen D. Crissinger University of South Alabama, Mobile, AL
Eosinophilic esophagitis (EoE) is an increasingly recognized entity in children with a variety of non-specific presenting symptoms. EGD features include esophagitis, vertical furrowing (VF), microabscesses, and trachealization. Esophageal biopsies show >15 eosinophils per high power field (eos/hpf). An effective treatment regimen is an elemental diet, but it has the disadvantage of poor patient compliance. Topical steroids have also been used for treatment. The purpose of this study was to examine the correlation among clinical symptoms, endoscopic and histopathologic findings in pediatric patients with EoE and to determine whether symptoms may be predictive of endoscopic and/or histologic findings.

Methods: Retrospective chart review (2002-2010).

Results: Of the 108 cases reviewed, 79% were male. The median age of presentation was 7.8 years. Presenting symptoms were vomiting (20%), abdominal pain (18%), regurgitation (11%), dysphagia (10%), and food impaction (9%). Asthma was reported in 33%, food allergy in 34%, and eczema in 26% of the cases. Patients were divided into 2 groups based on total eos/hpf on initial biopsy (15-30 eos/hpf, n=53; >30 eos/hpf, n=55). Eleven symptoms showed no correlation with eos/hpf in either group (p=0.9). VF (55%) was the most common endoscopic finding, which correlated with the eos/hpf (39.1±3.2; p=0.03). Follow-up
in 106 patients showed 81% compliance with treatment and 76% had symptom improvement. Treatment included topical steroids (23%), elemental diet (3%), or both (74%). Forty-five patients underwent a repeat EGD with a median elapsed period of 10.7 months. The mean eos/hpf was significantly reduced in this group (32.3±2.5 to 19.9±4.2; p=0.005).

Conclusions: Vomiting, abdominal pain, and regurgitation were the most common initial complaints. There is no correlation between the number or type of symptoms and eos/hpf at presentation. VF is a characteristic finding in this population. Compliant patients showed a significant reduction of eos/hpf at repeat EGD. Combination treatment is an effective regimen for EoE.

175* CHARCOT-LEYDEN CRYSTAL PROTEIN/GALECTIN-10: A NOVEL DISEASE-SPECIFIC BIOMARKER OF ACTIVE EOSINOPHILIC ESOPHAGITIS AS MEASURED BY THE ESOPHAGEAL STRING TEST.
Tarek Jazaerly1, Amir Kaghalwalla1, Brian Meybruck1, Preeth Alumkal1, Sophie Fillon1, Joanne Masterson1, Zachary Robinson1, Lindsay Hosford2, Shauna Schroeder2, Glenn Furuta2, 1University of Illinois at Chicago, Chicago, IL; 2Children’s Hospital Colorado, Denver, CO; 3Children’s Memorial Hospital, Chicago, IL.

Endoscopic esophageal histology is currently the only method to assess mucosal inflammation in Eosinophilic Esophagitis (EoE). We have reported that a minimally invasive Enterostest-based Esophageal String Test (EST) captures eosinophil granule proteins in children with EoE, distinguishing between active disease, remission, GERD and normal esophagus. Eosinophils express large amounts of Charcot-Leyden Crystal (CLC) protein/Galectin-10 (CLC/Gal-10), which is upregulated (~20-fold) in the EoE transcriptome. We hypothesized that in EoE: (1) the EST could be used to capture CLC/Gal-10 in the esophageal lumen, and (2) CLC/Gal-10 would be a biomarker that could be used to monitor disease activity during treatment. ESTs were performed in 42 children, removed at endoscopy and esophageal string segment identified by pH or endoscopic measurements. CLC/Gal-10 was measured using a lab-based ELISA in eluates from the strings, and in extracts of biopsies, obtained from children with active EoE (≥15 eos/HPF), treated EoE (<15 eos/HPF), GERD and normal esophagus. CLC/Gal-10 in EST samples from children with active EoE was significantly higher than EoE in remission, GERD and normal esophagus (Table 1). CLC/Gal-10 levels in both EST and biopsy samples were correlated with peak and mean eosinophils/HPF.

Summary: The EST captures CLC/Gal-10 in the esophagus of children with active EoE. Conclusion: EST measurement of CLC/Gal-10 may serve as a minimally invasive surrogate for endoscopy with biopsy to follow disease activity in EoE.

Table 1 - CLC/Gal-10 in String Tests vs. Biopsies

<table>
<thead>
<tr>
<th>Patient Group</th>
<th># of subjects</th>
<th>CLC/Gal-10 (ng/ml)*</th>
<th>p-value</th>
<th>CLC/Gal-10 (ng/mg protein)**</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EoE (active)</td>
<td>14</td>
<td>3,583 ± 990</td>
<td></td>
<td>23,840 ± 12,305</td>
<td></td>
</tr>
<tr>
<td>EoE (treated)</td>
<td>8</td>
<td>472 ± 209</td>
<td>0.003</td>
<td>2,457 ± 1,471</td>
<td>0.082</td>
</tr>
<tr>
<td>GERD</td>
<td>5</td>
<td>400 ± 27</td>
<td>0.008</td>
<td>1,985 ± 635</td>
<td>0.129</td>
</tr>
<tr>
<td>Normal control</td>
<td>15</td>
<td>80 ± 20</td>
<td>0.0001</td>
<td>150 ± 43</td>
<td>0.023</td>
</tr>
</tbody>
</table>

*mean ± SEM; **normalized to total extracted protein

176 EOSINOPHILIC ESOPHAGITIS - REVISITING EOSINOPHILIC COUNTING IN ESOPHAGEAL BIOPSIES.
Tarek Jazaerly1, Khaleed Bittar2, Yasir Hussein1, Hayan Jaratli1, Janet Poulak1, Vinod Shidham1, 1Pathology, WSU/DMC, Detroit, MI; 2Pediatrics, WSU/DMC, Detroit, MI

Background: Eosinophilic esophagitis (EE) is a clinicopathologic syndrome characterized by intraepithelial eosinophilic infiltration. The criteria from American Gastroenterological Association requires at least 15 intraepithelial eosinophils/high power field (HPF) in the appropriate clinical settings. However, in practice the small fragments of esophageal biopsies (EB) may not fill the whole HPF area. In addition, the focal nature of eosinophil infiltration adds further variation. The counting practice is not standardized to address this variability, which may lead to overlapping misinterpretation as GastroEsophageal Reflux Disease (GERD). The aim of our study is to explore different ways to evaluate intraepithelial eosinophil count (EC) in EE for improved objectivity and prevention of overlapping misinterpretation as GERD.

Design: Thirty one EB from 20 patients interpreted as EE and 21 EB from 20 patients interpreted as GERD were compared. Clinicopathologic correlation confirmed diagnosis in all EE cases. EC was performed in the areas with highest count. The squamous epithelial cells (SEC) were also counted in the field to compare with EC. The area in the HPF not occupied by the mucosa was corrected in order to fill the entire field with appropriate correction for EC and SEC numbers.

Result: See table

Conclusion: EC per HPF in EE is usually higher than GERD. EC in comparison to SEC can be evaluated easily in smaller biopsies. One or more eosinophils for 15 SEC in worst area is consistent with EE (in contrast to less than 1 EC for 100 SEC) in appropriate clinical setting. Prospective multi-institutional clinico-pathologic study is recommended to formalize the approach.
CONCLUSION:

DUODENAL WINDSOCK: A rare finding of duodenal windsock diverticulum was made by CE when abdominal CT suggested patients had IBD and 8 patients had celiac disease.

POLYPS: Seventeen patients were found to have polyps studies, small bowel findings were seen. Two patients were found to have isolated small bowel disease.

INFLAMMATORY BOWEL DISEASE: Fifty-eight patients had IBD. One patient was subsequently diagnosed with Polyposis coli. Two patients had FAP. Three patients had BD and 8 patients had celiac disease.

CELIAC DISEASE: Twenty nine children with elevated TTG levels were examined by CE. A novel finding of proximal small bowel polyps was found in 7 patients (24%). One patient was subsequently diagnosed with Bannayan-Riley-Ruvalcaba syndrome.

RESULTS: 288 CE procedures were performed. Indications for CE included suspected Crohn’s disease, anemia, abdominal pain, polyposis syndrome, celiac disease, and GI bleeding. The majority (263) of capsules were placed using the capsule delivery technique. In 25(8.68%) patients, the capsule could not be placed using the standard technique, and a novel technique was developed using laryngoscopic assistance. By this method, 24 of these 25 patients had successful capsule placement. There were no complications. Sometimes, capsule placement in children was difficult, particularly in boys over the age of 10. Conservative treatment has a good outcome of esophageal perforation in EoE patients.

Conclusion: Eosinophilic esophagitis should be considered in the differential diagnosis of spontaneous esophageal perforation, particularly in boys over the age of 10. Conservative treatment has a good outcome of esophageal perforation in EoE patients. Endoscopy with biopsy is recommended, once it’s safe to do, to delineate the etiology.

### 177 SPONTANEOUS ESOPHAGEAL PERFORATION: IS IT EOSINOPHILIC ESOPHAGITIS OR IDIOPATHIC?

TS Gunasekaran1, J. Berman2, H. Hernandez3, E. Garcia-Alvarez3, K. Gorla1,2, S. Weides1, Pediatrics, Lutheran General Children's Hospital, Park Ridge, IL; 2Pediatrics, Loyola University Medical Center, Maywood, IL; 3Pediatrics, University of Illinois, Chicago, IL.

Spontaneous esophageal perforation is uncommon in children. We report three children who had spontaneous esophageal perforation, two with classic eosinophilic esophagitis (EoE) and one with no clear cause. All perforations sealed with conservative treatment.

Age: 10-15 years, all boys.

Symptoms: Chest pain, breathlessness and vomiting. One patient had a mediastinal abscess. Prior to the perforation patients had no symptoms to suggest GERD or EoE or only had mild dysphagia.

An all three patients were treated with NPO, antibiotics. PPI and TPN. Esophageal perforation and the abscess healed in 3-4 weeks. Subsequent endoscopy showed: patients #1 and #2 had EoE; vertical lines and white spots, and a diverticulum at mid esophagus (Pt1). Biopsies of both showed 30-20 eosinophils/HPF, eosinophilic abscess, and increase in basal layer. Patient #3 had a normal endoscopy, but the biopsies showed 3-5 eosinophils/HPF, both in the distal and mid esophagus. Patients #1 and #2 were treated with fluticasone. For patient #3 all treatments were stopped once endoscopy was done. Follow up to 10 months showed no recurrence of perforation in all patients and histology in patient #1 showed eosinophils increase up to 50/HPF. Growth was normal.

Conclusion: Eosinophilic esophagitis should be considered in the differential diagnosis of spontaneous esophageal perforation, particularly in boys over the age of 10. Conservative treatment has a good outcome of esophageal perforation in EoE patients. Endoscopy with biopsy is recommended, once it’s safe to do, to delineate the etiology.

### 188 PEDIATRIC CAPSULE ENDOSCOPY

Stephen Nanton1, Philip Rosenthal2, Pediatrics, Avera Childrens, Sioux Falls, SD; 2Pediatrics, University of California, San Francisco, CA.

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

SUBJECTS: We studied 258 consecutive children referred for CE. Mean age 13 years (range 2.5 to 21.5 years). The weight of the smallest child was 14.6 kg.

RESULTS: 288 CE procedures were performed. Indications for CE included suspected Crohn’s disease, anemia, abdominal pain, polyposis syndrome, celiac disease, and GI bleeding. The majority (263) of capsules were placed using the capsule delivery device (Advace CE by US Endoscopy). In 25(8.68%) patients, the capsule could not be placed using the standard technique, and a novel technique was developed using laryngoscopic assistance. By this method, 24 of these 25 patients had successful capsule placement. There were no complications.

CELIAC DISEASE: Twenty nine children with elevated TTG levels were examined by CE. A novel finding of proximal small bowel polyps were found in 7 patients(24%). One patient was subsequently diagnosed with Bannayan-Riley-Ruvalcaba syndrome. Other CE findings included classic scalloping of duodenal mucosa, loss of villi and mosaic pattern.

INFLAMMATORY BOWEL DISEASE: Fifty-seven CE studies were performed on forty-four patients. In forty-two of the CE studies, small bowel findings were seen. Two patients were found to have isolated small bowel disease.

POLYPS: Seventeen patients were found to have polyps in the small bowel. Two patients were known to have FAP. Three patients had BD and 8 patients had celiac disease.

DUODENAL WINDSOCK: A rare finding of duodenal windsock diverticulum was made by CE when abdominal CT suggested intussusception.

CONCLUSION: The use of CE in children is feasible, safe and has a significant impact on the diagnosis and management of pediatric gastrointestinal diseases.
189 HIGH PREVALENCE OF CELIAC DISEASE AMONG SAUDI CHILDREN WITH TYPE 1 DIABETES.
Abdulrahman A. Al-Hussaini*, Nimer Sulaiman*, Masa Al-Zahrani*, Ahmed Almezzi*, Imad El Hag*, Pediatrics, King Fahad Medical City, Riyadh, Saudi Arabia; *Pediatrics, King Saud Medical City, Riyadh, Saudi Arabia

Background: Type I diabetes (T1D) is associated with increased risk of celiac disease (CD). The prevalence of CD in patients with T1D in European and North American countries has been reported at 1% to 16%. Review of the literature reveals a lack of comparable well designed study in Saudi community.

Objective: To estimate the prevalence of CD among Saudi diabetic children and to characterize the clinical and laboratory features of children with T1D and CD.

Methods and materials: Children with T1D following in diabetic clinic have been screened for presence of CD over a one-year period (2007 - 2008), by doing tissue transglutaminase IgA antibodies (TTG), endomyseal IgA antibodies (EMA), and total IgA. All children have been subjected to the following: history, physical examination, blood tests (CBC, iron profile, Hb A1C).

Children with positive TTG (> 30 units) and/or EMA had upper endoscopy and 6 duodenal biopsies.

Results: One hundred and six children with T1D have been screened for CD: age ranges between 8 months to 15.5 years (62 females). Nineteen children had positive TTG and/or EMA, however only 12 children had biopsy proven CD (11.3%). Five of 12 had gastrointestinal symptoms (42%) and seven were asymptomatic (58%). Children with T1D and CD had significantly lower serum iron than children with T1D without CD (8.5 µgm/L Vs 12.5 µgm/L; P = 0.014, respectively). The sensitivity and specificity of TTG and EMA were 91.6% and 83.3% Vs 93.6% and 99%, respectively. The positive and negative predictive value of TTG and EMA were 65% Vs 91% and 99% Vs 97%, respectively. ROC analysis for the best cut-off value of TTG for diagnosis of CD was 63 units (sensitivity 100% and specificity 98%).

In conclusion: CD has a prevalence of 11.3% among Saudi children with T1D. Children with T1D and CD have significantly lower serum iron than children with T1D without CD. TTG has high false positive results that can be reduced by setting the positive cut-off value at 63 units.

190 PUNCTATE ERYTHEMATOUS LESIONS IN THE DUODENAL BULB AT ENDOSCOPY SHOULD PROMPT CONSIDERATION OF CELIAC DISEASE. Adie Kalansky1, Elizabeth Siegel1, Dascha Weir1, Jeffrey Goldsmith1,2, Hongyu Jiang1, Alan Leichtner1, Children's Hospital Boston, Boston, MA; 2BIDMC, Boston, MA

INTRODUCTION: Classic endoscopic features of celiac disease (CD), such as flattening or scalloping of the mucosal folds, are insensitive and nonspecific. Diagnostic accuracy can be improved with high resolution endoscopy or other techniques which permit visualization of villi. Punctate erythematous lesions (PELs) in the duodenal bulb, sometimes referred to as "vascular markings", have been noted to be a feature of CD, but their utility in diagnosis is not established.

METHODS: PELs were defined as 1-3 mm pleomorphic red lesions in the absence of ulceration. Endoscopists performing EGD on 177 prospectively recruited patients being evaluated for CD were asked to record the presence of PELs, nodularity, and ulceration in the bulb, and flattened or scalloped folds, nodularity, ulceration, and loss of villi in the distal duodenum on macroscopic examination. Two biopsies were obtained from the bulb and 4 from the more distal duodenum. Patients were diagnosed with CD if one or more biopsies met standard Marsh 2 or 3 criteria.

RESULTS: 96/177 patients were female. The average age was 9.2 years (SD = 4.9 years). 78/177 patients met histopathologic criteria for CD. 24/78 (31%) were noted to have PELs in the bulb vs. 6/99 (6.1%) control patients (p<0.001). The calculated specificity, positive predictive value, and negative predictive value of PELs were 93.9%, 80.0%, and 63.3%, respectively. No histopathologic differences were noted between biopsies targeted at PELs and biopsies from other sites. When available, narrow band imaging (NBI) was used to examine PELs and enhancement of the lesions was noted.

CONCLUSIONS: Although the finding of PELs in the bulb at endoscopy had a high positive predictive value for CD, the diagnosis should be based upon standard histopathologic criteria. However, identification of incidental PELs should prompt the endoscopist to obtain sufficient duodenal biopsies to permit diagnosis of CD. NBI suggests that these lesions could represent submucosal blood, most likely within dilated vascular structures.

191 RICKETS AS A CLINICAL PRESENTATION OF CELIAC DISEASE IN SAUDI CHILDREN. Asaad M. Assiri, Anjum Saeed, Ahmed Al Sarkhi, Mohamed El Mouzan, Abdullah Al Sanie, Mona Al Asmi, Yassin Hamid, Pediatric, Faculty of Medicine & KSU, Riyadh, Saudi Arabia

Aim: To report rickets as a clinical presentation of celiac disease in Saudi children with unexplained rickets.

Patients and Methods: Children referred to Pediatric Gastroenterology and Hepatology unit of King Khalid University Hospital Riyadh for evaluation of unexplained rickets and osteomalacia were enrolled and screened for celiac disease. The diagnosis of rickets was made on the basis of clinical history, physical examination, biochemical and radiological investigations and the diagnosis of celiac disease was made according to the 1990 modified ESPGHAN criteria. The data included age, sex, presenting complaints, dietary practice, medication intake and celiac serology with histology of small bowel biopsies and recorded on a predesigned proforma.

Results: Of 26 children who were referred for evaluation of unexplained rickets to our unit, 10 patients (38.4%) had confirmed celiac disease, 9 were females and 1 male. Mean age was 9.5 years (range: 1-15 years). The main symptoms were bone pain, fatigue with signs of rickets including skeletal deformities, waddling gait, widening of wrists and ankles with rachitic rosary. All ten children had frank evidence of rickets on radiological investigations. The mean laboratory values were; hemoglobin 9.96 gm/dl, Ca 1.83 mmol/L, phosphate 1.31 mmol/L, alkaline phosphatase 868.8 IU/L. Serum concentration of 25-OH vitamin D ranged between 12-26 ng/ml (N: 10-45). Parathyroid hormone level was raised in 7 patients. Anti-endomyseal and anti-tissue
transglutaminase antibodies were positive in all patients. Small bowel histopathology showed total villus atrophy with crypt hyperplasia and intraepithelial lymphocytes consistent with the diagnosis of celiac disease. Conclusion: Rickets or osteomalacia is a rare presentation of celiac disease in Saudi children. Pediatricians should consider celiac disease in any child with unexplained rickets.

192 COHORT OF ITALIAN CHILDREN AT RISK FOR CELIAC DISEASE LACK BACTEROIDETES. C. Sturgeon1, F. Valitutti2,3, G. Serena1, E. Lionetti1, M. Barbato4, R. Francavilla5, C. Barbera6, G. Barera7, J. Ravel8, C. Catassi1,9, A. Fasano5,7, MBRC, University of Maryland School of Medicine, Baltimore, MD; 2Pediatrics, Universita di Roma, Roma, Italy; 3University of Catania, Catania, Italy; 4University La Sapienza, Roma, Italy; 5University of Bari, Bari, Italy; 6University of Turin, Turin, Italy; 7University of Milan, Milan, Italy; 8Institute of Genome Sciences, University of Maryland School of Medicine, Baltimore, MD; 9Department of Pediatrics, Universita Politecnica delle Marche, Marche, MD

Background: Celiac disease is an autoimmune enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. The role of gliadin causing celiac disease is well established. However, the early steps following mucosal exposure to gliadin leading to celiac disease are still unknown. Recent data suggests children with celiac disease have a different profile of intestinal microbiota than healthy controls. Aim: To determine the composition of the microbiota of children at risk for celiac disease. Methods: Stool samples from a subgroup of children at risk of celiac disease enrolled in a prospective interventional study were analyzed for microbiota composition. We received stools from 41 of the 722 enrolled infants. Fecal microbiota was analyzed by 454 pyrosequencing of 16S rRNA. Data was analyzed through the bioinformatics pipeline CloVR. Results: Phylum level comparisons of the proportions show an overall domination of Firmicutes. Interestingly, these children all show extremely low levels of Bacteroidetes. Log adjusted data revealed two clusters with significantly different levels of Bacteroidetes. These clusters did not group with the diagnosis or treatment group allocation (early vs. late gluten introduction). Furthermore, these clusters showed high levels of both Firmicutes and Actinobacteria. Proteobacteria had significantly different levels in the two clusters. Conclusions: The gut microbiota of this subset of children at-risk of celiac disease appears to separate into two clusters based on the level of Bacteroidetes. However, both clusters show extremely low levels of Bacteroidetes that remained in children up to 6 years of age.

193 SERUM COTININE LEVELS AND FOOD ALLERGIES, A CROSS SECTIONAL STUDY. Cade M. Nylund Pediatrics, Uniformed Services University of the Health Sciences, Bethesda, MD

Background: Perinatal cigarette smoke exposure has been linked to food allergy. Many food allergies resolve during early childhood. Less is known about smoke exposure and food allergies in later childhood. The risk of food allergies in pediatric participants exposed to cigarette smoke was evaluated.

Methods: The 2005-2006 National Health and Nutrition Examination Survey’s food specific IgE levels, serum cotinine levels (a biomarker of cigarette smoke exposure), and questions about smoke exposure were examined. Participants ages 1-18 years old were evaluated for milk, egg, and peanut allergy and participants ages 6-18 year old were additionally evaluated for shrimp allergy. Food-specific IgE and age-based criteria were used to define food sensitization (IgE >0.35 kU/L) or probable food allergy (milk, >15 kU/L; egg, 7 kU/L; peanut, >14 kU/L; shrimp, >5 kU/L) or for ages 1-2 years (milk, >5 kU/L; egg, >2 kU/L).

Results: Food specific IgE levels were measured in 3587 pediatric participants. Of these 3027 (84%) had a cotinine level measured. The median (interquartile range) age was 11.5 (5.75-15.50). Those with food sensitivity include: milk, 468 (13.1%); egg, 238 (6.6%); peanut, 384 (10.7%); shrimp, 229 (6.4%). Those with food allergy include: milk, 4 (0.1%); egg, 15 (0.42%); peanut, 30 (1.1%); shrimp, 42 (1.2%). Serum cotinine levels were significantly higher in those with shrimp (p<0.05) and egg (p <0.05) sensitization and shrimp allergy (p<0.05). In those with detectable cotinine there was higher total serum IgE (p<0.0001) and percent eosinophil count (p<0.005). Neither maternal reporting of smoking during pregnancy nor reporting a current smoker in the home was associated with food sensitization or allergy for all foods. However, 79 percent of those with a detectable cotinine level reported no household smoke exposure.

Conclusions: Cigarette smoke exposure as measured by serum cotinine levels is associated with shrimp allergy and shrimp and egg sensitization. Reported maternal smoking during pregnancy and reported current household smoke exposure was not associated with food allergies or sensitization.

194 SCHIZOPHRENIC SUBJECTS WITH A POSITIVE TTG2 AND ELEVATED LEVELS OF NEURONAL TISSUE TRANGLUTAMINASE (tTG)6 IN tTG2 POSITIVE
schizophrenia subjects.

Methods: Intestinal anti-TG 2, anti-gliadin IgA, anti-gliadin IgG and anti-endomysium antibodies (EMA) were assayed in 1401 schizophrenic patients who were part of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study and 900 controls. Neuronal anti-iTG6 antibodies were tested in those schizophrenic patients that were positive for anti-iTG2 antibodies and in matched controls with a ratio 1 patient: 2 controls.

195 DIFFERENT EXPRESSION OF FOXP3 GENE AND HLA DQ2/DQ8 HAPLOTYPE BETWEEN CELIAC AND NON-CELIAC PATIENTS WITH DOWN SYNDROME. G. Serena1, D. Libreri2, D. Kryszak1, C. Sturgeon1, K. Lammers1, A. Fasano1. 1MBRC, University of Maryland School of Medicine, Baltimore, MD; 2Pediatrics, University of Palermo, Palermo, Italy

Background: Down syndrome (DS) is associated with an increased prevalence of autoimmune disorders as celiac disease (CD). While the prevalence of CD is 0.5-1% worldwide in normal population, its prevalence among DS patients rises up to 5-15%. CD is an immune mediated enteropathy triggered by gliadin, a protein included in gluten-containing cereals among genetically susceptible individuals (95% has HLA DQ2 haplotype, 5% HLA DQ8). CD4+CD25+FoxP3+ regulatory T cells constitute a subpopulation of CD4+ T cells that regulate the immune homeostasis and self-tolerance. Dysfunction of Tregs is associated with autoimmunity and is hypothesized to result from a lack of exons within the FOXP3 gene that encode important functional sites. Aim: To study putative genetic correlations among DS patients that account for the higher prevalence of CD in this population. Methods: Venous blood was drawn from 89 DS patients and 16 DS patients with CD (DS-CD) in Department of Pediatrics in Palermo and HLA DQ2/DQ8 haplotype was evaluated using DQ-CD Typing Plus Kit of BioDiagnex. RNA was extracted from a subset of these samples (19 DS, 5 DS-CD) with the Midi Rneasy Lipid Tissue Kit (Qiagen). Real-time RT-PCR (SYBRgreen) was run to detect gene expression of total FoxP3, its full length and Δ2 isoforms. Results: Thirty-two out of 89 DS patients (35.9%) and 9 out of 16 DS-CD patients (56.3%) had the HLA DQ2/DQ8 haplotype. The real-time RT-PCR analysis showed that expression of total FoxP3 and isoforms was higher expressed in DS patients vs. DS-CD. Conclusions: Frequency of HLA DQ2/DQ8 haplotype in DS patients was similar to that of the normal population (30%), however, HLA DQ2/DQ8 haplotype was less frequent in DS-CD patients compared to non-Down CD population, suggesting the implication of an alternative HLA haplotype in DS-CD. Our preliminary data showing higher expression on FoxP3 (isoforms) gene expression in DS vs. DS-CD patients suggests a lack of functionality of autoimmunity regulation in DS-CD.

196 NEUTROPHIL CHEMOTAXIS TO PT-GLIADIN AND FMLP IS IMPAIRED IN CELIAC DISEASE PATIENTS COMPARED HEALTHY INDIVIDUALS. K. Lammers1, S. Khandelwal2, M. Janka-Juantilla1, M. Chiappi2, E. Leonard Puppo1, C. Parent2, V. Casalaro1, A. Fasano1, 1Mucosal Biology Research Center, University of Maryland School of Medicine, Baltimore, MD; 2Laboratory of Cellular and Molecular Biology, NCI, NIH, Bethesda, MD; 3NIAID, NIH, Bethesda, MD

Background: Celiac disease (CD) is triggered by the ingestion of gliadin, immunogenic component of gluten-containing grains. Gliadin induces a rapid, massive influx of neutrophils to the murine gut mucosa, suggesting that gliadin itself is a chemoattractant factor. Gliadin is also a chemoattractant factor for human neutrophils. We study whether gliadin has chemoattractant properties also for human neutrophils, and to assess neutrophil chemotaxis in healthy individuals (HC) and patients with CD. Methods: Neutrophils were isolated from venous blood of HC and CD patients and applied in 2 chemotaxis assays; (a) E2taxi-scan assay, an in vitro model for real-time monitoring of chemotaxis to pepsin-trypsin-digested gliadin (PTG) or N-formyl-methylene-leucyl-phenylalanine (fMLP; positive control), and (b) underagarose assay with both stimuli, in which recruitment was analyzed with fluorescent microscopy. Results: E2taxi-scan assay (HC, n=2) showed that PT-gliadin was also a chemoattractant factor for human neutrophils. The underagarose assay showed differences in chemotactic response between neutrophils from HC and CD patients. CD neutrophil migration to PTG was markedly reduced compared to HC (0.403 ± 0.259 (n=16) vs. 5.772 ± 1.338 (n=20) net neutrophil migration, respectively, P=0.0005). A similar difference was observed in the migration of CD vs. HC neutrophils to fMLP (4.790 ± 1.080 (n=12) vs. 11.93 ± 2.886 (n=14) net neutrophil migration, respectively, P=0.067). Conclusion: PT-gliadin is also a chemoattractant factor for human neutrophils. We also show that, compared to HC neutrophils, CD neutrophil chemotaxis to both PTG and fMLP is clearly impaired. These findings suggest that CD neutrophils are less responsive than HC neutrophils. This may result in a delayed arrival of neutrophils at the site of gluten-promoted inflammation and may critically contribute to the autoimmune pathogenesis of CD.

197 USE OF REAL TIME VIEWER FOR ENDOCOSCOPIC DEPLOYMENT OF CAPSULE ENDOSCOPE IN PEDIATRIC POPULATION. Lee M. Bass, Larry Misiewicz, Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL

Wireless capsule endoscopy (WCE) is an increasingly utilized procedure for visualization of the small intestine. One challenge in pediatric WCE is the placement of the capsule in a population too young or unable to swallow it. Here we present a novel use of the Real Time (RT) viewer in the endoscopic deployment of WCE. MATERIALS AND METHODS: Retrospective chart review performed on all WCE completed at the Children’s Memorial Hospital from February 2010 until May 2011. This study was approved by the Institutional Review Board of Children’s Memorial Hospital. All patients had diagnostic EGD prior to WCE placement. The AdvanCE capsule delivery device was utilized in all cases. The RT viewer was attached to the capsule recorder and image was noted on screen prior to insertion into oral cavity. The upper esophageal sphincter was visualized on RT viewer. The endoscope and delivery device were slowly advanced into stomach, through the pylorus and into duodenum while maintaining visualization on the RT viewer. RESULTS: 11 patients had endoscopic placement of the WCE. Ages ranged from 2 to 19 years. Reasons for WCE included GI Bleeding, anemia, familial polyposis, and evaluation for Crohn’s disease. Eight
patients required endoscopic placement due to inability to swallow the capsule, while 3 were placed as part of a previously scheduled procedure to take advantage of sedation and airway protection. All eleven patients had successful deployment of the capsule into the duodenal lumen. In each case, the endoscopist was able to confirm capsule location in the duodenum during scope withdrawal. One patient had retrograde transit of the capsule back into the stomach upon retching while waking up from anesthesia. There was no evidence of iatrogenic trauma or bleeding in any patient. There were 3 incomplete studies, a completion rate consistent with that described in the literature. CONCLUSION: Use of the RT viewer for endoscopic deployment of WCE is an effective technique to improve visualization of capsule placement in the pediatric population.

198 SHORT COURSE, SINGLE-DOSE POLYETHYLENE GLYCOL 3350 REGIMEN FOR COLONOSCOPY BOWEL PREPARATION IN CHILDREN. Mazen I. Abbas, Carol Bruch, Lucyminda Nazareno, Cade Nylund, Phillip Rogers, Pediatrics, Walter Reed AMC, Washington, DC

Background: Polyethylene glycol (PEG) 3350 is recently being used as a colonoscopy preparation in children. There is no standardized pediatric bowel preparation regimen recognized. A single-dose regimen of PEG 3350 + a sports drink is popular at many pediatric gastroenterology centers. We proposed a prospective study to assess the efficacy, tolerability, and safety of this regimen.

Methods: Prospective, open label study of children ages 8-18 years old of a colonoscopy bowel preparation including 238 grams of PEG 3350 mixed with 64 ounces of Gatorade® given the day before the procedure. Efficacy was determined using the Boston Bowel Preparation Scale (BBPS). A questionnaire was administered assessing side effects, acceptability and tolerability of the cleanout. Basic metabolic profiles pre/post cleanout were also obtained.

Results: A total of 28 of 33 patients were able to complete the study. Five of 28 patients were not able to complete the full 64 oz regimen. Patients were predominately male with a mean age of 14.83 years. All of the colonoscopies were completed to the cecum/or terminal ileum. Seventy-nine percent were found to be acceptable cleanouts according to study criteria (BBPS mean 6.07 +/- 1.61). Approximately half of the patients reported either nausea, vomiting or abdominal discomfort during the cleanout. Overall, patients felt the regimen was acceptable with main concern being the volume of the regimen. There was no clinically significant changes in basic metabolic profiles, although a statistically significant decrease in blood urea nitrogen (3.82 mg/dL) and carbon dioxide (1.82 mmol/L).

Conclusions: PEG 3350 + Gatorade® is a safe and effective colonoscopy bowel preparation regimen. We propose a standard regimen for older children that would include 238 grams of PEG 3350 mixed in 64 ounces of a sports drink over a 2-4 hour period the night before the colonoscopy. Main concerns of this regimen is the large volume to drink. Study limitations include the small study size, lack of a control group, and absence of blinding.

199 DOUBLE BALLOON ENTEROSCOPY IN CHILDREN. Melissa Jensen, Riad Rahhal, University of Iowa, Iowa City, IA

Double balloon enteroscopy is an endoscopic procedure that allows visualization of the small bowel and has been recently employed in pediatric gastrointestinal disorders. Limited studies have been published about the utility and complications in this population. We describe 4 procedures performed in 3 patients, with an age range of 7-13 years and weight range 28.2-43.9 kg. Indications included obscure intestinal bleeding, suspected small bowel abnormality in imaging study and known small bowel polyps. Diagnostic yield has high with the finding of a bleeding source, a small bowel ulcer and polyps. Estimated length of small bowel visualized ranged from 70 to 300 cm. All procedures were under general anesthesia. Therapeutic intervention was performed in 2 patients. One patient had successful cauterization of a bleeding anastomotic ulcer without complications. Another patient had several small bowel polyps (related to Peutz Jeghers syndrome) removed, but this was complicated by perforation. Double balloon enteroscopy can be performed in children with a high diagnostic yield. Complications can occur and should be assessed after such procedures.

200 POLYETHYLENE GLYCOL POWDER SOLUTION VS. SENNA FOR BOWEL PREPARATION FOR COLONOSCOPY IN CHILDREN: A PROSPECTIVE, RANDOMIZED, INVESTIGATOR-BLINDED TRIAL Natalie Terry1, Mei-Lin Chen Lim1, Rong Guo1, Muralidhar Jatla2, Salina Esch1, Lisa Farace1, Frances Jannelli1, Anita Puma1, Dean Carlow1, Petar Mamula1, 1Children's Hospital of Philadelphia, Philadelphia, PA; 2Children's Hospital at Scott and White, Texas A&M, Temple, TX

Background and Objectives: Safety and effectiveness of large volume polyethylene glycol-based solution (PEG-ES) has been documented, but the taste and volume can be barriers to successful preparation. Efficacy and safety of small volume electrolyte-free PEG-P (Miralax®, Schering-Plough HealthCare Products, Inc) for colonoscopy preparation has been rarely studied, although it is currently used at many pediatric centers. The primary objective of this study was to determine whether PEG-P results in a more efficacious and safe colonoscopy preparation as compared to senna.

Methods: The study design was prospective, randomized, and single-blind. Patients aged 6-21 years were randomized to a two-day clean-out regimen of PEG-P at a dose of 1.5 g/kg divided twice a day for two days versus senna 15 mL daily (ages 6-12) or 30 mL daily (ages 12-21) for 2 days. Both preparations required one day of clear liquids while senna preparation required an additional day of full liquid diet. A blinded endoscopist graded the quality of preparation with a standardized cleanliness tool (Aronchick scale). Serum chemistry panels were obtained. Patients rated symptoms and ease of preparation. The anticipated number of subjects was 166, however, the interim analysis demonstrated inferiority of senna preparation.

Results: Thirty-three patients were enrolled. One patient withdrew the consent for participation. Of the patients in the PEG-P arm, 88% (14/18) received an excellent/good score compared to 29% (4/14) with the senna preparation (p=0.0022). Both preparations were well-tolerated according to symptoms and patient-graded ease of preparation. Demographics and laboratory values did not differ significantly across the two groups. No serious adverse events were noted.
Conclusions: PEG-P is an effective colonoscopy preparation while senna preparation was insufficient. Both were well-tolerated and safe in a pediatric population.

201 DUODENAL BULB BIOSPIES ADD TO OUR DIAGNOSTIC YIELD OF CELIAC DISEASE. Osama F. Almadhoun, Thomas Rossi, Marilyn R. Brown, Pediatric GI, University of Rochester Medical Center, Rochester, NY

Background: Celiac disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten. The diagnosis of celiac disease requires the presence of characteristic histologic alterations in biopsy specimens taken from the descending duodenum, which are classified according to modified Marsh criteria. Several recent studies demonstrated the patchy nature of villous atrophy, with changes restricted to the duodenal bulb in some patients. On that basis, we revised our clinical practice by obtaining two biopsies from the duodenal bulb in addition to four from the descending duodenum in patients with positive celiac serology.

Objective: To assess whether the addition of duodenal bulb biopsies to distal duodenum biopsies in patients with positive celiac serology have increased the diagnostic yield of celiac disease.

Methods: The medical records of 156 patients with positive celiac serology from July, 2009 to December, 2010 were reviewed. The age, sex, symptoms, risk factors, Anti-tissue transglutaminase antibody-IgA levels, endoscopic, and histologic finding of descending duodenal biopsies and duodenal bulb biopsies were recorded.

Results: Of the 156 patients with positive celiac serology, 59% of patients (92/156) underwent an EGD to confirm the diagnosis of celiac disease. The diagnosis of Celiac disease was confirmed in 50% of patients (46/92). Duodenal bulb biopsies were obtained in 30/46. Among those patients, 23% (7/30) had histological changes consistent with celiac disease in their biopsies from duodenal bulb only. In 70% (21/30), the histological finding in both, duodenal bulb and descending duodenal biopsies were consistent with celiac disease. The histological changes were limited to the descending duodenal biopsies in only 7% of patients (2/30).

202 MANAGEMENT OF CELIAC DISEASE: IS THERE A NASPGHAN APPROACH? Rita Fleming, Lennie Clore, John Snyder, Children's National Medical Center, Washington, DC

Introduction: Celiac disease (CD) affects about one per cent of the US population and is known to have protein manifestations which can potentially involve every organ system in the body. Recent attention has been focused on the relationship of CD with bone health, associated endocrine disorders, impact on immunizations and use of genetic testing. To date, there has been no consensus about the optimal way to evaluate and follow these patients. To determine the standard of practice in the pediatric GI community, we sent a questionnaire to representative NASPGHAN members.

Methods: We developed a validated research instrument on the diagnosis and management of children with CD. Questionnaires were sent to 75 academic and private practice centers in the US and academic centers in Canada in May, 2011.

Results: These data summarize the responses of initial 18 respondents. For diagnosis, all programs screen with quantitative IgA and anti-tissue transglutaminase (tTG) antibody; 8 of the 18 programs also screen with anti-endomysial antibody. Two-thirds of the programs use the Marsh criteria for histologic diagnosis. Very little routine screening for bone health, associated endocrine disorders and impact on immunizations was reported. None of the programs do routine HLA testing; 10 of the programs feel that absence of HLA markers eliminates the diagnosis of CD.

Conclusions: These preliminary data indicate that there is a similar pattern of testing among the programs for most categories. All programs use similar diagnostic tests but rarely use routine screens for associated problems.

Comparison of US and Canadian Programs

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203 PEDIATRIC NEUROPSYCHIATRIC MANIFESTATIONS OF GLUTEN INTOLERANCE. T. Marciano1, F. Lazare1, H. Davidovich2, K. Grancher3, S. Acchacha4, J. Corrigan2, F. Daum3, 1Pediatric Gastroenterology and Nutrition, Winthrop University Hospital, Mineola, NY; 2Pediatric Endocrinology, Winthrop University Hospital, Mineola, NY; 3Pediatrics, State University of New York, Downstate Medical Center, Brooklyn, NY

Children with active celiac disease (CD) frequently have irritability and mood change. There are no data to indicate if gluten affects cognition and/or the emotional status of CD children. The study was to determine the effect of a gluten free diet (GFD) on behavior and cognition in CD. Methods: The Div, Peds GI, Winthrop University Hospital performed a prospective, controlled, non randomized single blinded study. Pts (N=14) were 6-18 years with newly diagnosed CD. Pts with comorbid disease affecting...
neurological status and cognition were excluded. Controls (N=5) were children without serologic evidence of CD. Cognitive assessment was made by the Pediatric Automated Neuropsychological Assessment Metrics(PANAM), which assesses sustained concentration, mental flexibility, spatial processing, cognitive processing, fatigue, learning, recall, and working memory. Parents completed the Youth Outcomes Questionnaire (YOQ), which tracks changes in behavior. Baseline cognitive and behavioral assessments were performed prior to starting a GFD in the CD group. Baseline testing was also performed in controls. A reassessment was performed in both groups at 6 months. Results: The mean age for CD was 12.8 years, controls 15.5 years. PANAM data showed that CD children performed slower with minimal improvement in their scores over the 6 months. The results of the initial YOQ testing and follow up was 27/18 for the CD group and 11/8 for controls. Conclusions: On PANAM, the controls performed faster and attained better scores over the test period than the CD pts. The CD group initially manifested more observed behavioral irregularities (raw score 27) than controls (raw score 11). The CD subjects demonstrated a 9 point improvement after a 6 month GFD (raw score 18) compared with only a 3 point improvement in controls (raw score 8).

204 IS SEROLOGIC SCREENING BEING PERFORMED PRIOR TO REFERRAL OF CHILDREN WITH CELIAC DISEASE? Toba Weinstein, Jeremiah Levine, Michael Pettei, Pediatric Gastroenterology and Nutrition, Cohen Children’s Medical Center, New Hyde Park, NY

BACKGROUND: Celiac disease (CD) is being diagnosed with increasing frequency. The classic triad of diarrhea, abdominal distention and failure to thrive is no longer the most common presentation of CD. CD is now recognized more frequently in two groups of pediatric pts - those with less severe GI symptoms and those from high risk populations (non-GI presentations). AIM: To determine if physicians are screening patients for CD before referral to GI subspecialists. METHODS: A retrospective chart review was performed of all children seen in the last year with biopsy-confirmed CD to determine if pts were referred with screening serology. All pts were diagnosed within the last five years. RESULTS: A total of 153 pts (52M,101F), mean age 9.7±4.5 yrs (range 1.3-17.8) were included in the study. 63 pts presented with GI symptoms while 90 had non-GI presentations (Table). Among the GI symptomatic pts, 36 (57%) presented without serology while only 7 (8%) of the non-GI pts presented without serology (p<0.001). There was no difference in the ages of those with or without serology in either group. CONCLUSION: The majority of our CD pts initially referred for GI complaints were sent without prior serologic screening. This is in contrast to CD pts from high-risk, non-GI populations who were almost uniformly screened. Increased awareness by physicians to screen pts with GI symptoms associated with CD is still needed.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No Celiac Serology on Referral</th>
<th>Celiac Serology on Referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>15</td>
<td>16</td>
</tr>
<tr>
<td>Constipation</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Vomiting/GER</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhea &amp; abdominal distention</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Short Stature/FTT</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>Family History of CD</td>
<td>1</td>
<td>33</td>
</tr>
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<td>Diabetes/Thyroid</td>
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<td>19</td>
</tr>
<tr>
<td>Anemia</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Dermatologic Manifestation</td>
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<td>1</td>
</tr>
</tbody>
</table>

205 SURGERY THROUGH NATURAL ORIFICES. Ulises Leal Quiroga, Endoscopy, Christus Muguerza Sur, Monterrey, Mexico

INTRODUCTION: The fenestrated duodenal membrane has a prevalence of 1:10,000 to 1:40,000 births; symptoms could be present or not since birth. The surgery technique mostly used is the duodenectomy, resection of the membrane through Mckulic's closure. The purpose for this presentation is to show three cases of patients with duodenal membrane resolved by endoscopy; two of them with previous surgeries. CASE 1. Male patient 47 days old started with persistent vomits since birth. The first surgery procedure reported duodenal bridle which was resected, having a torpid evolution. The patient continued with vomits. The Upper GI series showed occlusion at duodenal level. The upper GI endoscopy showed obstruction of 80% of the anastomoses and a preveterian fenestrated duodenal membrane. The membrane was incised and fulgurated with a papilotome. CASE 2. Male patient 5 days old with vomits, was diagnosed as having duodenal atresia, and a Kimura duodenumduodenum asastomoses was done. The patient continued vomiting, an Upper GI series and endoscopy were done finding an obstruction in the second portion of the duodenum as a result of a non fenestrated duodenal membrane. A second laparotomy was carried out and a longitudinal incision in the membrane was done, thirty days after surgery the patient started vomiting. Endoscopy was practiced finding a duodenal membrane with a central orifice and electrofulguration was done. CASE 3. Male patient 2 years and 2 month old vomiting since birth. Upper GI series done; the findings were gastromegaly and an important dilation of the first and second portion of the duodenum. An upper GI endoscopy was carried out finding a duodenal fenestrated membrane which could be incised and was fulgurated with a papilotome; the surgery time was of 100 minutes. Conclusion: We have the consideration that when fenestrated duodenal membrane is suspected upper GI endoscopy must be done for being less invasive helping in the diagnosis and treatment; besides being a secure and effective procedure, reducing surgery time and days of hospitalization.
206 COEXISTENCE OF CELIAC DISEASE WITH INFLAMMATORY BOWEL DISEASE IN CHILDREN. Veronica Busoni1, Judith Cohen Sabban1, Julieta Gallo1, Silvia Christiansen2, Carlos Lifschitz3, Marina Orsi1, 4Pediatric Gastroenterology Hepatology and Hepatointestinal Transplantation, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 5Pathology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Introduction: The coexistence of celiac disease (CD) with inflammatory bowel disease (IBD) has been described in adults. There are few reports regarding this association in the pediatric population.

Material and Methods: We performed a retrospective review of the clinical charts from patients with IBD who attended a Pediatric Gastroenterology Unit from 1980 to 2010.

Results: Of the 151 patients (89 male) seen during that period, no patient was diagnosed as having CD and IBD until 2004. Since 2005, 6 patients (3.97%) were identified with this association: 4 girls (3 with Crohn’s Disease (CrD) and 1 with ulcerative colitis (UC)) and 2 boys (both with CrD). Median age at diagnosis was: 5.2 yrs (r: 1.8-15.4 yrs). Diagnosis was made simultaneously in 4/6 and in the rest in a subsequent manner (1 was diagnosed first with IBD (CrD) and the other one initiated with CD and UC afterwards). In all of them, CD was confirmed with histology and specific serology. All of these patients presented with growth retardation, hypoalbuminemia and anemia that did not improve with adequate iron supplementation. Parents of patients in whom diagnosis was made simultaneously, were reluctant to accept the coexistence of both diseases and for a period of time did not comply with treatment. In most cases patients began gluten free diet, but had difficulty with IBD medications. Once both therapies were properly administered, patients normalized serologic markers and improved clinically.

Conclusions: It is important to consider the possible coexistence of CD and IBD when inadequate response to treatment for either entity is observed, mostly in areas where CD is prevalent. Parents’ reluctance to accept both diagnoses and comply with therapy may delay clinical improvement.

207 CALCIUM AND VITAMIN D SUPPLEMENTATION IN CELIAC DISEASE. PRELIMINARY RESULTS OF A PROSPECTIVE, DOUBLE BLIND, RANDOMIZED STUDY. Veronica Busoni1, Marina Orsi1, Ana Galich1, Guillermo Alonso1, Carlos Lifschitz1, Daniel D’Agostino1, 1Pediatric Gastroenterology Hepatology and Hepatointestinal Transplantation, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 2Nuclear Medicine, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; 3Pediatric Endocrinology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Introduction: Calcium and vitamin D malabsorption in newly diagnosed celiac patients, may compromise bone mass and lead to osteodystrophy.

Aim: To evaluate the role of calcium and vitamin D supplementation in bone health in patients with recent celiac disease (CD) diagnosis.

Materials and Methods: Patients recently diagnosed with CD, were enrolled in a prospective, double blind study. Subjects were randomized in 2 groups: G1 received calcium carbonate and vitamin D for 1 year after diagnosis and G2 received placebo. Bone mineral density (BMD) was measured by dual energy x-ray absorptiometry (DXA) technique in lumbar spine and total body at diagnosis and after 1 year of gluten free diet (GFD). Compliance with GFD was evaluated by antitransglutaminase serology.

Informed consent was obtained in all cases.

Results: 29 patients were enrolled. 19/29 (68.9%) reached the completed study (10/29 abandoned the study). The mean weight/height was 98.5% (SD 10.8) (r 81-122%) and the delta height after 1 year of GFD was +8.75 cm/y. (SD 2.14) for the whole group, not showing significant differences between G1 and G2. 10/19 were enrolled in G1 (5 girls) and 9/19 in G2 (8 girls). The mean age in G1 was 7.38 y. (r 1.9-11.42) and in G2, it was 5.4 y. (2.33-9.45). The delta BMD Z-score of both groups together was +0.58 (SD 0.67) for total body and +0.56 (SD 0.58) for lumbar spine. There was no significant difference in the mean annual increment of body composition and BMD parameters, between G1 and G2.

Conclusion: Calcium and vitamin D supplementation did not modify the improvement in densitometric measurements nor in height velocity of patients with CD recent diagnosis. Most BMD reports were normal at diagnosis, however each one of the bone mineral measurements improved after 1 y of GFD, as well as growth did.

208 A RARE CASE OF REFRACTORY CELIAC DISEASE (RCD) TYPE II IN A TEENAGE GIRL WITH LESIONS IN THE MID JEJUNUM. Winnie Szeto, Anca M. Safa, Pediatric Gastroenterology, University of Maryland Medical Center, Baltimore, MD

Refactory celiac disease is defined by recurrent malabsorptive or persistent symptoms and villous atrophy on biopsy despite 6 to 12 months of a strict adherence to a gluten- free diet (GFD). RCD can be further classified as type 1 or type 2. RCD type 2 is less responsive to alternative pharmacological therapies and is associated with a poor prognosis. RCD type 2 has never been reported in the pediatric population.

We report the first case of refractory celiac disease type 2 in pediatric patient.

A fourteen year old Caucasian female presented with a history of recurrent abdominal pain and nausea for 9 months. Serologies for celiac disease(CD) were positive and initial endoscopy was consistent with classic findings of CD. Despite 12 months of a strict gluten-free diet she continued to have persistent abdominal pain and nausea. She was started on oral steroids and imuran with minimal improvement. She was then referred to us for further management. A repeat upper and lower endoscopy were negative and it was decided that further imaging should be performed before dismissing RCD as a possible diagnosis. A capsule endoscopy demonstrated severe scalloping in the mid jejunum and, therefore, a double balloon enteroscopy was performed and biopsies were sent for pathology and immunohistochemical staining. She was found to have Marsh stage 3a lesions on pathology accompanied by the detection of CD3 intraepithelial lymphocytes (IEL)and with > 50% loss of CD8 surface markers by immunohistochemistry. These findings were consistent with the diagnosis of RCD type 2.

If a pediatric patient with CD has persistent symptoms after 6 months on a strict gluten-free diet and negative upper and lower
endoscopies then one must consider a capsule endoscopy study before dismissing refractory celiac disease. If further imaging studies are concerning then tissue biopsies should be sent for pathology and immunohistochemistry. RCD type 2 has been known to be a disease of the adult population but we report the first case of RCD type 2 in a pediatric patient.

209 CAPSULE ENDOSCOPY IN A LARGE PEDIATRIC POPULATION. Zev Davidovics, E. O'Brian Smith, Mark A. Gilger, Lina B. Karan, Pediatric GI, Baylor College of Medicine, Houston, TX

Wireless capsule endoscopy (CE) was approved by the US FDA in 2001 for evaluation of small bowel disease in adults. In 2009 CE was approved for use in children above 2 years of age. Several studies have reviewed the utility and safety of CE in the pediatric population, but further evaluation is warranted.

Methods: Retrospective analysis of CE studies performed at Texas Children’s Hospital from October 2008 to December 2010. Outcome measurements included demographic information, clinical indication, placement technique, small bowel transit time, study completion, and histopathologic results.

Results: 130 patients underwent CE studies. Ages ranged from 2 to 20 years (mean age=13.7±3.5) and 58% were female. The smallest child was 12kg. Indications for CE were evaluation of established inflammatory bowel disease (IBD) (35%), gastrointestinal bleeding (25%), abdominal pain (24%), suspected IBD (9%), Fe deficiency anemia (3%), and other (3%). Diagnostic yield of the CE was 49% in all studies, but was higher in patients with a history of gastrointestinal bleeding (61%). A colonoscopy with biopsies of the terminal ileum was performed in 75 patients. Patients with an abnormal CE study were more likely to have abnormal terminal ileum biopsies (77% vs. 43%, p=0.01).

A CE study was more likely to be completed in 8 hours if the patient swallowed the capsule versus if it was placed endoscopically (80.2% vs. 63.3%, p=0.04). This finding was not related to age, weight, BMI, gender, indication, or type of anesthesia used.

Conclusions: Our experience, which includes the largest number of pediatric patients to date, confirms that in children ages 2 and older CE is safe and has a high diagnostic yield. Endoscopic placement of the capsule lead to more incomplete studies. This finding may be related to the use of anesthesia and its possible motility effects.

The relationship between CE findings and ileal biopsy findings suggests that CE may be a useful surrogate for colonoscopy in the diagnosis of small bowel disease. No cases of capsule retention occurred.

210 WAIT TIMES FOR PEDIATRIC OUTPATIENT ENDOSCOPY: A SINGLE CENTRE EXPERIENCE. Tin Yan Tina Ngan1, Sylviane Forget1, Najma Ahmed1, 1Pediatrics, McGill University Health Centre, Montreal, QC, Canada; 2McGill University, Montreal, QC, Canada

BACKGROUND: Access to endoscopy in is an important issue in the adult population. As a result, benchmarks for wait times are being set. However, there is little data on wait times for pediatric endoscopy and therefore, until this is better understood, appropriate targets cannot be established.

OBJECTIVES: To assess wait times for outpatient elective pediatric endoscopy at a single university-affiliated pediatric centre over a six month period.

METHODS: Retrospective review of wait times, from time of placement on the endoscopy waiting list to date of the procedure.

RESULTS: 256 outpatients were wait-listed for endoscopy between December 2009 and June 30 2010. Median wait time overall was 36.5 days. The median wait time for patients undergoing their procedure under gastroenterologist-administered sedation (GA) was 24 vs. 43 days for general anesthesia (GA). The most common reasons for endoscopic evaluation were to rule out: inflammatory bowel disease (n=60), celiac disease (n=24) and eosinophilic esophagitis (n=23). Median wait times for these indications were 21.5, 31 and 59 days respectively.

CONCLUSIONS: At our centre, the median wait-time for endoscopy varied by diagnosis and sedation. Compared to Canadian adult benchmarks for IBD (<2 weeks) and celiac disease (n=24) and eosinophilic esophagitis (n=23), Median wait times for these indications were 21.5, 31 and 59 days respectively. Further assessment on a national/international level is needed to assess current waiting times and establish appropriate targets.

Distribution of Endoscopy Waiting Time

<table>
<thead>
<tr>
<th>Days</th>
<th>GA(n)</th>
<th>GS(n)</th>
</tr>
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<tbody>
<tr>
<td>&lt;16</td>
<td>40</td>
<td>37</td>
</tr>
<tr>
<td>16-30</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>31-45</td>
<td>15</td>
<td>11</td>
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<tr>
<td>45-60</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>&gt;60</td>
<td>65</td>
<td>32</td>
</tr>
</tbody>
</table>

GA-general anesthesia GS-gastroenterologist administered sedation
211 CLINICIANS POORLY DETERMINE READINESS FOR TRANSITION AMONG CHILDREN AND ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE. Jeannie Huang1, Allison Tobin1, Trevor Tompaine1
1Pediatrics, University of California, San Diego, San Diego, CA; 2Gastroenterology, Rady Children’s Hospital, San Diego, CA
Background & Aims: Adolescents with chronic disease must obtain the ability to obtain, process, and understand basic health information to make appropriate health decisions in preparation for the transition from pediatric to adult health services. We sought to objectively measure literacy readiness for transition among children and adolescents with inflammatory bowel disease (IBD), to determine predictors of readiness for transition, and to compare such measures with clinicians’ opinions.
Methods: We evaluated health knowledge of IBD, personal medical history knowledge, and health literacy in children and adolescents with IBD. Participants were recruited at a tertiary care pediatric gastrointestinal clinic and met the following criteria: age ≥10 years with a diagnosis of IBD for ≥6 months.
All participants performed surveys addressing health knowledge of IBD, personal medical history knowledge, and health literacy.
Participants’ clinicians were asked to report their perception of participants’ literacy readiness for transition.
ANOVA, chi-squared, and Spearman’s correlation analyses were used to determine relationships between survey measure outcomes, demographic variables, and clinician report of readiness for transition.
Results: 74 children and adolescents with IBD participated. Literacy readiness for transition based on validated measures was found in 12% of the cohort, while clinicians found 47% of the cohort ready to transition by literacy standards. Literacy readiness for transition was associated with greater age (p=0.05), white race (p=0.09), and longer duration of disease (p=0.008). Agreement was poor between measures-defined and clinician-defined literacy readiness for transition.
Conclusions: Clinicians inadequately judge the health literacy and transitional readiness of their pediatric patients. Objective measures may be required to determine the need to prepare adolescents with IBD for the transition from pediatric to adult health care services.

MOTILITY/FUNCTIONAL GASTROINTESTINAL DISORDERS

221 GASTROESOPHAGEAL REFLUX AND CYSTIC FIBROSIS: STOP THE BLAME GAME. Ajay Kaul, Richard Boesch, McPhail Gary, Rhonda VanDyke, Matthew Fenchel, Kartik Warkoo, William Campbell, Pediatrics, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH
OBJECTIVE: Evaluate characteristics of and associations between GER and nutritional parameters, feeding mode, and pulmonary function in children with CF. METHODS: All patients from our CF center who had undergone esophageal impedance monitoring (>18 hours) from 2005-2011 were identified. Impedance indices and clinical characteristics were studied. Wilcoxon rank-sum and Spearman correlations were used for comparisons of continuous variables, and chi-square or Fisher’s exact test for categorical variables. RESULTS: Analysis included 38 subjects, aged 2 months to 24 years (median 11 years). The median BMI-LFW% was 25%, 14 (37%) had gastrostomy tubes, and 11 (29%) received overnight continuous feeds. Best previous FEV1% ranged from 28-121% (median 80%) and 25 (66%) were studied during a pulmonary exacerbation. There were 2592 total reflux events recorded of which 1021 (29%) were acid, 1571 (61%) were non-acid, and 946 (36%) reached the proximal lead.
Prevalence of GERD (total reflux episodes >72) was 30%. Only 6 (16%) had an elevated acid exposure time of >4.2%. Reflux-cough correlation >50% was associated with total and proximal reflux episodes (p=0.009, 0.006). There were no differences in any parameter based on age or gender. Patients with gastrostomy or on overnight feeds were more likely to have a lower BMI-WFL% (p=0.05, 0.03) and lower FEV1% (p=0.08, 0.0005). They were not more likely to have increased GER, proximal events, or increased acid exposure time. No impedance index correlated to BMI-WFL%. There was no correlation between FEV1% and total reflux episodes, proximal reflux episodes, or acid exposure time. There was no association between GER and pulmonary exacerbation. SUMMARY: GER does not appear to be more common in those with poorer lung function, admitted for a pulmonary exacerbation, and receiving continuous overnight gastrostomy feeds. No association was found between frequency of reflux episodes, proximal reflux episodes and prolonged acid exposure time and decreased lung function in this cohort.

222* LACTULOSE BREATH TEST GAS PRODUCTION AND CLINICAL CORRELATION IN CHILDHOOD IRRITABLE BOWEL SYNDROME. Bruno P. Champitazi, Erica M. Weidler, Robert Shulman, Pediatrics, Baylor College of Medicine, Houston, TX
In adults with irritable bowel syndrome (IBS), hydrogen and/or methane gas production have been suggested to play a role in symptom genesis. Whether the same is true in children is not clear. The aims of this ongoing study were to determine in children with IBS: 1) the extent of hydrogen and methane production following carbohydrate (lactulose) administration; and 2) the relationships between hydrogen and methane production and clinical symptoms.
Methods: Children, ages 7-18, meeting Rome III criteria for IBS completed a 2-week daily diary capturing the number and severity of abdominal pain episodes, stooling frequency, stool form, and pain-related activity limitation. Subjects were subtyped based on Rome III guidelines. Children then underwent a 3-hr lactulose breath test after an overnight fast. Carmine red was added to the lactulose to measure whole intestinal transit time. Areas under the curve for hydrogen and methane production were calculated.
Results: 29 children were studied, of which 16 (55%) were female. Mean age was 13.3 ± 0.5 (SEM) years; 21 (72%) were White, 4 (14%) Black, 3 (10%) Hispanic, and 1 (3%) Asian. Fifteen (52%) were subclassified as IBS-C, two (7%) as IBS-D, and 12 (41%) as IBS-U. All children produced hydrogen and 13 (45%) produced methane. Hydrogen and methane production did not differ based on IBS subtype. Neither hydrogen nor methane production correlated with age, the number or severity of abdominal pain episodes, number of bowel movements, number of diarrheal episodes or hard bowel movements, longest interval between bowel movements, or abdominal pain-induced interference with activities of daily living. Methane, but not hydrogen production
Results: Twenty-six child/parent pairs were enrolled. Of the children, 20 (77%) were female, and the average age was 14.8 ± 0.4 (SEM) years. The mean number of foods identified by the child as inducing symptoms was 11.5 ± 1.2 (Range: 3-29) and did not differ in number (10.4 ± 1.7) or type from the parent’s assessment. The top foods identified by children as causing symptoms were: spicy foods (n=18), pizza (n=14), cow’s milk (n=14), fried foods (n=13), cheese (n=11), sodas (n=11), salsa (n=10), and ice cream (n=10). Older children (older than 10 years) identified more foods (14.4 ± 1.8 vs. 8.0 ± 1.0; P<0.01) and avoided more foods (11.0 ±1.8 vs. 5.8 ± 1.2; P<0.01). A child’s total number of identified or avoided foods did not correlate with overall QOL score. However, there was a trend for worsening PedsQL GI symptom score with increasing numbers of identified foods (P=0.06) and avoided foods (P=0.09).

Conclusions: 1) Children with FGIDs identify multiple foods as inducing a variety of GI symptoms; 2) Older children identify more foods as inducing symptoms and avoid more foods than younger children; 3) The number of identified foods did not correlate with overall QOL but did tend to correlate with a worsening PedsQL GI symptom score.

224 A MULTI-SUBSTRATE CARBOHYDRATE ELIMINATION DIET DECREASES GASTROINTESTINAL SYMPTOMS IN A SUBPOPULATION OF CHILDREN WITH IRRITABLE BOWEL SYNDROME. Bruno P. Chumpitazi, Erica M. Weidler, Robert J. Shulman, Pediatrics, Baylor College of Medicine, Houston, TX

Multi-substrate carbohydrate elimination diets (MCEDs) may improve gastrointestinal (GI) symptoms in adults with irritable bowel syndrome (IBS). The efficacy of MCEDs has not been studied in childhood IBS. The aims of this ongoing study were to determine in children with IBS the: 1) Efficacy of a MCED in reducing GI symptoms; 2) Clinical and dietary characteristics of those who benefit from a MCED; and 3) Impact of a MCED on overall dietary intake.

Methods: Children, ages 7-18, with Rome III IBS completed a baseline daily pain and stool diary for two week follow-up. Following this, children began a MCED diet for eight days during which they again completed a daily pain and stool diary. A 3-day diet record was completed during the baseline period and during the MCED diet. Resolution of pain was defined as a 75% decrease in both severity and frequency of abdominal pain. Food records were analyzed using Nutritionist Pro (Axxya Systems, Stafford, TX).

Results: Thirty-seven children enrolled (21 female). Mean age was 12.4 ± 0.4 (SEM) years. Seven (19%) of children had resolution of symptoms while on the MCED. Children with resolution of pain were younger (10.4 ± 0.5 years vs. 12.9 ± 0.5 years; P<0.05) but did not otherwise differ at baseline with respect to demographics, body mass index percentage. IBS subtype, or associated IBS symptoms. Children with resolution of pain could not be distinguished from those without resolution based on nutritional intake at baseline or during the MCED. While on the MCED, all children ate fewer kcal (P<0.001), fat (P<0.001), carbohydrates (P<0.001), crude fiber (P<0.02), glucose (P<0.01), fructose (P<0.01), sucrose (P<0.02), and lactose (P<0.001). However, intake of starches increased (P<0.01).

Conclusions: 1) A MCED may be effective in a subpopulation of children with IBS; 2) Those that benefit may be younger but otherwise clinical characteristics and baseline dietary factors do not predict efficacy; 3) A MCED may influence the intake of numerous nutrients beyond only those being restricted.

225 HIGH RESOLUTION ANORECTAL MANOMETRY IN CHILDREN: A MULTIYEAR SINGLE CENTER EXPERIENCE. Bruno P. Chumpitazi, Cynthia Tsai, Pediatrics, Baylor College of Medicine, Houston, TX

High resolution manometry using numerous closely spaced pressure channels, in conjunction with graphic pressure topography plots has been introduced as a new technology. The impact of using high resolution anorectal manometry (HRAM) in children is unknown.

Aims: 1) To determine the indications, and pathologic findings of using HRAM in children; and 2) To determine if HRAM may identify physiologic differences in children with retentive fecal incontinence (RFI) vs. those with constipation without incontinence.

Methods: Review of childhood HRAM evaluations at a single center during 2008-2011. HRAM was performed with eight to ten circumferential 0.6 cm spaced solid-state pressure sensors. A balloon was used for rectal distention with graded distentions used to elicit the rectoanal inhibitory reflex (RAIR). Both line tracings and graphic pressure topography plots (Manoscan, Sierra Scientific Instruments) were used to analyze the data.

Results: 209 children underwent HRAM, of whom 106 (50.7%) were male. The mean age was 6.5 ± 0.3 (SE) years (range 0.1-17.8 years). Indications were 161 (77%) for constipation, 42 (20.1%) for retentive fecal incontinence, and 6 (2.9%) for non-
retentive incontinence. Abnormal findings included lack of a rectoanal inhibitory reflex in 13 (3 new Hirschsprung’s disease (HD), 2 new internal anal sphincter achalasia, 8 previously known HD). Of 124 children formally tested, 56 (45.1%) had dyssynergia. Those with constipation without incontinence vs. those with RFI could not be differentiated on the basis of RAIR threshold, defection dynamics, EAS contraction with RAIR, baseline or squeeze pressure. Children with constipation alone had a non-clinically significant longer sphincter length than those with RFI.

Conclusions: HRAM can be successfully performed in children with defecation disorders with constipation being the most common indication. Pelvic floor dyssynergia is the most commonly identified manometric abnormality. HRAM was unable to physiologically differentiate those with constipation without incontinence versus those with retentive fecal incontinence.

226* ENDOTHELIN B RECEPTOR OVEREXPRESSION INCREASES ENS STEM CELL MARKER EXPRESSION IN GUT CELLS. Cheryl E. Gariepy1,2, Yu-Hwai Tsai3, Naoko Murakami1,3, Molecular and Human Genetics, The Research Institute at Nationwide Children’s Hospital, Columbus, OH; 2University of Michigan, Ann Arbor, MI; 3The Ohio State University, Columbus, OH

ENS stem cells express high levels of the p75 neurotrophin receptor (p75high) and can be isolated by cell sorting. They also express the endothelin B receptor (ETB), one of the genes implicated in Hirschsprung disease. Although some reports suggest that ETB is required for stem cell maintenance, others suggest that it does not prevent differentiation. We hypothesized that ETB overexpression and activation in ENS precursors would increase stem cell numbers and impair their differentiation in culture.

METHODS: We generated bicistronic retroviral expression vectors encoding GFP alone or GFP with ETB. We exposed dissociated embryonic gut cells to retroviruses in the presence or absence of BQ788, a selective ETB antagonist, followed by sorting for P75high. The capacity of GFP+ P75high cells to form multipotent colonies was evaluated. RESULTS: The retroviruses had similar infection efficiency and resulted in gene overexpression in isolated p75high cells. The proportion of p75high cells among cells infected with GFP-ETB retrovirus was higher (2.9±1.31, n=4) than among cells infected with the retrovirus containing only GFP (0.72±0.29, n=4; p<0.02). Culture of GFP-ETB expressing cells in the presence of BQ788 reduced the number of p75high cells (1.4±0.64, n=4; p<0.02). When GFP+ P75high cells were plated and cultured at clonal density, 2.18±1.83% of ETB-overexpressing cells formed multipotent colonies compared to 18.6±2.19% of cells infected with the GFP only vector (p<0.01). CONCLUSIONS: Constitutive ETB overexpression in gut cells increases the number of cells expressing an ENS stem cell marker but also reduces the ability of these cells to form clonal colonies. These findings suggest that ETB signaling may be manipulated to increase ENS stem cell isolation. The suppression of in vitro colony formation by constitutive expression of ETB in P75high cells may be due to alterations in proliferation, survival or cell adhesion characteristics of these cells.

227 RET SIGNALING REDUCES THE NUMBER OF ENS STEM CELLS ISOLATED FROM EMBRYONIC GUT

Cheryl E. Gariepy1,2, Yu-Hwai Tsai3, Naoko Murakami1,3, Molecular and Human Genetics, The Research Institute at Nationwide Children's Hospital, Columbus, OH; 2University of Michigan, Ann Arbor, MI; 3The Ohio State University, Columbus, OH

The RET receptor tyrosine kinase is the major susceptibility gene for Hirschsprung disease, a disorder of gut colonization by neural crest (NC) cells. Migrating NC cells are initially RET+. The RET receptor activates signaling pathways that play roles in NC migration and survival. The RET receptor tyrosine kinase is the major susceptibility gene for Hirschsprung disease, a disorder of gut colonization by neural crest (NC) cells. Migrating NC cells are initially RET+. The RET receptor activates signaling pathways that play roles in NC migration and survival.

METHODS: We generated bicistronic retroviral expression vectors encoding GFP alone or GFP with RET. We exposed dissociated embryonic gut cells to these retroviruses then sorted cells for high expression of p75 (p75high) cells. The capacity of RET+ p75high cells to form multipotent colonies was evaluated. RESULTS: The retroviruses had similar infection efficiency and resulted in gene overexpression in isolated p75high cells. The proportion of p75high cells among cells infected with GFP-RET retrovirus was higher (2.9±1.31, n=4) than among cells infected with the retrovirus containing only GFP (0.72±0.29, n=4; p<0.02). Culture of GFP-RET expressing cells in the presence of BQ788 reduced the number of p75high cells (1.4±0.64, n=4; p<0.02). When GFP+ P75high cells were plated and cultured at clonal density, 2.18±1.83% of ETB-overexpressing cells formed multipotent colonies compared to 18.6±2.19% of cells infected with the GFP only vector (p<0.01). CONCLUSIONS: Constitutive ETB overexpression in gut cells increases the number of cells expressing an ENS stem cell marker but also reduces the ability of these cells to form clonal colonies. These findings suggest that ETB signaling may be manipulated to increase ENS stem cell isolation. The suppression of in vitro colony formation by constitutive expression of ETB in P75high cells may be due to alterations in proliferation, survival or cell adhesion characteristics of these cells.

228 DECISION MAKING DURING THE ENDOSCOPIC EVALUATION OF CHILDREN WITH CHRONIC ABDOMINAL PAIN. Fareded Ahmad1, Thomas Imperiale2, Joseph Fitzgerald1, Steven Steiner3, Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Riley Hospital for Children, Indianapolis, IN; 2Division of Gastroenterology, Indiana university Hospital, Indianapolis, IN

BACKGROUND: The role of endoscopic evaluation in children with Chronic Abdominal Pain (CAP) is not well defined. Recent study showed a 60% change in the management plan based on endoscopy. No guidelines are available regarding biopsy of endoscopically normal-appearing mucosa in this patient population. AIM: 1-To measure the change of management based on endoscopy and biopsy. 2-To measure the efficacy of endoscopy in uncovering clinically significant histopathological abnormalities. METHODS: In this prospective study, we enrolled children, ages 5-18 years, with CAP scheduled for outpatient endoscopic evaluation. We asked the pediatric gastroenterologists to fill out a questionnaire regarding their management plan at three different times of the management process: before endoscopy; after endoscopy and before the biopsy result; and after the biopsy result. RESULTS: Sixty six patients were enrolled; 56(85%) were girls. Mean age was 14.2 years. Forty (61%) patients had esophagogastroduodenoscopy (EGD) and 26 (39%) had EGD and colonoscopy. The pediatric gastroenterologists changed
the management plan in 17 (25%) patients based on the endoscopy findings (16/17 due to EGD, and 1/17 due to colonoscopy). The biopsy led to a management change in 14 (21%) patients with normal endoscopy (eight due to histological abnormality, and six due to lactase deficiency). Using the biopsy as the gold standard, endoscopic visualization had a sensitivity of 62%, specificity 84%, positive predictive value 55%, and negative predictive value of 88% in uncovering histopathological abnormality. CONCLUSIONS: Endoscopy, primarily EGD, leads to change in the management of children with CAP. In this patient population, biopsy of endoscopically normal appearing mucosa adds only a small incremental yield in uncovering a histopathological abnormality.

229 IMPACT OF ENDOSCOPIC EVALUATION ON THE QUALITY OF LIFE OF CHILDREN WITH CHRONIC ABDOMINAL PAIN. Fareed Ahmad1, Thomas Imperiale2, Joseph Fitzgerald1, Steven Steiner1, 1Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Riley Hospital for Children, Indianapolis, IN; 2Division of Gastroenterology, Indiana University Hospital, Indianapolis, IN

BACKGROUND: Multiple methods of evaluation are used in the diagnostic process of children with Chronic Abdominal Pain (CAP), including endoscopy. Due to the absence of well defined end points in the treatment process, patient reported outcomes, including Quality of Life (QoL) measures, are used as tools to measure the response to treatment. AIMS: 1- To measure the QoL for children with CAP before and after endoscopic evaluation. 2- To identify the factors responsible for the change in QoL, as perceived by the parents and the treating gastroenterologist. METHODS: in this prospective study, we enrolled children, ages 5 - 18 years, with CAP scheduled for outpatient endoscopic evaluation. The parents were asked to fill out a generic QoL questionnaire (PedsQL™ - Pediatric Quality of Life Inventory), on behalf of their children, on the day of endoscopy, and two months after the endoscopy. The parents and the treating gastroenterologists were asked also to identify the most important factors contributing to change in the QoL in two months following the endoscopy. RESULTS: Twenty patients were enrolled; 17 (85%) were girls. Mean age was 13.3 years. Mean QoL before endoscopy was 65.06 +/- 18.1; It significantly increased to 76.97 +/- 18.4 two months following the endoscopy (P = 0.045). Parents rated endoscopy (30%), clinic visit evaluation (25%), and none (20%) as the most important factors in management. The treating gastroenterologists rated clinic visit evaluation (40%), endoscopy (40%), and the combination of clinic visit evaluation, endoscopy, and blood tests (18%) as the most important factors in the management. CONCLUSIONS: QoL of Children with CAP improved two months after the endoscopic evaluation. Parents perceive endoscopy as the most important factor in management, whereas, the treating gastroenterologists perceive both of the clinic evaluation and endoscopy to be the most important factors in management.

230 ASSOCIATION OF RECURRENT ABDOMINAL PAIN, DEPRESSION AND ANXIETY DISORDERS IN SCHOOL-AGED CHILDREN AND ADOLESCENTS. Guillermina Gomez-Navarro, Maria del Carmen Bojorquez-Ramos Gastroenterologia y Nutricion, Hospital de Pediatría Centro Medico Nacional de Occidente Instituto Mexicano del Seguro Social, Guadalajara, Mexico

Objectives: To establish an association between recurrent abdominal pain (RAP), depression and anxiety disorders in school-aged children and adolescents by using self-report questionnaires; investigate the main causes of RAP, both organic and functional, in a Mexican third-level hospital and classify functional RAP diagnosis according to the pediatric Rome III criteria. Patients and methods: We included children diagnosed with RAP, ages 6 to 15 years old, from January 2009 to June 2010. In this cross-sectional study, selected patients were asked to answer the Kovacs’ Child Depression Inventory and the Screen for Child Anxiety Related Emotional Disorders. Based on the clinical data, children were classified as either having organic of functional RAP and, based on the scores of the self-report questionnaires, were then evaluated for an association with anxiety disorder or depression.

Results and discussion: A total of 35 patients were included, 23 of them were female and 20 were classified as having functional RAP. Irritable bowel syndrome was the most common diagnosis in patients with functional RAP, which was present in 13 patients (65%). Gastro-esophageal reflux disease was the most common diagnosis in patients with organic RAP, being present in 6 patients (40%) followed closely by Helicobacter pylori-associated gastritis which was diagnosed in 5 patients (33%). 17 RAP patients had anxiety disorder (48.6%) and 16 had depression (45.7%).

Conclusions: The main finding of this study was that among RAP patients, both organic and functional, an association with depression and anxiety disorder was found. This implies that all RAP patients should be studied integrally, not only from a physically but also from a psychological basis in order to improve understanding and treatment of this gastrointestinal disorder.

231 DIAGNOSTIC YIELD OF WIRELESS MOTILITY CAPSULE AND ANTRODUODENAL MANOMETRY IN PEDIATRIC PATIENTS WITH UPPER GI SYMPTOMS. Jaime Belkind-Gerson1, Alex D. Green2, Brian C. Surjanahata2, Braden Kuo1, Carlo Di Lorenzo2, 1Massachusetts General Hospital, Boston, MA; 2Nationwide Children’s Hospital, Columbus, OH

Introduction: Antroduodenal Manometry (ADM) and Wireless Motility Capsule (WMC), a non-invasive measure of gastrointestinal transit and contractility, are used to evaluate GI motility. These techniques have not been compared directly in symptomatic patients.

Aims: Comparison of ADM and WMC prospectively in pediatric patients with UGI symptoms.

Methods: ADM: 4 hr fasting and 1 hr post-prandial. WMC: according to published standards. A gastric emptying time (GET) of ≤5 hr was considered nl, 5-12 hr mild gastroparesis (mGP) and >12 hr severe gastroparesis (sGP). Contractility. Area Under the Curve and Motility Index were calculated 1 hr before (Gastric contractility parameters: Gc) and 1 hr after (Small Bowel contractility: Sbc) gastric emptying.

Results: 20 patients completed both studies (16 F/4 M, age 9-17), 6 had nl GET by WMC and all had nl ADM, but 2 had abnl Gc/SBc and 1 isolated SBc abnl. There were 4 patients with mGP, all with nl Gc and SBc, but by ADM 3 had: hyperactive
motility, mild motility disorder and a pattern consistent with a neuropathy. In 10 patients with sGP by WMC, we could evaluate Gc/SBc in 7 (missing WMC data in 3); 5 had abnl Gc and 1 SBc. Only 2 with sGP had nl Gc/SBc, the ADM was nl in these 2. In the 10 patients with sGP by WMC, the ADM was abnl in only 1: antral hypomotility. Overall in the 20 pts, 20% of ADM studies were abnl. 50% of WMC studies had abnl Gastric/SB contractility (diff. in diagnostic yield p<0.01), 70% of WMC studies had abnl GET data (p<0.01), 85% of WMC studies had both abnl contractility/GET data (p<0.01). By ADM, 6 pts had rumination without an additional motility disorder.

Conclusions: Even in cases with nl ADM and GET, contractility abnormalities by WMC were noted. In cases of sGP, UGI contractility abnormalities by WMC were frequent (75%) despite the majority being nl by ADM. Rumination (the most common diagnosis by ADM in this series) has an increased prevalence (50%) of UGI contractile abnormalities revealed by WMC.

232 METABOLIC AND IMAGING ABNORMALITIES IN THE EVALUATION OF CHILDREN WITH CYCLIC VOMITING SYNDROME. Jonathan Moses, Ashley Keilman, Sarah Worley, A. David Rothen, Samit Parikh, Kadakkal Radhakrishnan, The Cleveland Clinic, Cleveland, OH

Cyclic vomiting syndrome (CVS) is a diagnosis made by exclusion of other organic diseases, which can lead to an extensive amount of testing. It has been suggested that patients with CVS can have mitochondrial dysfunction. The aim of the study was to examine the evaluation of our CVS patients as well as to determine whether they had associated, undiagnosed metabolic abnormalities.

Methods: The study included 106 consecutive patients less than 21 years of age at diagnosis. Information regarding medical history, laboratory and imaging studies was collected. Metabolic studies in serum and urine were obtained when patients were well and when patients were in a vomiting cycle, which included serum amino acids, urine organic acids, and acylcarnitine profile.

Results: The mean age at diagnosis was 8.9 ± 5.0 years. The patient population was 57% male and 77% Caucasian. Neuroimaging showed previously unknown intra-cranial abnormalities in less than 10% of patients, none of which explained the vomiting symptoms. Abdominal ultrasounds (US) showed abnormalities in 15% of patients during an acute episode and 7% of patients when well. The most common finding was renal abnormalities. 61 patients had an upper gastrointestinal series (UGI) done, all of which were normal. 34% of patients completed metabolic testing when well, of which 28% had findings suggestive of mitochondrial dysfunction. 37% of patients completed metabolic testing with an acute episode, of which 20% had findings suggestive of mitochondrial dysfunction. The most common finding was increased alanine.

Conclusions: The initial work-up of these patients could potentially be more individualized in regards to neuroimaging, abdominal US, and UGI. Almost one-third of our patients had abnormalities in blood and urine suggesting mitochondrial dysfunction. Additional and more detailed metabolic analysis is needed to further delineate these abnormalities.

233 CLINICAL PREDICTORS OF CROHN’S DISEASE IN PEDIATRIC PATIENTS WITH ABDOMINAL PAIN. Khalil El-Chammas1, Angela Majeskie1, Chia-Cheng Chen2, Pippa Simpson2, Manu Sood1, Adrian Miranda1

1Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI; 2Quantitative Health Sciences, Medical College of Wisconsin, Milwaukee, WI

Introduction: In patients with chronic abdominal pain (CAP), care providers often feel uncomfortable diagnosing a functional gastrointestinal disorder (FGID) without excluding an organic cause. In children presenting with CAP, Crohn’s disease (CD) is often in the differential diagnosis; however, studies investigating predictors are lacking. Aim: To determine predictors of CD in pediatric patients with CAP. Methods: All patients prospectively completed a detailed demographic, history and symptom questionnaire and the data were analyzed retrospectively from systematic chart reviews of patients seen in outpatient Pediatric Gastroenterology between 2005 and 2008. Patients included those with CD, based on histology, or with FGID, based on Rome III criteria. Predictors of CD were identified with tree analysis using SPSS. Results: A total of 604 patients (128 with CD, 476 with FGID) were studied and data of 78 variables was collected. The age distributions of males with CD and FGID were similar. Of 29 predictors, anemia and hematocrit were most predictive of CD (Receiver Operating Characteristic area-under-the-curve of 0.85) while other red flags such as wake from sleep, pain location, and fever were not. Patients with no anemia and no hematocrit were unlikely to have CD (23/366), but patients with anemia were likely to have CD (56/70). Compared with FGID patients, those with CD were less likely to have social stressors, emesis, or headaches (p<0.001). Those with CD were more likely to have hematocrit, weight loss, difficulty gaining weight, anemia, or low albumin (p<0.001). Patients with FGID were more likely to have a family history of irritable bowel syndrome (p=0.03), gastroesophageal reflux (p=0.044) or constipation (p=0.032). Conclusion: In pediatric patients presenting with CAP, anemia and hematocrit are most predictive of CD and may be useful for identifying patients who require additional evaluation prior to diagnosing a FGID.

234 HIGH RESOLUTION MANOMETRY: USING PRESSURE TOPOGRAPHY PLOTS TO EVALUATE PEDIATRIC COLON MOTILITY. Khalil El-Chammas, Neelosh Tipnis, Manu Sood, Medical College of Wisconsin, Milwaukee, WI

Introduction: Displaying high resolution manometry (HRM) data as pressure topography plots (PTP) has improved our understanding of esophageal motility disorders. Aim: To evaluate the use of HRM to study colon motility and interpreting colon motility data displayed as PTP. Method: We used HRM (36 sensors) and water perfused manometry (WPM) (8 sensors) to evaluate fasting, postprandial and post-bisacodyl colon motility. HRM data was converted to PTP and WPM data was displayed as conventional line plots (CLP). We evaluated 30 HRM and 20 WPM studies for high amplitude propagating contractions (HAPCs), gastrocolonic response (GCR) and other clinically relevant findings. Two gastroenterologists independently reported 10 studies with data displayed as CLP (8 sensors) and PTP (36 sensors) for intra and inter-observer variability. The percentage agreements and kappa values were calculated using SPSS software. Results: The median (range) age of subjects who underwent...
HRM and WPM was 7.7 (21) and 12.2 (17) years respectively. The median (range) fluoroscopy time for catheter placement for HRM and WPM studies was 1.2 (7) and 1.9 (10) minutes respectively. Using HRM, rectal propagating contractions and anal pressure changes could be studied in addition to colon motility in 7 subjects; this information was not available using WPM. Percentage agreements (kappa values) for interpreting data expressed as CLP and PTP are shown in Table 1. Conclusions: HAPCs and GCR are easily recognized when HRM data is expressed as PTP. Intra and inter-observer agreement comparing data expressed as CLP and PTP was good to excellent. HRM provides additional information regarding rectal propagating contractions and anal pressure changes in addition to colon motility data.

Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Intra-observer variability</th>
<th>Inter-observer variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting HAPCs</td>
<td>Observer 1</td>
<td>Observer 2</td>
</tr>
<tr>
<td></td>
<td>100% (1.00)</td>
<td>100% (1.00)</td>
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<tr>
<td>Post-prandial HAPCs</td>
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<td>100% (0.09)</td>
</tr>
<tr>
<td>GCR</td>
<td>67% (1.00)</td>
<td>60% (1.00)</td>
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<tr>
<td>Bisacodyl-induced HAPCs</td>
<td>100% (1.00)</td>
<td>90% (n/a)</td>
</tr>
<tr>
<td>Study conclusion</td>
<td>80% (0.62)</td>
<td>60% (0.09)</td>
</tr>
</tbody>
</table>

235 CYPROHEPTADINE IN THE TREATMENT OF DYSPEPSIA SYMPTOMS IN CHILDREN. Leonel Rodriguez1, Juan J. Diaz2, Samuel Nurko1, 1Gastroenterology, Children's Hospital Boston, Boston, MA; 2Pediatrics, Hospital Universitario Central de Asturias, Oviedo, Spain

Cyproheptadine is a serotonin receptor antagonist that may have an effect on gastric dysfunction. Objective: Describe use of cyproheptadine in the management of dyspepsia symptoms in children. Methods: Retrospective review of children treated with cyproheptadine for dyspepsia symptoms. Exclusion criteria: children receiving cyproheptadine for appetite stimulation, migraine headaches, cyclic vomiting syndrome and allergy. Results: A total of 65 children were included, mean age was 10 years, 45 (69%) were female. Mean dose was 0.5mg/kg/dose for a mean duration of 32 weeks (range 1-198 weeks) in cycles to avoid tolerance. Symptoms prompting therapy were nausea in 21, vomiting in 21, abdominal pain in 10, retching in 9 and early satiety in 4. Gastric emptying study was performed in 39 subjects, median emptying at 60 minutes was 43%. Antroduodenal manometry was done in 18 patients, showing antral hypomotility in 11. Favorable response was reported in 50 (76.9%) patients as follows: mild response (requiring further therapies) in 21, significant improvement (no further therapy required but still on cyproheptadine) in 21 and resolution (cyproheptadine successfully stopped) in 8. We found that age (p=0.048), weight (p=0.008) and duration of therapy (p=0.001) were individually associated with a favorable response unlike results of gastric emptying study, antroduodenal manometry and total dose and dose per kg of weight given. Multivariate analysis demonstrated younger age (p=0.038) is the only predictor of response unlike gender, idiopathic diagnosis, gastric emptying study, antroduodenal manometry results and dose of medication given. Side effects were present in 15 (23%) children including somnolence (6), irritability (4), increase appetite (4) and abdominal pain (1) and medication was stopped only in 1 child due to irritability. We also found a higher rate of side effects associated with higher wt (p=0.020). Conclusions: Cyproheptadine is a safe and effective therapy for dyspepsia symptoms in children. Younger children seem to respond better.

236 METABOLOMICS AND COLONIC MOTILITY IN CHILDREN WITH CONSTIPATION. Leonel Rodriguez1, Samuel Nurko2, Jessica Larosa1, Robert Gerszten2, Allan Goldstein1, 1Gastroenterology, Children's Hospital Boston, Boston, MA; 2Pediatrics, Massachusetts General Hospital, Boston, MA; 3Surgery, Massachusetts General Hospital, Boston, MA

Constipation may be associated with abnormal metabolic responses. Objective: Evaluate the serum metabolomic profile of constipated children during the performance of colon motility studies. Methods: Prospective study of children undergoing colon motility (CM) study for the evaluation of intractable constipation. CM was divided in 3 periods: 1 hour of fasting, meal and 1 hour for post-prandial evaluation and bisacodyl challenge followed by 1 hour of evaluation. Serum was obtained at 6 points in time during the CM: 1) at baseline (fasting early in the morning), 2) 10 minutes after a meal challenge, 3) 30 minutes after meal challenge, 4) 59 minutes after meal challenge and 1 minute before bisacodyl challenge, 5) 15 minutes after bisacodyl challenge and 6) 45 minutes after bisacodyl challenge. Serum was analyzed for a profile of 84 aminoacids and peptides. Results: a total of 20 patients were included, mean age was 12y and 14 were female. Overall analysis showed significant changes in levels in 62 metabolites throughout the study. Metabolites associated to changes only with a meal included 5-HIIA and 5-hydroxy-tryptophane. Metabolites associated to change only after bisacodyl included: adenosyl, methylhidroxido, NMMA and thyroxine. The rest were associated to changes after both. Patients with abnormal CM had a significantly lower baseline level of serotonin, 5-hydroxy-tryptophane, dymethylglicine, adenosine and methyl-histamine. Also importantly, patients with abnormal manometry showed significantly higher levels for glycine, asparagus, citruline and choline and lower levels of cystamine, methyl-histamine and histamine for the meal-associated times. In regards to the times associated to response to bisacodyl challenge, patients with abnormal CM had higher levels of glycine, alanine, glutamine and xanthosine. Conclusions: In this preliminary report of the metabolomic profile of constipated children we found significant changes that may help understand the pathophysiology of constipation.
237 AZITHROMYCIN STIMULATES GASTRIC MOTILITY DURING ANTRODUODENAL MOTILITY TEST IN CHILDREN. Leonel Rodriguez, Alejandro Flores, Gastroenterology, Children’s Hospital Boston, Boston, MA; Pediatrics, Floating Hospital for Children, Boston, MA

Background: Antroduodenal manometry is used to evaluate patients with upper gastrointestinal motility and functional disorders. The study includes a challenge with erythromycin to stimulate antral and duodenal motility. Some have suggested the use of amoxicillin/clavulanic acid as a substitute. We evaluated the utility of azithromycin as a substitute to erythromycin. Objective: report the effect of azithromycin on antroduodenal motility. Methods: retrospective review of antroduodenal manometry studies performed using intravenous erythromycin during a shortage of intravenous erythromycin. The antroduodenal motility study was divided in 4 periods: fasting (2 hours), azithromycin, octreotide and meal challenge (1 hour post-prandial evaluation). Antroduodenal motility studies with azithromycin were compared to studies performed using erythromycin on age and gender matched subjects. Results: 6 patients were included, mean age was 12.5 years (1-21) and 5 were female. We found that all patients receiving azithromycin had a normal antral response, 2 patients had abnormal antrum motility during fasting and all patients lacked an antral response to a meal. Interestingly, only one patient showed increased small bowel motility after challenge with azithromycin in comparison to the matched subjects receiving erythromycin. One patient reported nausea and abdominal pain during the azithromycin infusion. Conclusions: Azithromycin is a safe and effective alternative to erythromycin to evaluate gastric motility during the ADM.

238 A PILOT STUDY OF S-ADENOSYL METHIONINE FOR THE TREATMENT OF FUNCTIONAL ABDOMINAL PAIN IN CHILDREN. Lillian J. Choi, Jeanie S. Huang, Pediatric, University of California San Diego, San Diego, CA; Gastroenterology, Rady Children’s Hospital San Diego, San Diego, CA

Background: Functional abdominal pain (FAP) is one of the most common functional gastrointestinal disorders in children. Tricyclic antidepressants are widely used to treat FAP but have been associated with an increased risk of suicidal ideation and the benefits of treatment are often limited by side effects. S-adenosyl methionine (SAM-e) is a dietary supplement, which has efficacy as a treatment for both depression and chronic pain.

Methods: We performed an open-label, dose-escalation trial of oral SAM-e among children and adolescents with FAP. Measurement visits occurred at baseline, 2 weeks, 1 month, and 2 months. Self-reports of pain and quality of life were the primary outcomes. Participants were also monitored for potential toxicities (liver function tests and evaluations for mania and depression) throughout the trial. Repeated measures analyses were used to analyze the data.

Results: We enrolled 8 subjects with a median and mean age of 14 years. We demonstrated improvement in self-pain reports over the 2-month follow-up period (p=0.004). Liver function tests and psychological assessments for mania and depression did not change over the study period.

Conclusions: Oral SAM-e demonstrates promise in reducing abdominal pain among children with FAP. Associated toxicities were minimal in comparison to that reported in prior trials with antidepressants. Larger, placebo-controlled trials are needed to support our initial findings.

Study Measures Over Time

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline</th>
<th>2 weeks</th>
<th>1 month</th>
<th>2 months</th>
<th>p-value*</th>
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<tr>
<td>Child FACES Pain scale</td>
<td>4(0)</td>
<td>4(1)</td>
<td>3(0)</td>
<td>3(0)</td>
<td>0.004</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>23(4)</td>
<td>25(16)</td>
<td>23(4)</td>
<td>21(3)</td>
<td>0.656</td>
</tr>
<tr>
<td>ALT (IU/L) Score</td>
<td>17(7)</td>
<td>34(49)</td>
<td>21(12)</td>
<td>16(6)</td>
<td>0.361</td>
</tr>
<tr>
<td>Children’s Depression Scale scores</td>
<td>21(3)</td>
<td>18(6)</td>
<td>20(3)</td>
<td>19(4)</td>
<td>0.783</td>
</tr>
<tr>
<td>Young’s Mania Scale scores</td>
<td>0(1)</td>
<td>1(1)</td>
<td>1(2)</td>
<td>0.5(1)</td>
<td>0.150</td>
</tr>
</tbody>
</table>

Values are expressed as mean (standard deviation). * p-value from repeated measures analyses.


1 Pediatric Gastroenterology, School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil; 2 Student, School of Medicine, Federal University of Minas Gerais, Belo Horizonte, Brazil; 3 Epidemiology, IPSEMG, Belo Horizonte, Brazil

Goal: Treat constipated pediatric patients with polyethylene glycol (PEG) 4000 electrolyte-free(PEG-EF). Method: Analyze clinical parameters at two-time points of a prospective follow-up study protocol for constipated patients treated with PEG-EF at a tertiary Brazilian Public Health Service (BPHS). Rome criteria and the Bristol Stool Form Scale (BSFS) were applied. Results: 97 constipated patients were initially included. 34 patients (35%) were excluded: lost follow-up appointment (22/97); refused to use PEG (8/97); and interrupted PEG (12/97) due to cost (6/12), cutaneous rash (1/12) or unknown reasons (5/12). Comparing data from before and after treatment (mean time of 42.3 ± 34.1 days), respectively, 63 patients (64.9%) showed significant reduction of straining (70% vs. 24%, p<0.001), painful defecation (57% vs. 14%, p<0.001), fecal incontinence (8.0 ± 8.9 vs. 4.7 ± 6.8 events/wk., p<0.001) and retentive behavior (60% vs. 22 %, p<0.001). Stool frequency (3 ± 3.6 vs. 7.0 ± 6.1/wk., p<0.001) and consistency (BSFS was type 4 in 24.2% vs. 62.9%, p<0.0001) improved. After an average follow-up of 207 days, data from 30/63 patients was compared with their previous evaluation, respectively, retentive behavior (45.8% vs. 8.3%,p=0.004) and fecal incontinence (8.4 ± 86 vs. 4.3 ± 6.7 events/wk., p<0.001) showed significant decrease but painful defecation (30% vs. 13.3%, p=0.063) and straining (25% vs.10%, p=0.25) did not. There was improvement of the BSFS (27.6% vs. 58.6%,p=0.022), but stool frequency was stable (3.7 ± 3.3 vs. 7.3 ± 5.0,p=0.001). PEG-EF's average dose was...
240 CHILDREN WITH FECAL INCONTINENCE HAVE WORSE HEALTH RELATED QUALITY OF LIFE COMPARED TO CHILDREN WITH CONSTIPATION ALONE. Muna R. Sood1, Suzanne Magie2, Carlo DiLorenzo2, Sam Nurko1, Rina Sanghavi1, Pippa Simpson1, Anand Ponnambalam1, Margo Kinservik1, Alan H. Silverman1

1Medical College of Wisconsin, Milwaukee, WI; 2Nationwide Children’s Hospital, Columbus, OH; 3Children Hospital of Boston, Boston, MA; 4UT Southwestern Medical Center, Dallas, TX; 5University of South Alabama Children’s and Women’s Hospital, Mobile, AL

Introduction: Studies have reported sub-optimal health related quality of life (HRQOL) in children with constipation. The aim of this prospective study was to compare the HRQOL in children with constipation alone (CA) or constipation and fecal incontinence (CFI).

Method: We prospectively recruited 170 children with constipation between 2-18 yrs of age. All children met the Rome III criteria for the diagnosis of constipation. All parents completed a demographics questionnaire, PedsQL (Generic and Family Impact Modules), the Pediatric Symptom Checklist (parent report). The study was approved by IRBs of participating centers. Results: There were 72 children with CA, median (range) age 7.4 (2 to 17) years (44 females) and, 98 children with CFI, median (range) age 7.4 (4.1 to 17) years (28 females). There were significantly more males in the CFI group (p<0.001). Children with CFI scored significantly worse on social functioning (p=0.015) and psychosocial domains (p<0.05) compared to children with CA. As a group parents of children with CFI reported that their child was more likely to get into trouble with the teachers, less interested in making friends and got into fights more often compared to children with CA (p<0.05). Children with CFI had lower self-esteem compared to children with CA (p<0.05). Conclusion: Children with CFI have lower HRQOL compared to children with CA. Fecal incontinence more severely affects the social and psychosocial well being of the affected child. Strategies to improve fecal incontinence in children with constipation are likely to result in improved HRQOL. However, given the relative increased risk for psychosocial maladjustment consultation with appropriate mental health services may be indicated.

(Support provided by Takeda Pharmaceuticals North America, Inc.)

241 PATHOLOGY OF COLONS RESECTED FROM ANORECTAL MALFORMATION PATIENTS FOR CHRONIC UNMANAGEABLE CONSTIPATION. Marcia F. Torres2,3, Andrea Bischoff, Alberto Penâ1, Marc A. Levitt2, Rosalia F. Salazar2, Margaret H. Collins2,1Pediatric Gastroenterology, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; 2Colorectal Center for Children Department of Surgery, Cincinnati Children’s and Hospital Medical Center, Cincinnati, OH; 3Surgery, Centro Colorectal de Puebla, Mexico, Mexico; 4Pathology, Cincinnati Children's and Hospital Medical Center, Cincinnati, OH

Colonic dysmotility (CD), a debilitating disease, may require surgical therapy. CD may be a consequence of myopathy and neuropathy but often is idiopathic. The colon histology of patients with anorectal malformation (ARM) and CD has not been well described. Objective: Describe the histopathology of colonic specimens from patients with ARM who required surgery for unmanageable CD. Methods: H&E and immunohistochemical stained slides of colonic specimens and medical records of patients operated at The Colorectal Center for Children between 2005 and 2011 were reviewed retrospectively. Results and discussion: All patients had their ARM repaired; as part of their malformation, 5 patients had rectal-perineal fistula, 5 recto-vestibular, 3 recto-prostatic, 1 recto-urethral, and 2 cloacae. All specimens from 9 boys and 7 girls (2-12 y) have abnormal findings, the most frequent being nerve hyperplasia and large ganglion cell clusters (10/16), eosinophilic inflammation in the muscularis propria and myenteric plexus (10/16), and muscularis propria hypertrophy (8/16). Other findings include displacement of myenteric plexus (3/16), accessory smooth muscle layers (3/16), large gaps in the muscularis propria containing fat (2/16) and decreased Cajal cells (2/9). These data document significant structural abnormalities in the colon of ARM patients with CD, and some may represent maldevelopment. The importance of these findings in CD pathogenesis in ARM patients should be explored. The eosinophilic inflammation in the muscularis propria and myenteric plexus identified (67% of cases) could be a consequence of prior surgery, chronic constipation, or other. We speculate that the constipation could improve in these patients with elimination diet or anti-inflammatory medications.

242 EFFECTS OF NUTRITIONAL REHABILITATION ON GASTRIC MOTILITY AND SOMATIZATION IN ANOREXIA. Maria E. Perez, Brian Coley, Wallace Crandall, Carlo Di Lorenzo, Terrill Bravender, Nationwide Children's Hospital, Columbus, OH

Gastrointestinal disturbances have been well documented in adults with anorexia nervosa (A), but there is little data in pediatrics. This prospective study examined (1) differences in gastric motility in A before and after nutritional rehabilitation compared to controls (C), and (2) differences in self-reporting of somatic complaints, anxiety symptoms and functional gastrointestinal disorders (FGIDs).

Methods: 16 A patients (mean 16 yrs) undergoing nutritional rehabilitation and 22 C (mean 17 yrs) were enrolled. Patients underwent an ultrasound surrounding a liquid meal to obtain gastric measurements (T1). They completed the Children’s Somatization Inventory (CSI), the Screen for Child Anxiety-Related Emotional Disorders (SCARED), and the Questionnaire on Pediatric Gastrointestinal Symptoms- Rome III Version. All testing was repeated 3-4 months later (T2).

Results: The two groups had similar demographics. Initial BMI was lower in A (p=0.0006), and improved over time (p=0.012). Max post-prandial antral diameter was greater in C compared to A (p=0.008). While C had similar results at T2, A had an increase in max post prandial diameter at T2 (p= 0.009). There was no difference in residual gastric volume (RV) between the 2 groups at either time point. Initial CSI scores were higher in A vs C (p= 0.0001), including higher scores for nausea (p=0.0007), constipation (p=0.0004), diarrhea (p= 0.02), abdominal pain (p< 0.0001), bloating (p< 0.0001), and “food making you sick”
understanding or completing the QPGS questionnaire was then presented through Power Point to 406 children in Pasto, who were asked to report difficulties in understanding two of 12) from Pasto (population 400,000) and 17 children (mean age 14) from Cali (population 2,207,994) participated. Focus groups: A bilingual translation of the QPGS RIII into Spanish was performed by 7 children (Pasto) and 17 children (Cali), who expressed difficulties in understanding the questionnaire and referenced several criteria for FGIDs (p=0.003), and this improved over time.

Conclusions: Adolescents with A have impaired gastric accommodation compared to C which improves after nutritional rehabilitation, but they do not have delayed gastric emptying. Those with A have more somatic complaints and meet more criteria for anxiety disorders and FGIDs. Somatization improves after nutritional rehabilitation and FGIDs become less common, but symptoms of anxiety persist.

243 ABDOMINAL PAIN AND CONSTIPATION OUTPATIENT VISITS DURING MILITARY DEPLOYMENTS IN CHILDREN AGED 3-8 YEARS OLD. Mazen I. Abbas1, Cade Nylund2, Matilda Eide2, Elizabeth Hisle-Gorman2, Gregory Gorman1, Pediatrics, Uniformed Services University of the Health Sciences., Bethesda, MD; 2 School of Social Work, University of Maryland, Baltimore, MD

Children of military personnel face an increase in stress when a parent deploys. Functional gastrointestinal disorders can be provoked or exacerbated during times of stress. Functional abdominal pain and constipation are the two most common reported functional gastrointestinal disorders in children. We aimed to determine the effect of parent deployment on abdominal pain/constipation visits in children aged 3-8 years. Methods: Retrospective cohort of all outpatient claims data for military and civilian pediatric outpatient visits collected from the TriCare database. Results: Records of children aged 3-8 years old of active-duty personnel during 2006-2007 were linked with their parent’s deployment records obtained from the Defense Manpower Data Center. Abdominal pain and constipation visits were identified by ICD-9 codes. Results: 642,397 children aged 3-8 years and 442,722 military parents were included. There were 1,050,000 person-years with 95,796 abdominal pain and constipation health visits. The unadjusted IRR of abdominal pain and constipation visits for children with a deployed parent compared to when a parent was home was 1.25 [95% CI 1.23-1.27]. Attributable rate differences to deployment were 2.2 extra visits per 100 patient-years. Increases in all abdominal pain/constipation visits were noted during deployments if the parent was married, the child was older or the military parent was male.

Conclusion: Abdominal pain and constipation outpatient coded visits had an overall increase by 25% in children when a military parent deploys. These results are in line with a previous deployment data that noted an increase in pediatric behavioral health visits. Additional studies are warranted to evaluate the effect of deployment on functional gastrointestinal disorder especially in older children. Increased screening of these disorders are warranted when a child’s parent is deployed.

244 ABDOMINAL PAIN AND FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN WITH CELIAC DISEASE. Miguel Saps1, Papa Adams1, Diana Nichols-Vinueza2, 1 Children’s Memorial Hospital, Chicago, IL; 2 Universidad del Valle, Cali, Colombia

Celiac disease (CD) and abdominal pain-associated functional gastrointestinal disorders (AP-FGIDs) including IBS are common in adults and children. Symptoms of CD and AP-FGIDs frequently overlap. Studies on prevalence of CD in IBS have shown controversial results (studies showed an association and others did not). Children with immune conditions affecting the intestine have a higher risk of developing AP and FGIDs. Intestinal lymphocytes are common in CD. Aims: Assess whether patients with CD are more likely to develop FGIDs in long-term follow up than controls. Methods: Data of children (3-22 years of age) with CD diagnosed at Children’s Memorial Hospital, 2000-2010 was obtained. Parents of the children were contacted at least 6 months after the diagnosis of CD. The parents were asked to complete the Rome III Diagnostic Questionnaire for the Pediatric Functional GI Disorders (QPGS). Due to similar genetic/environmental background, the closest sibling of the same gender without history of CD and negative EGD or TTG was selected as control. If no sibling of the same gender existed, the next child in kinship selected as control. Children with abdominal pain (AP) were diagnosed with (QPGS) parent-report form. Sample size calculation: 44 patients in each arm (unidirectional alpha of 0.05, power of 0.80). Significance between groups was evaluated using relative risk and Fischer exact tests. 45 cases (mean 11.2 years, 20 males) and 45 controls (mean 11.5 years, 20 males) were enrolled. Results: Mean interval since the time of diagnosis of CD was 8.14 years (0-14 years). 22% of patients had AP at the time of diagnosis of CD. 12/45 (26.6%) of patients and 9/45 (20%) controls had AP at the time of study (p=0.6). 9 children (20%) in the CD group were diagnosed with various FGIDs: IBS in 33%, Functional dyspepsia in 22%, abdominal migraine (AM) in 22% and FAP in 22%; while children in the control group were diagnosed with: FAP in 50%, IBS in 33% and AM in 17%. Conclusion: CD and controls had similar risk of AP and FGIDs at diagnosis and follow-up.

245 SPANISH VERSION OF THE QUESTIONNAIRE ON PEDIATRIC GASTROINTESTINAL SYMPTOMS: ROME III (QPGS-RIII). Carlos A. Velasco1, Diana Nichols-Vinueza2, Miguel Saps1, 1 Children’s Memorial Hospital, Chicago, IL; 2 Universidad del Valle, Cali, Colombia

Functional gastrointestinal disorders (FGIDs) are common in children. Diagnosis of FGIDs is based on the Rome criteria. The QPGS-RIII is a validated questionnaire designed to facilitate the diagnosis of FGIDs in children and adolescents according to the current version of the Rome criteria. QPGS-RIII has been translated to various languages but was not translated into Spanish. Aim - Translate the English QPGS-RIII into Spanish. Methods - QPGS-RIII version was translated into Spanish by 2 bilingual researchers (senior medical student: DNV, and pediatric gastroenterologist: CV). To verify the accuracy of this translation, 3 focus groups of children from a middle sized and a large city of Colombia reviewed the Spanish version. 413 children (mean age 12) from Pasto (population 400,000) and 17 children (mean age 14) from Cali (population 2,207,994) participated. Focus groups: First, researchers presented QPGS-RIII translated version to 7 children (Pasto) and 17 children (Cali), who expressed difficulties understanding two of the words in the questionnaire that were then changed. Second, the modified Spanish version of the questionnaire was then presented through Power Point to 406 children in Pasto, who were asked to report difficulties in understanding or completing the QPGS-RIII. Children did not report any difficulties. Finally, the revised Spanish version of the
246 FIRST PROSPECTIVE STUDY OF FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS) IN COLOMBIA. Miguel Saps¹, Diana Nichols-Vinueza², Carlos A. Velasco³, ¹Children’s Memorial Hospital, Chicago, IL; ²Universidad del Valle, Cali, Colombia

Functional gastrointestinal disorders (FGIDs) are common. Aim- Follow-up of gastrointestinal symptoms (GS) in school children with and without FGIDs in Colombia. Methods- Prospective cohort study. 3 schools: 1 public (PU), 2 private (PR) of Pasto. Prevalence of FGIDs: children first completed the Questionnaire of FGIDs Rome III (QPGS) which was translated to Spanish and adapted to local common children language (reverse translation by bilingual doctors). Prevalence and progress of GS in children with and without diagnosis of FGIDs: confidential questionnaire validated questions assessing presence/severity of abdominal pain (AP), constipation, diarrhea, nausea, vomiting, chest pain (CP), headaches, limb pain for 8 consecutive weeks (time criterion Rome criteria for FGID) Results- 373 children, 9-11 years (50% girls) completed translated/adapted QPGS. 26.5% children met Rome III criteria (24% PU, 33% PR). Functional constipation (FC): 14%, IBS: 5.4%, Functional AP: 2.7%, Functional dyspepsia (FD): 1.7%, Non- retentive fecal incontinence (NFI): 1.5%, Abdominal Migraine (AM): 1%, Cyclic Vomiting (CV): 0.2%. Prospective follow up: 85% surveys completed. 265 (33PR, 232 PU) children completed surveys every week. Children who met Rome (FGID): Weekly prevalence GS: AP (47.6%), nausea (33%), constipation (20%), diarrhea (23%), vomiting (10%). AP interfered with activities: gym (30.8%), school (25.8%), sleeping (26.5%), and social activities (20.7%). 6% missed school for AP during study period. Extra-GS: headaches (44.8%), CP (26.7%), and pain in arms/leg (54.3%). Children not meeting Rome III (n-FGID): Weekly prevalence GS: AP (18%), nausea (5.4%). Extra-GS: headaches (11.3%), CP (4%). None complained of constipation, diarrhea, vomiting or reported AP interference with activities or school. AP interference with daily activities or school attendance in children with FGIDs (87.5%) vs. children n-FGIDs (0%) (p<0.0001). Conclusions- FGIDs are common in Colombian children. Children with FGIDs by Rome have more GS and daily interference than n-FGIDs children.

247 GASTROINTESTINAL SYMPTOMS IN SCHOOL-AGED COLOMBIAN CHILDREN. Miguel Saps¹, Diana Nichols-Vinueza², Carlos A. Velasco³, ¹Children’s Memorial Hospital, Chicago, IL; ²Universidad del Valle, Cali, Colombia

38% of American school children complain of abdominal pain (AP) weekly, nausea 23%, diarrhea 9%, constipation 8% and vomiting 7%. 2% seek medical attention for AP over 6 months. Biological, psychological and environmental factors vary among countries. No studies have prospectively explored gastrointestinal (GI) symptoms in South American children. Aim - Assess prevalence of GI symptoms in school-aged children in Colombia. Methods- Fourth and fifth-grade students from a public school (PU) and fifth-grade students from a private school (PR) in Colombia were invited to participate in a prospective study using same methods and questionnaires (Spanish version) than the American school study. Children completed weekly confidential surveys for 8 consecutive weeks (5 questions on GI symptoms and 3 questions on extra-GI complaints). Results - 332 children were invited to participate in the study (40% girls, mean age 10, range 8-12 years). All families/children accepted to participate: 288 (PU), 44 (PR). 85% of weekly surveys completed. 265 (33 PR, 232 PU) children completed 8/8 surveys of the study; 67 completed most surveys (6-7/8). Overall weekly prevalence of GI symptoms: AP (35.3%), nausea (25.5%), constipation (11.3%), diarrhea (8%), vomiting (7.3%). 56% of children with AP reported interference with activities: gym (18.9%), school (14%), difficulty sleeping (12.2%), social activities (10.6%). 2.5% of all children missed school for all causes during study period: 1.1% for AP. 5.7% of all children sought medical attention during study period (1% AP). Extra-GI complaints were common: pains in arms/legs (38.7%), headaches (30.8%) and chest pain (25.2%). Conclusions - GI symptoms are common in school-aged children in Colombia and interfere with both daily activities and school attendance. The prevalence of AP and other GI symptoms found in this study were similar to published prevalence of American children using similar methods. Similarly to the American study, children rarely seek medical attention for AP.

248 CHILDREN’S DESCRIPTION OF STOOLS. Diana Nichols-Vinueza¹, Papa Adams², Ashish Chogle³, Miguel Saps²
¹Universidad del Valle, Cali, Colombia; ²Children’s Memorial Hospital, Chicago, IL

Stool characteristics are important for diagnosis and assess treatment progress in constipation. There are no studies investigating the optimal wording for children interview. Use of children language may improve diagnosis and treatment. Aim- Investigate children’s description of stool forms. Methods- Bristol Scale (BS) is a stool chart that classifies stools in 7 types (hard to watery). Hard plastic three-dimensional models (3DM) resembling shape and texture of BS pictures (PT) inside a toilet bowl were made by artist. Focus group (nurses, doctors) approved 3DM. 50 children (group 1- G1) from general pediatrics and GI clinics were shown PT and plastic replica of each stool form and asked to name them. Most common words for each stool type were selected. Second group (G2) of 50 children was recruited. A researcher read selected words to G2 who were asked to indicate the corresponding stool PT and 3DM type. Results- None of the children in G1 used the words depicted in the BS to name the stools. Children correctly correlated the selected word with the PT type: “ball”-type 1 PT 49(98%); “round but together” 37(74%) and “bumpy” 38(76%) with PT type 2; “pine cone” 44(88%) and “corn” 40(80%) with PT type 3; “snake” and “banana” both 100% with PT type 4; “chicken nuggets” 45(90%) and “peanut” 36(72%) with PT type 5; “mashed potatoes” 40(80%) and “vomit” 27(54%) with PT type6; “pee” 48(96%), “liquid” or “honey” 44(88%) with PT type 7. Correct correlation of selected word with the 3DM: “balls” 100% and “cocoa puffs” 48(96%) with 3DM type 1; “balls-clumped” 46(92%) and “pine cone” 29(58%) with 3DM type 2; “sausage” 34(68%), “log” or “tree bark” 33(66%) with 3DM type 3; “long” 100% and “banana” 48(96%) with 3DM
type 4; “corn flakes” 47(94%) with 3DM type 5; “oatmeal” 49(98%) and “vomit” 42(84%) with 3DM type 6; “honey” 100% and 
“juice” 49(98%) with 3DM type 7. Conclusions- BS wording was not selected by any of the children. There was a good 
correlation between child’s wording and PT and 3DM. Children’s wording should be used for history collection.

249* NEUROSPHERE CULTURE ALTERS ENS STEM CELLS AND REQUIRES ENDOTHELIN-B 
ACTIVATION. Monalee Saha1, Naoko Murakami2, Cheryl E. Garthepy1,2,1 Molecular and Human Genetics, The Research 
Institute at Nationwide Children’s Hospital, Columbus, OH; 2The Ohio State University, Columbus, OH
Enteric nervous system stem cells (ENS-SCs) are multipotent, self-renewing and capable of forming neurons in the gut. ENS-SCs 
are isolated from the gut using neurosphere (NS) culture or selection of cells expressing high levels of p75, the neurotrophin 
receptor (p75
high
). ENS-SCs derived using these 2 techniques differ in their expression of RET and their response to endothelin-B 
receptor (ETB) activation, both of which are critical for ENS development. How these 2 types of ENS-SCs are related to each 
other and which has the greatest therapeutic potential is unclear. We hypothesized that direct comparison would reveal additional 
differences in stem cell marker expression and growth behavior between these ENS-SCs. METHODS: Using cells dissociated 
from embryonic rat intestine, NSs were cultured from unselected cells or p75
high
 cells in defined media containing the RET ligand 
GDNF, the ETB ligand ET3, or an ETB-selective antagonist BQ788. Individual cells and intact NSs were analyzed by 
immunohistochemistry. RESULTS: NSs derived from unselected cells express ETB, lesser amounts of Nestin, and little p75. 
P75
high
 cells express Nestin, ETB and RET, and NSs grown from these cells diffusely express Nestin, ETB, and p75, but not 
RET. Once dissociated from a NS, the selected cells have altered growth characteristics in adherent culture. P75
high
 cells generate 
fewer NSs than unselected cells (6x2/100 selected cells vs. 15x6/100 unselected cells; p<0.01) and ETB antagonism severely 
impairs culture of both types of NSs. CONCLUSION: NSs derived from selected and unselected cells show diffuse expression of 
ETB and require ETB signaling for propagation. This suggests that ETB plays a significant role in ENS-SC proliferation and/or 
cohesiveness. P75
high
 cells have a lower propensity than unselected cells to form NSs and the NS microenvironment may down-
regulate RET expression, a marker of a restricted enteric phenotype, on these cells. This finding suggests that cell-cell contact can 
modulate ENS-SC differentiation.

250* HRM EVALUATION OF UES DYSFUNCTION IN CHILDREN WITH CHRONIC THROAT PAIN. Neellesh 
A. Tipnis, Manu R. Sood, Pediatric Gastroenterology, Medical College of Wisconsin, Milwauke, WI
BACKGROUND: Throat pain is a common complaint in children, and is often recalcitrant to conventional GERD therapy. UES 
dysfunction has been attributed to the genesis of globus sensation in adults. The mechanism of the hyperdynamic UES is not 
clear. OBJECTIVE: To evaluate UES dysfunction in children with throat pain. Methods: HRM recordings in 34 consecutive 
children (13 females, median age 12.65 (6.32-17.89) y) evaluated for dysphagia were reviewed. 9 patients with achalasia, 1 with 
nutcracker esophagus and 2 with profound developmental delay were excluded. Simultaneous videofluoroscopy was used to 
identify bolus retention. Mean resting UES pressure, % change in UES pressure with respiration, and % change in UES pressure 
during periods of UES bolus retention were compared between 8 children with chronic throat pain and 14 children without. 
RESULTS: The mean UES resting pressure was similar between throat pain and control children (81 ± 30 vs 92 ± 44 mmHg, 
p=0.593). UES pressure increased with inspiration in all control children and in 75% of throat pain patients. The percent change 
of UES pressure due to respiration change was greater in throat pain children compared to controls (32% vs 12%, p=0.035). All 8 
children with throat pain had bolus retention at the thoracic inlet compared to 4 of 14 control patients. Change in UES pressure 
during periods of bolus retention was increased in throat pain patients compared to controls with bolus retention and controls 
without bolus retention (47% vs 21% vs. 10%, p=0.021 and p=0.01). DISCUSSION: Similar to adults with globus sensation, 
children with throat pain had a greater physiologic response to provocative maneuvers such as respiration. Furthermore, children 
with bolus retention had a greater percentage of change in UES pressure compared to controls and their resorption of the 
esophagus results in an increase in UES pressure. Therefore, repetitive stimulation of the esophago-UES closure reflex due to 
distension of the upper esophagus by chronic bolus retention may explain the hyperdynamic nature of the UES in children with 
throat pain.

251 FIRST PEDIATRIC STUDY ON CYCLIC VOMITING SYNDROME IN LATIN AMERICA. Pamela Jofré1, Natalia 
Zaloaga1, Miguel Saps1,1 Pediatría, Universidad de Valparaíso, Viña del Mar, Chile; 2Children’s Memorial Hospital, Chicago, 
IL
Studies show Cyclic Vomiting Syndrome (CVS) is fairly common in children of North America, Asia and Europe . CVS is 
multifactorial. Pathogenesis includes genetic , other biological or psychosocial factors. Triggers: emotional stress, infections, diet, 
exercise, weather, etc. Genotype,triggers, management, progress and daily life impact may vary by region. There are no studies 
on CVS in Latin-American children. Aims: Assess natural history, management, comorbidities and progress in Chilean children 
with CVS. Methods: Cohort study. Patients diagnosed CVS (NASPGHAN 2008) at 2 pediatric GI clinics (Gustavo’s Fricke’s 
Hospital, Reñaca Clinic, Viña del Mar, Chile) between 2001- 2011. Families completed written/phone survey on clinical 
characteristics, comorbidities, management, progress, disability. Results: 26 children (mean 9.6 y, 11 F) had CVS diagnosis 
during study period. 15 families participated, 66.7% (10/15) females. Average onset of symptoms: 5 years (range 1.5/11 y). 
Average interval-diagnosis: 1.1 years (range 8 months- 5 y). 40% (6/15) children had one episode/month, 26.67% (4/15) ≥two 
episodes/month, 33.3% (5/15) two months interval between episodes. Median duration episodes: 6 hours. 93.3% (14/15) missed 
school for CVS (median 10 days/year). 25% children missed ≥ 30 school days. 40% hospitalized ≥once. Triggers: 66% (10/15) 
emotional stress (birthday, tests, etc), 13% (2/15) sleep deprivation, 20% physical stress, 73% (11/15) food was possible trigger: 
chocolate, citric, cheese, fried food, etc. 40% (6/15) reported migraines, 33.3% (5/15) recurrent abdominal pain, 13% (2/15) 
depression. Treatment: 66% (10/15) managed with lifestyle changes (LC) alone. 2/15 (13%) LC and Cyproheptadine (CP) 
prophylaxis. 13 children (10 LC exclusively, 2 LC plus CP and 1 without changes) achieved ≥50% reduction in number of
episodes. 2 cases, frequency unchanged. 66.6% children received abortive treatment (Ondasentron) in ≥1 occasion. 6.6% family history CVS.Conclusions: CVS has great impact in daily life. LC alone or combination with abortive treatment reduced frequency of CVS.

252* ASSESSMENT OF ABDOMINAL PAIN THROUGH GLOBAL OUTCOMES AND RECENT FDA RECOMMENDATIONS IN CHILDREN. ARE WE READY FOR CHANGE? Saeed Mohammad1, Nader N. Youssef2, Adrian Miranda2, Samuel Nurko2, Paul Hyman1, Jose Cocjin1, Carlo Di Lorenzo2, Miguel Saps1,2,3. Children's Memorial Hospital, Chicago, IL; 4NO PAINS CONSORTIUM, Chicago, IL.

There is no consensus on the optimal outcome measures to assess abdominal pain (AP) progress in functional gastrointestinal disorders (FGID). FDA recently published guidelines for IBS research recommending against global assessment of AP and binary outcomes as clinical endpoints. FDA recommended using 2 co-primary endpoints (AP, altered bowel movements). AP improvement considered satisfactory if >30%. No studies have validated this recommendation in children. Aims: Evaluate 1) validity >30% improvement in AP; 2) validity of global assessment of AP improvement. Methods: database of randomized clinical trial in children with functional AP analyzed. At study entry and exit, children completed Pediatric Functional Disability Index (PFDI). AP assessed daily (100 mm scale). At end of trial, children answered questions on AP interference with activities and 2 global assessment questions (binary outcomes). We measured extent to which >30% AP improvement and global questions correlated with disability (interference activities and PFDI). Results: 77 children (F=70%).1) >30% AP improvement did not correlate with activity interference (p=0.62) or PFDI score change (p=0.37); 2) Overall improvement question correlated with improvement in PFDI scores (p<0.04) while positive responses to pain relief question inversely correlated with child’s activities interference (p<0.001). Both global questions correlated positively with each other (r=0.74; p<0.0001) and with >30% AP improvement (p<0.01). Global questions and >30% improvement correlated with daily AP intensity improvement (p<0.001). 30% change PFDI scores- arbitrary measure of minimally clinical important difference (MCID)- correlated with global questions: overall improvement (p<0.001) and pain relief (p=0.07) but not with >30% AP intensity improvement (p=0.26). Conclusions: Previously used global assessments and binary outcomes correlate well with disability, improvement of PFDI scores and MCID whereas newly recommended 30% improvement does not.

254 PREVALENCE OF ABDOMINAL PAIN AND FUNCTIONAL GASTROINTESTINAL DISORDERS IN COMMUNITY CHILDREN. Silvana Bonilla1, Ashish Chogle1, Diana Nichols-Vinueza1, Miguel Saps1.

1Children’s Memorial Hospital, Chicago, IL; 2University of Illinois, Chicago, IL; 3Universidad del Valle, Cali, Colombia

Functional gastrointestinal disorders (FGIDs) and abdominal pain (AP) are common. Severity of AP drives medical consultations and quality of life in adult patients with IBS. 38% of 8 to 15 year old school children report AP weekly with 24% of children reporting persistence of AP >8 weeks. Still, only 2% of school children seek medical attention for AP. Lack of parental knowledge on their child’s symptoms may constitute one of the factors affecting the low ratio of consultation in children reporting AP. Aims-To determine the prevalence of AP and FGIDs in healthy community children. Methods-Data of 4 studies with same methodology to assess GI symptoms in children with celiac disease (CD), cow’s milk allergy (CMA), pyloric stenosis (PS) and Henoch-Schönlein purpura (HSP) and their healthy siblings were reviewed. 1-a phone questionnaire on GI symptoms and, 2-Pediatric Gastrointestinal Symptoms Rome III version questionnaire (QPGS-R III). Inclusion criteria: healthy children 4-18 years with a sibling previously diagnosed with CD, CMA, PS or HSP. Results-208 healthy children, mean age (7.8 years, range 3-24, 118 boys:56.7%). Parents reported presence of AP in last 8 weeks in 20 (9.6%) children (age range 3-18 years, 10 girls). No significant difference in AP prevalence between boys and girls (p=0.64), 8 children met QPGS-R III diagnostic criteria for FGIDs (3.8%); 4 Functional AP (FAP), 3 IBS, 1 Abdominal Migraine and 2 were not classifiable by Rome III criteria. Conclusions-AP was common in community children. FAP was the most common FGID among healthy community children. Prevalence of AP by parental report is lower than the previously published prevalence of AP reported by children. Lack of awareness of children’s symptoms may play a role in the low ratio of consultation for AP in symptomatic children. Future prospective studies should confirm our findings and investigate the factors influencing the medical consultation decision including parental awareness of children’s symptoms.

CONCURRENT SESSION II - INTESTINAL DISORDERS/INFLAMMATION I
Fri, October 21, 2011
2:30pm – 4:00pm

260 ALTERATIONS IN DIVERSITY OF THE ORAL MICROBIOME IN PEDIATRIC INFLAMMATORY BOWEL DISEASE. Michael Dooktor1,2, Shelly Abramowicz1, Jay Ingram1, Yaoyu Wang1, Mick Correll1, Bruce J. Paster3, Athos Bousvaros1, Gastroenterology, Children's Hospital Boston, Boston, MA; 2CCC B, Dana Farber Cancer Institute, Boston, MA; 3Forsyth Institute, Cambridge, MA

BACKGROUND: Extra-intestinal manifestations (EIMs) of Inflammatory Bowel Disease (IBD) are signs and symptoms of systemic inflammation outside of the intestinal tract and are commonly seen, particularly in Crohn Disease (CD). One such EIM is oral pathology, which in CD can predate intestinal symptoms by years. The aberrant interaction between one’s microbiome and the immune system appears to play a critical role in the pathogenesis of CD and Ulcerative Colitis (UC). We hypothesize that microbial changes in the oral cavity may mirror the dysbiosis noted in studies of the intestinal microbiome. Our lab has developed a molecular technique using 16S rRNA known as the Human Oral Microbe Identification Microarray (HOMIM) to study this complex environment. METHODS: Tongue and buccal mucosal brushings were analyzed using HOMIM. Shannon Diversity Index (SDI) was employed to detect changes at the population and phyla level amongst study groups. RESULTS: 119
patients from Children’s Hospital Boston (Boston, USA) were enrolled in our study. 50 control(13+/−5 yrs, 48% male); 39 CD(14+/−, 59% male); 30 UC(14+/−, 57% male). Tongue samples from patients with CD showed a modest decrease in overall diversity as compared to healthy controls with the phyla Fusobacteria making up the majority of this perturbation (p<0.05). Buccal mucosal samples, showed a marked decrease in overall diversity across 6 of 9 phyla in CD (p<0.05). Samples from patients with UC showed smaller decreases in both overall diversity and at the phyla level for both tongue and mucosal samples. CONCLUSION: Distinct shifts in the oral microbiome of patients with IBD are detectable using HOMIM. Given the systemic inflammation seen in CD, not surprisingly the oral microbial signature was most dramatically altered in this cohort. Considering the proposed microbe-host interaction in IBD, microbial analysis of oral mucosal samples of IBD patients demonstrates great promise as a novel, non-invasive tool for IBD screening.

NASPGHAN Endoscopy Prize

261 THERAPEUTIC ERCP IN INFANTS. Victor Fox, Gastroenterology/Nutrition, Children’s Hospital Boston, Boston, MA

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is used therapeutically in adults and older children with comparable rates of technical success and clinical benefit. Infants present a greater technical challenge due to equipment limitations and low procedure volume. There are no published reports of therapeutic ERCP in a series of infants. This study was designed to evaluate the technical success, clinical benefit, and safety of therapeutic ERCP in infants less than 2 years of age.

Methods: A retrospective IRB-approved chart review was conducted of infants less than 2 years of age who underwent ERCP from April 2006 to April 2011 at a single institution. Recorded data included basic demographics, procedure indications, comorbid conditions, technical outcomes including selective duct cannulation, sphincterotomy, stone removal, stricture dilation, stent placement, clinical benefits including resolved obstruction or leak from bile or pancreatic ducts, avoidance of or simplified surgery, and complications.

Results: 22 procedures were performed by a single pediatric endoscopist in 17 infants, median age = 50 weeks (range 5 -103), 59% male, median weight = 8.3 kg (range 3.9-14), representing 12.7% of 173 total ERCPs (median age = 10 years) identified during study period. Biliary indications 20/22 (91%) were predominant. Comorbid conditions included partial hepatectomy (2) and liver transplantation (2) for hepatoblastoma, kidney transplantation (1), congenital heart disease (2), Langerhans cell histiocytosis (1), and respiratory insufficiency (1). Selective duct cannulation was successful in 19/20 (95%) procedures. Therapeutic interventions were planned during 20 procedures in 16 infants. Interventions including sphincterotomy (8), stone removal or drainage (11), dilation and stent placement (4) were successful in 15/20 (75%) leading to clinical benefit to 11/16 (69%) patients. Complications were limited to mild pancreatitis in 2 patients.

Conclusion: Therapeutic ERCP can be performed safely with substantial technical success and clinical benefit in infants with complex disease despite limitations of equipment design and procedure volume.

PLENARY SESSION II
Saturday, October 22, 2011
8:30am – 10:00am

Young Faculty Clinical Investigator Award

262 GASTROPARESIS IN CHILDREN. COST AND BENEFIT OF CONDUCTING 4 HOURS SCINTIGRAPHIC GASTRIC EMPTYING STUDIES. Ashish Chogle, Miguel Saps, Children’s Memorial Hospital, Chicago, IL

Scintigraphic gastric emptying study (GES) is the gold standard for diagnosis of gastroparesis. Adult studies demonstrated that extending GES to 4 hr increases sensitivity. Most pediatric centers assess GES up to 2 hrs post-meal. Shorter studies usually justified by need for longer technician time and higher resources use. Aim: Assess impact of extending GES from 2 to 4 hr in the evaluation of children with suspected gastroparesis. Methods: Exclusion GES from 2 to 4 hr increases number of symptomatic patients diagnosed with gastroparesis. Methods: Chart review of all children who underwent GES with a standard solid meal labeled with Tc 99m sulfur colloid (CMH 2009-10). Results of GES at 1, 2 and 4 hours were compared. Patients categorized as abnormal GES if gastric retention of meal > 90% at 1 hr, > 60% at 2 hours, >10% at 4 hours according to American Motility and Nuclear Medicine Society guidelines. Cost of evaluation of patients diagnosed with gastroparesis was estimated. Test differences in proportions: Chi-square, P < 0.05 significance. Results: 71 patients, 32 males, average: 10.8 years (range 3-21) had 4 hr GES. 4 hrs GES was more sensitive. Using adult guidelines of 4 hrs length, 56% (n=40) children with suspected gastroparesis had abnormal GES. 23% (8 of 35) had normal GES at 2 hrs but abnormal 4 hrs (Table 1; P<0.0001). 28% had delayed GES at 1 hour: all these patients persisted to have abnormal GES at 2 and 4 hrs. Cost evaluation of gastroparesis $6225/child. Transitioning from 2 hrs to 4 hrs only required scheduling adjustments. It did not result in cost increase or limitation in number of scheduled patients. Conclusion: 2 hrs GES misses high proportion of patients with gastroparesis Extending GES to 4 hrs results in significant increase in diagnosis that offsets the time invested in minor scheduling adjustments if compared with the total cost of evaluating a patient with suspected gastroparesis.
GES results at 2 and 4 hours

<table>
<thead>
<tr>
<th></th>
<th>Abnormal GES at 2 hours</th>
<th>Normal GES at 2 hours</th>
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<tr>
<td>Abnormal GES at 4 hours</td>
<td>32</td>
<td>8 (23%)</td>
</tr>
<tr>
<td>Normal GES at 4 hours</td>
<td>4 (11%)</td>
<td>27</td>
</tr>
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</table>

263 CHARACTERISTICS OF PAIN-PREDOMINANT FUNCTIONAL GASTROINTESTINAL DISORDER (FGID): PRELIMINARY RESULTS FROM THE PAIN FREE CONSORTIUM. Lucia G. Goncalves, Beth Skaggs, Samuel Nurko, Jeffrey Hyams, Heidi Sweeney, Miguel Saps, Paul Hyman, Carrie Firestone-Baum, Manu Sood, Adrian Miranda, Carlo Di Lorenzo, Gastroenterology, PAIN FREE Consortium, Columbus, OH

Background: The Pediatric Alliance for International Neurogastrointestinal Functional Research(PAIN FREE) registry is a prospective,observational research consortium aimed at characterizing clinical features and outcomes of pediatric patients with FGID.We report preliminary data evaluating characteristics of different subgroups of pain-predominant FGID.Methods: Patients presenting with the chief complaint of abdominal pain were enrolled in the consortium at 6 different centers (Hartford, CT, New Orleans, LA, Boston, MA, Chicago, IL, Columbus, OH and Milwaukee, WI). Data pertaining to the first visit of each patient were analyzed. Diagnoses were based on ROME III criteria as obtained through the QPGS questionnaire. Results: 190 patients were enrolled. Most of them (68.4%) were female. age ranging from 4 to 17 years, 61 (32.1%) patients fulfilled criteria for irritable bowel syndrome (IBS), 42 (22.1%) for abdominal migraine, 28 (14.8%) for functional dyspepsia, 12 (6.3%) for functional abdominal pain (FAP), and 47 (24.7%) had other diagnoses. There was no significant difference among the groups in regards to age (p=0.8), race (p=0.6), gender (p=0.6), body mass index (p=0.5) and recruiting center (p=0.09). No significant differences were found for alarm symptoms, such as frequency of waking up at night due to the pain (p=0.15), weight loss (p=0.7), growth deceleration (p=0.3), fever (p=0.9), hematochezia (p=0.3), dysuria (p=0.7), arthritis (p=0.5) or mouth ulcers (p=0.8). Groups did not differ statistically when we evaluated if the onset of the symptoms occurred after an infectious illness or not (p=0.7). Conclusions: In a cohort of patients presenting with chronic abdominal pain, IBS is the most common phenotype followed by abdominal migraines. The surprisingly high prevalence of abdominal migraines needs further study, as it maybe due to the diagnostic criteria used. There seems to be no demographic or clinical feature more prevalent in any specific subgroup of pain predominant FGID.

CONCURRENT SESSION III – INTESTINAL DISORDERS/INFLAMMATION II
Saturday October 22, 2011
10:30am – 12:00pm

264 EFFECT OF VITAMIN K2 (MK-7) ON BIOAVAILABILITY AND BONE QUALITY DURING GROWTH AND DEVELOPMENT. Douglas Bolster1, Marie-Noelle Horcajada2, Sandra Sacco2, Stephanie Viguet-Carrin2, Stephanie Pinaud2, Elizabeth Offord-Cavin2, Nestle Nutrition R&D Centers, Minnetonka, MN; Nestle Research Center, Lausanne, Switzerland

Introduction. The estimated requirement for vitamin K for bone mineral density (BMD) and bone microarchitecture, and serum biochemical markers of bone metabolism were determined using microcomputed tomography (µCT) and ELISA, respectively. A dose-dependent increase in plasma vitamin K2 (p<0.008) was observed in response to increasing dietary levels. No effect was found on blood coagulation suggesting no negative impact on hemostasis. Blood bone markers NTx and osteocalcin remained unchanged. Trabecular (p<0.05) and cortical (p<0.0001) BMD and bone microarchitecture (cortical thickness, marrow diameter-p<0.05) were improved with the highest dose of vitamin K2. Conclusion. Natto-derived K2 is bioavailable and does not contribute to coagulation abnormalities. Further, this is the first research study to demonstrate a significant effect on bone microarchitecture in vivo during growth and development in response to vitamin K2. These findings suggest K2 may provide improved bone quality during developmental periods and/or protection of bone microarchitecture under conditions of growth impairment.

265 NOVEL STAT3 PHOSPHORYLATION INHIBITOR AMELIORATES DEXTRAN SULFATE SODIUM (DSS)-INDUCED COLONIC INFLAMMATION IN MICE. Jeffrey V. Eckert1, Yuqin Chen1, Jessica E. Thorpe1, Bryan Disch1, Randle M. Gallucci1, Pui-Kai Li2, Chenglong Li3, Michael A. Ihnat4, Thomas J. Sferri1, 1University of Oklahoma HSC, Oklahoma City, OK; 2The Ohio State University, Columbus, OH

Inflammatory bowel diseases (IBD) are characterized by dysregulation of several pro-inflammatory cytokines. Inhibitors of IL-6, one of these cytokines, have a potential therapeutic role in IBD. Curcumin (a component of turmeric) has several biological activities including the inhibition of IL-6 signaling at STAT3 phosphorylation and is therapeutic in animal models of IBD.
**266 MENARCHE IN CROHN'S DISEASE.** Neera Gupta¹, Robert Lustig¹, Michael Kohn², Eric Vittinghoff³, ¹Pediatrics, University of California, San Francisco, San Francisco, CA; ²Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA

**Background:** Delayed puberty is frequently observed in Crohn’s disease (CD), yet the timing of menarche in CD is poorly described. Our aims were to study the age at onset and factors associated with menarche onset in CD.

**Methods:** Cross-sectional study of 34 female CD patients enrolled between 1/07 and 7/09. We compared age of menarche in CD versus a contemporary sample of 545 female controls, using data in the National Health and Nutrition Examination Survey (NHANES) collected between 1/07 and 12/08.

**Results:** Mean chronological age (CA) of CD patients was 15.6 ± 3.2 years and did not differ from the NHANES cohort (15.7 ± 2.4 years; p = .91). The median CA of menarche (13.9 years) in CD was older than in the NHANES sample (12.0 years) (p<0.0005). In CD patients, the cumulative incidence of menarche was 10% at CA 12 years, 51% at CA 14 years, and 100% by CA 16 years. 68% reached menarche by bone age (BA) 13.5 years and 100% by BA greater than 14.0 years. Menarche occurred earliest in South Asians, followed by East Asians, and then Caucasians (p=.02).

**Conclusions:** CA of menarche is delayed in CD compared with the NHANES cohort. BA of menarche in CD is similar to reported BA of menarche in healthy children. CA of menarche in CD differs by race/racial subcategory. Prospective studies should clarify understanding of timing and predictors of menarche in CD, and help determine when delayed menarche in CD may be due to other underlying etiologies. Our data suggest that determination of bone age should be included in the standard of care of patients with Crohn’s disease. Furthermore, our data suggest that if menarche has not occurred by a BA greater than 14.0 years, referral to endocrinology for further evaluation should be strongly considered.

**267 MICRONRNA REGULATORY PATHWAYS IN CHOLESTASIS.** Melissa Kennedy, Claire LeGuen, Amber Horner, LaTasha Boateng, Nicholas Hand, Joshua Friedman, Pediatric Gastroenterology, Hepatology, and Nutrition, Children’s Hospital of Philadelphia, Philadelphia, PA

**Introduction:** Cholestasis develops in response to a variety of insults, leads to hepatocellular injury, and is a significant cause of liver-related morbidity in the pediatric population. MicroRNAs (miRNAs) are small, noncoding RNA molecules that repress gene expression and play critical roles in many biologic processes. The specific role of microRNA in cholestatic liver disease is currently unknown.

**Methods:** Bile duct ligation (BDL) was performed in C57B/6 mice and liver samples were collected at day 3 (n=3) and day 15 (n=3) post ligation. Low density arrays were performed on RNA isolated from liver samples. Array results were confirmed using quantitative PCR in a separate set of BDL mice (Day 3, n=5; Day 15, n=6). Results were compared with another mouse model of cholestasis, the Mdr2/- knockout mouse, at 8 weeks of age. Bioinformatics tools were used to match significantly altered miRNAs to candidate target genes. Levels of the miRNAs were then measured in cholestatic human liver samples.

**Results:** Several miRNAs were significantly increased in the livers of BDL mice versus sham laparotomy controls (miR-376c, miR-182, miR-183, miR-184, miR-34c, and miR-495). Several of these miRNAs were also increased in Mdr2/- mice (miR-495, miR-182, miR-183, miR-184, and miR-34c). Bioinformatic investigation predicts that a possible target of miR-376c is CYP7A1, the gene which codes for cholesterol 7 alpha hydroxylase, the rate limiting step in bile acid synthesis. MirR-182 is predicted to regulate NR5A2, the gene which codes for Liver Receptor Homologue-1, a nuclear receptor which activates CYP7A1 and is also down-regulated in cholestasis. The miRNAs mir-183 and mir1-184 were elevated in the livers of infants with biliary atresia and other cholestatic conditions.

**Conclusion:** These results suggest a unique liver miRNA signature in cholestatic liver disease in mice and humans. These miRNAs may play a role in the regulation of genes involved in the biologic response to cholestatic liver disease.
268 EVALUATION OF THE USE AND SAFETY OF INFILIXIMAB IN THE TREATMENT OF PEDIATRIC IBD: A MULTICENTER REGISTRY EXPERIENCE. V. Martin1, C. Langton2, J. Markowitz1, A. Griffiths1, D. Mack1, A. Otley1, M. Oliva-Hemker1, D. Kelo1, R. Carvalho1, J. Evans1, S. Stephens1, A. Bousvaros1, M. Pfefferkorn2, J. Rosh1, C. Ashai-Khan3, M. Kappelman1, M. Kay1, R. Dimmitt2, B. Sudel1, W. Faubion3, M. Schaefer4, N. LeLeiko1, T. Lerer4, Jeffrey Hyams5,6
1Pediatric IBD Collaborative Research Group, Hartford, CT; 2CT Children’s Med Ctr, Hartford, CT

Background: Infliximab (IFX) use is common in pediatric IBD. Long-term safety data are lacking. Aim: To examine the use and safety profile of IFX. Methods: Data were obtained from the Pediatric IBD Collaborative Research Group Registry, a prospective observational study of newly diagnosed children ≥16 years of age started in 2002. Data are recorded at diagnosis (dx), 30 days, and then quarterly. Patients are treated by physician dictate, not protocol. Results: As of Feb 2011 1736 patients (pts) (57% male, mean age at dx 11.7yr, mean follow-up 3.2yr), were in the Registry. 1166 (67%) are still active. 568/1736 pts (33%) received IFX. 447/1173 CD (38%), 98/457 (21%) UC. 23/106 (22%) IBD-U. 327/568 (58%) received IFX within 1 year of dx, mean 15.7±16.3 mos from dx (range 0-88 mos). 65% were receiving a concomitant immunomodulator at first IFX. 7697 IFX infusions have been given since 2002. mean dose 6.3mg/kg (range 2.3-14.8 mg/kg). Total exposure years to IFX=1385. Since 1/1/05 a formal IFX infusion reaction capture system has been in place in the Registry. Of 6914 infusions (533 pts) since that time 1.9% were associated with acute infusion reactions (facial flushing, shortness of breath) representing 13.5% of pts on IFX. Delayed hypersensitivity reactions were seen in 11 (2.1%) pts. There were 10 opportunistic infections (2 PPD conversion without sequelae, 1 varicella, 3 CMV colitis, 2 shingles, 2 yeast infections). 7 pts (1.3%) had pancreatitis, 13 (2.4%) psoriasis, 4 abnormal LFT, 1 neutropenia, 2 seizures. Since 2002, 1 pt treated with IFX and thiopurine developed Hodgkin’s lymphoma of the bowel (pt alive and off chemotherapy), and 1 pt died of an unrelated arrhythmia. Conclusion: This large prospective multicenter experience with IFX therapy in children revealed no new signals of toxicity.

POSTER SESSION III
Saturday, October 22, 2011
10:00am – 12:00pm

ESOPHAGUS/STOMACH

269 DUODENAL BULB NODULARITY: A SIGN OF COW’S MILK PROTEIN INDUCED GASTRODUODENITIS IN INFANTS? Mosa A. Khormi1, Mosa Fagih1, Abdulrahman A. Al-Hussaini1, 1Pediatrics, King Fahad Medical City, Riyadh, Saudi Arabia; 2Pathology, King Fahad Medical City, Riyadh, Saudi Arabia

Background and objectives: Infants with food allergy have not been systematically examined with endoscopies and biopsies, therefore knowledge on endoscopic findings of the gastrointestinal tract remains limited. We report an association between lymphomonodular hyperplasia (LNH) of the duodenal bulb and cow’s milk allergy (CMA) in infants as a preliminary observation for a typical endoscopic finding.

Methods: During the year from 2004 through 2010, we had performed upper endoscopy for infants, previously diagnosed to have gastroesophageal reflux disease (GERD) and refractory to anti-GERD medications, presenting to our institution with hematemesis for variable duration of time. The diagnosis of CMA was based on complete resolution of symptoms on hypoallergenic milk formula and recurrence of symptoms on re-challenge with regular milk formula.

Results: Eight infants were diagnosed to have CMA (5 females) with median age 7 months (range 5-11 months). The main presenting complaint was intermittent hematemesis for a median duration of 4 weeks (1-8 weeks), however all 8 patients had experienced vomiting with a median age at onset of 2 months (birth-3 months). Four infants were on milk formula since birth and 4 had been breastfed for 1-2 months before switching to milk formula. Four infants had eczema. Endoscopic findings included: nodularity of the duodenal bulb and erythematous, hemorrhagic, and nodular antrum in all patients. Histopathological examination of biopsies from duodenum revealed presence of lymphoid nodules with focal flattening of villi and preservation of normal villous architecture. Mucosa of the duodenum and antrum were infiltrated with eosinophils at a median of 18/HPF (15-30). All infants demonstrated complete symptomatic response on hypoallergenic formula and recurrence of symptoms on re-challenge with regular milk formula.

Conclusion: The presence of duodenal bulb nodularity on upper endoscopy in infants with GERD like picture should be considered a pathologic finding that raises suspicion of CMA.

270 THE DIAGNOSTIC YIELD OF UPPER ENDOSCOPY IN CHILDREN. Melissa Sheiko1, Kelley E. Capocelli2, Robert E. Kramer3, 1GME, Childrens Hospital Colorado, Aurora, CO; 2Pathology, Childrens Hospital Colorado, Aurora, CO; 3Digestive Health Institute, Childrens Hospital Colorado, Aurora, CO

Objective: To ascertain the indications most predictive of significant endoscopic and histological findings by performing a large retrospective, single center review of initial diagnostic upper endoscopy in children at a large academic center in the US.

Methods: A review of 1000 patients who underwent diagnostic upper endoscopy between January 2009 and March 2010 was performed. Exclusion criteria included endoscopy within 5 years or as a follow-up to a known GI condition. Age, sex, primary indication, endoscopic findings and histologic findings were recorded.

Results: Patients ranged from 0.1 to 18.9 years (mean 9.3 +/- 3.3). The most common primary indications for endoscopy were generalized abdominal pain (28.7%), GE reflux (11.6%), FTT (9.4%), diarrhea (8.8%), vomiting (8.6%) and epigastric pain (8.5%). The overall incidence of an endoscopic finding was 34.7%, with findings in the esophagus, stomach and duodenum in 17.0%, 15.4%, and 9.9%, respectively. The number with a clinically significant histologic finding was 40.4%, with findings in the esophagus, stomach and duodenum at 21.9%, 26.4%, and 10.7% respectively. By chi-squared analysis, incidence of endoscopic and pathologic findings were found to vary significantly by indication (p<0.05). The highest rates of endoscopic
findings were found in patients with a stricture on UGI (100%), foreign body (87%), GI bleed (57%), dysphagia (56%) and positive celiac screening (52%). The lowest rates of endoscopic findings were in patients with feeding issues (13%), miscellaneous indications (17%) and FTT (20%). The highest rates of histologic findings were in patients with positive celiac screening (91%), foreign body (87%), dysphagia (51%), GI bleeding (49%) and epigastric pain (38%). The lowest rates of histologic findings were in patients with miscellaneous indications (17%), stricture on upper GI (25%) and reflux (26%).

Conclusions: The diagnostic yield of upper endoscopy varies widely by primary indication and should be considered in patient selection.

271 THE ACCURACY OF ENDOSCOPIC FEATURES IN EOE- THE EXPERIENCE IN CHILDREN FROM RURAL WEST VIRGINIA. Awni M. Al-Sabti1, Lauren E. Bevin1, Yulia Dementieva2, Yoram Elitsur1, 1Marshall University, Huntington, WV; 2Mathematics, Emmanuel College, Boston, MA

Eosinophilic Esophagitis (EoE) has a unique esophageal characteristics including: furrows, rings, plaques, and strictures. The sens. and spec. of these findings were not studies in children living in rural areas. Aim: To determine the accuracy of esophageal features in EoE children from rural WV. Methods: A review of endoscopic charts of patients diagnosed with EoE, GERD, and normal children was performed. Diagnosis was established clinically and by the number of eos in the mucosa (EoE: >20 eos/HPF, GERD: <6 eos/HPF, and normal: 0 eos/HPF). Demographic, symptoms, esophageal features, and histology was compared between the groups. Results: 271 charts reviewed, of which 53 had EoE, 103 had GERD and 115 were normal. Average age(y) was 9.4±5, 10.2±4.5 and 11.3±4.3, respectively (p=NS). Compared to both control groups, the sensitivity, specificity, positive and negative predictive values of ≥ 1 esophageal feature for the diagnosis of EoE were: 88% (95%CI 76-95), 98% (95%CI 92-99), 96% (95%CI 84-99), and 94% (95%CI 87-97), respectively. The accuracy rate was 94.8%. Recorded data described in Table 1. Conclusion: 1. The esophageal mucosal features are adequate markers for the diagnosis of EoE. 2. In a proper clinical scenario, therapy may be started before histological results are available. 3. Dysphagia and chocking are characteristic symptoms for EoE.

<table>
<thead>
<tr>
<th>Mucosal features</th>
<th>EoE</th>
<th>GERD</th>
<th>Normal</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furrows</td>
<td>40 (75%)</td>
<td>2 (1.9%)</td>
<td>0</td>
<td>0.0001*, 0.0001**</td>
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<tr>
<td>Plaques</td>
<td>13 (24%)</td>
<td>0</td>
<td>0</td>
<td>0.0001*, 0.0001**</td>
</tr>
<tr>
<td>Rings</td>
<td>6 (11.%)</td>
<td>0</td>
<td>0</td>
<td>0.001*, 0.0001**</td>
</tr>
<tr>
<td>Stricture</td>
<td>5 (9%)</td>
<td>0</td>
<td>0</td>
<td>0.004*, 0.002**</td>
</tr>
<tr>
<td>Any feature</td>
<td>47 (88%)</td>
<td>2 (1.9%)</td>
<td>0</td>
<td>0.0001*, 0.0001**</td>
</tr>
<tr>
<td>Erythema</td>
<td>43 (81%)</td>
<td>25 (24%)</td>
<td>8 (7%)</td>
<td>0.0001*, 0.0001**</td>
</tr>
<tr>
<td>Gender: Male%</td>
<td>75%</td>
<td>55%</td>
<td>42%</td>
<td>0.022*, 0.0001**</td>
</tr>
<tr>
<td>Symptoms: Abd pain</td>
<td>19 (35%)</td>
<td>59 (57%)</td>
<td>68 (59%)</td>
<td>0.0175*, 0.0076**</td>
</tr>
<tr>
<td>Vomiting</td>
<td>23 (43%)</td>
<td>27 (26%)</td>
<td>27 (23%)</td>
<td>0.0456*, 0.0111**</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>9 (17%)</td>
<td>2 (1.9%)</td>
<td>1 (0.9%)</td>
<td>0.0011*, 0.0001**</td>
</tr>
<tr>
<td>Chocking</td>
<td>9 (17%)</td>
<td>0</td>
<td>0</td>
<td>0.0001*, 0.0001**</td>
</tr>
<tr>
<td>Heartburn</td>
<td>3 (5.6%)</td>
<td>10.97%</td>
<td>3 (2.6%)</td>
<td>0.114*, 0.381**</td>
</tr>
</tbody>
</table>

p-values: Two-tailed Fisher Exact test, Kruskal-Wallis Test, * EE vs. GERD; ** EoE vs. normal.

272 NUTRITIONAL PROFILE OF CHILDREN WITH ACID GASTROESOPHAGEAL REFLUX DISEASE AND ITS ASSOCIATION WITH THE SEVERITY OF DISEASE. Christian G. Boggio Marzet, Maria L. Deforell, Susana Dozo, Hebe L. Gomez, Christian Palacios, Pediatric Gastroenterology & Nutrition Section, Hospital "Dr. Ignacio Pirovano", Capital Federal, Argentina

Introduction: Few pediatric studies related to nutritional status (NS) in patients with Gastroesophageal Reflux Disease (GERD) were reported.

Objective: To describe nutritional profile of children with GERD and its association with the severity of the disease.

Material and Methods: Sample: 40 children, 1 to 12 years, with diagnosis of acid GERD with refractory respiratory symptoms with dual channel 24 h pH probe, providing mild severity (5-10% reflux index, RI), moderate (RI 10-15%) and severe (RI > 15%). Study period: 01-01-10 to 31-12-2010. Z scores were estimated for weight, height and BMI according to WHO references adapted by the Argentine Ministry of Health. The NS was established according to BMI: normal-No (Pc 10 to 85), overweight/obesity-Ov/Ob (> Pc 85) and underweight-Un (< Pc 10).

Results: 42.5% female, 57.5% male, mean age 5y 4m ± 2y 8m. Diagnosis: a) Mild GER (70%), Moderate (12.5%), Severe (17.5%), with significantly higher percentages of Moderate–Severe GERD in children > 5 years (45%) rather than with lower age (11.1%) (Fisher p=0.03) and also among Ov/Ob children (50%) than No and Un (13.6%) (Fisher=0.017); b) No NS 47.5% (95%CI 32-62), Un 7.5% (95%CI 0-15), Ov/Ob 45% (95%CI 29.5-60) without gender differences, with average height z-score of -0.46 ± 1.1. The averages weight z-score and BMI z-score were significantly higher in children with mild reflux (weight z-score 1.22, BMI z-score 2.06) and severe (weight z-score 1.74, BMI z-score of 1.98) for those with mild reflux (weight z-score -0.12, BMI z-score 0.92) with higher values of BMI z-score in males (p=0.001) and females (p=0.001). Significant differences were found between mild, moderate, and severe reflux in the nutritional profile, with similar z-score values among mild and moderate reflux. Significant differences were also found in the nutritional profile between normal and overweight/obesity NS, with higher values of weight z-score in males with normal weight (p=0.001) and females (p=0.001). Significant differences were found between mild and moderate reflux in the nutritional profile, with higher values of BMI z-score in males with moderate reflux (p=0.001) and females (p=0.001).

Discussion: The nutritional profile of children with GERD is associated with the severity of the disease, with higher values of weight z-score in males with mild reflux (p=0.001) and females (p=0.001). The association between NS and BMI z-score is significant in males and females with mild reflux (p=0.001). The nutritional profile of children with GERD is associated with the severity of the disease, with higher values of weight z-score in males with moderate reflux (p=0.001) and females (p=0.001). The association between NS and BMI z-score is significant in males and females with moderate reflux (p=0.001). The nutritional profile of children with GERD is associated with the severity of the disease, with higher values of weight z-score in males with severe reflux (p=0.001) and females (p=0.001). The association between NS and BMI z-score is significant in males and females with severe reflux (p=0.001). The nutritional profile of children with GERD is associated with the severity of the disease, with higher values of weight z-score in males with normal weight (p=0.001) and females (p=0.001). The association between NS and BMI z-score is significant in males with normal weight (p=0.001) and females (p=0.001).
BMI z-score 0.43) (anova p = 0.003 and p = 0.008)
Conclusions: Nutritional profile of the population studied shows high prevalence of overweight. Severity of GERD in children depended on age group and NS, being more affected over 5 years and those with overweight or obesity. The average weight and BMI z-scores were higher in children with greater severity of disease.

273 HIGHER BODY MASS INDEX (BMI) AND WAIST CIRCUMFERENCE (WC) CORRELATE WITH GASTROESOPHAGEAL REFLUX-RELATED SYMPTOMS (GER-RS) BUT NOT GASTROESOPHAGEAL REFLUX DISEASE (GERD) IN CHILDREN. Cindy Haller, Jeremiah Levine, Pediatrics, North Shore-LIJ Health System Cohen Children’s Medical Center, New Hyde Park, NY

The prevalence of childhood obesity has reached epidemic proportions with over 40% of American children overweight or obese. GER-RS and GERD are prevalent in 5-8% of children. Obesity and GERD have been found to be associated in adults. We evaluated this association in children. Method: Prospective study of children aged 6-18 undergoing upper endoscopy. Exclusion: use of anti-reflux medication or medication affecting intestinal motility, constipation, presence of conditions pre-disposing to GER. Parents completed an age-appropriate validated GER-Questionnaire, which included questions about GER-RS (nausea, vomiting, chest pain, abdominal pain, eructation, dysphagia). Weight, height, BMI%, and WC% were measured. Patients were grouped as: BMI%<85 and <85 and WC%≥75 and <75. In addition, patients<10 were compared to those≥10. Subjects underwent an upper endoscopy and endoscopic (ES) and histologic scoring (HS) were performed. Results: 63 subjects (25 male, 38 female, mean age 12.2±3.5 yrs) were included. No difference in the age, gender, and ethnicity was seen between the groups. No difference was noted in GER-RS in those with BMI%<85 while those with WC%≥75 had more complaints of eructation than those<75 (p=0.045). In children≥10, those with WC%≤75 had more chest pain (p=0.008) and eructation (p=0.02) compared with WC%<75, and those with BMI%<85 had more chest pain (p=0.045). A difference in ES and HS was not seen with BMI%<85. WC%≥75 had a higher HS than those<75 (p=0.033). Conclusion: Overweight children, especially adolescents, with a large waist circumference have more frequent GER-RS such as chest pain, and eructation, although they did not have increased GERD. As GER and obesity remain a significant public health care concern in children, further study and a larger sample size may be helpful in finding more shared associations.

274 AIRWAY PEPSIN AND OUTCOMES OF GER AND MICROASPIRATION IN CARDIAC PATIENTS
Nichole Fields1, Zhaoping He2, Sam Soundar3, Karoly Horvath1, Jeff Bornstein1, Dev I. Mehta1, 1Pediatric Gastroenterology, Arnold Palmer Hospital for Children, Orlando, FL; 2Biomedical sciences, Alfred I duPont Hospital for Children, Wilmington, DE

Cardiac surgery is associated with increased risk of microaspiration, because of vocal cord dysfunction, chronic intubation, or other complications. We performed chart reviews among this high risk group of patients and selected those who had been evaluated for microaspiration using airway Pepsin assay and were referred for evaluations with feeding problems between 2006 and 2008. These patients have been followed over a two year period.
Method: Those who either had bronchoscopy or airway aspirates for Pepsin were selected and their evaluations including pH studies, UGI, as well as oro-pharyngeal motor function study (OPMS) were reviewed. Their current status were assessed based on the latest clinic visit.
Results: 14 patients met inclusion criteria, with the average follow up of 2.4 yrs (range 1.1-3.5 yrs). Cardiac procedures included Norwood procedure, VSD closure, PDA ligations and TOF repair. The airway pepsin assay was positive in 8/14 (57%). Of Pepsin positive, 7/8 had reflux seen in either on an UGI (6) or pH study (1). OPMS was abnormal in 2 patients and both were Pepsin positive. Of those 8 who were Pepsin positive, 4 underwent Nissen fundoplication due to ongoing clinical aspiration despite medical therapy, and one had GI-tube placed; another 2 remained on PPIs and prokinetics for chronic GERD and asthma. In contrast, only 1 of the 6 Pepsin negative patient needed fundoplication. (p=0.05, Fisher’s, Sensitivity 0.86, specificity 0.71).
Conclusions: Airway pepsin positivity is significantly associated with need for fundoplication or long term GER medications in cardiac patients with feeding disorder after cardiac surgery. If confirmed in a larger population, airway pepsin assay will be an important biomarker in identifying microaspiration as a cause of respiratory distress in other populations.

275 IS NON-SPECIFIC GASTRIC INFLAMMATION ASSOCIATED WITH PROLONGED USE OF PROTON PUMP INHIBITORS? Eduardo D. Rosas Blum1, Tatevian Nina2, Marc Rhoads, Syed Hashmi1, Fernando Navarro1, 1Pediatric Gastroenterology, University of Texas HSC-Houston, Houston, TX; 2Pathology Department, University of Texas HSC-Houston, Houston, TX

BACKGROUND: Although proton pump inhibitors (PPIs) have shown a remarkable tolerability profile, there are concerns regarding their long-term safety. Several studies have shown that PPIs are associated with an increased risk of infectious and nutritional complications. Non-specific gastritis has been widely reported without any identified cause.
OBJECTIVE: To determine if mild non-specific gastric inflammation (NSGI) is associated with the prolonged use of PPI.
METHODS: We performed an IRB-approved chart review of all the upper endoscopy and pathology reports done in our institution from July 2009 to June 2010. Demographic data, PPI use (duration and dosage), and biopsy results were recorded. Subsequently, all biopsies were independently reviewed by a pathologist. Patient with H pylori infection, as well as, acute or severe chronic gastric inflammation were excluded.
RESULTS: Altogether, 310 charts and 205 gastric biopsies were reviewed. A total of 193 patients were included; 88 (46%) had a history for PPI use, and 48 (25%) were found to have NSGI. The odds of NSGI were higher in patients who took PPI compared to those who did not (OR: 2.81, 95CI: 1.36-5.93) p=0.007. A longer duration of PPI use (>3 months) gave an even higher odd for having NSGI (OR: 5.44, 95CI: 1.46-20.28). PPI dosage was not independently associated with NSGI when adjusted for duration. Association with NSGI was highest for the combination of high dosage and prolonged use. Gender, ethnicity, age, and obesity
were not associated with NSGI in multivariable models.

CONCLUSION: Prolonged PPI use was associated with NSGI, with the highest ORs among patients using high doses for a long time. In patients with persistent symptoms despite PPI use, we question if therapy should be continued beyond 3 months. Our results do not establish cause-and-effect. Further investigation could focus on mechanisms by which prolonged PPI therapy could be detrimental.

276 FOLLOWING A FEED, CHEMICAL CLEARANCE BECOMES INCREASINGLY LESS EFFICIENT IN CHILDREN WITH CYSTIC FIBROSIS. Frederick W. Woodley1, Rodrigo Machado2, Ajay Kaul3, William Campbell3, Karen McCoy4, Alpa Patel5, Hayat Mousa1, 1Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH; 2Pediatric Gastroenterology, University of Sao Paulo, Sao Paulo, Brazil; 3Pediatric Gastroenterology, Cincinnati Children's Hospital, Cincinnati, OH; 4Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH

Background: Classic 2-phase acid gastroesophageal reflux (AGER) episodes are comprised of a bolus contact component and a chemical clearance (CC) component. We have shown that CC of 2-phase AGER episodes is significantly prolonged in cystic fibrosis (CF) children compared to non-CF children (JPGN 2009 49[supp 1]: E9, E35). Specific Aim: To compare CC in patients with and without CF during feeding, first hour post-prandial (1stPP), second hour PP (2ndPP), and later fasting. Methods: pH/impedance tracings from 21 CF patients (11M/10F, median age 16.8 yr, range 0.3-18.6 yr) and 21 age-matched non-CF patients (10M/11F, median age 16.1 yr, range 0.3-17.4 yr) were manually scanned for the presence of 2-phase AGER events. For each subject, mean duration of CC during 2-phase events was calculated for each of the 4 phases of the feeding cycle. Ultimately, mean of mean durations (in seconds, s) during each of the four phases of the feeding cycle were compared for CF and non-CF cohorts using Mann-Whitney with significance set at α = .05. Results: The mean of mean duration of CC was 64.1±18.8s and 41.0±18.0s during feeding (p=.782), 119.9±20.6s and 57.6±6.5s during 1stPP (p=.018), 174.6±51.7s and 61.4±13.1s during 2ndPP (p=.004), and 218.3±64.2s and 83.1±13.9s during fasting (p=.048) for CF and non-CF subjects, respectively. Within-subjects analysis shows that while CC was significantly more prolonged in CF children during 1stPP, 2ndPP, and fasting when compared to feeding (p<.05), CC in non-CF children was not significantly prolonged during any of the four phases of the feeding cycle (p>.05). Conclusions: CC becomes increasingly (and significantly) less efficient in CF children following a feed. CC is significantly less efficient in the CF children during each phase of the feeding cycle except feeding.

277 RE-REFLUX ACID GASTROESOPHAGEAL REFLUX EPISODES REACH THE HYPOPHARYNX SIGNIFICANTLY MORE OFTEN THAN OTHER PH/IMPEDANCE-DETECTABLE ACID REFLUX EVENTS IN CHILDREN. Frederick W. Woodley1, Rodrigo S. Machado2, Hayat Mousa1, 1Gastroenterology, Nationwide Children’s Hospital, Columbus, OH; 2Pediatric Gastroenterology, University of Sao Paulo, Sao Paulo, Brazil

Background: When esophageal pH monitoring (EPM) is used in combination with multichannel intraluminal impedance (MII), 4 unique types of acid gastroesophageal reflux (AGER) are detected: 1) classic two-phase AGER, 2) single-phase AGER, 3) pH only events (POEs), and 4) re-reflux AGER. It is unclear whether these different AGER types may vary in their ability to cause respiratory symptoms or be aspirated. Specific Aim: To compare the efficiency with which different types of impedance-detectable AGER (classic two-phase, single-phase and re-reflux) reach the hypopharynx. Methods: 24-hr EPM/MII tracings from 22 children (11M/11F, median age 9.7 yr, range 0.3-17.4 yr) were examined. Anti-reflux medications had been discontinued and no subject had received a fundoplication prior to testing. For each type of AGER, proximal extents were calculated. AGER episodes that reached MII channels 5 or 6 were considered proximal (hypopharynx), those that reached channels 3 or 4 were considered middle, and those that reached 1 or 2 were considered distal esophagus. Mean percentages of AGER reaching the hypopharynx were calculated and compared using the non-parametric Mann-Whitney test. Odds ratios were calculated to compare the chances of each AGER type of reaching the hypopharynx. Results: The data showed that significantly more re-reflux (94.3%) reached the hypopharynx than single-phase (67±6%)(p = .002) or classic two-phase (76±4%)(p = .001) AGER. Odds ratio calculations indicated that re-reflux AGER events are approximately 2 times more likely than classic two-phase AGER and 4-times more likely than single-phase AGER to reach the hypopharynx. Conclusions: The data show that re-reflux AGER events are more likely to reach the hypopharynx and therefore, are possibly more likely to be associated with aspiration of AGER. Also, this study underscores the importance of using EPM/MII for identifying AGER types that are more likely to be pathogenic.

278 CHILDREN WITH CYSTIC FIBROSIS MAY POSSESS AN INNATE “PROTECTIVE RESPONSE” TO PREVENT ACID REFLUX FROM THE PROXIMAL ESOPHAGUS. Frederick W. Woodley1, Rodrigo S. Machado2, Ajay Kaul1, William Campbell3, Karen McCoy4, Alpa Patel5, Hayat Mousa1, 1Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH; 2Pediatric Gastroenterology, University of Sao Paulo, Sao Paulo, Brazil; 3Pediatric Gastroenterology, Cincinnati Children's Hospital, Cincinnati, OH; 4Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH; 5Pediatric Gastroenterology, Nationwide Children's Hospital, Columbus, OH

Background: Combined esophageal pH monitoring (EPM) and multichannel intraluminal impedance (MII) permits detection of 4 unique types of acid gastroesophageal reflux (AGER): 1) two-phase, 2) single-phase, 3) pH only, and 4) re-reflux episodes. Aim: To evaluate the likelihood of different types of MII-detectable AGER events (2-phase, 1-phase and re-reflux) to reach the proximal esophagus (PE)in CF vs non-CF children. Methods: 24-hr EPM/MII tracings for 22 CF patients (9M/14F, median 9.7 yr, range 0.3 - 18.6 yr) and 22 age-matched non-CF controls (11M/11F, median 9.8 yr, range 0.3-17.4 yr) were examined. Anti-reflux meds had been discontinued and no subject had received a fundoplication prior to testing. For each type of AGER, proximal extents were determined. AGER episodes that reached MII channels 5 or 6 were considered proximal, those that...
reached channels 3 or 4 were considered middle, and those that reached channels 1 or 2 were considered distal. Mean percentages of AGER reaching the PE were calculated and then compared using Mann-Whitney. Odds ratios were calculated to determine the likelihood that each AGER type would reach the PE. Results: When collapsed across all the 3 AGER types, significantly more AGER events reached the PE in non-CF children (p=.023). However, when examined individually, significant differences were found for 2-phase (p=.006) and re-reflux (p=.004) AGER types, but not for 1-phase events (p=.18). Further examination showed that, for both CF and non-CF patients, 2-phase (pH=1.5±0.09) and re-reflux (pH=1.5±0.12) AGER were both significantly more acidic than 1-phase events (pH=2.3±0.11) (p<.0001). Conclusions: CF children may respond differently to strongly acidic AGER episodes (compared to non-CF children) to reduce the frequency with which they reach the PE.

279 A MULTI-CENTER, DOUBLE-BLIND, PARALLEL-GROUP STUDY TO EVALUATE SHORT-TERM SAFETY AND EFFICACY AND LONG-TERM MAINTENANCE OF TWO DOSE LEVELS OF RABEPRAZOLE SODIUM DELAYED-RELEASE PEDIATRIC BEAD FORMULATION IN 1 TO 11 YEAR-OLD PEDIATRIC SUBJECTS WITH ENDOSCOPICALLY PROVEN GERD. Gerhard Leitz1, Ibrahim Haddad2, Jaroslav Kierkus3, Eduardo Tron4, Peter Hu5, Andrew E. Mulberg6, Steven Silber6, 1Established Products, J&J Pharmaceutical Research & Development, L.L.C., Titusville, NJ; 2Pediatric & Adolescent Gastroenterology, Pediatric & Adolescent Gastroenterology & Nutrition, Youngstown, OH; 3Department of Gastroenterology, Hepatology and Immunology, The Children’s Memorial Health Institute, Warsaw, Poland; 4Geisinger Medical Center Clinic, Wilkes Barre, PA
Objective: The primary objective of this study was to evaluate the efficacy and safety of two target dose level of a Rabeprazole Sodium Delayed-Release Pediatric Bead formulation in pediatric subjects, 1 to 11 years of age with endoscopically proven gastroesophageal reflux disease (GERD). Methods: All subjects had to have a grade 1 or greater on the Hetzel-Dent and grade >0 on the Histological Reflux Esophagitis scales. The primary endpoint was endoscopic/histological healing defined as grade 0 on the Hetzel-Dent Scale or grade 0 on the Histological Reflux Esophagitis Scale. Results: Of the 127 randomized subjects, a total of 108 (85%) completed the 12-week double-blind treatment phase. The overall healing rate after the 12-week treatment period was 81%: 78% for 0.5 mg/kg and 83% for 1.0 mg/kg. Consistent with the endoscopic/histological healing rate, the frequency and severity of GERD symptoms decreased substantially. There was no apparent pattern between the two treatment arms regarding treatment emergent adverse events (TEAEs) and serious adverse events. Conclusions: Both, the 0.5 mg/kg and 1.0 mg/kg dose regimen of the Rabeprazole Sodium Delayed-Release Pediatric Bead Formulation were effective and safe in pediatric subjects, 1 to 11 years of age. The clinical effect and the safety profile were similar for both dose levels. No unexpected adverse events were reported in this population of children with endoscopically proven GERD.

280 GENERAL ANESTHESIA RESULTS IN A LONGER WAITING TIME THAN LIGHT SEDATION FOR PEDIATRIC ENDOSCOPY. Christine P. Edwards, Christopher Samuel, Vikram Kapoor, Robert M. Issenman, Herbert Brill Pediatrics, McMaster University, Hamilton, ON, Canada
Background: Waiting times are a recognized measure of the Canadian public health care system’s ability to function effectively. There is limited research regarding waiting time in pediatric endoscopy. Endoscopy may be performed with the administration of light sedation or general anesthesia (GA), though the latter is hypothesized to have a longer wait time, as it requires more resources. We wished to identify whether there was a difference in waiting time according to sedation type, and whether this difference would have any negative clinical consequences.
Methods: We retrospectively reviewed medical charts of all children <18 years of age who had been assessed in the pediatric gastroenterology clinic and underwent an outpatient endoscopic procedure at McMaster Children’s Hospital (January 2006 - December 2007). We extracted information regarding sex, age at consult, clinical characteristics, cancellations, lack of follow-up, and date of: consult visit, endoscopy, medical diagnosis and pathological diagnosis. Results: 386 charts were reviewed. Subjects receiving light sedation were more likely to be older (14.1 years) and female (51.9%) than patients receiving GA (7.2 years, p=0.0001; 40.7%, p=0.04). Average waiting time between consult visit and endoscopy was 28.1 days in patients administered light sedation and 63.0 days in patients administered GA (p=0.0001). The longer waiting time did not lead to increased emergency room visits or hospital admissions (<2% in all subject groups).
Conclusions: Children administered general anesthesia compared to light sedation will have a longer wait time for endoscopy; however, this does not lead to serious complications.

281 CAPILLARY ECTASIA AS A MARKER OF REFLUX ESOPHAGITIS. Dana Altenburger2, Dev I. Mehta1, Shuan Li2, Shadi Ashrafi2, Orlando Gonzalez2, Karoly Horvath1, Jeffrey Bornstein1, 1Pediatric Gastroenterology, Arnold Palmer Hospital for Children, Orlando, FL; 2Pathology, OrlandoHealth, Orlando, FL
Esophageal blood lakes (capillary ectasia) have an early marker of histological feature of reflux esophagitis in adults (Geboes 1979). However, they have not been studied in the pediatric population. Their presence often corresponds to the red streaks seen on endoscopy and they are often present in the absence of inflammatory cells.

E76
Method: Ninety-four pediatric patients (4-14 years old) were retrospectively identified who underwent evaluation for reflux disease between the years 2004-2006. Their work-up included endoscopy with biopsy and pH monitor (Bravo) placement. Their esophageal biopsies were evaluated for blood lakes and the presence of eosinophils. Criteria for inclusion as a blood lake included partial endothelial lining, dissection into surrounding mucosa and enlargement greater than surrounding vascular papillae. The results of the pH monitoring as well as endoscopic reflux score (H-D) were compared to presence or absence of blood lakes.

Results: A total of 36 patients with capillary ectasia were identified, with 26 having 1 per high power field (HPF), 6 have 2 per HPF and 4 having 3 per HPF. 58 patients did not have any capillary ectasia. No association between blood lakes and eosinophils (p-value=0.60), and no correlation (p-value=0.135) between the size of blood lakes and eosinophils was noted. However, there was a significant difference in the average size of blood lakes between those who had eosinophils versus those who did not (p-value=0.05). Using endoscopic grading, 26 patients had grade 1 or 2 changes; these did not correlate with presence of blood lakes, nor the number of blood lakes.

Conclusions: Our findings indicate that blood lakes should not be used as an exclusive criterion for the diagnosis of pediatric acid reflux esophagitis. Further studies are being pursued to assess role of blood lake formation from volume expansion rather than exposure to acidic stomach contents, using impedance pH studies.

282* PEPSIN IN SALIVA AS A BIOMARKER FOR ESOPHAGEAL REFLUX COMPARED WITH 24-HOUR ESOPHAGEAL IMPEDANCE/PH MONITORING IN PEDIATRIC PATIENTS. John E. Fortunato, Heather N. Lopez, Mark O. Lively, Pediatrics, Wake Forest University School of Medicine, Winston-Salem, NC

Background: Pepsin in the oropharynx is a biomarker for gastroesophageal reflux (GER) in adults and children. It has been measured previously in expectorated saliva/sputum and in bronchial alveolar lavage (BAL) fluid. Those methods are not well suited for children due to an inability to expectorate (infants) or the invasive nature of BAL. We hypothesize that measurement of pepsin in oropharyngeal saliva collected by adsorption can be used as a non-invasive diagnostic method to assess GER in pediatric patients. Aim: To correlate the presence of pepsin in saliva with associated GER events during 24-hour esophageal impedance/pH monitoring. Methods: Pediatric patients ages 1 month to 18 years (n=62) who were deemed clinically to require 24-hour esophageal impedance/pH monitoring were included in this pilot study. 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. Samples were collected: 1) immediately before catheter placement; 2) before and 30 minutes after meals (3 meals, 6 samples); and 3) upon awakening. Results: Mean pepsin concentration was 35.9 ng/mL in samples collected 30 minutes after meals (n=158). Mean pepsin was highest in all samples taken within 45 min of a GER event: 32.6 ng/mL (n=242). The duration of 62% of those events was less than 90 sec. Proximal GER events (82% of all events) had higher average pepsin concentrations than distal events: 34.2 ng/mL (n=225) vs. 11.5 ng/mL (n=50). Conclusion: ELISA measurement of pepsin in oropharyngeal saliva collected by adsorption is a sensitive diagnostic indicator of laryngopharyngeal reflux associated with GER events observed during 24-hour esophageal impedance/pH monitoring. This method may lead to development of a screening diagnostic test to identify patients for whom additional testing by impedance/pH monitoring is most appropriate.
283 US CHILDREN WITH *HELICOBACTER PYLORI* INFECTION AND CO-EXISTING GASTROINTESTINAL (GI) CONDITIONS. Kurt Brown, Hans Rydholm, Per Lundborg, Mingliang Zhao, Jeremy Levinson, Huying Yang
AstraZeneca, Wilmington, DE; AstraZeneca R&D, Molndal, Sweden

Objective: To investigate *Helicobacter pylori* infection and co-existing GI conditions in US children. Methods: This retrospective, multi-year, cross-sectional study used a health care claims database, Marketscan. The eligible population included children with full-year continuous enrollment data. Cases were identified by ICD-9-CM codes. Results: From 2005-2009, of the 4.2-8.5 million children enrolled, approximately 73% were enrolled continuously each year. Of children with an *H pylori*-positive diagnosis, about 50% had ≥1 co-existing GI condition diagnosed concurrently in the same year. The table shows specific findings. Conclusion: In this US population of *H pylori*-positive children, the most common co-existing GI condition reported was duodenitis. In comparison with duodenitis, the proportions of peptic, gastric, and duodenal ulcer were relatively low.

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284 LACK OF EFFICACY OF TOPICAL MITOMYCIN C APPLICATION IN REFRACTORY ESOPHAGEAL STRICTURES AFTER SURGICAL REPAIR OF ESOPHAGEAL ATRESIA. Laurence Chapuy, Kelly Grzywacz, Martine Pomerleau, Patricia Perreault, Christophe Faure, Division of Pediatric Gastroenterology, Sainte-Justine Hospital, Department of Pediatrics, Montreal, QC, Canada

BACKGROUND AND AIMS: There are few limited studies on esophageal strictures of various origins (caustic, peptic, postsurgical) suggesting a role of mitomycin C, an antifibrotic agent, in preventing secondary restricting. The aim of this study was to specifically evaluate the efficacy of topical application of mitomycin C in refractory anastomotic strictures occurring after surgical repair of esophageal atresia (EA).

PATIENTS AND METHODS: We retrospectively reviewed the medical records of 11 patients suffering from esophageal stricture after surgery for EA (type C, n=8; type A, n=3), who underwent esophageal dilation and concomitant topical application of mitomycin C (median age 12 months, range 2 months - 15 years). All patients received 1 or 2 applications of mitomycin C except one who received 8 applications. Mitomycin C was applied after the 1st dilation (n=2 patients), 2nd dilation (n=3), 3rd dilation (n=2) and the 4th (n=4). The endpoints of the study were (i) the need for subsequent dilation following the first application of mitomycin C and (ii) the resolution of dysphagia.

RESULTS: With a median follow-up after first application of mitomycin C of 32 months (range 9 - 128), only 2 out of the 11 patients did not need subsequent dilation. For the remaining 9 patients, 1 to 7 subsequent dilations were performed. All patients remained with dysphagia. No dysplasia related to mitomycin C was demonstrated. One patient presented with a tracheoesophageal fistula at 12 months, after 6 dilatations (2 with mitomycin C).

CONCLUSION: In the setting of anastomotic esophageal strictures after surgery for EA, local application of mitomycin C does not prevent restricting nor improve dysphagia.
285 THE ROLE OF NONACID REFLUX AND FULL COLUMN EPISODES IN CHILDREN WITH PERSISTANT RESPIRATORY SYMPTOMS. Marina Orsi, Judith Cohen Sabban, Federico Ussher, Renata Weinschelbaum, Julieta Gallo, DAgostino Daniel, Hospital Italiano, Buenos Aires, Argentina

Introduction: Gastroesophageal reflux (GER) if undetected, may aggravate patients with respiratory symptoms. Impedance-pH studies may help in the evaluation of the various aspects of this particular association.

Aim: To evaluate GER in children with lower respiratory symptoms by determining acid and nonacid episodes, column height, Symptom Index (SI) and Symptomatic Association Probability (SAP).

Material and Method: Since January 2005 to December 2010, all children referred from the Pulmonology Service for asthma and recurrent bronchospasm because of inadequate response to respiratory treatment were evaluated for 24 hrs with Sleuth Monitoring Recorder. Patients were divided into two groups according to age: Group I (GI): < 2 yrs and Group II (GII): > 2 yrs. Each age group was subsequently divided according to their pH score (Boix Ochoa < or >16.6) into normal (N) and pathological (P).

Results: 121 were evaluated. GI: 38 children with X age of 1.8 yrs (17 girls), N: 30 and P: 8 patients. GII: 83 children with X age of 9.3 yrs (35 girls), N: 61 and P: 22 patients. Although the SAP and SI with cough resulted positive in some patients in both groups, most were non acid reflux.

Conclusion: The presence of non acid reflux related symptoms and high proportion of episodes reaching the upper esophagus may explain treatment failures in patients with persistent respiratory symptoms. New medications are needed to provide an efficacious treatment to these other aspects of GERD in respiratory patients.

<table>
<thead>
<tr>
<th></th>
<th>GI N (X±SD)</th>
<th>GI P(X±SD)</th>
<th>p</th>
<th>GI N (X±SD)</th>
<th>GI P(X±SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid episodes</td>
<td>18.4 ± 12.83</td>
<td>50.2 ± 33.78</td>
<td>0.000</td>
<td>19 ± 14.6</td>
<td>36.4 ± 27.1</td>
<td>0.000</td>
</tr>
<tr>
<td>Nonacid Episodes</td>
<td>28.5 ±18.37</td>
<td>26.7 ±14.83</td>
<td>0.801</td>
<td>9.59 ± 7.58</td>
<td>17.69 ±15.33</td>
<td>0.02</td>
</tr>
<tr>
<td>pH Score</td>
<td>6.59 ± 4.78</td>
<td>49.1 ± 41.5</td>
<td>0.000</td>
<td>6.11 ± 3.82</td>
<td>38.86±36.26</td>
<td>0.000</td>
</tr>
<tr>
<td>Full column</td>
<td>25.6 ± 14</td>
<td>65 ± 24.8</td>
<td>0.000</td>
<td>19.46 ± 13.9</td>
<td>28 ± 21.07</td>
<td>0.036</td>
</tr>
</tbody>
</table>

286 PHARMACOKINETICS AND TOLERABILITY OF DEXLANSOPRAZOLE (15, 30, AND 60 MG) IN CHILDREN WITH SYMPTOMATIC GASTROESOPHAGEAL REFLUX DISEASE. Michael Kukulka, Sai Nudurupati, M. C. Perez Takeda Global Research & Development Center, Inc., Deerfield, IL

The pharmacokinetics (PK) and tolerability of dexlansoprazole (DEX) dual delayed release capsules (30 and 60 mg) have been characterized previously in healthy adults and adolescents aged 12 to 17 years with symptomatic gastroesophageal reflux disease (GERD). This current study assessed the PK and tolerability of DEX in children aged 1 to 11 years old with GERD.

Methods: Phase I, multicenter study in male and female patients aged 1 to 11 years with GERD. Using baseline weight, patients were randomized to DEX 15, 30, or 60 mg once daily (QD) for 7 days. Blood samples for determination of DEX plasma concentrations were drawn prior to dose and over the 24-hour period after dosing on Day 7. PK parameters were calculated using noncompartmental methods and summarized by regimen. Safety assessments included monitoring of adverse events (AEs).

Results: 36 patients (mean age 7.1 years), 24 male and 12 female, were enrolled. PK parameter data for 31 patients are summarized in the Table. There was little or no accumulation of DEX in plasma. After adjusting for the body weight of the patients, DEX Cmax and AUC increased in an approximately dose-proportional manner when DEX doses increased from 15 mg to 60 mg. Compared to historical data, the mean AUC of DEX 30 mg in patients aged 1 to 11 years was similar to that in 12 to 17 year olds and healthy adults: for the 60 mg QD regimen, these patients had slightly lower exposure to DEX compared with 12 to 17 year olds and healthy adults. Three patients reported 1 or more treatment-related AEs, all rated mild in intensity.

Conclusions: In patients 1 to 11 years old with symptomatic GERD, approximate dose proportional PK was observed after adjusting for body weight. The 3 dose regimens were well tolerated.

<table>
<thead>
<tr>
<th>DEX Dosing Regimen</th>
<th>N</th>
<th>Tmax (h)</th>
<th>Cmax (ng/mL)</th>
<th>AUC(0-t) (ng h/mL)</th>
<th>T1/2 (h)</th>
<th>CL/F (L/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 mg QD for 7 days</td>
<td>9</td>
<td>4.39 (72)</td>
<td>559 (40)</td>
<td>1914 (33)</td>
<td>0.85 (34)</td>
<td>7.5 (33)</td>
</tr>
<tr>
<td>30 mg QD for 7 days</td>
<td>11</td>
<td>4.09 (57)</td>
<td>1005 (74)</td>
<td>2892 (58)</td>
<td>1.26 (67)</td>
<td>16.2 (71)</td>
</tr>
<tr>
<td>60 mg QD for 7 days</td>
<td>11</td>
<td>4.09 (88)</td>
<td>964 (54)</td>
<td>3747 (75)</td>
<td>2.75 (96)</td>
<td>26.9 (79)</td>
</tr>
</tbody>
</table>

Values are arithmetic mean (% coefficient of variation). For T1/2 and CL/F, N=6, 8, and 6 for 15, 30, and 60 mg, respectively.

287 NOVEL TECHNIQUE FOR APPLYING MITOMYCIN C IN THE TREATMENT OF RECALCITRANT ESOPHAGEAL STRICTURES. M. W. Anjum, Russell Jennings, Michael A. Manfredi, Children’s Hospital Boston, Boston, MA

Background: Treatment of esophageal strictures can be challenging requiring multiple balloon dilations. Mitomycin C is a chemotherapeutic agent with anti-fibroblast activity that has been reported to be effective in the treatment of recalcitrant esophageal strictures. Since this is a chemotherapeutic agent care must be given to only contact the desired treatment areas. This drug is commonly administered by rigid esophagoscopy.
Methods: We described our technique of applying mitomycin C in two patients with esophageal strictures. A 7 mm endotracheal tube (ET tube) was placed over an Olympus N180 endoscope which has an outer diameter of 5.5mm. The N180 scope was then advanced to the area of the esophageal stricture. The ET tube was lubricated and advanced over the scope to the site of the esophageal stricture. The endoscope was withdrawn leaving the ET tube in place to serve as an overtube. The biopsy forceps were frontloaded into the endoscope and the pledget soaked in mitomycin C was grasped with biopsy forceps. The pledget was inserted into the overtube and applied directly to the esophageal mucosa at the stricture site.

Results: Patient 1 was a 12 month old with an anastomotic stricture who underwent two sessions of mitomycin C. Average diameter changed from 4.5 to 3 mm and average interval between dilations changed from 16.3 to 44.5 days before. This patient had surgical resection of the stricture.

Patient 2 was an 18 month old male with an anastomatic stricture who underwent a total of five sessions of mitomycin C. Average diameter went from 5.1 to 5.5mm and average interval between dilations changed from 22.8 to 15.4 days. Patient 2 also went on to have surgical resection of his stricture.

Conclusion: We describe a technique of placing mitomycin C using flexible endoscopy. This technique allows for direct visualizing of the mucosa during drug application. Despite our results, mitomycin C has been shown effective by others in the treatment of recalcitrant strictures. Prospective controlled trials are needed to study the effectiveness of this treatment.

288 THE UTILITY OF ESOPHAGEAL PRESSURE SENSORS IN THE DETECTION OF COUGH DURING MULTICHANNEL INTRALUMINAL IMPEDANCE TESTING (PH-MII), Rachel Rosen, Jessica LaRosa, Janine Amirault, Kristen Hart, Samuel Nurko, Children’s Hospital Boston, Boston, MA

Background: Correlation of cough with reflux events is difficult and relies on patient compliance with symptom log completion. However, patient report of symptoms is inaccurate. We hypothesize that intraesophageal pressure recording at the time of pH-MII testing improves cough detection beyond patient report.

Methods: We placed a 2 channel intraesophageal pressure catheter simultaneously with pH-MII probes in 11 patients undergoing testing for the evaluation of cough. A cough was determined manometrically by high pressure simultaneous spikes in all of the pressure channels in the absence of a swallow by pH-MII. Coughs were coded as patient-reported (PRC), computer-detected (CDC) or both. Reflux was associated with a cough if it occurred within a 2 minute window before or after a cough. The symptom index (SI) for cough was defined as the number of coughs associated with reflux/total number of coughs.

Results: The mean age of the patients was 8.2±2.7 yrs. We recorded 861 coughs; 377 (44%) were detected by both PRC and CDC. 463 (54%) coughs were only CDC and 20 (2%) were only PRC. PRCs occurred a mean of 12.7±19.5 seconds after CDCs. There were a total of 268 reflux-associated coughs. The mean time between a reflux event and cough was 38±40 sec. When there was a reflux-cough correlation, reflux preceded cough 60% of the time, and cough preceded reflux 40% of the time. For reflux-associated coughs, 35%, 41%, and 24% were associated with non-acid reflux, acid reflux, and pH-only events, respectively. Thirty percent of reflux events associated with cough were full column. Six patients had a positive SI; 2 patients had a positive SI using CDC that would have been negative using PRC alone and 2 patients had a positive SI using PRC that would have been negative using CDC alone.

Conclusions: Simultaneous pressure measurements during pH-MII testing is an effective way to determine cough occurrence and its relationship with reflux. Reliance on patient reporting of cough during pH-MII testing underestimates cough by more than 50%.

289 USE OF A NON-INVASIVE TEST (ENTERO-TEST) IN THE DETECTION OF HELICOBACTER PYLORI IN CHILDREN IN AN ENDEMIC AREA IN COLOMBIA, Richard N. Arboleda1, B. G. Schneider2, L. E. Bravo2, R. M. Peek2, R. M. Mera1, M. C. Yenez3, C. Campo1, P. Correa3,1Division of Gastroenterology, Department of Medicine, Vanderbilt University, Nashville, TN; 2Department of Pathology, Universidad del Valle School of Medicine, Cali, Colombia; 3Universidad de Nariño, Pasto, Colombia

Background: A high prevalence (~90%) of Helicobacter pylori (H. pylori) in untreated children exists in the Andean region of Colombia. Large-scale investigations of strain diversity of H. pylori in asymptomatic children have been limited. The Entero-test (HDC Corporation, San Jose, CA) has been validated as a non-invasive procedure to obtain H. pylori from gastric samples in adults, but few have included children in an endemic area. Our aim is to validate the use of the Entero-test to culture H. pylori from asymptomatic children in an endemic area. Methods: Asymptomatic children (n=122, age 8-14y) from Nariño-Genoy, Colombia were screened for H. pylori infection using a urea breath test (UBT). Positive UBT subjects had the Entero-test capsule swallowed and allowed to dissolve in the stomach lumen for 30 minutes to allow absorption of gastric juice that may harbor H. pylori. Strings were then removed and placed in transport media (thiglycolate +20% glycerol), frozen and sent to Vanderbilt for culture and PCR. Samples were cultured on antibiotic plates and incubated at 37°C at 5% CO2 for 5 days. H. pylori were identified by morphology and positive tests for urease, oxidase and Gram stain. Negative cultures underwent PCR for housekeeping genes (efp, ureI) and virulence factors (cagA, vacA) to confirm H. pylori. Results: Eighty of 122 children (66%) were UBT positive; 29/80 Entero-test samples (36%) were H. pylori culture positive; 31/51 (61%) UBT positive, culture negative samples were PCR positive for at least one housekeeping gene or virulence factor. Combined culture and +PCR samples had a yield of 60/80 (75%). Conclusion: The Entero-test may be used as a non-invasive alternative method to endoscopy to detect H. pylori in asymptomatic children living in an endemic area where there is an increased risk of gastric cancer in adulthood.
290 NONSURGICAL MANAGEMENT OF DYSPHAGIA SECONDARY TO CRICOPHARYNGEAL ACHALASIA IN INFANTS. Sarah Lauridson1, Mitchell Katz2, 3Peds Gastroenterology, CHOC Children’s, Orange, CA; 3Rehabilitation Services, CHOC Children’s Hospital, Orange, CA

Introduction: Cricopharyngeal achalasia is a rare structural abnormality that prevents liquid from appropriately entering the esophagus secondary to failure of relaxation of the upper esophageal sphincter. Symptomatic presentation is dysphagia and aspiration. Reported pediatric cases have been managed by cricopharyngeal myotomy, injection of botulinum toxin and balloon dilatation.

Methods: Four infants, ages 1, 9, 11, and 20 weeks presented with chronic aspiration including choking during feedings, chronic congestion since birth and failure to thrive. Each was diagnosed radiographically by pharyngeal retention, primary aspiration, and characteristic cricopharyngeal bar. All cases were treated with cricopharyngeal dilatations using Maloney dilators sequentially to a maximum size of 44 French under anesthesia scheduled every other week for a total of 3 sessions. Each dilatation was followed by swallowing therapy utilizing neuromuscular electrical stimulation (NMES) to the pharyngeal musculature.

Results: All infants tolerated the dilatation and NMES without complications and demonstrated immediate symptomatic improvement after the first dilatation. All were able to take full feedings orally without clinical signs or symptoms of aspiration preventing the need for nasogastric feedings. In all cases, repeat swallow study 3 weeks after the 3rd dilatation demonstrated no aspiration. A slight residual narrowing of the cricopharyngeus was noted but had no functional impact. All children maintained safe oral feedings throughout the dilatation series. No child required prolonged therapy or diet modification subsequent to the acute treatment phase. At follow-up all patients were safely eating an age appropriate diet.

Discussion: Dilatation with Maloney dilators combined with NMES provides a safe, effective, and sustained method for treating cricopharyngeal achalasia in infants.

291 RECOVERY FROM RECURRENT OR REFRACTORY IRON DEFICIENCY ANEMIA BY HELICOBACTER PYLORI ERADICATION IN CHILDREN. Seiichi Kato, Takako Osaki, Shigeru Kamiya, Infectious Disease, Kyorin University School of Medicine, Mitaka, Japan

Objectives: Helicobacter pylori (HP) cause iron deficiency or iron deficiency anemia (IDA) especially in a subset of the infected children and adolescents. However, there are few studies about whether HP infection is associated with the pathogenesis of recurrent and/or refractory IDA. We performed eradication therapy in the infected children with recurrent and/or refractory IDA.

Methods: Seven HP-infected patients with IDA (12-16 years old). At eradication therapy, the IDA status was the first recurrence in 5 patients, the fourth recurrence and refractoriness to iron supplementation therapy in one, and refractoriness in one. The lowest values of hemoglobin in each patient ranged between 5.3 and 8.3 g/dl (median, 6.5 g/dl); those of serum iron and ferritin ranged between 6 and 20 μg/dl (median, 10 μg/dl) and between 0.9 and 5.6 ng/ml (median, 2.5 ng/ml), respectively. Gastroduodenoscopy showed no bleeding mucosal lesion. Gastric histology showed chronic active gastritis without significant atrophy in all patients. Stool occult blood test was negative in all patients. HP eradication therapy was done with lansoprazole-based triple regimens. In addition, the patients received iron supplementation therapy for 1 to 4 months after eradication therapy was started. HP eradication was confirmed by 13C-urea breath test. Results: HP was successfully eradicated in all patients. The median follow-up period after eradication therapy was 21 months (6 to 76 months). At the end point of the follow-up, median values of hemoglobin, serum iron and ferritin significantly increased to 13.9 g/dl (p <0.001), 102 μg/dl (p <0.001), and 29.3 ng/ml (p <0.05), respectively, compared to those at the baseline. No recurrence of IDA was shown in any patient. Conclusions: Eradication of HP resulted in the recovery of recurrent or refractory IDA, suggesting that chronic infection with the microorganisms play a central role in the pathogenesis. HP test-and-treat strategy should be considered for children or adolescents with IDA of unknown cause.

292 PEDIATRIC POST-ENDDOSCOPY OUTCOMES: A PROSPECTIVE REVIEW OF SHORT-TERM COMPLICATIONS. Shahan Fernando, Mark McOmber, Brad Pasternak, Dana Ursea, Gary Silber, Phoenix Children’s Hospital, Phoenix, AZ

Background: Endoscopic procedures in the pediatric population are commonly utilized for a multitude of indications such as abdominal pain, gastroesophageal reflux, and emesis. Most pediatric gastroenterologists feel that these diagnostic tools are relatively safe. However, there is a paucity of studies that capture short term, minor complications of pediatric endoscopic procedures.

Objective: To determine the frequency and severity of acute, commonly observed complications in pediatric subjects who undergo esophagogastroduodenoscopy (EGD) alone or EGD with flexible sigmoidoscopy (with or without biopsy) under general anesthesia.

Methods: Informed consent was obtained from parents of subjects aged 4-18 years who underwent EGD or EGD with flexible sigmoidoscopy. They then participated in a standardized telephone interview 5-7 days after the procedure. We identified short-term complications such as abdominal pain, bleeding, fevers, nausea and vomiting, difficulty breathing, and sore throat. Additionally, we examined the time to return to daily activities.

Results: Ninety-four procedures were included in this study. Of those, 55 (58.5%) had at least one post-procedural complication. There was no significant correlation with age, gender, scope size, or procedure type. The most frequent complications included sore throat (50.5%) and abdominal pain (30.8%), which were consistent among all age groups. The majority of patients returned to their daily activities within 1-2 days after the procedure, including return to school, regular diet, and baseline energy.

Conclusions: In general, pediatric upper endoscopy and flexible sigmoidoscopy are well-tolerated procedures. Despite nearly 60% of procedures being associated with short-term complications, most children were able to return to their daily activities in a short period of time.
293 ROLE OF ANTIMICROBIAL PEPTIDES IN ESOPHAGITIS. Shauna Schroeder, Zachary D. Robinson, Sophie A. Fillon, Joanne C. Masterson, Lindsay Hosford, Glenn T. Furuta, Digestive Health Institute, Section of Pediatric Gastroenterology Hepatology and Nutrition, Gastrointestinal Eosinophilic Disease Program, Childrens Hospital Colorado, University of Colorado, Aurora, CO

Background: Defensins are antimicrobial peptides that contribute to the innate arm of mucosal defense. Changes in defensin expression may predispose patients to intestinal inflammatory diseases. Eosinophilic esophagitis (EoE) is an allergic/immune mediated chronic disease of undetermined etiology. We hypothesize that dysregulation of defensins contributes to the pathogenesis of EoE. Objectives: To compare defensin expression in well defined patients with EoE to normal controls and in an in vitro model system. HET-1A esophageal cells were grown to confluence with cytokines IL5 (100pg/ml) and GM-CSF(100pg/ml) for 24 and 48 hours to represent a Th2 microenvironment. Human tissue and HET-1A RNA was isolated (RNase Kit,Qiagen), reverse transcribed (cDNA kit, Applied Biosystems), and quantitative RT-PCR (Applied Biosystems 7300, Taqman® probes and Absolute Blue ® qPCR Master Mix) performed. Sample target expression was normalized to 18S RNA and presented as relative mRNA expression (culture system) and fold change (human biopsies).

Human beta defensin 1 (hβD1), hβD2, and hβD3 statistical analysis was performed by one-way ANOVA. Results: Esophageal mucosal defensin expression (hβD1-3) was significantly decreased compared to normal controls. See Table. HET 1A epithelial cells exposed to IL5/GM-CSF had decreased hβD1 expression at 48 hours and hβD3 at 24 hours compared to control cells p=0.03 and p=0.01 respectively. Conclusion: Diminished esophageal defensin expression may provide a susceptible microenvironment for the development of esophagitis.

<table>
<thead>
<tr>
<th>Esophageal Defensin Expression</th>
<th>hβD1</th>
<th>hβD2</th>
<th>hβD3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagitis (n=5)</td>
<td>0.48±0.86</td>
<td>0.4±0.60</td>
<td>0.16±0.21</td>
</tr>
<tr>
<td>Normal (n=11)</td>
<td>1.1±0.54</td>
<td>0.92±0.96</td>
<td>0.93±0.62</td>
</tr>
<tr>
<td>p-value</td>
<td>0.001</td>
<td>0.03</td>
<td>0.013</td>
</tr>
</tbody>
</table>

294 LACK OF CORRELATION BETWEEN BMI AND GASTROESOPHAGEAL REFLUX (GER) IN AN INNER CITY PEDIATRIC COHORT. Sridhar Goli,1 Rupinder Gill1, Jiliu Xu, Nazia Kulsum1, Virginia Anderson1, Steven Schwarz2, Simon Rabinowizt1, 1Division of Pediatric Gastroenterology, SUNY Downstate Medical Center, Brooklyn, NY; 2Department of Pathology, SUNY Downstate Medical Center, Brooklyn, NY

Obesity is correlated with GER and its complications in adults. Published data on this association in children is conflicting, perhaps related to variance in the criteria employed to diagnose pediatric GER. This retrospective study investigates the association between obesity and GER in a cohort of inner city children, utilizing published endoscopic and histologic diagnostic criteria. METHODS: Charts of all 367 patients (ages 1-18 yr, mean=10.5 yr) who had an upper endoscopy at our institution from 1/1/2007 to 12/31/2009 were reviewed. Complete data and inclusion criteria identified the study cohort (n=340). Patient demographics, BMI and gastroesophageal histologic findings were reviewed. A BMI >95th %ile (based on 2000 CDC data) was defined as obese and 85-95th %ile as overweight. Endoscopic GER was classified as normal, grades 1-4 or suggesting eosinophilic esophagitis (EoE). Histologic esophagitis was classified as mild, moderate and marked. RESULTS: There was a high proportion of obese (29%) and overweight (14%) children. 1/4 of the cohort (24%) had abnormal gastroesophageal findings on endoscopy. They were: grade 1(17%), grades 2-4(3%), and esophageal furrows and plaques (EoE)(4%). The proportions of obese children with all levels of esophagitis (grade 1: 30%, grade 2-4: 30%, and EoE: 20%) were similar to the proportion of obese children with normal esophageal endoscopy (29%). 21% had abnormal esophageal histology that were subdivided into: mild (13%), moderate (3%) and marked (5%). Again, there were similar proportions of obese children with all degrees of histological esophagitis (mild: 30%, moderate:18%, EoE: 19% and normal:30%). Reanalyzing the data by combining overweight and obese children yielded the same outcome. CONCLUSIONS: In our cohort of inner city, mostly African American and Caribbean children, we found no increased endoscopic or histologic features of GER in our overweight or obese patients.

295 INVERSE CORRELATION BETWEEN HELICOBACTER PYLORI (HP) COLONIZATION AND OBESITY IN A COHORT OF INNER CITY CHILDREN. Sridhar Goli1, Nazia Kulsum2, Rupinder Gill2, Jiliu Xu, Steven Schwarz2, Simon Rabinowitz1, 1Division of Pediatric Gastroenterology, SUNY Downstate Medical Center, Brooklyn, NY; 2Department of Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY

Obesity is an increasing problem among children in the US. Inner-city youth are particularly affected, with obesity prevalence rates approaching 30%. HP, because of its potential effect on gastric synthesis of leptin and ghrelin, may play a role in regulating body weight. Although organism eradication has been associated with weight gain in some adult studies, adult epidemiologic studies have failed to demonstrate a significant correlation between HP infection and body mass index (BMI). A retrospective analysis was performed to determine the prevalence of gastric HP colonization in groups of inner-city children with varying BMIs. METHODS: Clinical and endoscopic findings were reviewed in 345 symptomatic patients (ages 1-18 yr, mean= 10.5 yr) undergoing endoscopy between 1/1/07 to 12/31/09. Patient demographics, anthropometrics and histologic findings including HP immunostaining were determined. BMI was defined as obese (>95th %ile) and overweight (85th-95th %iles) based on 2000 CDC data. RESULTS: In this study group, the overweight prevalence was 43%, with 29% classified as obese. HP colonization was...
present in 19% of the entire cohort. The table demonstrates a substantially decreased prevalence of HP among the obese children (*p<0.05, compared with overweight and normal BMI). CONCLUSIONS: In this group of inner-city children, mostly African American and Caribbean, with upper GI tract symptoms, obesity was associated with reduced HP colonization when compared with both normal and overweight subjects. Whether HP infection may actually protect certain children from obesity, as previously suggested, remains to be elucidated.

<table>
<thead>
<tr>
<th>BMI</th>
<th>&gt;95% (Obese)</th>
<th>85-95% (Overweight)</th>
<th>5-85% (Normal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP+(n,%)</td>
<td>10, 10%</td>
<td>12, 25%</td>
<td>37, 22%</td>
</tr>
<tr>
<td>HP-(n,%)</td>
<td>88, 90%</td>
<td>36, 75%</td>
<td>133, 78%</td>
</tr>
</tbody>
</table>

**Prevalence of H. pylori in the study cohort**

296 **PILLCAM ESO™ IN THE EVALUATION OF ESOPHAGEAL VARICES IN PEDIATRIC PATIENTS WITH PORTAL HYPERTENSION.** Vivien A. Nguyen, Rula Harb, Sylvie Lebel, Chuan Hao Lin, Hillel Naon, Children’s Hospital Los Angeles, Los Angeles, CA

Background: Hemorrhage from esophageal varices is a serious complication of portal hypertension. The AASLD recommends that adults with portal hypertension undergo esophagogastroduodenoscopy (EGD) at diagnosis and on a periodic basis to screen for esophageal varices. In children with portal hypertension, these guidelines imply multiple EGDs over the course of a lifetime. EGD requires sedation or general anesthesia and is associated with significant cost, inconvenience, and risk. Adult studies comparing EGD to esophageal video capsule endoscopy (EVCE) for the detection of varices have shown 85% sensitivity and 80.5% specificity. However, similar studies have not been performed in children.

Hypothesis: EVCE is comparable to EGD in detecting varices in children with portal hypertension and is lower in cost.

Methods: This is a retrospective study that includes pediatric patients with portal hypertension undergoing evaluation for varices. Data were obtained using the Given Imaging PillCam ESO™, Given Imaging RAPID™ reporting system, and KIDS™ electronic medical record. EVCEs were reviewed separately by 3 Pediatric Gastroenterologists.

Results: 15 EVCEs were performed in 13 patients from 1/07 to 10/10. Esophageal varices were identified in 9 patients, 4 of whom also underwent EGD during the time period. Two patients, with grade 1-2 varices on EVCE, had no varices on EGD. Two patients, with grade 1-2 varices on EVCE, had varices on EGD. Another patient with no varices on EVCE, had grade 1 varices on EGD.

Conclusions: The differences noted between EVCE and EGD in the detection of varices may have arisen from variable time intervals between studies. These discrepancies did not affect patient management. The study did not include a sufficient number of patients to demonstrate statistical significance; therefore, a prospective study is planned. EVCE was tolerated well and was preferred by patients. The cost of EVCE ($4674) as compared to EGD ($11,472) favors the former as a screening modality.

**INTESTINE/COLON/IBD**

307 **DEVELOPMENT OF AN OBJECTIVE SKILL ASSESSMENT TOOL FOR PEDIATRIC COLONOSCOPY: A DELPHI APPROACH.** Catharine M. Walsh, Simon C. Ling, Thomas D. Walters, Heather Carnahan, University of Toronto, Toronto, ON, Canada

BACKGROUND: Colonoscopy is a technically challenging procedure; however, no objective measure of endoscopic competence currently exists for use in the pediatric setting. Using the Delphi approach, this study aimed to determine expert consensus regarding items required on a checklist and global rating scale designed to assess the competence of clinicians performing colonoscopy on pediatric patients.

METHODS: Checklist and global rating items were generated from a systematic literature review and a survey of core committee members. A Delphi group of pediatric endoscopy experts from across North America was established to aid with further item generation and reduction. Using a 1 to 5 Likert scale, experts rated the checklist and global rating items for their importance as an indicator of the competence of trainees learning to perform colonoscopy. Responses were summarized by an expert panel, analyzed, and resent to the group in an online survey. The process continued until consensus was reached and items were reduced to a number feasible for use in the clinical setting. Items that ≥80% of experts rated as ≥4 were included in the final instrument. Cronbach’s α was used to measure variability among experts.

RESULTS: 67 checklist and 34 global rating items were generated through a systematic literature review and survey of committee members. These were distributed to a Delphi group of 41 experts who added an additional 2 checklist and 4 global rating items. 5 rounds of surveys were completed with response rates ranging from 76 to 100%. α values for checklist items were 0.93, 0.96, 0.89, 0.83 and 0.73 for rounds 1 to 5, respectively. α values for global rating items were 0.94, 0.94, 0.91, 0.90 and 0.86 for rounds 1-5, respectively. 7 global ratings and 19 checklist items were included in the final tool.

CONCLUSIONS: The Delphi method allowed for the determination of consensus regarding essential items to be included in a tool designed to measure competence in performing colonoscopy. Next, we plan to assess the reliability and validity of the tool in the clinical setting.
308 COMPUTER-ASSISTED ASSESSMENT OF GASTROINTESTINAL ENDOSCOPY SKILLS: VALIDATION OF A NOVEL AND OBJECTIVE PERFORMANCE MEASURE. Catharine M. Walsh1, Sayra M. Cristancho2, Adam Dubrowski3, Heather Carnahan1, 1University of Toronto, Toronto, ON, Canada; 2University of Western Ontario, London, ON, Canada

BACKGROUND: Motion analysis systems, such as the Imperial College Surgical Assessment Device (ICSAD), are now being utilized for the evaluation of surgical skills as they provide an objective, reliable and valid measure of technical skills. Their utility in the assessment of gastrointestinal endoscopic skills, however, remains unknown. This study aimed to establish the construct validity of the ICSAD as an assessment tool for endoscopy skill performance by examining (a) its responsiveness to detecting changes in the performance level of novices trained on an endoscopy simulator task and (b) its ability to discriminate between operators of different experience levels performing the simulator task.

METHODS: 13 novice endoscopists viewed a 10 minute instructional video. They were then pretested on a bench-top colonoscopy simulator task. The validated simulator is composed of a series of 4 vertical panels with numbered targets (holes), which are navigated using a real colonoscope in defined sequences as quickly and accurately as possible. Novices then underwent one session of training on the simulator during which they were required to complete 12 sequences. After practice, novices completed a post-test requiring them to navigate the colonoscope through the same sequence as the pre-test. 6 experienced endoscopists (> 50 procedures) completed only the pre-test simulator task. Performances were measured using the ICSAD (number of hand movements, path length, and time).

RESULTS: Novices improved significantly with training as measured by path length, number of hand movements and execution time (p < 0.01). As compared with experienced endoscopists, trained novices had longer path lengths, made more movements and took more time for task completion (p < 0.01).

CONCLUSIONS: Construct validity of the ICSAD for the assessment of endoscopy skills was established by demonstrating that it can measure improvement in performance with training and distinguish between operators of different experience levels.

309 INFANTS WITH COLIC HAVE DIFFERENT STOOL OUTPUT CHARACTERISTICS THAN ASYMPTOMATIC HEALTHY INFANTS. Laura E. Flores-Fong1, Alfredo Larrosa-Haro3, Jesús Nájera2, Rocio M. Macías-Rosas12, Carmen A. Sánchez-Ramírez2, Mariana Gómez-Nájera3, Erika F. Hurtado-López32, Heriberto Pinto-Aguilar1, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2Servicio de Gastroenterología y Nutrición, UMAE Hospital de Pediatría CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; 3Servicio de Gastroenterología y Nutrición, Hospital General 16, Instituto Mexicano del Seguro Social, Torreón, Mexico; 4Facultad de Medicina, Universidad de Colima, Colima, Mexico; 5División de Pediatría, Hospital de Gineco-Obstetricia 48, Instituto Mexicano del Seguro Social, León, Mexico

Objective: To compare the stool output pattern between infants with colic versus healthy asymptomatic infants. Patient and methods: One-hundred infants consecutively seen by colic (Rome’s III criteria) at five GI outpatient clinics and the same number of infants seen at a General Pediatrician office were studied. Quantitative and qualitative stool characteristics and some other clinical data were obtained with an ad hoc questionnaire. The instrument was applied to the parents individually by each investigator. Comparison of variables was performed with Student’s t or chi2.

Results: The mean age was 10.9±6.2 weeks, 51.2% were females. There were no differences between the daily number of feedings and its type (breast milk, formula or both). In the colic group the excessive crying started at 2.8 weeks, it occurred 3.7 times a day, the total 24-hour crying time was > 3 hours, it occurred 6.7 times per week, more frequently at night; two-thirds had colic while passing stools and 53.1% during feedings. The statistically significant differences related to stool output were: a) Frequency of daily and weekly bowel movements was lower in infants with colic; b) Stool consistency was increased in infants with colic (Bristol criteria); c) Feces in the colic group were more frequently green, darker and bad smelling.

Conclusions: The stool output pattern showed differences between the colicky and asymptomatic infants studied. This finding may suggest and underlying motility disorder associated to infant colic.

310 REHYDRATION AND FEEDING PRACTICES CARRIED OUT BY PARENTS AND CAREGIVERS IN INFANTS AND CHILDREN WITH ACUTE DIARRHEA (AD). María C. Cortés-López1, Alfredo Larrosa-Haro2, Enrique Romero-Velarde1, Edgar M. Vázquez Garibay4, Teresa M. Torres-López3, Alfredo Nájar-Estrada1, Blanca A. Barragán-Guezmán1, 1Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 2Instituto de Investigación en Salud Ocupacional, Departamento de Salud Pública, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; 3Departamento de Pediatría, Hospital General de Zona 89, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; 4Unidad Docente Asistencial de Terapia de Hidratación Oral y Saneamiento, Hospital Civil de Guadalajara Dr. Juan I Menchaca, Guadalajara, Mexico

Objective: To evaluate the rehydrating and feeding practices in children with AD according to the WHO protocol. Patients and methods: One-hundred consecutive children with AD, 1-63 months, managed at oral rehydration centers of the ER of two pediatric hospitals in a four-month period are reported. Socio-demographic variables, rehydration and feeding practices were attained with ad hoc questionnaires. Energy, macro and micronutrient intake were estimated with a 24-hour dietary recall and a nutritional calculator (Nutrikal).

Results: The mean age was 14 months, 82 were infants and 18 preschoolers; 60% were males. The opinion that influenced the most the oral rehydration technique was the mother’s mother. In about two-thirds of the sample the rehydration practices of the 24-hour period previous to the admission were not performed according to the WHO criteria in the rehydration plan, the type of solution offered and the hydration technique. In most cases, the children’s diet during the 24 hours previous to the assistance to the ER was qualitatively close to the usual diet; however, water, macronutrient and electrolyte ingestion was lower than the daily
recommended intake for age and gender.
Conclusions: The WHO rehydration protocol was inadequately applied by parents or guardians in most of the patients with AD studied previously to their admission to the ER. These findings underline the insufficient information and ability of the parents or caregivers to handle adequately the diarrheal episode.

311 FAMILIAL AGGREGATION FOR INTESTINAL CONSTIPATION IN RELATIVES OF INFANTS WITH COLIC: CASE CONTROL STUDY. Laura E. Flores-Fong, Alfredo Larrosa-Haro, Jesús Náyera, Rocío M. Macías-Rosales, Carmen A. Sánchez-Ramírez, Mariana Gómez-Náyera, Erika F. Hurtado-López, Heriberto Pinto-Aguilar, Instituto de Nutrición Humana, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, Mexico; Servicio de Gastroenterología y Nutrición, UMAE Hospital de Pediatría, CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico; Servicio de Gastroenterología y Nutrición, Hospital General 16, Instituto Mexicano del Seguro Social, Torreón, Mexico; Facultad de Medicina, Universidad de Colima, Colima, Mexico; División de Pediatría, Hospital de Gineco-Pediatría 48, Instituto Mexicano del Seguro Social, León, Mexico
Objective: To compare the frequency of intestinal constipation between relatives of infants with colic vs relatives of healthy infants.
Methods: 104 infants attended by colic at 5 GI outpatient clinics (Rome III) and 101 infants seen at a General Pediatrician office for monthly control were studied. In an interview with the infant’s parents, the frequency of constipation (Rome III) in siblings, parents, uncles, aunts, grandparents and great-grandparents was investigated. The instrument was applied to the parents individually by each investigator. Statistics: chi2, OR and 95% CI.
Results: The infant’s mean age was 10.9±6.2 weeks; 51.2% were males. The relatives of the colicky infants had a higher frequency of constipation than the relatives of the asymptomatic ones with a strong predominance for females. The significant associations of constipation in the group of infants with colic are presented in Table.
Conclusion: These findings suggest a possible familial genetic involvement related to the occurrence of functional bowel motility disorders as infant colic and constipation.

<table>
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<tr>
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<td>Fathers</td>
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</tr>
<tr>
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</tr>
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<td>Paternal grandmothers</td>
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<td>1.4-6</td>
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</table>

312 MOLECULAR INSIGHTS IN CONGENITAL SUCRASE-ISOMALTASE DEFICIENCY (CSID). Stefanie Uhrich, Zaining Wu, C. Ronald Scott, Pediatrics, University of Washington, Seattle, WA
CSID is one of the intestinal malabsorption syndromes with reduced capacity to digest complex carbohydrates, resulting in chronic diarrhea, abdominal bloating/pain, and failure to thrive. The gene (SI) for sucrase-isomaltase is large (100 Kb, 48 exons) and encodes a protein of 1827 amino acids.
We have identified 36 affected persons and obtained DNA from oral fluids for gene sequencing. Forty-seven different mutations were identified. The majority were “private” mutations in single families, but three mutations were more frequent, with p.G1073D, p.V577G, and p.R1124X having frequencies of 0.28, 0.16, and 0.06, respectively. Assuming Hardy-Weinberg equilibriums, 75% of affected patients should have 1 or 2 of these mutations.
Molecular testing may offer a less expensive initial evaluation than intestinal biopsy and enzyme analysis for a child suspected of CSID. No obvious correlation was noted between the site of amino acid alteration within either the sucrase or isomaltase domains and dietary limitation.

313 PERCEPTIONS OF MOTHERS ON DIARRHEAL DISEASE IN CHILDREN IN PROVIDENCIA, COLOMBIA. Cesar Verbel, Carlos A. Velasco, Angela M. Jimenez, Pediatrics, University of Valle, Cali, Colombia; Group of Investigation GASTROHNUP, University of Valle, Cali, Colombia; Sociedad Colombiana de Pediatría, Regional San Andres, Isla, Colombia
Introduction: Perceptions, attitudes and practices of mothers on the island of Providencia, Colombia on diarrheal disease (DD) in children are extremely important to promote proper focus and prevent misuse. Objective: To describe the perceptions of mothers on the island of Providencia, Colombia on the etiology, medical care and management of DD in children. Materials and methods: We conducted 89 interviews with mothers of 152 children (1 month to 15 years) including identification data, anthropometric measurements and knowledge, practices and attitudes about the DD. The results are expressed as mean and standard deviation. Results: In terms of aetiology, 55% of mothers feel that “something” causes the DD for their children. As to where to go when their children have DD, 59% go to the doctor, 41% do not go to anyone, only 7% ask their grandmothers and 3% for their mothers. Finally, with respect to management, 75% offer in order hydration serum, liquid, cinnamon and tea, 29% indicated medications, most often anti-diarrhea, and in terms of food, 12% offer fruits, especially guava and 7% rice, especially rice-water.
Methods and findings: C5 susceptibility along with the colonic mucosal microbiome in mice. Disease group. Here, we studied the effects of transient pediatric dietary cellulose supplementation on young adult colitis adulthood. Therefore, the pediatric time period may be important in respect to the bowel diseases (IBD) where intestinal microbes are recognized to play an etiologic role. The peak onset of IBD is in young influences in humans. Indirect epidemiologic data suggests that dietary fibers su... 

Background: Dietary fibers have intestinal trophic and anticolitic effects in rodents, and can have beneficial gastrointestinal effects of colitis in mice with a neutrophil-targeted SHIP deficiency. Methods: SHIP (floxed/floxed) mice were interbred with congenic mice expressing Cre to cause experimental granulomatous ileitis. In order to dissect cell-specific roles for SHIP, we examined the course of colitis in mice with a neutrophil-targeted SHIP deficiency. Methods: SHIP (Iox/flox) mice were interbred with congenic mice expressing Cre-recombinase under the control of the granulocyte elastase promoter. Resulting Cre+ (with targeted deletion of SHIP) and Cre- (control) mice were given 2% dextran-sulfate sodium (DSS) colitis for 5 days with subsequent recovery over the following 9 days (total 14 days). Mice were harvested at day 7 and 14 for assessment of colitis. Results: Cre+ mice showed a trend to decreased weight loss during the course of DSS colitis as well as decreased diarrhea (Stool dry/total weight 26.0 (Cre+ vs 21.0% (Cre-) on day 7; 33.4 vs 29.5% on day 14). Colonic myeloperoxidase assay showed diminished neutrophil infiltration during DSS colitis in Cre+ compared to Cre- (Day 7: 4.1 vs 7.6 U/mg, p < 0.01; 4.0 vs 2.7 U/mg, p < 0.05). Histological scores in Cre+ mice were significantly lower than in the Cre- group (Day 14: 7.6 vs 12.4; p < 0.001). Interestingly, in spite of the diminished levels of inflammation seen in the colon by MPO assay and histological analysis, granulomata were noted in approximately 80% of the Cre+ mice at day 14, primarily in lymphoid follicles, with no granulomata noted in the Cre- group. Conclusion: Targeted neutrophil deletion of SHIP reduces neutrophil recruitment and histological damage in experimental colitis, but with the subsequent development of granulomata in the intestinal tract. This highlights a critical, cell specific role for SHIP in mediating intestinal disease. 

316 PEDIATRIC CELLULOSE SUPPLEMENTATION INDUCES TRANSIENT TROPHIC, ANTICOLITIC, AND SHORT-LIVED MICROBIOMIC EFFECTS IN MURINE COLON. Dorottya Nagy-Szakal1-3, Scott E. Dowd1, Lars Koenig1, James Versalovic1, 2, C. W. Smith1, Richard Kellermayer1, 2, 3 Pediatric Gastroenterology, Baylor College of Medicine, Houston, TX; 2Research and Testing Laboratory, Lubbock, TX; 3Department of Pediatrics, Baylor College of Medicine, CNRC, Houston, TX; 4Department of Pathology, Baylor College of Medicine, Houston, TX; 5Texas Children Hospital, Houston, TX Background: Dietary fibers have intestinal trophic and anticolitic effects in rodents, and can have beneficial gastrointestinal influences in humans. Indirect epidemiologic data suggests that dietary fibers such as cellulose may protect against inflammatory bowel diseases (IBD) where intestinal microbes are recognized to play an etiologic role. The peak onset of IBD is in young adulthood. Therefore, the pediatric time period may be important in respect to the nutritional developmental origins of this disease group. Here, we studied the effects of transient pediatric dietary cellulose supplementation on young adult colitis susceptibility along with the colonic mucosal microbiome in mice. Methods and findings: C57BL/6J male mice received a synthetic high (12.5%), or low (2.5% cellulose, control) fiber diet from postnatal days (P) 30 to P80. Thereafter, the high fiber group was reversed to control diet for 10 or 40 days. Colitis was induced...
by dextran sulfate sodium (DSS). The mucosal microbiome was studied by massively parallel pyrosequencing of 16S rRNA. Cellulose supplementation induced transient trophic effects on the colon (increased length) that persisted 10 days following reversal, but diminished by 40 days. Colitis susceptibility inversely correlated with colonic length measures. High cellulose diet stimulated a significant separation of the colonic mucosal microbiome from controls. However, this divergence was lost by 10 days after reversal.

Conclusions: Dietary cellulose dependent microbiome separation in the colonic mucosa of mice is short lived. The transient anticolitic effects of cellulose supplementation are independent from its microbiomic influence. These findings may have implications for dietary fiber supplementation in humans.

317 FECAL CALPROTECTIN IN HIV INFECTED HAART NAÏVE UGANDAN CHILDREN: A HOSPITAL-BASED SURVEY. Elin Hestvik1,2, Edda Olafsdottir2, Thorklid Tylleskar1, Lage Aksnes1,2, Deogratias Kaddu-Mulindwa1, Grace Ndeezzi1,1, James K. Tumwine3, Lena Grahunquist1,1, Centre for International Health, University of Bergen, Bergen, Norway; 2Department of Paediatrics, Haukeland University Hospital, Bergen, Norway; 3Department of Paediatrics and Child Health, Makerere University Medical School, Kampala, Uganda; 4Department of Microbiology, Makerere University Medical School, Kampala, Uganda; 5Department of Women’s and Children’s Health, Karolinska Institute, Stockholm, Sweden; 6Department of Clinical Medicine, University of Bergen, Bergen, Norway

Objective: Fecal calprotectin is a marker for gastrointestinal inflammation. A recommended cut-off value is established in children over 4 years of age. Our aim was to determine the concentration of fecal calprotectin in HIV infected HAART naïve Ugandan children and to compare it with concentrations found in healthy Ugandan children.

Method: We tested 193 HIV infected children aged 0-12 years in a hospital-based survey for fecal calprotectin. A standardized interview with socio-demographic information and medical history was used to assess risk factors. A CD4-cell percent was prevalent in all children, and was classified as high or low with limits concurrent with those recommended for starting HAART.

Results: The median fecal calprotectin concentrations decreased with increasing age, as in healthy children. The median concentration was 208 mg/kg in infants 0-1 year, 171 mg/kg among toddlers 1-4 years, and 62 mg/kg for children 4-12 years. Children with advanced disease and a low CD4-cell percent had significantly higher fecal calprotectin concentrations than those with a high CD4-cell percent. Children older than 4 years of age with diarrhoea had significantly higher fecal calprotectin concentrations compared to those without diarrhoea. There were no significant differences between concentration of fecal calprotectin and WHO stage, fever on examination or colonization by Helicobacter pylori.

Conclusion
HIV infected children older than 4 years of age had a median fecal calprotectin concentration 2.2 times higher than healthy Ugandan children. Children with more advanced disease had higher fecal calprotectin concentrations regardless of age.

318 FECAL CALPROTECTIN IN HEALTHY UGANDAN CHILDREN: A COMMUNITY-BASED SURVEY. Elin Hestvik1,2, Lena Grahunquist1, Thorklid Tylleskar1, James Tumwine3, Grace Ndeezzi1,1, Deogratias Kaddu-Mulindwa1, Lage Aksnes1,2, Edda Olafsdottir2, 1Centre for International Health, University of Bergen, Bergen, Norway; 2Dep. of Paediatrics, Haukeland University Hospital, Bergen, Norway; 3Dep. of Women’s and Children’s Health, Karolinska Institute, Stockholm, Sweden; 4Dep. of Paediatrics and Child Health, Makerere University Medical School, Kampala, Uganda; 5Dep. of Microbiology, Makerere University Medical School, Kampala, Uganda; 6Dep. of Clinical Medicine, University of Bergen, Bergen, Norway

Objective: Fecal calprotectin is a marker for gastrointestinal inflammation. Studies have established normal concentrations in healthy children living in high-income countries. The objective of this study was to determine the concentration of fecal calprotectin in apparently healthy Ugandan children.

Methods: We tested 302 apparently healthy children aged 0-12 years in urban Kampala, Uganda. The children were recruited consecutively by door-to-door visits. Fecal calprotectin was analyzed by an ELISA method. Feces were tested for H. pylori antigen, for growth of enteropathogens and microscopy was performed to assess protozoa and helminths. A short standardized interview with socio-demographic information and medical history was obtained to assess health status of the children.

Results: The median fecal calprotectin concentration was 249 mg/kg in infants 0<1 year, 75 mg/kg in toddlers 1-4 years, and 28 mg/kg for children 4<12 years. There was a significantly difference in the fecal calprotectin concentration across all three age groups. There was no significantly difference between fecal calprotectin and sex, education of female caretaker, wealth index, habits of using mosquito nets, being colonized with H. pylori, having other pathogens in the feces or have used antibiotics last 3 months.

Conclusion
Concentrations of fecal calprotectin among healthy Ugandan children, living in a low- income country, are comparable to those in healthy children living in high-income countries. In children older than 4 years, the fecal calprotectin concentration is low. In healthy infants fecal calprotectin is high. Healthy children living under poor circumstances do not have a constant inflammation in the gut.

319 MID-SIGMOID VOLVULUS: A PEDIATRIC CASE REPORT. Graciela Wetzler1, Amy Felix1, Asha Willis2, Steven Shamah1, Konstantin Vaizman2, 1Pediatric Gastroenterology, Maimonides Infants & Children’s Hospital of Brooklyn, Brooklyn, NY; 2Maimonides Medical Center, Brooklyn, NY

NS is an 8-year old female who presented with intestinal obstruction (severe abdominal pain and bilius vomiting) of 1-day duration. Her past medical history revealed less severe but similar episodes as well as constipation and poor growth. Blood tests were normal. Abdominal CT scan showed mid-sigmoid volvulus with dilatation and hyperemia of the trapped sigmoid colon, suggesting venous drainage compromise. The patient underwent an emergency colonscopy to decompress the volvulus. Decompression was successful with complete resolution of the presenting symptoms. Further work up included an upper GI series with SBFT which revealed a malrotation with a non-fixed colon; a barium enema which revealed an abnormal course of
the large bowel with abnormal fixation of the cecum; and a rectal biopsy which ruled out Hirschprung's disease. Patient underwent a Ladd procedure, appendectomy, and correctional placement of the cecum, which was found in the left upper abdomen. Incidental surgical finding was a carcinoid of the distal appendix. Although sigmoid volvulus is a rare occurrence in pediatrics, it can present with recurrent attacks of abdominal pain and vomiting, and can be decompressed through emergency colonoscopy rather than barium enema and surgery. After decompression, imaging of the GI tract is indicated as well as rectal biopsy to rule out Hirschprung's disease, a frequent associated condition. This is the first report of carcinoid tumor associated with malrotation and sigmoid volvulus.

320 RAPID 1 HOUR INFILXIMAB INFUSIONS ARE SAFE: A META-ANALYSIS. Haley C. Neef, Jeremy Adler
Pediatric Gastroenterology, University of Michigan, Ann Arbor, MI
Introduction: Infliximab (IFX) is a mainstay of therapy for inflammatory bowel disease (IBD). Currently, IFX is routinely given as a 2 hr IV infusion. Prolonged infusions are burdensome for both patients and the healthcare system, because time, space, and resources are inadequate at many infusion centers. There are limited data on the safety of rapid IFX infusions. We performed a systematic review of the literature and meta-analysis to identify studies of the safety of rapid compared to standard 2 hr IFX infusions.

Methods: Search of OVID, Embase, Web of Science and references identified 941 papers. Inclusion required human subjects and documentation of numbers of 2 hr duration IFX infusions (D2), 1 hr IFX infusions (D1), and infusion reactions (IR). Sixteen studies met criteria; 8 were excluded for duplicate or incomplete data. All studies required at least four D2 without IR to be eligible for D1. The 8 remaining studies included 7,328 D2 and 6,063 D1. Six studies were specific to IBD, including 5,930 D2 and 5,070 D1. Additionally, 4 studies included 978 thirty minute infusions (D½). Data were extracted by 2 independent reviewers. The primary outcome measured was rate of IR. Bivariate random effects regression model meta-analysis was performed with Stata.

Results: Across 8 studies, there were 82 (1.4%) D1 and 346 (4.7%) D2 IR. Pooled analysis showed decreased risk of IR with D1 relative to D2 (relative risk (RR) 0.41, 95% confidence interval (CI) 0.27-0.63; p<0.001). In 6 studies specific to IBD, there were 43 (0.8%) D1 and 130 (2.2%) D2 IR (RR 0.42, 95% CI 0.23-0.77; p=0.005). In 3 studies with D½, there were no differences in IR rates between D½ (1.0%) and D2 (3.7%) (p=0.16).

Conclusions: Rapid IFX infusions are not associated with increased risk of infusion reactions compared to standard 2 hr infusions. In fact, selected patients who previously received 2 hr infusions without reaction had lower rates of infusion reactions to subsequent 1 hr infusions than occur in the general population of all patients receiving 2 hr infusions. One hr IFX infusions should be standard for patients without prior infusion reactions.

321 COMPARING MANUAL, SEMI-AUTOMATED AND ROBOTIC METHODS OF MUCOSAL DISACCHARIDASE ASSAYS. Janet Conrad, Patrick Pignon, Karoly Horvath, Jeffrey Bornstein, Dev I. Mehta, Pediatric Gastroenterology, Arnold Palmer Hospital for Children, Orlando, FL
Introduction: Mucosal disaccharidases are typically assayed using a manual method. We compared this method with a thermal cycler based assay and a robotic assay.

Methods: Samples (N=15) were divided into 3 aliquots and assayed using a method described by Dahlqvist, a thermal cycler method, or a robotic method. Differences in values were compared.

Results: The robotic assays for all enzymes except Palatinase were consistently higher compared to the other 2 methods (Table 1). The degree of agreement with the thermal cycler based and manual assay was very close (Table 2). Operator time is 30 min for robot, 3 hours for thermal cycler and 3 hours and 30 min for manual.

Conclusion: Both the thermal cycler method and manual method are very comparable, however, the robotic method yields higher values. None of the samples required changes in interpretation. The robotic method may require new normal ranges, but potentially more cost effective.

### Disaccharidase activities and paired tests for 3 methods

<table>
<thead>
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<th>Method Ave (μM/min/g)</th>
<th>N=15 Robot</th>
<th>Semi-automated</th>
<th>Manual</th>
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<td>53.8</td>
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</tr>
<tr>
<td>Glucoamylase</td>
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<tbody>
<tr>
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<td>Palatinase</td>
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<td>Glucoamylase</td>
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### Correlation between assays

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<th>semi-automated vs manual</th>
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</tbody>
</table>

### 322 PITFALLS IN SAMPLE PREPARATION OF MUCOSAL DISACCHARIDASE ASSAYS.

**Janet Conrad, Patrick Pignon, Karoly Horvath, Jeffrey Bornstein, Dev I. Mehta, Pediatric Gastroenterology, Arnold Palmer Hospital for Children, Orlando, FL**

Introduction: Several laboratories involved in sharing quality control samples use variable specimen homogenization. Automation of mucosal biopsy disaccharidase assays requires use of both homogenization and sonication to yield finer suspensions. We studied impact of various conditions to help develop a standard approach.

Method: Frozen samples were either homogenized only using a Kontes Pellet Pestle motorized mixer, or homogenized and then sonicated, using a Fisher Scientific Sonic Dismembrator Model 500. We tested several combinations to assess ranges of both that would be optimal in triplicate. We adjusted homogenization by sampling at incremental time points. Sonication was also altered both by duration, and %Amps. Lactase, Sucrase, Palatinase and Glucoamylase activities were measured.

Results: Homogenization alone showed a gradual reduction after 15 seconds for all disaccharidases (Lactase only shown, Table 1)

Sonication had a biphasic pattern. Set at 30 Amps, progressive reduction in lactase activity was seen initially, with a rise after 15 seconds. At 15 Amps, the activity stayed constant (Table 2)

Combining 15 seconds of homogenization with 10 second of sonication at 10% Amp gave optimal results, with no decay even with samples with low level disaccharidases.

Conclusion: Disaccharidases are sensitive to homogenization and sonication. Small changes can lead to large, potentially misleading effects. We have defined settings that allowing consistent peak activity using homogenization and sonication. These setting should be suitable for automation, and provide a basis to develop standardized assays across laboratories. Additional marker of percent of denaturation may be a useful quality indicator.

<table>
<thead>
<tr>
<th>Time/sec</th>
<th>15</th>
<th>30</th>
<th>45</th>
<th>60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactase Activity</td>
<td>86.6±14.4</td>
<td>84.0±14.2</td>
<td>69.4±8.6</td>
<td>84.1±11.3</td>
</tr>
</tbody>
</table>

### 323 WITH UNIVERSAL FOOD FOLATE FORTIFICATION, CHILDREN WITH INFLAMMATORY BOWEL DISEASE TREATED WITH SULFASALAZINE DO NOT NEED FOLIC ACID SUPPLEMENTATION.

**Jean-Francois Turcotte, Jessica Sawyer-Bennett, Hien Q. Huynh, Stollery Children’s Hospital, Edmonton, AB, Canada**

BACKGROUND: Sulfasalazine is used in the treatment of children with inflammatory bowel disease (IBD). It is known as an inhibitor of folate absorption. Folic acid supplementation is recommended. However, the evidence is scarce and no deficient folate levels have been reported in children. It has been recently suggested that folate could act as a cancer promoter. With universal food folate fortification in place, adding folic acid supplementation could be deleterious.

AIM: To assess folate levels in children treated with sulfasalazine

METHODS: It is the practice of our IBD clinic not to routinely give folic acid supplements to patients receiving sulfasalazine but to instead monitor levels. A chart review of IBD patients treated with sulfasalazine for more than one year was performed. In our laboratory, red blood cells (RBC) folate was the test of choice until November 2007. Since, serum folate measurement was introduced as the initial assessment because of its lower cost, easier technique and good correlation with RBC folate. Hemoglobin, mean corpuscular volume (MCV) and vitamin B12 levels were also assessed.

RESULTS: Twenty nine patients were reviewed. Mean initial dose of sulfasalazine was 52mg/kg/day and mean duration of treatment was five years. A first folate level following introduction of therapy was conducted after a mean time of 31 months (mean serum folate of 31nmol/L; mean RBC folate of 1229nmol/L). Folate levels were assessed on average 1.5 times per year per patient; only one patient had a borderline low serum folate level of 11.9nmol/L (normal >12nmol/L) that normalized without
supplementation. Low RBC folate levels were not detected and no patient was ever supplemented with folic acid. No vitamin B12 deficiency was identified.

CONCLUSION: In places where universal food folate fortification has been introduced, our study does not support the use of folic acid supplementation in children treated with sulfasalazine for IBD. Yearly folate level measurement is a better strategy in monitoring patients on sulfasalazine.

324 GD3 GANGLIOSIDE AMELIORATES THE NECROINFLAMMATORY LESION IN A MURINE MODEL OF NECROTIZING ENTEROCOLITIS (NEC). Jilin Xu1, Virginia Anderson2, Steven Schwarz2, 1Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY; 2Pathology, SUNY Downstate Medical Center, Brooklyn, NY

NEC is the most common devastating gastrointestinal emergency in newborn, particularly preterm infants. Gangliosides are glycosphingolipids that signal enterocyte growth, differentiation, and immune response. Recent studies in an in vitro NEC model have shown that gangliosides exert a protective effect against lipopolysaccharide/hypoxia-induced bowel necrosis, by suppressing proinflammatory signals (JPGN 2009; 49:382). However, the protective role of gangliosides in vivo is unknown. The aim of this study was to investigate the effects of orally administered GD3, the predominant ganglioside expressed in rat neonatal intestine, in our established murine NEC model. METHODS: Newborn rats were gavage-fed with either formula (NEC), formula supplemented with 15 μg/ml GD3 or a combination of GD3 and 500 ng/ml epidermal growth factor (GD3-EGF). Dam-fed littersmates served as controls. NEC was induced by asphyxia and cold stress. At 96 h, all animals were killed and gross and histological changes in the ileum were evaluated. RESULTS: In pups supplemented with GD3 or GD3-EGF, the necroinflammatory lesion of NEC was significantly ameliorated, compared with the NEC group. CONCLUSION: These data suggest that gangliosides, when supplemented to an artificial formula diet, reduce the incidence and severity of NEC.

SPECULATION: Our in vivo results suggest that gangliosides represent new potential therapeutic agents for prevention and possibly for treatment of NEC.

325 CO-EXISTENCE OF SUPERIOR MESENTERIC ARTERY SYNDROME AND NUTCRACKER SYNDROME IN A CHILD. Fouseena Pazheri, Jonathan Moses, Victor Uko, Oliver Soldes, Naim Alkhouri, The Cleveland Clinic, Cleveland, OH

Superior mesenteric artery (SMA) syndrome is a rare disorder with gastrointestinal symptoms due to compression of the third part of duodenum between the abdominal aorta and SMA. Similarly, compression of the left renal vein between the abdominal aorta and SMA leads to the nutcracker syndrome which may manifest as hematuria, proteinuria or flank pain. Co-existence of these two syndromes in a patient is extremely rare and has not been reported in the pediatric literature. We report a 16 year-old adolescent girl who presented with a two year history of chronic postprandial abdominal pain, nausea and poor weight gain, in addition to left flank pain that started 6 months prior to her initial visit. Her initial work up including complete blood count, complete metabolic panel, sedimentation rate and celiac panel was normal. Due to concern for small bowel Crohn’s disease, a CT enterography was done and showed proximal dilation of the third part of the duodenum with narrowing as it passes between the SMA and aorta concerning for SMA syndrome. Moreover, she had narrowing of the left renal vein between the SMA and aorta with left para-vertebral collaterals. UGI series confirmed the diagnosis of SMA syndrome. Urinalysis demonstrated proteinuria without hematuria or other renal dysfunction. Due to failure of medical treatment, she underwent a duodenojejunalostomy anastomosis and a left renal vein bypass with femoral vein graft with marked improvement in her postprandial pain and left flank pain and progressive weight gain. To our knowledge, this is the first case report describing the association between SMA syndrome and nutcracker syndrome in a child. Clinicians should consider SMA syndrome in patients presenting with weight loss and postprandial pain. The presence of nutcracker syndrome should be sought after in the appropriate clinical settings.

326 TRANSITIONAL CARE: EXPECTATIONS AND EXPERIENCE IN YOUNG PEOPLE WITH INFLAMMATORY BOWEL DISEASE. Jose M. Cabrera1, Michaeal V. Chiorean2, Steven J. Steiner1, 1Pediatric Gastroenterology, Indiana University, Indianapolis, IN; 2Internal Medicine/Gastroenterology, Indiana University School of Medicine, Indianapolis, IN

Background: Little is known about the transition of patients with inflammatory bowel disease (IBD) from pediatric to adult care. Current recommendations for transitional care are based on expert opinion and extrapolated data from other chronic pediatric diseases Aim: To evaluate the expectations and the experiences of patients with IBD during transition care. Methods: Using telephone questionnaires, two cohorts of IBD patients were interviewed seeking demographic data and qualitative data. The first cohort of patients included 26 adolescents nearing the transition from a pediatric to adult gastroenterologist. The second cohort included 21 young adults who have already completed the transition of care. The telephone survey consisted of questions about communication between pediatric and adult gastroenterologists, timing of transition, school and employment issues, meeting other IBD patients, and discussing sensitive issues. Participants answered using a Likert scale. Statistical differences between these cohorts were examined. Results: The adolescent cohort had significantly higher scores concerning: contact with their pediatric gastroenterologist following transition, knowledge of their adult gastroenterologist prior to transition, notifying their school or employer about special needs, and supporting their independence. The adult cohort had significantly higher scores concerning discussion of sensitive or difficult issues. Scores were similar between the cohorts concerning: timing and involvement of family in transition, communication with primary care providers, decisions about who should be present in the examination room, and facilitating meeting other patients with IBD. Conclusions: By exploring the disease specific expectations and experiences in young people with inflammatory bowel disease, gastroenterologists can provide more appropriate transitional care for these patients. Further studies in this area are warranted.
327 EVALUATION OF CURRENT TREATMENT STRATEGIES IN CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN AT A TERTIARY CARE CHILDREN’S HOSPITAL: A RETROSPECTIVE STUDY. Khaled Bittar1, Rodrigo Rodrigues2, Hossein Salimnia2, Mohammad El-Baba1,1 Pediatric Gastroenterology, Children’s Hospital of Michigan, Detroit, MI; 2 Pathology, Children’s Hospital of Michigan, Detroit, MI; 3 Pediatrics, Children’s Hospital of Michigan, Detroit, MI

Background: Reports suggest that Clostridium difficile infection (CDI) has been increasing in both incidence and severity which has incited interest in its optimal treatment. We describe all pediatric patients diagnosed and treated for CDI in our institution over a 6-year period and identify their response to treatment.

Methods: Data maintained by clinical laboratory at Children’s Hospital of Michigan was used to identify children with a positive CD toxin assay between 2004 and 2009. Chart review was performed on children tested positive who were treated for CDI. Persistent diarrhea longer than 5 days of treatment was considered as failure of treatment.

Results: 154 patients tested positive for CD toxin and received therapy. Over the 6 years of the study, there was an increase in the number of patients diagnosed and treated for CDI from 16 cases in 2004 to 42 in 2009. Majority (82%) had chronic illness mainly oncologic (36%) followed by gastrointestinal, neuromuscular and cardiac conditions. Treatment consisted of metronidazole (MN), oral vancomycin or both. Initial treatment was MN in 147 patients, and combination of MN and vancomycin in 7. 13 patients received vancomycin; 6 were in 2009. Vancomycin was used due to failing MN treatment in 3 cases, not tolerating MN in 3 and in combination with MN for severe infection in 7 (6 in 2009). 138 patients responded to MN monotherapy. 3 patients failed MN and subsequently responded to vancomycin. 3 patients had unknown outcome due to lack of follow up in our institution.

Conclusions: Metronidazole remains the first line of treatment for CDI. However, the use of vancomycin alone or in combination with metronidazole in the pediatric population has increased from 2004 to 2009. This result correlates with studies from the adult population. Further investigation on antimicrobial susceptibilities in the pediatric setting is warranted.

328 ADVANCES IN PEDIATRIC DRUG LABELING IN GASTROENTEROLOGY. Laurie S. Conklin1,2, Lisa Mathis3, Hari C. Sachs4, US Food and Drug Administration, Silver Spring, MD; 2 Gastroenterology, Hepatology, and Nutrition, Children’s National Medical Center, Washington, DC

INTRODUCTION: In 1999, >80% of drugs had no dosing or safety information in children(1). Legislation, including requirements and incentives, has increased pediatric drug development and research. METHODS: A list of 73 drugs used in pediatric gastroenterology (GI) was compiled based on review of 10 NASPghan and ACG practice guideline recommendations. The following data were collected by searching public FDA information: approval and indication in children, boxed warnings, Pediatric Research Equity Act (PREA) trigger, issuance of Written Request (WR), Pediatric Exclusivity. RESULTS: 53% of these drugs contain pediatric dosing, safety, and efficacy information in labeling (36 approved, 3 negative studies). The majority (78%) are used off-label for the recommended gastroenterology (GI) indication in children and 23% of these drugs have a boxed warning. Studies were required under PREA for 12 products. WRs for studies under the Best Pharmaceuticals for Children Act (BPCA) that could result in 6 months of marketing exclusivity have been issued for 28 drugs (38%). To date, pediatric marketing exclusivity has been granted for 16 GI products studied under BPCA. CONCLUSIONS: PREA and BPCA have been effective in increasing pediatric studies and labeling information. Many commonly used GI drugs are now approved for use in children, although frequently not for the recommended GI indication. Although there has been progress, ongoing collaborative effort is needed to to make pediatric dosing, safety, and efficacy information from clinical trials available in labeling for drugs used commonly by pediatric gastroenterologists.


No official support or endorsement by The Food and Drug Administration is intended or should be inferred

329 ROLE OF P38 MAPK IN TNF-α MEDIATED NEUTROPHIL PRIMING: A MODEL FOR CHRONIC INFLAMMATORY STATES. Melissa Jensen, Emily Gross, Brianna Hilkin, Gina South, Jessica Moreland

University of Iowa, Iowa City, IA

Crohn’s disease and Ulcerative Colitis are inflammatory disorders of the gastrointestinal tract that cause significant morbidity. The inflammatory cytokine tumor necrosis factor alpha (TNF-α) is a well-described activator of neutrophils (PMNs), which can contribute to host tissue damage, as can be seen in inflammatory bowel disease. Treatment of these conditions includes the use of TNF-α inhibitors. Priming is an intermediate state of PMN activation, whereby the PMNs functional response to a secondary stimulus is enhanced by previous interaction with a priming agent such as TNF-α. Priming not only occurs in vitro, but also in vivo during both acute and chronic inflammatory states. Our laboratory has demonstrated a required signaling role for NADPH oxidase derived ROS in neutrophil priming by TNF-α. We hypothesized that low concentrations of TNF-α elicit a “chronic” primed state in neutrophils that is p38 MAPK-dependent and regulated by NADPH oxidase-derived ROS. p38 MAPK is known to be a required cell signaling intermediate during TNF-α priming necessary for activation of p47phox, a component of the NADPH oxidase complex. Our preliminary data demonstrate that early blockade of p38 MAPK activity, concurrent with initial exposure to TNF-α, blocks both generation of low-level direct ROS and blocks priming of the respiratory burst to subsequent stimulation with fMLF as measured by chemiluminescence. However, “late” p38 MAPK blockade (following generation of initial ROS) does not inhibit the primed respiratory burst. As an additional endpoint for priming, we examined stimulated elastase release. TNF-α priming enhances elastase release in response to both fMLF and PMA. Early p38 inhibition blocks TNF-α priming of PMA-induced elastase release, but not fMLF induced release. These data suggest that the role of p38 MAPK in TNF-α priming is finely regulated and occurs in the initial activation phase. These data will help us to better understand the cell biology of PMN activation states and the mechanisms of therapeutic TNF-α inhibition in inflammatory diseases.
330 CITRULLINE LEVEL AS A PREDICTOR OF TPN INDEPENDENCY IN CHILDREN WITH SHORT BOWEL SYNDROME. Pablo J. Palomo1, David F. Mercer1, Brandy D. Hobson2, Ryan T. Fischer1, Brandi K. Gerhardt2, Wendy J. Grant1, Jean F. Botha3, Stephen C. Raynor2, Alan N. Langnas4, Ruben E. Quiros-Tejeda1, 1Pediatric Gastroenterology, University of Nebraska Medical Center, Omaha, NE; 2Transplant Surgery, University of Nebraska Medical Center, Omaha, NE; 3Pediatric Surgery, University of Nebraska Medical Center, Omaha, NE

Background: Short bowel syndrome is a heterogeneous condition in children. The vast majority of patients with short bowel syndrome have a significant dependency on total parenteral nutrition (TPN) as their primary source of nutrition. Prolonged TPN use has been associated with increased risk of infections and parenteral nutrition associated liver disease (PNALD) that can ultimately lead to cirrhosis. Citrulline is an amino acid that is primarily synthesized by the enterocytes from glutamine. In the face of no renal pathology, normal citrulline levels correlate with a healthy enteral environment and good absorption capacity.

Aim: Evaluate the role of citrulline levels as a predictor of intestinal adaptation in patients with short bowel syndrome.

Methods: We reviewed medical records and citrulline levels from 49 patients followed from January 2009 until March 2011 at the intestinal rehabilitation program (IRP) at the University of Nebraska Medical Center. Results: in our sample (41 patients), the most common cause of short bowel syndrome was necrotizing enterocolitis (NEC) = 12, followed by gastroschisis= 11, intestinal atresia= 9, malrotation= 8 and omphalocele = 1. Out of 41 patients, 25 patients (54%) were completely TPN independent at the end of the study. The citrulline level of the adapted patients was 22.9 ± 8.2 mg/dl vs 12.6 ± 7.3 mg/dl of the TPN dependent group (p<0.001). 79% of patients with citrulline level > 15 mg/dl adapted vs only 23% of the patients with citrulline level < 15 mg/dl (p<0.001). Conclusion: Citrulline level could be useful when assessing small bowel adaptation potential in patients with short bowel syndrome. Patients with levels less than 10 mg/dl had poor potential for adaptation.

331 PROBIOTICS IN PRACTICE: A SURVEY OF NASPGHAN. Peter Church1, Najma Ahmed1, Hien Huynh1, Jackie Fiander1, Jeff Critch1, 1Memorial University, St. John's, NF, Canada; 2University of Toronto, Toronto, ON, Canada; 3McGill University, Montreal, QC, Canada; 4University of Alberta, Edmonton, AB, Canada

Aims: To assess NASPGHAN members' knowledge, attitudes and experience using probiotics for acute diarrhea (AD), antibiotic-associated diarrhea (AAD), C. difficile-associated diarrhea (CDAD), necrotizing enterocolitis (NEC), pouchitis (P) and irritable bowel syndrome (IBS). Methods: An internet based survey was emailed to NASPGHAN members in February 2011. Responses were anonymous. Results: 213 responses were obtained from 1594 delivered surveys (13%). 73% (n=155) felt fellowship teaching was sufficient, but 60% felt it was insufficient. 93% (n=163) who felt fellowship teaching on probiotics was sufficient were satisfied with their knowledge compared to 74% (n=163) who reported no or insufficient education (p=0.007). Overall 78% of respondents expressed satisfaction with their knowledge of probiotics. Most felt the evidence was strongest for AAD, CDAD and pouchitis, and that probiotics were generally safe. There was less familiarity with the literature on NEC. This is reflected in their recommendations for the use of probiotics as reported in the table. 70% had discussed probiotics within the preceding week and 87% had treated patients with probiotics within the last month. OTC preparations were recommended most frequently, followed by food products and then prescription probiotics. Conclusions: NASPGHAN members are comfortable with their knowledge base on probiotics and they are using them in practice. Education on probiotics during fellowship training was associated with an increased satisfaction of their knowledge. Practices may be different among members not completing the survey.

### Percent Recommending Probiotics

<table>
<thead>
<tr>
<th></th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>23%</td>
<td>51%</td>
</tr>
<tr>
<td>AAD</td>
<td>71%</td>
<td>84%</td>
</tr>
<tr>
<td>CDAD</td>
<td>63%</td>
<td>75%</td>
</tr>
<tr>
<td>NEC</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>P</td>
<td>54%</td>
<td>69%</td>
</tr>
<tr>
<td>IBS</td>
<td>44%</td>
<td>75%</td>
</tr>
</tbody>
</table>

332 ZINC SUPPLEMENTATION IN CHILDREN WITH ACUTE GASTROENTERITIS: A DOUBLE BLIND RANDOMIZED CONTROLLED TRIAL. Judy Castañeda1,2, Rafael Guerrero-Lozano1, 1Pediatrics, Universidad Nacional de Colombia, Bogotá, Colombia; 2Hospital de la Misericordia, Bogotá, Colombia

Introduction: Acute gastroenteritis is a common disease in childhood, being among the top 5 causes of infant mortality in many countries. There are studies supporting the use of zinc to reduce the duration of the disease.

Aim: To evaluate the effect of zinc supplementation on the duration of disease and on the number of stools per day in children with acute gastroenteritis.

Methods: This was a randomized double-blind trial in children aged 6 months to 5 years, who attended the casualty unit with acute gastroenteritis less than 48 hours in duration prior to enrolment. A group of 27 patients received zinc sulphate, while a group of 35 received placebo. In both groups, the number of loose stools per day and the total duration of the episode were recorded.

Results: Groups were comparable. Children in the supplemented group showed a reduction of 8% in the total duration of...
diarrheal episode and of 15% in its duration after initiation of zinc, as compared to the placebo group. The number of loose stools was lower at the seventh day in the supplemented group. The rate of treatment failure showed no differences between groups. No side effects of zinc administration were observed.

Conclusion: This study suggests that the use of zinc during acute gastroenteritis is of benefit because it reduces the duration of the episode, as well as the number of loose stools at day seven. Thus, it could be recommended.

333 ETIOLOGY OF SHORT BOWEL SYNDROME MAY PREDICT RISK OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN CHILDREN. Ryan Fischer, Shaia Shelby, Shilpa Singh, Steven Raynor; David Mercer; Ruben Quiros-Tejeira, University of Nebraska Medical Center, Omaha, NE

Purpose: Small intestinal bacterial overgrowth (SIBO) is a common concern in children with short bowel syndrome (SBS). SIBO is implicated as a cause of malabsorption and subsequent poor growth in children. We sought to analyze the incidence of SIBO in SBS at a tertiary referral center with a dedicated intestinal rehabilitation program.

Methods: We performed a retrospective chart review of patients seen in the dedicated intestinal rehabilitation program at our center. Children seen at the center between 2004 and 2010 were included in the study (99 patients). Collected data included age, gastrointestinal diagnosis and anatomy and duodenal aspirate culture results (if available). SIBO was defined by the growth of > 10^5 colony forming units/L from the aspirate.

Results: SIBO was diagnosed by duodenal aspirate in 66 patients (66%). Thirty-one of those patients (46%) had more than one positive aspirate. Organisms included E. Coli (21% of aspirates), Klebsiella spp (18%), S. Viridans (9%), and Enterococcus spp (6%) among others. Mean small bowel length was not significantly different between patients with and without SIBO (45 cm versus 43 cm, respectively; p = 0.4). The absence of an ileocecal valve was associated with a higher likelihood of SIBO (OR = 1.9), though this was not statistically significant (p = 0.2). However, the underlying diagnosis of atresia was associated with a statistically significant increased risk of SIBO (OR = 6.4; p < 0.04) as was the diagnosis of gastroschisis (OR = 2.6; p < 0.05).

Conclusion: Duodenal aspirates from children with SBS are frequently positive for SIBO. This may contribute to morbidity and mortality in these patients. Interestingly, it seems that intestinal anatomy may not be as important in predicting which children have SIBO as the etiology of the SBS.

334 THE ROLE OF PLATELET ACTIVATING FACTOR ACETYLHYDROLASE SINGLE NUCLEOTIDE POLYMORPHISMS IN THE ETIOLOGY OF NEC. Senthilkumar Sankararaman1, Krishna Yanamandra1, Jay G. Aryama1, Dawn Napper1, Arun Pramanik1, Joseph A. Bocchini1, Ramasubbareddy Dhanireddy2, 1Pediatrics, LSU Health Sciences Center, Shreveport, LA; 2Pediatrics, UT Health Science Center, Memphis, TN

Necrotizing enterocolitis (NEC) in premature babies is the most common gastrointestinal emergency with high mortality and morbidity. The etiology is multifactorial and studies have shown that platelet activating factor (PAF) may play a significant role through its inflammatory effects. PAF acetylhydrolase (PAFAH), the enzyme that degrades PAF and reduces its activity may be involved in the etiology of NEC. We retrospectively included a total of 285 babies (18 patients with NEC, 267 controls) and genotyping was done by microplate PCR method. Genotypes were stratified by ethnicity and disease status. Results are shown in the table. Interestingly, variant PAFAH genotype frequencies were significantly lower in NEC group, compared to the healthy controls. Because of the controversial relationship of variant genotypes to PAFAH enzyme levels, the significance of our observations is unknown at present, but we speculate a protective role for PAFAH polymorphisms in the etiology of NEC. This is the first study in the literature showing the association of PAFAH genotypes in the etiology of NEC.

Distribution of PAFAH Ile198Thr & Ala379Val genotypes in Caucasian NEC patients and controls.

<table>
<thead>
<tr>
<th>PAFAH genotypes (Ile198Thr &amp; Ala379Val)</th>
<th>NEC infants (#)</th>
<th>NEC infants (Frequency)</th>
<th>Non-NEC infants (#)</th>
<th>Non-NEC infants (Frequency)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>198ThrThr + 379ValVal</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>198IleIle + 379ValVal</td>
<td>1</td>
<td>0.05</td>
<td>36</td>
<td>0.19</td>
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<td></td>
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<tr>
<td>198IleIle + 379ValVal</td>
<td>17</td>
<td>0.95</td>
<td>149</td>
<td>0.78</td>
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<tr>
<td>Total genotypes</td>
<td>18</td>
<td>1</td>
<td>192</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alleles - 198Thr/379Val</td>
<td>1</td>
<td>0.03</td>
<td>50</td>
<td>0.13</td>
<td>0.17 (0.03-1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Alleles - 198Ile/379Ala</td>
<td>34</td>
<td>0.97</td>
<td>334</td>
<td>0.87</td>
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<tr>
<td>Total Alleles</td>
<td>35</td>
<td>1</td>
<td>384</td>
<td>1</td>
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<td></td>
</tr>
</tbody>
</table>

African American Genotypes between cases and controls were similar (data not shown)
335 DIAGNOSIS AND MANAGEMENT OF ANASTOMOTIC ULCERATION IN PEDIATRIC PATIENTS. Tara A. Altepeter, Denise B. Angst, Rajeev Nagpal, Pediatric Gastroenterology, Advocate Hope Childrens Hospital, Oak Lawn, IL; Pediatrics, Advocate Hope Childrens Hospital, Oak Lawn, IL; Center for Pediatric Research, Advocate Hope Childrens Hospital, Oak Lawn, IL.

Background: The goal of our study was to understand how pediatric gastroenterologists diagnose and treat anastomotic ulceration (AU) in children, a complication which may present at any time after bowel surgery with end to end anastomosis.

Methods: We collected data on diagnosis, management and outcomes for 52 children with AU via an anonymous, web-based survey of NASPGHAN members. Twelve of these cases, relating to transplantation and IBD, were excluded due to differences in underlying pathology.

Results: Most cases were diagnosed endoscopically (98%), presented with GI bleeding (occult: 40%, gross blood per rectum: 58%), and were located at the ileo-colic junction (73%). After initial surgery, time to presentation varied from 3 months to more than 5 years. Many patients (38%) presented with severe anemia (Hgb <7g/dl). Among those patients who were treated medically (23 patients), successful resolution of symptoms (10 patients) was noted only in those treated with antibiotics, 5-ASAs, or both. Recurrence of symptoms occurred in 2 of these 10 patients. Treatment using antacids, sucralfate, probiotics, and bile-acid sequestrants were not successful. Two patients were treated with electrocautery without recurrence. Two additional patients were treated with intralesional steroid injections but had recurrence. Outcomes for surgical patients (revision of anastomosis with or without further resection) were not encouraging, with 6 out of 12 having recurrence of symptoms despite undergoing a major abdominal surgical procedure.

Conclusions: A high index of suspicion is required to identify children with AU, whose initial presenting sign may be only mild iron deficiency anemia. The optimal treatment choice is unclear. Surgical resection is not always a definitive cure, and careful consideration of non-invasive treatments including 5-ASAs and antibiotics is warranted. Further research is required.

336 AN EVALUATION OF BEHAVIORAL INTERVENTIONS TO INCREASE ORAL INTAKE OF CHILDREN WITH INTESTINAL FAILURE. Valerie Volkert, Cathleen C. Piazza, David F. Mercer, Brandy Hobson, Brandi Gerhardt, University of Nebraska Medical Center, Omaha, NE.

Background: Although it may be ideal to transition patients with intestinal failure (IF) to oral feeds or oral and enteral feeds rather than enteral feeds only, many children with IF do not cooperate with oral feeding. In fact, the results of a number of studies have suggested that many children with IF fail to transition to oral feeding at all. Behaviorally based treatments may be effective in improving oral intake in children with IF.

Aim: To determine whether behavioral treatments resulted in increases in appropriate (acceptance and swallowing of solids and liquids) and decreases in inappropriate mealt ime behavior.

Methods: We analyzed data from children with IF, who participated in the intestinal rehabilitation program at the University of Nebraska Medical Center or received a small bowel transplant, admitted to the Munroe-Meyer Institute Pediatric Feeding Disorders Program between 2006 and 2011. The mean age of the children was 2.6 years (range, 0.8 to 4.8 years). The children received behavioral interventions to increase intake of liquids and/or solids. We examined data for acceptance, mouth clean (swallowing), and inappropriate mealt ime behavior (e.g., turning head away from spoon, pushing feeder’s hand) during baseline and treatment.

Results: We analyzed data from 19 assessments. Mean acceptance increased from 29.4% to 95.7% and 40.5% to 89.5% from baseline to treatment for liquids and solids, respectively. Mean inappropriate mealt ime behavior per minute decreased from 8.7 to 1.4 and 8.1 to 1 from baseline to treatment for liquids and solids, respectively.

Conclusion: Preliminary data suggest that behaviorally based treatments are effective in improving the oral intake of children with IF.

337 RESOLUTION OF ILEOCOLITIS WITH THE SPECIFIC CARBOHYDRATE DIET IN A 4-YEAR-OLD FEMALE. Vrunda Bhardwaj, Hillel Naon, Department of Pediatric Gastroenterology, Hepatology and Nutrition, Childrens Hospital Los Angeles, Los Angeles, CA.

Background: The exact role of complex carbohydrates in the pathogenesis and progression of Inflammatory Bowel Disease (IBD) has not been elucidated. A potential role in dysbiosis is hypothesized, as suggested by the Specific Carbohydrate Diet (SCD) (Breaking the Vicious Cycle; by Elaine Gottschall). This consists of easily digestible mono-saccharides and elimination of complex carbohydrates, which in theory depletes intestinal bacteria of the substrates needed to survive, reducing bacterial growth and the harmful products of fermentation.

Purpose: We report a response to SCD and clinical remission in a patient with biopsy evident ileocolonic ulcerations marked by normalization of fecal calprotectin, resolution of anemia, diarrhea, rectal bleeding and abdominal pain.

Methods: A 4-year-old female born at 28-week gestation, with resection of terminal ileum and cecum post necrotizing enterocolitis and ileostomy take-down, developed abdominal pain, diarrhea and rectal bleeding. She was treated with Flagyl and Pentasa for 6-months with no change in symptoms. She subsequently commenced the SCD with taper off of medications.

Results: On initial presentation her upper endoscopy and colonoscopy showed severe acute colitis and ileocolonic anastomotic site ulcerations. Laboratory data revealed a hemoglobin (HB) 9.7g/dl, ESR 27mm/hr, fecal calprotectin 1848mcg/g and anti-OmpC IgA 19.9EU/ml. CT scan showed small bowel and colonic wall thickening. She was found to have negative stool infectious studies and celiac panel. Within 3-months on the SCD she demonstrated resolution of symptoms with Hb 14.0g/dl and fecal calprotectin 20.6mcg/g suggesting a therapeutic remission presumably secondary to the diet.
Conclusions: The apparent effectiveness of the SCD in IBD warrants further controlled trials to elucidate its specific role, if any, in IBD. Also further studies to investigate gut microbiota in patients on SCD are indicated. If the SCD works by changing the gut bacterial flora, then it will support the role of bacteria in the pathogenesis of IBD.

HEPATO BILIARY/TRANSPLANT

354 LOBULAR RATHER THAN PORTAL CONNECTIVE TISSUE GROWTH FACTOR IS BETTER CORRELATED WITH ROUTINELY PERFORMED BLOOD TESTS IN ADVANCED BILIARY ATRESIA.

Allah Haufig, Christian Farrington, Regino P. González-Peralta, Joel Andres, Pediatrics, University of Florida, Gainesville, FL

Hepatic fibrosis (HF) is a prominent feature of biliary atresia (BA). Despite its significance in BA, HF can not be evaluated during routine patient care. Therefore non-invasive tools to assess HF are needed.

Aim: This work was done to determine if routine blood tests can be correlated with hepatic connective tissue growth factor (CTGF) and if the hepatic distribution of CTGF affect this correlation?

Methods: Using liver explants from patients with BA, immune-expression of CTGF was determined using horseradish peroxidase labeled antibodies. Mean expression intensities of lobular (L) & portal (P) CTGF were determined by using ImageJ software. These intensities were correlated with blood tests performed at the time of LT. Correlation coefficients were determined for each blood test vs mean L-CTGF and P-CTGF expression intensities. A P-value of less than 0.05 was considered significant.

Results: Kendall tau (τ) rank correlation coefficient for L-CTGF and WBC was inversely (τ = -0.52; p ≤ 0.02). Similar but non-significant inverse relationships were noted for L-CTGF and prothrombin time (PT) (τ = -0.15; p ≤ 0.4), international normalized ratio (INR) (τ = -0.14; p ≤ 0.5), and platelet count (τ = -0.36; p ≤ 0.09). Inversely correlations were also evident between P-CTGF and GGT, PT, INR, and platelet count. Pearson correlation coefficients for combinational analysis of total bilirubin, alkaline phosphatase, GGT, and platelet with L-CTGF (0.33; p = 0.3) and P-CTGF (0.06; p = 0.8), were not significant. Similar analysis for alanine aminotransferase (ALT), TB, and GGT combination (L-CTGF, 0.16; p = 0.5; P-CTGF, 0.3; p = 0.2) as well as WBC, platelet count and TB (L-CTGF, -0.36; p = 0.09; P-CTGF, -0.33; p = 0.13) also revealed non-significant results.

Conclusions: 1. Hepatic CTGF expression can be correlated with routinely performed blood tests in patients with BA. 2. CTGF expression has an inverse relationship with select hematological parameters in advance BA. 3. L-CTGF expression is better correlated with hematologic parameters than P-CTGF.

355 AUTOIMMUNE HEMOLYTIC ANEMIA IN PEDIATRIC LIVER AND INTESTINAL TRANSPLANT RECIPIENTS AT A LARGE SINGLE-CENTER.

Christopher Fink1, Robert Venicker1, Suzanne McDermid1,2, Douglas Farmer3. Pediatric Gastroenterology, UCLA, Los Angeles, CA; 1Transplant Surgery, UCLA, Los Angeles, CA

Background: Pediatric liver (LTx) and intestinal transplant (ITx) recipients have many reasons to be anemic. Marrow suppressive medications, viral infections, frequent phlebotomy, gastrointestinal blood loss, renal insufficiency, and hypersplenism, may all contribute. However, autoimmune hemolytic anemia (AIHA) can be the most severe and difficult cause to treat. The aim of this study is to describe in detail the incidence, management, clinical outcomes and complications associated with AIHA at a large pediatric LTx and ITx center. Methods: Retrospective review of an IRB-approved electronic database and medical records was initiated of all LTx and ITx between 1/2000 and 6/2011. Results: 293 LTx and 73 ITx were performed during this time. While chart review is ongoing, 8 cases of clinical and serological AIHA have been identified to date. Diagnosis ranged from 9 months to 2.5 years after transplantation in all but one patient. All patients developed warm AIHA, and two had concomitant cold agglutinins. All except one patient required various combinations of steroids, IVIG, rituximab, plasmapheresis, native splenectomy and vincristine. We did not withdraw tacrolimus although we did dose adjust in some cases. Five patients achieved remission two weeks to three months after onset. Discussion: With the capture of all clinically apparent AIHA in the pediatric LTx and ITx cohort at UCLA we hope to clearly establish the following regarding AIHA: incidence, risk factors for the development of AIHA, clinical outcomes before and after the use of rituximab, and a general standard of management including the role of splenectomy and ways to approach the treatment refractory patient.

356 RANGE OF NICU PRACTICE IN ENGLAND AND WALES REGARDING THRESHOLDS FOR NEONATAL CONJUGATED HYPERBILIRUBINAEMIA AND RELEVANT INVESTIGATIONS.

Christos Tzivinikos, Paediatrics, Luton and Dunstable Hospital, Luton, United Kingdom

Conjugated jaundice is a common problem in a NICU setting and is generally seen as a reversible complication of prolonged parenteral nutrition. However, several investigations are performed to exclude underlying liver disease.

Methods: Questionnaire survey of lead neonatal consultants from all NICUs in England and Wales. Questions included definition of conjugated jaundice, bilirubin cut off that prompted investigations and tests performed. Clinicians were also requested to give their opinion on the yield from these investigations.

Results: 102/194 NICUs (52%), responded to the survey of which 33 were level 3 units, 50 level 2 and 19 level 1 units. 96 units (94%) performed conjugated jaundice screen and 6 units (6%) did not. 77 units (75%) had a written policy. 49% of responders defined conjugated jaundice as conjugated bilirubin >20% of total bilirubin and 46% as >5% of total bilirubin and 5% of units did not have a clear definition. Conjugated bilirubin levels that prompted investigations varied between units with 28 (30%) using conjugated bilirubin >20% of total, 33(36%) a conjugated bilirubin >15% of total and 20 (21%) with no definite threshold. Majority (>76%) of units performed liver and thyroid function tests, Galactosaemia screen, α1 antitrypsin and liver ultrasound. In addition to above investigations, 65% of units performed urine culture and hepatitis serology, 32% performed urine organic acids, NH3 and lactate. 19 units performed CF genetics and 23 HIDA scan. 71% of responders (which included 2 out of 3 neonatal units with in-house paediatric hepatology services) thought ‘diagnostic yield’ from these tests ‘poor’ and 44% based this on their personal view, 29% on local data and 27% on anecdotal evidence.
Conclusion: Our study identified a wide variation in definition and investigation of conjugated jaundice in neonates. Most neonatologists believe yield from these investigations is poor. Further studies are needed to support or refute this view. National consensus guidelines are required to standardize practice.

357 PILOT STUDY: LACTULOSE VS. PLACEBO IN TREATMENT OF MINIMAL HEPATIC ENCEPHALOPATHY IN CHILDREN. Girish Subbarao1, Meltem Zeytinoglu2, Eric Scott1, Elizabeth Byam1, Jean Molleston1, 1Riley Hospital for Children, Indianapolis, IN; 2University of Chicago, Dept of Internal Medicine, Chicago, IL.

Background and Aim: Minimal hepatic encephalopathy (MHE) is seen in patients (pts) with cirrhosis. There is paucity of information on treatment of MHE in children.

Methods: We conducted placebo controlled, double blind, randomized controlled trial with cross over in children with cirrhosis between the ages of 5 and 18 years with evidence of MHE. Pts were considered to have MHE if they had one or more abnormal cognitive function tests (CFT) [pts scored 2 standard deviations [SD] below mean]. Pts were randomized to receive either placebo (5% Dextrose in water) or lactulose (1-3ml/kg/day) for 3 months. Thereafter, underwent repeat psychometric testing. After a month of wash out period, pts crossed over to the opposite treatment group for 3 months, then underwent repeat psychometric testing.

Results: 13 pts (Female 8, Child-Pugh (CP) Class A 10, Class B 3) were screened. The mean age 10.4±5 years. Six pts (46.2%, CP Class A 4, Class B 2) failed at least one CFT, indicating presence of MHE (Table 1). Four pts completed the treatment study (Table 2).

Conclusions: MHE is common in children with cirrhosis. Large scale studies are needed to delineate the role of lactulose in treatment of children with MHE.

Table 1: Cognitive Function Tests and Baseline Results

<table>
<thead>
<tr>
<th>Cognitive parameter</th>
<th>Cognitive Function test (n=number of study subjects tested)</th>
<th>Standard Mean Score±SD</th>
<th>Score for the Study Cohort (Mean±SD)</th>
<th>Number of Study Subjects with score ≤-2 SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention/Concentration</td>
<td>Wechsler Intelligence Scale for Children Digit Span (n=11)</td>
<td>10±3</td>
<td>7.7±3.1</td>
<td>1</td>
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<tr>
<td></td>
<td>Connor’s Continuous Performance Task (n=8)</td>
<td>50±10</td>
<td>55.5±16.4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Stroop Test (n=10)</td>
<td>50±10</td>
<td>47.3±11.9</td>
<td>1</td>
</tr>
<tr>
<td>Fine Motor Skills</td>
<td>Wechsler Intelligence Scale for Children Block Design (n=13)</td>
<td>10±3</td>
<td>8±3.3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Delis Kaplan Trail Making Test (n=7)</td>
<td>10±3</td>
<td>7.3±3.8</td>
<td>3</td>
</tr>
<tr>
<td>Processing Speed</td>
<td>Woodcock-Johnson-III Cognitive Abilities Visual Matching (n=13)</td>
<td>100±15</td>
<td>94.7±18.2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Woodcock-Johnson-III Cognitive Abilities Decision Speed (n=13)</td>
<td>100±15</td>
<td>100±17.4</td>
<td>0</td>
</tr>
<tr>
<td>Visual Memory</td>
<td>Wide Range Assessment of Memory and Learning Finger Windows Test (n=12)</td>
<td>10±3</td>
<td>7.1±3.2</td>
<td>2</td>
</tr>
</tbody>
</table>

Table2. Effect of Lactulose/Placebo on MHE

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Lactulose</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No Change in MHE</td>
<td>No Change in MHE</td>
</tr>
<tr>
<td>2</td>
<td>No Change in MHE</td>
<td>MHE resolved</td>
</tr>
<tr>
<td>3</td>
<td>No Change in MHE</td>
<td>MHE resolved</td>
</tr>
<tr>
<td>4</td>
<td>MHE resolved</td>
<td>MHE resolved</td>
</tr>
</tbody>
</table>
358 FEASIBILITY AND SAFETY OF HEPATIC VENOUS PRESSURE GRADIENT MEASUREMENT IN CHILDREN WITH LIVER DISEASE. Jessica Woolfson1, Vicky L. Ng1,2, Binitha Kumath1,2, Nicola L. Jones1,2, Yaron Avitzur1,2, Philip John1, Simon C. Ling1,1, Division of Gastroenterology, Hepatology & Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 2Department of Diagnostic Imaging, The Hospital for Sick Children, Toronto, ON, Canada; 3Department of Paediatrics, University of Toronto, Toronto, ON, Canada

Background: Hepatic venous pressure gradient (HVPG) measurements are recommended in cirrhotic adults for evaluation of prognosis and to monitor pharmacological primary prophylaxis of variceal hemorrhage. Data describing such measurements in children are scarce. We present our retrospective experience with HVPG measurements.

Methods: We searched our Image Guided Therapy database (2000-2011) for consecutive patients with HVPG measurements. Medical charts were reviewed for clinical, procedural and outcome details.

Results: 21 patients (12 male, mean age 7.8±5.3y, range 1m-17y) underwent 24 HVPG measurements. Diagnoses included acute liver failure (n=5), vascular abnormalities (4), acute hepatitis (2), chronic graft injury (2), portal vein thrombosis, GVHD, VOD, PSC, Wilson disease, autoimmune hepatitis, biliary atresia and neonatal hemochromatosis. Measurements were mostly taken at the time of transjugular liver biopsy, with additional specific indications being the evaluation of vascular abnormalities (n=4) and the evaluation of portal hypertension (n=4). There were no complications related to HVPG measurement. Mean±SD HVPG measurements in 21 patients were 9.6±5.1 mmHg, excluding one patient with arterialization of portal flow (HVPG 45 mmHg). Although the group was not primarily evaluated for complications of portal hypertension, HVPG in patients who had or who developed ascites (n=16, 9.4±4.7 mmHg), varices on imaging or endoscopy (n=12, 10.8±5.8 mmHg) or variceal bleeding (n=8, 9.0±4.0 mmHg) tended to be higher than in children with no such complications (n=6, 6.9±4.5 mmHg).

Conclusions: HVPG measurement is feasible in children, has a low risk, and should be considered for use within future research studies of pharmacological interventions to reduce portal hypertension in children.

359* EARLY ISOLATED IntEStmNAL TRANSpLANTATION VERSUS MULTIVISCERAL TRANSpLANTATION FOR PATIENTS WITH INTESTINAL FAILURE. Khalid Khan, Chirag Desai, Angelika Gruessner, Rainer Gruessner, University of Arizona, Tucson, AZ

Background: The available data (mainly from individual centers) indicate a trend towards a better outcome in the pediatric population for isolated intestinal transplantation (IITx) as compared to multivisceral transplantation (MVTx). We examined this further using the composite data from the United Network of Organ Sharing (UNOS) database.

Methods: UNOS Star files were used and all cases from 10/1987 to 8/2009 were included. MVTx was defined as combined liver and intestinal grafts and there was no further categorization based on any additional organ grafts transplanted.

Results: A total of 1822 patients received intestinal grafts; of those, 1063 (58.3%) were pediatric recipients: 316 (29.7%) underwent IITx and 747 (70.3%) MVTx. 1-, 3- and 5-year patient survival rates were 84%, 70% and 63% respectively for IITx vs. 65%, 54% and 50% for MVTx (p<0.0001) (Fig.1). 1-, 3- and 5-year graft survival rates were 77%, 58% and 46% respectively for IITx vs. 65%, 53% and 47% for MVTx (Fig.2). IITx graft survival was significantly higher for the first 3 years post-transplant (p=0.001, Wilcoxon test). A subanalysis of the last 10 years confirmed these results, with slightly improved outcome in both groups.

Conclusion: Higher survival rates of IITx vs. MVTx warrant early patient referral i.e before development of endstage liver disease, thus making more liver grafts available to patients with other liver diseases.

360 ARE INFANTS AT HIGH RISK TO GET CYTOMEGALOVIRUS INFECTION POST LIVER TRANSPLANT? Neelam Mohan, Sharat Varma, Sakshi Karkra, Arvinder Soin, Medanta Hospital, Gurgaon, India

Introduction: Cytomegalovirus (CMV) has remained the single most common viral pathogen influencing the morbidity, mortality and outcome of liver transplantation. The incidence of CMV infection after liver transplantation varies between 18-30% overall and between 35-65% among the high-risk recipients. The common high-factors for CMV infection currently considered include D+/R-, anti-thymocyte globulin therapy, high dose mycophenolate therapy, co-existing renal disease among others.

Aim: To evaluate whether infants are at high risk for CMV infection post liver transplantation.

Methods: Retrospective analysis of our data from 56 pediatric living related liver transplants was done. Children without the known high risk factors for CMV (D+/R- or having received ATG / Daclizumab or having a co-existing renal disease) were included. CMV infection status on the basis of NASBA/PCR was ascertained upto 3 months post transplantation. A comparative analysis of CMV infection incidence in the recipients of less than 1-year and more than 1-year age was done. Symptomatic and asymptomatic CMV infection rates in both the age groups were analyzed.

Results: 42 of 56 (75%) children were evaluated for CMV in the first 3 months post transplant. 2 of 42 didn’t satisfy the inclusion criteria. Total study population was 40. 12 of 40 (30%) were less than 1 year and 28 more than 1-year age. 9 of 12 (75%) less than 1 year developed CMV infection. All 9 (100%) were symptomatic. 8 of 28 (28.5%) more than 1-year age developed CMV infection of which 7 (87.5%) were symptomatic.

Conclusion: Infants had CMV infection more than twice as often, compared to the other children. CMV infection is usually symptomatic in the pediatric recipients.

Suggestion: Infancy should be included as a high risk factor for CMV infection post LT. Need for CMV prophylaxis should be evaluated in this age group.

Background: Biliary atresia (BA) is a neonatal liver disease of unknown etiology that leads to the fibro-inflammatory destruction of extrahepatic bile ducts, resulting in cholestasis. BA patients typically present with acholic stools within the first 4 to 8 weeks of life, and if untreated, will die by 24 months. No medical therapy exists, and biliary atresia is the leading indication for pediatric liver transplantation worldwide.

Chemokines are important mediators of inflammation and immune function. Previous work has shown that the interferon-gamma induced chemokine CXCL10 (IP-10) and its only known receptor, CXCR3, are overexpressed in liver in both experimental and clinical BA. Here we address the functional role of these factors in experimental BA.

Methods: To address the role of the CXCL10/CXCR3 axis in BA we took advantage of existing null alleles of both genes in the established Rhesus rotavirus (RRV)-BALB/c mouse model of BA. Each gene was extensively (>8 generations) backcrossed onto a BALB/c background. To correct for litter-to-litter variation, we set up crosses to yield both control and mutant litters. We collected serum, tissue samples, and isolated liver RNA at 3, 8, and 12 days post infection (dpi). In addition, in the case of CXCR3, we performed a survival study with n=29.

Results: Despite the fact that CXCL10 gene expression increases ~30-fold by 7 dpi in experimental BA, we have not found any significant difference in cholestasis, hepatic damage, gene expression, inflammation, or disease outcome, between BALB/c mice mutant either for CXCL10 or CXCR3, and their corresponding control litters. We conclude that parallel induction of other chemokine axes likely accounts for the unexpected redundancy of CXCL10/CXCR3 in this model, and present these data as a caution to targeting these molecules for potential therapeutic intervention.

362 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN THE PEDIATRIC COMMUNITY HOSPITAL SETTING. Patricia M. Notario1, Tennille N. Webb1, Denise B. Angst1, Rajeev Nagpal1, 1Pediatrics, Advocate Hope Children's Hospital, Oak Lawn, IL; 2Advocate Center for Pediatric Research, Advocate Hope Children's Hospital, Oak Lawn, IL; 3Pediatric Gastroenterology, Advocate Hope Children's Hospital, Oak Lawn, IL

Endoscopic retrograde cholangiopancreatography (ERCP) is a well-established diagnostic and therapeutic tool for use in adult pancreaticobiliary disorders. There is a small but rising amount of evidence showing its safety and usefulness in the pediatric setting which is limited by the fact that pancreaticobiliary disease is less common in children. Most pediatric ERCPs are performed by adult gastroenterologists at tertiary or quaternary academic referral centers. The purpose of our study is to describe our experience with ERCP in children over a 12-year period in a pediatric community hospital setting. Our specific aims were to: 1) Describe the demographic and clinical features of children who have undergone ERCP; 2) Evaluate the safety of this procedure in children; and 3) Identify any complications. We conducted a retrospective chart review for patients less than 18 years old who had an ERCP performed at Advocate Hope Children’s Hospital between 1999 and 2011 and performed appropriate data analysis to collect descriptive statistics. We compared our results with recently published studies. Fifty children underwent ERCP from 1999 to 2011 at our institution. Most ERCPs were performed for biliary etiologies in adolescent children. Our success rate overall was 94% and our complication rate was 14%, which was composed predominantly of post-ERCP pancreatitis. There was no significant difference between our success and complication rates and those of the only published study (Paris et al., 2010) examining ERCP in the pediatric community hospital setting (p>0.05). This retrospective study, the largest study to date examining the safety of pediatric ERCP in the community hospital setting, provides further evidence that endoscopists properly trained in ERCP can confidently and safely address the hepatopancreaticobiliary needs of children even in the pediatric community hospital.

363 EVIDENCE FOR BILIARY ATRESIA AS A CONGENITAL RATHER THAN ACQUIRED CHOLANGIOPATHY
Sanjiv Harpavat, Milton Finegold, Saul Karpen, Pediatrics, Baylor College of Medicine, Houston, TX

Background: Although biliary atresia accounts for 40% of pediatric liver transplants, its etiology remains poorly understood. BA’s favored model is that healthy infants acquire disease, through infection which triggers autoimmunity against bile ducts. This study tests the acquired model. We hypothesize that if acquired, BA infants would have i) normal direct bilirubin (DB) levels at birth, and ii) subsets of normal and abnormal bile ducts after infection. Alternatively, if BA is congenital, infants would have elevated DB levels at birth and all bile ducts abnormal.

Methods: This study uses statistical and immunohistochemical techniques. First, BA patients cared for at Texas Children’s Hospital and born between 2007-2010 were identified. Second, their DB and total bilirubin levels (TB) at birth were compared to normal newborn levels (n=300). Third, their liver biopsy specimens were probed with antibodies against CK19 and CD56 (n=11). CK19 marks normal and reactive bile ducts, whereas CD56 marks only reactive ducts.
Results: BA patients had i) elevated DB levels at birth, and ii) all bile ducts abnormal. Their DB levels were significantly higher than controls (mean 1.4±0.43 mg/dL vs. 0.19±0.075 mg/dL, p<0.0001). The DB:TB ratio was also elevated but below the 0.2 value considered abnormal by NASPGHAN guidelines (mean 0.17±0.068 vs. 0.02±0.012, p<0.0001). In addition, liver biopsies from BA patients lacked normal bile ducts. Instead, all ducts were CD56-positive, including those from early samples in which duct proliferation and fibrosis were not yet evident.

Conclusions: Our data suggest BA is a congenital, rather than acquired, cholangiopathy. The serum results support screening newborns to identify BA patients early. They also emphasize investigating elevated DB levels regardless of the DB:TB ratio. The histology results suggest injury starts in the intrahepatic ducts, rather than in the extrahepatic ducts as is commonly assumed. Together, the findings challenge BA’s current model and favor a genetic or epigenetic, rather than infectious or autoimmune, cause.

364 GASTROINTESTINAL AND HEPATIC MANIFESTATIONS IN CHILDREN WITH VISCERAL LEISHMANIASIS. Stephanie Oliveira¹,², Geraldo Bezerra Silva Junior², Natalia Rocha², Alexandre Liborio², Michelle Oliveira², Luiz Franco², Graziela Aquiart², Rodrigo Pimentel², Krasnalhia Abreu², Elizabeth Daher²
¹Pediatries, University of Medicine and Dentistry of New Jersey, Newark, NJ; ²Federal University of Ceara, Fortaleza, Brazil

Background: Visceral leishmaniasis (VL) is a multisystemic disease with multiple clinical and laboratorial manifestations within the gastrointestinal/hepatic tract that is endemic in tropical areas.

Objective: To describe the gastrointestinal and hepatic abnormalities in children with VL (kala-azar).

Methods: A retrospective study was conducted at the Sao Jose Infectious Diseases Hospital, Fortaleza, Brazil with 146 consecutive patients admitted between 2003 and 2008 with confirmed clinical, laboratorial and epidemiological diagnosis of VL.

Results: The patients were predominantly male (53.4%), aged 5 months to 14 y/o. The diagnoses were confirmed predominantly by bone marrow aspirate (57.5%). Splenomegaly was present in 94.5% of the cases, while hepatomegaly was observed in 82.1%. Other unspecific GI symptoms included abdominal pain (25%), vomiting (25%), diarrhea (16%), constipation (11%), coluria (2%) and epigastric pain (2%). Elevation of liver enzymes was observed with most of the cases presenting with mild elevation of AST (mean 96.9±109.1). Elevation of ALT was seen in 51% of the patients that had this test done on admission, but the elevation was less prominent than the AST elevation (mean 58.6±64.1). 69 % of the patients that had prothrombin time (PT) measured on admission, had that value below 70%. The inversion of the albumin/globulin ratio was observed in 48% of the patients that had those tests done on admission.

Conclusions: Visceral leishmaniasis should be well known by pediatricians in endemic areas due to the fact that can affect children at all ages. In those areas, splenomegaly should rise the high suspicious for the disease and the condition should be one of the differential diagnoses of unspecific GI signs and symptoms, as it can present oligosymptomatic and with minimal laboratorial changes. Pediatricians in non-endemic areas should be aware that VL should be suspected in every febrile children returning from endemic areas.

365 RECURRENCE OF NORMAL GGT CHOLESTASIS MIMICKING PRIMARY BSEP DISEASE AFTER LIVE DONOR LIVER TRANSPLANTATION IN PFIC 2. Vrinda Bhardwaj, Sylvie Lebel, Department of Pediatric Gastroenterology, Hepatology and Nutrition, Childrens Hospital Los Angeles, Los Angeles, CA

Background: Progressive Familial Intrahepatic Cholestasis Type 2 (PFIC2) is a recessive hereditary condition caused by mutations in ABCB11 gene encoding bile salt export pump (BSEP). Progression to end stage liver disease (ESLD), lack of an effective medical treatment, and increased risk of hepatic malignancy make liver transplantation (LT) necessary for patients with severe form of disease that is thought to be curative.

Purpose: We report a 7-year-old patient who developed recurrent normal gamma-glut amyl transferase (GGT) cholestasis mimicking primary BSEP disease after LT with anemia and neutropenia suggesting an autoimmune phenomenon.

Methods: PFIC2 diagnosis was made in infancy with elevated total and direct bilirubin, normal GGT and a liver biopsy with severe cholestasis, giant cell transformation and bridging fibrosis. There was absence of canaliculare BSEP on immunodetection and live donor liver transplantation was performed at 4-years of age. Cholestasis with normal GGT developed 2.5 years after LT with anemia and neutropenia during the immunosuppression reduction period after treatment with thymoglobulin and prednisone for possible rejection.

Results: Liver biopsy 2.5 years post LT showed canaliculare cholestasis, new giant cell hepatitis, bile plugging without evidence of rejection. New giant cell hepatitis on the liver biopsy was postulated to be from recipient antibodies to ABCB11, acting as a neoantigen, suggesting an immune mediated liver dysfunction.

Conclusions: The occurrence of allo-immune mediated BSEP dysfunction after LT in PFIC2 patients, immunologically “naive” to BSEP may lead to a PFIC2 like phenotype. This represents a novel clinicopathological condition more than a rare and sporadic phenomenon. An increase in immunosuppression before normal GGT cholestasis onset may avoid progression of fibrosis in the liver graft. Prospective strategies are warranted to prevent “disease recurrence” in high-risk patients.

366 DECISION-MAKINGS FOR MANAGING CHILDREN WITH SUSPECTED BILIARY DYSKINESIA. Warapan Nakayuennongsak¹, Wikrom Karsakul¹, ¹Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR; ²Pediatrics, Johns Hopkins Hospital, Baltimore, MD

Objective: There has been no consensus decision-making for the management in children with suspected biliary dyskinesia. The purpose of the study is to collect data from pediatric gastroenterologists (pedGIs) on how they manage chronic right upper quadrant (RUQ) pain in children who had normal RUQ ultrasound.

Method: Questionnaires were designed to collect decision-makings for managing children who have chronic RUQ pain and sent to pedGIs worldwide via the Pediatric Gastroenterology Internet Bulletin Board.
Results: 111 responses include pedGIs practicing in the US (60.3%), and outside the US (10.8%). Only 19.1% primarily chose to use medications with proton pump inhibitor or PPI (66%) and antispasmodics (42%) as most prescribed drugs. The mean duration of treatment was 1.6 months (1-3 months) before further investigations. 79.1% of pedGIs would schedule test(s) prior to any treatment with HIDA scan in 68.4%, EGD in 55%, and repeat RUQ ultrasound in 21%. HIDA scan technique mostly used is rapid cholecystokinin injection over 2-3 minutes (77.8%) with the cut off limit of gallbladder ejection fraction (GBEF) of < 35% as abnormal results in 55.3%. Of 75.7% who would refer to surgeons for laparoscopic cholecystectomy, 64% would do so if both decreased GBEF and RUQ pain during CCK injection are presented.

Conclusion: PedGIs prefer to perform further investigations first and HIDA scan is the test of choice for most pedGIs. A referral to pediatric surgeons is considered when patients having decreased GBEF and RUQ pain during CCK injection.

CONCURRENT SESSION IV – PANCREAS AND NUTRITION
Saturday, October 22, 2011
2:00pm – 3:30pm

381 TLR2 CORECEPTOR TLR6 IS NOT NECESSARY FOR DEVELOPMENT OF OBESITY AND ADIPOSE TISSUE INFLAMMATION IN A MOUSE MODEL. Ryan W. Himes, C. Wayne Smith, Pediatrics, Baylor College of Medicine, Houston, TX

INTRODUCTION: We have previously shown that toll-like receptor 2 (Tlr2) is necessary for diet-induced obesity and adipose tissue inflammation in mice. TLR2 forms heterodimers with TLR1 or TLR6 to affect downstream MYD88-dependent signaling. TLR2/TLR6 heterodimers were hypothesized to be the critical TLR pair relevant to obesity due to its interaction with scavenger receptor CD36, which others have shown is necessary for obesity and tissue inflammation. We tested whether genetic deletion of Tlr6 was sufficient to recapitulate the obesity-resistant phenotype we previously reported in the Tlr2 knockout mouse.

METHODS: Tlr6-deleted mice on the C57BL/6J background or wild type C57BL/6J mice were exposed to a high fat, high sucrose Western diet model for five weeks. Body and fat pad weights as well as QMRI were used for body composition analysis. Serum glucose, insulin, leptin, adiponectin, cholesterol, free fatty acids and triglycerides were measured in serum. QPCR was performed on epididymal adipose tissue for genes encoding canonical inflammatory proteins.

RESULTS: Tlr6-deleted mice had an equivalent increase in fat pad weight and total body adiposity, as assessed by QMRI, over the five week experiment. Serum insulin, leptin, adiponectin, cholesterol, free fatty acids and triglycerides were not different among either genotype exposed to Western diet. Adipose tissue gene expression of Ccl2, F4/80 and Il6 were similar among wild type and Tlr6-knockout mice fed Western diet.

CONCLUSION: Deletion of Tlr6 in mice was not associated with protection from diet-induced obesity or adipose tissue inflammation. This may indicate that TLR2/TLR1 heterodimers are more relevant in our model of exogenous obesity than that compensatory pathways are activated early absent the Tlr6 gene product.

382 THE CA2+ TARGET CALCINEURIN MEDIATES EARLY PANCREATITIS EVENTS. Abrahim I. Orabi, Kamaldeen M. Muili, Yuhuan Luo, Dong Wang, Syeda M. Mahmood, Mahwish U. Ahmad, Sohail Z. Husain Pediatric Gastroenterology, Yale University, New Haven, CT

Acute pancreatitis accounts for over 200,000 annual hospital admissions and thus ranks as the third most common inpatient gastrointestinal diagnosis in the US. The premature activation of digestive proenzymes, specifically proteases, within the pancreatic acinar cell is an early and critical event during the disease process. Our previous studies demonstrate that pathologic protease activation requires a high amplitude, sustained rise in cytosolic Ca2+. In this study, using both a pharmacologic and genetic approach, we tested the hypothesis that a target of aberrant Ca2+ in acinar cells is the Ca2+/calmodulin dependent protease activation by 93, 67, and 80% down to control levels, respectively (n=3; P<0.05). Cell injury was recapitulated by 77.8% with the cut off limit of gallbladder ejection fraction (GGEF) of < 35% as abnormal results in 55.3%. Of 75.7% who would refer to surgeons for laparoscopic cholecystectomy, 64% would do so if both decreased GBEF and RUQ pain during CCK injection are presented.

CONCLUSION: Deletion of Tlr6 in mice was not associated with protection from diet-induced obesity or adipose tissue inflammation. This may indicate that TLR2/TLR1 heterodimers are more relevant in our model of exogenous obesity than that compensatory pathways are activated early absent the Tlr6 gene product.

383 IMPACT OF JEJUNAL INFUSIONS OF LINOLEIC ACID ON BODY WEIGHT AND MEAL PATTERNS IN DIET-INDUCED OBSESE RATS. Luis Caicedo1, Ann Scheimann1, Alexander Moghadam2, Ryan Purcell1, Timothy Moran2
1Pediatrics, Johns Hopkins Children’s Center, Baltimore, MD; 2Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD

Background: The rise in obesity and associated co-morbidities is one of the most pressing issues facing the medical and scientific community. Currently surgical approaches for management of severe obesity have shown the greatest impact on weight loss. The mechanisms of weight loss following Roux-en-Y bariatric surgery (RYGB) are incompletely understood but a role for increased secretion of gut hormones has been proposed. Our preliminary data in non-obese rats demonstrated significant reductions in food intake (FI) and body weight (BW) in response to small volume jejunal nutrient infusions (NI) suggesting an important role for
lower gut nutrient delivery in the efficacy of RYGB. Aims: In the present study we sought to extend these findings to a relevant rodent obesity model - the diet induced obese rat (DIO). The experiments sought to determine whether 1) jejunal FI of free fatty acids induce weight loss in DIO rats, and 2) how such FI affect FI, gut peptide secretion, adiposity and hypothalamic gene expression.

Methods: We used male DIO Sprague Dawley rats. Chronic intestinal cannulas were surgically implanted. Intestinal fatty acid NI began during the dark phase and represented approximately 12% of the daily caloric intake. NI continued daily for 10 days then rats were sacrificed for measurements of gut peptides and adiposity. Results: Rats receiving linoleic acid NI had a 7% decrease in BW (P<.05), consumed fewer meals with no significant effect on meal size, had decreased fat pads, decreased levels of ghrelin, elevated GLP-1 and decreased expression of arcuate NPY. No significant levels of steatosis were found. Conclusions: Jejunal linoleic acid may decrease FI and BW via alterations in signaling of the gut-brain axis by decreasing meal numbers. These data provide insight into the mechanisms that may contribute to the effectiveness of RYGB. This study may help in the identification and development of pharmaceuticals and different surgical procedure to treat obesity.

CONCURRENT SESSION V – FUNCTIONAL/MOTILITY DISORDERS
Saturday, October 22, 2011
3:45pm – 5:15pm

Motility and Neurogastroenterology Prize
384 GASTRIC ELECTRICAL STIMULATION IMPROVES OUTCOMES OF PEDIATRIC PATIENTS WITH FUNCTIONAL DYSPESIA AND GASTROPAESIS. Hayat Mousa1, Carla Di Lorenzo1, Jaya Punati1, Steven Teich2
1Pediatrics Gastroenterology, Nationwide Children Hospital, OSU, Columbus, OH; 2Pediatric Surgery, Nationwide Children Hospital, Columbus, OH

Permanent Gastric electrical stimulation (GES) has been used in adult patients with gastroparesis or refractory nausea and vomiting. No available data on children. Aim: To assess the clinical outcomes and feasibility of GES therapy in children. Methods: We placed GES on 16 children (10F/6M) median age 15 yrs (range 4-19 yrs). All pts were evaluated for chronic nausea and vomiting refractory to medical therapy for a median duration of 2 yrs (3 mos-14 yrs). Pts met ROME III criteria for functional dyspepsia with 50% of them having delayed gastric emptying. At referral, 3 pts were on total parenteral nutrition (TPN) exclusively, 3 on jejunal feeds and 10 on oral feeds (PO). Symptoms, route for nutrition and satisfaction with procedure were recorded at baseline and after GES. Overall global health condition and complications after GES were also recorded. Statistical analysis was performed using a paired Student’s t test. Results: Data showed significant improvement in the severity and frequency of combined symptoms score (CSS) p<.0001 and p<.0001 respectively. There was also significant improvement in the severity of vomiting P= 0.0001, frequency of vomiting p=0.0003, severity of nausea P<.0001 and frequency of nausea P<.0001. Follow-up ranged from 0.5 to 23 mos, with 13/16 pts reporting sustained improvement. After GES, 13/16 were on PO exclusively, 2 on PO+G-tube and 1 on TPN + PO+ G-tube + intermittent TPN. Overall global health condition much improved in 63%, better in 31% and same in 6%. GES was complicated with skin infection in 1 pt. Conclusions: 1. Gastric electrical stimulation can be successfully applied to children with functional dyspepsia and gastroparesis. 2. Combined dyspeptic symptoms significantly improved after GES. 3. Overall global condition is much improved in the majority of children and adolescents after GES. 4. There are no serious adverse effects of the GES. 5. Long-term efficacy / dependency on this therapy in children needs to be established.

385 GLUCOCORTICOID-MEDIATED UPREGULATION OF DUSP4 IN EOSINOPHILIC ESOPHAGITIS. Marcia F. Torres1, Julie M. Caldwell2, Carine Blanchard3, Marc E. Rothenberg1. 1Pediatrics, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; 2Division of Allergy and Immunology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH

Background: Eosinophilic esophagitis (EE) is a Th2-associated disorder characterized by marked eosinophil infiltration in the esophageal epithelium. Although no curative treatment for this disease exists, a subset of patients responds to treatment with topical (swallowed) glucocorticoids such as fluticasone propionate (FP).

Aim: To elucidate the molecular mechanisms that underlie the remission induced by swallowed FP.

Methods: Microarray analysis was undertaken to observe global gene expression differences in the esophageal tissue of untreated non-EE patients, untreated EE patients with active disease, FP-treated EE patients who responded to the treatment, and FP-treated EE patients who did not respond to the treatment. Genes that exhibited altered expression specifically in patients who responded to FP compared to untreated patients were identified. Transcript levels in a separate patient cohort were verified by RT-PCR. Primary esophageal epithelial cells were treated with FP in vitro and transcript levels were monitored by RT-PCR. Results and Discussion: The normalized signal for two probes representing dual specificity phosphatase 4 (DUSP4) was upregulated 2.1- and 2.0-fold in patients who responded to FP compared to untreated patients (P<0.01). Interestingly, the majority of patients with EE who were treated with but did not respond to FP showed DUSP4 expression levels similar to untreated patients. Quantitative PCR revealed that esophageal DUSP4 mRNA was increased 163-fold (P<0.0001) in FP-responder patients compared with non-EE and active EE patients. Next, we tested whether glucocorticoids promoted DUSP4 expression in primary esophageal epithelial cells. We observed that DUSP4 mRNA was upregulated approximately 2-fold (P<0.05) after 24 h of FP-treatment of cells derived from two patients. We speculate DUSP4 may dephosphorylate key proteins involved in the inflammatory response in EE and promote remission in a subset of patients.
386 SLEEP INTERRUPTION ACTIVATES THE PERIAQUEDUCTAL GREY REGION AND RESULTS IN VISCERAL AND SOMATIC HYPERSENSITIVITY IN RATS. Adrian Miranda, Mitchel Bruckert, Pradeep Kannampalli, Jyoti N. Sengupta, Pediatrics, Medical College of Wisconsin, Milwaukee, WI

Introduction: Short-term sleep loss is known to cause temporary difficulty in cognition, behavior and health. The objective of the study was to determine if short-term sleep interruption (SI) in rats alters colonic sensitivity and to investigate the neuroanatomical sites involved and the role the sleep hormone, melatonin. Methods: Male Long-Evans rats were subjected to SI during the 12 hour “lights-on” period (cage oscillation every 90 sec) for 2 consecutive days. Rats were allowed to recover without interruption during the 12 hour “lights-off” period. Sham SI rats had the same total duration of cage oscillation during the 12 hours, but condensed to allow for 45 minutes of undisturbed sleep every hour. In all rats, the paw withdrawal reflex to von Frey filaments (PWR) (n=17) and the visceromotor response (VMR) to graded colorectal distension (CRD) (n=9) was recorded prior to and immediately following SI (n=4) and compared to control. Results: SI significantly increased the VMR from baseline at CRD pressures >30mmHg (p<0.05). There was no difference in the VMR recorded after sham SI (n=4). SI resulted in a significant decrease in the PWR threshold (p<0.05). Melatonin significantly decreased the VMR in the SI group (p<0.05), but had no effect in the control group. The SI group had higher serum cortisol levels (93.9 ng/ml) compared to control (50.8 ng/ml) and increased expression of c-fos in all areas of the PAG: DMPAG (68.5 vs 21.2), DLPAG (92.0 vs 21.3), LPG (166.7 vs 27.7), VLPAG (231 vs 23.3) (p<0.05). Conclusion: Two days of SI results in somatic and colonic hypersensitivity that is attenuated by melatonin. High serum cortisol levels and c-fos expression in the area of the PAG following SI suggests that the HPA axis and/or the descending pain modulatory system play an important role.

387 ADAM10 IS ESSENTIAL FOR INTESTINAL CRYPT HOMEOSTASIS. Riha Bhatt, Yu-Hwai Tsai, Peter Dempsey

Pediatric Gastroenterology, University of Michigan, Ann Arbor, MI

INTRODUCTION: ADAM10 acts as a cell surface sheddase that regulates various physiologic processes. Using intestine-specific ADAM10KO mice, we have recently shown that ADAM10 is required for Notch-dependent cell lineage specification. In this study, we examined the requirement for ADAM10 (A10) signaling in the adult crypt stem cell compartment.

METHODS: To investigate the role of A10 in the intestine, tamoxifen (TX)-inducible Villin-CreER (VilCrE) A10KO mice were analyzed. Mice were given various TX regimens to induce different levels of crypt recombination. Changes in cell proliferation, apoptosis and lineage markers were assessed by IHC and qPCR analysis.

RESULTS: VilCrE A10KO mice given a single TX treatment showed a dose-dependent reduction in body weight and viability. Next, we induced recombination with a high-dose TX regimen to achieve maximum A10 deletion in all intestinal crypts. Crypt progenitors were replaced by two distinct, post-mitotic secretory cell populations: enteroendocrine cells and an intermediate-Paneth (MMP7+)/goblet (MUC2+) cell. To study the fate of individual A10-deficient crypts over time, a lower TX dose was used to achieve reduced and mosaic crypt recombination. Changes in cell proliferation, apoptosis and lineage markers were assessed by IHC and qPCR analysis.

RESULTS: VilCrE A10KO mice given a single TX treatment showed a dose-dependent reduction in body weight and viability. Next, we induced recombination with a high-dose TX regimen to achieve maximal A10 deletion in all intestinal crypts. Crypt progenitors were replaced by two distinct, post-mitotic secretory cell populations: enteroendocrine cells and an intermediate-Paneth (MMP7+)/goblet (MUC2+) cell. To study the fate of individual A10-deficient crypts over time, a lower TX dose was used to achieve reduced and mosaic crypt recombination. Histology revealed dramatic changes in the crypt-villus architecture: crypt degeneration and intestinal remodeling. All degenerating crypts were A10-deficient, had lost cell proliferation (Ki67-) and showed increased apoptosis. Finally, to study the role of A10 in long-lived, multipotent ISCs, we used the Rosa26YFP reporter for lineage tracing analysis. At day 28 of chase, A10+/YFP+ crypt-villus units were readily detected in control mice. However, no A10-/YFP+ crypt-villus units were detected in VilCrE A10KO mice, indicating that A10 is required for maintenance of long-lived ISCs.

CONCLUSIONS: These results demonstrate that ADAM10 acts at multiple levels in the crypt compartment to regulate crypt homeostasis. Specifically, ADAM10 is essential for crypt progenitor proliferation, cell fate specification and for the long-term maintenance of ISCs. Ongoing studies will follow to investigate A10’s role in intestinal injury and regeneration.