ROLE OF WIRELESS CAPSULE ENDOSCOPY IN RECLASSIFYING IBD IN CHILDREN
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Background: Capsule endoscopy is a diagnostic tool allowing visualization of the small bowel. Between 5–20% of newly diagnosed cases of IBD are indeterminate, known as IBD type unclassified (IBDU); cases where endoscopy and histology fail to reveal diagnostic features of either CD or UC. The objective was to evaluate the role of capsule endoscopy in identifying small bowel lesions, in pediatric patients with newly diagnosed IBDU, to better characterize their type and extent of disease. Secondary outcome is to evaluate if findings from the capsule endoscopy translates changes on patient management.

Methods: Ten pediatric patients (7 boys, 3 girls; age 8–17 y) recently diagnosed with IBDU were recruited from the pediatric GI clinic at McMaster Children’s Hospital, to undergo capsule endoscopy using the Pillcam SBTM (Given Imaging) capsule. Images were analyzed by a pediatric GI and patients were followed for 12 months after the capsule endoscopy. Findings consistent with a diagnosis of Crohn’s disease required the identification of at least three or more ulcerations of small bowel.

Results: The capsule was easily swallowed by 9 of our patients (1 had GA insertion). They all excreted the capsule normally with no complications. Three patients had newly identified findings on capsule endoscopy that met our criteria for CD. Three other patients had findings suspicious of CD, but failed to meet our diagnostic criteria. As for secondary outcome, findings from capsule endoscopy allowed for a better characterization of the type and extent of disease in all cases and no adverse outcomes occurred in our cohort.

Conclusions: The early use of capsule endoscopy in pediatric IBDU showed to be useful to reclassify and manage pediatric patients. Given the limitations of this pilot study, further investigation is warranted to better characterize the use of capsule endoscopy in this population.

GLUCOSE-GALACTOSE MALABSORPTION IN ARAB INFANTS
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Four infants with chronic diarrhea from glucose-galactose malabsorption from three different families are presented. Two are Saudi Arab from the same family, the third is Syrian Arab and the fourth infant is Yemeni Arab. The mean age of the infants at the time of presentation was 6 months. They were first presented with chronic diarrhea and severe growth failure since birth, one infant who is from Yemen Arab develops gangrene of both legs as complication of dehydration and hypernatremia. This complication required below knee amputation of both legs at his original country before his presentation to Saudi Arabia. Two infants developed nephrocalcinosis on follow-up. Laboratory investigation including small bowel biopsies confirmed the diagnosis of glucose galactose malabsorption. All the infants responded clinically to fructose based formula. Pediatrician should think of glucose-galactose malabsorption as a cause of diarrhea since early infancy which start after breast or bottle-fed fructose based formula will improved the disease and this will save our infants from the long-term complications of the disease. Four Arab infants presented with chronic diarrhea since early infancy which was associated with breast and bottle feed. One of those infant developed gangrene of both feet and another two infants developed nephrocalcinosis as long-term complications of the disease. A diagnosis of glucose-galactose malabsorption was made in those infant, pediatrician should think of glucose-galactose malabsorption as a cause of chronic diarrhea since early infancy which is associated with breast or bottle feed. Fructose based cause of chronic
diarrhea since early infancy which is associated with breast or bottle feed. Fructose based formula will save the life of the infants.

3

EFFECT OF ROTAVIRUS VACCINATION ON HOSPITALIZATION AND SEASONALITY OF DISEASE FROM ROTAVIRUS INFECTION

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Background: To determine changes in hospitalization rate and seasonality of rotavirus AGE in infants and children from birth to 6 years of age, before and after institution of RV.

Methods: This was a retrospective, descriptive, comparative study. Data were obtained from databases of FHMC, the microbiology lab and the New York City Vaccine Registry for patient vaccination histories. Stool tests for rotavirus antigen were done using enzyme immunoassay. An historical control group comprised patients 0–6 years of age admitted to FHMC from Sept 2004-Aug 2005 with a diagnosis of rotavirus AGE, and a comparator group comprised similar patients admitted from Sept 2007-Aug 2009 (after institution of RV).

Results: Total monthly pediatric admissions during the study periods and discharge diagnoses were derived from the database. We recorded the date of admission and results of rotavirus testing for all patients, and immunization histories for the study group only. We excluded patients who received RV <3 weeks before being tested for rotavirus and patients with unknown immunization histories. Data were analyzed using frequency distribution analysis.

Results: We reviewed 494 patients tested for rotavirus during the study periods; 97 were marked. Positive in the hospitalization rates from rotavirus AGE in the pre-RV year (12.5% total admissions) to the two post-RV years (1.8% for 1st year, 3.5% for 2nd year) were seen, and there was a notable change in the seasonality of disease. In the pre-RV era, rotavirus admissions rose from Nov-Feb, peaked from Feb-May, and then declined. In the post-RV era, there were fewer cases, wider scatter, and a peak in April. Among patients who developed rotavirus AGE, none were fully immunized with RV.

Conclusions: There was a decrease in the hospitalization rate from rotavirus AGE after institution of RV at our institution between March 2007 and May 2010. Diagnosis of celiac disease was confirmed by endoscopic biopsy of the small intestine. Subjects included in the study had both TTG IgG and IgA testing in the presence of small intestine biopsy consistent with celiac disease.

Methods: Forty-seven patients (ages 2–21; 35 F) were identified as having biopsy confirmed celiac disease, and TTG IgG and IgA testing in the past 5 years. For these 47 patients, TTG IgA was found to be 98% sensitive (46/47) whereas TTG IgG was 10.6% sensitive (5/42).

Conclusions: In our series, TTG IgG sensitivity was not similar to TTG IgA sensitivity for predicting celiac disease in the pediatric population. This is unlike published series of adults reporting sensitivities for TTG IgG above 70%. In this review, no patients with IgA deficiency were identified. These findings suggest that the current practice of using TTG IgG as an additional screening test for celiac disease at this institution has limited value. Larger scale studies evaluating sensitivity in an IgA deficient pediatric population may be beneficial.

5

SEROLOGY CORRELATION WITH FINDINGS ON CAPSULE ENDOSCOPY (CE) IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE (IBD)

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Background: To evaluate the diagnostic yield of IBD serology in the absence of histology for findings on CE.

Methods: Retrospectively reviewed the records of children who all underwent CE, IBD serology testing, small bowel radiographic studies, EGD and colonoscopy with biopsies at our institution between March 2007 and May 2010.

Results: Total 50 patient. Twenty-five females (50%) were part of the study. Age ranging from 8 to 18 years with a mean age of 16 years. The indications were unexplained abdominal pain, diarrhea, hematochezia and/or weight loss. In the selected patients, findings were suggestive of small bowel Crohn’s disease (CD) on CE in 15/50 (30%). Serologic testing for IBD was positive for CD in total of 11/50 patients (22%) and only 4/15 (26.6%) had findings on CE suggestive of CD. Furthermore IBD serologies were positive for CD in 7/35 patients (20%) with normal small bowel on CE.
Conclusions: In the diagnosis of small bowel CD in children, Serologic testing for IBD did not add significant diagnostic value to CE.

6

MAGNETIC RESONANCE ENTEROGRAPHY (MRE) IDENTIFIES ACTIVE INFLAMMATION, CHRONIC DISEASE/NARROWING, UNKNOWN COMPLICATIONS, AND EXTENT OF SMALL BOWEL INVOLVEMENT IN PEDIATRIC IBD

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Background: Children with inflammatory bowel disease (IBD) often undergo small bowel series or CT scans which expose them to ionizing radiation. Magnetic resonance enterography (MRE) evaluates the abdomen without radiation exposure. The purpose of this study was to evaluate MRE in pediatric IBD.

Methods: We performed an IRB-approved chart review from 2007-2010 on IBD patients at a tertiary referral pediatric hospital who underwent MRE. MRE findings, history and laboratory results, and demographics were recorded.

Results: A total of 52 patients with IBD (45 Crohn Disease (CD), 7 Ulcerative Colitis (UC)) underwent MRE for symptomatic disease. Thirty displayed active and/or chronic disease while 22 had a normal MRE. Extent of small bowel involvement was evaluated by estimating the length of disease. MRE identified 13 unknown complications including 7 fistulae, 2 non-specific liver disease findings, and one each of intra-abdominal abscess, sclerosing cholangitis, tethering and a blood clot. MRE active inflammation of the small intestine/colon was associated with a higher CRP (3.2 vs 0.5, P < 0.05) but not ESR (36 vs 25, P = 0.14) when compared to patients with a normal MRE. Comparison between terminal ileum/colon histology and MRE suggests high inter-observer agreement (kappa 0.71 and 0.68 respectively).

Conclusions: MRE detects active inflammation, chronic disease and narrowing/strictures. MRE identifies unknown complications and evaluates the extent of small bowel involvement in IBD. Active inflammation on MRE correlates with CRP but not ESR and shows good agreement with histology for both the terminal ileum and colon. This study adds to a growing body of evidence that MRE is an excellent assessment of active inflammation, chronic disease, extent of small bowel involvement, and unknown complications without the risk of radiation exposure. Therefore, MRE should be considered effective for IBD diagnostic imaging and the preferential radiographic study in IBD.

7

COMPARATIVE GROWTH IN CELIAC CHILDREN UNDER TREATMENT IN PUBLIC AND PRIVATE INSTITUTIONS

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Background: To monitor physical growth, adherence to gluten-free diet (GFD) and food transgression is essential in pediatric celiac patients. To evaluate growth and adherence to GFD of celiac children before and after treatment according to the institution in which they are treated (public and private).

Methods: Retrospective study, n = 29 children (76% women). Minimum follow up = 5 months. Age x 5 y 11 m ± 3 y 4 m (diagnosed (baseline) and treated with a team at Public Hospital (PUB) (n = 14) and Private Center (PRI) (n = 15). Follow-up x = 15 months. Monitored with z score of weight (zW) and height (zH), food history and serology (EMA IgA, AtG IgA/IgG and AGA IgA/IgG). zW and zH variation was evaluated (DIF = z basal - later), according to PUB or PRI, transgressions and serology.

Results: At baseline: 55% (16) had z-weight <-1 and 27% (8) z-height <-1. Average values weight x -0.98 ± 1.33/height x -0.40 ± 1.11, with more PUB affected children but not significantly differences from those of PRI (Test T P = 0.38/P = 0.28). zW and zH significantly improved in PUB children after treatment x = 15 months (Paired T Test DIF zW P = 0.04 DIF zH P = 0.02). No significant differences were found comparing DIF between PUB and PRI for either zW [PUB Me = -0.23 (C1: -1.3 C3: 0.17) PRI Me = -0.15 (C1: -0.42 C3: 0.06) Wilcoxon Test P = 0.67] or zH [PUB Me = -0.03 (C1: -0.4 C3: -0.0007) PRI Me = -0.02 (C1: -0.25 C3: 0.04) Wilcoxon Test P = 0.40] having improved their zW 52% (15) and zH 59% (17) of children, with no differences by group treatment (Fisher P = 0.32 and P = 0.22). Patients who report transgressions are similar in both groups (14% PUB, 20% PRI) but serologies differ significantly with positive serology (PUB 85.7%, PRI 13.3%) (P = 0.0001) showing better diet adherence in PRI children.

Conclusions: zW and zH of celiac children improved in PUB and PRI institutions with no significantly differences between treatment groups. Apparent transgressions are less than the evidence of positive serology in children PUB, suggesting weaker adhesion to diet or presence of unintentional transgressions.

8

A NOVEL IMMUNOGENIC PEPTIDE FROM THE α-GLIADIN SYNTHETIC PEPTIDE LIBRARY IS RESPONSIBLE FOR CXCR3-DEPENDENT INTERLEUKIN-8 PRODUCTION IN CELIAC DISEASE PATIENTS

Karen Lammers1,2, Sunaina Khandelwal1,2, Debby Kryszak1,2, Elaine Leonard Puppa1,2, Vincenzo Casolaro1,3, Alessio Fasano1,2,1Center for Celiac Research, University of Maryland School of Medicine, Baltimore, MD; 2Mucosal Biology Research Center, University of Maryland School of Medicine, Baltimore, MD; 3Johns Hopkins Asthma and
Background: The chemokine receptor, CXCR3, serves as a receptor for gliadin. At intestinal epithelial level, CXCR3 engagement by gliadin causes zonulin release and opening of tight junctions, e.g. increased intestinal permeability. Various immune cells express CXCR3, and at this level, gliadin causes IL-8 production in a CXCR3-dependent manner only in celiac disease (CD) patients but not healthy controls (HC).

To search for the peptide sequence within α-gliadin that is responsible for this celiac disease-restricted immune effect.

Methods: PBMC from HC (n=16) and CD patients (n=17) were incubated with 11 out of the 25 overlapping twenty-mer peptides from the α-gliadin synthetic peptide library in the presence or absence of a blocking anti-CXCR3 antibody (10 μg/ml). Choice for these peptides was made after a prior set of experiments in which PBMC were stimulated with 5 peptide pools each consisting of 5 randomly chosen peptides and in the presence or absence of a CXCR3 blocking antibody; the peptides from 2 pools showing a CXCR3-dependent IL-8 production pattern, and 1 CXCR3-binding peptide from another pool were then incubated separately to the PBMC cultures. Supernatants were assessed for IL-8 production.

Results: Out of the 11 peptides, 1 α-gliadin 20-mer synthetic peptide, peptide 4037, appeared to be responsible for the CXCR3-dependent IL-8 production pattern specific for CD patients.

Conclusions: In addition to the different peptides of α-gliadin which have been described before to be implicated in its immunotoxic (31–43 aa), immunomodulatory (57–89 aa) and zonulin-inducing (111–130 aa and 151–170 aa) effects, we here show a novel immunogenic peptide of α-gliadin, 258–277 aa, that has a specific function in regulation of IL-8 production in CD.

PT-GLIADIN AS A CHEMOATTRACTANT FACTOR FOR NEUTROPHILS

K. Lammers1, M. Chieppa2, S. Khandelwal1, M. Janka-Junttila3, C. Parent3, V. Casolaro1,4, A. Fasano1,1 University of Maryland School of Medicine, Baltimore, MD; 2National Institute of Gastroenterology “Saverio de Bellis”, Bari, Italy; 3National Institute of Health, Bethesda, MD; 4Johns Hopkins University School of Medicine, Baltimore, MD.

Background: Gliadin triggers celiac disease (CD) in genetically predisposed individuals. Neutrophil influx is implicated in CD. We have shown that gliadin increases gut permeability through zonulin release, so gaining access to the lamina propria and initiating the host immune process. The aim was to establish whether neutrophil recruitment is triggered by gliadin.

Methods: Ten C57BL/6 mice were given gliadin (1 mg/ml) or PBS by gavage. After 2h mice were sacrificed and duodenal tissue analyzed for (a) tight junction (TJ) disassembly by fluorescence microscopy and (b) immune cells (dendritic cells, T cells, granulocytes) by flow cytometry. Effects on neutrophil recruitment caused by gliadin was monitored in vivo after luminal exposure to gliadin (n=5) or PBS (n=5) for 2h by intravitral microscopy technique using Lys-GFP mice that have green-fluorescent neutrophils. Furthermore, neutrophils were isolated from bone marrow of 8 C57BL/6 mice, and applied in the so-called taxi-scan assay, an vitro model that allows monitoring neutrophil chemotaxis. Gliadin, and, as positive control N-Formyl-Methionyl-Leucyl-Phenylalanine (N-terminus) which have been described before to be implicated in gliadin, and that binding of gliadin to intestinal epithelial cells. The aim was to investigate whether gliadin induces CXCR3+ B cells to undergo expansion and differentiation into IgA-producing plasma cells.

Methods: PBMC from HLA-DQ2/DQ8+ healthy controls (HC; n=15), active CD (n=14) and CD in remission (n=28) were stained with B-cell marker CD19 and CXCR3 and analyzed by flow cytometry. B-cell activation and differentiation into IgA-secreting plasma cells in the intestinal mucosa were assessed by measuring expression of the AICDA gene and of IgA germinine and Ca mature transcripts, respectively, by real-time RT-PCR of biopitic RNA from HC (n=12) and active CD (n=16).
Results: A significantly higher percentage of CXCR3+ B cells was detected in the peripheral blood of CD patients, irrespective of their disease status, compared to HC ($P < 0.05$). At the intestinal level, compared to HC, CD showed significantly higher expression of B-cell activation marker AICDA ($P = 0.004$), and of IgA isotype switch markers $\text{Ig} A$ ($P = 0.021$) and $\text{C} A$ ($P = 0.003$).

Conclusions: CD is associated with increased systemic expansion of CXCR3+ B cells. Furthermore, higher numbers of recently activated B cells and IgA-isotype switched plasma cells can be detected in the active CD intestinal mucosa. We hypothesize that a CXCR3+ B-cell subset may be uniquely responsive to gliadin exposure to differentiate into IgA-secreting plasma cells. Whether gliadin-induced B-cell activation and switch into IgA-producing plasma cells occurs in the intestinal mucosa or in mesenteric lymph nodes is under current investigation.

11

EFFICACY AND SAFETY OF A NEW TWO-DAY BOWEL PREPARATION USING POLYETHYLENE GLYCOL 3350 AND BISACODYL FOR COLONOSCOPY IN CHILDREN

Uma Phatak, Susanne Johnson, Sohail Husain, Dinesh Pashankar. Pediatrics, Yale University, New Haven, CT.

Background: Polyethylene glycol 3350 without electrolytes (PEG) based bowel preparations (prep) are gaining popularity for colonoscopy in children. The aim was to assess the efficacy, safety, and acceptance of a two-day bowel prep with PEG and bisacodyl for colonoscopy in children.

Methods: In a prospective study, 111 children (61 boys, 50 girls) were given PEG at a dose of 2 gm/kg in divided doses and a 5 mg tablet of bisacodyl daily for two days prior to the colonoscopy. Patients were allowed to mix the PEG in a beverage of their choice. Adverse effects, stool frequency and consistency (on a scale of 1-hard to 5-watery) were monitored during the prep. Compliance, tolerance, and quality of the colon prep were assessed.

Results: The mean age of children was 11.9 years (range 2.5 to 19). The patients used different beverages to mix the PEG which included fruit juices (66), sports drink (32), water (31), and other (35). The mean daily stool frequency increased from baseline of 2, to 4+ on day 1, and 6.5+ on day 2. The mean stool consistency changed from baseline of 3, to 4+ on day 1, and 5+ on day 2. ($**P < 0.001$ for difference vs baseline). Adverse effects were mild nausea (19%), abdominal pain (11%), and vomiting (4%). The compliance, tolerance, and quality of the colon prep were assessed. The colon prep was rated as excellent or good by the endoscopists in 92% and 93% of the patients in the right and left colon, respectively. The endoscopists reached the cecum or terminal ileum in 98% of the cases.

Conclusions: This new 2-day bowel prep with PEG and bisacodyl is safe and effective for colonoscopy in children. It is well accepted and tolerated by children without any major adverse effects.

| Table. Compliance, tolerance, and quality of the colon prep |
|-------------------|------------------|----------------|-----------------|
|                   | Excellent | Good | Fair | Poor |
| Compliance, %     | 95 | 4 | 1 | 0 |
| Tolerance, %      | 75 | 22 | 3 | 0 |
| Right Colon, %    | 48 | 44 | 7 | 1 |
| Left Colon, %     | 52 | 41 | 7 | 0 |

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CELIAC DISEASE IN A CHILD WITH CROHN’S DISEASE

Sam Cheng, Philip Stein, Uma Phatak, Dinesh Pashankar. Pediatrics, Yale University, New Haven, CT.

Crohn’s disease and celiac disease are immune-mediated enteropathies and can present as diarrhea, anemia, and weight loss. It is rare for both to occur together. We report a 10-year-old boy who presented with bloody diarrhea for 2 months. He had a history of intermittent diarrhea and poor growth for one year before presentation. Laboratory evaluation showed anemia and increased inflammatory markers. Endoscopy revealed gastric and duodenal erythema, with multiple ulcerations, friability and inflammation in the colon consistent with a diagnosis of Crohn’s disease. Therapy with intravenous steroids was started, and hematocrit and diarrhea resolved. On histology, there was mild gastritis and inflammatory changes in the colon consistent with Crohn’s disease. Duodenal histology revealed partial villous atrophy and intraepithelial lymphocytosis. These changes were compatible with both Crohn’s disease and celiac disease. Serology revealed a strongly positive tissue transglutaminase (TTG) IgA antibody (146 U/ml; normal <20). Endomysial antibody and repeat TTG were also positive. The diagnosis of celiac disease was made. Gluten-free diet was initiated, and anemia and growth improved. Patient is growing well and remains in remission for the last 3 years without any gastrointestinal symptoms on 5-aminosalicylic acid and gluten-free diet. Repeat duodenal biopsy showed normal mucosa, and repeat serology revealed normal TTG-IgA. We conclude that although rare, celiac disease and Crohn’s disease can occur together. While abnormal duodenal histology can occur in Crohn’s disease, high TTG antibody titers are suggestive of celiac disease. Celiac disease should be suspected in patients with Crohn’s disease with unexplained gastrointestinal symptoms and poor growth.

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CELIAC DISEASE TESTING IN HOSPITALIZED CHILDREN WITH TYPE I DIABETES MELLITUS

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Background: The incidence of celiac disease (CD) in diabetes mellitus (DM1) is reported between 3–10%. We examined tissue transglutaminase (tTG) serologies to characterize CD in a hospitalized population.

Methods: We reviewed DM1 patients (n = 311) hospitalized at Texas Children’s Hospital from 7/2008–1/2010 with IRB approval. Inclusion criteria were: DM1 (+) antibodies or C-peptide value <0.6 ng/mL and tTG test completion. Demographics, GI symptoms, DM1 antibodies, timing of tTG and methodology for CD diagnosis were recorded. tTG testing was performed at multiple labs, and cutoffs were based on individual reference labs.

Results: Of 311 patients, 29 (10M/9F) had a positive tTG result (9.3%). 6 pts (3M/3F) met DM1 criteria (1.9%) with positive tTG and histologic confirmation of CD. A known CD pt (tTG negative with abnormal histology) was diagnosed during study period with DM1. One patient was excluded as DM1 labs unavailable. All tTG values in CD pts were above 100 units regardless of reference lab. The distribution for ethnicity was white (n = 5), Hispanic (n = 4) and asymptomatic (n = 2). Five additional pts had serological evidence of CD without histologic confirmation. Borderline tTG values at DM1 onset were found in 14/29 (48%). Of the remaining pts, 9 were retested. tTG values confirmed a positive result in two. The remaining (n = 7) were initially elevated, and later; normal (n = 4); borderline (n = 3). Two borderline retests underwent EGD to reveal no histological evidence of CD.

Conclusions: Using strict criteria for DM1 diagnosis in hospitalized pts, we found a lower incidence of CD (1.9%) in an ethnically mixed DM1 population than previously reported. For patients with new-onset DM1, tTG may be falsely positive, or demonstrate latent celiac disease at a similar rate (2.2%). Further long-term data is needed in this subset of patients to formulate recommendations for the timing of tTG testing in DM1.

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HIGH RISK OF DEVELOPING CELIAC DISEASE IN CHILDREN CARRYING HLA DR3-DQ2: THE TEDDY STUDY

Edwin Liu1, Hye-Seung Lee2, William Hagopian3, Carin A. Aronsson4, Sibylle Koletzko5, Marian J. Rewers1, George S. Eisenbarth6, Olli Simell6, Daniel Agardh4

Abstracts JPGN

Table.

<table>
<thead>
<tr>
<th>HLA DR-DQ haplotype</th>
<th>Persistent TGA positivity (n)</th>
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<td>DR4-DQ8/DR4-DQ8</td>
<td>29</td>
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<tr>
<td>Others</td>
<td>8</td>
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</table>

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THE VALUE OF TRANSGLUTAMINASE AUTOANTIBODY WORKSHOPS IN QUALITY IMPROVEMENT AND HARMONIZATION

Marcela Li, Edwin Liu. Pediatrics, University of Colorado, Aurora, CO.

Quantitative and qualitative differences amongst assays exist amongst different transglutaminase autoantibody (TGA) assays. Such disparities can lead to uncertainty when the same patient is tested serially using different assays. Our first International Transglutaminase Autoantibody Workshop reported in 2009 demonstrated such marked variability in TGA assays. The aim of this second workshop was to follow up on the performances of prior participating labs, to expand proficiency testing to other labs, and to explore the best approach for assay harmonization. A total of 23 laboratories participated in this 2nd International Transglutaminase Autoantibody Workshop, including 18 ELISA and 5 radio-binding assays (RBA). Eight of the ELISA assays were run by commercial vendors. Each laboratory received 82 samples coded and blinded; 50 control sera from healthy donors and 26 sera from untreated CD patients. Of these celiac samples, 8 out of 26 were prediluted with control sera.
to simulate lower-titer samples. There were an additional 6 samples derived from a single patient that was serially diluted from 1:8 to 1:256 to test limits of detection (these were not included in the final analysis). Finally, a reference set of unblinded sera diluted 1:2 serially x 10 was provided to make a standard curve. One control sample was found to be positive for TGA by all participating labs, and by consensus, was considered to be a true positive test. Five out of the 6 CD sera that were most commonly reported as negative had the lowest TGA levels by the reference laboratory (our assay, run by RBA). There continues to be marked variability amongst TGA assays, particularly between ELISA and RBA. The greatest disparities occur in the low TGA range, which is very important in screening for CD. This TGA workshop was designed with international participation to compare assays and will hopefully lead to a standardization program for TGA.

Table.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Limits of Detection</th>
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<tr>
<td>ELISA</td>
<td>69–92%</td>
<td>98–100%</td>
<td>none:1–64</td>
</tr>
<tr>
<td>RBA</td>
<td>81–100%</td>
<td>100%</td>
<td>1:128–1:256</td>
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<td>Commercial vendors</td>
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**LACTOBACILLUS REUTERI STRAINS REDUCE INFLAMMATION IN NEONATAL NECROTIZING ENTEROCOLITIS IN RATS**

Yuying Liu, Nicole Fatheeree, Nisha Mangalat, J. Marc Rhoads. Pediatrics, University of Texas Medical School, Houston, TX.

**Background:** Abnormal gut microbiota and aberrant immune responses can lead to necrotizing enterocolitis (NEC) in the premature infant. Lactobacillus reuteri (LR) modulates immune responses in a strain-dependent manner in monocytes. Hypothesis: Human-derived LR strains will differentially affect inflammatory response in the intestine and prevent NEC.

**Methods:** NEC was induced in rat pups by formula feeding LR (10^6 cfu/g.bw/day) (strain DSM 17938 or ATCC PTA 4659) or formula without LR. Intestinal (ileal) histology was evaluated for NEC score. qRT-PCR was performed to detect mRNA expression of Toll-like receptors (TLRs) and cytokines. Protein levels of IL-6 and TNF-α. Protein levels of TNF-α, IL-1β, and IL-13 were all significantly decreased in the intestine of pups fed either strain. Ileas of rats that were formula-fed without hypoxia also demonstrated mild histological inflammation and high levels of proinflammatory cytokines. Formula-associated inflammation was suppressed by LR (strain 17938). Messenger RNA levels of TLRs 2, 4 and 6 in the intestines of NEC rats were significantly increased compared to those of formula-fed rats. Surprisingly, there were no significant changes in TLR1–9 mRNA levels in response to LR treatment in the NEC rats.

**Conclusions:** Even though LR strains have been called either immunosuppressive or immunostimulatory, each strain has potential therapeutic value in NEC. Additionally, cow milk formula induces inflammation in the newborn rat intestine that is ameliorated by LR.

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**PSYCHOSOCIAL AND BEHAVIORAL CORRELATES OF GLUTEN-FREE DIET ADHERENCE IN YOUTH WITH CELIAC DISEASE**

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**Background:** To determine the influence of psychosocial, behavioral and family functioning on gluten-free diet (GFD) adherence in youth with celiac disease (CD).

**Method:** Nineteen youth (ages 8 to 17) with biopsy-confirmed CD on the GFD for >3 months and their primary caregivers participated in the study. Youth completed surveys of depression, anxiety, quality of life (QoL), family functioning, CD symptoms, and CD and GFD knowledge, in addition to providing a blood sample analyzed for tTG and a 3-day food record for evaluation of GFD adherence by an expert dietitian. Primary caregivers completed surveys about their youth’s overall behavioral and emotional functioning, QoL, and family functioning, in addition to engaging in the dietitian evaluation of their youth’s GFD adherence.

**Results:** Lower levels of tTG in the blood were significantly associated with GFD adherence as rated by the expert dietitian [r = −0.519, P = 0.05]. Significant associations were found between GFD adherence difficulties and parent reported youth overall emotional and behavioral difficulties [r = −0.539, P = 0.05], externalizing problems [r = −0.469, P = 0.05], aggression [r = −0.46, P = 0.05], attention problems [r = −0.644, P = 0.05], and youth reported depressive interpersonal difficulties [r = −0.614, P = 0.01]. Parent reported youth physical [r = +0.52, P = 0.05], emotional [r = +0.485, P = 0.05], social [r = +0.512, P = 0.05], and school [r = +0.528, P = 0.05] QoL and overall family functioning [r = +0.646, P = 0.01] and family cohesion [r = +0.691, P = 0.05] as reported by youth were associated with GFD adherence. Knowledge of gluten-free foods [r = +0.505, P = 0.05], time on the GFD [r = +0.466, P = 0.05], and belonging to a support group [r = 2.867, P = 0.011] were associated with GFD adherence.
Conclusions: Psychosocial, behavioral, and family-functioning characteristics may be used to identify patients at risk for poor dietary adherence and may inform GFD adherence interventions at the family systems level.

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ILEAL CYTOKINE DYSREGULATION IN EXPERIMENTAL NECROTIZING ENTEROCOLITIS (NEC)
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Background: CD40, a co-stimulatory molecule, plays a critical role in coordinating immune responses in enteric inflammations. Up-regulation of IL-10, a CD40-modulated cytokine, in NEC has been described, but the role of the CD40/CD40 ligand (CD40L) on IL10 signals and on the expression of intestinal disease has not been elucidated. Here we investigated the expression of CD40, CD40L and IL-10 receptor (IL-10R) in the ileum of rats with experimental NEC.

Methods: NEC was induced in newborn rats by formula feeding, asphyxia and cold stress. Breastfed littermates served as controls. After 96 h, rats were killed and the distal ilea were resected. Histopathology was evaluated by H&E stained sections. Immunoblots examined expression of CD40, CD40L, IL-10R and toll-like receptor (TLR)-4 and IL-18. Ileal infiltration by macrophages/monocytes and T cells was examined by immunofluorescence confocal microscopy.

Results: Histological changes consistent with NEC were noted in the small intestine of NEC pups. NEC pup ileum showed increased expression of TLR-4, IL-18 and IL-10R. Ileal sections from both NEC and control groups demonstrated preservation of cells expressing CD40/CD40L. However, while both CD40 and CD40L were expressed in the distal ileum of controls, neither was detected in the samples from NEC pups. Additional studies showed that enteral administration with epidermal growth factor previously shown to ameliorate the histological changes of NEC nor restore CD40 expression.

Conclusions: These data suggest that ileal cytokine dysregulation associated with a decreased CD40 and CD40L expression, is involved in NEC pathogenesis. Dampened CD40 signaling may be related to enhanced IL-10 expression, and result in a suppressed T-cell response to potential injury.

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A CELIAC DISEASE SCREENING ALGORITHM: EFFECT ON PROVIDER BEHAVIOR AND HEALTH CARE COSTS
Julia Bracken, Marilyn Hamilton, Uttam Garg, Gary Wasserman, Keith Mann. Children’s Mercy Hospital, Kansas City, MO.

Background: Widespread variability in provider ordering exists in the serologic screening for celiac disease. Tissue Transglutaminase (tTG) is recommended for initial screening, with EMA, a more specific yet costly test, used for confirmation. Both tests require sufficient IgA for interpretation. To standardize screening at our institution, an updated

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algorithm was implemented. In the new algorithm, an IgA level is obtained from the electronic medical record or laboratory prior to tTG testing. EMA is performed on the original specimen only when the tTG is elevated. The current study evaluated the impact of this algorithm on the frequency of IgA, tTG, and EMA orders and the cost of celiac disease screening.

Methods: In a retrospective review, frequencies of IgA, tTG and EMA results during six-month periods before and after implementation of the algorithm were tabulated. Total number of tTG results was considered representative of total attempts to screen for celiac disease. Difference in proportion tests compared pre- and post-algorithm proportions of IgA to tTG and EMA to tTG. Compliance to the algorithm was estimated by the proportion of EMA to positive tTG results. Cost-savings was estimated by absolute differences of IgA to tTG and EMA to tTG. Compliance to the algorithm was estimated by the proportion of EMA to positive tTG results. Cost-savings was estimated by absolute differences in patient charges.

Results: The proportion of celiac screens performed with an IgA level increased from 36% to 100% after implementation of the new algorithm \((z = -38.13, P < 0.001)\). The proportion of total EMA to tTG decreased from 30% to 13% \((z = 11.35, P < 0.001)\). The proportion of total EMAs ordered appropriately in the setting of abnormal tTG increased from 20% to 45% after the algorithm \((z = 6.54, P < 0.001)\). Annual cost savings of $55,160 was estimated based on reduction of EMA charges post-algorithm.

Conclusions: Implementation of the celiac screening algorithm at our institution increased the proportion of celiac screening performed correctly, including increasing the frequency of IgA orders and decreasing the ordering of unnecessary EMA. This simple intervention appeared to promote best ordering practices among multiple providers and reduce screening cost.

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PREVALENCE OF COLONIC POLYPS IN CHILDREN UNDERGOING COLONOSCOPY
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Background: The epidemiology of colorectal polyps in children is unclear. There is little information on the prevalence and types of polyps in unselected groups of children who undergo colonoscopy, and the associated clinical and endoscopic characteristics of colon polyps in children.

Methods: We conducted a cross-sectional study to determine the frequency and determinants of polyps in all children (0–20 years) who underwent colonoscopy at 13 pediatric facilities between Jan 2000 and Dec 2007 and were recorded in Pediatric Endoscopy Database System Clinical Outcomes Research Initiative (PEDS-CORI). We compared colonoscopy procedures in which polyps were identified to colonoscopies without polyps with respect to procedure indication, gender, age, and anesthesia type. We also analyzed the number, size, and distribution of polyps seen during colonoscopy.

Results: We analyzed 12,305 procedures performed in 10,932 patients. Polyps were reported in 705 patients (6.4%; 95% CI: 6.0% to 6.9%). Children with colorectal polyps identified during colonoscopy were significantly younger (8.9 y vs. 11.9 y; \(P < 0.0001\)), male (58.3% vs. 49.0%; \(P < 0.001\) and of Black or Hispanic background (38.1% vs. 26.0%; \(P < 0.001\)) compared to children without polyps. There were 641 colonoscopies with a single polyp, and 169 with multiple polyps. The most common polyp location was in the sigmoid (29.5%) and rectum (23.0%), followed by descending (11.9%), transverse (8.7%), ascending colon (7.9%), and cecum (7.6%). Review of available pathology records in one facility showed that the most common histological types were juvenile (n = 112, 60.6%) and inflammatory (n = 30, 17.4%), followed by adenoma (n = 25, 9.1%), hyperplastic (n = 5, 4.6%) and hamartoma (n = 3, 1.5%).

Conclusions: This is the largest study to examine the prevalence and determinants of colorectal polyps in children and adolescents. Polyps are present in 6.4% of children undergoing colonoscopy, and approximately two third of polyps are found in the left colon. Young age, non Caucasian race, and male sex are possible risk factors.

EPCAM STAINING IN THE EVALUATION OF DIARRHEAL DISEASES
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Congenital diarrheal diseases can be difficult to diagnose. Some diseases, such as microvillus inclusion disease and congenital tufting enteropathy (CTE), require biopsy diagnosis. CTE is characterized by intestinal epithelial cell dysplasia leading to severe malabsorption and significant morbidity. The pathology in CTE is not uniform making diagnosis even more difficult. Last year, we identified mutations in the gene for epithelial cell adhesion molecule (EpCAM) in CTE. Immunohistochemical staining for EpCAM was found to be absent in duodenal specimens from patients with CTE as compared with normal tissue. In this study we hypothesize that lack of EpCAM staining in the intestinal epithelium is specific to CTE. After IRB consent, fluorescent immunohistochemistry of available formaldehyde-fixed, paraffin-embedded duodenal biopsy tissue was performed. Tissue from 4 patients with Ulcerative Colitis, 4 patients with Crohn’s disease, 4 patients with Celiac disease, 1 patient with microvillus inclusion disease, 2 patients with non specific duodenitis and 4 normal age matched controls was included. Immunohistochemical staining for EpCAM was performed using mouse monoclonal anti-EpCAM antibody (clone 323/A3; Abcam, Cambridge, MA). Fluorescent secondary antibody (mouse IgG) was applied. Isotype controls were also performed. EpCAM was found to be present in the epithelia of all tissue specimens except for those from patients with CTE and isotype controls. In this study we describe lack of EpCAM staining in
patients with CTE that is not seen in other gastrointestinal diarrheal diseases. Immunohistochemical staining for EpCAM may be a useful tool in the evaluation of congenital and chronic diarrheal diseases and specifically in making the diagnosis of CTE.

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FURTHER EVIDENCE FOR EPCAM AS THE GENE FOR CONGENITAL TUFTING ENTEROPATHY

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Congenital Tufting Enteropathy (CTE) is a rare autosomal recessive diarrheal disorder presenting in the neonatal period. Last year, we identified mutations in the gene for epithelial cell adhesion molecule (EpCAM) in CTE studying only two affected patients from the same family of Mexican-American origin. Earlier this year we indentified the first nonsense mutation in an affected Pakistani patient. In this study we describe two additional families in whom novel mutations of EpCAM are identified. Our observations provide further the evidence for EpCAM as the gene responsible for congenital tufting enteropathy.

After IRB consent, sequencing of EpCAM in patient genomic DNA was undertaken. Patient A is a 4 yo female with CTE who remains TPN dependent. Patient B is a 16 yo male with CTE and hepatitis C currently weaned from TPN therapy. Patient A and B are affected siblings of Kuwaiti origin without known consanguinity. Homozygous insertion of C at c.498 in exon 5 was identified in patients A and B causing a frameshift which results in a premature stop codon. Sequencing of EpCAM in 6 yo female (Patient C) from a consanguineous family of Pakistani origin with known CTE as well as multiple epiphyseal dysplasia and renal calculi was undertaken. DNA from Patient C revealed a homozygous substitution of G>A at c.307. Parents were found to be heterozygous for these variants consistent with autosomal recessive inheritance. These mutations were not identified in 200 control DNAs.

In this study we describe novel EpCAM mutations associated with congenital tufting enteropathy. Identification of additional EpCAM mutations is necessary before genotype-phenotype correlations can be established. EpCAM is best known for its overexpression in multiple carcinomas. While normal EpCAM expression appears to be needed for normal gut development and function, the specific role of EpCAM in the intestine is still unclear and worthy of further exploration.

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ENDOSCOPIC DIAGNOSIS OF GRAFT-VERSUS-HOST DISEASE

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Background: Graft-versus-host disease (GVHD) is a major cause of GI morbidity following bone marrow transplant (BMT). EGD and colonoscopies are frequently done to obtain a tissue diagnosis. There is no consensus as to what portion of the GI tract is most likely to yield the diagnosis of GVHD or whether bx of both the upper and lower GI tracts are necessary in children. The aim was to determine the frequency of histological abnormalities in different parts of the GI tract in children with acute GI GVHD.

Methods: We reviewed the charts of all patients younger than 18 years with suspected acute GVHD who had endoscopic evaluation within the first 100 days after BMT.

Results: 48 patients met the above criteria. The median age was 8 y (range 0.5–18 y), 71% had leukemia. The median time following BMT of endoscopic biopsies was 54 (range 21–98) days. The number of bx sites per patient ranged from 1–8 (median 2). The most common symptoms were diarrhea (70%) and a combination of nausea and vomiting (67%). The most common endoscopic finding was gastric erythema (48%). GVHD was diagnosed in at least one bx site in 40 patients (83%); 22 (55%) of these 40 patients had simultaneous endoscopic bx of the esophagus, stomach, duodenum, and rectosigmoid. The sensitivity for diagnosing GVHD was 77% for both rectosigmoid and upper endoscopic bx. 33/40 patients with GVHD had EGD with biopsies. The sensitivities and negative predictive value of gastric and duodenal bx were 72%, 47%, 42% and 29.6% respectively. 13 cases had positive stomach and negative duodenum whereas in only 3 cases was the reverse true (NS P = 0.06). 6 patients had positive esophageal bx. One patient had a positive esophageal bx while the other biopsies were negative.

Conclusions: Rectosigmoid biopsies are equally sensitive to upper endoscopic bx for diagnosis of acute GI GVHD. Although not statistically significant gastric bx are more likely to diagnose GVHD than duodenal biopsies. EGD and lower endoscopy may both be needed in the BMT patient in whom GVHD is suspected.

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POUCH OUTCOMES IN PEDIATRIC PATIENTS AFTER ILEAL POUCH ANAL ANASTOMOSIS—A HISTORICAL COHORT STUDY

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Background: Ileal pouch anal anostamosis (IPAA) with preserved anal continence is a surgical procedure of choice for patients with refractory ulcerative colitis (UC). Majority of the patients tolerate this procedure very well, however a subset of population develop complications leading to pouch
failure. The aim of the study was to describe the clinical characteristics of pouch in pediatric patients in comparison to adults and to identify possible predisposing factors for pouch failure in pediatric patients.

Methods: All pediatric patients under 21 years at the time of pouch creation for UC were identified from pouchitis database at the Cleveland clinic from 2002 to 2009. Demographic, clinical and endoscopic data were collected. A control group of 789 adult patients with IPAA was used for comparison.

Results: A total of 142 pediatric patients with IPAA were identified, predominantly Caucasian (98.6%) and male (71%). The preoperative diagnosis was UC in 128 patients and indeterminate colitis in 12. The mean age at pouch creation was 16.4 ± 3.8. Compared to adults, the incidence of toxic megacolon was higher (16.9% vs. 9.6%, P = 0.02), dysplasia was less common (14.7% vs. 2.1%, P < 0.0001), duration of IBD from diagnosis to pouch creation was shorter (2 vs. 6 yrs, P < 0.0001) and post-op hospitalization was more common (13.4% vs. 6.2%, P = 0.01) in pediatric patients. Acute and chronic pouchitis rate was identical in both groups. Pouch failure was more common in pediatric patients (11.3 vs. 7.4%, P = 0.11) with Crohn’s disease of the pouch being the most common cause of pouch failure (62%). The duration of pouch creation to failure was shorter (4 vs. 6 yrs) in pediatric patients; however, Cox regression analysis failed to show any significant risk factors for pouch failure.

Conclusions: In comparison to adult patients, children had high incidence of toxic megacolon, short duration of IBD before creation of IPAA and higher rates of postoperative hospitalizations. No predisposing factor for pouch failure in pediatric patients has been identified.

PREDICTING THE NEED FOR HOME PARENTERAL NUTRITION AFTER NEONATAL ENTEROCOLITIS DUE TO NECROTIZING ENTEROCOLITIS
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Background: Necrotizing enterocolitis (NEC) is a common etiology intestinal failure (IF). We hypothesized residual small bowel (length and adjusted percentage) predicts the need for parenteral nutrition (PN) and duration of home PN (HPN) in NEC patients undergoing laparotomy.

Methods: We analyzed data from neonates admitted to the Children’s Hospital of Alabama between 1998 and 2008 undergoing laparotomy with intestinal resection for NEC. Intestinal rehabilitation (IR) was defined as weaning from PN prior to discharge. Univariate and multivariate analyses of variables associated with IR were utilized.

Results: IR was accomplished in 24 patients with 25 IF patients. In univariate analyses, IR prior to discharge was associated with early laparotomy, younger gestational age, and residual bowel (length and %). Increased age adjusted residual bowel % predicted IR prior to discharge in a multivariate model. Using multiple linear regression, shorter duration of HPN was associated with increased residual bowel (length and %), no colectomy, total number of operations, and white race. Total colectomy and male gender predicted more days of HPN.

Conclusions: Increased residual small bowel and colon in patients in patients with surgical NEC is predicts IR. Accurate reporting of post-operative intestinal anatomy may assist in determining IR plans for these patients.

THE USE OF POLYETHYLENE GLYCOL 3350 FOR COLONOSCOPY PREPARATION IN CHILDREN: A LOOK AT THE SAFETY, EFFICACY, AND TOLERANCE
Ritu Walia, Christine Carter-Kent, Marsha Kay, Franziska Mohr, Rita Steffen, Lisa Feinberg, Worley Sarah, Lori Mahajan. Pediatric Gastroenterology, Cleveland Clinic; Cleveland, OH.

Methods: 45 pediatric patients were enrolled in a prospective pilot study. Patients weighing less than 45 kg were given 136 grams of PEG 3350 mixed in 32 ounces of Gatorade; those weighing 45 kg or more were given 255 grams of PEG 3350 in 64 ounces of Gatorade the day prior to colonoscopy. Patients also received clear liquids the day prior to the procedure. Tolerance was evaluated by patient questionnaires and the efficacy was graded by the endoscopist. A basic metabolic panel was performed at the time of the preoperative visit and just prior to colonoscopy to evaluate for electrolyte changes.

Results: The PEG 3350 colon preparation was completed in 44 patients (mean age 14 years; r: 7–20 years); 29 (66%) were females and the mean BMI was 22.6 kg/m². No patients required nasogastric administration of the preparation. One patient was excluded from final analysis due to a breach in protocol. All patients (100%) rated the prep as easy or tolerable to complete. 100% stated if required they would take the same colonoscopy prep. Symptoms reported were nausea (34%), abdominal pain (23%), vomiting (16%), dizziness (7%), and abdominal bloating (23%). No significant changes in the pre and post colonoscopy levels of sodium, potassium, chloride, BUN and creatinine were observed. The prep procedure bicarbonate and glucose levels were higher. These values though statistically significant were not clinically significant. Complete colonoscopy was rated by the staff endoscopist as excellent in 23%, good in 52%, fair in 23 % and poor in 2%.

Conclusions: Electrolyte-free polyethylene glycol 3350 is a safe, effective and tolerable bowel preparation in children prior to colonoscopy.
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JEJUNAL ADAPTATION IN A PREPUBERTAL BOY AFTER TOTAL ILEAL RESECTION AND JEJUNOSTOMY PLACEMENT: A 5-YEAR FOLLOW-UP
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Intestinal adaptation is the process by which the gut augments fluid and nutrient absorption after intestinal resection. It is known that the colon and ileum can undergo adaptation in the absence of jejenum. However, there is little evidence for jejunal adaptation without ileum. Here, we report the case of an 8 year old boy who underwent total ileal resection, right hemicolectomy, and jejunostomy placement after a motor vehicle accident. He initially presented with jejunostomy outputs of about 2 L per day, despite a low carbohydrate diet, proton pump inhibition therapy, an antibiotic trial, and anti-motility agents. No intrinsic intestinal disease was identified. Over a five-year follow-up period, stoma output gradually decreased from an initial level of 1.9 ± 0.1 L/day to 1.3 ± 0.1 L/day 10 months later and then a slow gradual reduction by 40% total. The child eventually underwent at age 13 years jejunocolic anastomosis, and despite the absence of the right colon, after the post-operative period he passed semi-formed stool and had fecal continence with-no diarrhea. Our case illustrates that 1) jejunal output even in a pre-pubertal child is normally as high as in adult age; 2) the jejunum can undergo adaptation in the absence of ileum; and 3) the right colon reabsorbs the majority of small intestinal fluid, but the left colon can compensate as well.

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PEDIATRIC CAPSULE ENDOSCOPY: LESSONS FROM THE LITERATURE
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Background: Capsule endoscopy (CE) represents a relatively non-invasive tool for examination of the small bowel. We compiled the available data on safety and application of capsule endoscopy for diagnosis and clinical management, evaluating the clinical impact and the differences between pediatric and adult patients.

Methods: A search of the Medline and PubMed databases between 2001 and May 2010 was performed for English-language citations on CE in patients (pts) ≤18 yrs of age. Reports ≤5 pts and duplicate studies were removed.

Results: 15 source documents with 723 pts were found. The youngest was 10 months of age (11.5 kg). Suspicion or evaluation of IBD was the most common indication, accounting for 54% of the use of CE (34% suspected CD, 16% known CD, 1% UC, 3% IC). Evaluation of GI bleeding and/or undiagnosed anemia comprised 17% of indications, followed by evaluation of abdominal pain (13%), polyposis (11%) and other (5%). The predominant indication in those <8 yrs of age was GIB. CE demonstrated diagnostic superiority over traditional SB endoscopy and radiography, leading to 413 (58%) positive procedures (vs 59% in adults). Of those reported, 134 (57%) resulted in a new diagnosis and 106 (60%) directed a change in therapy. Gastric (20 pts, 2.8%) and SB (16, 2.2%) retention required intervention in 17 (2.4%), an increase over adult rates, where 1.4% was retained, with 0.6% requiring endoscopy or surgery.

Conclusions: CE is as effective in pediatrics as in adults, though the frequency of indications vary. CE aids in diagnosis and evaluation of extent and severity of disease, assisting the physician in directing patient management for the pediatric patient population. Retention remains relatively infrequent for both groups.

Table.

<table>
<thead>
<tr>
<th>Indications/Population</th>
<th>Adults* (22,840)</th>
<th>Pediatrics (723)</th>
<th>&lt;8 Years** (83)</th>
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<td>GIB</td>
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<td>17%</td>
<td>36%</td>
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PEDIATRIC CAPSULE ENDOSCOPY: A SINGLE-CENTER, 5-YEAR RETROSPECTIVE
Stanley A. Cohen1, Hagit Ephrath2, Ari Bergwerk2, Jeffery D. Lewis1, Dinesh Patel1, Steven Liu1, Akanksha Shah1, Bonney Reed-Knight1, Angela Stallworth1, Tamara Wakhisi1. 1Children’s Center for Digestive Health Care, Children’s Healthcare of Atlanta, Atlanta, GA; 2Given Imaging, Yoqneam, Israel.

Background: Capsule endoscopy (CE) allows a patient-friendly examination of the small intestine. Many large studies have demonstrated the utility and safety of this diagnostic tool in adults but few such series are reported in children. We report a single pediatric center’s experience with the use and safety of CE.

Methods: Retrospective review of consecutive CE studies between July 2004 and June 2009.

Results: 285 CE studies were performed in 282 patients with a mean age of 15 (± 3.7) years, range 3.4–23 years. In 31 patients <10 years of age, 20 were placed. Overall, 244 (82%) were for suspected (184, 61%) or confirmed (60, 21%) Crohn’s disease (CD); 26 (9%) for anemia or GI bleeding; 6 (2%) for polyposis; 6 (2%) for celiac. Of those assessing CD, 67 (29%) had small bowel lesions found on CE that confirmed or led to the diagnosis of CD in the small intestine. In
138 of the entire population, no significant small bowel disease was identified but CE showed gastric lesions in 53 studies and severe colitis in two. In order to assess functional patency of the intestine prior to administration of the video capsule, a patency capsule (PC) was used prior to CE in 21 patients. In 4, the PC did not confirm patency and the video capsule was not administered. 5 CE studies (1.8%) resulted in retention of the video capsule including 1 with PC patency (4 required surgery; 1 had endoscopic removal of the retained capsule through an ileostomy). 65 (21%) were described as incomplete because the capsule did not enter the colon before the video’s end. Of the incomplete examinations, 36 (65%) had significant findings including 27 (49%) in which CD of the small intestine was diagnosed.

**Conclusions:** CE is a useful and relatively safe procedure to diagnose small bowel disease in children. Even in a study population of children with a high prevalence of confirmed and suspected CD, the risk of retention remains small. CE may identify gastric disease even when small bowel lesions are not present.

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**ROTAVIRUS-ASSOCIATED SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN AN INFANT**

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Rotavirus is a leading cause of morbidity and mortality in infants and children worldwide. Systemic Inflammatory Response Syndrome (SIRS) attributed to rotavirus is very unusual. We report a case of a 10 month old infant who, following two days of vomiting and diarrhea, presented to a hospital emergency with hypotensive seizures. Soon she developed hyperalbuminemia with generalized edema, ascitis and pleural effusion leading to respiratory distress warranting pleural and peritoneal fluid drainage. Absence of protein in the urine sample and preserved hepatic synthetic functions supported the diagnosis of PLE. The patient stabilized after receiving albumin infusions with a loop diuretic and Total Parenteral Nutrition (TPN) support until day 3, when dropping serum hemoglobin, falling platelet count with a high serum D-DIMER heralded a DIC (Disseminated Intravascular Coagulation)-like picture. She required packed RBC, Fresh Frozen Plasma (FFP) and platelet transfusions. Stool samples sent at admission were reported positive for rotavirus antigen but the bacterial cultures were all negative. The elevated C-reactive protein (CRP) as well as the picture of DIC found in our patient is not usual in viral infections so superimposed, concurrent or secondary bacterial or candidal infections were suspected but the blood, urine and stool cultures were negative. Broad spectrum antimicrobial coverage was still provided against possible secondary bacteremia. The recovery started eleven days post admission. We conclude that this was likely a severe rotavirus infection with SIRS, complicated by hypotensive seizures, ascitis and pleural effusion. Secondary bacteremia or candidemia and sepsis, although still possible, were not found in our patient.

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**IMPORTANCE OF PAN-BIOPSY OF THE UPPER GASTROINTESTINAL TRACT IN CELIAC DISEASE**

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**Background:** Celiac disease (CD) is an autoimmune mediated process triggered by gluten exposure in a genetically susceptible host leading to defined pathology in the GI tract. While at times CD gives rise to only patchy pathologic changes, small bowel biopsy is still considered the gold standard for diagnosis. There have been recent reports questioning the importance of distal duodenal (DD) biopsy over duodenal bulb (DB) biopsy. In addition, there have been isolated reports of CD-associated abnormalities in the esophageal or gastric mucosa. The aim was to determine the importance of obtaining biopsies from multiple sites in the GI tract at the time of original diagnosis of CD.

**Methods:** A retrospective review was performed of all newly diagnosed children with CD who had at least 4 biopsies from the DB and DD as well as esophageal and gastric biopsies performed by a single endoscopist from 4/06 to 4/10. The diagnosis of CD was made by standard combination of histology and serology.

**Results:** There were a total of 93 patients (33M, 60F), mean age 10.2 years (range 1.7–17.9). 9.7% of patients had findings consistent with CD in only one location with 7 (7.5%) having abnormalities in the DB only and 2 (2.1%) in the DD only. 84 (90.3%) had pathologic findings present in both locations. Of those, 20 (23.8%) had differing histopathologic findings between the DB and DD with 17 having more severe findings in the DB and DD with more severe findings in the DD. Reflux esophagitis was documented in 8.6% and eosinophilic esophagitis in 2.1%. Neither group had esophageal symptoms. Lymphocytic gastritis was found in 8.6% and *Helicobacter pylori* antritis in 2.1%.

**Conclusions:** CD tends to be present and most severe in the DB but DD biopsies still add to the diagnostic accuracy. 21.5% of our patients with CD had clinically unsuspected pathologic findings in the antrum and esophagus. Appropriate endoscopic mucosal biopsy for the investigation of CD should include a sufficient number of biopsy specimens from both the DB and DD as well as the antrum and esophagus.
ONE-DAY BOWEL PREPARATION WITH POLYETHYLENE GLYCOL 3350 (MIRALAX®) IS AS EFFECTIVE AND SAFE AS THREE-DAY PREPARATION FOR COLONOSCOPY IN CHILDREN

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Background: Polyethylene Glycol 3350 (Miralax®) without electrolyte is commonly used for 3–4 days for bowel preparation for colonoscopy in children. One-day preparation has been anecdotally reported to be effective for this purpose but there have not been any published prospective studies comparing the safety and efficacy of one-day preparation with that of three-day preparation with PEG 3350.

Objective: To compare the efficacy and safety of one-day bowel preparation with Polyethylene Glycol 3350 with that of three-day preparation for colonoscopy in children.

Methods: We conducted a prospective, randomized controlled trial with children aged 2–21 yrs, undergoing elective colonoscopy. Patients were randomly assigned to receive Miralax® as bowel preparation for either one or three days prior to colonoscopy. Children with known electrolyte disturbances, dehydration, fecal impaction, metabolic or renal disease were excluded. Electrolytes, BUN, creatinine and serum osmolality were measured before and after bowel preparation. Effectiveness of the bowel preparation was assessed using a stool diary and the gastroenterologist’s grading of degree of bowel cleansing during colonoscopy.

Results: 32 subjects were enrolled, 18 in the one-day and 14 in the three-day preparation group. There were no differences between the groups in efficacy of bowel preparation based on colonoscopic grading (Fisher exact test, \( P = 0.437 \)) or in the safety of the preparation (\( P = 0.266 \)). The one-day preparation was not tolerated less well than the three-day preparation (\( P = 0.492 \)).

Conclusions: Polyethylene Glycol 3350 (Miralax®) used for just a single day in children to prepare the bowel for elective colonoscopy is safe, effective and well tolerated.

THE FECES AND INTESTINAL MICROFLORA PATTERNS OF TOLL-LIKE RECEPTOR 4–DEFICIENT MICE

Yen-Hsuan Ni1, Chia-Hui Yu2, Shu-Chen Wei3. 1Pediatrics, National Taiwan University Children’s Hospital, Taipei, Taiwan; 2Physiology, College of Medicine, National Taiwan University, Taipei, Taiwan; 3Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan.

Background: The intestine flora plays roles in initiating and perpetuating the process in inflammatory bowel disease (IBD) patients. Toll-like receptor4 (TLR4) is a receptor for lipopolysaccharide (LPS). This study aimed to investigate the bacteria patterns of the TLR4 deficient (TLR4-d) mice models. By comparing the microflora patterns of the control and TLR4-d mice, we may explore the role of microflora in intestinal inflammation.

Methods: 0.1–0.2 g of the mice fecal and/or colon mucosal scraping samples were collected snap frozen at −80°C until analysis. After extracting DNA from the feces and colon mucosal scrapings, the V2-V3 region of the 16S rRNA gene was amplified by eubacterium-specific universal primers. The forward primer of each set is extended with a 40-bp GC clamp at the 5' end to allow the separation of all amplicons with denaturing gradient gel electrophoresis (DGGE). Distinct amplicons from DGGE gels were excised from the gels and purified. After purification, cloning and sequencing were carried out. The histologic examination of the intestines was performed in all mice.

Results: A more versatile microflora pattern of TLR4-d mice was observed than that of control mice in feces, but not in mucosal scrapings. Lachnspiraceae sp. were seen in the mucosa scraping of TLR4-d mice but not in control. Bifidobacteria sp. were seen in the feces of TLR4-d mice but not in control. Though found in both feces, \( E. coli \) in TLR4-d mice outnumbered that in control mice. \( Clostridium saccharolyticum \) and \( Clostridium jejeunese \) are the same amount in the feces of both TLR4-d and control mice. The intestine of LPS-stimulated TLR4-d mice owned increased inflammatory cells while the control did not.

Conclusions: TLR4-d mice owned a diverse microflora pattern. The number of Lachnspiraceae sp., Bifidobacteria sp. and \( E. coli \) are distinguishable in TLR4-d mice. These may imply the significance of these specific microbes in the initiation of IBD.

A GLUTEN-FREE DIET DECREASES BMI Z-SCORES IN OVERWEIGHT AND OBSE CHILDREN WITH CELIAC DISEASE

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Background: Decreased BMI in obese adults with celiac disease (CD) adherent to a gluten-free diet (GFD) has recently been described. We reviewed growth data of overweight and obese (O/O) children with CD to observe their response to a GFD.

Methods: We identified patients meeting the CDC criteria for O/O (BMI for age >85th-95th%ile or >95th%ile, respectively) from a database of 318 children with biopsy-proven CD diagnosed from 2000–2008, and compared their growth indices pre- and post-treatment with a GFD.

Results: A total of 32 patients (10%) were overweight or obese (19 and 13 patients, respectively). Most O/O patients
presented with mild villous atrophy (VA) (Marsh II-IIIa) while severe VA (Marsh IIIb-IIIc) predominated in the general cohort (Table 1). O/O patients presented most frequently with abdominal pain (25%) and detection by serological (autoimmune and familial) screening (38%). Mean length of follow up (n = 20) was 34.8 months (SD 18). Following a GFD, 75% of O/O patients had decreased BMI z-scores, with increased mean height but no change in mean weight z-score (Table 2). Pre-treatment VA did not significantly affect changes in BMI, height or weight z-scores. Mean age at diagnosis did not significantly differ among those with increased or decreased BMI.

**Conclusions:** Children with CD are not infrequently overweight. Adherence to a GFD may reduce BMI in these patients by improving longitudinal growth.

**Table 1.** Characteristics of Overweight/Obese Patients vs Cohort

<table>
<thead>
<tr>
<th>Variable</th>
<th>O/O</th>
<th>Cohort</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation, mean (SD)</td>
<td>8.4 (5)</td>
<td>8.3 (5)</td>
<td>0.9</td>
</tr>
<tr>
<td>Male Gender (%)</td>
<td>56</td>
<td>43</td>
<td>0.2</td>
</tr>
<tr>
<td>Severe Villous Atrophy (%)</td>
<td>36</td>
<td>62</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Table 2.** Growth Indices Pre- and Post-GFD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-GFD</th>
<th>Post-GFD</th>
<th>Az</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height z score, mean (SD)</td>
<td>-0.5 (1.8)</td>
<td>0.1 (1.0)</td>
<td>0.6 (1.1)</td>
<td>0.2</td>
</tr>
<tr>
<td>Weight z score, mean (SD)</td>
<td>1.0 (1.0)</td>
<td>1.0 (0.9)</td>
<td>0.0 (0.7)</td>
<td>1.0</td>
</tr>
<tr>
<td>BMI z score, mean (SD)</td>
<td>1.7 (0.6)</td>
<td>1.2 (0.7)</td>
<td>-0.5 (0.9)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Methods:** Diagnosis of EoE was based on presence of >20 eosinophils/high power field (eos/hpf) following 8 weeks of PPI therapy. Only children with EoE who had cow’s milk eliminated from their diet were included in this analysis. Complete histological remission, for the purpose of this study, was defined as peak eosinophil ≤0–1/hpf in esophageal biopsies obtained 4–6 weeks after elimination of cow’s milk from the diet.

**Results:** Nine (7M/2F) children who were treated with a single food elimination diet were identified. Mean age was 3.9 (range 1–9) years. The pretreatment peak esophageal eosinophilic count was 63.4 (35–150) per hpf. All 9 children experienced clinical improvement. Seven of nine (78%) treated with cow’s milk protein elimination had complete histologic remission. Histology improved with decrease in eosinophil count to 12 eos/hpf in one patient and the histology in the one was unchanged from the pre-treatment levels. The posttreatment peak eosinophil count for the entire group was 8 (range 0–60).

**Conclusions:** Empiric single food elimination of cow’s milk protein successfully induced clinical and histological remission in a small cohort of children with EoE. It should be considered as one of the options when elimination diet is being considered for treatment EoE. Larger prospective studies are needed to validate this finding and determine the percentage of children who may benefit from this approach.

**37**

**PEDIATRIC EOSINOPHILIC ESOPHAGITIS: THE NORTHERN VIRGINIA EXPERIENCE**

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Despite increasing prevalence of eosinophilic esophagitis (EoE) among children in the United States (US), there is limited data on its epidemiology, clinical course and management. We reviewed charts of 70 children with ≥15 eosinophils per high power field in the mid and distal esophagus, and diagnosed with EoE. Forty-nine (70%) patients were male, aged 7.0 ± 3.6 years (mean ± SD) (range 1–16 years). Children < 5 years [n = 24 (34%)] commonly presented with poor weight gain and vomiting, children aged 5–10 [n = 18, (26%)] presented with dysphagia and abdominal pain, and children aged >10 [n = 15 (21%)] mostly presented with dysphagia and food impaction. Forty-one (58%) patients had co-existing allergic conditions [food allergies (58%), environmental allergies (48%) and asthma (25%)]. Four patients (6%) had celiac disease. A prick test and/or patch test were positive in 62 (89%) patients. Endoscopic visualization commonly revealed edema with white spots, linear furrowing or trachealization of the esophagus. Only 16 (23%) patients had an normal appearing esophagus.
despite severe eosinophilia, and 13 (83%) of these patients were aged <10. Twenty-nine (42%) patients were prospectively followed with esophageal biopsies to evaluate for histological resolution of eosinophilia after initiating them on dietary allergen elimination, anti-acid therapy, fluticasone swallow or a combined approach. The dietary allergen elimination therapy (n = 13) was associated with histologic resolution in 60% of patients. One patient had fibrosis and narrowing of the esophagus, and had to undergo endoscopic dilation. The changes in clinical symptoms correlated poorly with the resolution of eosinophilia in the esophagus. Our data emphasizes the association between pediatric EoE and allergic conditions, and the heterogeneity with respect to its clinical presentation, endoscopic findings especially in young children and their responses to current therapeutic options. This study will contribute to better understanding of EoE among children in the US.

**38 REDUCED LUMBAR SPINE BONE MINERAL DENSITY IN PEDIATRIC EOSINOPHILIC ESOPHAGITIS**

James Squires1, James E. Heubi1, Charles W. DeBrosse2, J.P. Abonia2, Tommy Grojanc2, Marc E. Rothenberg3, James P. Franciosi3. 1Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 2Division of Allergy and Immunology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 3Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

**Background:** Eosinophilic esophagitis (EoE) has the potential to compromise bone mineral density in growing children. The aim of this study was to describe a cohort of children with EoE with respect to their growth and lumbar spine bone mineral density (BMD).

**Methods:** Retrospective cohort of Caucasian, male children with EoE who had undergone a dual energy x-ray absorptiometry (DXA). This cohort was compared to age, race and sex matched reference data.

**Results:** A convenience cohort of 25 pediatric EoE subjects had an average of 23.7 months between a diagnosis of EoE and DXA measurement (SD 26.3; range 0–101 months), a mean age of 7.7 years (SD 3.3; range 3 to 15 years of age), a mean height z-score of −0.29 (SD 1.18), a mean weight z-score of −0.18 (SD 1.14) and a mean BMI z-score of −0.08 (SD 1.16). The mean lumbar spine BMD z-score was −0.84 (SD 0.89; range −2.1 to 1.4) and was significantly reduced compared to a reference cohort of 1,554 children (P < 0.0001). There was a trend towards BMD DXA z-score correlation with disease duration (r = 0.37; P = 0.065). There were also differences in mean DXA z-scores between EoE subjects with and without the combination of current PPI therapy and dietary restriction (−1.11 vs −0.48; P = 0.057).

**Conclusions:** Lumbar spine BMD DXA z-scores are significantly reduced in this cohort of pediatric EoE subjects. Further research is needed to determine the effect of EoE on BMD with regard to treatment and underlying disease factors.

**39 CONTENT VALIDATION OF THE PEDIATRIC EOSINOPHILIC ESOPHAGITIS HEALTH RELATED QUALITY OF LIFE INSTRUMENT (PEEHRQOL VERSION 1.0): A PATIENT AND PARENT PROXY REPORTED OUTCOME MEASURE**


1Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 2Division of Allergy and Immunology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 3Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 4Department of Pediatrics, Texas A&M University, College Station, TX.

**Background:** Currently there is no disease-specific outcome measure to assess pediatric eosinophilic esophagitis (EoE) Health Related Quality of life (HRQOL). The primary objective of this study was to identify and develop key patient-reported outcome (PRO) elements of EoE disease-specific HRQOL as an EoE-specific module for the validated Pediatric Quality of Life Inventory™ (PedsQLTM).

**Methods:** Content validation for pediatric EoE was developed according to the well-established methodology utilized for the generic PedsQLTM as well as previously established disease-specific modules. Child self-reports were obtained for patients in the 5–7, 8–12 and 13–18 year old age groups and parent proxy-reports were obtained in each age range (ages 2–4, 5–7, 8–12, 13–18). Individual qualitative focus interviews and cognitive interviews of pediatric patients with EoE and their parents as a proxy were conducted in each of these subsamples.

**Results:** A total of 84 subjects met our study criteria to identify and develop questions and domains of interest from patient and parent proxy interviews. Specific themes that emerged from these interviews included, but are not limited to, feelings of being different than their family and peers, diet and medication adherence, difficulties with eating food, worry about their symptoms and illness, and discussing EoE with others.

**Conclusions:** The Pediatric Eosinophilic Esophagitis Health Related Quality of Life (PEEHRQOL version 1.0) module has been developed as a parent proxy-report and patient self-reported outcome measure with face and content validation.

**40 CONTENT VALIDATION OF THE PEDIATRIC EOSINOPHILIC ESOPHAGITIS SYMPTOM SEVERITY SCORE (PEESS VERSION 2.0): A PATIENT AND PARENT PROXY REPORTED OUTCOME MEASURE**

James P. Franciosi1, Kevin A. Hommel1, Charles W. DeBrosse2, Allison B. Greenberg2, Alexandria Greenler2,
Background: Previous non-validated attempts to measure symptoms in pediatric Eosinophilic Esophagitis (EoE) have not focused on what patients and their families define as important. The primary objective of this study was to identify and validate key patient-reported outcome (PRO) elements of EoE disease symptoms.

Methods: Content validation for PRO in EoE was developed using the FDA guidelines on PRO development as well as the validated generic Pediatric Quality of Life Inventory 4.0TM (PedsQL) guidelines. Qualitative focus interviews of pediatric patients with EoE and their families were conducted followed by qualitative cognitive interviews in a separate cohort.

Results: We describe items and domains of a new instrument that were identified and developed from patient and parent interviews. From patient and parent responses, a combination of Likert rating and visual analog scale item response choices were developed. Child self-reports were obtained for patients 8–18 years of age, and parent proxy-reports for parent of children 2–18 years of age.

Conclusions: The Pediatric Eosinophilic Esophagitis Symptom Severity of EoE (PEESS v2.0) has been developed as a parent proxy-report and patient self-reported outcome measure with face and content validation. In the next phase, the PEESS v2.0 will undergo construct validation, internal consistency testing as a measurement of instrument reliability, and responsiveness testing.

A NATIONAL REGISTRY FOR EOSINOPHILIC GASTROINTESTINAL DISORDERS: AN INTERNET-BASED PLATFORM THAT COMBINES THE ELECTRONIC MEDICAL RECORD AND PATIENT REPORTED OUTCOMES

James P. Franciosi1, J.P. Abonia2, Keith Marsolo3, Michael D. Eby2, Sean Jameson2, Shalana Hottenger2, Bridget Buckmeier Butz2, Ron Bryson2, Margaret H. Collins2, Marc E. Rothenberg2, J.P. Abonia2, Marc E. Rothenberg2, James W. Varni4, J.P. Abonia2, Marc E. Rothenberg2, James W. Varni4

1Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 2Division of Allergy and Immunology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 3Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 4Department of Pediatrics, Texas A&M University, College Station, TX.

Background: Current treatments of eosinophilic esophagitis (EE) including restrictive diets or glucocorticoids provide only transient improvement in symptoms and/or histology. Use of proton-pump inhibitors (PPI) in children with EE does not lead to short-term histologic improvement; however, the long-term use of PPI on symptoms and prevention of complications has not been evaluated.

Methods: A retrospective chart review of patients diagnosed with EE from 1/95–12/09 was performed. The diagnosis was made based on symptoms, initial endoscopic biopsies with >15 eosinophils per high-power-field and persistent eosinophilic inflammation despite PPI therapy. Follow-up was calculated based on time to most recent endoscopic biopsies. Inclusion criteria included diagnosis of EE and long-term PPI use as treatment.

Results: Forty patients (30 male, 10 females, mean age 6.9 ± 5.8 years) fulfilled inclusion criteria. The average time of follow-up was 3.7 ± 4.1 years. Treatment included PPI in all patients along with restrictive diet following allergy testing (9) and swallowed fluticasone (4). At follow-up, 31 patients were asymptomatic and the remaining 9 patients’
symptoms were significantly improved. There were no complications of stricture or food impaction although significant eosinophilic inflammation on esophageal biopsies persisted in 26 patients. Absolute blood eosinophil count significantly decreased from 0.68 ± 0.44 K/μL at presentation to 0.47 ± 0.28 K/μL at follow-up; P < 0.05. The BMI of the treated EE patients significantly improved from 48.9 ± 31.5% at presentation to 56.0 ± 31.3% at follow-up; P < 0.01.

**Conclusions:** Patients with EE treated with long-term PPI show an improvement in symptoms along with a decrease in eosinophil count and improvement in BMI over time. Longer follow-up is important to determine whether persistent EE in PPI-treated patients is associated with any long-term complications. PPI treatment may be useful maintenance therapy in children with EE.

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**CORRELATION OF ENDOSCOPIC FINDINGS AND TISSUE EOSINOPHIL COUNTS IN EOSINOPHILIC ESOPHAGITIS (EOE)**


**Background:** Linear furrows, white plaques, and esophageal rings are endoscopic features associated with EoE. To date, no studies have looked at the correlation of these findings with eosinophil counts.

**Methods:** We performed a retrospective chart review of upper endoscopies (EGD) performed on patients diagnosed with EoE. The gross visual appearance of the esophagus and histological findings with eosinophil counts in both the mid (ME) and distal (DE) esophagus were noted. We assessed whether there was a correlation between the eosinophil counts and the endoscopic findings using the Student’s t test (two-tailed) with significance assigned at P < 0.05.

**Results:** We reviewed 71 records with a total of 210 EGDs. 81% of the patients were male and the average age was 80.5 ± 81 months. 30% of the procedures were for the initial diagnosis while 87% were repeat EGDs. In patients with a normal appearing esophagus, the mean eosinophil count was 10 ± 5 in the DE and 8 ± 3 in the ME. An abnormal visual finding correlated with an eosinophil count of 55 ± 9 (P < 0.01) in the DE and 45 ± 10 (P < 0.01) in the ME. Furrowing alone correlated with an eosinophil count of 36 ± 12 (P < 0.01) in the DE and 31 ± 12 (P < 0.01) in the ME. Furrowing with edema correlated with an eosinophil count of 69 ± 34 (P < 0.01) in the DE and 57 ± 54 (P = 0.11) in the ME. Furrowing with white plaques correlated with an eosinophil count of 77 ± 19 (P < 0.01) in the DE and 73 ± 21 (P < 0.01) in the ME. White plaques alone correlated with an eosinophil count of 56 ± 15 (P < 0.01) in the DE and 51 ± 11 (P < 0.01) in the ME. Edema alone correlated with an eosinophil count of 28 ± 18 (P = 0.09) in the DE and 33 ± 25 (P = 0.08) in the ME.

**Conclusions:** Abnormal visual findings in patients with EoE are associated with a statistically significant increased tissue eosinophil count in the ME and DE. The highest correlation was found with furrowing with white plaques. These findings suggest that visualization is a reliable surrogate for tissue histology.

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**COEXISTENCE OF EOSINOPHILIC ESOPHAGITIS WITH GASTROESOPHAGEAL REFLUX**

Judith Cohen Sabban1, Gabriela Donato1, Silvia Christiansen1, Maria Davila2, Carlos Lifschitz2, Marina Orsi1. 1Hospital Italiano, Buenos Aires, Argentina; 2Garrahan Hospital, Buenos Aires, Argentina.

**Background:** Eosinophilic Esophagitis (EE) is considered in patients with gastroesophageal reflux (GER) symptoms non responsive to proton pump inhibitors (PPI). However, these 2 clinical conditions can coexist. 24 hr. multichannel intraluminal impedance and pHmetry (MII-pH) are able to detect all types of reflux and symptom correlation, helpful in determining a possible association between EE and GER. The aims were to determine the presence of pathological GER in patients with EE and evaluate the behavior of GER with MII-pH before and after treating both entities.

**Methods:** Patients with symptoms of GER received omeprazole 1 mg/kg/d (O) for 1 mo. Those without improvement underwent upper endoscopy (UE) and MII-pH. Patients whose esophageal biopsies confirmed the diagnosis of EE received topical budesonide 2 mg/day bid for 3 mo. Patients with abnormal MII-pH also received a 3 mo. of O. A second UE and MII-pH was performed off medication.

**Results:** EE was diagnosed in 7 patients, mean age: 12.8 yr; 4/7 also had GER by pHmetry (J. De Meester score >22), of whom 3 had pathological MII as well (SIs >50% with regurgitation, epigastric pain, SAP >95%). EE resolved in all patients after budesonide, but only 3 resolved symptoms of GER.

No statistical significant differences were observed in the number of acid and non acid episodes before and after therapy. Table shows MII-pH results before and after treatment.

**Conclusions:** MII-pH enabled the diagnosis of coexistence of GER in children with EE. Persistence of symptoms in patients treated for EE may be the result of coexistent GER and not necessarily unresolved or relapsing EE.

**Table.**

<table>
<thead>
<tr>
<th></th>
<th>MII-pH before Treatment</th>
<th>MII-pH after Treatment</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>SD</td>
</tr>
<tr>
<td>pHmetry Score</td>
<td>19</td>
<td>10.6</td>
</tr>
<tr>
<td>N</td>
<td>32</td>
<td>18.9</td>
</tr>
<tr>
<td>MII Acid</td>
<td>24.4</td>
<td>8.5</td>
</tr>
<tr>
<td>Nonacid</td>
<td>6.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Clearance</td>
<td>21</td>
<td>7.39</td>
</tr>
</tbody>
</table>

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IS THYMIC STROMAL LYMPHOPOIETIN (TSLP) A KEY PLAYER IN EOSINOPHILIC ESOPHAGITIS (EE)? A PILOT STUDY
Kiranmai Gorla, Judy B. Splawski. Pediatric Gastroenterology, Rainbow Babies and Children's Hospital, Cleveland, OH.

Background: EE is an inflammatory disease of the esophagus involving Th2 type inflammation. This is similar to atopic dermatitis and asthma. Esophageal epithelium is a stratified squamous epithelium like that of skin and airways. TSLP is a chemokine produced by airway and skin epithelial cells and stimulates dendritic cells to promote differentiation of naïve T cells into Th2 cells and this is shown to be an important factor in atopic diseases. TSLP production by esophageal epithelial cells contributes to Th2 mediated inflammation seen in EE. Limitation of TSLP to the squamous epithelium might explain limitation of EE to the esophagus.

Methods: Patients (0–18 yrs) who are scheduled to undergo EGD were screened for EE criteria. Esophageal, gastric and duodenal samples from patients with normal EGD and from those with gross picture of EE were collected and assigned to Control or Test groups after confirming the pathology. Staining with TSLP antibody was done with TSLP: Rabbit polyclonal antibody/Sigma-Aldrich/Cat #: PRS4203/Lot. no. 40230604. IHC analysis:TSLP staining was scored depending on the location of staining (st. germinativum/spinosum/corneum); cytoplasmic vs. nuclear; and intensity of staining. We are currently staining the gastric and duodenal samples to see if TSLP is limited to the esophageal epithelium or more pervasive. H and E staining was also done on the same biopsy sections to confirm the histology.

Results: A total of 30 patients were consented. Only 27 subject samples were collected: 10 controls and 11 EE sample sets were secured, 6 sets were discarded. TSLP was present in normal samples in the esophagus in the basal layers. In EE, TSLP staining was more prominent through the basal epithelial cells and is increased in the esophageal epithelium of EE patients. We speculate that TSLP has a role in the Th2 type inflammation seen in EE. This suggests that the epithelium plays a major role in Th2 type inflammation seen in EE.

Conclusions: TSLP is expressed in the normal esophageal basal epithelial cells and is increased in the esophageal epithelium of EE patients. We speculate that TSLP has a role in the Th2 type inflammation seen in EE. This suggests that the epithelium plays a major role in Th2 type inflammation seen in EE.

SUBEPITHELIAL FIBROSIS CORRELATES WITH BASAL CELL HYPERPLASIA IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS
Jaime Grubert1,2, Kelly Maples3, Sarah Poff3, Amy Fantaskey1, Scott Stanley1, Maria Aguiar1,5, Erin McGuire1,5, Lauren K. Willis1,3,1. Pediatric Gastroenterology, Eastern Virginia Medical School, Norfolk, VA; 2Pediatric Allergy, EVMS, Norfolk, VA; 3Pathology, EVMS, Norfolk, VA; 4Statistics, EVMS, Norfolk, VA; 5Department of Pediatrics, EVMS, Norfolk, VA.

Background: In addition to intraepithelial eosinophilia, basal cell hyperplasia (BC) is a consistent feature of eosinophilic esophagitis (EoE) and many specimens reveal subepithelial fibrosis, even in young children. It is thought that the presence of fibrosis leads to dysphagia with progression to esophageal strictures. Data is necessary to establish whether the accepted treatments reverse the fibrosis in EoE.

Methods: A review of subjects diagnosed with EoE (using ≥20 eos/hpf) at a single tertiary pediatric facility at an academic medical center from 2000–2006 was performed to retrospectively assess presence of esophageal subepithelial fibrosis before and after initiation of treatment and to analyze relationships between eosinophil count, subepithelial fibrosis, and BC. H&E and trichrome stained proximal and distal esophageal biopsies at diagnosis (Pre) and post-treatment 1 (Post 1) and post-treatment 2 (Post 2) were then evaluated by pathologists for eos/hpf, BC, and subepithelial fibrosis (Chehade 2007). 31 subjects with pre-treatment and post treatment esophageal biopsies were included. Spearman rank correlations for eos/hpf with BC and fibrosis were calculated.

Results: For each subject, there was a positive correlation between fibrosis score and BC within each time point: Pre (n = 31) R = 0.603, P < 0.001; Post 1 (n = 26) R = 0.667, P < 0.001; Post 2 (n = 25) R = 0.773, P < 0.001. Post 1 samples demonstrated significant positive correlations between eos/hpf and FS and BC in both proximal and distal samples.

Conclusions: Basal cell hyperplasia and subepithelial fibrosis were present together and correlated positively within each time point suggesting that they are reliable predictors of one another. BC may be a useful surrogate marker for fibrosis, particularly in patients in whom biopsies are not adequate to assess subepithelial fibrosis.

CLASSIFICATION OF EOSINOPHILIC ESOPHAGITIS (EOE): CRUCIAL STEP TO UNDERSTAND THE CLINICAL COURSE OF EOE
T.S. Gunasekaran1,2, M. Dahlberg3, K. Luther General Children’s Hospital, Park Ridge, IL; 2Loyola University Medical Center, Maywood, IL; 3Center for Children’s Digestive Health, Park Ridge, IL.

Background: Eosinophilic Esophagitis (EoE) is increasing in incidence and prevalence. Diagnostic criteria based on eosinophil (eos) count is exact, but leaves physicians with challenges correlating symptoms with biopsy findings, and current treatment options result in varied outcomes. Our aim is to determine if subtypes of EoE can be classified based on symptoms and if those subtypes lead to different outcomes.

Methods: Chart review was done on EoE patients diagnosed by standard criteria. We classified Type 1 as presenting...
primarily with dysphagia, Type 2 as generalized upper gastroenterological (GI) symptoms such as heartburn, abdominal pain, or nausea, and Type 3 as other symptoms such as short stature, failure to thrive, or anorexia. Symptoms were scored on a scale of 0–14 based on number and severity. Patients were treated with many options including fluticasone, diet change, or proton pump inhibitor. Patients were considered improved if they had a reduced symptom score or reduced eos.

Results: 80 patients included, follow-up 1.3 years (±1.2), 84% male. 35% were classified as Type 1, 46% Type 2, 19% Type 3. Table shows differences in symptoms. Type 2 had the highest initial symptom score. Type 2 had higher follow-up symptom scores than the other subtypes. Type 3 had the greatest change in symptom score at follow-up. A similar percent of patients’ symptoms improved in each subtype. The number of eos at initial biopsy and follow-up did not differ among subtypes, nor did the percent of improved patients.

Conclusions: Initial symptom scores differed among groups. Type 2 continued to have the highest symptom score at follow-up. Patients with Type 2 symptoms may benefit from more aggressive therapy. Subtyping EoE patients may be beneficial to predict outcomes, but more studies are needed to support this hypothesis.

Table. Differences in Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Initial Symptom Score</th>
<th>Follow-up Symptom Score</th>
<th>Average Change in Symptom Score</th>
<th>% of Improved Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>2.0 (±0.6)</td>
<td>0.5 (±0.7)</td>
<td>1.3 (±1.1)</td>
<td>80%</td>
</tr>
<tr>
<td>Type 2</td>
<td>2.7 (±1.3)</td>
<td>1.4 (±1.1)</td>
<td>1.3 (±1.5)</td>
<td>71%</td>
</tr>
<tr>
<td>Type 3</td>
<td>3.7 (±1.4)</td>
<td>0.6 (±0.5)</td>
<td>3.0 (±1.6)</td>
<td>100%</td>
</tr>
<tr>
<td>P Value</td>
<td>&lt;0.0001</td>
<td>0.0004</td>
<td>0.0005</td>
<td>0.15</td>
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Results: Demographics showed: age 3–67 years, mean 14.81 ± 14.48; 67.74% male; mean 38 ± 17 e/hpf; common presentation abdominal pain 25.8%; 74% previously PPI-treated; 41.94% with family GI disorders, mostly reflux 25.8%; 41.94% had pets. Positive allergy testing to foods was present in 32.14%; 64.12% to environmental allergens, negative tests in 9.6%. 48% had reflux, but no significant correlation between e/hpf and reflux index (r = −0.16, P = 0.42) or DeMeester score (r = −0.15, P = 0.45). All patients who accepted treatment (96.77%) were given topical fluticasone or budesonide; 33.33% were also prescribed an elimination diet. Patients with abnormal pH-impedance also were treated with PPI. Repeat endoscopy (EGD) was performed in 76.6% of treated patients after at least 3 months. In compliant patients (87%), there was only 1 non-responder (26 e/hpf increased to 36 e/hpf) and 1 partial responder (60 e/hpf decreased to 22 e/hpf), all others (90%) had less than 10 e/hpf (range 0–9). In the 13% who admitted medication noncompliance, all had active EE (30–70 e/hpf) on repeat EGD. No side effects were reported.

Conclusions: Adult and pediatric EE patients may be managed successfully in the private practice setting with topical steroids and diet, along with PPI if reflux is present; non-compliance is the most common cause of failure.

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PRESENTATION, MANAGEMENT, AND OUTCOME OF ADULT AND PEDIATRIC EOSINOPHILIC ESOPHAGITIS PATIENTS IN THE PRIVATE PRACTICE SETTING

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Background: Eosinophilic esophagitis (EE), characterized by ≥20 eosinophils (e) per high power field (hpf) and unresponsiveness to proton pump inhibitors (PPI), is treated with diet and topical steroids. Natural history is unknown; most research is from tertiary centers. The aim of this study was to characterize the presentation, management, and outcome of pediatric and adult EE patients in private practice.

Methods: Outpatient chart review using code for EE identified 41 patients (2006–10), 31 who completed allergy and GI evaluations were included. SAS Statistical analysis software version 9.2 was used.

Results: Of adult and pediatric EE patients in the private practice setting, 95% were male. 35% were classified as Type 1, 46% Type 2, 19% Type 3. Table shows differences in symptoms. Type 3 had the highest initial symptom score. Type 2 had higher follow-up symptom scores than the other subtypes. Type 3 had the greatest change in symptom score at follow-up. A similar percent of patients’ symptoms improved in each subtype. The number of eos at initial biopsy and follow-up did not differ among subtypes, nor did the percent of improved patients.

Conclusions: Initial symptom scores differed among groups. Type 2 continued to have the highest symptom score at follow-up. Patients with Type 2 symptoms may benefit from more aggressive therapy. Subtyping EoE patients may be beneficial to predict outcomes, but more studies are needed to support this hypothesis.

Table. Differences in Symptoms

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PHENOTYPIC DIFFERENCES OF EOSINOPHILIC ESOPHAGITIS (EE) IN NON-CAUCASIAN (NC) VS. CAUCASIAN (C) POPULATION

Rupinder K. Gill1, A. Al-Subu2, H. Chamdawala1, Y. Elitsur2, S. Schwarz1, W. Treem1. 1Pediatric Gastroenterology, SUNY Downstate Medical Center, New York, NY; 2Pediatric Gastroenterology, Joan C. Edwards School of Medicine at Marshall University, Huntington, WV.

Background: EE is found predominantly in C males. To date, no studies compare the NC v. C EE phenotype. The aim of the present study was to compare the clinical characteristics of EE in a NC urban vs. a predominantly C rural population.

Methods: From January 2003 to April 2010, EE cohorts of 54 NC patients from an urban, inner-city population and 53 C patients from rural W. Virginia were studied retrospectively. EE was histologically defined as ≥15 esophageal eosinophils (Es)/hpf. Age, presenting symptoms, personal or family history of atopy (asthma, seasonal allergies, eczema), absolute peripheral Es, total IgE, RAST results, endoscopic/histological findings, treatment and response to treatment were analyzed.

Results: The M: F ratio was 3.5:1 and 3:1 in the NC and C cohorts, respectively. Age at diagnosis was significantly younger in NC subjects [NC: C = 4.7: 9.5 yr, P = 0.01, 95% CI (3, 6)]. A history of atopy was reported in 63% NC and 42% of C patients (P < 0.0001); however, a family history of atopy was lower in the NC group (NC: C = 35% v. 55%, P < 0.0001). Gross EE endoscopic findings were significantly less common in the NC v. C patients (42% v. 83%, P < 0.0001). Oral steroids and elimination/elemental
diets were the preferred treatment in the NC group compared to Fluticasone in the C group (P < 0.0001).

Conclusions: Our data show that significant phenotypic differences of EE in the NC vs. C group include younger age at presentation, higher incidence of atopy, relative paucity of gross endoscopic findings and a predilection for non-inhaled steroid therapy in the NC group compared to the C group. These results may have significant implications for future diagnosis and management of this disorder.

EOSINOPHILIC ESOPHAGITIS (EE): MORE THAN JUST EOSINOPHILS (ES) IN THE ESOPHAGUS?
Rupinder K. Gill, N. Hundal, W. Treem, S. Schwarz. Pediatric Gastroenterology, SUNY Downstate Medical Center, New York, NY.

Background: EE is defined as focally ≥15Es/hpf in the esophagus. Patients with eosinophilia in other parts of the GI tract have been excluded from the diagnosis of EE. We present a subset of EE patients with esophageal and intestinal eosinophilia.

Methods: Duodenal mucosal biopsies from EE patients between January 2003 to April 2010 were reviewed for the presence of Es, where eosinophilia was defined as >20 Es/hpf. Patients were divided into 2 groups: Intestinal EE (IEE) or non-Intestinal EE (nIEE). IEE subjects manifested both esophageal and duodenal eosinophilia, whereas patients with nIEE demonstrated increased Es only in the esophagus. Age, presenting symptoms, personal or family history of atopy (asthma, seasonal allergies, eczema), absolute peripheral Es, total IgE and RAST results were analyzed.

Results: Fifty-four patients met the diagnostic criteria of EE. 17/54 patients (31%) also demonstrated duodenal eosinophilia. The M: F ratio was 3.3:1 and 3.6:1 in the IEE and nIEE groups, respectively. No between-group mean age difference was found (IEE vs. nIEE = 4.1 v. 5 yr). Vomiting, abdominal pain and poor wt gain were the most common symptoms in both groups. 76% of IEE patients had a personal history of atopy compared with 49% in the nIEE group (P = ns). Similarly, no significant, group difference in the percent of patients with positive RASTs were found. Both diagnostic groups received similar therapeutic interventions and exhibited a similar response to treatment.

Conclusions: These data indicate that a significant percentage of patients with EE also demonstrate duodenal eosinophilia, according to established criteria. At present, the importance of this observation is unclear. Larger EE cohorts are required to determine phenotypic differences between IEE and the nIEE patients.

MONTELUKAST AS MAINTENANCE TREATMENT OF EOSINOPHILIC ESOPHAGITIS

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Montelukast doses ranged from 5 mg to 20 mg daily. Patients treated with 5 mg of montelukast daily had lower post treatment eosinophil counts in the distal esophagus (median 2.4 ± 2) when compared to patients treated with 10 or 20 mg of montelukast daily (median 18 ± 30 vs 56.5 ± 50, respectively) (P = 0.037). Remission rates were 60% for those receiving 5 mg therapy and 24% for those receiving 10 or 20 mg therapy (P = NS).

Conclusions: There was a high rate of histologic recurrence of EE with montelukast, although 5 mg tablets were found to maintain remission better than 10 or 20 mg of montelukast daily. It is possible that the chewable form of montelukast may have a topical effect on EE and maintain remission better than the film coated tablet. A randomized double blind placebo controlled trial will best elucidate the impact of chewable montelukast on EE.

PPI USE IS NOT RELATED TO DIAGNOSIS OF PEDIATRIC EOSINOPHILIC ESOPHAGITIS
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Background: Eosinophilic Esophagitis (EE) is an inflammatory disorder of the esophagus characterized by increased eosinophils of >20 per high powered field. The etiology is still unclear however PPIs have recently been implicated in the disease’s pathophysiology. The link has been made with...
the increasing use of PPIs and proposed mechanisms such as altering mucosal permeability. Clinically, it has been suggested that the probability of diagnosing EE is decreased if patients respond to PPI therapy. The purpose of this study was to evaluate the use and response to PPIs prior to diagnosis among pediatric EE patients and controls who underwent upper endoscopy.

**Methods:** Data including symptoms leading to endoscopy, past medication use, response to medications, endoscopic details and pathology reports was gathered from 1052 children who had upper endoscopies performed in 13 centers across Canada over a one year period. Ethics approval was obtained in each of the centers. Children undergoing upper endoscopy related to IBD, Celiac Disease, Transplantation and Cystic Fibrosis were excluded.

**Results:** 119 patients of the 1052 patients who underwent upper endoscopy with biopsies were found to have EE. Of the patients who had EE, 55% (65/119) had used a PPI prior to diagnosis. This was the same percentage of PPI use in the non EE population (56% or 520/933). There was an equal proportion of EE patients amongst PPI users (65/585) and non users (54/467) (11.1% vs. 11.6 %, \( P = 0.82 \)). There was no difference in clinical response to PPIs in the EE population vs. the non EE population (71% symptom improvement vs. 59% symptom improvement, \( P = 0.07 \)).

**Conclusions:** PPI use does not seem to be an important factor in the development of pediatric Eosinophilic Esophagitis. Also response to PPI is not a predictor of an ultimate diagnosis of EE in our study.
Results: Patients: 8 cases, 7 controls. Ten were females, median age 5 months. Anthropometrics: Length and head circumference z-scores increased negative values in the controls while they were preserved in the enteral group. Arm anthropometric indicators showed significant loss of fat stores in the oral group while they improved in the intervention group; the muscle arm area decreased in the control group while it kept preserved in the intervention group. Safety: The frequency of respiratory infections, diarrhea and abdominal distension was higher in the intervention group. At the end-point, hemoglobin and ammonia were higher in the enteral group; GGT, alkaline phosphatase and leukocyte count were higher in the control group.

Conclusions: Enteral nutrition preserved linear growth, head circumference growth and arm muscle area and increased fat stores. The main adverse effect of the nutritional intervention was respiratory infection.

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ENERGY INTAKE, DIETARY HABITS, AND PHYSICAL ACTIVITY OF OBESE CHILDREN’S MOTHERS: OBESEGENIC FAMILY ENVIRONMENT

Clio Chávez-Palencia1, Alfredo Larrosa-Haro1,2, Edgar M. Vázquez-Garibay2, Enrique Romero-Velarde2, Leticia Salazar-Preciado3, Rogelio Troyo-Sanromán2, Ana Karina Rodríguez-Anguiano3, Maria Elena Cámara-López2, Hugo E. Sepúlveda-Vázquez3. 1Gastroenterology and Nutrition, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; 2Instituto de Nutrición Humana, Universidad de Guadalajara, Guadalajara, Mexico; 3Unidad de Investigación en Epidemiología Clínica UMAE HE CMNO, Instituto Mexicano del Seguro Social, Guadalajara, Mexico.

Background: The aim was to compare the energy intake (EI), dietary habits (DH) and physical activity (PA) of mothers of children with obesity with mothers of children with healthy weight.

Methods: Design: Case-control (cases: mothers of obese children, n = 63; controls: mothers of healthy weight children, n = 62). Setting: An elementary school at Guadalajara Mexico, 2009. EI was evaluated by a 24-hour recall questionnaire; HA and PA were evaluated with an ad hoc questionnaire. Analyses: OR, CI95%, logistic regression.

Results: Overweight and obesity were significantly more frequent in the mothers of the obese children. They ingested a higher amount of energy and protein and with a significant higher frequency had lunch or dinner at work and watched TV at mealtimes. Their PA differed from controls mothers PA in outdoors or indoors moderate PA, less time of transportation to school and work and longer periods of sedentary activity. The regression models included the variables of the energy equation (energy and protein intake, active plus sedentary PA) plus specific DH and some socio-demographic characteristics (as families with one son and fathers job as independent professionals).

Conclusions: The obese children’s mothers’ lifestyle seems to be obesogenic in variables related to energy intake and consumption both as a part of the energy equation as well as in dietary habits and the socio-demographic condition, underlining the multifactorial condition of childhood obesity.

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INFLUENCE OF A LIQUID MILK–BASED FORMULA MATRIX ON BIOLOGICAL ACTIVITIES MEDIATED BY YEAST β-GLUCAN WGP

Anja Wittke1, Yali Wang2, Jun Yan2. 1Mead Johnson Nutrition, Evansville, IN; 2Tumor Immunobiology Program, University of Louisville School of Medicine, Louisville, KY.

The beneficial properties of β-glucans have been recognized for centuries. During the past decades they have been used as biological response modifiers to stimulate the immune response. The objective of the study is to determine if liquid milk based formula matrix has any influence on biological activities mediated by particulate yeast whole β-glucan particle (WGP) both in vitro and in vivo. In vitro the biological activity of 100 μg/ml WGP in the presence or absence of a liquid milk based formula matrix was evaluated. In vitro studies demonstrated that WGP significantly upregulated CD86 expression on macrophages and CD80, CD86, CD83, MHC class II molecules on dendritic cells (DCs). Cytokine studies revealed that WGP predominately stimulated macrophages to secrete IL-6 and TNF-α but low level of IL-12. In contrast, WGP stimulates DCs to predominately secrete IL-12 and TNF-α but low level of IL-6. Formula matrix did not significantly change WGP’s stimulatory effect in vitro. For in vivo studies mice (n = 10 per group) were fed WGP 1 mg/mouse/day for 10 days. These studies demonstrated that orally administered WGP and formula matrix treatment significantly increase peripheral blood neutrophil counts and promote neutrophil respiratory burst activity. However, the frequency of other hematopoietic cell populations including basophils, eosinophils, monocytes, lymphocytes, and red blood cells were not significantly altered in the steady condition. In addition, no significant difference was observed on macrophages and DC activation in vivo. However, serum level of IL-6 was significantly increased upon WGP plus formula matrix oral treatment. Taken together, these data demonstrate stimulatory effects of WGP on the immune system and a liquid milk based formula matrix did not significantly alter WGP’s effect. Moreover, combined WGP and formula matrix treatment in vivo significantly augment neutrophil counts and activity.

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BIOELECTRICAL IMPEDANCE ANALYSIS FOR THE MEASUREMENT OF BODY COMPOSITION IN PEDIATRIC INTESTINAL FAILURE

Bram Raphael1, Nilesh Mehta1, Nicolle Quinn2, Tom Jaksic1, Christopher Duggan1. 1Center for Advanced
Intestinal Rehabilitation, Children’s Hospital Boston, Boston, MA; Clinical and Translational Study Unit, Children’s Hospital Boston, Boston, MA.

Background: A reliable and valid bedside test of body composition is desirable for nutrition assessment in children with intestinal failure (IF). The accuracy of bioelectrical impedance analysis (BIA) in this population is not known. The aim was to compare BIA and deuterium oxide (D2O) dilution technique for the measurement of total body water (TBW), fat-free mass (FFM) and fat mass (FM) in children with IF.

Methods: Deuterium (0.2 g/kg) was administered enterally, and urine samples at 0 and 4 hours were analyzed by mass spectrometry for isotopic enrichment. TBW and FFM from BIA were calculated according to standard equations. Subjects underwent simultaneous multi-frequency BIA. TBW and FFM from BIA were calculated according to Horlick equations. Correlation and agreement between the 2 methods were analyzed using linear regression and Bland-Altman method.

Results: 16 measurements were performed in 11 subjects. Six subjects (55%) were receiving parenteral nutrition at the time of the study. Median (IQR) age was 8.5 (5.6 to 10.3) years, weight z-score −0.9 (−1.4 to −0.3), height z-score −1.5 (−3.5 to −1), BMI z-score 0.5 (−0.7 to +0.8). Median (IQR) citrulline level was 24 (16–27) micromoles/L. The correlation between TBW (BIA) and TBW (D2O) was \( r = 0.89 \) (\( P < 0.05 \)) and mean difference was \(-0.2 \) kg (limits of agreement \(-5.0 \) to \(+4.6\)). For FFM, \( r = 0.89 \) (\( P < 0.05 \)) and the mean difference was \(-1.4 \) kg (limits of agreement \(-7.6 \) to \(+4.8\)). For FM, \( r = 0.20 \) (NS) and the mean difference was \(-1.4 \) kg (limits of agreement \(-4.8 \) to \(+7.6\)).

Conclusions: BIA provides a reliable and valid measurement of TBW in children with IF, as compared with the gold standard of deuterium dilution. The agreements between BIA and D2O for FFM and FM are less strong. The applicability of BIA for serial measurement of TBW and body composition deserves evaluation.

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KNOWLEDGE OF GENERAL PRACTITIONERS IN CALI, COLOMBIA ON FEEDING IN THE FIRST YEAR OF LIFE
Carlos A. Velasco1, Marna R. Ortiz1, Diana Vinueza1, Maria M. Uribe2. 1Pediatrics, University of Valle, Cali, Colombia; 2Gastrohup Ltda., Cali, Colombia.

Background: Health professionals should make up the process of breastfeeding (BF) and complementary feeding of children during the first year of life. The aim was to determine what knowledge of general practitioners (GP) of healthy infant feeding during the first year of life.

Methods: Cross sectional observational study. \( N = 78 \) GP who worked in health institutions in Cali, Colombia. The survey included identification data, questions about knowledge in nutrition and normal dietary recommendations. SPSS Database. Description frequencies, averages, standard deviations and proportions and bivariate analysis using student t and Chi2.

Results: 82.1% recommended exclusive BF. 85.9% BF suspending BF by maternal infections, 38.5% know that the BF prevent chronic diseases, 12.8% suggests elimination diet in a mother allergic, 33.3% recommended commercial
infant formula, 98.7% do not recommend cow’s milk (CM) before one year of age, 83.3% starts complementary foods in >6 months: 57.7% fruits, 35.9% cereals, 2.6% meat and eggs, 73.1% prefer one food at a time, 56.7% tested every 3 to 5 days new foods, 73.1% changes the food consistency in >6 months and 73.1% starts meat in >6 months, 15.4% fish, 69.2% legumes and 73.1% tubers; 78.3% removes allergens in allergic children. 70.5% not recommended vitamins and 67.9% nutritional supplements. 65.4% acquire their knowledge from their teachers. No significant differences in terms of background, occupation, gender, but yes in GP unmarried, childless, with a history of allergenicity, and female GP and BF and GP with 30 and 35 years of age.

Conclusions: 61.5% GP have enough knowledge about normal feeding during the first year of life, between what stands out positively that the BF should be indicated by >1 year old and negatively elimination diet in the mother allergic.

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PROSPECTIVE COMPARATIVE STUDY OF GASTROSTOMY BALLOON TUBES IN CHILDREN
Dina Al-Zubeidi, Riad Rahhal. Pediatrics, University of Iowa Children’s Hospital, Iowa City, IA.

Background: Gastrostomy tubes are frequently utilized for nutritional support in children with various medical conditions when oral intake is inadequate or compromised. Complications related to the use of gastrostomy tubes include infections, leakage, granulation tissue growth, tube obstruction and balloon rupture. A variety of balloon gastrostomy tubes exist but prospective comparative studies are lacking in children.

Methods: We prospectively studied the use of two balloon gastrostomy tubes in a cohort of children in a crossover design. Patients were randomly assigned to use one tube (MINI One) for 4 months and then another type (MIC-Key) for another 4 months. Patients were evaluated at enrollment, and at 4 and 8 months, with monitoring phone calls at 2 and 6 months. Variables measured included caregiver satisfaction, tube related complications and tube durability.

Results: 22 patients were recruited, of which 19 finished the study. Infection rate and overall leakage was similar in both groups. Formula leakage, granulation tissue growth and satisfaction scores were slightly more favorable in the MINI One tube (not statistically significant). Balloon durability was relatively comparable.

Conclusions: Both balloon gastrostomy tubes performed well in this cohort. Longer study duration would be helpful to better assess tube durability.

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A PEDIATRIC ACADEMIC CENTER’S EXPERIENCE WITH ENDOSCOPICALLY PLACED GASTROJEJUNAL FEEDING TUBES
Dina Al-Zubeidi, Riad Rahhal. Pediatrics, University of Iowa Children’s Hospital, Iowa City, IA.

Background: Enteral feeding through gastrojejunal (GJ) tubes is an established method of nutrition for patients who do not tolerate gastric feedings. Literature about the safety and complications of different GJ tubes and placement methods remains lacking in children.

Methods: Retrospective chart review for GJ tube placements at our center from January 1999 to July 2009. Data collected included patient’s age, gender, weight, placement indication and underlying diagnosis. GJ tube parameters included tube type, durability, placement method, complications, fluoroscopy exposure and use of sedation.

Results: Preliminary data analysis for the first 20 patients showed 119 procedures (placements/replacements) performed. Mean age at initial placement was 4.7 years (range: 0.8–18), number of procedures per patient was 6, mean follow-up duration (SD) was 30.8 months (40.6) and mean tube durability was 4 months. Initial placement indications included GERD (90%), aspiration (35%), recurrent pancreatitis (20%), and poor gastric emptying (5%). Replacement indications included tube clogging (21%), tube coiling in stomach (15%), balloon rupture (12.6%), accidental dislodgement (9.2%) and tube breakdown (8.4%). Sedation was used in 11% of cases. The low profile MIC-Key transgastric jejunal tube was placed in 77% of cases. GJ tube placement in 45% using endoscopy and fluoroscopy with remaining cases with fluoroscopy alone.

Conclusions: The study offers practical information to both pediatric gastroenterologists and families of children that may benefit from GJ tubes particularly about placement methods and expectations including tube durability and common reasons for replacement.

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BRIEF AUTISM MEALTIME BEHAVIOR INVENTORY (BAMBI-R): PSYCHOMETRIC CHARACTERISTICS AND ASSOCIATION WITH CHILDREN’S DIET
Douglas Field1, Keith Williams1, Helen Hendy2. 1Pediatrics, Penn State Hershey Medical Center, Hershey, PA; 2Psychology, Penn State Schuylkill, Schuylkill, PA.

Background: Feeding problems are common in pediatrics, occurring in up to 70% of children with developmental disabilities and 20% of typically developing children. We evaluated the psychometric characteristics of the Brief Autism Mealtime Behavior Inventory (BAMBI) when applied to a larger and more clinical group of children from a hospital based feeding program to determine the BAMBI’s subscales and items within them. We also examined the usefulness of the revised BAMBI (BAMBI-R) for understanding children’s food consumption patterns and how parents help them learn to accept a variety of foods.

Methods: 202 children were divided into 3 groups: 46 with autism, 90 with other special needs and 64 with no special needs. Questionnaires completed by parents included demographic information, the original BAMBI, Child Eating...
Behavior Questionnaire (CEBQ) and Parent Mealtime Action Scale (PMAS). Parents described their child’s food consumption patterns by stating whether they eat each of 84 foods from 5 food groups.

**Results:** BAMBI-R revealed 3 subscales similar to those in BAMBI: LIMITED VARIETY, DISRUPTIVE BEHAVIOR and FOOD REFUSAL. Children with LIMITED VARIETY had higher BMI’s and were more likely male. LIMITED VARIETY was associated with FOOD FUSSINESS/CEBQ) and preparation of SPECIAL MEALS (PMAS). FOOD REFUSAL was more common in younger children and those with other special needs compared to those with autism/no special needs. Children with FOOD REFUSAL had less FOOD ENJOYMENT (CEBQ). Those with DISRUPTIVE BEHAVIOR had less FOOD ENJOYMENT (CEBQ) and were more likely to have parents who reported INSISTENCE ON EATING and USE OF REWARDS. Children who consumed fewer dairy products were more likely to have parents concerned about FOOD REFUSAL. Children with the combination of less protein, fruit and more consumption of starches were more likely to have parents concerned about LIMITED VARIETY.

**Conclusion:** BAMBI-R had 3 subscales similar to those in BAMBI. BAMBI-R subscales are useful for understanding specific food group problems.

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**BIFIDOBACTERIUM LACTIS BB12 ENHANCES INTESTINAL ANTIBODY RESPONSE IN FORMULA-FED INFANTS**

Hannah D. Holscher, Kelly A. Tappenden, Division of Nutritional Sciences, University of Illinois, Urbana, IL.

**Background:** In non-exclusively breastfed infants, the use of probiotics in infant formula may positively affect immune function. This study aimed to investigate the effect of infant starter formula containing the probiotic *Bifidobacterium animalis* subsp. *lactis* (BB12) on intestinal immunity and inflammation.

**Methods:** Six-week old healthy, full-term infants (n = 139) were enrolled in a prospective, randomized, double-blind, controlled clinical trial with 2 groups studied in parallel to a breastfed comparison group. Intervention: ad libitum feeding of partially hydrolyzed whey formula containing DHA and ARA (control group, CON) vs an identical formula supplemented with 10^6 CFU BB12/g powder (probiotic group, PRO) for 6 wks. Fecal samples were collected at enrollment (V0), after 2 wks of feeding (V1) and after 6 wks of feeding (V2). Infants received poliovirus and rotavirus vaccinations between V1 and V2. Fecal secretory IgA, poliovirus-specific IgA, rotavirus specific IgA and calprotectin were determined by ELISA. BB12 was quantified in fecal samples using qPCR, lactate concentrations using a colorimetric assay and pH using a pH meter. Data were analyzed using linear regression and ANCOVA where appropriate; log transformations were utilized to meet model assumptions, as needed.

**Results:** BB12 was detected in 93% and 88% of PRO feces at V1 and V2, respectively. Poliovirus-specific IgA concentration increased from V1 to V2 in PRO vs CON (P = 0.023). Vaginally-delivered PRO infants had increased fecal IgA concentration from V0 to V2 compared to CON (P = 0.047). Calprotectin increased from V0 to V1 in the PRO group (P = 0.048); however, this increase was not maintained at V2. Fecal pH, rotavirus-specific IgA and lactate concentration did not differ in formula-fed infants.

**Conclusions:** BB12 is found in feces of infants consuming supplemented formula and induces an immunologic response that may provide enhanced protection from viruses by increased production of virus neutralizing antibodies, up-regulated fecal secretory IgA abundance and enhanced neutrophil activity.

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**IMPROVED SURVIVAL OF INTESTINAL FAILURE CHILDREN UNDER A MULTIDISCIPLINARY PROGRAM**


**Background:** Intestinal failure (IF) is the inability of the intestine to digest and absorb sufficient nutrients to maintain health and in children to support growth. Children with IF rely on parenteral nutrition (PN) for survival; this can lead to death from sepsis or liver failure. Multidisciplinary care may improve outcomes. The aim was to evaluate the impact of a multidisciplinary program, the Children’s Intestinal Rehabilitation Program (CHIRP) established in 2004 on the outcomes of IF children at the Stollery Children’s Hospital, University of Alberta.


**Results:** 31 children formed the CHIRP cohort and we have identified 30 IF children on long term PN (≥100 days) to form the preCHIRP cohort. Demographics and clinical characteristics including gut anatomies were equivalent in the two groups. Overall survival was improved from 63.3% to 90.3% under CHIRP (P = 0.024). There was a significant rise in the survival of the severe short gut population (≤25% remnant bowel) from 14.3% (preCHIRP) to 100% (CHIRP) and a reduction of mortality from liver cholestasis to liver failure from 47.1% (preCHIRP) to 4.5% (CHIRP) (P = 0.005). Catheter line sepsis episode was reduced from 11.44 to 6.74 per patient/1000 catheter days (P = 0.001).

**Conclusions:** A coordinated multidisciplinary approach improves the survival of children with IF by the application of medical, nutritional and surgical managements that promote gut adaptation, better line care and ultimately survival.
ALUMINUM CONTENT OF PARENTERAL NUTRITION SOLUTION PRODUCTS

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Background: Aluminum (Al) toxicity is associated with significant central nervous system, bone, liver, and hematologic damage. Al is a contaminant in products used to make parenteral nutrition (PN) solutions including calcium (Ca), phosphate (Phos), and other additives. Premature infants are at a potentially high risk for toxicity. The Food and Drug Administration (FDA) has mandated standards for PN solution product labels and recommended a maximum patient Al daily exposure limit of 5 μg/kg/day. The objective of this study was to compare the labeled Al content to the measured Al content of the PN solution products and determine which manufacturers have the least amount of Al contamination.

Methods: Nearly 100 PN solution products from different manufacturers were sampled and sent for Al content measurement. The products identified to have the lowest contamination were then analyzed using our PN patient database to determine actual daily Al exposure.

Results: Comparing measured values, Ca contains 20–30%, Phos contains 13–16%, and Acetate contains 1–20% of the labeled Al content. The PN patient database found that neonates were receiving 28.3–47.6 μg/kg/day exposure to Al, using the least contaminated products, was 8.8–12.9 μg/kg/day, P < 0.001.

Conclusions: The actual Al content of PN solution products is significantly less than the labeled content. There is a difference between different manufacturers’ Al content. We previously found that neonates were receiving 28.3–47.6 μg/kg/day exposure to Al, using the labeled Al concentrations and 14.9–23.1 μg/kg/day Al exposure when actually measuring the PN (JPGN 2010;50:208–11). When we look at the same patients, using the measured Al concentrations of the least contaminated products, the daily exposure is significantly less, 8.8–12.9 μg/kg/day. Though still above the FDA recommended 5 μg/kg/day, this study reveals that by using a combination of the least contaminated PN solution products available, the Al exposure can be significantly reduced.

ACHIEVEMENT OF BMI STABILIZATION IN A PEDIATRIC CLINIC SETTING

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Background: Family-based action-oriented counseling (FAOC) is a strategy used to promote diet and lifestyle change through assessing current habits, identifying opportunities for change, identifying behaviors amenable to change and concrete goal setting. This study examines the extent to which the use of FAOC by a clinician is effective in stabilizing BMI among overweight children and adolescents. A secondary aim was to assess how overweight children with known non-alcoholic fatty liver disease (NAFLD) respond to FAOC as compared to overweight children without NAFLD.

Methods: Retrospective cohort study. This is a clinic based chart review of patients arriving in the clinic between January 2006 and February 2010. Information was extracted from medical records at baseline and at each of the subsequent clinic visits and BMI and BMI z-score was calculated. Patients’ BMI z-scores measured at baseline and then at the closest follow-up visit after 90 days were compared. Weight stabilization was considered to be achieved if BMI z-score was within 0.04 of the baseline BMI z-score.

Study Population: 111 patients referred to the liver clinic at Children’s Healthcare of Atlanta at Eggleston by their primary care pediatrician, for childhood NAFLD (n = 42) or for excess weight gain (n = 69). The overall mean BMI z-score at baseline was 2.45 (SD = 0.49), and was 2.46 (0.29) and 2.45 (0.58), for NAFLD and non-NAFLD patients, respectively. Analyses were conducted using SAS 9.2 and Microsoft Excel.

Results: Of the 111 patients, 32.4% (n = 36) met the criteria for 90 days minimum follow-up (26.1% of the non-NAFLD group and 42.9% of the NAFLD). Among those who met criteria for follow-up, 75% of the patients stabilized, 67% and 83% in the NAFLD and non-NAFLD groups respectively and this was not statistically different.

Conclusions: The results suggest that family-based, action oriented counseling (setting lifestyle and physical activity goals) in an office setting can be effective in short-term stabilization of BMI in both overweight children with NAFLD and those without.

DEGREE OF PARENTERAL NUTRITION SUPPORT CORRELATES WITH SERUM CITRULLINE LEVELS IN SHORT BOWEL SYNDROME

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Background: Several intestinal markers, including length of residual bowel, presence of an ileocecal valve, and age at the time of resection, are useful tools to assess the likelihood of intestinal adaptation in patients with short bowel syndrome (SBS). Recently, serum citrulline, an amino acid produced by the intestinal mucosa, has been proposed as a marker of functional intestine. Serum citrulline levels (SCL) have been shown to correlate with residual bowel length in SBS, supporting the potential utility of SCL in a clinical setting. Successful intestinal adaptation is manifested by decreasing requirements for parenteral nutrition (PN). We therefore
investigated whether SCL correlated with the degree of nutritional support provided by PN in our patients with SBS. **Methods:** Serum citrulline was measured in 19 subjects with short bowel syndrome; 10 were female and 17 utilized PN at the time of measurement. Subjects ranged from 7 mo to 21 y, with bowel lengths of 5 to 150 cm, and percentage of PN providing 0–100% of caloric intake. SCL was compared to PN intake as well as bowel length. Comparisons were made using linear regression analysis. **Results:** Of the 19 subjects, SCL decreased with increased PN intake (R = 0.69). Of the 17 subjects with known residual bowel length, SCL correlated with bowel length (R = 0.73). **Conclusions:** Our findings support a correlation between SCL and degree of PN support, as well as bowel length, in our SBS subjects. These findings raise the question as to whether SCL is associated to bowel length or intestinal adaptation. Further studies are warranted investigating longitudinal measurements of SCL as a dynamic marker for intestinal adaptation.

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**VASUALRITY IN OVERWEIGHT CHILDREN**

Diego Rodriguez1,2, Mauricio Coll1, Rafael Guerrero-Lozano1, Liliana Henao2, 1Pediatrics, Universidad Nacional de Colombia, Bogota, Colombia; 2Hospital de la Misericordia, Bogotá, Colombia.

**Background:** Endothelial dysfunction associated with obesity in children can be determined by impaired flow-mediated vasodilation (FMV). Available data show reversibility of such alterations through diet and exercise programs. **Methods:** Prospective study in two phases. In the initial descriptive phase, FMV was compared in overweight (OWC) and eutrophic children. In a second, interventional part, an attempt was made to ascertain the impact of healthy habits on endothelial dysfunction associated with short bowel syndrome; 10 were female and 17 utilized PN at the time of measurement. Subjects ranged from 7 mo to 21 y, with bowel lengths of 5 to 150 cm, and percentage of PN providing 0–100% of caloric intake. SCL was compared to PN intake as well as bowel length. Comparisons were made using linear regression analysis. **Results:** Of the 19 subjects, SCL decreased with increased PN intake (R = 0.69). Of the 17 subjects with known residual bowel length, SCL correlated with bowel length (R = 0.73). **Conclusions:** Our findings support a correlation between SCL and degree of PN support, as well as bowel length, in our SBS subjects. These findings raise the question as to whether SCL is associated to bowel length or intestinal adaptation. Further studies are warranted investigating longitudinal measurements of SCL as a dynamic marker for intestinal adaptation.

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**SUGAR-SWEETENED BEVERAGE CAUSES OXIDATIVE STRESS UNDER ISOCALORIC CONDITION**

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**Background:** Sugar-sweetened beverage (SSB) intake causes fatty liver (FL) and oxidative stress (OS) in animal and human studies. In rodent model of FL using SSB, we found that decreased sulphur amino acid intake did not cause OS. Recent human data suggests that OS may be due to hypercaloric state. The aim was to assess if SSB causes OS under isocaloric condition. **Methods:** 5 wk old C57BL6 mice were single-housed, divided into control and glucose groups and fed regular chow ad libitum. Control group received regular and glucose group received 30% dextrose water, ad libitum. After 5 weeks, FL was quantified by liver triglyceride (TG) measurement, OS was measured by redox states of oxidized/reduced glutathione (GSSG/GSH) and cystine/cysteine (CySS/Cys) using high performance liquid chromatography (HPLC). Steady state redox potential (Eh) for these redox couples was calculated using the Nernst equation. **Results:** Initial weight was similar in both groups (18.7 ± 0.2 g each). Glucose group had increased water intake (10 ± 0.3 vs. 5.5 ± 0.8 mL/day), decreased solid food intake (1.7 ± 0.7 vs. 4.3 ± 0.7 g/day), increased weight gain (final weight 30 ± 0.4 vs. 24 ± 0.4 g) and similar total caloric intake (19.8 ± 4 vs. 17.5 ± 3 kcal/day) compared to control group, respectively. Glucose group received 63% of its total caloric intake from dextrose water. Liver TG content directly correlated with plasma (but not liver) CySS/Cys (r = 0.84, P = 0.001) and GSSG/GSH (r = 0.73, P = 0.007) redox potentials. **Conclusions:** Even under isocaloric condition, glucose-sweetened beverage causes plasma OS.

**Table.**

<table>
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<tr>
<th>HPLC</th>
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<td>−136 ± 9</td>
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<td>TG (nmol/mg)</td>
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<td>6 ± 0.5</td>
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WEIGHT GAIN IN CHILDREN PARTICIPATING IN A MULTIDISCIPLINARY OUTPATIENT FEEDING PROGRAM
Sarah Hagin1,2, Debra J. Lobato1,2, Beth Pinkos1, Carolina S. Cerezo1,2, Neal S. LeLeiko1,2. 1Rhode Island Hospital, Providence, RI; 2Alpert Medical School, Brown University, Providence, RI.

Background: Multidisciplinary programs are the standard of care for the treatment of children with feeding disorders. However, there is limited research evaluating multidisciplinary feeding disorder treatment outcomes. Previous research has focused on behavior change (i.e., food refusal) in single or small, selected samples, limiting the generalizability of results and omitting important health outcomes, such as weight gain. The objective was to evaluate weight change in children participating in a multidisciplinary outpatient feeding disorder program.

Methods: Medical records of 75 children were reviewed. Inclusion criteria consisted of children younger than 6 years old, not receiving enteral nutrition, and participating in at least 6 months of treatment. Children were 58% male and averaged 30 months old. Weight measurements were converted into z-scores according to CDC norms. A repeated measures analysis of variance was conducted examining weight change over 6 months of treatment by specific age groups.

Results: Using Wilks’ criterion, results revealed a significant main effect for weight, F(2,67) = 6.13, P < 0.01 and a significant age by weight interaction, F(12,134) = 2.47, P < 0.01. Follow-up polynomial contrasts revealed a significant overall linear effect for weight with means increasing over time, F(1,68) = 12.10, P < 0.01, partial η² = 0.151. Confidence intervals of pairwise comparisons revealed significant differences in mean weight between baseline and 6 months, (95% CI from -.35 to -.06) and 3 months and 6 months (95% CI from −0.20 to −0.02).

Conclusions: To our knowledge this is the first study evaluating growth outcomes in a clinic-based sample of children in a multidisciplinary outpatient feeding disorder program. Results revealed overall weight gain over the course of treatment. Future research should include pre-treatment growth parameters to assess treatment impact on growth trajectories, compare patient growth to a norm group, and include change in feeding behavior to further assess outcomes and their predictors.

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) IN SMALL (<6 KG) INFANTS
Philip Minar1, Jeffrey Garland2, Alfonso Martinez1,2, Steven Werlin1. 1Pediatrics, Medical College of Wisconsin, Milwaukee, WI; 2Pediatrics, Wheaton Franciscan Medical Center, Milwaukee, WI.

Background: Percutaneous endoscopic gastrostomy (PEG) tubes have been placed in children for over two decades to provide safe and adequate nutrition. Sparse data exists documenting the safety of PEG placement in small infants. In pediatric PEG studies the major complication rate ranges from 0.5–17%. The aim was to evaluate the incidence of major complications of PEG placement in medically complicated infants weighing less than 6 kg.

Methods: We reviewed the charts of all infants who weighed <6 kg at time of PEG placement in a single NICU from January 2001- June 30, 2008. Patient characteristics and complications within the first 30 days were recorded.

Results: 40 infants with mean gestational age 29 weeks (range 23–41 weeks) with mean weight 3250 grams (range 2100–5600 grams) at PEG placement were evaluated. 19/40 infants weighed <3000 g of which 6 were <2500 g. The primary indication for PEG was dysphagia or unsafe oral feeding. A 12–14 French PEG was successfully placed in 38/40 (95%) infants. A major complication occurred in 1/39 (2.5%) of the completed procedures; a 38 week infant with Prader-Willi syndrome who weighed 2730 g at time of PEG had an upper esophageal tear with resulting pneumomediastinum. A surgical gastrostomy tube was placed during the same procedure and the patient did well with conservative, non-operative treatment. In a second infant the PEG bumper could not pass the upper esophageal sphincter and a surgical gastrostomy was placed. 15/40 infants had other surgical procedures performed at the time of PEG. For those infants only having a PEG placed, the mean procedure time was 10 minutes (range 4–18 min). Initiation and advancement of feeds were dependent on the clinical status of the patient and managed by the neonatology attending. The mean time to initial feeding was 20 hours (range 3–103 hours) and the mean time to full feeding (100 kcal/kg) was 60 hours (range 18–145 hours).

Conclusions: PEG placement can be safely and successfully performed in a majority of small (including <3 kg), medically complicated infants.

EARLY USE OF OMEGAVEN IN PATIENTS WITH SHORT BOWEL SYNDROME ON PARENTERAL NUTRITION: TRANSIENT CHOLESTASIS, LIVER FIBROSIS AND ESSENTIAL FATTY ACID DEFICIENCY
Valerie Marchand1, Moshe Bibas1, Marjolain Pineault2, Lise Bouthillier1. 1Gastroenterology, Hopital Ste-Justine, Montreal, QC, Canada; 2Pharmacy, Hopital Ste-Justine, Montreal, QC, Canada; 3Nutrition, Hopital Ste-Justine, Montreal, QC, Canada.

Parenteral nutrition (PN) has become an essential tool in the management and the survival of patients with short bowel syndrome (SBS). As a consequence of its long term patients may develop parenteral nutrition-associated liver disease (PANLD) characterized by progressive cholestasis, liver...
fibrosis, cirrhosis and finally end stage liver disease. Recently, addition of fish oil emulsion (Omegaven®) or complete substitution of soybean oil emulsion by fish oil emulsion was associated with reversal of PANLD. We present the case of two PN-dependant patients with SBS who initially received a mixture of fish (1 g/kg) and soybean (1 g/kg) oil emulsions and for whom we eventually completely stopped soybean oil and left them solely on fish oil emulsion (1 g/kg). Patient 1: A 2-year-old boy with 29 cm of small bowel developed cholestasis (maximum total/direct bilirubin 117/70 µmol/L) while on a mixture of fish and soybean oil emulsion. Bilirubin normalized 32 weeks after discontinuation of soybean oil emulsion despite no significant change in enteral nutrition. Patient 2: An 18-month-old boy with 35 cm of small bowel developed cholestasis (maximum total/direct bilirubin 196/122 µmol/L) while on a mixture of fish and soybean oil emulsion. Bilirubin normalized 17 weeks after discontinuation of soybean oil emulsion despite negligible enteral intake. Both patients had fibrosis on liver biopsy. They both developed essential fatty acid (EFA) deficiency while sustaining adequate growth. When soybean oil emulsion was reintiated at 0.25 g/kg, bilirubin remained normal. In our patients, the use of Omegaven® seemed to improve cholestasis but did not prevent the development of liver fibrosis. Both our patients developed EFA deficiency while solely on fish oil emulsion.

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**USE OF FISH OIL EMUSION IN PARENTERAL NUTRITION: A REVIEW OF 31 CASES**

Valerie Marchand¹, Veronique Groleau¹, Maxime Thibeault².

¹Gastroenterology, Hopital Ste-Justine, Montreal, QC, Canada; ²Pharmacy, Hopital Ste-Justine, Montreal, QC, Canada.

**Background:** Parenteral nutrition (PN) is used to provide adequate nutrition when the gastrointestinal tract is nonfunctional or partly functional. Unfortunately, complications such as parenteral nutrition associated liver disease (PNALD) are often seen. Recently, substituting part or the totality of the soybean oil emulsion with fish oil emulsion (Omegaven®) was associated with reversal of PNALD.

**Methods:** We retrospectively reviewed the charts of all the patients who received fish oil emulsion in our institution between October 2007 and December 2009. Values of conjugated bilirubin, ALT and GGT were recorded.

**Results:** Thirty-one patients received fish oil emulsion, 11 had received fish oil emulsion for less than a month and were excluded from further analysis. Diagnosis for the remaining 20 patients were as follow: short bowel syndrome 8, intestinal resection without short bowel 4, necrotizing enterocolitis without resection 3, gastrochisis without resection 2, intractable diarrhea 1, diaphragmatic hernia 1 and immune deficiency 1. Patients had been on PN with soybean oil emulsion for an average of 9 weeks (2–42 weeks) before initiation of fish oil emulsion. Sixteen patients received a 1:1 mixture of the 2 lipid emulsions (total 2 g/kg), among them only 3 showed an improvement of their bilirubin.

One was on soybean oil emulsion alone (1 g/kg) then was switched to fish oil emulsion alone (1 g/kg) and normalized his bilirubin. Three patients received a 1:1 mixture of both lipid emulsions followed by fish oil emulsion alone (1 g/kg). All 3 improved their bilirubin only after soybean oil emulsion was discontinued and they remained on fish oil emulsion alone (1 g/kg). Essential fatty acid (EFA) deficiency was seen in 3 patients, all of them were on fish oil emulsion alone.

**Conclusions:** The use of fish oil emulsion results in improvement of conjugated bilirubin in patients on PN. The best results are seen in patients who receive fish oil emulsion alone. There is a risk of EFA deficiency when fish oil emulsion is the sole source of intravenous lipids.

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**ACANTHOSIS NIGRICANS AS A CLINICAL MARKER FOR INSULIN RESISTANCE IN OBESE CHILDREN**

Rohit Ostwani, Amy Lochow, Yoram Elitsur. Pediatrics, Section of Gastroenterology, Marshall University, Huntington, WV.

**Background:** Obesity has been recognized as a major risk factor for various illnesses including cardiovascular, endocrine, and skeletal diseases. Insulin resistant diabetes mellitus type 2 (IR-DM2) in obese children is a major risk factor for developing diabetes mellitus and cardiovascular complications. Increased skin pigmentation around the neck and/or at the armpits (Acanthosis nigricans, AN) is a common clinical finding observed in obese children. The aim was to investigate the accuracy of AN to detect IR-DM2 in obese children.

**Methods:** Obese children (>95%tile) who attended the gastroenterology and the outpatient general clinics were prospectively recruited to the study. Demographic data, BMI value, and fasting serum levels of glucose, insulin, lipid profile, and liver enzymes were obtained at first visit in all children. The presence or absence of AN was recorded and the insulin resistant was calculated (HOMA equation). Insulin resistant was compared to AN, and the accuracy rate was calculated.

**Results:** A total of 69 children participated. The mean age was 12.9 ± 3.3 years and the Male:Female ratio was 1.6:1.0. The mean BMI value was 32.75 ± 5.83. The mean (mg/dl) cholesterol level, TG, HDL, and LDL were 162 ± 33, 132 ± 88, 42 ± 10, and 95 ± 26, respectively. AN documented in 43 (62%) children, and IR-DM2 calculated in 38 (55%) children. AN detected IR-DM2 in obese children with Sen. of 73.7%, Spec. - 51.6%, PPV- 65.1%, NPV- 51.6%, and accuracy rate of 63.7%. A weak correlation was calculated between AN and lipid profile (cholesterol, TG, HDL, or LDL; r² < 0.20), or between IR-DM2 and the degree of Obesity (BMI >95%-tile) (r² = 0.044).
Conclusions: AN is a common physical finding in obese children and could be used as a clinical marker to detect IR in obese children.

Cellular/Molecular Biology

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ROTAVIRUS (RV) INFECTION OF HUMAN CHOLANGIOCYTES RESULTS IN RELEASE OF IL-6 AND IL-8
Maria Grazia Clemente1, John T. Patton2, Edwin Oh3, Robert Anders4, Robert H. Yolken5, Kathleen B. Schwarz1. 1Department of Pediatric GI, Johns Hopkins University, Baltimore, MD; 2Department of Pathology, Johns Hopkins University, Baltimore, MD; 3Department of Internal Medicine, Johns Hopkins University, Baltimore, MD; 4Department of Genetics Medicine, Johns Hopkins University, Baltimore, MD; 5The Stanley Division of Developmental Neurovirology, Johns Hopkins University, Baltimore, MD.

Background: Biliary atresia (BA) is a severe hepatobiliary disease of infancy of unknown etiology. A murine rotavirus (RV) BA model suggests that a perinatal RV infection targets cholangiocytes and, through the release of proinflammatory cytokines, causes an irreversible fibro-obliterative cholangiopathy. Sera from infants with BA exhibit increased levels of IL-1ra, IL-6, IL-8 and hepatocyte growth factor while the liver remnants show increased expression of TGF-beta1, IFN-gamma, TNF-alpha. The aim of this study was to determine if RV infection of human cholangiocytes results in release of cytokines.

Methods: Human cholangiocytes were grown until confluence and exposed or not to RV in serum-free medium. After 15 hours, post-infection (p.i.) media were collected and screened for 23 different cytokines using a human cytokine array; total mRNA isolated from cell lysates was used for cytokine gene expression by real-time PCR. The rate of infection was estimated by immunofluorescence experiments using an anti-RV antibody.

Results: Under basal conditions only 3 of the 23 cytokines studied were detected in the medium from H69 cells. These were CXCL8 (IL-8), CCL5 (RANTES) and growth related oncoprotein (GRO). RV-infected H69 cells released IL-6 and IL-8 mRNA expression in RV-infected cells was 4.5 fold higher compared to mock infected H69 cells. IL-15, MCP-1, IFN-gamma, TGF-beta1, TNF-alpha and CXCL1 (GRO-alpha were not detected either before or after RV infection.

Conclusions: Human cholangiocytes infected with RV in vitro release IL-6 and IL-8 and exhibit increased production of IL-8. As IL-8 has been implicated as a marker of disease progression and liver fibrosis in children with BA, our finding offers a mechanistic support of a possible role of RV in the pathogenesis of human BA.

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THE ROLE OF BREAST MILK AND ANTIBIOTIC USE IN THE DEVELOPING PREMATURE INFANT INTESTINAL MICROBIOME
Mem M. Zolak, Philip M. Tatum, Reed A. Dimmitt. Pediatrics, University of Alabama at Birmingham, Birmingham, AL.

Background: Breast milk (BM) feeding and probiotic use have been shown to decrease the incidence of necrotizing enterocolitis (NEC) in premature infants theorized to be associated with establishing a normal intestinal microbiome. We hypothesized that the early perinatal clinical course in premature infants influences the bacterial composition of these infants.

Methods: Weekly fecal samples were obtained from 75 patients with a birth weight less than 1,500 grams. Total DNA was extracted and amplified using SYBR Green quantitative PCR. Degenerative 16s ribosomal primers were used to quantify the total number of bacteria. Specific 16s primers were used to quantify Lactobacillus sp and Enterobacteriaceae family bacteria. Clinical influences including mode of delivery, antibiotic use, and feeding practices were collected on each patient. Backward stepwise linear regression was performed to link clinical variables with the number of bacteria.

Results: The BM feeding was associated with significantly less total bacteria and presumed pathogenic Enterobacteriaceae at week one. At week two, an operative delivery was associated with less copies of Lactobacillus. At the third week of life, duration of initial postnatal antibiotic use, days to full feeds, and subsequent days of antibiotic use were all associated with decreased total bacteria. In addition, BM feeding continued to decrease the number of Enterobacteriaceae. By week four, BM feeding was associated with increased total bacteria but significantly less Enterobacteriaceae. No correlation between clinical variables, bacterial copy number, and NEC was found.

Conclusions: The early postnatal intestinal microbiota of the premature infant appears to be dynamic and influenced by clinical practice. The lack of correlation of the microbiome with NEC may indicate that other bacteria play a role in both protection and pathogenesis. Further elaboration of these bacteria may aid in specific novel probiotic therapies to prevent NEC.

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INTESTINAL TOLL-LIKE RECEPTOR DEFICIENCY RESULTS IN DECREASED JUNCTIONAL PROTEIN AND INCREASED DEFENSINS EXPRESSION IN NEONATAL MICE
Philip M. Tatum, Randy Bullock, Reed A. Dimmitt. Pediatrics, University of Alabama at Birmingham, Birmingham, AL.

Background: Probiotics have been shown to decrease the incidence of necrotizing enterocolitis (NEC) in premature...
infants. These bacteria signal through host toll-like receptors (TLR) found in many cell types. We have previously shown that neonatal mice lacking specific TLR have decreased intestinal development and increased injury in an NEC model. We hypothesized that TLR expression is necessary for postnatal development of intercellular junctional protein expression and barrier formation.

**Methods:** Two-week old TLR 2/−/−, 4/−/−, 2−/− 4−/−, 9−/−, wild-type (WT), and microbial reduced mice were sacrificed and the mid-jejunum harvested (n = 10/strain). RNA was isolated and cDNA produced. Quantitative PCR was used to determine the expression of several junctional protein genes as well as those for defensins. Gene expression was determined by the crossing threshold compared to 18 s expression. Fold change difference relative to WT was analyzed using Student’s t-test, significance P < 0.5.

**Results:** Mice lacking combined TLR2 and 4 had decreased expression of tjp1, ocln, and dag2. The TLR 9−/− mice had decreased ocln and ctnnb1. Only ocln expression was reduced in the TLR 4−/− mice. Defensin expression was markedly increased in the TLR 9−/− mice, specifically defcr-r, CAMP, pap, and reg3g.

**Conclusions:** The presence of TLR is essential for the early postnatal development of junctional proteins in the intestine. The increased expression of defensins in TLR deficient mice may reflect a decreased barrier function with activation of innate mucosal immunity. Determining which TLR ligands are essential for this postnatal development may provide insight into specific probiotic therapies to prevent NEC.

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**FRIDAY, OCTOBER 22, 2010**

**Plenary Session I:**

**Fellow Research Award**

8:15 AM–10:00 AM

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**PROSPECTIVE EVALUATION OF THE PEDIATRIC NAFLD FIBROSIS INDEX AND ELF MARKERS IN CHILDREN WITH FATTY LIVER DISEASE**

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**Background:** Nonalcoholic fatty liver disease (NAFLD) encompasses a spectrum of disease from simple steatosis to steatohepatitis, to fibrosis and ultimately cirrhosis. The diagnosis of fibrosis is based on liver biopsy. Previous studies have identified the pediatric NAFLD fibrosis index (PNFI) and the enhanced liver fibrosis (ELF) test as potential noninvasive markers for fibrosis. The aim of this study was to prospectively evaluate the performance of PNFI, ELF and their combination in assessing fibrosis in a group of children with biopsy-proven NAFLD.

**Methods:** 111 consecutive children diagnosed with NAFLD were included. The stage of fibrosis was scored according to the Nonalcoholic Steatohepatitis Clinical Research Network. PNFI was calculated using age, waist circumference and triglycerides. The ELF test involved the assessment of hyaluronic acid, amino-terminal propeptide of type III collagen, and tissue inhibitor of metalloproteinase 1 levels.

**Results:** 76-six patients (68.5%) had some degree of liver fibrosis (62 had stage 1, 5 had stage 2, and 9 had stage 3). Patients with fibrosis had higher BMI and waist circumference and they were more likely to have the metabolic syndrome. Moreover, Patients with fibrosis had more advanced steatosis, inflammation, ballooning and higher NAFLD activity score. Both PNFI and ELF test values were increased in patients with fibrosis (P < 0.001). The area under the receiver operating characteristic (ROC) curve for predicting fibrosis of PNFI and ELF test were 0.761 and 0.924, respectively. The best performance was obtained by combining PNFI and ELF test with an area under the ROC curve of 0.944. The combined use of PNFI and ELF test as a first-line approach could predict the presence or absence of fibrosis in 86.4% of children with NAFLD.

**Conclusions:** In pediatric patients with NAFLD, the combination of PNFI and ELF test can be used to accurately assess the presence of liver fibrosis and to identify patients in whom liver biopsy is correctly indicated.
least two consecutive positive TGA tests at least 3 months apart.

**Results:** TGA seroconversion continues throughout the first 10 years of life and can fluctuate over time. One-third of those with initial evidence of celiac autoimmunity but who remain on a regular diet, have become TGA negative $x$ 2 with the last measurement during follow-up still negative. Those transient subjects had significantly lower peak TGA levels compared to those with persistent celiac autoimmunity. The cumulative incidence of celiac autoimmunity is shown in the table. To date, 53 of the total 1370 children being followed have been diagnosed with celiac disease by intestinal biopsy.

**Conclusions:** 1. Children born with a high-risk HLA for celiac disease will have continued TGA seroconversion throughout at least the first decade of life; 2. High risk populations are identifiable based on number of HLA alleles; 3. Screening strategies will need to account for seroconversion throughout the first decade of life as well as the occurrence of fluctuating and sometimes even transient TGA positivity over time.

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<tr>
<th>HLA risk group</th>
<th>No. newborns followed (%)</th>
<th>Cumulative incidence of celiac autoimmunity at 10 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR 3/3</td>
<td>129 (9.4%)</td>
<td>22%</td>
</tr>
<tr>
<td>DR 3/x or 3/4</td>
<td>619 (45.2%)</td>
<td>15%</td>
</tr>
<tr>
<td>DR 4/4 or 4/x</td>
<td>573 (41.8%)</td>
<td>5%</td>
</tr>
<tr>
<td>DR x/x</td>
<td>49 (3.6%)</td>
<td>0%</td>
</tr>
</tbody>
</table>

$x =$ not DR3 or DR4.

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**Concurrent Session I:**

**Hepatobiliary and Pancreatic Disease**

10:30 AM – 12 PM

**ALCOHOL PREDISPOSES TO PATHOLOGICAL PANCREATIC ACINAR CELL CA2+ SIGNALS BY HYPERPHOSPHORYLATING RYANODINE RECEPTORS**

Abraham I. Orabi, Ahsan I. Shah, Zahir M. Mannan, Mahwish U. Ahmad, Sohail Z. Husain. *Pediatrics, Yale University, New Haven, CT.*

Alcohol abuse is a leading cause of pancreatitis, accounting for 30% of acute cases and 60%-90% of chronic cases, yet the mechanisms leading to alcohol-induced injury are unclear. An early and critical feature of this disease is the aberrant signaling of Ca2+ within the pancreatic acinar cell. An important conductor of this Ca2+ release is the basolaterally localized, intracellular calcium channel ryanodine receptor (RYR). In this study, we examined the role of the RYR in mediating Ca2+ signals during alcohol exposure. We hypothesized that alcohol triggers the release of acinar cell Ca2+ from pathologically leaky, hyper-phosphorylated RYRs. Acinar cells were freshly isolated from rat, loaded with the Ca2+ dye Fluo-4, and imaged by time lapse confocal microscopy. Spatial and temporal changes in Ca2+ release were examined using the Ca2+ activating agonist carbachol (1 μM) with or without ethanol (100 mM), a concentration that is achievable during heavy intoxication. Ethanol accelerated the speed of the apical to basolateral Ca2+ wave from 9 μm/sec to 18 μm/sec ($P < 0.0005$; $n = 18–22$ cells/group). Ethanol also caused a similar doubling in intra-acinar cAMP levels from 1.5 fmol/control to 3 fmol/control ($P < 0.05$; $n = 3$). Acceleration of the acinar cell Ca2+ wave by alcohol was abrogated by the PKA inhibitor PKI (1 μM; $P < 0.05$; $n = 10–16$ cells/group). Using a phospho-antibody that recognizes the PKA site on the RYR, we found that ethanol increased RYR phosphorylation by nearly five-fold ($P < 0.05$). Finally, the alcohol induced acceleration of wave speed was reduced by 100% relative to control levels by the RYR inhibitor dantrolene ($P < 0.05$; $n = 10–16$ cells/group). Our results implicate a pathological role for RYR-Ca2+ release in the pathogenesis of alcohol-induced pancreatitis via cAMP/PKA hyperphosphorylation of the RYR.

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**HEPATIC STEATOSIS IN TYPE 2 AND TYPE 1 DIABETES MELLITUS IS MEDIATED BY INSULIN SIGNALING VIA FATTY ACID TRANSPORT PROTEINS**

Samir Softic, Michelle Kirby, Noah Shroyer, Rohit Kohli. *Gastroenterology, Hepatology, and Nutrition, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.*

Obesity related type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD) are characterized by hepatic triglyceride (TG) accumulation though hepatic steatosis is also observed in poorly controlled type 1 DM (T1DM). Free fatty acid (FFA) flux mediated via liver specific fatty acid transport proteins (FATP-2&5) may in part be responsible for this hepatic TG accumulation. We studied the role of FATPs in-vitro using AML-12 cells fed FFA and treated with varied insulin concentrations or FATP-2/5 knock-down using siRNA. Cells were assayed for TG, ALT, FATP-2&5 mRNA, and FATP immunofluorescence. We further studied the role of FATPs in-vivo using obese T2DM mice and streptozotocin treated T1DM mice. Cells fed FFA had increased TG content ($P = 0.015$) and higher ALT levels ($P = 0.002$) compared to albumin controls. Varying insulin concentrations in-vitro produced TG levels with a “U” shaped curve. TG nadir was 174 mg/dL at 10 mU/ml of insulin, while peak levels were at 0 mU/mL (291 mg/dL) or 100 mU/ml (249 mg/dL) of insulin. Similar U-shaped insulin dose effect curves were seen for FATP-2&5 mRNA levels. FATP immunofluorescence mimicked FATP mRNA
expression. Knockdown of FATP-2 or FATP-5 resulted in a 50% reduction in TG accumulation, while double knockdown almost completely abrogated TG accumulation. Obese T2DM mice developed hyperglycemia (235 vs 160 mg/dl) and hyperinsulinemia (10.28 vs 1.87 ng/ml) compared to chow controls. In contrast T1DM mice developed hyperglycemia (380 vs 195 mg/dl) with hypo-insulinemia (0.62 vs 1.57 ng/ml). Interestingly we observed similar two-fold increases in FATP-2 & 5 mRNA expressions for both T2DM and T1DM mice. Conclusion: Hepatic steatosis is regulated by insulin in a “U” shaped dose dependent fashion via FATP-2 & 5. This indicates an optimal window of insulin concentration, wherein deviations from this optimum lead to increased hepatic TG accumulation. This resembles steatosis seen in humans with either poorly controlled T1DM or obesity associated T2DM and NAFLD.

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DNA HYPMETHYLATION CAUSES BILE DUCT INJURY IN ZEBRAFISH AND IS A DISTINGUISHING FEATURE OF INFANTILE BILIARY ATRESIA

Randolph P. Matthews1, Steven F. EauClaire1, Monica Mugnier2, Shuang Cui1, Kristin Lorent2, Michael Pack2, Zhe Zhang3, Pierre Russo4. 1Division of GI, Hepatology, and Nutrition, The Children’s Hospital of Philadelphia, Philadelphia, PA; 2Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA; 3Pathology, The Children's Hospital of Philadelphia, Philadelphia, PA; 4Center for Biomedical Informatics, The Children’s Hospital of Philadelphia, Philadelphia, PA.

Biliary atresia (BA) is a progressive fibroinflammatory disorder of extra- and intrahepatic bile ducts that occurs exclusively in infancy, and is the most common indication for liver transplantation in children. The etiology of BA is unclear, and there is evidence both for and against viral, toxic, and genetic causes, although non-Mendelian inheritance patterns argue against a single gene defect. Interferon-γ (IFNγ) signaling is activated in patients and in the frequently utilized Rhesus rotavirus mouse model of BA, and is thought to play a key mechanistic role. Here we demonstrate intrahepatic biliary defects and upregulated hepatic expression of IFNγ pathway genes caused by genetic or pharmacological inhibition of DNA methylation in zebrafish larvae. The intrahepatic defects were reversed by treatment with prednisone. DNA methylation was significantly reduced in bile duct cells from BA patients compared to patients with other pediatric liver disorders, thereby establishing an etiologic link between decreased DNA methylation, activation of IFNγ signaling, and biliary damage in patients. Genomic DNA methylation patterns can be altered by environmental factors such as viruses and toxins, and can be inherited in a non-Mendelian fashion. We propose epigenetic activation of IFNγ signaling as a common etiologic mechanism of bile duct injury in biliary atresia.

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INNATE IMMUNE FUNCTION IN PLACENTA AND CORD BLOOD OF HEPATITIS C-SEROPOSITIVE MOTHER-INFANT DYADS

Christine E. Waasdorp Hurtado1, Lucy Golden-Mason1, Megan Brocato1, Mona Krull2, Michael Narkewicz2, Hugo Rosen1. 1University of Colorado, Aurora, CO; 2Obstetrics and Gynecology, Denver Health Medical Center, Denver, CO.

Background: Vertical transmission accounts for the majority of pediatric cases of hepatitis C viral (HCV) infection. In contrast to the adult population who develop persistent viremia in ~80% of cases following exposure, the rate of mother-to-child transmission (2–6%) is strikingly low. Protection from vertical transmission likely requires the coordination of multiple components of the immune system. Placenta and decidua provide a direct connection between mother and infant.

Methods: We hypothesized that innate immune responses would differ across decidua, placenta and cord blood and that HCV exposure would modify innate immunity in these tissues. The study was comprised of 12 HCV-infected and 16 healthy control mother and infant pairs from whom cord blood, placenta and decidua were collected with isolation of mononuclear cells. Multiparameter flow cytometry was performed to assess the phenotype, intracellular cytokine production and cytotoxicity of innate immune cells.

Results: In keeping with a model where the maternal-fetal interface provides antiviral protection, we found a gradient in frequencies of natural killer T (NKT) and γδ-T cells being higher in placenta than cord blood. HCV exposure increases the frequency of non-conventional T cells (NKT cells and γδ T cells) in the placenta. HCV exposure results in a decrease in plasmacytoid dendritic cells in both placenta and cord blood of exposed infants. HCV exposure leads to a decrease of activation markers CD69, TRAIL, and NKP44 on NK cells in both placenta and cord blood. Paradoxically, HCV infection increased cytotoxicity of NK and NKT cells.

Conclusions: HCV dysregulates the expression of natural cytokotoxicity receptors and activation markers on innate immune cells. The placenta represents an active innate immunological organ that provides antiviral protection against HCV transmission by increased innate cell cytotoxicity.

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ORAL-VANCOMYCIN TREATMENT OF PEDIATRIC PRIMARY SCLEROSING CHOLANGITIS

Scott M. Seki1, Kathy Eng1, Yinka Davies2, Muhammad Khan1, Kathleen Cox1, Kari C. Nadeau1, Ken Cox1. 1Pediatric Allergy and Immunology, Stanford University School of Medicine, Stanford, CA; 2Pediatric GI, Sutter Medical Group, Sacramento, CA.
**Background:** Primary Sclerosing Cholangitis (PSC) is a disease characterized by chronic inflammation of the biliary tree which often progresses to cirrhosis and liver failure. Recent clinical studies have shown that oral vancomycin is an effectively therapy for PSC in children. We hypothesized that oral vancomycin may play a role in regulating the inflammation associated with PSC and further that this modulation would be observable in the cytokine levels in plasma.

**Methods:** A study was conducted in 7 children with PSC. Blood samples were obtained before starting and while oral vancomycin. All samples were analyzed for cytokine levels, sedimentation rate (ESR), alanine aminotransferase (ALT) and γ-glutamyl transpeptidase (GGT). Oral vancomycin dose was 50 mg/kg/day up to a maximum dose of 1500 mg/day.

**Results:** In 4 patients, IL-7 levels were elevated within 3 months on vancomycin therapy from a mean of 19.56 pg/mL to 46.126 pg/mL (HC mean = 0 pg/mL). MIP-1A levels were elevated from a mean of 32.07 pg/mL to 74.21 pg/mL in 6 patients following treatment within 3 months of initial dosing (HC mean = 0.47 pg/mL). RANTES levels decreased from a mean of 10429.26 pg/mL to 4421.70 pg/mL in 5 out of 7 patients (HC mean = 554 pg/mL). GGT, ALT and ESR levels normalized in all patients on oral vancomycin within 6 months on therapy.

**Conclusions:** Oral vancomycin has been shown to treat the chronic hepatic inflammation associated with PSC. We have shown in this study that oral vancomycin may accomplish this by altering IL-7, TGF-β, MIP-1A, and RANTES levels. Further studies are now underway to confirm these findings.
Methods: We employed mouse primary hepatocytes; Huh7 and Hep 3B cell lines treated with palmitate for these studies.

Results: PA induced GSK-3 activation was identified by phosphorylation of its direct substrate glycogen synthase. GSK-3 pharmacologic inhibition, by GSK-3 inhibitor IX and enzastaurin, significantly reduced PA-mediated lipoapoptosis. More importantly Huh7 cells in which either GSK-3 α or β isoforms were stably and selectively knocked down by shRNA, displayed resistance to PA induced cytotoxicity. GSK-3 pharmacological inhibitors and sh targeted knockdown of GSK-3 α or β also reduced JNK activation, following treatment with PA as assessed by phospho-immunoblot analysis. GSK-3 pharmacologic inhibition also reduced PUMA mRNA expression by PA. On the other hand the GSK-3 inhibitors did not prevent PA induction of the ER stress marker CHOP.

Conclusions: Our results suggest GSK-3 is activated downstream of free fatty acid mediated ER stress. Activation of this pro-apoptotic kinase initiates a JNK cytotoxic signaling cascade culminating in lipoapoptosis.

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PORTAL FIBROBLAST AND CHOLANGIOCYTE INTERACTIONS IN ARPKD ASSOCIATED CONGENITAL HEPATIC FIBROSIS

Jessica Wen1,2, Katherine Dell3, Lisa Guay-Woodford4, Rebecca Wells2,1 The Children’s Hospital of Philadelphia, Philadelphia, PA; 2University of Pennsylvania, Philadelphia, PA; 3Case Western Reserve University, Cleveland, OH; 4University of Alabama, Birmingham, AL.

Autosomal recessive polycystic kidney disease (ARPKD) results from mutations in fibrocystin/polyductin, located in the primary cilia of cholangiocytes. The mechanism by which it causes biliary abnormality and liver fibrosis is unknown. The aim was to determine whether fibrosis precedes biliary abnormality in ARPKD-associated congenital hepatic fibrosis (CHF); to identify the major fibrogenic cell type; to identify signaling molecules that lead to myofibroblastic differentiation. Methods: Several rodent models were utilized, including PCK rats and PKHD1 mice, which are orthologues of ARPKD; BPK and CPK mice, which are recessive models that demonstrate ductal plate malformation. Immunostain for fibrogenic cell markers and Kupffer cells were performed. Portal fibroblasts and Kupffer cells were isolated from wild type rats, co-cultured and treated with various cytokines. Cytokine production by cholangiocyte line was measured by ELISA and qRT-PCR. Result: Immunostain of livers from young rodents showed that biliary abnormalities precede fibrosis. Portal fibroblasts, as identified by elastin stain, were the predominant myofibroblastic cells. Kupffer cells in PCK rats were increased compared to wild type. Monocyte Chemotactic Protein-1 (MCP-1) was highly expressed by PCK cholangiocytes compared to wild type, as measured by ELISA and qRT-PCR. However, primary portal fibroblasts were not directly activated to undergo myofibroblastic differentiation when treated with MCP-1. Instead, their activation by MCP-1 required the presence of Kupffer cells, and disappeared when treated with TGF-β inhibitor. Conclusion: Biliary abnormalities precede fibrosis in ARPKD associated liver disease. Portal fibroblasts are the predominant myofibroblastic cells in CHF. MCP-1 is a potential signaling molecule that leads to myofibroblastic activation of portal fibroblasts. However, its effect requires the presence of Kupffer cells, and it is likely mediated by TGF-β.

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SERUM MICRORNAS ARE NOVEL BIOMARKERS FOR BILIARY ATRESIA


Biliary atresia is an idiopathic, neonatal liver disease characterized by an inflammatory and fibrotic occlusion of the bile ducts, resulting in cholestasis and jaundice. The only therapies are Kasai portoenterostomy (KPE) and liver transplantation. The success of KPE falls with age at the time of surgery. Diagnosing biliary atresia is a multi-step process typically involving serum biochemical testing, radionuclide scanning, liver biopsy, and intra-operative cholangiography. Novel biomarkers that expedite an accurate diagnosis would likely improve long-term outcome and reduce the need for transplantation. MicroRNAs (miRNAs) are short nucleotides that decrease target mRNA stability and hinder 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. Recently, specific serum miRNA profiles have been associated with various conditions, including liver disease. We describe a pilot study designed to identify a serum miRNA profile in biliary atresia. Biliary atresia and cholestatic control serum samples were obtained from the Childhood Liver Disease Research and Education Network. A preliminary screening of serum miRNA was performed by low-density microarray. TaqMan RT-PCR subsequently verified changes in serum miRNA levels observed via microarray. Several miRNAs were found to be significantly upregulated at least 2-fold in biliary atresia patients, whereas a single miRNA was present at lower levels compared to controls. This panel of miRNAs showed partial overlap with findings in an experimental mouse model of biliary atresia previously performed in our laboratory. A number of miRNAs identified have known functions in T cell or cholangiocyte biology. These findings indicate that biliary atresia is associated with a serum miRNA profile distinct from indeterminate cholestasis and indicate that serum miRNA should be explored as a non-invasive diagnostic biomarker for biliary atresia.
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RELATIONSHIPS BETWEEN VITAMIN K AND D STATUS AND BONE MINERAL DENSITY (BMD) IN CHILDREN WITH NEWLY DIAGNOSED CELIAC DISEASE
Justine Turner1,2, Jing Qiao2, Leanne Shirton1, Carla Rodriguez-Dimitrescu2, Diana Mager1,2. 1Department of Pediatrics, University of Alberta, Edmonton, AB, Canada; 2Department of Agriculture, Life & Environmental Sciences, University of Alberta, Edmonton, AB, Canada.

Background: Childhood and adolescence are critical periods in which to optimize bone mass. Children with celiac disease (CD) are at risk for decreased bone mineral density (BMD) due to malabsorption of fat soluble vitamins, inflammation and undernutrition. The aim of our study was to determine the role of vitamin D and K deficiency for altering bone metabolism in newly diagnosed children with CD.

Methods: Children and adolescents between the ages 3–18 yrs (mean ± SD: 9.4 ± 4.2 y; n = 43) with biopsy proven CD were recruited at time of diagnosis. BMD was measured using dual-energy x-ray absorptiometry. Relevant data regarding anthropometrics, bone mass and size at whole body, hip and spine sites, bone age, dietary intake and plasma vitamin D, parathyroid hormone (PTH) and calcium were collected. Vitamin K status was assessed by plasma PIVKA-II (prothrombin induced in vitamin K absence).

Results: Dietary vitamin K, D and calcium intake were less than 50% of recommendations for adequate intake in 81%, 45% and 32% of children, respectively. Low total, lumbar spine and hip BMD (z scores less than −1.0) were observed in 11%, 27% and 14% of patients respectively. In 53% of children vitamin D levels were indicative of suboptimal status for bone health (25–80 nmol/L) and in 35% plasma PTH levels was elevated. PIVKA-II levels indicative of vitamin K insufficiency were observed in 23% and plasma PIVKA-II levels were negatively related to spinal BMC (P < 0.05). Adjusted whole body BMD z-scores were positively correlated with serum vitamin D (r = 0.48. P < 0.05), and negatively related to PTH (r = −0.5, P < 0.05).

Conclusions: Children and adolescents with newly diagnosed CD are at risk for suboptimal bone health at time of diagnosis. Treatable risk factors include low vitamin K and D intake/status. Therapeutic strategies aimed at optimizing vitamin K and D intake may contribute to improved bone health in children with CD.

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EOSINOPHILIC ESOPHAGITIS: A TISSUE-ORIENTED APPROACH

Background: Eosinophilic esophagitis (EoE) is known to be a heterogeneous disease with respect to clinical presentations and response to therapy. We tested if the immune mechanisms that lead to eosinophilic infiltration of the esophagus also varied from patient to patient, and correlated with response to a specific treatment.

Methods: We performed immunofluorescence studies and confocal microscopy on esophageal biopsy samples from 20 EoE patients (aged 3–16) using two different antibody sets. Patients’ records were reviewed for food allergy history, total serum IgE levels and treatment. Primary antibodies against IgE, tryptase and IL5 were used to test whether IL5 positive mast cells expressed IgE, whereas eotaxin-3, IL13 and IL5 were used to evaluate the relationship between the major eosinophilic factors implicated in the mechanism of EoE.

Results: Although the clinical phenotypes were uniform regarding multiple food allergies and elevated serum total IgE titers (349 IU/L ± 102), the tissue phenotypes were heterogeneous, with four different staining patterns detected in confocal microscopy. In half of the samples (n = 10), there was co-localization of IgE, IL5, and tryptase. In the remainder, either only IL5 co-localized with tryptase (n = 4), or did not (n = 3), suggesting its non-mast cell origin. Finally, there was no significant staining either for IL5 or IgE in 3 samples. Patients with biopsy samples where IL5 and IgE co-localized to mast cells responded the best to food avoidance determined by resolution of the esophageal eosinophilia at repeat endoscopy. Patients with pathologies revealing either a non-mast cell source of IL5 or no IL5 staining did not improve by food avoidance and required swallowed steroids for clinical remission.

Conclusions: Our data, for the first time, provides evidence that there is immunological heterogeneity of EoE at the tissue level. These different set of markers could not only serve as a diagnostic tool, but can also be utilized for clinical decision making to choose between different treatment options.

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GASTROESOPHAGEAL REFLUX AND SWALLOWING DISORDERS: COINCIDENCE OR CONSEQUENCE?
Annela Gnesetti1,2, Daniela Armas1,2, Alicia Munyro1,2, Ines Perez Puig1,2, Agustina Barriola1,2, Silvina Moo1,2, Silvia Palermo1,2, Patricia Nacif1,2, Clara Jasinski2. 1Feeding Disorders Unit, Hospital Britanico, Montevideo, Uruguay; 2Gastroenterology, Hepatology and Nutrition Unit, Centro Hospitalario Pereira Rossell, Montevideo, Uruguay.

Background: The association of Gastroesophageal Reflux (GERD) and Swallowing Disorders (SD) can be seen in
children under 2 yr of age. Not much can be found in the literature about this association. The aim was to analyze the characteristics of the association between GER and SD in children.

**Methods:** Charts of children referred from a public health center (Centro Hospitalario PereiraRossell, CHPR) and a private hospital (Hospital Britanico, HB) between August 2005 to May 2010 to evaluate for GER were reviewed. Patients who at the time of consultation were receiving antireflux medication were excluded. GER evaluation was performed with pH probe or combined 24-h Multichannel Intraluminal Impedance (MMI-pH). A brief questionnaire in search of clinical SD symptoms was conducted in patients with confirmed GER. Particular interest towards choking, suffocation, coughing/choking with food/saliva, dribbling, vomiting, fluids through nose, cyanosis, tongue thrust. When SD was suspected a swallow study and upper GI series were performed.

**Results:** 211 patients (<2yr) with suspected GER were seen of whom 116 (72.%) were <1yr, and 70 were former preterm 33.2%. 153 patients (72.5%) were evaluated for GER and confirmed in 69 (45%). Only 26 children were evaluated with MMI-pH and 46% of this group had non-acid reflux. 57 (83%) patients with confirmed GER presented SD and 73% had pharyngeal dysfunction. Aspiration was seen in 40.6%. Only 12% of the patients had Cerebral Palsy. Predominant symptoms were coughing and choking; 22 (35%), vomiting; 13 (23%), suffocation; 12 (21%), dysphonia; 8 (14%), chronic cough; 6 (10%), dribbling; 7 (12%), apnea; 6 (10%), food refusal: 4 (7%), regurgitation: 4 (7%), regurgitation through nose: 3 (5%). Pharyngeal incoordination was present in 43%. Conclusions: SD is very common in young children with GERD and neurologically normal. Given the frequency of SD, with mainly pharyngeal dysfunction and a high percentage of airway aspiration, we believe it is important to investigate SD in children with GER.

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**FOREIGN BODY INGESTION IN CHILDREN: 10-YEAR EXPERIENCE IN THE SOUTHERN REGION OF PUERTO RICO**

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**Background:** Ingestion of foreign body is a common pediatric problem. Most of them passes spontaneously but others need to be removed. Management depends on the object ingested, location, patient’s age and any underling medical condition. The aim of this study is to recall and evaluate the foreign bodies in the upper airway in children from the southern region of Puerto Rico.

**Method:** A retrospective review of hospital records in 2 different institutions in the southern region of Puerto Rico with ICD-9 (International Classification of Diseases) code 938 which occurred in children 0–15 years of age during the last 10 years (1999–2009). Data was recorded during May 2010. Demographic data, type and location of object and what was the patient doing at the moment of the incident.

**Results:** Foreign bodies were detected in 69 (93%) of the 75 children evaluated. The age of the children range from 6 months to 14 years (mean: 3.7 years old), of the 75 children: 59% were male and 41% were female. The most common objects were coins (65%) followed by earrings, pins and small toys. There were three cases of lithium battery ingestion that required admission. At the moment of the incident most of the children were playing. Most of the children were evaluated within 48 hours of ingestion and were mostly asymptomatic. Localizations of the foreign body were the stomach, esophagus and distal small intestine. Endoscopic interventions were performed in all the patients. No major complication was observed during the procedure and none of the patients underwent surgery. The frequently used accessories device were: rat tooth forceps and retrieval net basket. The child reach the hospital using always private transport and never in an ambulance.

**Conclusions:** Our results showed epidemiological similarities with the experience of other centers in the world. Efforts for prevention of ingestion of inanimate foreign objects should focus in the preschool toddler group. Absence of symptoms does not preclude presence of foreign body in children.

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**EFFECTS OF AGING ON SALIVA TRANSPORT EFFICIENCY IN PATIENTS WITH CYSTIC FIBROSIS**

Frederick W. Woodley1,2, R. Machado 1, B. Skaggs 1, K. McCoy1,2, A. Patel1,2, H. Mousa1,2. 1Gastroenterology, Nationwide Children’s Hospital, Columbus, OH; 2Pediatrics, Ohio State University, Columbus, OH.

**Background:** Persons with cystic fibrosis (CF) are now living well into their 40s and 50s due to advances in both science and medicine. When compared to non-CF age-matched controls, children with CF have significantly delayed chemical clearance (CC) of acid gastroesophageal reflux (AGER). The aim was to assess the effects of aging on the rate of saliva transport to the distal esophagus in patients with CF.

**Methods:** 24-h pH/impedance (pH/I) tracings for 29 CF patients were analyzed. Patients were divided into 4 groups: infants (0–2 y, n = 3), children (2–12 y, n = 10), adolescents (12–19 y, n = 6), and adults (>19 y, n = 10). All were off anti-reflux meds and had no fundoplications prior to testing. Dry swallows from pH/I tracings were divided into 2 groups; when the pH in the distal esophagus was <4 (group A) and ≥4 (group B). For each subject, 20 of each type of swallow were measured during non-feeding periods. Velocities were calculated by determining the time duration from bolus entry into the proximal impedance channel to bolus entry into the distal channel, and then dividing this
number into the distance traveled. Outcome variables are expressed as mean of means cm/s ± SEM.

**Results:** While neither velocity type was significantly different between infants (i) and children (c) (P > 0.05), both were significantly faster when adolescents (a) were compared to children (6.1 ± 0.5 [Aa] vs 4.3 ± 0.25 [Ac], P = 0.014, and 4.5 ± 0.44 [Ba] vs 3.1 ± 0.27 [Bc], P = 0.022) and to infants (P = 0.019 [A] and = 0.016 [B]). Both velocities declined slightly in adults but not significantly when compared to adolescents (P = 0.439 [A] and = 0.197 [B]). Collapsed across all age groups, group A swallows were significantly faster than group B swallows (4.9 ± 0.25 vs 3.7 ± 0.22, P < 0.0001).

**Conclusions:** Saliva transport efficiency increases as CF patients grow older. Differences between group A and group B swallows suggest that CF patients may compensate for reduced CC efficiency by increasing the rate of saliva transport during clearance of AGER.

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**DO CYSTIC FIBROSIS PATIENTS BENEFIT FROM CONTINUED PROTON PUMP INHIBITOR TREATMENT FOLLOWING FUNDOPPLICATION?**

Frederick W. Woodley1,2, R. Machado1, B. Skaggs1, K. McCoy1,2, A. Patel1,2, H. Mousa1,2.1Gastroenterology, Nationwide Children’s Hospital, Columbus, OH; 2Pediatrics, Ohio State University, Columbus, OH.

**Background:** Patients with cystic fibrosis (CF) are known to have increased acid gastroesophageal reflux (AGER). Classic treatment includes medicinal treatments that include a proton pump inhibitor (PPI), surgical treatment to reduce GER (eg, fundoplication), and sometimes a combination of the two. The aim was to compare different groups of CF patients on the basis of the frequency of association of AGER with coughing.

**Methods:** Four CF cohorts were studied: 1) patients who were off meds and had no fundoplication (n = 29, median age [m] 15 y [0.3–48.9 y], 13M/16F), 2) patients who were on PPI and had no fundoplication (n = 13, m 25.9 y [7.8–46.2 y], 8M/5F), 3) patients who were off meds and post-fundoplication (n = 10, m 18.1 y [7.1–30.8 y], 3M/7F), and 4) patients who were on PPI and post-fundoplication (n = 9, m 18.5 y [4.7–28.3], 2M/7F). For each patient, coughing was considered to be associated with AGER when it occurred within a 5 minute interval of an AGER episode and when linear regression produced a corresponding symptom association probability (SAP) that was ≥95%.

**Results:** Cohort 1 – 11/29 (38%), Cohort 2 – 5/13 (38%), Cohort 3 – 3/10 (30%), and Cohort 4 – 1/9 (11%). Chi square analysis for trend reveals that the “trend” was not statistically significant (P = 0.1664). However, when compared to Cohort 4, odds ratio for having a positive association between AGER and cough was 0.2 (95% CI 0.01 – 1.97) for Cohort 1, 0.2 (95% CI 0.01 – 2.67) for Cohort 2, and 0.29 (95% CI 0.01 – 4.73) for Cohort 3.

**Conclusions:** Although there were no significant differences among treatment groups, patients who continued PPI treatment following fundoplication were 5 times less likely than Cohorts 1 and 2, and 3.4 times less likely than Cohort 3, to have a positive association of AGER with cough. Odds ratio data suggest that, given a larger sample size, a significant difference between Cohort 4 and Cohorts 1, 2, and 3 is likely to emerge.

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**SALIVA TRANSPORT IN PATIENTS WITH CYSTIC FIBROSIS IS SIGNIFICANTLY MORE RAPID WHEN THE DISTAL ESOPHAGUS IS ACIDIFIED**

Frederick W. Woodley1,2, R. Machado1, B. Skaggs1, K. McCoy1,2, A. Patel1,2, H. Mousa1,2.1Gastroenterology, Nationwide Children’s Hospital, Columbus, OH; 2Pediatrics, Ohio State University, Columbus, OH.

**Background:** We recently showed that chemical clearance (CC) of acid gastroesophageal reflux (AGER) in the distal esophagus of children with cystic fibrosis (CF) is significantly prolonged. The aim was to compare the rates of saliva transport to the distal esophagus in children with CF and in non-CF (NCF) age-matched controls.

**Methods:** 24 h pH/impedance (pH/I) tracings for 15 CF children (9F/5M, median age 7.6 [0.3–17 yr]) and 15 age-matched NCF children (8F/7M, median age 7.3 [0.3–18.2 yr]) were analyzed. Mean AGER Indices were 11.7 ± 2.4 and 5.7 ± 0.87 for CF and non-CF children, respectively (P = 0.028). All patients were off meds and had no fundoplications prior to testing. Dry swallows from pH/I tracings were divided into 2 types; when the pH in the distal esophagus was < pH 4 (acidified [A]) and ≥ pH 4 (non-acidified [NA]). For each subject, 20 swallows were measured during non-feeding periods for each swallow type. Swallow velocities were calculated by determining the time duration from bolus entry into the proximal impedance channel to bolus entry into the distal channel, and then dividing this number into the corresponding distance traveled (cm/s ± SEM).

**Results:** For CF and non-CF (NCF) subjects, mean velocities were not significantly different either when the distal esophagus was acidified (4.6 ± 0.33 [CF] vs 4.0 ± 0.24 [NCF], P = 0.128) or when the esophagus was not acidified (3.4 ± 0.27 [CF] vs 3.6 ± 0.26 [NCF], P = 0.599). However, while both velocity types were not significantly different in the non-CF subjects (3.6 ± 0.26 [NA] vs 4.0 ± 0.24 [A], P = 0.102), they were different in CF cohort (3.4 ± 0.27 [NA] vs 4.6 ± 0.33 [A], P = 0.001).

**Conclusions:** In children with cystic fibrosis, saliva transport to the distal esophagus is significantly more efficient when the distal esophagus is acidified. These data suggest that CF patients may compensate for reduced CC efficiency by increasing the rate of saliva transport to the distal esophagus during clearance of AGER.
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IMPEDANCE-PHMETRY PARAMETERS IN CHILDREN WHO UNDERWENT NISSEN FUNDOPLICATION
Judith Cohen Sabban, Gabriela Donato, Silvia Christiansen, Marina Orsi. Hospital Italiano, Buenos Aires, Argentina.

Background: Laparoscopic Nissen Fundoplication is the treatment of choice for patients with Gastroesophageal Reflux Disease (GERD) not responding to Proton Pump Inhibitors (PPI). Not all non responders have severe esophagitis as their main feature, others mechanism may be the cause of the persistence of the disease. In that regard, the 24 hr Multichannel Intraluminal Impedance-pHmetry (24hrMII-pH) which evaluates reflux quality, bolus clearance and column height can help characterize patients who eventually will need surgery. The aim was to compare results of 24 hr MII-pH of patients with GERD who had a Nissen fundoplication with those of an age matched group with GERD not operated and evaluate if there are any parameters which may help identify patients who required surgery.

Methods: We reviewed the charts of 16 patients (11 boys) (X age: 9.5 yr, r 6–14) with persistent symptoms of GERD despite adequate treatment with PPI for at least 6 mo. Eight had undergone fundoplication (G I) and the others (G II) matched for age with those who were operated, did not require surgery. All of them were off medications for one week before studies were performed. An upper endoscopy (multiple biopsies) and simultaneous 24 hr MII-pH were performed.

Results: 24 hr MII-pH parameters are shown in the Table below. P = 0.038 with SI in Non acid reflux and P = 0.05 in SAP.

Conclusions: In this small sample the only parameters of the 24 hr MII-pH which differed significantly between the operated and the non operated were the Symptom Index related to Non acid reflux and the SAP.

Table.

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<td>Clearance Bolus</td>
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HELICOBACTER PYLORI INFECTION IN HOUSEHOLD CONTACTS OF HELICOBACTER PYLORI-INFECTED CHILDREN
Karen D. Crissinger, Diana A. Moya. Pediatrics, University of South Alabama, Mobile, AL.

Background: Positive follow-up testing after H. pylori treatment may be due to inadequate treatment, resistant organisms, or reinfection. The study objective was to determine if household contacts of H. pylori-positive children are also positive and if positive follow-up testing of H. pylori infection in children is decreased by simultaneous treatment of all H. pylori-infected family members.

Method: Patients 6 months of age and under who presented to Pediatric GI clinic at UMass between Dec 2006 - July 2009 and had fecal lactoferrin sent were included, except those born preterm or with other confounding factors. Charts were analyzed for correlation with symptoms and response to treatment.

Results: There were 49 infants, ranging from 26 days, to 6 months and 22 days, in age. All had GI symptoms including fussiness, spitting, crying and vomiting. 32 were FL positive. Of the 28 FL + that had fecal occult blood tested, 16 were negative. 9/17 FL- had undergone dietary changes prior. 11/49 were breast fed, of which 10/11 were FL +. Of 32/49 with one of their diagnoses as GE reflux, 21/32 were FL +. 13/20 with respiratory symptoms such as gagging and nasal congestion were FL +. Symptom resolution followed treatment of CMPI and associated conditions in all. Normal controls are currently being recruited.

Conclusions: FL is a useful test in aiding the diagnosis of CMPI in infants in whom it is suspected, replacing an invasive test like a mucosal biopsy in these young patients. It is more sensitive than fecal occult blood, and will allow for earlier treatment. Results of controls will be important.

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RELEVANCE OF THE FECAL LACTOFERRIN (FL) TEST IN IDENTIFYING COW’S MILK PROTEIN INTOLERANCE (CMPi) AMONGST COLICKY INFANTS
Jyoti Ramakrishna, Jay Fong, Mohsina Alom, Denise Stefanczyk. 1Pediatric GI & Nutrition, UMass Memorial Childrens Medical Center, Worcester, MA; 2Pediatrics, UMass Memorial Childrens Medical Center, Worcester, MA.

Background: Colicky infants pose a challenge to pediatricians/pediatric gastroenterologists. A proportion have CMPI, yet diagnosis is difficult. Fecal occult blood is often used but unreliable. Empiric treatment is the norm. FL is a neutrophil-derived marker of inflammation of GI mucosa, reported to correlate with flares of inflammatory bowel disease. Infants with CMPI have inflamed GI mucosa, which should cause positive FL, a potentially useful clinical marker. We previously reported on 14 patients, hypothesizing that FL is useful to identify a subset with CMPI amongst colicky infants. Although this seemed to hold true, a larger cohort was needed. We have identified 35 more patients who presented with colic and had FL tested, these are included here.

Methods: We reviewed the charts of 16 patients (11 boys) (X age: 9.5 yr, r 6–14) with persistent symptoms of GERD despite adequate treatment with PPI for at least 6 mo. Eight had undergone fundoplication (G I) and the others (G II) matched for age with those who were operated, did not require surgery. All of them were off medications for one week before studies were performed. An upper endoscopy (multiple biopsies) and simultaneous 24 hr MII-pH were performed.

Results: 24 hr MII-pH parameters are shown in the Table below. P = 0.038 with SI in Non acid reflux and P = 0.05 in SAP.

Conclusions: In this small sample the only parameters of the 24 hr MII-pH which differed significantly between the operated and the non operated were the Symptom Index related to Non acid reflux and the SAP.

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Methods: A retrospective study involving chart review of patients <18 years between February 1991 and September 2009 was performed.

Results: H. pylori testing was positive in 166 patients via upper endoscopy (64%), urea breath test (28%) and serology (8%). The mean age was 11 years. In 86 (52%) of 166 patients who had follow-up testing, 37 (43%) were positive after treatment. Before August 2003 when household contact testing was not performed, 48 (61%) of 78 patients had follow-up testing after treatment and 25 (52%) tested positive for H. pylori. Since August 2003, 39 (45%) of 87 patients had follow-up testing after treatment and 12 (31%) tested positive (P = 0.0065). Since August 2003, 29 (33%) of 87 patients had testing of contacts and 24 (83%) had at least one contact who was positive for H. pylori (P = 0.0036; 95% confidence interval 66–97%).

Conclusions: A significant percentage of children who tested positive for H. pylori had at least one household contact who tested positive. The percentage of patients who tested positive for H. pylori on follow-up decreased significantly after initiation of testing of household contacts. Thus, before assuming that recurrent disease is due to resistant H. pylori, it may be beneficial to test household contacts and treat all H. pylori -positive persons simultaneously to attempt to eradicate the organism from the household and prevent reinfection.

BENEFICIAL RESULT OF INCLUDING A LOWER ENDOCOPY WITH UPPER ENDOSCOPY TO DIAGNOSE EOSINOPHILIC GASTROENTEROPATHY IN PATIENTS 6 MONTHS TO 5 YEARS OF AGE
Karla Au Yeung. Division of Pediatric Gastroenterology and Nutrition, The Johns Hopkins Hospital, Baltimore, MD.

Background: Esophagogastroduodenoscopy (EGD) is often utilized to diagnose eosinophilic gastroenteropathy (EGE) when infants and children present with symptoms of food refusal, gastroesophageal reflux disease (GERD), or failure to thrive (FTT) and laboratory or radiologic workup do not reveal a cause. A retrospective chart review was conducted to determine whether performing a flexible sigmoidoscopy (FS) or colonoscopy (C) in addition to EGD improved diagnostic yield for EGE. This study also elicited the common symptoms leading to referral for endoscopy.

Methods: Charts were reviewed of patients who underwent EGD with or without FS or C from Jan 2007 to Dec 2009, ages 6 months to 5 years old. Pathology results on EGD and FS or C and up to 4 symptoms were recorded. Patients were excluded with a history of organ transplant because of immunosuppressant medication, prior diagnosis of EGE, severe GI bleeding, cancer, and severe cardiac disease. Data was only included from the patients’ first endoscopy.

Results: There were 232 charts with 31 charts excluded and 201 reviewed. There were 44.8% (90/201) patients who had FS/C with EGD; only 30% (27/90) had positive biopsy findings on the FS/C. Of the patients referred for EGD and FS/C, only 61% had lower GI symptoms, which were constipation, diarrhea, blood in the stool. The most common diagnoses leading to lower endoscopy without an associated lower GI symptom were FTT (38%), GERD (33%), feeding problems (24%), and atopy (24%). This correlated with the most common reasons for EGD referral as follows: FTT (21.5%); feeding disorder (18.7%); and GERD (16%). Including a FS/C with EGD added to the diagnosis in 23% (21/90) because eosinophils were found in the colon, but not on the EGD. Of these, 95% (20/21) had lower GI symptoms leading to either FS or C being ordered.

Conclusions: Lower endoscopy potentially improves diagnostic yield for eosinophilic gastroenteropathy in children less than 5 years old, specifically in cases where lower GI symptoms occur.

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ATOPY PATCH TEST IS A STRONG COMPLEMENTARY TEST TO SKIN PRICK TEST IN EOSINOPHILIC ESOPHAGITIS
Kelly Grzywacz1, Seema Khan2. 1Department of Pediatrics, A.I. duPont Hospital for Children, Wilmington, DE; 2Gastroenterology, A.I. duPont Hospital for Children, Wilmington, DE.

Background: The majority of patients with Eosinophilic Esophagitis (EE) have food allergies (FA). Dietary restrictions are usually guided by in vitro serum and skin prick tests (SPT), but are often ineffective. Atopy patch test (APT) is proposed as useful in evaluating the role of non-IgE FA, but not routinely available due to lack of standardization. The aim was to show that APT is successful at identifying a greater number of FA than SPT alone.

Methods: We undertook a retrospective review of electronic medical records of 87 children with EE (>20 eos/hpf) seen in GI and FA clinics during 2006–2009. Baseline characteristics (age, sex, atopic disease, use of anti-reflux medicines, and topical steroids), SPT and APT results were reviewed. Post therapy esophageal biopsies were reviewed to assess remission (≤5 eos/hpf) and partial response (6–20 eos/hpf and >50% decreased density from baseline).

Results: 36 patients (26 male), mean age 9 yr (2–19) who had both SPT and APT, were included in further data analysis. The frequency of associated atopic diseases was: reactive airway disease 56%, allergic rhinitis 75% and atopic dermatitis 31%. 67% of patients (24 of 36) had used topical steroids. The mean number of foods tested per case was 21 (2–44). 94.4% (34/36) of patients had FA by either test. 50% of patients had between 2–8 FA. The 8 most common food allergens were corn, soy, egg, peanut, milk, chicken, oat, and rice. 58% (21 of 36) of patients had at least one positive APT result. 32% (21 of 66) additional food allergens were identified by performing APT on foods that had previously tested negative to SPT. 33% of patients were found to be in remission and 22% had a partial response on follow-up biopsies.
Conclusions: EE is strongly associated with both IgE and non-IgE mediated food allergies. Therefore, APT is a useful adjunct to SPT in the diagnosis of non-IgE mediated food allergens in EE.

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PROTON PUMP INHIBITOR USE IN NEONATES AND INFANTS
Marta Illueca, Berhanu Alemayehu, Yan Liu, Nze Shoetan, Huiying Yang. AstraZeneca LP, Wilmington, DE.

Proton pump inhibitor (PPI) use in outpatients and inpatients aged <1y from the US was evaluated through a real-world claims data analysis from the PharMetricsTM (outpatients; January 1, 2003-December 31, 2007) and Premier PerspectivesTM (inpatients; January 1, 2004-December 31, 2008) databases. Gastroesophageal reflux disease (GERD) diagnoses were determined using ICD-9-CM code 530.81.

Outpatient Results: Of 246,236 newborns and infants, 48,849 (19.8%) had GERD, of which 4018 (8.2%) received a PPI dose. Overall, 1.6% of newborns and infants received a PPI. Overall, 1.6% of newborns and infants received a PPI dose. Of 4018 (8.2%) received a PPI. Overall, 1.6% of newborns and infants received a PPI dose. Of 4018 (8.2%) received a PPI.

Inpatient Results: Data from 2008 showed that of 620,899 hospitalized newborns and infants, 0.19% and 4.42%, respectively, were prescribed ≥1 PPI dose. PPI prescriptions increased from 2004 to 2008 in newborns (0.09% to 0.19%) and infants (1.94% to 4.42%). Over 50% and 65% of newborns and infants, respectively, with GERD were treated with a PPI. Overall, 1.6% of newborns and infants received a PPI dose. Of 4018 (8.2%) received a PPI.

In this multicenter, randomized, double-blind study (D9614C00004; NCT00427635), neonates (premature to 1mo corrected age) with signs/symptoms of GERD received esomeprazole (ESO) 0.5 mg/kg or placebo (PBO) 30 min before AM feeding for ≤14 d. A pH/impedance probe was placed in the esophagus prefeeding (data recorded for 18–24 h at baseline and final visit). Mean change from baseline in number and type of reflux episodes (acidic [pH <4.0], weakly acidic [pH 4.0–6.9], nonacidic [pH ≥7.0]) measured by combined pH/impedance monitoring and number of acidic episodes >5 min and % time pH >4.0 and pH 4.0–6.9 measured by pH monitoring alone was analyzed via ANCOVA adjusting for treatment and baseline. LSMs of absolute change from baseline were calculated for each treatment group. 42/51 patients (20 ESO, 22 PBO) with ≥18 h of pH0–8 data at baseline and final visit and no continuous hour of data outside pH 0–8 were included. Based on 24-h pH/impedance monitoring, there was no significant difference between treatments in reflux episodes (P = 0.5338). ESO treatment resulted in a significant decrease in acidic reflux episodes (−30.40 vs −4.32; P < 0.0001) and a significant increase in weakly acidic episodes (26.05 vs 0.46; P = 0.0207) vs PBO. Based on 24-h pH monitoring alone, ESO treatment resulted in a significant decrease in acidic reflux episodes lasting >5 min (−4.96 vs 0.51; P = 0.0009) and % time pH <4.0 (−0.78 vs 0.37; P = 0.0017) vs PBO. Concomitantly, the % time pH 4.0–6.9 significantly increased after ESO treatment vs PBO (7.83 vs −0.77; P = 0.0022). The greater decrease in acidic reflux episodes with ESO vs PBO was not significant (−19.10 vs 6.05; P = 0.0737). ESO treatment significantly reduced esophageal acidity and concomitantly increased the number of weakly acidic reflux episodes in neonates with GERD signs/symptoms.

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ORAL ERYTHROMYCIN IN CHILDREN LESS THAN 12 MONTHS WITH GASTROESOPHAGEAL REFLUX ASSOCIATED WITH GASTROPARESIS
Background: The aim was to evaluate the effect of oral erythromycin on clinical manifestations, gamagramic results, and nutritional status in children less than 12 months of age with gastroesophageal reflux and gastroparesis.

Methods: We carried out a prospective, interventional, comparative, unblinded study in 34 pediatric patients less than 12 months of age. Oral erythromycin (10 mg/kg/day) was prescribed in patients with a clinical diagnosis of gastroesophageal reflux. These patients were evaluated twice, at baseline and after 3 months of continuous oral prokinetic therapy. A questionnaire was answered by the patients’ mothers to obtain data on clinical manifestations. Average gastric half-emptying time and percentage of gastric residual volume was determined by gammagram; nutritional status was assessed by measuring weight and height.

Results: There was no significant statistical difference in the nutritional status. The most common symptom was regurgitation; all symptoms decreased after treatment (P < 0.05). There were five positive symptoms before treatment and two after treatment (P = 0.0001). Gastric half-emptying time was statistically significant before and after treatment (mean of 170.47 ± 73.8 minutes, 106.8 ± 36.4 minutes respectively) (P = 0.0001). The percentage of gastric retention was statistically significant before and after treatment (79 ± 8.7% and 61.3 ± 7.5%) (P < 0.0001). A correlation was observed between the percentage of gastric retention and the hydrodized formula (r = 0.407, P = 0.01) with a determination coefficient of 0.17.

Conclusions: The use of oral erythromycin is effective in reducing symptoms and gastric emptying time in patients younger than 12 months with gastroparesis.

PHARMACOKINETICS AND SAFETY OF DEXLANSOPRAZOLE DUAL DELAYED RELEASE CAPSULES (30 MG AND 60 MG) IN ADOLESCENTS WITH SYMPTOMATIC GASTROESOPHAGEAL REFUX DISEASE

Michael Kukulka, Jingtao Wu, M. Claudia Perez. Takeda Global Research and Development Center, Inc., Deerfield, IL.

Background: Dexlansoprazole dual delayed release (DEX) capsule (30 mg QD) is approved in adults for treatment of heartburn associated with non-erosive gastroesophageal reflux disease (GERD) and maintenance of healed erosive esophagitis (EE); 60 mg is approved for healing EE. The current study assesses the pharmacokinetic (PK) profile and safety of DEX in adolescent patients.

Methods: Phase 1, open-label, parallel group, multicenter study in male and female adolescents with GERD (12 to 17 yrs). Patients were randomized to receive DEX capsules (30 or 60 mg, QD) for 7 days. Blood samples for the determination of DEX plasma concentrations and PK parameters were summarized by regimen. Safety assessments included monitoring of adverse events (AEs).

Results: 36 patients (mean age 14.6 yrs), 14 male and 22 female, were randomized, and PK data are available for 35 patients. PK parameters for DEX capsules (30 or 60 mg, QD) for 7 days are shown in the Table. The overall exposure of DEX after administration of the 60 mg capsule was slightly less than double the exposure from the 30-mg capsule. Cmax and AUC values observed for adolescents were similar to results from previous Phase 1 studies in healthy adults. Six of 36 patients (16%) reported >1 treatment-related AE (22.2% in the 30 mg group and 11.1% for the 60 mg group). All AEs were considered to be of mild severity.

Conclusions: The PK data for the DEX 30 and 60 mg capsules in adolescent patients with symptomatic GERD was similar to that in adults. Both 30 and 60 mg doses were well tolerated.

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*Data from adolescent study. N = 17 for 30 mg dose and N = 18 for 60 mg dose. *Data pooled from phase 1 studies in healthy adults.

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A COMPARISON OF SHORT AND LONG-TERM FEEDING OUTCOMES IN INFANTS WITH ESOPHAGEAL ATRESIA

Thomas Ciecierega 1,2, David Lal 1,2, Katherine Frontier 2, Neelesh A. Tipnis 1,2, Medical College of Wisconsin, Milwaukee, WI; 2Children’s Hospital of Wisconsin, Milwaukee, WI.

Background: Esophageal Atresia (EA) is a common congenital defect affecting between 3,000 and 4,500 live births. It prevents infants from early oral feeding exposure which may play a role in long-term feeding outcomes. We evaluated early and long-term feeding outcomes of infants born with esophageal atresia.

Methods: Records of infants born between Jan 2004-Jan 2010 with esophageal atresia at a single tertiary care medical center (Children’s Hospital of Wisconsin, Milwaukee, WI, USA) were reviewed. Demographic, surgical, and nutrition outcomes were abstracted. The percentage of oral feedings at discharge and 1 year follow-up were compared between two groups, based on the type of surgical repair.

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Results: 16 infants (7 females, mean weight of 2.17 kg, mean gestational age of 35.7 weeks) with esophageal atresia were identified. 10 of 16 patients had an accompanying tracheo-esophageal fistula. 1 patient died, 1 was lost to follow-up. 10 infants had esophago-gastrostomy anastomosis (EEA) and 4 had esophago-gastrostomy anastomosis (EGA). Infants with EEA were older at birth (mean gestational age of 36.3 vs 34.8 weeks, \( P < 0.05 \)) and in EEA and 4 had esophago-gastrostomy anastomosis. 10 infants had esophago-esophagostomy tracheo-esophageal fistula. 1 patient died, 1 was lost to follow-up. 10 infants had esophago-esophagostomy anastomosis. A greater percentage of infants with EEA achieved full oral feeds at discharge (60% vs 25%, \( P < 0.05 \)) compared to infants with EGA. Type of surgical repair plays a role in short- and long-term feeding outcomes in infants with esophageal atresia.

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PHARMACOKINETICS AND TOLERABILITY OF RABEPRAZOLE IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE: AN OPEN-LABEL, SINGLE- AND MULTIPLE-DOSE STUDY

Gerhard L eitz\(^1\), Dennis Doose\(^1\), Peter Zannikos\(^1\), Sarah Rusch\(^1\), Martha Gonzalez\(^1\), Blaha Solanki\(^1\), Ibrahim Haddad\(^2\), Andrew Mulberg\(^1\), Bhavna Solanki\(^1\), Ibrahim Haddad\(^2\), Andrew Mulberg\(^1\), Johnson and Johnson FRD, Titusville, NJ; \(^2\)Pediatric & Adolescent Gastroenterology & Nutrition, Youngtown, OH.

Background: Rabeprazole (RBZ) pharmacokinetics (PK) has been characterized in adults and adolescents previously.

Methods: This phase I study evaluated the PK and safety of RBZ after a single oral dose and daily administration for 5 days in children 1 to 11 years of age with gastroesophageal reflux disease (GERD). Subjective evaluations of GERD severity, RBZ effectiveness, palatability, and safety were also evaluated. In part I, 8 patients received RBZ 0.14 mg/kg; in part II, 20 patients were randomized to receive 0.5 mg/kg or 1 mg/kg. PK parameters of RBZ and the thioether metabolite (formed by a non-P450-dependent pathway) were calculated using noncompartmental methods.

Results: RBZ was rapidly absorbed with mean Tmax values ranging from 1.5 to 2.4 hours across dose groups. RBZ and metabolite levels increased in a dose-dependent manner, with little or no accumulation after once-daily administration. The mean AUC of RBZ on Day 1 for the 0.5-mg/kg (346 ng·h/mL) and 1-mg/kg (785 ng·h/mL) dose groups were close to those targeted. Plasma AUC values of RBZ and the metabolite were poorly correlated with individual age and body weight and oral RBZ clearance values (unadjusted for weight) were similar to historical adult data. These results imply RBZ dose-adjustment based on age or total body weight in this age group is not warranted. Weight-adjusted clearance values were higher for the pediatric patients; approximately 2 to 3 times the mg/kg dose of RBZ in these children was necessary to achieve comparable concentrations in adults. Improvement of GERD symptoms was observed in most patients. Palatability of the formulation was reported to be good or excellent. RBZ was well tolerated with no notable differences in safety among the dose groups.

Conclusions: RBZ was safe and the PK in children was comparable to those in adults. RBZ is currently being evaluated during an ongoing phase III study in children 1–11 years old with GERD.

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SERUM GHRELIN AND OBESTATIN LEVELS IN CHILDREN WITH FAILURE TO THRIVE AND OBESITY

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Background: The regulation of appetite and caloric intake is a complex process involving neural and hormonal pathways. Ghrelin and obestatin are two gastric peptide hormones which have opposite effects on food intake and body weight gain. We investigated the role of serum levels of ghrelin, obestatin and the obestatin/ghrelin ratio in children with failure to thrive and obesity as compared to controls.

Methods: A total of 78 children were included, 19 with FTT, 21 with obesity, and 38 aged-matched controls. Children were enrolled before routine endoscopic procedures and were fasting for at least 8 hours prior to the specimen collection. Serum ghrelin and obestatin were measured using commercially available EIA kits.

Results: There was no significant difference in age between the FTT group and controls, and the obesity group and controls. In the control group, the fasting total ghrelin level was higher in children <3 years than that >3 years of age (\( P = 0.0004 \)). There were no significant differences between age groups 3–10, >10 years of age or in obestatin levels. In children with FTT, the total ghrelin level was significantly lower compared to controls (\( P = 0.032 \)). The obestatin level was not significantly different. The obestatin/total ghrelin ratio was increased in the FTT group but was not significantly different (\( P = 0.07 \)). In children with obesity, the total ghrelin was significantly lower compared to controls (\( P = 0.001 \)). The obestatin/total ghrelin ratio was significantly higher in the obese patients compared to controls.

Conclusions: In our study children with FTT and obesity both had lower levels of circulating total ghrelin. This may suggest lower circulating ghrelin is a marker for poor nutrition in FTT, while in obesity it may be a consequence of negative feedback. The obestatin/ghrelin ratio was also
higher in children with obesity. These data support the hypothesis that an imbalance of ghrelin and obestatin may play a role in the pathophysiology of both FTT and obesity. Further studies are necessary to elucidate their precise roles.

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PROPOFOL SEDATION FOR GASTROINTESTINAL ENDOSCOPY (GIE): SINGLE INSTITUTIONAL EXPERIENCE

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Pediatric GIE is difficult to perform under moderate sedation due to tolerance issues. General anesthesia is expensive and has fatal complications. Propofol, a hypnotic sedative has good safety and amnesia effect. It can be used with other narcotics. We report our Initial experience in our children’s Hospital from 2005 to 2006. We performed 480 GIE during this period in 464 children. (age: 3 yrs to 20 yrs; mean 13.7 ± 1.7 yrs (Fe:M 241:223). colonoscopy:111, Esophagogastroduodenoscopy (EGD): 369. 48 children had complications; 45 were Respiratory; 3 were low blood pressure due to tolerance issues. Propofol is a safe hypnotic agent. In conjunction with Glycopyrrolate and Fentanyl it can be used in the outpatient sedation unit for Pediatric GIE.

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DOES SWALLOWING VELOCITY IN THE PROXIMAL AND/OR DISTAL ESOPHAGUS CORRELATE WITH ACID GASTROESOPHAGEAL REFLUX INDICES IN CHILDREN WITH CYSTIC FIBROSIS?

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Background: Cystic Fibrosis (CF) patients are known to have increased acid gastroesophageal reflux (AGER). We previously showed that chemical clearance (CC) after AGER events is delayed in the CF population. Theoretically, CC could be affected by swallow velocity. The aim of the study was to test the possible correlation of declining swallowing velocity with increasing AGER Indices.

Methods: 24-hr pH/impedance tracings for 16 CF patients (N = 16, median age 8 yr [range 3 mo-18.5 yr], 8F/8M) were analyzed. For each patient, the velocities of 30 dry swallows were measured. For each swallow, three velocities were calculated; proximal, distal, and a full-length esophageal velocity. Proximal and distal esophageal swallow velocities were calculated by dividing the distance from channel 1 to channel 2 (proximal) and from channel 5 to channel 6 (distal) by the corresponding time duration of saliva travel (cm/s). The full-length velocity was calculated according to standard methods. These velocities were then plotted against the
AGER Index to test for correlation. A linear regression model was used to test each correlation.

**Results:** Swallow velocities in the proximal esophagus were significantly correlated with increasing AGER Indices ($P = 0.041$). Neither the swallow velocity in the distal esophagus ($P = 0.146$) nor the full-length swallowing velocity was correlated with decreasing AGER indices ($P = 0.19$). There was no significant difference when swallowing velocities (mean of means) in the proximal esophageal ($1.4 \pm 0.13$ cm/s) and distal esophagus ($1.1 \pm 0.10$ cm/s) were compared ($P = 0.106$).

**Conclusions:** Decreased swallowing velocity in the upper esophagus in CF patients correlates with increasing AGER index. These data suggest a possible relationship between the efficiency of saliva transport and acid exposure.

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**111 RELATIONSHIPS BETWEEN SLEEP QUALITY AND GASTROESOPHAGEAL REFLUX IN OBESE CHILDREN**

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**Background:** Obese children frequently suffer from sleep disordered breathing and poor quality of sleep. Few studies have assessed the impact of GER on reported quality of sleep in obese children. The aim was to evaluate the relationship between quality of sleep and GER in obese children.

**Methods:** 12 obese (group A, 5 M, age 13.5 yrs $\pm 3.9$, none on antisecretory drugs) and 21 patients older than 1yr (group B, 14M, age 11 yrs $\pm 11.9$, 11 on antisecretory drugs) were evaluated. Simultaneous polysomnography and intraluminal esophageal impedance/pH monitoring were done in both groups and compared. Number of reflux events, proportion of time with reflux and mean duration of each reflux event were evaluated and compared during sleep, wakefulness after sleep onset (WASO) and daytime. Arousal index = number of arousals per hour. We considered a sleep event associated with GER if it happened up to 2 min after a GER episode, and a symptom association probability (SAP) positive in 5 of group A and 2 from group B, $P = 0.07$.

**Results:** Patients presented 367 non-acid (10–211, median 61) and 2,167 (0–55, median 6) acid reflux episodes. 25 patients presented desaturations (3–1208 events, median 61) and 2,167 (0–55, median 6) acid reflux episodes. 25 patients presented 367 non-acid (10–211, median 8) and 2,167 (0–55, median 6) acid reflux episodes. 25 patients presented 367 non-acid (10–211, median 8) and 2,167 (0–55, median 6) acid reflux episodes. 25 patients presented 367 non-acid (10–211, median 8) and 2,167 (0–55, median 6) acid reflux episodes. 25 patients presented 367 non-acid (10–211, median 8) and 2,167 (0–55, median 6) acid reflux episodes. 25 patients presented 367 non-acid (10–211, median 8) and 2,167 (0–55, median 6) acid reflux episodes.

Obese patients presented more often acid reflux episodes during WASO (A: median 2.5 interquartile range [IQR] 0.9–4.0, B: median 0 IQR 0–2.3).

**Conclusions:** Obese children awaken more often than non-obese patients with GER. As arousals are more frequently associated with reflux episodes among obese children, GER may play a role in the poor quality of sleep among obese patients and important interactions may exist between GER and sleep quality.

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**112 EVALUATION OF GASTROESOPHAGEAL REFLUX EVENTS USING COMBINED ESOPHAGEAL PH MONITORING (EPM) AND MULTICHANNEL INTRALUMINAL IMPEDANCE (MII) IN OBESE VS NONOBESE CHILDREN DURING SLEEP**

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**Background:** Obesity is associated with gastroesophageal reflux disease (GERD). Sleeptime reflux pattern is different in patients with GERD, with higher incidence of reflux. However, it has not yet been evaluated among obese children. The aim was to evaluate the gastroesophageal reflux events using EPM/MII in obese vs non-obese children during sleep.

**Methods:** EPM/MII tracings of 19 children (10 male) were retrospectively evaluated, seven of whom were obese (BMI ranging from 27.56 to 54.2, mean 37.66). Total number of reflux episodes, the types of reflux, the reflux index, the number of reflux events by hour, the number of acid and not acid (pH $\geq 4$) events by hour, the nadir pH, the bolus contact time, the proportion of total time of exposure to acid and non acid reflux events were measured. Only episodes during sleep were evaluated.

**Results:** Patients presented 4 to 164 reflux events (median 33). Obese patients presented slightly less non-acid reflux events in (median 4, range 0–7) than non-obese patients (8, 0–18, $P = 0.19$), but the number of acid reflux events were similar (37 [19–163] vs 52.5 [10–105], $P = 0.89$). Among 734 (467 among obese) reflux events evaluated, 113 were non-acid, only 25 of them among obese patients ($P < 0.001$). The most frequent type of acid reflux was pH-only events (285, 38.8%), which was evenly distributed in both groups. Mean nadir pH of reflux events was 2.56 (standard deviation 1.44), and lower among obese patients (mean difference between two groups 1.41, 95% confidence interval [CI] 1.22 to 1.61, $P < 0.0001$). Interestingly, the nadir pH was higher during sleep (difference 0.5, 95% CI 0.27–0.73, $P < 0.0001$).

**Conclusions:** Obese patients present significant particularities in the reflux pattern, mainly lower nadir pH and less frequent nonacid events.
DETECTION OF PEPSIN IN MOUTH SWAB, A NONINVASIVE METHOD OF DETECTING GASTROESOPHAGEAL REFLUX IN PRETERM INFANTS

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Background: Gastroesophageal reflux (GER) is very common in premature infants. The currently available methods for the diagnosis of GER are invasive and unreliable in premature infants. Detection of pepsin in a mouth swab may correlates with GER in premature infants. The objective was to study the relationship between pepsin in a mouth swab and clinical GER in preterm infants.

Methods: Preterm infants (Birth weight <2000 gram) on full enteral feeds were enrolled in this study. Mouth swabs from cheek and pharynx were collected 1, 2 and 3 hours after the feeds. An enzymatic assay with FITC-casein as substrate was used to detect pepsin activity. Pepstatin was used to selectively inhibit pepsin A. The final Pepsin A activity was obtained by subtracting pepsin C activity from the total activity. Mouth swab was considered positive if pepsin A or C was detected in any of the samples. GER was diagnosed clinically by two blinded investigators after reviewing infant’s medical record.

Results: Ninety nine premature infants were enrolled [birth weight 1185 ± 366 gram, gestational age 29.0 ± 3.0 weeks]. The median age of collecting sample was 48 days (range 6–104 days). Pepsin was detected in 42/99 (42%) infants in at least one sample. A clinical diagnosis of GER was made in 34/99 (34%) infants. Mouth swab was positive in 24/34 (71%) infants with GER and only 18/65 (28%) infants without GER ($P < 0.001$). The sensitivity and specificity of detecting GER by measuring pepsin in a mouth swab was 71% and 72% respectively.

Conclusions: The detection of pepsin in a mouth swab correlates with clinical GER in premature infants.

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IMPACT OF ACID SUPPRESSION ON THE DIAGNOSIS OF HELICOBACTER PYLORI AND GASTRIC HISTOLOGY

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Background: Determine the effects of acid suppression on three major variables: sensitivity of Clo rapid urease test, gastric histology, and mucosal distribution of Helicobacter pylori (Hp) in pediatric patients.

Methods: Gastric biopsies from pediatric patients undergoing upper endoscopy at Vanderbilt Children’s Hospital between Jan 2006-Dec 2007 were evaluated after IRB-approval. Inclusion criteria were Hp infection based on histology and age less than 18 years. Only the first biopsy for each patient was included. Exclusion criteria included Crohn’s disease. A pediatric pathologist, blinded to the clinical history, examined the biopsies and applied the revised Sydney analog scale. Mucosal distribution of the Hp was also assessed, including the presence of Hp within parietal cells or lamina propria macrophages, using the anti-Hp immunoperoxidase stain (IPS) when available. Acid suppression use, gross endoscopy results, and Clo urease data were obtained via retrospective review of the medical record.

Results: 51 cases met study criteria. 55% of patients were on acid suppression at the time of endoscopy. Gross endoscopic findings and chronicity based on Sydney criteria were similar amongst the two groups. Of those patients tested with Clo urease, patients on acid suppression had a sensitivity of 66% (12/18) vs. 83% (10/12) for those not on acid suppression. Additionally, the acid suppression group appeared to be less likely to have moderate or marked activity (10/28, 36% vs. 16/23, 70%) and more likely to have Hp seen intracellularly with the IPS (9/28 or 32% vs. 4/23 or 17%).

Conclusions: Pediatric patients on acid suppression may be more likely to have a negative Clo, less activity and more intracellular Hp compared to those not on acid suppression. Next, we plan to evaluate more cases and obtain IPS on all biopsies for a better assessment of significance.

HIGHER RATES OF H PYLORI REINFECATION IN CHILDREN IS LIKELY DUE TO THE GENDER-SPECIFIC HEALTH CARE-SEEKING BEHAVIOR OF THEIR PARENTS

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Background: Higher H pylori re-infection rates in children raises the question of the status of H pylori prevalence in their adult caregivers which is often unknown. The study addresses the potential role of the gender difference in health...
care seeking behavior of the adults in causing higher re-infection rates in children.

Methods: This was a hospital-based descriptive study. Data was collected retrospectively by chart review from the patients who were referred for urea breath test (UBT) due to their GI complaints.

Results: In one year 84 patients sought medical attention for the symptoms of dyspepsia out of which 63 (75%) were females and 21 were males. The median age of the patients at the time of initial assessment for GI complaints was 28.5 yrs. Compared to the males, the female nationals were more likely to seek medical attention for dyspepsia (\(P = 0.0001\)). The preferred method of initial investigation for a patient with dyspepsia was Urea Breath Test (UBT) (83%) compared to Endoscopy + CLO/biopsy (5%) or stool antigen test (12%). Female patients were more likely to get post treatment UBTs in subsequent visits to confirm eradication of \(H. pylori\) (NS). Although the male nationals were found less inclined to seek medical attention, they were more likely to get referrals to GI and endoscopy clinic in their initial visit to the hospital (\(P = 0.031\)). Due to poor follow up the success of \(H. pylori\) eradication remained uncertain in the male patients.

Conclusions: There is a greater need to use evidence-based and culturally appropriate approach to \(H. pylori\) management. Any guidelines for children must take into account the gender differences of the adult family members in their attitude toward illness and medical attention.

SAFETY OF MULTIPLE DOSES OF INTRAVENOUS ESOMEPRAZOLE IN PEDIATRIC PATIENTS

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This multicenter, open-label study (NCT00474019; D9615C00021) of hospitalized patients aged 0–17 y considered for acid suppression therapy (including those with presumptive or clinical symptomatic or endoscopically-proven GERD). Patients received IV esomeprazole (ESO; 8 mg/mL, 2 mg/mL, or 0.2 mg/mL) once daily over 3 min for 4 d. Newborns (0–1 mo) received ESO 0.5 mg/kg; infants (1–11 mo inclusive) received ESO 1.0 mg/kg; children (1–5 y inclusive) received ESO 10 mg; children (6–11 y inclusive) were randomized to ESO 10 or 20 mg; and adolescents (12–17 y inclusive) were randomized to ESO 20 or 40 mg. Adverse events (AEs), physical examinations, clinical laboratory evaluations, vital signs, and electrocardiogram (ECG) parameters were assessed. Fifty-seven patients mostly from ICUs were included in the safety analysis (6 aged 0–1 mo; 9 aged 1–11 mo, 8 aged 1–5 y, 17 aged 6–11 y, and 17 aged 12–17 y). The youngest patient was a neonate of 33 wk corrected age. Thirty-one patients (54.4%) experienced ≥1 AE. The most common AEs were constipation (10.5%) and pyrexia (8.8%). Six patients experienced AEs classified as administration site conditions. Eight serious AEs (but no deaths) were reported by 6 (10.5%) patients; none were considered drug related. Two patients (3.5%) discontinued due to AEs (infusion site extravasation, pneumonia, and acute respiratory failure). AEs considered related to ESO treatment were of mild to moderate intensity and reported in 3 patients (1 patient from each group: 1–11 mo [1 mg/kg ESO], 1–5 y [10 mg ESO], 12–17 y [40 mg ESO]); none led to discontinuation of ESO. No clinically significant changes from baseline or in individual patients were observed for clinical laboratory values, vital signs, or ECG parameters. IV ESO was well tolerated in this population of 57 pediatric patients.

GASTROESOPHAGEAL REFLUX-ASSOCIATED DENTAL EROSION IS UNRELATED TO SALIVARY FLOW OR BACTERIAL LOAD

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Background: Dental erosion is a recognized extra-esophageal complication of gastroesophageal reflux (GER). While high bacterial load and decreased salivary flow is seen in caries, an association between erosion and salivary flow or bacterial load that leads to tooth destruction from caries is unknown. We performed an investigator-blinded cross-sectional study of the association of salivary flow rate and salivary bacterial load with dental erosion in children with and without GER symptoms.

Methods: Children (9–17 yrs) were identified as symptomatic or asymptomatic with GER by questionnaire. Permanence teeth were examined for dental erosion into dentin, erosion location (upper, lower, anterior, posterior), affected surface (facial, occlusal, lingual), and caries (Decayed, Missing, Filled Surfaces index). Stimulated salivary volume was measured over 2 min while chewing paraffin. Salivary bacterial load was calculated for all bacteria, Streptococcus mutans and Lactobacilli. Descriptive data are expressed as mean ± SD. Salivary flow was analyzed by Wilcoxon rank sum. Bacterial load was log-transformed and correlated using Spearman’s R.

Results: 79 children were studied: 69 (13.8 ± 2.4 yrs) with symptoms and 20 (12.4 ± 2.0 yrs) without symptoms of GER. Salivary flow rates were similar between groups (\(P = 0.77\)). Occlusal erosions correlated with salivary Lactobacilli (\(R = 0.29, P = 0.01\)) and predicted occlusal caries (\(P < 0.001\)), independent of facial or lingual surface
erosions. Total bacteria and Streptococcus mutans did not correlate with either erosions or caries.

**Conclusions:** Salivary flow does not associate with erosion. Occlusal erosion and Lactobacilli likely reflect caries activity in subjects with existing occlusal erosions. Location-specific erosions, not salivary flow or bacterial load, may aid in diagnosing GER before esophageal symptoms and injury. Further study is needed to examine the pathogenesis of GER-associated dental erosion.

**Motility/Functional Gastrointestinal Disorders**

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**FAMILIAL AGGREGATION FOR CONSTIPATION AND IRRITABLE BOWEL SYNDROME IN FAMILIES OF CHILDREN WITH CHRONIC FUNCTIONAL CONSTIPATION**

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**Background:** The aim was to evaluate the familial aggregation for intestinal constipation (IC) and irritable bowel syndrome (IBS) in families of children with chronic functional constipation (CFC).

**Methods:** Design: Case-control. Patients: Children with CFC taken care of in a pediatric referral hospital (cases) and children without CFC (controls). Dependent variable: Frequency of parents, aunts, grandparents and siblings with IC and/or IBS (Rome III criteria). Independent variables: socio-demographic, housing conditions, genogram, toilette control, physical activity, familial APGAR and food groups’ frequency intake. Analyzes: comparison of frequencies in 2 × 2 tables, risk estimation with OR and significance with CI 95%.

**Results:** Patients: 210 children, 70 cases and 140 controls; mean age: 8.8 ± 3.4 months, 111 (52.6%) were females. The proportion of relatives with IC and IBS was significantly higher in families of children with CFC (OR = 2.3, IC 7.8–3 and OR = 2, IC 1.6–2.7 respectively). When the data were analyzed by gender, children’s mother or father family lines and brothers or sisters, no statistical difference was demonstrated. The age at toilet control onset and its conclusion was significantly lower in the group with CFC. Comparison of sociodemographic variables, housing conditions, familial APGAR, intake food frequency and physical activity did not show differences.

**Conclusions:** Our study demonstrated familial aggregation for constipation and IBS in families of children with CFC. The search for other proposed factors associated to CFC showed no differences with the exception of age at toilet control.

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**USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE IN UNITED STATES PEDIATRIC PATIENTS WITH IRRITABLE BOWEL SYNDROME AND FUNCTIONAL DYSPEPSIA AND THEIR PARENTS: A PILOT STUDY**

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**Background:** Complementary and alternative medicine (CAM) use has been characterized in pediatric gastroenterology populations, but has not been specifically investigated in irritable bowel syndrome (IBS) and functional dyspepsia (FD). Conventional treatment of IBS and FD is generally unsatisfactory. In general pediatrics, CAM users were more likely to have a parent that used CAM. The aim was to identify patterns of CAM use in US pediatric patients with IBS and FD and their parents, including frequency and access.

**Methods:** Patients were identified via ICD-9 codes or GI office visit diagnosis of IBS or FD to enroll in a prospective survey. Survey packets, including CAM and questionnaire on PGI symptoms Rome III criteria, were distributed to 250 patients via mail or office visit. Of 40 consented patients, 20 met Rome III criteria for IBS or FD.

**Results:** 95% patients were Caucasian, 75% were female, 75% had IBS and 25% had FD, age 7 to 17 yrs, median 13 yrs. The prevalence of CAM use among patients and their parents was 40% and 60%, respectively. Both were most likely to use biologically-based CAM, such as vitamins and herbs. No children used CAM whose parents used no CAM or only one type of CAM. 92% of parents would consider using CAM if recommended by their PCP or GI specialist. 45% of parents reported that they did not discuss CAM at the visit because they were never asked.

**Conclusions:** CAM use is reported by a large number of both patients and parents of those with IBS and FD in this pilot study and is comparable to other pediatric diseases. We need to ask about CAM use, as parents often do not mention it. Further study with a larger sample size will investigate factors relating to intensity of CAM use and assess the factors that influence CAM choice.
NO RESPITE FROM ABDOMINAL PAIN ON SCHOOL WEEKENDS?
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Background: Previous studies have shown lower prevalence of abdominal pain (AP) consultations in summer than winter. This pattern has been commonly attributed to school stress. No studies have definitively proven a relation between school stress and AP. If school stress could solely explain this difference, AP intensity should parallel school stress. No studies have definitively proven a relation between school stress and AP intensity.

Methods: Post-hoc analysis of data obtained from a double-blind, randomized placebo-controlled prospective trial in children with functional GI disorders (FGIDs). Children 8–17 years from 6 centers with AP predominant FGIDs (Rome II) were recruited. Patients recorded AP (presence, frequency and intensity) daily for one month using a validated 0–100 mm VAS-Likert scale. Statistical comparison of AP intensity over weekday and weekends, both during school year and vacations, was calculated using unpaired 2-tailed t-test and Fisher’s exact tests. Post-hoc analysis of data obtained from a double-blind, randomized placebo-controlled prospective trial in children with functional GI disorders (FGIDs). Children 8–17 years from 6 centers with AP predominant FGIDs (Rome II) were recruited. Patients recorded AP (presence, frequency and intensity) daily for one month using a validated 0–100 mm VAS-Likert scale. Statistical comparison of AP intensity over weekday and weekends, both during school year and vacations, was calculated using unpaired 2-tailed t-test and Fisher’s exact tests.

Results: 76 children (58 girls, mean age 12.5). AP intensity was higher during school year (mean 41.3) than vacations (mean 31.3) (P < 0.0001). Weekdays AP intensity (mean 40.1) was similar to weekends (mean 40.3) (P = 0.8). Similar AP intensity during vacations weekdays (mean 35.3) and weekends (mean 33.3) (P = 0.9) and similar AP intensity during school year weekdays (mean 41.2) and weekends (mean 41.5) (P = 0.8). 37.3% of children had > 20% improvement in AP intensity on weekends over weekdays during school days and 33.3% children in vacation days (P = 1).

Conclusions: The study showed lower AP intensity during vacations over school time. There was no improvement in weekends over weekdays in school time or vacations. The study questions the exclusive role of school stress in AP.

ESOPHAGEAL LENGTH: ESOPHAGEAL MANOMETRY REMAINS SUPERIOR TO MATHEMATICAL EQUATIONS
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The pH probe study remains the gold standard to evaluate gastroesophageal reflux disease. Many mathematical equations based on height have been developed to estimate the esophageal length (EL) in normal children. The aim of this study is to re-evaluate the precision of 3 mathematical equations used to calculate EL when compared to measured EL by esophageal manometry (EM). Finding a relationship between patient’s height and measured EL was our secondary goal. Since 2000, at the Montreal Children Hospital, 127 children between the ages 4 to 17 years old, without previous esophageal surgery, had an EM (n = 144). During the same period, 54 EM were performed on 34 children with a previous history of esophageal surgery. For both groups, we compared the measured EL by EM to the calculated EL determined by the Strobel, the Song and the Jolley formulas. We also determined a correlation between subject’s height and EL measured by EM. All three equations were inaccurate in predicting the EL. The Strobel formula calculated an average EL 2.9 ± 0.17 cm too long compared to the measured EL. The Song and Jolley formulas calculated respectively an EL 3.4 ± 0.16 cm and 4 ± 0.16 cm shorter than the EM measurements (P < 0.001). The same inaccuracy was found for the surgical group. The height of nonsurgical children was found to be highly predictive of the lower esophageal sphincter location (LES) (r² = 0.85) and the relationship between the location of LES and height can be calculated with the regression equation: LLES = 0.23 (H) + 5.68. This study confirms that no actual known mathematical equation should be used for the placement of pH catheters, as they inaccurately predict the EL when compared to EM. As high resolution manometry becomes more available and easier to perform, pH probe placement by EM should become a standard clinical practice in the paediatric population, especially in surgical patients. As height is highly predictive of LES location in nonsurgical paediatric patients, the use of our mathematical equation could be considered for the placement of the ph probe in children between 4 to 17 years old, if EM is unavailable.

FUNCTIONAL GASTROINTESTINAL DISORDERS ARE MORE COMMON IN FAMILY MEMBERS OF CHILDREN WITH FUNCTIONAL ABDOMINAL PAIN AND IRRITABLE BOWEL SYMPTOMS THAN FAMILY MEMBERS OF CONTROL CHILDREN
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Background: Although functional gastrointestinal disorders (FGID) such as irritable bowel syndrome (IBS) are believed to have a genetic component and often “run in the family,” the occurrence of FGID in family members of children with functional abdominal pain (FAP) and IBS remains unclear.
Methods: We identified children 7–18 years of age who met the Pediatric Rome II criteria for FAP or IBS and age and sex matched children without abdominal complaints (Controls). Parents of both groups completed a self-report questionnaire to determine if any relatives had a FGID (i.e., IBS, FAP, constipation) or common GI symptoms (nausea, vomiting, diarrhea, bloating, or gas).

Results: There were 140 children in the FAP/IBS group and 85 children in the Control group. The mean age (± SD) and sex of the groups was 9.1 ± 2.1, 92 F vs 8.6 ± 1.1, 57 F, respectively. Ethnicity/race was similar between groups: 70.2% White, 9.8% Black, 17.3% Hispanic, and 2.7% Asian vs 74.1%, 3.5%, 18.8%, and 3.5%, FAP/IBS vs Controls, respectively. More children in the FAP/IBS group had a family member with a FGID overall than did Controls (Table). Similarly, specific types of FGID (IBS, FAP, and constipation) were found more often in the FAP/IBS vs Control groups (Table). In contrast, there were no differences between groups in the number of children with family members with symptoms of nausea, vomiting, diarrhea, bloating, or gas.

Conclusions: 1) IBS, FAP, and constipation are reported to be more common in family members of children with FAP/IBS than in Controls; 2) In contrast, the reported prevalence of GI symptoms is similar.

Table. Number of children who had a relative with the respective FGID and (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>All FGID</th>
<th>IBS</th>
<th>FAP</th>
<th>Constipation</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAP/IBS</td>
<td>56 (40.0)</td>
<td>34 (24.3)</td>
<td>20 (14.3)</td>
<td>11 (7.9)</td>
</tr>
<tr>
<td>Control</td>
<td>16 (18.8)</td>
<td>11 (12.9)</td>
<td>4 (4.7)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>P</td>
<td>0.001</td>
<td>0.039</td>
<td>0.026</td>
<td>0.033</td>
</tr>
</tbody>
</table>

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SINGLE-CENTER EXPERIENCE USING HIGH RESOLUTION ANORECTAL MANOMETRY IN CHILDREN
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Background: High resolution manometry using numerous closely spaced pressure transducers in conjunction with graphic pressure topography plots has been introduced as a new technology. The impact of high resolution anorectal manometry (HRAM) in children is unknown. The aims were: 1) To determine the indications and pathologic findings of using HRAM in children; and 2) To determine if HRAM may differentiate healthy children with defecation disorders with pelvic floor dyssynergia being the most commonly identified abnormality. HRAM was unable to add physiologic information to differentiate healthy children with constipation alone versus those with retentive fecal incontinence.

Results: 109 children underwent HRAM, of whom 60 (55%) were female. The mean age was 6.4 ± 0.5 (SE) years (range 0.2–17.8 years). 66 (60.6%) were Caucasian, 22 (20.2%) African-American, 18 (16.5%) Hispanic, and 3 (2.7%) Asian. Indications included 82 (75.2%) for constipation, 25 (23%) for retentive fecal incontinence, and 2 (1.8%) for non-retentive fecal incontinence. 7 children (6.4%) had undergone previous anorectal surgery. Abnormal findings included lack of a rectoanl inhibitory reflex in 5 (1 new Hirschsprung’s diagnosis, 1 new internal anal sphincter (IAS) achalasia, 3 previously known Hirschsprung’s). Of 62 children tested, 28 (45.1%) were identified with pelvic floor dyssynergia. Healthy children with constipation vs. those with RFI could not be differentiated on the basis of anal sphincter length, recto-anal inhibitory reflex threshold, external anal sphincter (EAS) contractile strength, or EAS contraction relative to IAS relaxation during the rectoanal inhibitory reflex.

Conclusions: HRAM may be successfully performed in children with defecation disorders with pelvic floor dyssynergia being the most commonly identified abnormality.
However, the convergence of symptom endorsement between children and parents was not strong \( (P > 0.06) \). A symptom endorsed by the child was not endorsed by the parent 56% of the time for Pstool, 38% of the time for Pfreq, and 37% of the time for Pform. 40% of children versus 26% of parents indicated the child met criteria for IBS. However, there was not significant agreement between child and parent \( (P = 0.91) \) with only 54% of the categorizations congruent between the pair. There were no significant differences in the proportion of participants classified as IBS between the child and parent respondents, and discordant categorizations were fairly balanced \( (P = 0.11) \).

**Conclusions:** There is a high discordance between child versus parent endorsements of IBS symptoms. These data have important implications for the use of questionnaires to assess occurrence of IBS symptoms in young children.

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**ARE MULTICHANNEL INTRALUMINAL IMPEDANCE MEASUREMENTS USEFUL IN ESOPHAGEAL ATRESIA?**

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**Background:** Patients with esophageal atresia (EA) frequently have esophageal dysmotility and gastroesophageal reflux which is often hard to characterize as these patients are often asymptomatic. Multichannel intraluminal impedance (MII) detects intraesophageal bolus movement. Our aim was to determine if MII is able to effectively detect the retrograde bolus movement (i.e. reflux) in patients with EA.

**Methods:** We reviewed MII tracings and medical records of 20 patients at our institution. Patients were categorized into 3 groups: patients with repaired EA (6), patients with documented gastroesophageal reflux disease (GERD) without EA (7) and patients with normal studies and without EA (7). Diagnostic accuracy of MII and symptom association were measured in the three groups. The baseline amplitudes of all 6 channels of the catheter were compared between the three groups at rest and in the recumbent position. In the subgroup of patients with EA, analysis of the impedance measurements in the 6 individual channels was performed, when the patient was upright.

**Results:** Symptoms of reflux captured by MII were higher in patients with GERD (50%) vs. pts with repaired EA (10%) which was statistically significant \( (P < 0.001) \). The baseline impedance value at rest in the recumbent position was significantly lower in patients with repaired EA \( (1108 \pm 110 \Omega) \) compared with patients with GERD \( (3263 \pm 186 \Omega) \) and controls \( (3219 \pm 200 \Omega) \) \( (ANCOVA, P < 0.001) \). The comparison of the individual values of the 6 impedance channels in the EA patients showed significant difference between the upper channels (channel 1: 6007 ± 1278 Ω) and the lower channels (channel 6: 564 ± 137 Ω; ANOVA, \( P < 0.001) \).

**Conclusions:** The low baseline impedance observed in EA patients with repaired EA appears to impair the capacity of MII to capture the changes associated with reflux in EA patients. This is postulated to be secondary to the poor esophageal function and/or stasis of liquid. A crucial first step in evaluating the efficacy of treating autistic behaviors with the various dietary restriction methods is to determine the prevalence of gastrointestinal symptoms in children with ASD.

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**PREVALENCE OF GI COMPLAINTS IN CHILDREN WITH AUTISM SPECTRUM DISORDER IN AN URBAN HOSPITAL-BASED PEDIATRIC PRACTICE**

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**Background:** Autism Spectrum Disorders (ASD) are neurodevelopmental disorders that emerge by age three. ASD involve deficits in communication and social interaction as well as repetitive behaviors. Research has sought to define the prevalence of GI complaints in pediatric patients with ASD; but estimates of prevalence have varied widely and referral biases are present. Many children with ASD are subjected to dietary restrictions (excluding casein and gluten, for example), despite the lack of objective evidence about the prevalence of gastrointestinal complaints and absent evidence to support the utility of restricted diets. A crucial first step in evaluating the efficacy of treating autistic behaviors with the various dietary restriction methods is to determine the prevalence of gastrointestinal symptoms in children with ASD.

**Methods:** A retrospective chart review was performed using the hospital-based electronic medical records of subjects age 3–21 years with ICD-9 codes or clinical documentation of a diagnosis of autism. The specific GI complaints assessed were abdominal pain, constipation, diarrhea, vomiting, failure to thrive, GERD, and presence of food allergies. Exclusion criteria were inflammatory bowel disease, motility disorders, anatomical abnormalities or malabsorptive disease.

**Results:** Preliminary data are available for 93 subjects with ASD who met inclusion criteria. 84% of these subjects were male; 66% were covered by private insurance and 34% by entitlements. 28 of the 93 subjects had at least one GI complaint, a prevalence of 30%; 12% had constipation, 7% food allergy, 6% GERD/vomiting/gastritis, and 2% had diarrhea. In addition, 5% of these subjects had FTT and 2% had gastrostomy tubes. Of note, 10% of these subjects currently were on or previously had tried a gluten- and casein-free diet.

**Conclusions:** GI complaints are prevalent in children with autism and should be screened for regularly during routine pediatric visits.
USE OF HIGH-RESOLUTION ESOPHAGEAL MANOMETRY IN THE EVALUATION OF CHILDREN WITH SUSPECTED ESOPHAGEAL MOTILITY DISORDERS
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Background: High-resolution esophageal manometry (HREM) has revolutionized the characterization of esophageal motility disorders in adults in terms of ease of performance and new analysis parameters. There is limited experience in children. The aim was to evaluate the use of HREM in pediatric clinical practice.

Methods: Fifty-four pediatric patients with dysphagia who underwent evaluation with a solid-state HREM assembly incorporating 36 manometric sensors were reviewed. At least ten saline swallows in each study were systematically evaluated with calculation of lower esophageal sphincter integrated relaxation pressure and analysis of the 30 mmHg isobaric contour plot for characterization of peristalsis and pressurization front velocity. HREM results were also compared with radiographic findings.

Results: The mean age was 14.3 ± 4.4 yr. Presenting complaints were: dysphagia (83%), gastroesophageal reflux (33%), chest pain (22%), vomiting (13%) and abdominal pain (7%). Based on HREM analysis, the esophageal motor findings were: normal peristalsis (33%), chest pain (22%), vomiting (13%) and abdominal pain (7%). On HREM analysis, the esophageal motor findings were: normal peristalsis (n = 16), peristaltic dysfunction (n = 21), and achalasia (n = 17). Of subjects with abnormal findings on HREM, 23/38 (61%) had abnormal findings on upper GI (UGI) contrast study suggestive of an underlying motility disorder, while 15/38 (39%) had normal UGI results. Of these 15 subjects, two subjects were diagnosed with achalasia and 13 were diagnosed with peristaltic dysfunction. HREM catheter placement and esophageal landmark localization was reported to be easier compared to conventional manometry by physicians and staff at our institution. The HREM procedure was well-tolerated by all patients and no adverse events were reported.

Conclusions: This study demonstrates that HREM is easy to perform, well-tolerated and a safe technique which provides important information in the evaluation of pediatric esophageal motility disorders. Further studies are needed to establish whether HREM provides a diagnostic advantage over conventional esophageal manometry.

FUNCTIONAL GASTROINTESTINAL DISORDERS (FGID): NOT JUST A GI PROBLEM
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Background: Many children with FGID suffer from complaints in other systems. There is no data about the non-psychiatric comorbidities of FGID in children. The aim was to assess the comorbidities of FGID in children in a questionnaire based study.

Methods: Prospective IRB approved study. We enrolled children with FGID who met ROME II criteria. The children or parents filled an extensive questionnaire to evaluate for non-GI complaints.

Results: 40 children were enrolled in the study (IBS: 19; Functional dyspepsia: 13; abdominal migraine: 4; Cyclic vomiting syndrome: 4). Orthostatic symptoms were very common, with 87% reporting orthostatic symptoms (dizziness, feeling sweaty, nauseated, etc). 20% reported having fainted >3 times in their lifetime. 52% reported more than 50 headaches in their lifetime, with 37% having headaches lasting >4 hours. Most of the headaches were described as throbbing and/or unilateral, with photo or phonophobia (85%) and associated with nausea/vomiting (65%). Chronic pains >3 month duration in the back, neck, and extremities were quite common (48%). Many children reported lack of energy (64%) and not feeling refreshed after sleep (52%). Other sleep complaints like difficulty falling asleep, waking up earlier than needed and having trouble staying awake during the day time were common (about 60%). Raynaud-like syndrome was reported in 31% (fingers turning white, blue or red with cold). Urinary symptoms were not common.

Conclusions: Children with FGID have many other associated symptoms that may contribute to poor quality of life. These symptoms may be exacerbate one another, for example poor quality of sleep worsening migraine or pain perception, and strongly suggest an interdisciplinary approach in the treatment of these disorders.

COMBINED MULTICHANNEL INTRALUMINAL IMPEDANCE-PH (MII-PH): A MULTICENTER REPORT OF NORMAL VALUES FROM 138 CHILDREN
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Background: Although combined intraluminal esophageal impedance pH monitoring (MII-pH) has replaced prolonged pH monitoring in detecting symptom association with gastroesophageal reflux (GER), the method does not have reference values established for children. Normal values for MII-pH parameters have been well established in healthy adults, the same is not true of the pediatric population. The aim of this collaborative study is to define normal pediatric values for MII-pH.

Methods: Multicenter retrospective chart review of all patients who were referred for esophageal multichannel intraluminal impedance (MII) from 2002–2010. MII-pH
variables included number of acid and non-acid reflux episodes, and time of reflux exposure for both types of GER episodes. The upper limit of normal was set to the 95th percentile. Inclusion Criteria: Children referred for impedance due to only respiratory symptoms and were found to have normal acid reflux index per age (<12% for <1 yr, <6% for children >1 yr). Exclusion Criteria: 1. acid suppression medication at the time of or up to 7 days before the MII/pH testing; 2. enteral feeding via NG or NJ tubes; 3. abnormal esophageal biopsies within 6 weeks of the impedance study; 4. previous fundoplication; and 5. studies lasting less than 20 hours.

Results: Forty-nine infants (21 F; age 0.25–11.89 months) were evaluated. The 95th percentiles for acid GER episodes (78), non-acid GER episodes (73), total GER episodes (108), acid GER exposure time (7.83%), non-acid GER (3%), and for total GER exposure time (8.94%). Eighty-nine patients age >1 yr (33F, age 1.29–18.17y) were evaluated. The 95th percentiles for acid GER (73), non acid GER (45), total GER (97), time acid exposure (5.32%), non-acid GER (1.95%) and total GER exposure time (5.9%).

Conclusions: This collaborative study characterizes the frequency and duration of acid and non-acid reflux in healthy children and provides normal values for 24 hour MII-pH monitoring for future comparison with GERD patients.

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COMPARISON OF SEASONAL PATTERNS OF ABDOMINAL PAIN CONSULTATIONS (APC) AMONG ADULTS AND CHILDREN
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Background: Consultations for chronic non-specific AP are frequent in adults and children. A seasonal pattern of APC with winter predominance is evident in pediatric studies; however no studies have investigated whether such a pattern exists in adults. Differences in seasonal patterns of APC between adults and children may indicate that either different mechanisms exist for common chronic conditions or that triggering factors may vary by age. The aim was to investigate whether a seasonal variation in APC patterns exists among adults and children.

Methods: The number of outpatient consultations among children (5–17 years) and adults (≥18 years) with a diagnosis of AP of non specified origin (ICD-9 code 789.0) from 5/2000 to 12/2008 was identified in an administrative claims database. The outcome measure was the rate per 1,000 (total number of APCs/total number of consultations × 1000) of APCs by season for children and adults. Seasons were defined as follows: winter (Dec-Feb), spring (Mar-May), summer (Jun-Aug), and fall (Sept-Nov). A trend test determined the degree of linearity in the patterns among the two groups. Among children, subanalysis by age 5–11 years and 12–17 years and gender were conducted.

Results: A total of 15.6 M patients with AP were identified (10.1% children; 89.9% adults) with 516.6 M total consultations (12.4% children; 87.6% adults). Children demonstrated a non-linear trend in APCs (R² = 0.030) with a quadratic trend found as the best fit (polynomial; R² = 1.000). This indicates a seasonal pattern in APC among children but not adults (linear; R² = 0.621). Seasonal variation of APCs among children stratified by age and gender was consistent with the overall child population.

Conclusions: Abdominal pain consultations in children are less common during summer months while APC among adults do not vary during the year. Factors involved in the pathogenesis of AP in adults and children may differ.

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SIMULTANEOUS HIGH-RESOLUTION MANOMETRY AND VIDEOFUOROSCOPY FINDINGS IN CHILDREN WITH ESOPHAGEAL SYMPTOMS
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Background: An esophageal motor disorder is considered when symptoms cannot be explained by conventional approaches. Aim: Compare conventional manometry (CM), high resolution manometry (HRM) and videofluoroscopy (VF) in children with unexplained esophageal symptoms.

Methods: Children evaluated by synchronized esophageal manometry and VF were evaluated (MMS, Netherlands). HRM was performed with 25 or 36 channel solid-state catheter. Barium liquid, coated solids and free drinking swallows were evaluated. HRM data was converted to 8 channel CM manometry.

Results: 23 combined HRM/VF studies were performed in 21 children (10 females, median age 10.1y range 0.7–19.5y). All had dysphagia, regurgitation 14, vomiting 8, chest pain 8, heartburn 6, throat pain 8, and choking 6. 11 had 2 or more symptoms. CM was abnormal in 16 (achalasia 8, nutcracker 1, non-specific motor disorder 6). HRM was abnormal in 19 (achalasia 8, nutcracker 1, hypertensive peristalsis 3, hypotensive peristalsis 5). With chest pain, 6 had esophageal spasm (4 diffuse spasm over 2 esophageal segments and 2 focal) and hypertensive peristalsis in 2. 5 with chest pain also had isolated high pressure esophageal contractions. 5 with regurgitation had hypotensive peristalsis. Throat pain had wide transition zone 6, focal esophageal spasm 2, diffuse esophageal spasm 2, and achalasia 1. VF was abnormal in 15 studies. VF findings were: slow bolus transit 13, retrograde bolus movement (14), functional LES obstruction 12, and anatomic abnormality 1. VF abnormalities were noted in: 7/14 regurgitation, 4/8 vomiting, 7/8 chest pain, 4/6 heartburn, 6/8 throat pain and 4/6 choking. Retrograde bolus
movement (bolus escape) occurred with achalasia 8, hypertensive peristalsis 3, and hypotensive peristalsis with transition zone abnormality 3.

Conclusions: Combined HRM and VF techniques are feasible in children. In children with chest pain symptom, esophageal spasm may be focal, and missed with CM. Bolus transit abnormalities were noted with VF. Further study will improve correlation of HRM and VF findings in children.

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ORTHOSTATIC INTOLERANCE AND ANTRODUODENAL DYSMOTILITY IN ADOLESCENTS WHO MEET ROME III CRITERIA FOR CHRONIC ABDOMINAL PAIN (CAP)

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Background: Functional abdominal pain (FAP) affects 10% of adolescents. Orthostatic intolerance (OI), as either neurally mediated hypotension (NMH) or postural orthostatic tachycardia syndrome (POTS), was noted in 20% of patients between the ages of 11 to 19 years. The Kennedy Krieger Institute has implemented the use of the Rome III questionnaire to better assess these patients. Adolescents who met the Rome III criteria for functional dyspepsia, IBS, abdominal migraine, functional abdominal pain or functional abdominal pain syndrome will have a higher prevalence of OI than by random chance.

Methods: Patients evaluated for CAP, ages 11–19, at our Motility Center who met criteria for the above stated functional disorders underwent tilt table testing (TTT) and concurrent AD assessment using MMS software.

Results: Twenty-two patients (9M:13F, ages 11 y 1 m to 19 y 8 m) underwent testing after completing the Rome III questionnaire. Twenty-one patients completed TTT and AD manometry successfully. Sixteen of twenty-two patients were noted to have OI (9 with POTS, 6 with NMH and POTS, 1 with NMH alone). Of the 21 patients who completed AD manometry, 5 were noted to have antral hypomotility, 2 with neurogenic intestinal dysmotility (NID), 5 with signs of rumination syndrome, 3 with NID during TTT and 8 with no dysmotility. Statistics: Using Stata TM 10.1 Data Analysis, we noted a prevalence of 0.727. Comparing against historical values, we find a $P < 0.001$, 95% CI 0.497–0.893; as determined by a one-sided test of binomial proportion. The prevalence of AD dysmotility was noted to be 0.62. Binomial proportion was not reported, due to the lack of reliable historical normative values.

Conclusions: In our experience, patients who meet Rome III criteria for CAP have a significantly higher prevalence of OI than by random chance. Future studies may include the treatment of OI as an adjuvant therapy for CAP patients.

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ENCOURAGING REGULAR TOILET USE: EFFECTIVENESS IN THE TREATMENT OF CHILDREN WITH FUNCTIONAL CONSTIPATION

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Background: Constipation is a common problem in pediatric practice. One of the recommendations for its treatment is to advise children to sit on the toilet after each meal; however, to date no studies support such recommendation. The aim of the study was to evaluate the effectiveness of a measure of intestinal training (postprandial toilet sitting) in managing children with functional constipation.

Methods: In a randomized clinical controlled study, 96 patients aged 4 to 18 years, diagnosed with functional constipation, were included. After initial assessment and after defining the basic therapy, children were randomized into two groups to receive the recommendation of sitting on the toilet after meals or not.

Results: Both groups showed clinical improvement regarding stool frequency, form and consistency, as well as retention behaviors and clogging the toilet. In the first review visit, 44.7% of patients reported following the studied recommendation, whilst only 15% did in the second. Improvement in stool frequency and retention behaviors was higher in the intervention group ($P < 0.01$). No differences were found in the second visit.

Conclusions: Advising children to sit on the toilet after meals may be useful in increasing stool frequency and diminishing fecal retention during the initial phase of management. As with other aspects of the treatment of constipation it may be recommended on an individual basis.

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SYMPTOMS OF PEDIATRIC CHRONIC CONSTIPATION: RESULTS OF QUALITATIVE INTERVIEWS WITH CHILDREN AND THEIR PARENTS

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Background: Chronic constipation (CC) is prevalent in children. Existing measures of pediatric CC symptoms do not meet regulatory requirements for Patient Reported Outcome (PRO) trial endpoints due to lack of patient input. This study’s aim was to develop a CC PRO symptom measure based on qualitative interviews with children and parents/caregivers.

Methods: Semi-structured concept elicitation interviews were conducted with children diagnosed with CC aged: 6–8 ($n = 10$), 9–11 ($n = 10$) and 12–17 ($n = 10$) years.
One parent per child and 20 parents of infants aged 6 months–5 years were also interviewed. Play-doh® and drawing activities helped children talk about their bowel habits and related impacts. Thematic analysis was used to identify concepts and evaluate saturation. Age appropriate items and response options developed were reviewed by expert clinicians.

**Results:** Bowel movement (BM) symptoms reported included: infrequent BMs (“not pooping”), difficulty defecating (“hard to poop”), straining (“I have to push hard”), rectal pain during a BM (“bottom hurts”), large stools (“big poops”), and a feeling of incomplete evacuation (“it won’t come out”). Non-stool/BM symptoms mentioned included: abdominal pain (“tummy hurts”), bloating (“puffy tummy”) and “gas.” For infants, behaviors parents associated with difficulty defecating included: crying, going red in the face, making a strained face, and hiding. Saturation was achieved for the above concepts.

**Conclusions:** Bowel, rectal and abdominal symptoms are important and bothersome to pediatric CC patients and should be included in treatment assessments. These qualitative interviews were used to develop comprehensive, developmentally appropriate, child self-report and parent/caregiver observation measures of CC symptoms for use in pediatric CC treatment trials. These methods are consistent with scientific standards and regulatory guidelines. The instruments are currently undergoing cognitive testing.

**DEVELOPMENT OF PEDIATRIC IRRITABLE BOWEL SYNDROME WITH CONSTIPATION MEASURES: RESULTS OF QUALITATIVE INTERVIEWS WITH CHILDREN AND THEIR PARENTS**

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**Background:** The Rome criteria for children/adolescents define Irritable Bowel Syndrome with Constipation (IBS-C) as abdominal pain or discomfort associated with constipation symptoms. Few, if any, pediatric IBS-C trials have used symptom measures that have been developed with patient input. The aim of this study was to conduct qualitative interviews with children with IBS-C and their parents/caregivers to develop a pediatric PRO measure of IBS-C symptoms.

**Methods:** Semi-structured interviews were conducted with children diagnosed with IBS-C aged: 6–8 (n = 10), 9–11 (n = 10) and 12–17 (n = 10) years. One parent per child aged 6–11, and 5 parents of the 12–17 year olds were also interviewed separately. Play-doh® and drawing activities were used to help children talk about their abdominal and bowel symptoms. Thematic analysis of transcripts was used to group quotes by concept and to evaluate conceptual saturation. Age appropriate items were developed to measure each concept and were reviewed by expert clinicians.

**Results:** IBS-C symptoms identified as being bothersome to children included: abdominal symptoms - abdominal pain (“stomach hurts”) and bloating (“tummy like a balloon”), and bowel symptoms - infrequent bowel movements (“don’t go often”), difficulty defecating (“it won’t come out”), straining on defecation (“have to push hard”), rectal pain during defecation (“butt hurts”), hard stools, large stools, and a feeling of incomplete evacuation (“some that won’t come out”). Saturation was achieved for the above concepts.

**Conclusions:** Results suggest bowel, rectal and abdominal symptoms are all important and bothersome to pediatric IBS-C patients and should be included in treatment assessments. These qualitative interview results were used to develop age-appropriate questions to evaluate this multi-symptom disorder, using methods consistent with regulatory guidelines. The instrument is currently undergoing cognitive testing.
Conclusions: There was no significant association between performance of endoscopies and persistence of AP or its severity. The study does not suggest that performing endoscopies with negative results improves the outcome of children with FGIDs.

Hepatobiliary/Transplant

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PREVALENCE OF LIVER DISEASE AMONG TYPE 1 DIABETIC CHILDREN
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Background: To determine the prevalence of liver disease among Type 1 diabetic (T1D) children.

Methods: Children with T1D in follow up in diabetic clinic at Children’s Hospital–King Saud Medical Complex, have been examined for existence of liver disease over a one year period. All have undergone the following: History, physical examination, blood tests (LFT, lipid profile, HbA1C, autoimmune markers: ANA, SMA, Anti-LKM antibodies), and U/S of the liver. A bright white liver on U/S was labeled as fatty liver due to T1D after extensive work up to rule out other underlying liver diseases.

Results: A total of 106 children, aged 8 months to 15.5 years, were evaluated (62 females). Twenty two patients (20.7%) were identified to have abnormal findings on U/S of the liver: 10 had enlarged liver with normal echogenicity, and 12 had hyperechogenic fatty liver. None of the patients in both groups had elevated liver enzymes. The group with hepatomegaly had better glycemic control and higher insulin dose when compared to patients without hepatomegaly: Mean HbA1c 9.4% vs 10.7%; Mean insulin dose 0.83 vs 0.74 U/kg/day, respectively. The group with fatty liver had poorer glycemic control when compared to patients without fatty liver (Mean HbA1c 12.14% vs 10.7%; P = 0.09). Four patients with fatty liver have celiac disease (33%) compared to 8 in the non-fatty liver group (8.5%) (P = 0.04). Autoantibody screen revealed a girl with positive anti-LKM antibodies and 4 had positive ANA, without evidence of liver disease.

Conclusions: Fatty liver is not uncommon in children with T1D and is more prevalent among children with poor glycemic control. All children with liver abnormality in this study are asymptomatic with normal liver enzymes which emphasize the importance of U/S of liver in screening for liver disease in children with T1D. Celiac disease could be a predisposing factor for development of fatty liver in patients with T1D. Anti-LKM antibodies can rarely be found in sera of patients with T1D; the clinical significance of which is unknown.

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FATTY LIVER IDENTIFIED BY ULTRASOUND AND SERUM TRANSFERSASES IN OBESE CHILDREN OF WEST MEXICO: CASE-CONTROL STUDY
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Background: The aim was to evaluate the association between obesity and fatty liver (FL) identified by ultrasound (US) and/or increased serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in children taken care of at a pediatric referral hospital.

Methods: Design: Case control. Patients: Children with obesity (BMI >95 percentile) and with healthy weight (BMI percentile between 5 and 85). Setting: West Mexico pediatric referral hospital. Protocol: Liver US and liver function tests were performed in 28 obese and 26 healthy weight children. US criteria for FL were liver-kidney eco-discrepancy and diminished portal vein ecogenicity. US, and transferases results were analyzed as dichotomic variables in 2 × 2 tables. Difference of frequencies was tested with χ² and Fisher. Risk was estimated with odds’ ratio and significance was evaluated with 95% CI.

Results: The mean age was 130.2 ± 35 months, without statistical difference between groups. Mean weight of cases and controls was 60.6 ± 22.1 and 39.7 ± 11.5 kg, respectively. In the obese, transferases were above normal values in 35.7% and 39.3% respectively; the OR was 6.7 and 7.8 with CI >1. The cases’ estimated risk of FL was 7.7 when evaluated with liver-kidney eco-discrepancy and 4.1 with diminished portal vein ecogenicity, both with significant CIs.

Conclusions: A significant association between obesity and FL was found in children from West Mexico, a novel finding in this population. The proportion of cases with FL doubles the cases of a similar report in Mexico City.

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ARM ANTHROPOMETRICAL INDICATORS PREDICT GROWTH IN CHILDREN WITH CHRONIC LIVER DISEASE
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Background: To correlate arm and growth anthropometrical indicators in children with chronic liver disease.

Methods: Design: Cross-sectional. Setting: A referral pediatric hospital. Patients: n = 94, 2–194 months, chronic liver disease. Variables: a) Mid upper arm circumference (MUAC); tricipital skinfold (TSK); subscapular skinfold (SSK); total arm area (TAA); fat arm area (FAA); and muscle arm area (MAA). b) Height for age (HA) and head circumference (HC). Analyses: Bivariate and multivariate regression.

Results: Mean age 64 months, 57% female. Diagnoses: Biliary atresia 37%, idiopathic CLD 13%, metabolic liver disease 11%, autoimmune hepatitis 7%. HA-TAA r = 0.61 P < 0.001; HA-MUAC r = 0.55 P < 0.001; HA-SSK r = 0.51 P < 0.001. HC-SSK and HC-TAA r = 0.53, P < 0.001 and r = 0.49, P < 0.001. Multivariate analyses led to 3 prediction models being the strongest for HA with MAA and TTA (r = 0.55, r² = 0.30, P < 0.001).

Conclusions: Growth was predicted by arm and fat body compartments in children with chronic liver disease of all age groups. This reflects the close relationship between growth and muscle plus fat reserves, as the substrate of growth.

LYSOSOMAL ESTERIFIED AND UNESTERIFIED CHOLESTEROL ACCUMULATION DIFFERENTIALLY AFFECTS LIVER CELL SURVIVAL: COMPARISON BETWEEN TWO MURINE MODELS OF CHOLESTEROL-ASSOCIATED LYSOSOMAL STORAGE DISEASE

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Background: Wolman disease (WD) and Niemann-Pick C disease (NPC1) are lysosomal storage disorders resulting from impaired intracellular cholesterol trafficking. WD is caused by loss of lysosomal acid lipase (LAL) while NPC1 is due to defective NPC1 protein. Hepatomegaly and liver dysfunction are seen in these two syndromes. The aim was to compare clinical, biochemical, and molecular features of liver involvement in murine models of WD and NPC1 disease.

Methods: 49 day old LAL (lal−/−) and NPC1 (npc1−/−) mice, and their corresponding wild types, were used to quantify relative liver weight, esterified (CE) and unesterified cholesterol (C) content, rate of cholesterol synthesis, relative mRNA levels of inflammatory markers and liver histology.

Results: Liver weights were 11 ± 0.3, 8 ± 0.1, and 5 ± 0.1% of body weights in lal−/−, npc1−/− and controls, respectively. Liver cholesterol contents (mg/organ) were 133 ± 8, 29 ± 1, and 3.2 ± 0.1 in lal−/−, npc1−/− and controls, respectively. CE was 91 ± 0.4% of the liver cholesterol in lal−/− mice while C was 98 ± 0.1% in npc1−/− mice. Rates of cholesterol synthesis (nmol/hr/organ) were 665 ± 281, 1013 ± 208, and 606 ± 93 in lal−/−, npc1−/−, and controls, respectively. While liver relative mRNA levels of CD68 and CD11c were about the same in both models, those of TNFβ were 11 fold higher in lal−/−. However, plasma ALT and AST were more elevated in npc1−/− mice. In support of the biochemical studies, histological examination showed more extensive lipidosis of hepatocytes in lal−/− than in npc1−/−.

Conclusions: In lal−/− mice, lysosomal cholesterol accumulation in the liver is almost entirely esterified in contrast to npc1−/− where it is mainly unesterified. This accumulation of liver CE in lal−/− mice results in greater hepatomegaly, much higher cholesterol accumulation, greater cholesterol synthesis, and strikingly higher TNFβ levels. Nevertheless, liver cell injury reflected by liver enzymes is greater in npc1−/−.
PORTAL VEIN COMPLICATIONS IN PAEDIATRIC LIVER TRANSPLANTATION

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Background: The aim was to determine the prevalence of portal vein (PV) complications and predictive factors for the same in our paediatric liver transplant population.

Methods: Retrospective review of all patients who received a liver transplant at the St. Justine Hospital (Montreal, Canada) from Jan 1986 to Dec 2008. PV complications were classified into three groups based on abdominal ultrasound findings: (A) all anomalies of PV blood flow and/or PV dilatations, (B) PV stenoses and (C) PV thromboses.

Results: During the 22 year study period, there were 194 cadaveric liver transplantations in 164 children. The median age of the children at transplantation was 3 years, the gender ratio was 1:1 and median weight was 14 kg. Biliary atresia was the most common indication for liver transplantation. The donors had a median age of 21.5 years and median weight of 57.5 kg. Ninety-four of the children received a reduced liver graft. The PV anastomosis was end-to-end in 148 and end-to-side in the remaining. PV complications were found in 41 patients and included 247 abnormalities of PV blood flow/dilatations (A), 9 PV stenoses (B) and 14 PV thromboses (C). The median time from transplant to the diagnosis of a PV complication was 3.7 months. No medical or surgical interventions were required in group A, 2 PV stents were placed in group B and 2 thrombectomies and 8 repeat liver transplantations were required in group C. There were 4 deaths in the PV thrombosis group. Greater PV complications were found in children receiving a complete liver graft versus a reduced liver graft and in transplants with a longer cold ischemia time. No other recipient, donor or surgical variables were predictive of the development of a PV complication.

Conclusions: Portal vein thrombosis post liver transplant in children has serious consequences requiring surgery or re-transplantation in most affected children while other abnormalities of PV blood flow and PV stenoses are generally benign. Complete liver graft and longer cold ischemia time are associated with an increased risk of developing a PV complication.

ASSOCIATION OF CONGENITAL HEPATIC FIBROSIS WITH PRADER-WILLI SYNDROME

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A 4 year old male Saudi child with history of recurrent rectal bleeding, delayed motor and speech development. He was born at full term by caesarean section. He was born to consanguineous parents. On physical examination he is pale but not jaundice. His weight and height were on the 90th and less than the 5th percentile, respectively. He has almond shape eyes, small hands and feet. His abdominal examination revealed hepatosplenomegaly. His CNS examination showed generalized hypotonia, his dysmorphic
features and hypotonia consist with the diagnosis of Prader-Willi Syndrome. His full blood count showed low hemoglobin and low platelets, his liver enzymes were normal. Abdominal ultrasound showed hepatosplenomegaly, upper gastrointestinal endoscopy showed esophageal varices, fundal varices and multiple erosion in the fundus. The liver biopsies confirm a diagnosis of congenital hepatic fibrosis. Molecular genetic studies confirm a diagnosis of UPD Type of Prader-Willi Syndrome. So in summary, we report a 4 year male Saudi child with UPD-Type Prader-Willi Syndrome in association with congenital hepatic fibrosis. This is the first association in the literature which is reported from Saudi Arabia.

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AUTOIMMUNE LIVER DISEASE IN CHILDREN: DIAGNOSTIC CHALLENGES AND OUTCOMES AT A CANADIAN PEDIATRIC CENTRE
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Background: Autoimmune liver diseases comprise a spectrum of clinical, biochemical, radiological and histological findings. The aim was to describe clinical presentation and outcomes in an Eastern Ontario/Western Quebec population served through a tertiary care pediatric hospital.

Methods: Retrospective chart review of patients diagnosed with autoimmune hepatitis (AIH), primary sclerosing cholangitis (PSC) and autoimmune sclerosing cholangitis (ASC) between 1998 and 2009.

Results: There were 14 children with AIH (57% female) and 10 with PSC (60% female). Mean age was 12.1 ± 3.8 years and 13.3 ± 4.4 years, AIH and PSC, respectively. Two males had ASC (mean age = 7.5 ± 0.7 years). Abdominal pain and jaundice were the most common complaints. 10 had ulcerative colitis (3 AIH, 6 PSC and 1 ASC). Liver enzymes were higher in AIH compared to PSC (AST: 851 vs. 71 IU/L, P < 0.001; ALT: 755 vs. 101 IU/L, P < 0.001). ALP:AST ratio was higher in PSC compared to AIH (1.1 vs. 0.1, P < 0.001); similarly GGT:AST ratio was higher in PSC compared to AIH (7.4 vs. 0.7, P < 0.001). GGT:AST ratio >2.7 was indicative of PSC. Autoantibodies were present in 13/14 children with AIH (8/14 ASMA, 1/14 anti-LKM and 10/14 ANA); 4/7 PSC were ANA+. Liver biopsies confirmed diagnosis of AIH in 11/14 children and PSC in 6/10. 13 patients underwent MRCP (5 AIH, 6 PSC and 2 ASC) and was diagnostic in 4 PSC cases. Celiac disease was found in 2/7 patients (1 AIH and 1 PSC). Treatment for AIH included steroids (12/14) and azathioprine (11/14). 8/10 children with PSC received ursodeoxycholic acid; one child with ASC received mycophenolate. Two patients underwent liver transplantation, one for fulminant AIH and one for cirrhosis in PSC.

Conclusions: Autoimmune liver diseases are uncommon in children and adolescents and many have associated gastrointestinal inflammatory conditions. The GGT:AST ratio seems to be a useful indicator of PSC. Many AIH children remain on immunomodulators however the need for liver transplantation is unusual.

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USE OF INTRAOPERATIVE CHOLANGIOGRAM TO EVALUATE FOR BILIARY ATRESIA
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Background: The diagnosis of biliary atresia (BA) in neonatal cholestasis (NC) remains challenging. While some centers perform a percutaneous liver biopsy (PLB) prior to a laparotomy, others proceed directly to an intra-operative cholangiogram (IOC) feeling that a negative PLB does not rule out BA. Little consensus on the optimal approach exists, and scarce literature is available on an acceptable rate of negative IOC when evaluating NC. We determined the rate of negative IOC in our institution and reviewed wedge liver biopsy results to identify patients in whom a PLB may have avoided an IOC. We also compared lab values between patients with BA and other causes of NC.

Methods: We performed a retrospective chart review of 30 patients with NC who underwent a laparotomy with IOC between 1/1/2008 to 3/31/2010.

Results: The overall rate of negative IOC was 47%. No difference was seen in the median age at presentation between patients who had BA and patients who had a negative IOC. The GGT was statistically higher in patients with BA (P < 0.05). Other lab values (ALT, AST, and bilirubin) did not differ significantly. All of the patients with BA who had a HIDA scan showed no excretion into the duodenum. Bile duct and/or cholangiolar proliferation was seen in the wedge liver biopsy of all patients with BA. Of those with negative IOCs, 50% did not have bile duct or cholangiolar proliferation. TPN hepatopathy was the most common diagnosis of those with negative IOCs. No cases of BA were missed during the study period.

Conclusions: The rate of negative IOC appears high at 47%. It is possible that more aggressive use of PLB could have avoided some of the negative IOCs. However, given that BA is a progressive disorder, patients with no evidence of bile duct proliferation on PLB would have needed serial liver biopsies to be sure evolving BA was not present. The cost and morbidity of IOC and wedge biopsy should be compared to serial liver biopsy.

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ANALYSES OF LIVER: BODY MASS REGULATION
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Liver mass is regulated in health and restored (by regeneration) after injury in proportion to body mass. For example, the liver:body mass ratio in wild-type C57Bl6/J mice is $\sim 4.5 \pm 0.1\%$. Following two-thirds (2/3) partial hepatectomy (PH), which is a model of liver regeneration, this ratio is restored over ~2 weeks. Despite long recognition of the precision with which liver:body mass is regulated, the mechanisms responsible remain incompletely characterized. For example, it is not known to what body mass compartment liver mass is proportionately regulated? To begin to address this question, we investigated the regulation of liver:body mass ratio in wild-type C57Bl6/J, heterozygous or wild-type controls (25 g/C24 g) from 2008–2010. Seven pts (4F/3M) ranged from age 2–21 (mean 12 yrs). Diagnostic indications were sclerosing cholangitis (n = 1), and referral for bile duct reconstruction (n = 1). Complications included post-procedure abdominal pain with normal pancreatic enzymes (n = 1), and bacteremia/sepsis (n = 1).

**Conclusions:** Choledochoscopy is an important diagnostic and therapeutic tool for children with hepatobiliary disease. Usage altered management and provided important clinical data in the majority of pts. Further experience with this technique will better define specific indications in pediatric populations.

### CHOLEDOCHOSCOPY IN PEDIATRIC PATIENTS: THE TEXAS CHILDREN’S HOSPITAL EXPERIENCE
Sanjiv Harpavat1, Isaac Raijman2, J.A. Hernandez1, Douglas S. Fishman1. 1Pediatric Gastroenterology, Texas Children’s Hospital, Houston, TX; 2Digestive Associates of Houston, Houston, TX.

**Background:** Choledochoscopy offers both diagnostic and therapeutic capabilities in patients with biliary disease, including direct visualization of biliary mucosa and the ability to take directed biopsies. We have previously reported our experience in adults, but choledochoscopy use has not been widely reported in children.

**Methods:** Eight cases of choledochoscopy were performed from 2008–2010. Seven pts (4F/3M) ranged from age 2–21 (mean 12 yrs). Diagnostic indications were sclerosing cholangitis (n = 4), abnormal imaging with obstruction (n = 3) and congenital anomalies (n = 2). Four of six were performed as part of pre- or post-OLT care. Two different choledochoscopes were used: Spyglass Spyoscope (n = 7) and Olympus SIF-180 (n = 1) in a patient with Roux-en-Y anatomy. Six cases were done perorally and two percutaneously. All peroral choledochoscopy pts had a prior biliary sphincterotomy and percutaneous usage was done as adjunct to primary percutaneous catheter (10 or 11F) placement. All pts received prophylactic antibiotics.

**Results:** Choledochoscopy was used to view biliary mucosa in all cases; demonstrated complete bile duct obstruction (n = 1), and endoscope unable to pass beyond the distal bile duct due to stricture (n = 1). Ductal tissue was biopsied (n = 2), facilitated cannulation (n = 2) of which an obstructed hepatic duct not visualized by ERCP was cannulated and decompressed with stent placement. In 6/8 (75%) cases, a suspected diagnosis was confirmed. In 7/8 (83%), results determined future management including OLT evaluation (n = 1) and referral for bile duct reconstruction (n = 1).

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**IMPACT OF PERINATAL PERIOD ON THE DEVELOPMENT OF HEPATOMEGALY IN OBESE CHILDREN**
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**Background:** The prevalence of obesity and comorbidities have dramatically risen over the past 2 decades. Although data suggests a role for early “imprinting” upon the development of chronic diseases, limited data exists regarding the relationship between the neonatal environment and non-alcoholic fatty liver disease (NAFLD) or hepatomegaly (H).

**Methods:** IRB-approved chart review of children (pts) presenting to the Weigh Smart(tm), pediatric weight management program, to determine the association between perinatal nutrition (i.e. breastfeeding and size for gestational age) with H and HOMA-IR (homeostasis model of insulin resistance). Data was analyzed using SPSS.

**Results:** From 2005 to present, 654 pts were enrolled - mainly female (64%) with a mean age of 12.4 years (SD = 2.7, range 7–19). Ethnicity data was available for 638 pts and included 117 (17%) Caucasians, 483 (76%) African-Americans, 18 (3%) Latinos, and 2 (0.3%) Asians. 121 pts (20%) had H. Of 187 pts who were breastfed (BF), 28 (15%) had H vs. 89/419 (22%) bottle fed pts. After adjusting for ethnicity and BMI in logistic regression model, a history of BF was independently associated with, and protective against, H (P = 0.022; OR = 0.54, 95% CI 0.32–0.91). Among 611 pts born at term, 89 (13%) had birth weight (BW) of <2.5 kg or small for gestational age (SGA), 504
(74%) had BW 2.5–4.5 kg or appropriate for gestational age (AGA), and 18 (2.7%) had BW >4.5 kg or large for gestational age (LGA). Size at gestational age was not associated with H in a univariate or adjusted model but was inversely associated with HOMA-IR score \( (P = 0.044) \) with differences noted between SGA and AGA \( (P = 0.047) \). Additionally, the mean HOMA-IR scores were higher in the H group as compared to pts without H \( (P = 0.002) \).

**Conclusions:** BF was an independent predictor, and protected against H. HOMA-IR scores were associated with supernumerary HB. Differences noted between SGA and AGA \( (P = 0.047) \). Additional studies that investigated supernumerary HB as previously reported. Additional studies that further define pts with liver disease (i.e., NAFLD, NASH), as well as prospective studies regarding perinatal influences upon liver disease, are needed.

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**150—WITHDRAWN**

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**USE OF ENTECAVIR IN CHILDREN WITH CHRONIC HEPATITIS B INFECTION**

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**Background:** Patients with chronic hepatitis B infection are at considerable risk for the development of cirrhosis and hepatocellular carcinoma. There is a paucity of reports on the treatment of children with chronic hepatitis B infection. Currently FDA approved drugs for the treatment of chronic hepatitis B in children included interferon alpha, lamivudine and adefovir. However, current approved treatment has limited virological response and a low rate of hepatitis B e antigen seroconversion. Entecavir which is an approved drug for HBV infection in adults is still in clinical trials for use in children. We report our experience with Entecavir treatment in children with chronic hepatitis B.

**Methods:** A retrospective analysis of data retrieved from medical records was performed. Four naive pediatric patients aged 6–17 years with active viral replication (HBV DNA > 20 x 10^5 IU/ml), histological and chemical evidence of liver inflammation (grade 1–2) and liver fibrosis (stage 1–2) were started on a fixed and off-label dose of Entecavir (0.5 mg po once daily). Liver biochemistry, hepatitis B DNA levels, serology, and safety were monitored. Our final objectives are sustained viral suppression and hepatitis B e antigen seroconversion.

**Results:** By week 12 all patients had normalization of their liver enzymes and a significant decrease in viral load. Two of the four patients after 56 weeks of treatment did not show seroconversion. The two other patients on treatment for 20 weeks have similar results. All the four patients remain with normal liver enzymes and a persistent decrease in their viral loads. None of our patients have any side effects so far.

**Conclusions:** Entecavir resulted in a significant viral suppression and decreased in liver enzymes without side effects. However, did not show promising results so far regarding seroconversion.

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**MINIMAL HEPATIC ENCEPHALOPATHY IN CHILDREN WITH CIRRHOSIS**

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**Background:** Minimal hepatic encephalopathy (MHE) is seen in patients (pts) with chronic liver disease (CLD). MHE is associated with altered cognitive function. There is paucity of information on MHE in children.

**Methods:** We prospectively evaluated children with cirrhosis between the ages of 5 and 18 years for evidence of MHE. The diagnosis of cirrhosis was based on biopsy/imaging/physical findings of portal hypertension in the context of CLD. Pts with neurologic, psychiatric, vision/hearing defects which might contribute to impaired cognitive function were excluded. Pts were considered to have MHE if they had one or more abnormal cognitive tests (pts scored 2 standard deviations [SD] below mean).

**Table.** Cognitive function tests and results

<table>
<thead>
<tr>
<th>Cognitive parameter</th>
<th>Cognitive function test (n = no. study subjects tested)</th>
<th>No. study subjects with score ≤-2 SD</th>
<th>Standard mean score ± SD</th>
<th>Scores for the study cohort (Mean ± SD)</th>
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<tr>
<td>Attention/Concentration</td>
<td>Wechsler Intelligence Scale for Children Digit Span (n = 11)</td>
<td>1</td>
<td>10 ± 3</td>
<td>7.7 ± 3.1</td>
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<tr>
<td></td>
<td>Connor’s Continuous Performance Task (n = 8)</td>
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<td>50 ± 10</td>
<td>55.5 ± 16.4</td>
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<tr>
<td></td>
<td>Stroop Test (n = 10)</td>
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<td>50 ± 10</td>
<td>47.3 ± 11.9</td>
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<tr>
<td>Fine Motor Skills</td>
<td>Wechsler Intelligence scale for Children Block Design (n = 13)</td>
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<td>10 ± 3</td>
<td>8 ± 3</td>
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<tr>
<td></td>
<td>Delis Kaplan Trail Making Test (n = 7)</td>
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<td>10 ± 3</td>
<td>7.3 ± 3.8</td>
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<tr>
<td>Processing Speed</td>
<td>Woodcock-Johnson-III Cognitive Abilities Visual Matching (n = 13)</td>
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<td>100 ± 15</td>
<td>94.7 ± 18.2</td>
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<td></td>
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<tr>
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<td>Wide Range Assessment of Memory and Learning Finger</td>
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<td>10 ± 3</td>
<td>7.1 ± 3.2</td>
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<tr>
<td></td>
<td>Windows Test (n = 12)</td>
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</tbody>
</table>

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**E62**

www.jpgn.org
Results: There were 13 pts (Female 8, Child-Pugh (CP) Class A 10, Class B 3). The mean age 10.4±5 years. The etiology of cirrhosis included: biliary atresia 5, primary sclerosing cholangitis 3, autoimmune hepatitis 1, alpha1 antitrypsin deficiency 2, cryptogenic cirrhosis 1, and cystic fibrosis related cirrhosis 1. The summary of the cognitive function test (CFT) results are given in Table 1. Six pts (46.2%, CP Class A 4, Class B 2) failed at least one CFT, indicating presence of MHE. One pt failed 4 CFT, one pt failed 3 CFT and 4 pts failed one CFT. Serum ammonia level was <50 mCmol/L in all pts except for one pt (62 mCmol/L).

Conclusions: MHE is common in children with cirrhosis. Visual memory and fine motor skills are especially affected. Larger studies are needed to better characterize MHE in children.

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THE SIGNIFICANCE AND SPECTRUM OF SLC25A13 GENE MUTATION IN CHINESE INFANTS WITH INTRAHEPATIC CHOLESTASIS AND AMINOACIDEMIA

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Background: SLC25A13 gene mutations cause citrin deficiency, which leads to neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD). The aim of this study is to explore the significance and the spectrum of the SLC25A13 gene mutation in Chinese infants with intrahepatic cholestasis and aminoacidemia.

Methods: 39 infants with intrahepatic cholestasis and various aminoacidemia were enrolled. All the exons of SLC25A13 gene was sequenced and previously reported big insertions were analyzed accordingly. Homology and structural predictions were analyzed for the novel mutations. Western blot were performed in the cases with liver specimens available.

Results: Genetic tests combined with Western blot analysis showed SLC25A13 gene mutations existed in 28 cases, including 9 heterozygotes, 6 homozygotes and 13 compound heterozygotes. 19 cases could be definitely diagnosed as citrin deficiency, account for 48.7% of the total. Eleven types of mutation including 8 known mutations and 3 novel mutations were found. Out of 46 mutated alleles, the known mutations include 851del4 in 26 alleles (56.5%), 1638ins23 in 6 alleles (13.0%), IVS6+5G>A in 2 alleles (4.3%), E601K in 2 alleles (4.3%), IVS11+1G>A in 1 allele (2.1%), R184X in 1 allele (2.1%), R360X in 1 allele (2.1%) and R585H in 1 allele (2.1%). The three novel mutations were splice site change IVS6+1G>A, deletion mutation 1092_1095delIT and missense mutation L85P each in 1 allele. Absence or abnormal citrin protein was demonstrated for novel mutation L85P and IVS6+1G>A.

Conclusions: Mutation spectrum of the SLC25A13 gene in Chinese is different from that of other population groups in East Asia. SLC25A13 gene mutation is the most important cause of infantile intrahepatic cholestasis with various aminoacidemia.

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ASSESSMENT OF RISK TAKING BEHAVIOR IN ADOLESCENTS AFTER LIVER TRANSPLANTATION

Joshua D. Prozialeck, Krista Tuzinkiewicz, Estella M. Alonso. Children’s Memorial Hospital, Chicago, IL.

Background: Adolescence is a period of tremendous change. This transition may be compound in liver transplant patients due to stressors associated with their chronic condition including parental dependence, peer acceptance, delayed or stunted growth and changes in physical appearance. The aims for this study were to assess the risk behavior profile of our transplant population and to identify specific health topics that should be addressed after surgery.

Methods: Modified versions of the 2007 Youth Risk Behavior Surveillance (YRBS) published by the Centers for Disease Control and Prevention were administered anonymously. Questions were added about transplantation history. The results were compared to age, race, and gender matched respondents of the 2007 YRBS. Guardians answered socioeconomic status questions.

Results: Twenty-six patients completed the survey. There were no significant differences in smoking, marijuana use or sexual behaviors between the groups. Transplant patients reported significantly less lifetime alcohol use (42.3%) than their peers (75%, P = 0.001). Those who chose to drink started at similar ages (54.5% vs 57.5% were <15 years old, P = 0.858) and with the same monthly use (54.5% vs 58.9% had >2 drinks a month, P = 0.768) and binge-behavior (36.4% vs 33.8% had ≥5 drinks in a row within hours P = 1.0) as controls. Teens after transplant had significantly fewer periods of sadness and hopelessness for two or more weeks in a row than peers (3.8% vs 31.7%, P = 0.002). There were no significant differences in bike helmet or seat belt use, fighting, drinking and driving, violence or suicide.

Conclusions: Liver transplant adolescents were less likely to drink underage and reported fewer feelings of sadness; however, in all other areas evaluated, they took similar health risks as their peers. A more comprehensive assessment of attitudes related to behaviors that might impact graft function and of anticipatory guidance programs that highlight high-risk behaviors as detrimental to post-transplant health are warranted.

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EFFECTS OF RURAL STATUS ON HEALTH OUTCOMES IN PEDIATRIC LIVER TRANSPLANTATION


Background: The objectives were (1) To determine whether living in rural areas with less access of care impacts health outcomes after pediatric liver transplantation (LT). (2) To
determine whether rural status correlates with poorer health at the time of LT.

**Methods:** Urban influence codes published by the USDA were used to stratify patients as urban or rural depending on zip codes and county of residence. 388 patients who had LT between the years of 1998 and 2008 were included in our investigation. Graft rejection, PTLD, and survival were used as primary outcome measures of post-LT health. UNOS Status 1 and PELD/MELD scores > 20 were used as secondary outcome measures of poorer pre-LT health. Adjusted and unadjusted logistic regression models were run using predictor variables of age, gender, distance to LPCH, and rural status.

**Results:** 9.3% were identified as residing in a rural area. Age and gender were comparable between the two groups. Patients in rural areas traveled farther to LPCH for LT than patients from urban areas (mean of 889 vs 380 miles). General trends show that rural patients may have decreased incidence of graft rejection (25.0 % vs 33.4 %; OR 0.64, 95 % CI 0.39–1.43), increased risk of PTLD (5.6 % vs 3.4 %; OR 1.86, 95 % CI 0.36–3.31), and decreased survival (OR 0.85, 95 % CI 0.29–1.44), increased risk of PTLD (5.6% vs 3.4%; OR 1.20, 95% CI 0.59–2.45). Though not statistically significant, trends show that patients from rural areas were sicker at the time of LT with increased proportion of Status 1 (OR 1.17, 95% CI 0.51–2.70) and PELD/MELD scores > 20 (OR 1.59, 95% CI 0.59–2.45).

**Conclusions:** From a single center experience, rural status did not significantly affect health outcomes after LT; although patients in rural areas may have decreased rejection, increased PTLD and mortality, and be in poorer health at the time of LT.

<table>
<thead>
<tr>
<th>Table. Effects of Rurality on Outcome Measures</th>
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<tr>
<td>Effect of Rurality (dy/dx)</td>
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<tr>
<td>Rejection risk</td>
</tr>
<tr>
<td>PTLD risk</td>
</tr>
<tr>
<td>Survival</td>
</tr>
<tr>
<td>PELD/MELD &gt; 20</td>
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<tr>
<td>UNOS Status 1</td>
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</table>

**Methods:** SRTR data was reviewed on CF patients who underwent transplantation between 1987 and 2009.

**Results:** A total of 3252 patients were transplanted (746 pediatric). The most common organ transplant was lung, n = 3013, 88.93% followed by liver, n = 259, 7.64% and Lung-heart, n = 56, 1.65%. Patient survival for adults was 55% at 5 years and 38% at 10 years. Survival for children was 52% at 5 years and 36% at 10 years. Outcome for abdominal organs in adults (n = 60) at 5 years was 64%, and at 10 years, 45%. Combined thoracic and abdominal transplant (n = 19) survival at 5 years was 62%. In children thoracic organ (n = 541) survival at 5 years was 43%, and at 10 years, 26%. Abdominal organ (n = 197) survival was 76% at 5 years and, at 10 years 61%. Combined thoracic and abdominal transplant (n = 8) survival was 75% and at 5 and 10 years.

**Conclusions:** The most favorable outcome for solid organ transplantation in the CF population is liver transplantation which is mainly performed in pediatric patients. There appears to be a survival advantage to combined abdominal and thoracic organ transplantation primarily in children although the sample is small.

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**INTRACTABLE PARENTERAL NUTRITION-ASSOCIATED CHOLESTASIS IN INFANTS: CLINICAL EFFICACY OF BILIARY IRRIGATION**


**Background:** Parenteral nutrition-associated liver disease is a major complication encountered with prolonged parenteral nutrition (PN). Aim: To describe our experience in treating intractable PN-associated cholestasis (PNAC) with biliary irrigation (BI).

**Methods:** A retrospective chart review of infants diagnosed with intractable PNAC that were treated with BI between 2005 and 2009. Intractable PNAC was defined as a sustained or elevation of direct bilirubin (DB) above 3 mg/dl despite being on trophic or full enteral feeds. Results were compared using paired Student’s t test.

**Results:** Six infants were identified (3 months to 11.5 months of age). Four subjects were former premature infants (31, 32, 33, 34 wks). The time on PN was 78 days to more than 12 months. Four subjects were on goal enteral feedings when they had worsening of serum DB, and rest of the LFT panel. All subjects had long-term ursodioxycholic acid. Hepatobiliary ultrasonography showed no abnormalities. A HIDA scan on three subjects showed poor uptake and no biliary excretion. Liver biopsies were performed on all subjects. Histopathology showed moderate-severe biliary duct proliferation and fibrosis stages ranging from Metavir F1-F2 (4/6) F3 (1/6) and F4 (1/6). Cholangiogram studies intra-operatively or via ERCP showed normal intra- and extra-hepatic biliary...
systems. BI procedures with normal saline or gastrografin/saline were performed. One subject developed a small intra-abdominal hematoma post-procedure. Five patients had improvement in the DB level 2–4 wks post-BI. Three subjects had normalization of liver panels at 2–3 months post-BI. 2 had normalization of liver panel at 6 months, and 1 did not show any improvement and required a liver transplant 6 wks later. Mean DB pre-BI (excluding the liver Tx) declined from 9.6 mg/dL to 0.5 mg/dL. (P = 0.0019).

**Conclusions:** BI is relatively safe and effective in reversing intractable cholestasis in non-cirrhotic PN-associated liver disease.

**Mean Direct Bilirubin:**

<table>
<thead>
<tr>
<th>Prebiliary Irrigation</th>
<th>9.6 mg/dL</th>
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<tbody>
<tr>
<td>6 Months Postbiliary Irrigation</td>
<td>0.5 mg/dL</td>
</tr>
<tr>
<td><strong>P</strong></td>
<td>0.0019</td>
</tr>
</tbody>
</table>

### 158

**PREVALENCE OF ACUTE ASYMPTOMATIC GROUP A ROTAVIRUS INFECTION IN INFANTS ENROLLED IN THE BILIARY ATRESIA RESEARCH CONSORTIUM (BARC)**

Maria Grazia Clemente, John T. Patton, Umesh D. Parashar, Peter F. Whittington, Robert H. Yolken, Trivellore E. Raghunathan, Kathleen B. Schwarz, 1, Daniel D’Agostino. Johns Hopkins University, Baltimore, MD; 2NIH/NIAID, Bethesda, MD; 3Children’s Memorial Hospital, Northwestern University, Chicago, IL; 4Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA; 5The Stanley Division of Developmental Neurovirology, Johns Hopkins University, Baltimore, MD.

**Background:** Biliary Atresia (BA) is a severe cholangiopathy of unknown origin; a murine model secondary to rotavirus (RV)suggests a viral etiology. Acute asymptomatic RV (ARV) infection—defined by positive anti-RV IgM in absence of gastroenteritis—affects 5% of normal newborns. The aim was to investigate the prevalence of ARV in infants with BA and with other causes of cholestasis enrolled in BARC, at ~2 mos of age.

**Methods:** 40 BA infants and 38 controls matched for RV season and birth year were studied. RV-IgM and RV-IgG were measured by ELISA using plates coated with purified RV. Results were expressed as enzyme immunoassay unit (EIU) or as negative/positive when cut-off (CO) = 3SD > mean of NC (low CO) or when CO = x 3 the mean of NC (high CO).

**Results:** No difference of RV IgM and IgG was found between BA and controls. The prevalence of ARV ranged between 10% and 40% depending on the cut-off used. Low cut-off = all samples were RV-IgG positive, while 16 of 40 BA (40%) and 14 of 38 controls (36.8%) were RV-IgM positive (P = NS). High cut-off = 35 of 40 BA (87.5%) and 33 of 38 controls (86.8%) were RV-IgG positive (P = NS) while 4 of 40 BA (10%) and 7 of 38 controls (18.4%) were RV-IgM positive (P = NS). Table shows EIU results.

**Conclusions:** The prevalence of ARV does not differ between cholestatic young infants with BA and other diagnoses. However the prevalence of 10 - 40% is higher than previously published rates in this age group. Whether a proportion of BA is secondary to RV infection in genetically susceptible infants awaits further study.

| BA infants | Non-BA infants |
| n = 40 | n = 38 |
| Mean EIU (SE) | Mean EIU (SE) | t-test value | 2-sided P |
| Serum-RV-IgG | 45.6 (6.2) | 63.5 (7.5) | 1.85 | 0.07 |
| Serum-RV-IgM | 10.0 (1.45) | 13.2 (2.8) | 1.02 | 0.31 |

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**SENSITIVITY AND SPECIFICITY OF PELD SCORE IN FULMINANT HEPATIC FAILURE TO ASSESS BAD PROGNOSIS**


**Background:** Although accurate prognosis in FHF is a paramount goal, prognostic scoring systems still fail to achieve success. PELD model has been found to be an excellent predictor of mortality in children with chronic liver disease listed for OLT. However, experience with PELD in FHF is limited. The aim was to investigate the prognostic accuracy of the PELD in children with FHF admitted to our liver transplant center and to investigate the prognostic value of hyponatremia and encephalopathy in FHF.

**Methods:** PELD score was calculated on the results of blood tests obtained on hospital admission in 40 consecutive patients aged <18 years who presented with FHF from June 1999 to January 2009. Bad outcome was defined as liver transplantation or death. Hyponatremia was defined as serum sodium <135 mEq/L.

**Results:** Mean age was 5.3 ± 4.4 years (7.6 mo-17 years) A total of 52.5% were females (n = 21). Etiology of FHF was Hepatitis A in 14 (42.5%), indeterminate in 17 (32.5%), autoimmune hepatitis in 5 (12.5%), autoimmune hepatitis 2 in 2 (5%) and toxic in 2 (5%). PELD mean score was 34.92 ± 10.48 (r 6–55). PELD scores obtained on admission were significantly higher among nonsurvivors (39.8 ± 9.5) and patients receiving transplants (39.7 ± 1.7) compared to those who survived without OLT (31.3 ± 3) (P < 0.001). A cutoff of 33 in PELD score using ROC curve showed 81% specificity and 86% sensitivity for bad outcome (PPV 92% y NPV 69%, AUC 0.88). Mean serum sodium level was 136 ± 4 mEq/L. Using logistic regression, hyponatremia wasn’t associated with an increased risk in patients with FHF listed for LT. The presence or grade of encephalopathy didn’t increase the risk of transplantation with a PELD higher than 33 (OR 1).
Conclusions: PELD score obtained upon admission may be of help to establish the optimal timing for pre-OLT evaluation and listing. Further validation in larger and different populations is needed. This study showed that the presence of hyponatremia or encephalopathy was not associated with an increased risk.

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THE ASPARTATE AMINOTRANSFERASE TO PLATELET RATIO INDEX (APRI) PREDICTS LIVER FIBROSIS PROGRESSION IN INFANTS WITH SHORT GUT ON PARENTERAL NUTRITION

Michael G. O’Connor, Shane R. Mangus, Rodrigo Vianna, A.J. Tector. Indiana University School of Medicine, Indianapolis, IN.

Background: Infants with parenteral nutrition (PN) dependence may develop cholestatic liver dysfunction. We have previously shown that aspartate aminotransferase to platelet ratio index (APRI) has good correlation with liver fibrosis progression in infants with short gut. This study applies APRI to PN-dependent short gut infants to determine hepatic fibrosis progression in patients stratified into study groups: estimated gestational age (EGA), age at initial intestinal resection, and residual intestinal length.

Methods: Study inclusion criteria included infants less than 1 year at initial intestinal resection with subsequent continuous PN-dependence of 3 months or greater. Laboratory values (total bilirubin, AST, ALT, calculated APRI) and biopsies were collected from initial intestinal resection, and thereafter for 26 weeks. Fibrosis scoring used the META VIR system and ranged from F0 (normal) to F4 (cirrhosis). For each study group, children were divided into three stratifications. Liver function values over time were analyzed as predictors of fibrosis progression.

Results: Thirty-one children, less than two months at time of initial intestinal resection (range 0–58 days, mean 12.6 days), were included in the study. APRI was the only tested liver function value statistically associated with META VIR score F ≤2:1.87, F3: 5.71 F4: 14.74 (P = 0.02). All liver function values for all groups increased with time. For EGA and age at initial intestinal resection, APRI shows points of statistical separation of younger ages and greater variability amongst age stratifications in relation to PN duration. For residual intestinal length, APRI has the least variability across all residual lengths and no statistical separations seen amongst the stratifications.

Conclusions: APRI clearly delineates fibrosis grades. Post resection while on continuous PN, APRI has less variability across residual intestinal length stratifications and demonstrates an ability to show separation of younger children.

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DE NOVO NONALCOHOLIC FATTY LIVER DISEASE AFTER LIVER TRANSPLANT IN CHILDREN

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1Pediatric Gastroenterology, Hepatology and Nutrition, Emory University School of Medicine, Atlanta, GA; 2Department of Pathology, Children’s Healthcare of Atlanta at Egleston, Atlanta, GA; 3Department of Surgery, Division of Transplantation, Emory University School of Medicine, Atlanta, GA.

Background: It is well known that non-alcoholic fatty liver disease (NAFLD) is contributing to morbidity and mortality in liver transplant recipients. Previous reports in adults have shown that NAFLD can develop in post transplant patients. As obesity has increased in children, more pediatric transplant patients have features of metabolic syndrome, which can lead to NAFLD a common complication of overnutrition and obesity. The prevalence of NAFLD in the pediatric population is increasing and is a particular challenge when it develops in post transplant livers.

Methods: We performed a retrospective case-control study and examined all liver biopsies reporting steatosis in pediatric liver transplant recipients over the last 5 years at our center.

Results: Of the 306 liver transplant patients that are followed in our center, 10 were found to have steatosis on post transplant liver biopsy. Two had focal steatosis and 8 had at least moderate steatosis. Two cases were identified as non-alcoholic steatohepatitis (NASH). One child had 3 liver biopsies over 3 years and progressed from steatosis to NASH. The majority of the patients were on a very low dose of prednisone but 3 patients were on high doses of prednisone or received intravenous steroid boluses several days prior to the biopsy. Six of the 10 patients were overweight at the time of biopsy.

Conclusions: De novo NAFLD and steatosis is a rare complication in children post liver transplant and can progress rapidly to NASH. Both medications and excess weight gain likely contributed to our cases of steatosis. We did not have donor liver biopsies in the majority of our patients. To identify if the disease was present in the donor liver further studies are required to examine the potential role of mild NAFLD donor livers in the long term graft survival.

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REGRESSION OF INTESTINAL FAILURE INDUCED HEPATIC FIBROSIS

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The development of hepatic fibrosis in pediatric patients is traditionally believed to be progressive and irreversible. We present two patients with parenteral nutrition associated liver disease (PNALD) enrolled in the UAB Intestinal Rehabilitation Program that previously had extensive complete portal
to portal bridging fibrosis determined by liver biopsy. Case 1: CZ is a former 27 week infant that developed necrotizing enterocolitis (NEC). He underwent numerous surgical procedures and is PN dependent secondary to short-bowel syndrome (108 cm of small bowel) and intestinal failure (IF). A liver biopsy performed at 7 months of age revealed PNALD with complete portal to portal bridging fibrosis. Over the subsequent months, his enteral nutrition was advanced but continued to require PN to achieve appropriate weight gain. His serum transaminase and direct bilirubin values returned to normal during his ongoing IR. A follow up liver biopsy performed at 16 months of age during an operation for central venous line placement revealed marked improvement with regression of hepatic fibrosis. Case 2: JW is a former 29 week infant with IF following NEC and multiple surgical interventions. At his last operation, he had 48 cm of residual small intestine. Intestinal rehabilitation (IR) was undertaken, including the use of intravenous omega-3 containing lipids and enteral feeding advancement. A liver biopsy performed at 8 months revealed complete bridging fibrosis. Over the next 6 months, his serum transaminase levels and direct bilirubin normalized. A repeat liver biopsy obtained at 15 months of age demonstrated only focal portal fibrosis. Some patients with IF undergoing IR have biochemical and histological evidence of resolving PNALD. These findings demonstrate that the IF associated hepatic fibrosis can be reversible, thus providing a longer period for attempted IR and possibly avoiding the need for visceral transplantation.

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INTESTINAL TRANSPLANTATION IN INFANTS YOUNGER THAN 1-YEAR OF AGE IN THE CURRENT ERA

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Background: Parenteral nutrition (PN)-dependent infants with short gut are at high risk of cholestatic liver disease and cirrhosis. Intestinal transplantation may be indicated for these children when the infant develops bridging liver fibrosis or cirrhosis, loss of vascular access or recurrent life-threatening central venous catheter infections. Intestinal transplantation in children less than 1-year of age, or less than 10 kg in weight, carries a high risk for lack of organ donors and risk of surgical complications. This study reports the results of 10 infants that underwent intestinal transplantation between 2007 and 2010.

Methods: Inclusion criteria for this analysis included pediatric intestinal transplant patients less than 1-year of age and less than 10 kg in weight. There were no exclusions. The primary study outcomes included PN-independence and patient survival.

Results: Ten infants underwent intestinal transplantation. Their ages ranged from 3 months to 12 months of age. Weight at transplant ranged from 4.5 kg to 9 kg. Donor ages ranged from 6 weeks to 13 months of age. Three infants received isolated intestinal transplant while 7 underwent multivisceral transplant (MVT; liver, stomach, pancreas, intestine). All 3 isolated intestine patients had lost their entire small intestine, while the MVT patients developed end-stage liver disease secondary to PN and short gut. Two patients (both isolated intestine patients) died within 3 months of transplant from viral respiratory illnesses (80% survival). All other patients are alive and well with normal growth and development. Median time to PN-independence was 21-days post-transplant.

Conclusions: These results demonstrate that infants less than 1-year of age can successfully undergo both isolated intestine and multivisceral transplant with good outcomes. Very young infants, less than 3 months of age, can be used routinely as organ donors for these children. Intestinal transplantation remains a viable alternative for young infants with life-threatening complications of intestinal failure.

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ROLE OF PHENOBARBITAL IN PREVENTION OF TOTAL PARENTAL NUTRITION-ASSOCIATED CHOLESTASIS IN PREMATURE INFANTS

Farhana Basit, Sabeena Farhath, Judy Saslow, Suganya Kathiravan, Vishwanath Bhat, Gary Stahl, Kee Pyon, Nicole Kemble, Zubair H. Aghai. Department of Pediatrics/Neonatology, Cooper University Hospital, UMDNJ - Robert Wood Johnson Medical College, Camden, NJ.

Background: Total parental nutrition (TPN)-associated cholestasis is common in premature infants and can lead to short and long term morbidities. Phenobarbital (PHENO) may prevent TPN-associated cholestasis by enhancing the excretion of bile. The aim was to study the effect of PHENO therapy on prevention of TPN-associated cholestasis in preterm infants.

Methods: Preterm infants (<1200 grams) born between 2000–2009 and treated with PHENO for seizures or neonatal abstinence syndrome starting within two weeks of life (study group) were compared with infants who did not receive PHENO (control group). Cholestasis is defined as direct bilirubin ≥ 2.0 mg/dl. The groups were compared for baseline demographics, risk factors for TPN associated cholestasis, and incidence and severity of cholestasis.

Results: 46 preterm infants (mean ± SD, BW 856 ± 221 g, GA 26.7 ± 2.5 weeks) were treated with PHENO and 90 infants did not receive PHENO (BW 806 ± 140 g, GA 26.2 ± 2.0 weeks). Median (range) age of starting PHENO was 3 days (1–13 days) and median duration was 55 days (21–186 days). There was no significant difference in baseline demographics and risk factors for cholestasis between the two groups. The incidence and severity of cholestasis was significantly higher in infants who were treated with PHENO compared to control group. The number of infants
Conclusions: Prophylactic PHENO started during second week of life did not prevent TPN-associated cholestasis in preterm infants. Early use of PHENO may worsen TPN-associated cholestasis in premature infants.

Table.

<table>
<thead>
<tr>
<th></th>
<th>PHENO group</th>
<th>Control group</th>
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<tr>
<td></td>
<td>(n = 46)</td>
<td>(n = 90)</td>
<td></td>
</tr>
<tr>
<td>Cholestasis</td>
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<td>19 (21.1)</td>
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<td>Direct Bilirubin &gt;5 (%)</td>
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</tr>
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<td>6 (13.0)</td>
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<tr>
<td>Cholestasis at discharge (%)</td>
<td>14 (30.4)</td>
<td>8 (8.8)</td>
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OUTCOME OF PEDIATRIC AND YOUNG ADULT PATIENTS WITH HCV INFECTION TREATED AT A PUBLIC SECTOR HOSPITAL OF KARACHI

Sina Aziz1,2, Jamila Rajper2, Wajeeha Noorulain2, Ayesha Mehnaz2,1 Pediatrics, Dow University of Health Sciences, Karachi, Pakistan; 2 Sarwar Zuberi Liver Centre, Dow University of Health Science, Karachi, Pakistan.

Background: To determine the outcome of pediatric and young adult patients treated with PEG-IFN-α or conventional interferon (IFN) plus ribavirin at a public sector hospital of Karachi.

Methods: Observational study, conducted at Sarwar Zuberi Liver Centre (SZLC), CHK, from 2007 to 2010. Patients up to 20 yrs of age at SZLC, were tested for Anti HCV (hepatitis C virus antibodies by 4th generation ELISA and 2nd generation antibody-capture lateral flow immunoassay) done. Patients with HBV, HIV and other comorbidities such as thalassemia, hemophilia, kidney disease and coexisting serious illness requiring treatment other than that for HCV were excluded. Depending upon the genotype, patients were treated for 24–48 wks with IFN 3 MIU 3 X per week or PEG-IFN-α 1.5 μg/kg plus ribavirin 15 mg/kg/day.

Results: Mean age of 45 patients, was 18.22 ± 2.88 years (range 8–20 years) and BMI 19.5 ± 2.49. Females were 66.7%. More than 80% had genotype 3 (a or b subtype). Remaining had genotype 1 or 4 or mixed. A slight decrease in Hemoglobin, platelet and white cell count was noted at 1, 3 and 6 months of treatment. No significant side effects were noted. There was a marked decrease in the ALT pretreatment vs post treatment. End treatment response (ETR) was 88%, of these sustained viral response (SVR) was achieved in 93%.

Conclusions: HCV infected pediatric and young adult patients treated with PEG-IFN-α or conventional interferon plus ribavirin (combination therapy) achieved an ETR of 88% and SVR of 93%.

A MULTIDISCIPLINARY CLINICAL PROGRAM IS EFFECTIVE IN REDUCING BMI AND ALT IN PEDIATRIC PATIENTS WITH NAFLD

S. DeVore, K. Lake, L. Nicholas, K. Dietrich, W. Balistreri, R. Kohli, S. Xanthakos. Division of Gastroenterology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background: There is currently no FDA-approved treatment for NAFLD, which affects 10% of children in the United States. Weight loss through diet and exercise effectively reduces ALT in research protocols, but outcomes of clinical programs are lacking.

Methods: 76 patients were evaluated in our steatohepatitis clinic from 11/07–5/10 due to chronically elevated liver enzymes and after standard testing to exclude other liver disease. We examined outcomes of 39 patients eligible for 1 year follow-up (range 9–18 mos) as of 5/10. Patients met with a gastroenterologist and dietitian every 3 months to set individualized dietary and exercise goals and monitor progress. Dietary goals focused on reducing added sugar and saturated fat intake. Change in mean BMI Z score and ALT was evaluated by paired t test and weighted least squares regression.

Results: 23 of 39 patients (59%) eligible for 1 year follow-up returned. Mean age was 14 ± 3 yrs (range 4–18), 65% male; 91% white and 9% biracial; 9% Hispanic ethnicity. All were obese (BMI ≥ 95th percentile); mean BMI Z score 2.61 and insulin resistant (HOMA-IR > 3.17); 4% had type 2 diabetes, 70% dyslipidemia and 48% hypertension. At 1 year follow-up, mean BMI Z score (−0.2 units, P = 0.08) and ALT levels (−60 U/L, P = 0.02) declined. Declines in BMI Z score and ALT adjusted for baseline values were both significant (P < 0.05). Decreases in serum triglyceride (−18 mg/dL), insulin (−9 μU/mL), total cholesterol (−8 mg/dL) and LDL (−5 mg/dL) were not statistically significant.

Conclusions: A clinically feasible multidisciplinary NAFLD program of every 3 month visits to set and monitor nutrition and exercise goals significantly improved mean BMI Z score and ALT levels at 1 year follow-up in obese pediatric patients with NAFLD. Attrition of 41% was less than reported for an intensive 16 week behavioral pediatric weight management program (55%).


FATTY LIVER IN CHILDREN POST LIVER TRANSPLANTATION: A NEW ENTITY

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Background: Fatty liver is a post liver transplantation recognized entity in adults and it has been recently described in children. The aim was to evaluate the presence of fatty liver in the post liver transplantation in children, and to correlate it with different variables.

Methods: A retrospective study from December 2000 to March 2010, was performed on 130 liver transplant children, 40.7% (n=53) were biopsied for alteration of liver profile laboratory within 3 months post transplant. Patients were grouped according to the presence or absence of steatosis.

Results: Whereas Group 1 more significantly required therapy with spironolactone, salt restriction, and albumin infusion ($P<0.05$) and had severe ASC, anemia, thrombocytopenia, varices, HE, hepatosplenomegaly, and PVT ($P<0.05$) than Group 2, presence of fever, abdominal pain and tenderness was significant in Group 2 ($P<0.05$). No significant difference in mortality outcome was found in the two groups ($P>0.05$). The only statistically significant predictive variables for mortality overall in 2 groups were ASC grade [hazard ratio (HR) 2.79 (95% CI, 1.40–5.50)]; thrombocytopenia [HR 1.72 (95% CI, 1.07–2.76)]; and hydrothorax [HR 1.28 (95% CI, 1.03–1.60)].

Conclusions: Presence of severe ASC, thrombocytopenia, and hydrothorax had significant effect on mortality irrespective of etiology of ASC.

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BLOOD TRANSFUSIONS: A RISK FOR PARENTERAL NUTRITION ASSOCIATED LIVER DISEASE (PNALD) IN PREMATURE INFANTS

K. Friedman1, A. D’Souza1, J. Weedon2, W.R. Treem1.
1Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY; 2Scientific Computing Center, SUNY Downstate Medical Center, Brooklyn, NY.

Background: Prior studies confirm the use of frequent blood transfusions (RBCs) in preterms; and that liver iron correlates with the volume of blood received. Chronic RBCs in children with hemoglobinopathies cause liver iron deposition and toxicity. Aims: In preterms on PN, we hypothesized that RBCs were a risk factor for PNALD.

Methods: We reviewed charts of all infants on PN >30 days. Data included serial measures of direct bilirubin (db), AST, ALT during PN days 30–100; and timing and cumulative volume of RBCs. PNALD was defined by db ≥2.0 mg/dl; AST >39 U/L; ALT >32 U/L. Kaplan-Meier analysis estimated median age at PNALD onset. Proportional hazards regression analysis used age at PNALD onset as the dependent variable, and cumulative RBCs as the time dependent predictor of interest. Potential confounders were cumulative days on PN (time-dependent) and birth wt (BW). Hazard ratios (HR) and confidence intervals (CI) are reported.

Results: 51 patients were studied including 5 with necrotizing enterocolitis (NEC); and 2 excluded due to diagnoses of CF and Hirschprung’s. Median number RBCs was 5 (range 0–38). 22 infants (45%) reached db ≥2.0 at estimated median age of 56 d (95% CI [49,67]). Multiple regression analyses, controlling for BW and PN duration, showed RBCs volume was a marginally significant predictor of...
We report 3 cases of acute liver failure during a peak outbreak of influenza H1N1. Incidence of acute liver failure at our institution increased only moderately from 9 in 2008 to 11 in 2009; with these 3 cases occurring in a short span, H1N1 may be relevant. This series raises awareness that hepatotoxic factors specific to the H1N1 strain as well as medication use (eg, AEDs or oseltamivir) may be important to pathogenesis. Further epidemiologic studies may be indicated.

Conclusions: Cumulative RBCs may be a risk factor for PNALD. Future prospective studies could substantiate these findings and determine the need for more restrictive guidelines for RBCs in preterm infants.

ALANYL-GLUTAMINE (ALA-GLN) PROMOTES INTESTINAL EPITHELIAL CELL SURVIVAL IN VITRO AND IN A MOUSE MODEL OF WEANLING MALNUTRITION
Priscilla M. Ueno1, Reinaldo B. Oria2, Lee A. Denson1, Sean R. Moore1. 1Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 2Federal University of Ceara, Fortaleza, Brazil.

Background: Malnutrition is linked to >50% of child deaths in developing countries and is associated with intestinal villous atrophy and increased gut permeability. Ala-Gln—a stable glutamine dipeptide—has been shown to enhance growth and gut integrity in underweight children from Northeast Brazil. We sought to test the hypothesis that Ala-Gln mediates these effects via anti-apoptotic mechanisms.

Methods: Colorimetric viability assays were performed in mouse small intestine epithelial (MSIE) cells in the presence of varying concentrations of Ala-Gln. Apoptosis was assessed by annexin and 7-AAD staining and flow cytometry. To determine Ala-Gln’s in vivo effects, we randomized dams of 10-day old C57/B6 mice to standard chow or an isocaloric, Northeast Brazil “regional” diet deficient in protein and fat. Upon weaning, pups were randomized to Ala-Gln solution or plain drinking water. At 6 weeks of age mice were sacrificed to obtain jejunal specimens for morphology, immunohistochemistry, and Ussing chamber permeability analysis.

Results: Ala-Gln promoted MSIE viability in a dose-response manner and reduced early apoptosis. Pups of dams that received the regional diet exhibited failure to thrive, villous blunting, decreased epithelial proliferation and increased epithelial apoptosis (as measured by BrdU and caspase-3 staining, respectively), and increased mucosal permeability to FITC-dextran. Despite continuing the regional diet, undernourished pups randomized to Ala-Gln showed significant improvements in villous height, epithelial proliferation/apoptosis, and barrier function.

Conclusions: The regional diet induces failure to thrive and enteropathy in weanling mice. Ala-Gln promotes enterocyte survival, normal villous architecture, and gut integrity in the setting of malnutrition. Further studies are needed to define
the signaling pathways by which Ala-Gln mediates these cellular responses critical to intestinal homeostasis.

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ENDOGENOUS GLP-2 AND ADAPTATION IN SHORT-BOWEL PIGLETS WITH AND WITHOUT ILEUM
Zheng Hua1, Justine Turner1, Patrick Nation1, Pamela Wizzard1, Ron Ball1, Paul Pencharz2, David Sigal3, Paul Wales1,2, 1University of Alberta, Edmonton, AB, Canada; 2University of Toronto, Toronto, ON, Canada; 3University of Calgary, Calgary, AB, Canada.

Background: Neonatal short bowel syndrome (SBS) is a malabsorptive state occurring as a result of small bowel resection or congenital disease. After resection the remnant bowel will adapt in order to increase absorptive capacity, a process regulated by trophic factors, including glucagon-like peptide-2 (GLP-2), secreted principally from ileum. We hypothesized endogenous GLP-2 production was reduced in piglets with ileal resection, associated with limited adaptation.

Methods: JI piglets (n = 13) had 75% mid-small bowel resection with jejunoileal anastomosis; JC piglets (n = 15) had 75% distal resection with jejunoileal anastomosis and no ileum; sham piglets (n = 11) had no resection. Piglets were maintained for 14 days on parenteral nutrition decreased as enteral nutrition increased. Data collection included weight gain; plasma intact GLP-2 measured day 0, when piglets were on 50% parenteral nutrition, and day 14; repeat measurement of small bowel length and histology to evaluate adaptation.

Results: Weight gain was least in resected piglets (1.8 kg JC vs 2.0 kg JI vs 2.5 kg sham; \( P < 0.015 \)). Small bowel lengthening was limited in JC piglets (0.0 cm JC vs 35.8 cm JI vs 191.9 cm sham; \( P < 0.01 \)). Only JI piglets had evidence of crypt hyperplasia (2.0 \( \mu m \) JI vs 1.7 \( \mu m \) JC vs 1.4 \( \mu m \) sham; \( P < 0.001 \)). GLP-2 levels increased from baseline across all groups, but only significantly for JI piglets on day 14 (27.2 pM JC vs 73.3 pM JI vs 44.5 pM sham; \( P < 0.05 \)).

Conclusions: Following bowel resection neonatal piglets show progressive increase in endogenous GLP-2, with highest levels observed in piglets with ileum. This is associated with bowel lengthening and adaptation that is not observed in piglets without ileum. Therefore neonates with ileal resection appear to have GLP-2 deficiency and impaired adaptation. The role of GLP-2 treatment in neonatal SBS warrants further investigation.

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COST-EFFECTIVENESS OF COLECTOMY AFTER DIAGNOSIS OF SEVERE PEDIATRIC ULCERATIVE COLITIS
K.T. Park1, Ray Tsai1, Felipe Perez1, William Berquist1, Alan Garber2. 1Pediatrics, Stanford University, Stanford, CA; 2CHP/PCOR & VA Palo Alto Health Care Systems, Stanford University, Stanford, CA.

Background: It is often unclear when UC patients may benefit from a subtotal colectomy with ileal pouch anal anastomosis (IPAA). Escalating expensive medical therapies for severe pediatric UC may reduce patients’ quality of life and potentially be cost-ineffective. The aim was to determine the cost-effectiveness of colectomy + IPAA after diagnosis of severe UC compared to delaying surgical intervention after all medical therapies have failed.

Methods: We performed a systematic review of the literature and created a Markov model using TreeAgePro 2009. Hypothetical 10 year old UC patients were enrolled at the time of initial UC flare to receive either traditional therapies with escalating medical strategies or a referral for colectomy + IPAA. Transition state probabilities and utilities were collected from literature and used as input data. Cost data were collected from Lucile Packard Children’s Hospital billing records, the Office of Statewide Health Planning and Development tables, and 2 different online pharmacies. Incremental cost per quality adjusted life-years (QALYs) were measured compared to the base case of traditional therapy alone.

Results: Immediate colectomy + IPAA after diagnosis of severe pediatric UC produced a net savings of $79,051 over a lifetime, but resulted in a net loss of 0.99 QALY. This resulted in an incremental cost effectiveness ratio of $80,156 per QALY. One and two-way sensitivity analyses showed that the intervention was most sensitive to the utility of the post-operative state. If the quality of life after surgery were 0.94 of the remission state controlled with medical therapy alone, immediate colectomy + IPAA would be the dominant strategy.

Conclusions: Immediate colectomy + IPAA in severe pediatric UC is cost-effective, but cannot be the recommended treatment option because of the loss of quality of life. Early surgical referral may become the optimal management strategy for moderate to severe UC if the quality of life after a surgically created pouch becomes comparable to UC in full remission.

SATURDAY, OCTOBER 23, 2010
Plenary Session II:
Fellow Research Award
8:30 am–10:00 am

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TELOMERASE-EXPRESSING INTESTINAL STEM CELLS ARE ACTIVATED IN RESPONSE TO PHYSIOLOGIC STRESS
Camilla A. Richmond1,2, Robert K. Montgomery1, Dana M. Ambruzs1,2, Diana L. Carlone2, David T. Breault1. 1Pediatrics, Division of Gastroenterology, Children’s Hospital Boston, Camilla A. Richmond, MD, 2Division of Pediatric Gastroenterology, Children’s Hospital Boston, MA.
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INFLUENCE OF NOD2 ON THE GUT MICROBIOTA
Ajay S. Gulati, Lieselotte Kreuk, Balfour Sartor. University of North Carolina at Chapel Hill, Chapel Hill, NC.

Background: The importance of the gut microbiota in the development of chronic intestinal inflammation is well established. Consistent with this concept is the high incidence of mutations of the bacterial receptor NOD2 in patients with Crohn’s disease (CD). While many studies have investigated the role of NOD2 in the development of CD, its influence on the intestinal microbiota is not established. We hypothesize that NOD2 dysfunction leads to dysbiosis of the commensal microbiota through alterations in innate immune function and production of antimicrobial peptides (AMPs).

Methods: Total DNA was extracted from ileal and cecal tissue, as well as cecal contents from wild-type (WT) and Nod2−/− mice. Faecalibacterium prausnitzii was chosen as a prototypic anti-inflammatory bacterium, while Escherichia coli was chosen as a representative pro-inflammatory organism. Bacteria were quantified using qPCR of the 16S rRNA gene. Transcript levels of selected AMPs were assessed using qRT-PCR.

Results: F. prausnitzii levels were ~9-fold higher in WT versus Nod2−/− ileal tissue (P < 0.01), and ~4-fold higher in WT versus Nod2−/− cecal tissue (P < 0.01). No differences in F. prausnitzii were found between cecal contents from WT versus Nod2−/− mice. For all specimens tested, E. coli was below the lower limit of detection. Regarding AMP expression, the cryptds Defcr and Defcr-rs10 were undetectable in both WT and Nod2−/− mice. However, Reg3γ was elevated in ileal (~2.5-fold, P < 0.01) and cecal (~7-fold, P < 0.03) specimens from Nod2−/− mice relative to WT controls.

Conclusions: Mucosally-associated levels of the anti-inflammatory bacterium F. prausnitzii are decreased in the ileum and cecum of Nod2−/− mice. This is consistent with the hypothesis that alterations in Nod2 function may lead to a more pro-inflammatory composition of the intestinal microbiota. Additional studies will be needed to determine if the described AMP alterations contribute to the observed bacterial changes. This disruption of the commensal microbiota may be a predisposing factor for the initiation of inflammation in CD patients with NOD2 mutations.

Young Faculty Investigator Award

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IMPACT OF PHYSIOLOGIC ROUTES OF ANTIGEN EXPOSURE ON ALLERGIC SENSITIZATION
David Dunkin1, M. Cecilia Berin2, Lloyd Mayer2. 1Pediatric Gastroenterology, Mount Sinai SOM, NY, NY; 2Immunology Institute, Mount Sinai SOM, NY, NY.

Background: Allergic sensitization to foods has been presumed to occur via the oral route, but infants are often exposed to significant quantities of food proteins through other routes such as the skin. Our aim was to determine how route of food exposure influences the development of allergic sensitization in mice.

Methods: C3H/HeJ mice were exposed weekly for 6 weeks to the milk protein α-lactalbumin (ALA), with or without cholera toxin (CT) as adjuvant. Routes of allergen exposure included intragastric, sublingual, cutaneous, or intranasal. Mice were then challenged orally with ALA, and anaphylaxis was assessed by symptoms and drop in body temperature. ALA-specific immunoglobulins were measured in serum by ELISA. The mechanism of skin sensitization...
was examined using an adoptive transfer model with transgenic T cells.

**Results:** As we have previously found, mice exposed to ALA by intragastric administration with the adjuvant CT responded to oral OVA challenge with anaphylaxis symptoms and a drop in body temperature. This was also observed in mice exposed to ALA plus CT by sublingual, cutaneous, and intranasal routes. Cutaneous ALA + CT exposure resulted in the largest allergic IgE response and lowest protective IgA response. Mice exposed to ALA by any route without CT did not become allergic. Cutaneous CT induced a migration of dermal DCs to the draining lymph node, and promoted antigen-specific CD4+ T cell proliferation and Th2 cytokine production.

**Conclusions:** Sensitization can occur via gastrointestinal, respiratory, and cutaneous routes of allergen exposure in an adjuvant-dependent manner, with cutaneous exposure being the most effective at inducing IgE. Exposure to foods on the skin during infancy may be a risk factor for development of allergic sensitization, especially in the context of skin inflammation or infection that could act as adjuvant.

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**NASPGHAN Endoscopy Prize**

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**ANALGESIA DURING PEDIATRIC DIGESTIVE ENDOSCOPY: A COMPARISON OF TWO PROTOCOLS FOR PROCEDURAL SEDATION**

Hamid Khour1, Edith Villeneuve2, Steven Martin1, Denise Herzog1. 1Division of Gastroenterology, Department of Pediatrics, Sainte Justine Hospital, Montreal, QC, Canada; 2Department of Anesthesia, Sainte Justine Hospital, Montreal, QC, Canada.

**Background:** Procedural sedation for diagnostic digestive endoscopies in patients 11 years of age and older is current practice. However, analgesia can be insufficient when using meperidine and midazolam alone. The aim of our study was to compare the analgesic efficacy of our current protocol (meperidine, midazolam) with that of a triple combination (ketamine, midazolam, meperidine) in upper and lower digestive endoscopy.

**Method:** Randomized, double-blind trial including patients between 11 and 19 years of age, and undergoing diagnostic procedures. All patients received midazolam (0.1 mg/kg, max 5 mg iv), and meperidine (1 mg/kg, max 50 mg iv). Placebo vs ketamine (0.5 mg/kg iv) was randomized. All patients were given nasal oxygen to maintain SaO2 ≥96%. Meperidine and midazolam rescue doses were administered if necessary.

**Results:** Groups did not differ for age, gender and weight. No reversal agent or cardiopulmonary intervention was necessary. Nystagmus was noted in 29 and hallucinations in 5 patients of the ketamine group while hypotension and nausea were present in 5 patients of the placebo group.

**Conclusions:** The level of analgesia was the same in both groups. Ketamine was safe and significantly decreased the frequency of rescue doses in colonoscopies.
Table. Procedural sedation with or without ketamine: analgesia and side effects

<table>
<thead>
<tr>
<th>Groups (n)</th>
<th>Ketamine (42)</th>
<th>Placebo (42)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper/lower endoscopy</td>
<td>18/24</td>
<td>20/22</td>
<td>ns (χ²)</td>
</tr>
<tr>
<td>OAAS score (mean ± SD)</td>
<td>4.5 ± 0.9</td>
<td>4.8 ± 0.6</td>
<td>ns (Mann-Whitney)</td>
</tr>
<tr>
<td>Interventions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5x verbal stimulation, 1x O₂</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain score (0–2 points) (mean ± SD)</td>
<td>6.1 (5.1–8.0)</td>
<td>3x verbal stimulation</td>
<td>ns (χ²)</td>
</tr>
<tr>
<td>Minutes to Aldrete discharge score</td>
<td>34.5 ± 14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colonoscopy patients with rescue doses</td>
<td>8</td>
<td>14</td>
<td>0.04 (χ²)</td>
</tr>
</tbody>
</table>

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PHARMACOKINETICS OF REPEATED DOSING OF INTRAVENOUS ESOMEPRAZOLE IN PEDIATRIC PATIENTS

Vasundhara Tolia1, Geoffrey Davidson2, Kurt A. Brown3, Lisa McCaff1, Göran Långström4, Per Lundborg4, Marie Sandström2, 1 Providence Hospital, Southfield, MI; 2 Centre for Paediatric and Adolescent Gastroenterology, Women’s and Children’s Hospital, North Adelaide, SA, Australia; 3 AstraZeneca LP, Wilmington, DE; 4 AstraZeneca R&D, Mölndal, Sweden; AstraZeneca, Södertälje, Sweden.

In this multicenter open-label study (NCT00474019; D9615C00021) hospitalized patients aged 0–17 y. Observed maximum steady-state plasma concentration (Css,max) was lower in patients aged 0–1 mo vs other groups. 17 y. Mean weight, kg 2.8 (2.4–4.1) 6.1 (5.1–8.0) 16.8 (8.5–23.0) 30.0 (24.8–49.7) 32.8 (18.5–69.0) 58.0 (38.0–76.0) 52.4 (45.0–60.0)

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JAUNDICECHIP: TWO-YEAR SUMMARY OF PATIENTS

Kerry Shooner, Brian Richardson, Grant Maddox, Amanda Schalk, Kejian Zhang. Division of Human Genetics, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background: The discovery of gene mutations for neonatal intrahepatic cholestasis allows for diagnostic specificity despite similar clinical phenotypes in patients. The JaundiceChip Resequencing Array provides a tool to assign a molecular diagnosis in children with idiopathic cholestasis; this report aims to summarize clinical findings to date.

Methods: The JaundiceChip was validated as a clinical test by Cincinnati Children’s Hospital Molecular Genetics Laboratory in 2008. From July 2008 to April 2010, 180 patients with presumed cholestatic liver disease were referred to CCHMC for testing. DNA was surveyed for mutations or variants in genes SERPINA1, JAG1, ATP8B1, ABCB11, and ABCB4 by the JaundiceChip. All abnormalities were confirmed by Sanger sequencing.

Results: 79 (43.8%) of presumed symptomatic patients tested by the JaundiceChip (n = 180) were found to have genetic defects in SERPINA1, JAG1, ATP8B1, ABCB11, or ABCB4. 19 of these patients had a variant in SERPINA1;

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Table.

<table>
<thead>
<tr>
<th>Age, ESO Dose</th>
<th>0–1 mo, 0.5 mg/kg (n = 6)</th>
<th>1–11 mo, 1 mg/kg (n = 6)</th>
<th>1–5 y, 10 mg (n = 7)</th>
<th>6–11 y, 10 mg (n = 8)</th>
<th>6–11 y, 20 mg (n = 8)</th>
<th>12–17 y, 20 mg (n = 8)</th>
<th>12–17 y, 40 mg (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean weight, kg</td>
<td>2.8 (2.4–4.1)</td>
<td>6.1 (5.1–8.0)</td>
<td>16.8 (8.5–23.0)</td>
<td>30.0 (24.8–49.7)</td>
<td>32.8 (18.5–69.0)</td>
<td>58.0 (38.0–76.0)</td>
<td>52.4 (45.0–60.0)</td>
</tr>
<tr>
<td>AUCt, μmol·h/L</td>
<td>7.5 (4.5–20.5)</td>
<td>10.5 (4.5–22.2)</td>
<td>7.9 (2.9–16.6)</td>
<td>6.9 (3.5–10.9)</td>
<td>14.4 (7.2–24.3)</td>
<td>8.1 (4.7–15.9)</td>
<td>17.6 (13.1–19.8)</td>
</tr>
<tr>
<td>Cmax, μmol/L</td>
<td>3.7 (2.7–5.7)</td>
<td>8.68 (4.5–14.0)</td>
<td>9.37 (4.4–17.2)</td>
<td>5.60 (3.3–13.2)</td>
<td>8.33 (3.6–29.4)</td>
<td>7.10 (4.7–9.02)</td>
<td>10.5 (7.8–14.2)</td>
</tr>
<tr>
<td>CL, L/h</td>
<td>0.5 (0.1–1.0)</td>
<td>1.7 (0.9–3.1)</td>
<td>3.4 (1.6–9.5)</td>
<td>3.8 (2.7–5.1)</td>
<td>3.6 (1.1–8.0)</td>
<td>7.0 (3.4–12.3)</td>
<td>6.4 (5.5–8.7)</td>
</tr>
<tr>
<td>Vss, L</td>
<td>11.0 (8.8–22)</td>
<td>1.6 (1.5–1.7)</td>
<td>3.3 (2.4–4.6)</td>
<td>6.7 (4.0–14.0)</td>
<td>6.8 (4.9–10.7)</td>
<td>9.5 (7.8–11.3)</td>
<td>10.9 (8.0–15.9)</td>
</tr>
<tr>
<td>Ifosfamide, L/kg</td>
<td>0.17 (0.04–0.32)</td>
<td>0.26 (0.12–0.58)</td>
<td>0.24 (0.09–0.66)</td>
<td>0.12 (0.08–0.17)</td>
<td>0.11 (0.02–0.25)</td>
<td>0.12 (0.09–0.21)</td>
<td>0.12 (0.10–0.16)</td>
</tr>
<tr>
<td>Vss, L/kg</td>
<td>0.38 (0.28–0.53)</td>
<td>0.25 (0.21–0.29)</td>
<td>0.23 (0.17–0.29)</td>
<td>0.21 (0.15–0.29)</td>
<td>0.20 (0.13–0.32)</td>
<td>0.17 (0.14–0.21)</td>
<td>0.21 (0.16–0.29)</td>
</tr>
</tbody>
</table>

[a1] patient excluded from analysis.
16 of these either the S- or Z-allele. 24 individuals had JAG1 sequence variants (7 of these had at least one abnormality in a second gene); 15 individuals with 1+ variants in ATP8B1, 24 with 1+ variants in ABCB11, and 15 with 1+ variants in ABCB4. Of 118 total variants identified in all patients, 53 were previously reported and 65 were novel (42 missense, 12 splice site, 8 nonsense, 3 deletion). Five Chip-tested individuals had reflex testing by direct Sanger sequencing to detect a possible 2nd mutation; none of this sequencing uncovered a mutation undetected by the Chip.

Conclusions: The JaundiceChip offers the unique ability to study several genes involved with neonatal cholestasis in a single analysis. This tool has effectively uncovered diagnoses in numerous patients; however, in some, a diagnosis remains elusive. As additional clinical information is gathered and more patients resequenced, this Array is having increasing utility as a frontline tool for efficient molecular diagnosis of inherited liver diseases.

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A COMMON VARIANT IN PNPLA3 GENE AND THE RISK OF PEDIATRIC NONALCOHOLIC FATTY LIVER DISEASE

Yu-Cheng Lin1, Pi-Feng Chang1, Fu-Chang Hu2, Wei-Shiung Yang2, Mei-Hwei Chang2, Yen-Hsuan Ni2. 1Pediatrics, Far Eastern Memorial Hospital, Taipei, Taiwan; 2National Taiwan University Hospital, Taipei, Taiwan.

Background: The PNPLA3 rs738409 G allele is strongly associated with increased liver fat content in adults. This study aimed to examine whether this genetic polymorphism would increase the susceptibility of non-alcoholic fatty liver disease (NAFLD) in obese children.

Methods: A total of 520 obese children aged 6–18 years were recruited. Obesity was defined as the body mass index (BMI) > age- and gender-specific 95 percentile in Taiwan. NAFLD was determined by liver ultrasonography. Their PNPLA3 rs738409 genotypes were detected by the 5’-nuclease assay. We assessed the effects of variant PNPLA3 rs738409 genotypes on pediatric NAFLD in obese children using multiple logistic regression models.

Results: 19.6% of the obese children had NAFLD. After conditioning on the effects of gender, age- and gender-adjusted BMI, waist circumference, and adiponectin, variant PNPLA3 rs738409 genotypes increase the odds ratio of pediatric NAFLD by 2.96 (95% C.I.: 1.57–5.59, P = 0.0008) in subjects with GG allel and 5.84 (95% C.I.: 2.59–13.16, P < 0.0001) for GG alleles, as compared to CC alleles. The fact that the odds ratio of homozygous GG alleles versus homozygous CC alleles (5.84) was close to two times of the odds ratio of heterozygous GG alleles versus homozygous CC alleles (2.96) implied that the G allele was hazardous and its effect on pediatric NAFLD might follow a dominant genetic model.

Conclusions: The variant PNPLA3 rs738409 genotypes increased the risk of NAFLD development in obese children. The hazardous effect of G allele on pediatric NAFLD followed a dominant genetic model.

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DEPRESSION, ANXIETY AND QUALITY OF LIFE ARE NOT CORRELATED TO COLONIC 5-HT ALTERATIONS IN CHILDREN WITH IBS AND FAP

Stephanie Willot1,2, Cindy Gauthier2, E. Brookes3, G. Mawe1, Christophe Faure1,2. 1Division of Pediatric Gastroenterology, Ste Justine Hospital, Montreal, QC, Canada; 2Sainte-Justine Research Centre, Ste Justine Hospital, Montreal, QC, Canada; 3Department of Anatomy and Neurobiology, University of Vermont, Burlington, VT.

Background: Rectal hypersensitivity is a symptom of both irritable bowel syndrome (IBS) and functional abdominal pain (FAP). In IBS patients, serotonin (5-HT) signalling alterations have been reported in the colonic mucosa. IBS and FAP are similarly associated with anxiety and depression, disorders that are also associated with abnormal 5-HT metabolism. The aim of this study was to test the hypothesis that in children with FAP and IBS, depression and anxiety are related to colonic 5-HT alterations.

Methods: 42 children (33 girls, median age 14 yrs, range 8–18) were prospectively studied. All underwent a colonoscopy indicated by their attending physician. They all filled validated questionnaires on pain and GI symptoms, anxiety (STAIC), depression (CDI) and quality of life (PedsQL). Biopsies were taken from the rectum. 5-HT content was determined by enzyme immunoassay, and mRNA levels for the serotonin transporter (SERT) were assessed by quantitative real-time RT-PCR. Three months after the endoscopy the final diagnosis was documented.

Results: 17 patients with a functional gastrointestinal disorder (FGID) (IBS n = 12; FAP n = 5) were recruited. They were compared to 12 age-matched controls. Results (mean; SD) are reported in the Table. In patients with FGID, no correlation was found between 5-HT or SERT mRNA levels and anxiety, depression or quality of life.

Conclusions: Children with IBS and FAP have higher 5-HT content in the rectal mucosa and have significant anxiety, depression and quality of life alteration as compared to controls. Colonic 5-HT alterations are not directly related to depression, anxiety or severity of symptoms.

<table>
<thead>
<tr>
<th></th>
<th>FGID n = 17</th>
<th>Controls n = 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-HT content (pmol/mg)</td>
<td>129 (75)</td>
<td>74 (53)</td>
</tr>
<tr>
<td>SERT mRNA</td>
<td>6.6 (4.7)</td>
<td>8.2 (4.6)</td>
</tr>
<tr>
<td>STAIC</td>
<td>72 (11)</td>
<td>65 (11)</td>
</tr>
<tr>
<td>CDI</td>
<td>11 (5)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>PedsQL (child)</td>
<td>67 (10)</td>
<td>82 (10)</td>
</tr>
</tbody>
</table>

Note: NS indicates not significant.
### Intestine/Colon/IBD

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**SERUM MICRO RNAs AS A NOVEL BIOMARKER FOR PEDIATRIC INFAMMATORY BOWEL DISEASE**

Adam M. Zahm, Amber M. Horner, Meena Thayu, Joshua R. Friedman. *Children’s Hospital of Philadelphia, Philadelphia, PA.*

Crohn disease, one of two predominant inflammatory bowel diseases (IBD), is characterized by an aberrant and chronic immune response within the gastrointestinal tract. Approximately one-third of newly diagnosed IBD patients are under the age of 18. Currently the diagnosis of Crohn disease is a multi-step procedure generally involving biochemical and serological testing, radiological imaging, and endoscopy. The development of novel biomarkers has the potential to simplify the diagnostic process by reducing the need for costly and invasive procedures. MiRNAs are short nucleotides that negatively regulate target mRNA stability and translational efficiency. Altered tissue miRNA profiles have previously been reported in the intestinal epithelia of IBD patients. It has recently been discovered that miRNAs are present in cell-free preparations of serum or plasma. Remarkably, specific serum miRNA profiles have been associated with various conditions, including heart and liver disease. Here we describe a pilot study examining the potential of serum miRNA as novel biomarkers of pediatric Crohn disease. An initial screening (n = 6) of serum miRNA was performed by microarray, and subsequently confirmed by TaqMan RT-PCR. We identified several miRNAs that are significantly increased in the serum of Crohn disease patients compared to age-matched controls. A panel of these altered miRNAs was measured in a larger, independent sample set (n = 24) by TaqMan RT-PCR. Serum levels of miR-192, a miRNA highly expressed in colonic epithelial cells, were significantly increased in Crohn patients. Other miRNAs, such as miR-16 and let-7b, were increased more than 10-fold compared to controls. Receiver operating characteristic (ROC) curves generated showed high AUC values, implying strong diagnostic potential. These findings suggest that pediatric Crohn disease is associated with a unique serum miRNA profile. This profile could be used as an inexpensive, non-invasive diagnostic tool. Future work may identify serum miRNA profiles with prognostic value.

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**MUTATION IN XIAP REVEALED BY WHOLE EXOME SEQUENCING IN A YOUNG BOY WITH SEVERE INFAMMATORY BOWEL DISEASE**

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*Background:* We report a boy presenting at 15 months with perianal abscesses and proctitis, progressing to transmural pancolitis with colocutaneous fistulae, consistent with a Crohn’s disease-like illness. The presentation suggested an underlying immune defect, but a comprehensive evaluation did not lead to a definitive diagnosis.

*Methods:* We performed whole exome sequencing, identifying variants in our patient not found in reference datasets. The leading candidate mutation was confirmed by Sanger sequencing and functional assays to test the predicted effects of the mutation on known signaling pathways.

*Results:* We identified a germline missense mutation in the X-linked inhibitor of apoptosis (XIAP) gene, encoding a cysteine to tyrosine substitution at residue 203 of the protein. XIAP has been shown to play a role in activation-induced cell death, as well as a lack of detectable NOD2 signaling.

*Conclusions:* The child was diagnosed with a functional defect in the XIAP protein causing a novel presentation of X-linked lymphoproliferative disease, Type 2. Allogeneic BMT has been recommended. This report demonstrates the power of exome sequencing to render a novel diagnosis in the setting of an intractable disease. Particular to this case, these findings suggest a novel role for XIAP in the pathogenesis of inflammatory bowel disease.

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**CD4/CD8 LYMPHOCYTE SUBPOPULATIONS AND IGA IN LARGE BOWEL MUCOSA OF CHILDREN WITH UNTREATED ULCERATIVE COLITIS**

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*Background:* The aim was to compare the CD4/CD8 lymphocyte subpopulations and IgA in colonic mucosa of
children with untreated ulcerative colitis (UC) and controls (CON).

**Methods:** Design: Pilot case-control. Setting: A GI department at a pediatric referral hospital, 2000–2008. Protocol: Large bowel biopsies were handled with immune-histochec- technical techniques (CD4, CD8 and IgA antibodies) and were evaluated blindly by 2 pathologists. Eleven children with UC and 5 CON were included. An ad hoc semi-quantitative protocol was used for reviewing the biopsies. Analyses: Results are presented as medians and 25/75 quartiles. Statistics: χ², Fisher, Man-Whitney U.

**Results:** Age (years): CU 15 ± 6–15, CON 10 ± 5.5–10.2. No intra-epithelial CD4L were observed in any of the study groups. Intraepithelial CD8L counts were lower in UC than in controls (P = 0.077). Lamina propria CD4L and CD8L counts were higher in UC (P = 0.004 and 0.026). IgA was significantly increased in UC. CD8L were increased around high-endothelium venules.

**Conclusions:** Presence and location of CD4L, CD8L and IgA in our children differ from reports of adults with UC. Location of CD8L around high-endothelium venules may identify the inflammation recruiting site.

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**186 SEASONALITY OF ONSET OF INFLAMMATORY BOWEL DISEASE IN CHILDREN**

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**Background:** The pathogenesis of inflammatory bowel disease (IBD) is not completely understood. It has been suggested that the onset of IBD follows a seasonal variation that mirrors the pattern of common infections. Also studies have suggested the clustering of date of births with the adult and childhood onset of IBD. The objectives were to determine if the onset of IBD in children and if the birth of children diagnosed with IBD follows a seasonal pattern.

**Methods:** Retrospective review of medical records of children diagnosed with IBD at our institution from 7/1992–2/2010. To determine the season of onset we used a specific date of onset of symptoms. Data obtained: date and season of birth, age, gender, race, presenting symptoms, date and season of onset and diagnosis. Children from Birth to 21 years diagnosed with IBD by endoscopic and histologic criteria [Crohn’s disease (CD), Ulcerative colitis (UC), and Indeterminate colitis (IC)]. Patients who had incomplete records, no clear date of onset, onset of symptoms more than 6 months, or non-specific symptoms at onset were excluded from the analysis of onset of symptoms but included in the analysis of birth date season.

**Results:** 170 patients were reviewed (CD: 90, UC: 77, IC: 3). 38 patients were excluded from the analysis of onset. By mere chance it is expected that the onset of symptoms should occur equally in the 4 seasons. 34% of patients with IBD had their onset in the fall and 19% of them had it in the summer while the rest divided equally between the winter and spring, the result being statistically significant. When breaking down the group to CD and UC, the onset of the diseases continued to be more in the fall but with no statistical significance. On the other hand the four seasons had roughly similar percentage of patients’ births with no statistical significance.

**Conclusions:** The onset of symptoms of inflammatory bowel disease tends to have a seasonal trend with the highest incidence in the fall and the lowest in the summer. There is no specific season in which children with IBD tend to be born.

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187 **BEYOND GWAS: EVALUATION OF METHYLATION AND GENE EXPRESSION IN PEDIATRIC CROHN DISEASE (CD)**


To date, >40 gene loci have been linked with Crohn disease (CD) susceptibility, yet these account for only 20% of genetic predisposition. The discordance between monozygotic twins affected by IBD, along with a number of other clinical and molecular findings in IBD, provide evidence that epigenetic regulation plays an important role in the etiology of this disease. Inherited and/or acquired epigenetic defects may be of etiologic and pathogenic importance in IBD. In this study we evaluate DNA methylation, a tissue specific genetic modulation that is “heritable” and affects gene expression. Using the Infinium Human Methylation 27 Illumina platform we performed DNA bisulfite sequencing of colonic tissue to compare the methylation status of 2 groups of pediatric patients (11 with new onset CD vs 13 controls). The Illumina platform determines the methylation status of over 27,578 CpG dinucleotides spanning 14,495 genes. We compared these results to gene expression profiles in the same tissues determined by the Affymetrix microarray. Compared to controls, hypomethylation was noted in 17 genes corresponding to elevated expression profiles in CD tissues, while hypermethylation was found in 19 genes with decreased expression. Of the up-regulated genes, many are previously described as associated with CD but not found on GWAS studies, including: IFI27, CTLA4, ITK, ICOS, IKZF1. Also identified were genes not previously reported to be associated with the disease: APP1, TRPS1, GIMAP5, CFL1, CCL18, IDO1. In addition, we noted genes of interest that were down regulated and hypermethylated including IL-11, S100A16, RBO2, TM4SF5. Finally, upon analysis using the DAVID v6.7 we defined 11 (P < 1.59E-07) of the upregulated, hypomethylated genes were involved in the immune response and 14 (P < 6.81E-03) were involved in STAT5b signaling. This data suggests that DNA methylation of cis regulatory CpG islands plays an important role in CD and may help define genes crucial to CD etiology.
INCREASED SUSCEPTIBILITY TO DEXTRAN SODIUM SULFATE-INDUCED COLITIS AND DELAYED EPITHELIAL REPAIR IN MILK FAT GLOBULE PROTEIN EGF FACTOR 8-DEFICIENT MICE
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Background: Milk fat globule-EGF factor 8 (MFG-E8) is expressed in intestines. MFG-E8 plays important role in maintaining integrity and accelerates healing of intestinal mucosa in septic mice. We examined the potential protective role for MFG-E8 in inflammatory bowel disease (IBD) using dextran sulfate sodium (DSS)-induced colitis model.

Methods: MFG-E8+/+ and MFG-E8−/− mice (C57BL/6) were fed distilled water for 1 week. Mice were fed only regular drinking water after 1 week until they were sacrificed. Control mice were fed only regular drinking water. Clinical (diarrhea, hematocrit, weight loss) and histological colitis scores (inflammatory injury score and crypt-epithelial injury score) were calculated. MFG-E8 mRNA and protein expression quantified by real-time PCR and Western blotting.

Results: MFG-E8−/− mice developed more severe crypt-epithelial injury than MFG-E8+/+ mice during exposure to 3.5% DSS drinking water. They showed delayed healing of damaged intestinal epithelium during water recovery phase. MFG-E8 gene expression was increased in colon and rectum of MFG-E8−/+ mice during induction of inflammation by DSS treatment. Higher levels of MFG-E8 were revealed to persist in rectum as compared to colon on day 7 of DSS exposure. The MFG-E8 levels in both tissues decreased to baseline during water recovery phase in mice with colitis. Histological analysis of colonic and rectal tissues demonstrated that alteration of MFG-E8 gene expression was correlated to levels of inflammatory response and crypt-epithelial injury in both colonic and rectal mucosa in MFG-E8−/+ mice.

Conclusions: Increased expression of MFG-E8 could be playing an important role in protecting the colonic and rectal mucosa from histological damage in the first week of DSS treatment. Absence of MFG-E8 causes increased susceptibility to colitis. MFG-E8 may be implicated in the pathophysiology of IBD.

CLINICAL EFFECTIVENESS OF THIOPURINES IN MAINTAINING REMISSION FOR PEDIATRIC CROHN’S DISEASE
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Background: Thiopurines are thought to be effective for maintaining remission in pediatric Crohn disease (CD). This study aimed to evaluate the clinical effectiveness of thiopurines for maintaining remission in routine clinical practice.

Methods: Data was obtained from the PIBDNet database (2004–2008). Patients entered the study if they achieved remission by physician global assessment (PGA) within 70–365 days of thiopurine initiation and had > 3 mos of follow-up. Exclusion criteria included concomitant use of methotrexate, infliximab, cyclosporin or tacrolimus or heterozygous TPMT geno/phenotype. Patients were included until treatment failure, defined as active disease by PGA, addition of methotrexate, infliximab, cyclosporin, tacrolimus or corticosteroids (CS), thiopurine discontinuation, hospitalization, or surgery. Patients treated with CS at study entry remaining on CS after 30 days were considered treatment failures.

Results: 65 patients (60% male, mean age 13.4 ± 2.8 yrs) met inclusion criteria. 22/65 patients (34%) were receiving CS at study entry. 8 patients were lost to follow-up by 6 months. 32 of the remaining 57 patients (56%) were treatment failures by 6 months. 16 patients were lost to follow-up by 12 months. 42 of the remaining 49 patients (86%) failed treatment. 45 of the initial 65 patients (69%) failed therapy by the end of the study period. 32/45 (71%) failed due to a subsequent PGA of mild, 6/45 (13%) moderate/severe, 14/45 (31%) secondary to CS therapy, 2 patients (4%) for hospitalization, and 2 (4%) discontinued thiopurines. 10 patients had > 1 reason for failure.

Conclusions: Long term thiopurine treatment was effective in some patients in maintaining remission for pediatric CD in routine clinical practice. However, treatment failure was common during the first year after achieving remission.

MEDICAL RADIATION EXPOSURE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE: ESTIMATES POTENTIALLY DANGEROUS CUMULATIVE DOSES
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Background: Children with Crohn Disease (CD) and ulcerative colitis (UC) often undergo imaging using ionizing radiation and may be exposed to high cumulative radiation. Literature suggests even moderate radiation doses increase the risk of cancer, especially in the young. The aim of this
study is to estimate radiation exposure in a cohort of children diagnosed with IBD.

**Methods:** An IRB-approved retrospective chart review from 2002-2008 was performed on all patients with IBD at a tertiary referral pediatric hospital. All radiographic studies were recorded. Radiation exposure for each study was estimated based on current protocols, age of patient, and dose estimates in the literature.

**Results:** A total of 117 children with IBD (86 CD, 31 UC) were evaluated. The median cumulative total exposure was 15.1 mSv in CD and 7.2 mSv in UC ($P = 0.005$). CT scan and SBFT were responsible for 43% and 36% of all radiation. Six children (4%), all with CD, were over 50 mSv of radiation exposure. Using the annual dose rate, an estimated 79 (68%) children would exceed 50 mSv by 35 years of age. The mean estimated exposure at age 35 was higher in CD compared to UC.

**Conclusions:** Radiation exposure from medical imaging is high in a subset of children diagnosed with IBD, mostly due to abdominal CT and SBFT. Almost half of children were estimated to have high radiation exposure at age 35. Non-ionizing imaging such as MRI and ultrasound should be offered to children with IBD as an alternative to current imaging that employs radiation.

**Table. Radiation Estimate per Patient (Effective Dose)**

<table>
<thead>
<tr>
<th>Crohn Disease</th>
<th>Ulcerative Colitis</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current total exposure (mSv)</td>
<td>15.1 (0–71.5)</td>
<td>7.2 (0–33.8)</td>
</tr>
<tr>
<td>Rate (mSv/yr)</td>
<td>4.3 (0–22.7)</td>
<td>2.2 (0–9.7)</td>
</tr>
<tr>
<td>Exposure estimated at Age 35 (mSv)</td>
<td>104.0 (0–436.1)</td>
<td>53.5 (0–275.8)</td>
</tr>
<tr>
<td>Conservative Exposure estimated at Age 35 (mSv)</td>
<td>52.4 (0.5–218.0)</td>
<td>29.1 (0.6–137.9)</td>
</tr>
</tbody>
</table>

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GROWTH PROFILE IN CHILDREN WITH COW’S MILK PROTEIN ALLERGY AND THEIR RELATIONSHIP TO THE AGE AT DIAGNOSIS AND ILLNESS DETECTION TIME


**Background:** Current data suggest that cow’s milk protein allergy (CMPA) could have a negative effect on physical growth. The objective was to describe the growth profile (GP) in children with CMPA and this degree of correlation with age at diagnosis (AD) of the pathology and the detection time (DT) of the same.

**Methods:** Descriptive, correlational, and retrospective study. Sample of 23 children with CMPA who attended in the Gastroenterology and Nutrition Section at Hospital Pirovano during the period 2004–2007. By medical records were recruited: sex, age, date of baseline medical consultation, at 3, 6 and 9 months (m) after diagnosis, weight and height/length of each of the medical consultations, AD, age of onset of symptoms and type of formula used. Calculation of z-score was made to determine the GP.

**Results:** Mean weight z-score was $-1.08$ in baseline control (95% CI $-1.53$/$-0.63$), showing improvement from treatment with values that tend to approach zero at 3 m: $-0.67$ (95% CI $-1.06$/$-0.29$), 6 m: $-0.51$ (95% CI $-0.99$/$-0.03$) and 9 m: $-0.61$ (95% CI $-1.23$/$-0.003$) but not significantly different ($P = 0.25$ ANOVA). Mean height z-score showed similar trend with less marked differences: Basal $-0.92$ (95% CI $-1.43$/$-0.40$), 3 m: $-0.84$ (95% CI $-1.32$/$-0.36$), 6 m: $-0.73$ (95% CI $-1.31$/$-0.15$) and 9 m: $-0.78$ (95% CI $-1.38$/$-0.17$) ($P = 0.95$ ANOVA). There was a statistically significant inverse correlation between AD and z-score in control at 3 m for both weight $r = -0.54$ ($P = 0.018$) and for height $r = -0.48$ ($P = 0.037$). Same inverse correlation was observed between pathology DT and z-score in control at 6 m for both weight $r = -0.62$ ($P = 0.007$) and for height $r = -0.54$ ($P = 0.019$).

**Conclusions:** Inverse association between AD and DT with z-score of weight and height in children with CMPA warrants the interdisciplinary nature for diagnosis and treatment, to minimize negative impact on growth profile of these children.

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**SALMONELLA ENTERICA SEROVAR TYPHI INDUCES INCREASED MUCOSAL PERMEABILITY AND ELICITS A STRONG EPITHELIAL PROINFLAMMATORY RESPONSE AMELIORATED BY VACCINE CANDIDATES IN VITRO**

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**Background:** Salmonella species are a major cause of food poisoning and can induce a broad spectrum of diseases from mild diarrhea to typhoid fever. The World Health Organization estimates that 16 million cases of typhoid fever occur annually, resulting in ~600,000 deaths. Infection is initiated in the intestinal tract, and severe disease causes widespread destruction of the intestinal mucosa. The aim was to study the effects of wild-type Salmonella typhi and vaccine strains, CVD 908-htrA and CVD 909, on the intestinal barrier function and cytokine production.

**Methods:** Enterocyte-like cell line, Caco2, was inoculated with wild-type Salmonella typhi and vaccine strains to evaluate initial host-pathogen interactions and the effect of exposure and colonization of these strains on mucosal barrier function. Changes in epithelial permeability were recorded and pro-inflammatory cytokines interleukin-8 (IL-8), interleukin-6 (IL-6) and TNF-α were measured in culture supernatants.
Results: Caco2 cells infected with wild-type Salmonella enterica serovar typhi exhibited marked changes in tight junction proteins organization, an increase in the paracellular flux of dextran, and a rapid decrease in transepithelial electrical resistance (TEER) as early as 4 h post-infection. Cell viability tests showed that barrier function disruption was not associated with cell death caused by bacterial infection. S. typhi-induced production of IL-8, IL-6 and TNF-α. Infection of Caco2 cells with the new oral vaccine strains, CVD 908-htrhA and CVD 909, showed that both strains, but in particular CVD909, elicits immune response with minimal disruption of the barrier integrity, and hence offers reason for optimism for vaccine development.

Conclusions: S typhi causes specific and transient intestinal mucosal epithelial events, including changes in TEER and cytokine production that seem to be ameliorated by the engineering of specific vaccine candidates.

SHIGELLA FLEXNERI CAUSES SEVERE IMPAIRMENT OF MUCOSAL BARRIER INTEGRITY BY DISRUPTING TIGHT JUNCTION-MEDIATED FUNCTION IN VITRO

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Background: Shigellosis, a major form of bacillary dysentery, is caused by infection with Shigella organisms. In poor countries, Shigella-caused dysentery is endemic and causes an estimated 163 million illness episodes annually and more than 1 million deaths. The pathogenesis of S. flexneri is based on the bacteria’s ability to invade and replicate within the colonic epithelium, which results in severe inflammation and epithelial destruction. The aim of the study was to study the intestinal mucosal biological effects triggered by wild-type Shigella flexneri and vaccine strain CVD 1208S.

Methods: To model the interactions of Shigella with human intestinal mucosa, we have studied Shigella flexneri infection in human colonic cell line Caco2 by monitoring its effect on intestinal permeability and intestinal epithelial immune response.

Results: Inoculation of Shigella into human Caco2 cells caused severe mucosal damage, which was apparent as a drastic reduction of the transepithelial electric resistance (TEER) to basal level in less than 24 hours from infection. This decrease in epithelial permeability can be accounted for a breakdown of the tight junction integrity, as shown by immunofluorescence staining of infected cells in which we observed the disruption of tight junction components at the cell-cell boundary. Cell viability tests following Shigella infection indicate that the effects on epithelial barrier function induced by the bacteria are not caused by epithelial cell death. Infection of Caco2 cells with an attenuated vaccine strain of Shigella (CVD1208S) did not cause damage to the intestinal permeability barrier.

Conclusions: Collectively, our experiments support a model in which S. flexneri can interfere with the intestinal epithelium barrier function by disrupting the role of components of tight junctions. In addition, the preliminary data with CVD 1208S make this strain very attractive as a candidate vaccine.

PATIENT PERSPECTIVE ON IMPACT OF CROHN’S DISEASE (CD): RESULTS FROM GROUP INTERVIEWS

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Background: The impact of Crohn’s disease (CD) on patients’ lives is wide-ranging. It can be substantially disruptive, and often not recognized immediately by patients. The objective was to determine CD effects on patients’ lifestyles and assess patient relationships with their CD physicians.

Methods: CD patients from 3 US cities were given video cameras for “day-in-the-life” videos, and then interviewed in group settings. Group interviews delved more deeply into issues that arose in the personal videos, focusing on the overall impact of CD on patients’ lives and their interactions with physicians.

Results: 44 CD patients were recruited (mean age, 40 years; 50% women). Nearly all patients described CD as “embarrassing” (because of frequency of using bathroom, fear of self-soiling, and frequent flatus). Many patients initially reported they felt well, but upon reflection, explained this view was relative to past symptoms or to other CD patients. CD was frequently said to be silent (no easily visible manifestations), causing misperceptions among family and friends. Many patients, especially males, reported withholding quality of life information from their physicians.

Conclusions: Patients described dramatic impacts of CD on their lives, including fear, embarrassment, and the withholding of information from their physicians.

SOLITARY RECTAL ULCER SYNDROME IN A PEDIATRIC REFERRAL CENTER

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Background: Solitary rectal ulcer syndrome (SRUS) is rare, particularly in children. Diagnosis is often delayed, and treatment is often frustrating.
Methods: We reviewed all biopsy-proven pediatric cases of SRUS at a tertiary care center between 1997 and 2009. SRUS was defined by characteristic changes on rectal biopsy including fibromuscular hyperplasia, focal ulceration, ectasia of superficial capillaries, and minimal surface inflammation or cryptitis.

Results: Eight cases of SRUS were diagnosed in patients between 10.5 and 16.6 yrs of age. Symptoms common to all cases included rectal bleeding, alternating constipation and loose stools, and perianal pain with defecation. Six of eight children complained of cramplng abdominal pain. Mean duration of symptoms prior to diagnosis was 3.6 (range 1.0–7.7) yrs. No patient had significant anemia (hemoglobin 11.0–15.8 g/dL). In 4 patients, erythrocyte sedimentation rate ranged from 1 to 17 mm/hr, and serum albumin was 4.1 to 4.5 g/dL. Two patients were also diagnosed with inflammatory bowel disease, (one indeterminate and one ulcerative colitis). Four patients were treated with mesalamine suppositories; two achieved remission but later relapsed. Two patients were treated with stool softeners. One patient required prototectomy.

Conclusions: Differential diagnosis for SRUS includes juvenile polyps, inflammatory bowel disease, and sexual abuse, all of which are treated quite differently than SRUS. Clinical symptoms are non-specific, but common features of clinical history include blood or mucous in stools, pain with defecation, and mucosal prolapse. Histologic features are diagnostic. Cases are often refractory to medical management. Awareness of the constellation of symptoms suggestive of SRUS is essential to prompt diagnosis and initiation of treatment.

INTERNATIONAL TRENDS IN THE EPIDEMIOLOGY OF PEDIATRIC INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW

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Background: Estimates of international trends in incidence of pediatric inflammatory bowel disease (IBD) are controversial. We conducted a systematic review of research describing the epidemiology of childhood-onset IBD to evaluate temporal changes in incidence and assess international differences.

Methods: Multiple electronic databases were searched for articles published 1950–2009. Included studies reported incidence or prevalence of IBD, Crohn disease (CD) or ulcerative colitis (UC). Incidence and prevalence per 100,000 population of residents <21 years were extracted independently by two authors to ensure accuracy. Choropleth maps demonstrated international incidence of IBD, CD and UC, with incidence quintiles derived using Jenk’s natural breaks. Temporal changes in incidence were graphed using data from studies reporting rates over multiple time periods.

Results: Our search yielded 139 included studies. IBD incidence estimates are lacking for most countries, but data reported indicate substantial worldwide variation. Only 28 studies (20.1%) statistically analyzed trends over time. Of these, 77.8% reported statistically significantly increased incidence of pediatric IBD, 60% reported significantly increased CD incidence, and 20% reported significantly increased UC incidence. Of studies reporting incidence over multiple time periods (whether or not statistical trends were calculated), increasing CD incidence was demonstrated in most countries, while UC trends were inconsistent. No clear north-south gradient was demonstrated.

Conclusions: In both developed and developing nations, rates of pediatric IBD are rising (due primarily to the rising incidence of CD). Unfortunately, most countries lack accurate estimates. There is a need for comprehensive international and regional incidence trends to assist in identification of specific environmental risk factors for IBD.

CHANGES IN SURGICAL AND HOSPITALIZATION RATES IN PEDIATRIC INFLAMMATORY BOWEL DISEASE IN ONTARIO, CANADA (1994–2007)

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Background: Changes to the treatment of children with IBD over the past decade may have resulted in changes in outcomes. The aims of this study were to describe trends in medication use, associated health services (physician visits), and outcomes (hospitalization and surgical rates) between 1994–2007 in children with IBD.


Results: 2801 children were diagnosed between 1994–2004. IBD-related care was increasingly provided by pediatric gastroenterologists (GIs), with decreasing care by adult GIs and surgeons. Coincident with changes in care provision, children diagnosed in 2001–2004 with Crohn disease (CD) were more likely to use immunomodulators (P = 0.0001) or biologics (P = 0.004) within three years of diagnosis. Odds of being hospitalized at least once within three years was higher in the recent cohort for both CD (adjusted odds ratio
Background: An intestinal dysbiosis may exist in patients with Crohn’s disease (CD). Genetic variants such as CARD15 have implicated an innate immune defect in some patients with CD. We hypothesized that the dysbiosis in CD impairs innate immune function to compound the genetic defect. We aimed to assess the direct effects of bacterial products within fecal supernatant (FS) on innate immunity by measuring in vitro functional changes in immune cells exposed to FS from children with and without CD.

Methods: Fresh stool was collected from children ages 2–17 yrs with and without CD (13 CD, 5 healthy). No patient had received pre/pro/antibiotics in 4 weeks. Stool was homogenized with PBS then underwent 3 rounds of differential centrifugation. We evaluated the effect of FS on: neutrophil survival, bactericidal activity of neutrophils and macrophages, bacterial invasion (AIEC, LF82) of macrophages, and neutrophil superoxide production (SOP). Assays were run in triplicate. Results were analyzed by t-tests.

Results: Macrophage bactericidal activity was impaired after incubation with CD FS compared to healthy FS (HFS) (CD 2.09 ± 0.35, HFS 1.53 ± 0.26 fold-difference vs. PBS, P = 0.021). Neutrophil bactericidal activity decreased after CD FS exposure (CD 107.3 ± 24.5 × 10^3 surviving bacteria; HFS 24.3 ± 24.7 × 10^3, P = 0.004). Macrophage invasion also decreased after exposure to CD FS (lysate bacteria: CD 0.8 ± 0.29, HFS 1.96 ± 1.02 fold-difference vs. PBS, P = 0.004). Incubation with CD FS and HFS decreased neutrophil survival equally, but had no effect on macrophage/epithelial cell survival. Neutrophil SOP was reduced equally by both CD FS and HFS.

Conclusions: Fecal supernatant from children with CD produced a more profound impact on certain in vitro parameters of innate immune function than did FS from healthy children. This suggests an important mechanism in the pathophysiology of CD by which products from the gut microbiome may impair innate immunity.

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SODIUM PICOSULFATE AND POLYETHYLENE GLYCOL USED AS PREPARATION FOR COLONOSCOPY: A COMPARISON OF EFFICACY AND TOLERABILITY IN PEDIATRIC PATIENTS
Hamid Khour, Patricia Perreault, Denise Herzog. Division of Gastroenterology, Department of Pediatrics, University of Montreal, Sainte Justine Hospital, Montreal, QC, Canada.

Background: Tolerance for bowel cleansing with polyethylene glycol (PEG) when preparing for colonoscopy has always been a problem in pediatric patients. Sodium picosulfate recently became available for the same indication. The aim of our study was to compare the efficacy of the two drugs for colon cleansing. As a secondary outcome the tolerability of the two laxatives was compared.

Methods: Prospective assessment of the quality of cleansing by the endoscopy nurse and using the Aronchick scale for colon cleansing. Prospective assessment of tolerability of the laxative via a validated questionnaire filled out by the patient and his parents immediately before the colonoscopy.

Results: 123 children taking picosulfate (14.1 ± 3.5 y) and 48 taking PEG (13.4 ± 5.5 y) were evaluated. Of those, 36/171 were ≤ 10 years of age, and 20 of these latter required preparation via nasogastric tube and with PEG. We found no difference for the quality of colon cleansing between the two groups. Preparation was acceptable or more in 104/123 and 44/48 patients, respectively. Children rated picosulfate more palatable than PEG. Nausea and vomiting were reported less frequently with picosulfate than with PEG. The latter difference may be due to the rapid administration of PEG via nasogastric tube.

Conclusions: Both laxatives are equally effective for colon cleansing. Children rated picosulfate more palatable than PEG. We therefore use PEG when nasogastric tube is required and picosulfate for oral colon cleansing.

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OUTCOME FOLLOWING AMINOSALICYLATE (SASA) THERAPY IN CROHN’S DISEASE (CD)
Henna Patel1, Trudy Lerer2, Jeff Hyams2, Athos Bousvaros2, Wallace Crandall1, Jonathan Evans2, William Faubion2, Anne Griffths1, Andrew Grossman2, Michael Kappelman2, Marsha Kay2, David Keljo2, Neal Leleiko2, David Mack2, Sonia Michail2, Maria Oliva-Hemker2, Anthony Otley2, Marianne Pfefferkorn2, Joel Rosh2, Shehzad Saeed2, Charles Samson2, Michael Stephens2, Boris Sudel2, James

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www.jpgn.org
Markowitz1,2, 1Cohen Children’s Medical Center of NY, New Hyde Park, NY; 2The Pediatric IBD Collaborative Research Group, Hartford, CT.

Background: Despite little supporting data, oral 5ASA are commonly used in children with CD. The aim was to describe the outcome of children newly diagnosed with CD given 5ASA as their exclusive initial therapy.

Methods: Data were drawn from the Pediatric IBD Collaborative Research Group Registry, a prospective observational database. Children <16 yrs of age are recruited at diagnosis (dx) and managed by their treating physicians, not standard protocols. All children with CD followed ≥1yr who received oral 5ASA monotherapy at dx were included. Remaining free of steroids, surgery, biological and/or immunological therapies at 30 days, 3 months and 1 yr was considered a successful outcome. Univariate and multivariate analyses were performed to identify baseline clinical (age, gender, CD activity, CD location, height Z score) and lab (Hgb, albumin, ESR, CRP, platelets) characteristics associated with 5ASA success or failure. CD activity was assessed by Physician’s Global Assessment (PGA: mild, moderate/severe).

Results: 173 children (age 11.5 yrs, 56% male, 55% mild CD at dx) initially received only 5ASA. 5ASA success: 30 days: 122 (70%), 3 months: 97 (56%), 1 yr: 61 (35%). Univariate analysis identified 3 baseline characteristics associated with 5ASA success or failure. CD activity was assessed by Physician’s Global Assessment (PGA: mild, moderate/severe).

Conclusions: At 1 yr only 35% of children given 5ASA alone do not require additional therapy. These data raise questions regarding the appropriateness of 5ASA monotherapy in children with CD.

Table.

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<th>30-day failure</th>
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<th>1-yr failure</th>
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<td>OR 95% CI P</td>
<td>OR 95% CI P</td>
</tr>
<tr>
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<td></td>
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<tr>
<td>2.1 1.0–4.3 0.054</td>
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<td>3.8 1.9–7.7 &lt;0.001</td>
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POTENTIAL NEW BIOMARKERS OF COLONIC DYSPLASIA IN ULCERATIVE COLITIS SCREENING

Jason M. Shapiro1,2, Rolf I. Carlson2, Jack R. Wands2. 1Pediatric Gastroenterology, Rhode Island Hospital, Providence, RI; 2Liver Research Center, Rhode Island Hospital, Providence, RI.

Background: Colon cancer is a complication of ulcerative colitis (UC). Current guidelines support regular screening colonoscopies starting 10 years from diagnosis. There are no good biomarkers to evaluate a pre-dysplastic state in colon cancer screening. It is known that aspartyl asparaginyl β-hydroxylase (AAH) expression is up-regulated in malignant tumors and invasive tissues (placental trophoblasts). Up-regulation of this protein may be a sign of malignant transformation. Also, the antigens of the AF20 and SF25 antibodies have been implicated in malignant transformation. The aims were to establish the presence of 3 new biomarkers of colon dysplasia in colon cancer cell lines and evaluate their up-regulation in tumor-associated human tissues.

Methods: Immunohistochemistry was done on three colon cancer cell lines (LS180, CaCO2, SKCO1) and a fibroblast control (NIH3T3). These cells were stained using the antibodies of interest: FB50 (AAH), AF20, SF25 as primary antibodies and an HRP conjugated secondary antibody. Cell lysates were obtained from LS180, CaCO2 and NIH3T3 cells and western blots were performed and probed. Lastly, paraffin-embedded human colonic biopsies containing a range of histopathologies were stained.

Results: Immunohistochemistry with all three antibodies revealed a strong staining pattern for the colon cancer cell lines compared to control. Similarly, western blots revealed up-regulation of the respective antigens in the colon cancer cell lines with a paucity of banding noted for the fibroblasts. Preliminary staining of human tumor and associated tissues revealed strong staining of dysplastic polyps and frank tumor with minimal reactivity against normal colonic mucosa.

Conclusions: We have shown that AAH, AF20 and SF25 are up-regulated in colon cancer cell lines, dysplastic human tissue and tumors. Thus, these antigens may be associated with malignant transformation of colonocytes and prove invaluable biomarkers of colonic dysplasia in the future of both general colonoscopy and UC screening.

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DIAGNOSTIC MEDICAL RADIATION IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Certain diagnostic radiology procedures may expose patients to radiation and increase the risk for cancer. This may be particularly important among patients with chronic, cancer-associated conditions such as inflammatory bowel disease (IBD).

Methods: Patients with IBD were identified from the medical records of a pediatric tertiary care center. The number and type of radiology procedures for each patient
was determined from medical record review. Cumulative effective radiation dose was calculated using published standard radiation effective dose estimates.

**Results:** 105 patients with inflammatory bowel disease underwent radiation associated abdominopelvic diagnostic radiology procedures with an average cumulative radiation exposure dose of 19 (18) [mean (SD)] mSv. 83% of the patients were exposed to acute radiation doses ≥10 mSv and nine patients (8%) were exposed to levels of cumulative radiation exposure ≥50 mSv which has been associated with an increased risk of cancer development. Patients with Crohn’s disease, an increased number of hospital admissions, and a prior history of surgery were more likely to have been exposed to higher levels of cumulative radiation than clinical counterparts.

**Conclusions:** A majority of IBD patients are exposed to radiation from typical diagnostic radiology procedures. Radiation-sparing procedures should be strongly considered in certain pediatric IBD patients to reduce their risk for cancer given an already-present increased lifetime malignancy potential. Multivariate model predicting Cumulative Effective Dose among IBD patients (N = 105).

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<tr>
<td>History of surgery (yes vs. no)</td>
<td>15.78</td>
<td>0.0008</td>
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**INFLIXIMAB AS PRIMARY THERAPY FOR CROHN’S DISEASE IN CHILDREN**


**Background:** Infliximab (IFX) is effective for the treatment of moderate to severe Crohn’s disease (CD) in children. Its use usually follows immunomodulators (IM) and there are little data on outcomes following IFX used as primary therapy. The aim was to describe outcome following primary IFX therapy in children with CD in a large pediatric IBD center.

**Methods:** Chart review of all IFX therapy for CD at Connecticut Children’s Medical Center from 4/06 until 5/10.

**Results:** During the study period 116 patients with CD were exposed to acute radiation doses ≥10 mSv and nine patients (8%) were exposed to levels of cumulative radiation exposure ≥50 mSv which has been associated with an increased risk of cancer development. Patients with Crohn’s disease, an increased number of hospital admissions, and a prior history of surgery were more likely to have been exposed to higher levels of cumulative radiation than clinical counterparts.

**Conclusions:** A majority of IBD patients are exposed to radiation from typical diagnostic radiology procedures. Radiation-sparing procedures should be strongly considered in certain pediatric IBD patients to reduce their risk for cancer given an already-present increased lifetime malignancy potential. Multivariate model predicting Cumulative Effective Dose among IBD patients (N = 105).

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**AGREEMENT BETWEEN PATIENT- AND PHYSICIAN-COMPLETED PEDIATRIC ULCERATIVE COLITIS ACTIVITY INDEX (PUCAI) SCORES**

Jessica J. Lee,1 Ruben J. Colman,1 Paul D. Mitchell,2 Melissa L. Atmadja,1 Athos Bousvaros,1 Jennifer R. Lightdale.1

1Medicine/Gastroenterology, Children’s Hospital Boston, Boston, MA; 2Clinical Research Program, Biostatistics Core, Children’s Hospital Boston, Boston, MA.

**Background:** Currently validated ulcerative colitis (UC) activity measures are physician-based, but incorporate patient reports of symptoms. We aimed to assess whether patient-completed pediatric UC activity index (PUCAI) scores are comparable to those of physician scores.

**Methods:** We performed a single-center prospective study to assess agreement between patient- and physician-completed PUCAI scores. Seventy UC patients (ages 4–29) representative of all disease activity categories (inactive, mild, moderate and severe) in the currently published physician-completed scoring system were recruited. Agreement was analyzed for PUCAI scores both as continuous and categorical measures. In order to ascertain validity, we compared both patient- and physician-completed PUCAI scores to the Physician Global Assessment (PGA) and serum inflammatory markers.

**Results:** Patient- and physician-completed PUCAI summary scores were identical 49% of the time, were different but within the minimal clinically important difference (MCID) of 20 points 48% of the time, and were at or beyond the MCID only 3% of the time. In general, patients reported higher mean disease activity on their questionnaires than did their physicians, with a mean difference in PUCAI scores of 3 ± 8 (95% CI, 2–5). A categorical comparison of the two sets of questionnaires using the disease activity groups
demonstrated perfect agreement for 60 (86%) pairs (kappa coefficient = 0.78; 95% CI, 0.65–0.90). Both patient- and physician-completed PUCAI scores also correlated well with the PGA and serum inflammatory markers.

Conclusions: Our data indicate that PUCAI scores obtained directly from patients are comparable to those of physician scores. Hence, a patient-based PUCAI could complement existing instruments in both clinical and research settings.

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LONG-TERM ADA LUMIMUB THERAPY IS SAFE AND EFFECTIVE IN PEDIATRIC CROHN’S DISEASE
Joel R. Rosh, Trudy Lerer, James Markowitz, Petar Mamula, Marian Pfefferkorn, Anne Griffiths, Subra Kugathasan, David Keljo, Maria Oliva-Hemker, Wallace Crandall, Ryan Carvalho, David Mack, Jeffrey Hyams. Pediatric IBD Collaborative Research Group, Hartford, CT.

Background: To characterize dosing, clinical response and safety of long-term adalimumab (ADA) in pediatric Crohn’s Disease (CD).

Methods: Retrospective chart review from 12 sites of the Pediatric IBD Collaborative Research Group identifying all CD patients given > 1 year of ADA. Clinical and demographic characteristics including dosing used; disease activity using Physician Global Assessment (PGA) and PCDAI; and serious adverse events including surgery, hospitalization, infection, malignancy, and death, were recorded.

Results: 24 patients (50% male) received >1 year of ADA. Mean age at CD diagnosis was 10.7 ± 2.4 yrs (6.6–16.4), first ADA was given at 4.1 ± 2.1 yrs (1.0–8.4) after diagnosis and duration of follow-up was 21.2 ± 7.6 months (12–40). Induction regimens were 80/40 in 50%, 40/40 in 29% and 160/80 in 8%. Initial maintenance dosing was 40 mg every other week in 87.5% but escalated to weekly dosing in 42% by one year. IFX treatment preceded ADA in all patients, with a mean of 9 IFX infusions (range 3–22). IFX was discontinued because of loss of response (42%) and infusion reaction or IFX intolerance (54%). Concomitant corticosteroids use was 33% at ADA baseline, 8% at one year and 17% at end of follow-up. Concomitant immunomodulator (thiopurine/methotrexate) use was 71% at baseline, 46% at 12 months and 37.5% at end of follow-up. Using PGA, 33% had mild/inactive disease at ADA baseline compared to 87.5% at 12 months and end of study. Mean PCDAI scores at baseline, 12 months and end of study were 28 ± 12.5, 7.5 ± 7.9, and 11.8 ± 12.7 respectively. There were no malignancies, serious infections or deaths.

Conclusions: ADA was a well-tolerated and durable rescue therapy for moderate-severe pediatric CD patients previously treated with IFX. Steroid free remission through a mean of 21 months was maintained in the majority of this cohort. ADA dose escalation and decreased use of concomitant immunomodulators was common.

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HEPATITIS B VIRUS IMMUNITY IN PEDIATRIC PATIENTS ON BIOLOGICS FOR INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE CROSS-SECTIONAL STUDY
Jonathan Moses, Naim Alkhouri, Angela Shannon, Kathy Raig, Rocío Lopez, Ariel Feldstein, Nizar Zein, Robert Wyllie, Christine Carter-Kent. The Cleveland Clinic, Cleveland, OH.

Background: Biologics have revolutionized the treatment of inflammatory bowel disease (IBD); however, these medications are potent immunosuppressants. Hepatitis B virus (HBV) infection is a vaccine-preventable infection that can be reacti- vated in chronic HBV carriers receiving biologics. The aims of this study were to determine hepatitis B immunity and prior exposure in children with IBD on infliximab therapy for IBD.

Methods: This was a prospective, cross-sectional, single-center study that included 100 pediatric IBD patients on infliximab. Serologic specimens were tested for HBsAg, anti-Hbc, and anti-HBs. Patients with an anti-HBs level ≥10 mIU/mL were considered to be immune.

Results: The mean age of patients was 17.8 (±4.0) years. None of the patients were positive for HBsAg or anti-Hbc. Regardless of vaccination history, 49% of patients had immunity to HBV as defined by anti-HBs ≥10 mIU/mL. The mean concentration of anti-HBs levels in immune patients was 295.6 (±350.6) mIU/mL. Vaccination records were available for 67 patients, of these 61 (91%) had received HBV vaccination in the past and 6 (9%) had not. In patients who were vaccinated, only 28/61 (46%) had anti-HBs level ≥10 mIU/mL indicating the absence of protective antibodies in 54% of vaccinated patients. Lower albumin levels and presence of pancolitis were associated with loss of protective immunity in 62%. The concurrent use of infliximab did not affect HBV immunity. Data on response to the HBV vaccine booster and full series are pending.

Conclusions: Only half of pediatric IBD patients had protective anti-HBs levels. Patients with IBD treated with infliximab without protective immunity against HBV are potentially at risk for severe liver disease if exposed to the virus or if the virus is reactivated in chronic carriers. Checking HBV immunity in children with IBD should be strongly considered when patients are started on therapy with infliximab.

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THE PREVALENCE OF HEPATITIS A ANTIBODIES IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE
Naim Alkhouri, Jonathan Moses, Angela Shannon, Kathy Raig, Rocío Lopez, Ariel Feldstein, Nizar Zein, Robert Wyllie, Christine Carter-Kent. The Cleveland Clinic, Cleveland, OH.
Blood samples were tested for IgG anti-HAV. Participants were documented to obtain from medical records and factors related to IBD (type, severity, location, treatment, etc.) were documented. Clinical data were obtained for IgG anti-HAV. P < 0.05 was considered statistically significant.

Results: The mean age for IBD diagnosis was 12.6 (±3.2) years, 60% were male and 88% were Caucasian. Crohn’s disease was present in 91% and ulcerative colitis in 9%. Only fourteen patients (14%) were positive for IgG anti-HAV, suggesting immunity from previous exposure or vaccination. Of these patients, ten were vaccinated against hepatitis A (71.4%). There were no significant epidemiological differences between immune and non-immune patients, including mean age, gender, ethnicity, history of blood transfusion, family history of hepatitis, severity and location of IBD, and immunosuppressive therapy for IBD.

Conclusions: The seroprevalence of HAV antibodies in our pediatric patients with IBD is very low (14%). Given the potential complications of liver disease in children with IBD, vaccination to the HAV virus should be administered on a routine basis. If providers cannot obtain documentation of previous vaccination, children with IBD should be screened for anti-HAV antibodies to identify vaccine candidates and the vaccine administered to patients who are determined to be negative for the antibodies.

We performed a retrospective chart analysis, and a review of liver and colonic biopsies.

Results: In all patients PSC was confirmed with either a cholangiogram or a liver biopsy (mild portal hepatitis with few plasmocytes associated with portal fibrosis; classical pericirrhal fibrosis in 33%). For 10 (67%) of the initial clinical presentation included digestive symptoms and abnormal biological liver tests, leading to a simultaneous diagnosis of PSC and IBD. During follow up, 67% of patients were in remission without steroids or immunosuppressive therapy. None had complications of their colitis. Endoscopic pancolitis was the most frequent feature (9/15), with rectal sparing in 2 cases; 4 patients had normal endoscopy with histologic pancolitis. Histologically, colonic biopsies demonstrated an important architectural distortion (50%) and focal glandular destruction (60%) or cryptic abscesses (30%). Most often, mucosecretion was conserved (80%). Colonic infiltration was mild (25%) to moderate (75%) and was predominantly composed of plasmocytes and eosinophils. No granulomas were found. Interestingly, 2 of the 3 patients with the most severe rectal disease also had histological ileal disease without macroscopic disease.

Conclusions: Pancolitis in pediatric patients with PSC appears to have a less severe clinical and histological pattern than what is observed in pediatric-onset UC or Crohn’s disease.

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COST-EFFECTIVENESS OF VSL#3 IN INDUCTION AND MAINTENANCE OF REMISSION IN PEDIATRIC ULCERATIVE COLITIS
K.T. Park1, Felipe Perez1, Anita Honkanen1, William Berquist1, Alan Garber2. 1Pediatrics, Stanford University, Stanford, CA; 2CHP/PCOR & VA Palo Alto Health Care Systems, Stanford University, Stanford, CA.

Background: Clinicians must promote cost-optimizing strategies in IBD amidst rising healthcare expenditures. Expensive medical therapies in ulcerative colitis (UC) may not be cost-effective. VSL#3 is shown to be beneficial in induction and maintenance of remission in UC. The aim was to determine the cost-effectiveness of adding VSL#3 as adjunct therapy to traditional medical therapy options.

Methods: We performed a systematic review of the literature and created a Markov model using TreeAge Pro 2009 software. Hypothetical 10 year old UC patients were enrolled at the time of initial UC flare to receive traditional therapy or VSL#3 + traditional therapy. Transition state probabilities and utilities were collected from published literature and used as input data. Cost data were collected from Lucile Packard Children’s Hospital billing records, the Office of Statewide Health Planning and Development tables, and 2 different online pharmacies. Incremental cost per quality adjusted life-years (QALYs) were measured compared to the base case of traditional therapy alone.
Results: We assumed a willingness-to-pay threshold of $50,000 per QALY. Adding VSL#3 to traditional therapy produced an incremental cost of $9454 per 0.64 QALY gained. This resulted in an incremental cost effectiveness ratio of $14,685 per QALY. One and two-way sensitivity analyses showed that the intervention was robust across a wide range of variables. A Monte Carlo simulation validated our findings. Adding VSL#3 became less cost-effective as the probability of inducing remission on traditional therapy alone approached the probability of inducing remission with traditional therapy alone.

Conclusions: VSL#3 appears to be a cost-effective strategy when added to mesalamine and steroid induction at the onset of UC flare.

CHARACTERISTICS OF PEDIATRIC IBD IN TEXAS
Kalpesh Thakkar1, Ashish Patel2, Carolyn Thibodeaux1, Kristin Tang1, Alejandra Perez1, George Ferry1, 1Baylor College of Medicine, Houston, TX; 2Dallas Children’s, 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 (eg, Hispanic, Black, Asian) 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 7 pediatric facilities in Texas between Jan 2009 and March 2010. We included all children with new diagnosis of IBD at each center. 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 93 children with newly diagnosed IBD (mean age 11.3; SD 2.8) including 48 (51.6%) female patients and 58 (62.4%) patients with Crohn’s disease (CD), 31 (33.3%) with Ulcerative Colitis, and 4 (4.3%) with Indeterminate Colitis. Race was described as “White/Caucasian” (56, 60.2%), followed by “Black/African-American” (21, 22.6%), “Hispanic” (11, 11.8%) and “Asian” (3, 3.2%). A family history of IBD was reported in 24 (25.8%) patients. 48 (51.6%) of patients presented with weight loss, 14 (15%) with arthritis/arthralgia, and 44 (47.3%) had gastrointestinal bleeding. Initial therapy included corticosteroids in 55 (59%), 5ASA products in 46 (49%), infliximab in 18 (19%), 6-mercaptopurine in 12 (13%), and azathioprine in 14 (15%) children. The presence of anemia, hypoalbuminemia, elevated ESR was not associated with race. Elevated CRP was associated with new-onset IBD in African American children (P = 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. CRP may have additional utility in African-American children presenting with IBD symptoms.

A NOVEL ENTERAL NUTRITIONAL THERAPY PROTOCOL FOR THE TREATMENT OF PEDIATRIC CROHN’S DISEASE

Background: Enteral nutritional therapy (EN) is an effective modality for inducing and maintaining remission of pediatric Crohn’s disease (CD). The current protocol for EN provides patients with 100% of their caloric needs. The aim of this study was to determine the efficacy of delivering 80–90% of patients’ caloric needs via EN to induce remission. This approach will allow patients to consume remaining calories from a normal diet.

Methods: Retrospective review of charts from 1998–2008 was conducted at CHOP. Inclusion criteria: age <18 years at diagnosis, active CD at start of EN and treatment with EN ≥ 4 weeks. Exclusion criteria: patients not on stable doses of steroids, anti-TNF α agents or immunomodulators at the initiation of EN. Remission was defined by an abbreviated PCDAI <10.

Results: 39 of 82 reviewed charts satisfied the inclusion criteria. Mean age at diagnosis was 11.2 years (8–17yrs), 27 (70%) were male, 12 (30%) were female. At diagnosis, 77% had small intestinal and colonic disease, whereas 23% had isolated colonic disease. Mean time from diagnosis to start of EN was 17 months (0–36 months); 7 patients started EN at diagnosis. Other medical treatments added on to EN included antibiotics (41%), immunomodulators (56%), 5-ASA (82%), steroids (28%), and Anti-TNF α agents (10%). Induction of remission was achieved in 35 (90%) at mean follow-up of 2 months (1–4 months). A significant increase in weight and height were seen in the population with median increases in z-scores of 0.91 [0.58–1.5] for weight and 0.32 [0–0.67] for height (P < 0.01).

Conclusions: This EN protocol, where patients receive 80–90% of their daily caloric needs, appears to be effective for the induction of remission in pediatric CD and contributes to significantly increasing weight and linear growth and improving patient quality of life. This protocol may result in improved EN acceptance and compliance, and will continue to be evaluated retrospectively as well as prospectively.

INVASIVE SALMONELLOSIS IN INFANTS VARIES BY AGE AND SEASON
Lay Har Cheng1, Barbara Mahon2, Andi Shane1, Conrad Cole1. 1Emory University School of Medicine, Atlanta, GA; 2CDC, Atlanta, GA.

Abstracts
**Background:** Infants are at increased risk for infection with Salmonella. However, little is known about variations in risk within infancy or seasonally.

**Methods:** The Foodborne Diseases Active Surveillance Network conducts active surveillance for Salmonella infections and collects data on case age and outcome (alive vs. dead at 7 days after specimen collection or at hospital discharge). We defined invasive infections as those in which Salmonella was isolated from a normally sterile site such as blood. We analyzed data for 1996–2008 on case-patients <18 years old, defining infants as <12 months old at specimen collection, and used census estimates to calculate average annual incidence and mortality. We compared incidence rates and proportions of invasive disease and examined the seasonal distribution of infections.

**Results:** In all, 30,359 infections were reported, 7930 in infants. Among infants, the lowest incidence of salmonellosis was in the first month of age (6.0/100,000), rising to a peak in the fourth month (13.7/100,000), relative risk (RR): 2.3, 95% confidence interval (CI): 2.0–2.6), then declining to 8.9 by the twelfth month (RR compared with first month: 1.5, CI: 1.3–1.7). In contrast, the proportion of infections that was invasive was highest in the first month (12%), falling to a nadir in the fourth month (4%, P < 0.0001), then stabilizing at 4–6% for the remainder of the year. The seasonal pattern of infections varied by invasiveness: stool isolations in infants peaked in August, but invasive infections peaked twice, in June and December. In older children, stool isolations peaked in July; invasive infections also peaked twice, but in August and December.

**Conclusions:** Infant salmonellosis peaks in the fourth month of age, but the proportion of infections that is invasive is highest in the first month. The seasonal distribution of Salmonella infection in infants varies by invasiveness and also differs from the patterns seen in older children. These findings suggest unexplained variability in susceptibility to invasive and noninvasive salmonellosis during infancy and across the seasons.

**HUMAN STOOL CONTAINS A PREVIOUSLY UNRECOGNIZED DIVERSITY OF NOVEL ASTROVIRUSES**

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Human astroviruses are a leading cause of diarrhea. Since 1975, 8 closely related serotypes have been described in humans, and recently, two new astrovirus species, astrovirus MLB1 and astrovirus VA1, were identified in diarrhea patients. In this study, we used consensus astrovirus primers targeting the RNA polymerase to define the diversity of astroviruses present in pediatric patients with diarrhea on two continents. From 416 stool specimens collected in Vellore, India, 35 samples were positive. These positive samples were then analyzed by several sequencing of the ~400 bp ampiclon generated by the consensus PCR or by performing additional RT-PCR specific for individual astroviruses. 19 samples contained the classic human astrovirus serotypes 1–8 while 7 samples were positive for the recently described astrovirus MLB1. Strikingly, from samples that were positive in the consensus PCR screen but negative in the specific PCR assays,
5 samples contained sequences that were highly divergent from all previously described astroviruses. Sequence analysis suggested that 3 novel astroviruses, tentatively named astroviruses VA2, MLB2 and VA3, were present in these 5 patient specimens. Using the same RT-PCR screening strategy, 13 of 466 stool specimens collected in St. Louis were positive. Nine samples were positive for the classic human astroviruses. One sample was positive for AstV-VA2, and 3 samples were positive for AstV-MLB2 demonstrating that these 2 viruses are globally widespread. Collectively, these findings underscore the tremendous diversity of astroviruses present in fecal specimens from diarrhea patients. Given that a significant fraction of diarrhea is of unknown etiology, it is plausible that these or other yet unrecognized astroviruses may be responsible for at least part of the undiagnosed cases.

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RELIABILITY OF THE MONTREAL CLASSIFICATION FOR PEDIATRIC INFLAMMATORY BOWEL DISEASE
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Background: The Montreal Classification was developed to provide a uniform system of designating subgroups of patients with inflammatory bowel disease (IBD), with the aim of facilitating multi-center genotype-phenotype correlation studies.[1] Although the classification is frequently used for pediatric IBD patients, its reliability in this population has never been evaluated. The aim of the study was to determine the reproducibility with which experienced IBD clinical researchers apply the Montreal Classification in pediatric settings.

Methods: Case scenarios were constructed using de-identified data from the medical records of 50, randomly-selected, pediatric IBD patients. Data pertaining to clinical presentation, radiologic and endoscopic investigations were recorded. International IBD experts classified these cases using the Montreal Classification on two separate occasions. Inter-rater and intra-rater reliability was determined using the kappa statistic. A kappa of >0.6 and >0.8 was considered to indicate good and excellent reliability respectively.

Results: 12 international pediatric IBD experts participated. The inter-rater reliability for the diagnosis of Crohn disease (CD), Ulcerative colitis (UC) or IBD-unclassified (IBDU) was moderate with a kappa statistic of 0.63. The median kappa statistic for intra-rater reliability for diagnosis was 0.70 (range 0.57 to 0.80). Incomplete diagnostic workup, the presence or absence of perianal disease and upper GI tract findings led to variation in classification.

Conclusions: Variability exists in the phenotypic classification of pediatric IBD patients. Rigorous classification is essential in order to realize the true impact of genotype-phenotype correlations.

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THE ORAL MICROBIOME IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE
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Background: Patients with inflammatory bowel disease (IBD) often have oral inflammation. Our prior studies have demonstrated that the oral microbiome is altered in periodontitis and in systemic diseases. The aim of this study was to assess the feasibility of utilizing a novel technology (Human Oral Microbe Identification Microarray, HOMIM) to characterize oral microbial populations in children with IBD.

Methods: In this case-control investigation, tongue brushings from 13 children with IBD (7 CD, 6 UC) and 10 controls were sampled. Of these 23 patients, 3 IBD patients and 1 control had buccal ulcers; for this subset, the buccal lesion and the contra-lateral unaffected mucosa were sampled. Bacterial DNA was isolated using standard techniques and PCR amplified with universal 16s rRNA primers. PCR products were labeled in a nested PCR with a Cy3 fluorescent dye, and hybridized to the HOMIM microarray. This technology allows for the simultaneous detection of nearly 300 of the most predominant oral bacterial species, including microbes that have yet to be cultured.

Results: From tongue brushings, we found decreased microbial diversity in IBD patients compared to controls (mean 28 species per person in IBD vs. 23 species in controls, P < 0.05). This observation was most pronounced in the Bacteroidetes phylum (mean 0.8 in IBD patients vs. 2.4 in controls, P < 0.05). Tongue samples demonstrated greater microbial diversity than buccal samples (mean 25 species per person in tongue samples vs. 10 species in buccal samples, P < 0.001).

Conclusions: In our pilot study, we identified decreased diversity in the tongue microflora of children with IBD compared to controls. In addition, we have demonstrated that the tongue microbiome is more varied than the buccal mucosa, as has been shown in our prior studies. Our findings suggest that patients with IBD may have an altered oral microbiome. Further work is underway to validate these initial findings by increasing our sample size.

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PSYCHOSOCIAL INFLUENCES ON PAIN IN PEDIATRIC IBD
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Abstracts

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Background: Pain is a symptom of IBD thought to signify ongoing disease activity. Psychosocial variables impact pain in many chronic diseases, but few have evaluated the interface of psychosocial factors and pain in pediatric IBD. Catastrophizing (CAT) is one factor shown to be a robust correlate of pain intensity, duration, and treatment efficacy. CAT is a cognitive-emotional process whereby a person has difficulty disengaging attention from pain, ruminates about pain sensations, and feels helpless in managing/escaping from the pain. The aim of the study was to evaluate the impact of child and parent CAT on associations between IBD activity, pain and functioning.

Methods: Children and parents answered questionnaires assessing CAT and pain. Children also completed measures of depression and functional disability. IBD activity was assessed by the PGA as inactive/mild or moderate/severe. Hierarchical regressions were employed to examine main effects of IBD activity and CAT on child’s pain, as well as interactions between IBD activity and CAT. Covariates included depression and IBD activity.

Results: 40 child/parent pairs enrolled; mean age 15.2 yr (9.6–18.9 yr); CD (81%), UC (19%); 71% inactive/mild, 28% mod/severe; mean IBD duration 36.2 (0.2–137 mo). A significant interaction between IBD activity and child CAT on functional disability (P = 0.014) was observed, such that child CAT was associated with greater functional disability among children with mod/severe IBD activity. A significant interaction between IBD activity and parent CAT emerged for pain (P = 0.003), such that parent CAT was associated with greater pain in children with mod/severe IBD activity.

Conclusions: Results suggest parent and child CAT may worsen pain and functioning in mod/severe IBD, thus psychosocial interventions involving parent and child may be beneficial in managing pain and functioning in pediatric IBD. Understanding factors that contribute to pain in pediatric IBD is necessary for the development of appropriate screening, treatment, and prevention tools and strategies.

IGF-1 LEVELS MAY EXPLAIN SEX DIFFERENCES IN GROWTH IMPAIRMENT IN PEDIATRIC PATIENTS WITH CROHN’S DISEASE

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Background: Growth impairment is more common in males than females with Crohn’s disease (CD) for unknown reasons. Since insulin-like growth factor 1 (IGF-1) is required for maximal growth potential, we hypothesized that IGF-1 levels are lower in males with CD.

Methods: Cross-sectional study of 82 CD patients <21 years old (43% female) enrolled between 1/07 and 7/09. We examined sex differences in hormone Z scores based on chronological age (CA-Z) and bone age (BA-Z). Estradiol and follicle stimulating hormone (FSH) Z scores in females were compared to testosterone and luteinizing hormone (LH) Z scores in males.

Results: IGF-1 CA-Z and BA-Z scores were –0.50 units (P = 0.04) and –1.24 units (P = 0.003) lower in males compared with females. Mean bone age (12.2 years) was lower than chronological age (13.1 years) (P < 0.0001), and bone age delay did not differ by sex (P = 0.10). ESR, CRP, and albumin did not differ by sex (P ≥ 0.08), and predicted IGF-1 CA-Z and BA-Z scores (P < 0.02). Insulin-like growth factor binding protein 3 (IGF-BP3) CA-Z and BA-Z scores were –0.71 units (P = 0.004) and –1.26 units (P < 0.001) lower in males. Sex hormone CA-Z (P = 0.98) and BA-Z (P = 0.19) scores did not differ by sex. Male LH CA-Z scores did not differ from female FSH CA-Z scores (P = 0.39), but male LH BA-Z scores were lower than female FSH BA-Z scores at Tanner stage (TS) 1 (P = 0.01) and 2 (P = 0.06). Urine growth hormone (GH)/serum IGF-1 ratio was higher in males at TS 1 (P = 0.02) and 2 (P = 0.04), which may indicate greater GH resistance.

Conclusions: Lower IGF-1 levels in males may explain sex differences in growth impairment in CD. Prospective longitudinal study is required.

PRESENTATION OF PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD) IN SOUTH ASIANS COMPARED WITH CAUCASIANS

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Background: Data on the presentation of pediatric IBD in South Asian patients are lacking. We compared the presentation of pediatric IBD in South Asian (SA) with Caucasian (C) patients followed at the UCSF Pediatric IBD clinic.

Methods: Retrospective cohort study of UCSF SA IBD patients < 18 years, diagnosed between 4/1/94 and 4/1/09. Four C for each SA patient were randomly selected as controls. Demographic data, IBD subtype, presenting symptoms, and disease location were compared by race. The Fisher’s Exact Test was applied.

Results: 108 patients (13% SA; 58% female). Mean age at diagnosis was 11.2 ± 4.0 (standard deviation). SA and C did not differ by gender (P = 0.99), age at diagnosis (P = 88), or initial classification of disease (P = 0.99). SA more
commonly presented with fever (36% vs. [C] 13%, \(P = 0.04\)), poor weight gain (21% vs. [C] 2%, \(P = 0.02\)), and vomiting (36% vs. [C] 11%, \(P = 0.03\)). Prevalence of upper GI tract (\(P = 0.22\)), terminal ileal (\(P = 0.69\)), ileocolonic (\(P = 0.33\)), and colonic (\(P = 0.78\)) disease did not differ by race. Perianal disease was more common in SA (43%) than C (8%) (\(P = 0.002\)). In patients with Crohn’s disease, although the prevalence of granulomas did not differ by race (\(P = 0.19\)), a higher proportion of SA (36%) had granulomas in the right colon compared with C (7%) (\(P = 0.02\)).

**Conclusions:** SA with pediatric IBD appear to have a more severe presentation of disease compared with C. Prospective multi-center studies, incorporating patient genotype and geographic birth history, will improve our understanding of racial differences in the presentation of pediatric IBD.

**PATHOGENIC YERSINIA DNA IN INTESTINAL SPECIMENS OF PEDIATRIC PATIENTS WITH CROHN’S DISEASE**

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**Background:** Although there is no proof that infectious agents are the cause of Crohn’s disease (CD), several reports indicate a close pathogenic relationship with intestinal microbiota and CD demonstrated by increased serology against bacterial components. Lamps et al previously reported identifying *Yersinia* species by PCR in intestinal specimens from 31% of adult patients they studied with CD. *Yersinia* infection in children has a higher prevalence than in adults. Our study was aimed to determine the presence of *Yersinia* in intestinal tissue in children with CD.

**Methods:** We tested 62 intestinal biopsy or resection specimens from 58 pediatric patients with CD for presence of *Yersinia* DNA by a validated PCR assay. Control cases included 55 specimens from 45 patients with ulcerative colitis (UC) and 10 patients with appendicitis (ie, non-IBD controls). All cases had a firm diagnosis of CD determined by colonoscopy and biopsies without any clinical or bacteriological evidence (negative stool cultures) of *Yersinia* infection at diagnosis or during follow up.

**Results:** Seven of 62 CD cases (11%) contained pathogenic *Yersinia* DNA. None of the 55 controls (0%) were positive for *Yersinia* DNA. The presence of *Yersinia* in CD specimens was significantly increased compared to the control groups (11% vs 0%, \(P = 0.0055\)).

**Conclusions:** This is the first study demonstrating the presence *Yersinia* DNA in pediatric CD intestine. Our study adds evidence to the literature that increased pathogenic bacteria such as *Yersinia* can be seen in CD despite no clinical evidence of such infection. This indicates the close relationship between CD and microbiota, which is presumably due to genetic defects in bacterial handling (such as NOD2 and ATG16L1 mutations), defects in intestinal permeability, and mucosal barriers in ileum.

**DISCREPANCIES IN SELF-REPORTED AND OBJECTIVE THIOPURINE ADHERENCE IN TEENS WITH IBD**

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Thiopurines are a widely used treatment for teens with IBD, and previous research has documented variable rates of medication adherence in this group. Inconsistencies in adherence rates may be due to the use of different assessment methods. Self-reports have been criticized as overestimating adherence, but no studies have examined the extent of overestimation in teens with IBD. This study examined discrepancies in thiopurine adherence via objective (MEMS cap electronic monitors) and subjective (monthly interview ratings of missed doses) methods and explored demographic and psychosocial correlates of MEMS adherence. 30 teens ages 11–18 participated. Participants were 63% male, 93% Caucasian, and most (93%) had Crohn’s disease. Youths used a MEMS cap for their thiopurine for 6 months (mean days of use = 195, SD 32) and completed monthly phone interviews for 6 months, during which they reported the number of missed thiopurine doses in the last week. Although correlations between objective and subjective adherence indicators were high (\(r = 0.77 - 0.80, P < 0.001\)), significant discrepancies in adherence rates were found depending upon method utilized. MEMS cap indices ranged from 12% to 100% (mean 83%), while interview ratings were much higher (99% to 100%; mean = 100%). Across the full sample, interview ratings overestimated adherence by 17% on average. Youths who were nonadherent (took < 80% of doses based on MEMS) had far greater overestimation of adherence (mean = 47%) based on self report than did youths who were adherent (took 80% or more of doses based on MEMS; mean = 7%). No differences in MEMs adherence rates as a function of sex, age, thiopurine knowledge, or involvement in condition management were found (\(r = 0.06 – 0.34, P < 0.05\)). Self reported adherence had limited utility in identifying nonadherent teens with IBD. Clinicians should be cautious in using teen report when nonadherence is suspected.
DEFINING DNA METHYLATION SIGNATURES IN ULCERATIVE COLITIS DIFFERENTIATES IL10 IN A SUBSET
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Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease of unknown etiology. Since there is a higher risk of dysplasia and colorectal cancer in long standing UC we hypothesize that DNA methylation signature of oncogenes could be different in UC. IL-10 has been studied in UC extensively since IL-10 is an potent anti-inflammatory cytokine. IL-10 knockout mice develop spontaneous colitis and adenomas, genome wide association studies and candidate gene approaches have identified IL-10 as a susceptibility gene in UC. To that end, we investigated aberrant methylation signatures of 806 oncogenes, including IL-10 in UC. The aim was to determine whether distinct methylation pattern in genomic DNA is present in UC.

Methods: Narrow phenotypes of UC (Caucasians with pancolitis and onset <16 yrs, n = 23) were compared to age, gender and race matched controls (n = 23). Illumina GoldenGate Cancer Panel I, a validated microarray bead assay for the detection of methylation patterns of 1505 loci from 807 oncogenes was used. Differential loci were assessed using multiple methods. The final differential loci were calculated using a differential analysis module. Replication of our finding was performed by cloning and sequencing of 30 clones per selected samples to validate initial findings.

Results: After analysis, 21 loci of 1505, including IL-10 promoter region, showed significant methylation patterns (P < 0.0001) compared to controls. Heatmaps and unsupervised hierarchical clustering using complete linkage showed patients with UC had significant differences in methylation patterns at IL-10 promoter region. Validation with cloning and sequencing of the IL-10 region with bisulfite treated PCR products showed significant correlation with these results. Pearson correlation of 0.747.

Conclusions: Patients with UC showed distinct methylation signatures at 21 loci. We have replicated the IL-10 loci in a subgroup of patients with UC.

THE “UPOPOLIS” SECURE SOCIAL NETWORK: AN EFFECTIVE WAY TO EDUCATE CHILDREN AND TEENS ABOUT INFLAMMATORY BOWEL DISEASE (IBD)
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Background: In a previous study, we reported that pediatric IBD patients, in contrast to their parents did not make much use of a free IBD information CD distributed to our clinic patients and families. As youth commonly use the internet, we examined the effectiveness of presenting the same information to hospitalized pediatric patients using the “Upopolis” secure social network.

Methods: A Child Life Specialist (CLS) administered a pre-questionnaire, then orientated new and previously diagnosed pediatric IBD (<18 years) admitted January 2009 - April 2010 to our previously developed educational program about IBD on Upopolis, a hospital wide patient oriented intranet. The post-questionnaire examined the change in knowledge suggested. The aim was to describe the age of presentation and distribution of disease phenotype in siblings affected by IBD.

Methods: A retrospective chart review of patients seen at our pediatric IBD center was performed to identify families with more than one child who was diagnosed with IBD. The age of each child at diagnosis, presence of IBD in the parent(s), clinical disease phenotype (Crohn’s Disease = CD, Ulcerative Colitis = UC, Indeterminate Colitis = IC) and time to diagnosis of the second sib were recorded.

Results: There were a total of 632 affected families. Sixteen families (2.5%) had more than one child diagnosed with IBD. There were only 3 families with an affected parent (one UC, 2 CD). In 10 families (63%) both siblings had the same disease phenotype (8 CD and 2 UC). One family had all three siblings with IBD (2 UC; 1CD). The younger sibling was the first to be diagnosed in 11 of 16 (69%) of the families. Median time of diagnosis from first to second sib was 3.9 yrs. (1–6 yr). Mean time of diagnosis from CUC to CR was 3.5 yrs (1–5.5 yr). Mean time of diagnosis of CD to CR was 4.0 yr (2–7 yr). Of the 7 “mixed” phenotype siblings, CUC presented first in 6 and CD first in 1 family.

Conclusions: Compared to the general population, siblings have an increased rate of IBD. There was a trend for the younger sibling to be diagnosed before the older sib. There was a slight trend towards concordance of phenotype amongst siblings however in a significant number of siblings there was non-concordance. In the siblings with both phenotypes, the onset of CUC predominated as being first onset. Siblings would be expected to have a high degree of homology and very similar life environments. Our study suggests a more complex set of factors and interactions play a role in the etiology of IBD.
and the patient’s comfort level explaining IBD to their friends. Four categories were measured: self-reported knowledge, misconceptions, comfort with explaining IBD, and evaluation of information. Categories 1, 3, and 4, were measured using a 5 point Likert scale. Category 2 was scored based on correct answers. 

**Results:** 17 patients (aged 10–17 yrs.; mean 14.5; 7 males, 10 females; 13 Crohn’s disease, 3 ulcerative colitis, 1 indeterminate colitis) participated. Improvements in knowledge and comfort level explaining IBD improved significantly; 82% of patients demonstrated increased knowledge (P = 0.002); 41% of patients had increased knowledge (P = 0.014), (most of the others already had near perfect or perfect scores prior to viewing the information); 94% of patients had increased comfort explaining IBD (P = 0.001). 85% of the patients liked the information and found it applicable.

**Conclusions:** In contrast to a freely distributed CD, IBD information posted on the Upopolis secure social network effectively educated young patients about IBD and increased their comfort level explaining IBD. Participants positively evaluated the experience, demonstrating that electronically accessible health information introduced by a CLS is an effective way to educate pediatric patients with IBD.

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**INCIDENCE OF SURGERY IN PEDIATRIC CROHN’S DISEASE**

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**Background:** Pharmacotheraphy is the mainstay of treatment for pediatric Crohn’s disease while surgery is reserved for cases refractory to medical treatment or for complications of the disease. In the past, rates of surgery in pediatric Crohn’s disease have ranged from 19% to 46%. However, many studies addressing the rate of surgery were performed prior to the advent of biologic therapies. In this study, we evaluated the incidence of surgery over the past decade, a period during which medical modalities such as biologic medications have been approved.

**Methods:** Patients treated for Crohn’s disease at the Children’s Hospital of Wisconsin between January 1999 and September 2009 were retrospectively reviewed. Data collected included date of diagnosis, medications used, whether surgery was required, time from diagnosis to surgery, type of surgery, and whether repeat surgery was necessary. Patients were grouped based on use of biologic versus non-biologic medications and descriptive statistical analysis was performed.

**Results:** Of the 544 patients reviewed, 78 (14.3%) had a surgical procedure related to their diagnosis of Crohn’s disease. The rate of surgery for patients on biologics was 15% versus 13.8% for patients on non-biologics. Mean time from diagnosis to surgery was 33 months for the biologic group versus 19 months for the non-biologic group. Ileocecectomy was the most common operation (78%). 46% of the patients requiring surgery were treated with a biologic prior to operation. Repeat surgery was required in 9 of 78 patients (11.5%).

**Conclusions:** The rate of surgical treatment in pediatric Crohn’s disease has decreased in the past decade. While there were similar rates of surgery for patients on biologic versus non-biologic therapies, patients treated with a biologic had a mean time from diagnosis to surgery that was 14 months longer compared to the non-biologic group.

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**USE OF HIGH-DOSE INFlixIMAB BY PEDIATRIC GASTROENTEROLOGISTS FOR TREATMENT OF ULCERATIVE COLITIS IN PEDIATRIC PATIENTS**

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**Background:** Infliximab (IFX) for the medical treatment of moderate-to-severe and fulminant ulcerative colitis (UC) is initiated at 5 mg/kg. In adults who lose responsiveness, the dose is commonly increased to 10 mg/kg. No published data support this dose increase among pediatric patients with UC. The aim was to determine dosing practices of IFX among pediatric gastroenterologists (PGI) for treatment of pediatric UC.

**Methods:** A 19-item survey was distributed to subscribers of the PEDSGI listserv. Responses were submitted anonymously and results compiled in a secure Web site.

**Results:** 113 subscribers (88% based in the USA) responded (101 PGI attendings and 12 PGI fellows). 46% were in academic medical institutions and 39% in hospital-based practices. 91% were treating >10 patients with UC; 13% were treating >100 patients with UC. 91% prescribed IFX 5 mg/kg; 72% prescribed 10 mg/kg. Using a Likert scale, factors that influenced the decision not to increase IFX dosing in patients with UC included “improvement on initial dose of IFX” (mean 3.83) and “decision to move to colectomy” (3.65). Lowest mean Likert scores were “Lack of guidelines or literature regarding increased IFX dosing” (1.93) and “Insurance authorization or other insurance issues” (2.37). 39.0% identified “Insurance authorization or other insurance issues” as at least somewhat of a factor (Likert score ≥3) in their decision not to increase IFX dose. 78% reported induction of remission and 81% reported maintenance of remission with IFX 10 mg/kg. One responder reported a mortality with IFX 10 mg/kg.

**Conclusions:** IFX 10 mg/kg is commonly used for the treatment of pediatric UC. A significant number of responders identified insurance issues as a hindrance in their decision to increase IFX dose. Further prospective controlled studies will help determine efficacy and safety of IFX 10 mg/kg for treatment of pediatric UC.
EVALUATING PEDIATRIC CROHN’S DISEASE IN A NONHISPANIC BLACK AND MIXED RACE COMMUNITY

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Background: Variations in Crohn’s disease (CD) phenotype and serology exist among ethnic and racial populations. IBD serology (ASCA IgA, IgG, ANCA, anti-Cbir1 and anti-OmpC) as a correlate of complicated disease (i.e. penetrating or strictureing disease) in non-white children has not been studied. The objective was to characterize pediatric CD in a non-Hispanic black and mixed race population. We hypothesize that children with complicated CD will have a higher mean number of positive antibodies and higher median titers at presentation compared to children with non-complicated CD.

Methods: We reviewed charts of 58 patients diagnosed with CD at the Children’s Hospital at Montefiore from 2001 to 2009. Only 22 patients had IBD serology at presentation. Clinical records were reviewed and phenotypic information was obtained.

Results: In our population, 32% were black, 36% mixed race, 9% Asian and 5% white. Eighteen percent of patients declined to report racial status. Ileocolonic disease was present in 15/22 (68%) of patients. Non-penetrating, non-stricturing disease was present in 14/22 (64%), penetrating disease was present in 6/22 (27%) and perianal involvement in 9/22 (41%). ASCA IgA was positive in 10/22 (45%), ASCA IgG in 8/22 (36%), anti-OmpC in 9/22 (41%), anti-Cbir1 in 17/22 (77%) and ANCA in 4/22 (22%). Five of twenty-two (23%) had 4 positive antibodies, 3/22 (14%) had 3 positive, 7/22 (32%) had 2 positive, 5/22 (23%) had 1 positive and 2/22 (9%) had 0 positive. There was no difference in the mean number of positive antibodies when comparing patients with complicated versus non-complicated disease (2.5 vs. 2.0). Median ASCA IgA titers were significantly higher in patients with complicated versus non-complicated disease (56.2 vs. 12.0, P = 0.05).

Conclusions: Non-Hispanic black and mixed race children with CD have a high prevalence of penetrating and perianal disease at presentation. ASCA IgA titers may correlate with complicated Crohn’s disease in this population.

INFLAMMATORY BOWEL DISEASE IN PEDIATRIC PATIENTS WITH CEREBRAL PALSY

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Background: Enteric nervous system is a complex network that includes, in the digestive mucosa, neuronal bodies and neurites interacting with the immune system and mucosal mast cells (MC). These interactions involve the secretion of messengers such as the neurotrophins neuronal growth factor (NGF), neurophin-3 (NT3) and brain-derived neurotrophic factor (BDNF). This study was designed to test the hypothesis that, in children with IBS or IBD, colonic mucosal innervation is altered. The aims were to measure MC infiltration, number of neuronal bodies, distance from MC to neurites and NGF, NT3 and BDNF content in colonic mucosa of pediatric patients with IBS or IBD as compared to controls.

Methods: Rectal biopsies from children (median age 14 yrs, range 8–18) with IBS (n = 11), IBD (n = 9) and controls (n = 14) were studied. MC and neuronal mucosal structures were identified by tryptase and PGP9.5 immunofluorescence. NGF, NT3 and BDNF were quantified in situ by ELISA.

Results: MC infiltration was not significantly different between IBS, IBD and controls. The number of neuronal bodies was increased in patients with IBD compared to controls (9.1 ± 2.3/field vs 5.5 ± 0.6/field; P = 0.06) but similar to controls for IBS patients. Number of MC in close proximity to neurites (<5 µm) were not different in the 3 groups. The distance between MC and neurites was different in IBS compared to controls (5.2 ± 0.3 vs 5.0 ± 0.3 µm), but MC were significantly further from neurites in patients with IBD (7.4 ± 0.5 µm) compared to controls (P = 0.02). NT3 content was similar to controls in IBS and IBD. However, NGF was higher than controls in IBS (0.93 ± 0.3 vs 0.62 ± 0.3 pg/mg protein, P < 0.05) and BDNF was higher in IBD than in controls (0.3 ± 0.08 vs 0.018 ± 0.006 pg/mg protein, P < 0.01).

Conclusions: Colonic mucosal innervation, assessed in rectal endoscopic biopsies, is altered in IBS and in IBD.

COLONIC MUCOSAL INNERNATION AND MAST CELL INTRILATION IN CHILDREN WITH IRRITABLE BOWEL SYNDROME (IBS) OR INFLAMMATORY DISORDERS (IBD)

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Background: Enteric nervous system is a complex network that includes, in the digestive mucosa, neuronal bodies and neurites interacting with the immune system and mucosal mast cells (MC). These interactions involve the secretion of messengers such as the neurotrophins neuronal growth factor (NGF), neurophin-3 (NT3) and brain-derived neurotrophic factor (BDNF). This study was designed to test the hypothesis that, in children with IBS or IBD, colonic mucosal innervation is altered. The aims were to measure MC infiltration, number of neuronal bodies, distance from MC to neurites and NGF, NT3 and BDNF content in colonic mucosa of pediatric patients with IBS or IBD as compared to controls.

Methods: Rectal biopsies from children (median age 14 yrs, range 8–18) with IBS (n = 11), IBD (n = 9) and controls (n = 14) were studied. MC and neuronal mucosal structures were identified by tryptase and PGP9.5 immunofluorescence. NGF, NT3 and BDNF were quantified in situ by ELISA.

Results: MC infiltration was not significantly different between IBS, IBD and controls. The number of neuronal bodies was increased in patients with IBD compared to controls (9.1 ± 2.3/field vs 5.5 ± 0.6/field; P = 0.06) but similar to controls for IBS patients. Number of MC in close proximity to neurites (<5 µm) were not different in the 3 groups. The distance between MC and neurites was different in IBS compared to controls (5.2 ± 0.3 vs 5.0 ± 0.3 µm), but MC were significantly further from neurites in patients with IBD (7.4 ± 0.5 µm) compared to controls (P = 0.02). NT3 content was similar to controls in IBS and IBD. However, NGF was higher than controls in IBS (0.93 ± 0.3 vs 0.62 ± 0.3 pg/mg protein, P < 0.05) and BDNF was higher in IBD than in controls (0.3 ± 0.08 vs 0.018 ± 0.006 pg/mg protein, P < 0.01).

Conclusions: Colonic mucosal innervation, assessed in rectal endoscopic biopsies, is altered in IBS and in IBD.
10.7 years (range: 3–21 years). Disease type was ulcerative colitis in 5, Crohn’s disease in 6, and indeterminate colitis in 2. The most common symptoms were bloody stools (n = 10), weight loss/poor weight gain (n = 5), and abdominal pain (n = 3). Histology often revealed moderate inflammation (n = 6), with the distal colon affected in 11 of 12. Distribution of colon involvement was pan-colitis in 4, distal colitis only in 3 and mid-distal or patchy disease in 4. Also, 4 patients had small bowel disease and 4 had esophagus and/or stomach disease. 2 patients had perianal fistula. Within five years of diagnosis, 3 patients underwent colectomy for severe disease, including one with perforation, and one had partial small bowel resection. Of 887 IBD patients seen during the same time interval, 1.5% had CP, compared to published CP prevalence of 0.35% in a general pediatric population.

Conclusions: The incidence of IBD in pediatric patients with CP may be higher than in the general pediatric population. The low frequency of abdominal pain complaints at diagnosis and common surgical intervention for severe disease suggest that CP may be recognized later in the disease course than in patients without cognitive impairment. The association between IBD and CP requires further study.

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NUTRITIONAL INFLUENCES ON EARLY COLONIC MUCOSAL EPIGENETIC DEVELOPMENT AND COLITIS IN MICE

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Background: Inflammatory Bowel Diseases (IBD) are chronic illnesses that are thought to develop secondary to a pathologic interaction between the immune system and the intestinal microflora. Based on monozygotic twin studies, IBD has been recognized as disorders in which epigenetic changes may play an important role. The most stable epigenetic alteration is methylation of cytosines at CpG dinucleotide sites (DNA methylation) and can be influenced in mammals by dietary exposures. We addressed whether prenatal exposure to a methyl-donor diet (MDD) induces alterations in colitis susceptibility and whether it leads to stable colonic mucosal epigenetic changes.

Methods: C57Bl/6j mothers received MDD or control diet (CD) 2 weeks prior to and throughout pregnancy, and through lactation. Offspring of both the MDD and the CD mothers were transitioned to CD at weaning/postnatal day 21 (P21) until P30. Colonic mucosa was collected and whole genomic DNA methylation specific amplification microarrays (MSAM), as well as gene expression microarrays were performed. Other groups of P30/P90 mice were transiently exposed to DSS, and their weight was followed for a total of 14 days, when the mice were sacrificed and colonial lengths measured.

Results: Mice that received MDD during prenatal and postnatal development became more ill, lost more weight and had shorter colons by the end of the DSS experiment (P < 0.01) supporting an increased severity of colitis. MSAM and gene expression microarrays have been performed and 18 overlapping genes were identified and are currently being confirmed via bisulfite pyrosequencing and RT-PCR.

Conclusions: Early developmental nutrition can induce prolonged phenotypic changes, such as alteration in chemically induced colitis susceptibility. Colonic mucosal DNA methylation and gene expression can also be altered by early nutritional exposures in a similarly prolonged fashion.

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RECTAL MEDICATION COMPLIANCE IN ADOLESCENTS WITH IBD

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Background: Low compliance rates have been found in IBD patients with regards to maintenance therapy. We proposed to identify barriers to compliance with rectal medications in pediatric IBD patients.

Methods: A 30-question survey was performed in adolescent patients (12–21 years) and their parents. Questions included demographics such as current age, age at diagnosis, diagnosis, and ethnicity. A history of their disease was established with respect to surgical management and time of most recent colonoscopy. Current disease activity was assessed with questions regarding abdominal pain, stools, and function. The remainder of the survey determined the rate of compliance with respect to rectal medications and identified the barriers to compliance with ranging from physician-patient communication to adverse effects. Subjects who had never used rectal medications answered questions about whether they would consider using of the medications and what were potential concerns.

Results: Preliminary data showed the mean age of diagnosis is 13 y and the mean age at time of survey completion of 16 y. 85% of respondents had Crohn’s disease and 15% had ulcerative colitis. 80% reported low disease activity and a high quality of life, as assessed with frequency and severity of symptoms, as well as function. 80% reported being compliant “some of the time” with rectal medications. The most commonly identified barrier to adherence was not liking the sensation (75%). 20% of patients were prescribed oral medications while on rectal medications. 95% of patients reported they would not or did not take the medication at school. The responses of adolescent patients were compared to their parents with respect to compliance rates and barriers to compliance. Parents reported 95% compliance rate compared to 80% reported by adolescents. Parents and patients both identified disliking the sensation as the most common barrier to adherence.

Conclusions: Identifying barriers to compliance with rectal medications among teens is important when considering medication options.
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THIOPURINES WITH ALLOPURINOL ARE AN EFFECTIVE WAY TO MAXIMIZE THERAPY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE
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Background: Thiopurines (TP) like 6-Mercaptopurine (6MP) and Azathioprine (AZA) are mainstays in therapy of pediatric inflammatory bowel diseases (IBD) like Crohn’s Disease (CD) and Ulcerative Colitis (UC), but are often associated with adverse events like hepatitis due to elevated 6-methylmercaptopurine (6-MMP) and preferential metabolism away from its therapeutic metabolite, 6-Thioguanine (6TG). Manipulation of the metabolism of these drugs with allopurinol (AL) has been reported. The aim was to report our experience with thiopurine/allopurinol (TP/AL) combination therapy in pediatric IBD.

Methods: Institutional Review Board approved retrospective chart review of first 10 patients treated with TP/AL.

Results: Average age: 13.7 years, males: 3, females: 7, CD: 9, UC: 1. Main indication: preferential metabolism with ongoing symptoms/lack of efficacy (10/10), steroid dependence (5/10), hepatitis (4/10). AZA: 5, 6MP: 5. Average 6TG pre-AL: 176.7, post-AL: 378.1 (P<0.001), average 6MMP pre-AL: 9157, post-AL: 966.5 (P<0.001). Adverse events were seen in 5 patients: nausea (3), one of which stopped the AL, leukopenia (2). 4 had clinical improvement, 4 continued symptoms and went on to biologics, 1 has continued symptoms but is not on steroids/biologics. All patients (9/9) required adjustments to dosing to achieve appropriate levels of 6TG. 4/4 patients with hepatitis had resolution of their ALT with the addition of AL. Steroid dependent patients were able to wean from steroids. After dose adjustments, average AZA dose: 0.76 mg/kg/d and average 6MP dose: 0.38 mg/kg/d.

Conclusions: TP with AL are an effective way to maximize therapy and minimize preferential metabolism/hepatitis. Levels must be monitored closely because each individual patient has a narrow range for adequate dosing. Dosing TP at 25% regular dosing when given with AL seems to be an appropriate starting point.

Motility/Functional Gastrointestinal Disorders

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COMPARISON OF RED FLAGS AND ASSOCIATED FACTORS IN PEDIATRIC FUNCTIONAL GASTROINTESTINAL DISORDERS AND CROHN’S DISEASE
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Background: Gender, age, family history, social stressors and “red flags” may be important predictors for diagnosing painful FGIDs in children. We aimed to examine the prevalence of these factors in children with FGIDs and Crohn’s disease (CD).

Methods: All patients prospectively completed a detailed demographic, history and symptom questionnaire and the data were analyzed retrospectively. Systematic chart reviews were completed in 606 patients (478 FGID and 128 CD) who presented in 2005–2008. Only FGIDs that involved abdominal pain based on the Rome III criteria were included. Only patients with histologic findings consistent with Crohn’s disease were included as controls. Chi square analysis was used to compare FGID patients to CD patients. Further analysis of red flags was performed using the logistic regression model.

Results: The mean (SD) age at presentation for FGIDs was 11.4±3.4 vs. 13.1±3.0 for CD. Overall, there were more females in FGID group than CD (65.1 vs. 40.6%; P<0.001). Only 6.3% of all patients with FGID (n=478) were male over age 13 years (P<0.05). Social stressors were identified by 35% of children with FAP vs. 5% with CD (P<0.0001). A positive family history of IBS, reflux or constipation was significantly higher in patients with FGID compared to CD (+P<0.05). Prevalence of red flags is shown in Table 1.

Conclusions: Blood in the stool and weight loss are the only red flags that may be useful in distinguishing from CD. Patients with FGIDs are more likely to report more stressors and have a positive family history of FGIDs. Post-pubescent males are far less likely than females to present with FGID.

Table. Multivariate analysis of red flags

<table>
<thead>
<tr>
<th>Red flag</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake from sleep</td>
<td>1.288</td>
<td>0.922–1.799</td>
<td>0.1374</td>
</tr>
<tr>
<td>Blood in stool</td>
<td>0.216</td>
<td>0.140–0.333</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.350</td>
<td>1.372–4.025</td>
<td>0.0018</td>
</tr>
<tr>
<td>Fever</td>
<td>1.041</td>
<td>0.626–1.734</td>
<td>0.8761</td>
</tr>
<tr>
<td>Weight loss</td>
<td>0.374</td>
<td>0.263–0.531</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Problems gaining weight</td>
<td>0.790</td>
<td>0.527–1.185</td>
<td>0.2546</td>
</tr>
<tr>
<td>Joint pain</td>
<td>0.872</td>
<td>0.564–1.346</td>
<td>0.5353</td>
</tr>
</tbody>
</table>

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FUNDOPPLICATION DOES NOT PREVENT PROGRESSION OF LUNG DISEASE IN CYSTIC FIBROSIS
Jaime Echartea-Gonzalez, Kartik Warikoo, Cade Nylund, Ajay Kaul. Gastroenterology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background: Gastroesophageal Reflux Disease (GERD) is believed to worsen lung disease in CF and a fundoplication is often performed to prevent this progression. The aim was to compare lung function over time in CF patients who had a fundoplication with matched controls who did not.
LONG-TERM OUTCOMES AND QUALITY OF LIFE IN CHILDREN WITH AN ANTEGRADE CONTINENCE ENEMA (ACE)

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Background: The Antegrade Continence Enema (ACE) is an effective therapeutic modality in select patients with intractable constipation and/or fecal incontinence. The aim of the study was to determine long term outcome and quality of life impressions in children that have undergone the ACE.

Methods: ACE patients were contacted and a brief questionnaire was administered. Families were also asked to rate pre and post ACE functioning on a subjective 10 point scale. Objective clinical outcome (successful/unsuccessful) was measured manually using standard criteria.

Results: 84 of 117 families were successfully contacted. Mean age was 17 ± 6 years. Mean time since ACE placement was 76 ± 38 months. 55 (66%) patients were successful with the ACE at the time of their response to this questionnaire. The mean subjective functioning scores pre-ACE were 1.8 ± 1.1, and post-ACE were 7.9 ± 2.3 (P < 0.001). The table shows responses to the questionnaire in all 84 patients.

<table>
<thead>
<tr>
<th>Question</th>
<th>Strongly Agree/Agree</th>
<th>Neutral</th>
<th>Strongly Disagree/Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happy with the ACE</td>
<td>80%</td>
<td>5%</td>
<td>15%</td>
</tr>
<tr>
<td>Better off with the ACE</td>
<td>93%</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Would recommend the ACE to another patient</td>
<td>88%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Would repeat the ACE again</td>
<td>92%</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>ACE gives greater control over bowel movements</td>
<td>80%</td>
<td>5%</td>
<td>15%</td>
</tr>
<tr>
<td>ACE helps avoid embarrassing social situation</td>
<td>71%</td>
<td>15%</td>
<td>14%</td>
</tr>
</tbody>
</table>

Conclusions: The ACE was successful in 66% of patients. The majority of families whose children undergo ACE placement have a favorable impression of the procedure independent of objective final outcome, as a result of perceived clinical improvement.

SMALL INTESTINAL BACTERIAL OVERGROWTH IN CHILDREN WITH MIGRATING MOTOR COMPLEX ABERRATIONS

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Background: Small Intestinal Bacterial Overgrowth (SIBO) has been associated in adults with disturbances in the migrating motor complex (MMC) of the small bowel. There are no similar pediatric studies.

Methods: We retrospectively identified 62 patients who underwent 67 antroduodenal manometry (ADM) studies and had duodenal aspirates collected for culture at the time of catheter placement. Positive cultures were defined as greater than 1 × 10^5 CFU/mL of pathogenic aerobic or anaerobic bacteria, or yeast. The manometry tracings were measured manually using standard criteria.

Results: The mean age was 8.1 ± 5.5 years. There were 34 (55%) females. Indications for ADM were: Vomiting/Feeding Intolerance (68%), Abdominal Pain (13%), and staging of a motility disorder (19%). Phase III of the migrating motor complex was normal in 48 (72%) patients and abnormal in 19 (28%). Of those that were abnormal, it was present but abnormal in 13 (68%) studies and absent in 6 (32%).

Duodenal aspirates met our criteria for positive cultures in 21 studies (31%). Ten of 19 children (53%) with abnormal phase III had positive cultures, compared to 11 of 48 patients (23%) with normal phase III (P = 0.038). There was no difference in the incidence of positive cultures in patients with present but abnormal phase III (54%), and absent phase III (50%).

Conclusions: Duodenal cultures identified the presence of bacteria in children undergoing evaluation with antroduodenal motility testing. Children with aberrations in phase III of the MMC are at increased risk of SIBO. Further studies are needed to assess the significance of this finding and the effect of treatment.
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ACCURACY OF ABDOMINAL PAIN RECALL IN CHILDREN
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Background: Chronic AP (AP) is common in children. Recall of symptoms is used clinically to determine management and treatment progress in drug studies to determine outcomes. Limited data exists on accuracy of AP recall in children. The aim was to assess ability to accurately recall AP in children.

Methods: The study was a post-hoc analysis of data obtained from a prospective double-blind, randomized placebo-controlled interventional trial in children with functional GI disorders (FGIDs). Children 8–17 years with AP predominant FGIDs by Rome II criteria recruited from 6 centers. Those with evidence of organic disease were excluded. Patients maintained AP diary daily for one month (presence, frequency and intensity). At end of study patients reported number of days of AP during previous month. Agreement between daily pain reports and recalled pain was assessed. Univariate analysis with Spearman rank correlations was used.

Results: 63 children (45 girls, mean age 12.8) participated. 1- Correlation between recall and diary: r = 0.4 P < 0.0001. 16% had perfect agreement on number of days of AP. 54% recalled fewer episodes of pain. Average number of AP days by recall was 17.7/month while by diary: 23.5/month (P = 0.001) 2- To understand patients recall we assessed if recall only reflects last week of AP by comparing the recalled answers to previous week answers: r = 0.467, P < 0.0001. 3- To assess if children only recall higher intensity of AP, we compared AP recall vs. various intensities of AP. Reported AP did not reflect AP of greater severity. 4- To assess if adolescents have better recollection of symptoms, we compared recall between children ≤11 years and >11 years. Higher correlation was noted in ≤11 years (r = 0.59 moderate) than >11 years (r = 0.26 weak).

Conclusions: Few children can accurately recall the episodes of AP. Children commonly recall a lower frequency of AP than that assessed by prospective diary reports. Reported recall does not reflect a shorter recollection period. Recall is not related to intensity of pain. Adolescents have worse recall of symptoms than pre-adolescents.

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BRISTOL STOOL SCALE: AN OLD FRIEND REVISITED
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Background: Bristol stool form scale (BSS) is a clinical and research tool in constipation. Stool form/consistency are primary outcomes in many clinical trials. Still, there is paucity of studies validating BSS in children. The aim was to assess validity of BSS in children.

Methods: Pediatric subjects prospectively recruited. Subjects’ interpretation of ordinal ranking of stool types: BSS picture cards and custom made 3-D models (6 × 3 cm stool resin models depicting stool types of BSS in water placed in mock toilet bowl) were given in random order. (1) 50 subjects ranked picture cards and another 50 subjects ranked 3-D models from hardest to softest. Correlation between rank order of BSS and subjects’ ranking was analyzed. (2) 50 children matched BSS picture cards with descriptions from BSS for each stool type and another 50 children matched cards with descriptions from modified pediatric stool scale (MPS). (3) Children also matched 3-D models with BSS and MPS descriptions for respective stool types. Percentage of concordance between text definitions of stool type and appropriate pictures or 3-D models was calculated.

Results: (1) Ordinal ranking: 2% and 0% children ranked BSS stool picture cards and 3-D models correctly. Only stool types 6 & 7 of picture cards and 3-D models were ranked correctly by >70% children. (2) Correlation between BSS pictures & words: Subjects correlated stool pictures with appropriate BSS words: 33% and MPS words: 46%. There was >70% agreement between stool pictures and appropriate words from BSS for stool types 1, 2, 3, 4, 6 and 7 and with words from MPS for stool types 1, 3, 4, 5, 6 and 7. (3) Correlation between 3-D models & words: Subjects correlated 3-D stools models with appropriate BSS words: 50% and MPS words: 44%. There was >70% agreement between 3-D stool models and appropriate words from BSS for all stool types except type 5 and with appropriate words from MPS for all stool types except type 2.

Conclusions: In children, BSS had similar construct validity as MPS. Poor assessment of consistency noted for all 3 scales. BSS has better agreement after eliminating type V category of stool. BSS can be improved for research purposes by using custom made 3-D models instead of cards.

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CHILDREN’S RELIABILITY USING A MODIFIED BRISTOL STOOL SCALE TO INDICATE STOOL FORM
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Background: Identification of stool form and changes in stool form are important in clinical practice and research. Self-report of stool form in children may be uniquely important given that caregivers often do not observe all passed stools. However, procuring accurate descriptions from children may be challenging. The aim was to determine the ability of children of various ages to reliably use a modified Bristol Stool Form Scale (MBFS) to indicate stool form.
Methods: The original Bristol Stool Form Scale was modified to reduce the number of discriminations from seven to five choices (types 3 and 5 omitted). Ten color photographs of expelled stool (two for each of the 5 stool types) that had high agreement among a prior sample of pediatric gastroenterologists were used. Participants included 191 patients or siblings ages 3–18. Children were presented with the 10 stool photographs by a trained research assistant and were asked to use the MBSFS to assign a stool form category to each photograph. Intra-class correlation coefficients were calculated for the total sample and for each of 5 age groups. Results: The single measures intra-class correlation coefficient for the total sample was 0.80. As expected, child age impacted the ability of the children to reliably use the scale, with intra-class correlation coefficient values ascending with each age group: 0.65 (3–5 years), 0.74 (6–7 years), 0.82 (8–10 years), 0.86 (11–13 years), and 0.90 (14 and older).

Conclusions: (1) Overall, children were able to use the MBSFS to reliably indicate stool form, though reliability increased with age; (2) Children ages 3–5 did not exceed the MBSFS to reliably indicate stool form, though reliability impacted the ability of the children to reliably use the scale; (3) Children ages 8 and older evidenced outstanding inter-rater reliability; (3) Children ages 8 and older evidenced outstanding inter-rater reliability. These results support that a modified pictorial stool scale can be used to obtain reliable reports of stool form by children.

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GASTROINTESTINAL TRANSIT PROFILES IN CYSTIC FIBROSIS PATIENTS
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Background: CF patients have non-specific gastrointestinal (GI) complaints, which may be due to intestinal dysmotility such as altered gastric emptying, malabsorption, small intestinal bacterial overgrowth (SIBO), or distal intestinal obstruction syndrome. We hypothesized that a wireless motility capsule (WMC) could define GI transit profiles in patients with CF.

Methods: A single-site, pilot study of 10 adult subjects with CF and 10 healthy subjects matched by age, gender, and body mass index. Subjects could not be taking acid-suppressing medicines. CF subjects on cycled inhaled antibiotics were used. Participants included 191 patients or siblings ages 3–18. Children were presented with the 10 stool photographs by a trained research assistant and were asked to use the MBSFS to assign a stool form category to each photograph. Intra-class correlation coefficients were calculated for the total sample and for each of 5 age groups. Results: The single measures intra-class correlation coefficient for the total sample was 0.80. As expected, child age impacted the ability of the children to reliably use the scale, with intra-class correlation coefficient values ascending with each age group: 0.65 (3–5 years), 0.74 (6–7 years), 0.82 (8–10 years), 0.86 (11–13 years), and 0.90 (14 and older).

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Results: Ten subjects (7 F) were recruited in each group. Control subjects were matched to CF subjects based on gender, age (mean 22.5 vs 21.6 yr) and BMI (mean 23.2 vs 23). There was a statistically significant increase in small bowel transit among CF (mean 6 hr 9 min) compared to the control patients (mean 3 hr 46 min) P = 0.005. There was no statistical difference between gastric emptying, colonic transit or total WMC transit.

Conclusions: Patients with CF have slower small bowel transit compared to healthy controls. This may facilitate SIBO that can interfere with nutrient absorption and cause non-specific GI complaints. WMC did not demonstrate a difference in gastric emptying or colonic transit between CF and control patients.

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RETROSPECTIVE REVIEW OF PROPOFOL DOSING FOR PROCEDURAL SEDATION IN PEDIATRIC PATIENTS

Background: The purpose was to determine the total propofol dose in milligrams per kilogram used for procedural sedation of pediatric patients and evaluate differences in doses with regard to multiple patient characteristics. Additionally, adverse events were recorded to evaluate the safety of propofol for pediatric procedural sedation.

Methods: Expedited IRB approval was granted. All pediatric patients at St. Luke’s Hospital Bethlehem sedated for non-emergent gastrointestinal imaging studies from January 2008 to November 2009 were included. Patient characteristics identified included age, weight, body mass index (BMI), gender, procedure performed, chronic medical conditions, chronic medication use, and the use of other sedatives, anxiolytics, or narcotics. Additionally, incidences of hypotension, bradycardia, and bradypnea were recorded.

Results: A total of 151 procedures were identified and 74 met inclusion criteria. Of those included, procedures were colonoscopies (7), esophagogastroduodenoscopy (EGD) (57), and combination colonoscopy/EGD (10). The mean patient age was 11 ± 3.6 years and procedure duration was 12.3 ± 5.4 minutes. The mean dose for colonoscopy was 4.74 ± 2.3 mg/kg, EGD was 3.75 ± 2.3 mg/kg, and EGD/colonoscopy was 4.33 ± 2.9 mg/kg. A total of 37 patients (43.2%) had a documented adverse event. They included hypotension in 25 patients (33.8%), bradycardia in 7 (9.5%), and bradypnea in 11 (14.9%). Only 3 adverse reactions were considered to be serious and required intervention, but none required a longer than planned length of stay or had any known long term adverse outcomes.

Conclusions: This study suggests there are differences in dosing based on age, procedure performed, BMI, dosing scheme and procedure duration, however, further studies
with larger sample sizes should be conducted to establish statistical significance. While adverse reactions were common, the majority were mild and required no intervention. Based on these results, propofol can safely and effectively be administered by practitioners experienced in airway management.

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INVESTIGATING THE ADDITIVE VALIDITY OF PSYCHOLOGICAL SERVICES TO PATIENTS WITH FECAL RETENTIVE ENCOPRESIS
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Background: Patients with Fecal Retentive Encopresis currently seen by the embedded GI psychologist appear clinically to improve more rapidly with regard to soiling than patients not receiving these adjunctive services. When the behavioral aspect of Fecal Retentive Encopresis is addressed, symptoms appear to improve quickly, costly medical resources are conserved and patients are spared the emotional consequences of continued soiling. If proven effective, elements of the psychological protocol such as psychoeducation and/or motivational interviewing could quickly and easily be implemented by GI providers into standard patient visits. The objective was to investigate the additive validity of psychological interventions provided to patients with Fecal Retentive Encopresis.

Methods and Results: 20 patients with Fecal Retentive Encopresis ages 7–14 will either receive the standard of care, which includes laxative therapy, dietary recommendations and routine education, or will receive the standard of care plus psychological services, which include psychoeducation, motivational interviewing and institution of a positive reinforcement paradigm. Patients will be contacted once weekly for four weeks and followed up at 3 and 6 month intervals to evaluate improvement in soiling and retention.

Conclusions: Patients receiving adjunctive psychological services will have decreased frequency of retention and therefore soiling. If proven effective, the psychological protocol will be detailed for use by GI providers during routine patient visits.

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ENDOTHELIAL DYSFUNCTION IN OBESE PATIENTS MAY BE RELATED TO ABNORMAL GASTROESOPHAGEAL REFLUX
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1Pediatrics, Nationwide Children Hospital, OSU, Columbus, OH; 2Sleep lab, Nationwide children Hospital, Columbus, OH; 3Endocrinology, Nationwide Children Hospital, Columbus, OH.

Background: Obesity is associated with low ghrelin, a gastrointestinal hormone that enhances GI motility and improves endothelial cell function. Although obesity is associated with gastroesophageal reflux (GER), the relationship between GER and endothelial function has not been studied. The aim was to evaluate the endothelial function and its correlation with quality of sleep and GER in obese children.

Methods: Prospectively we performed synchronized polysomnography and multichannel intraluminal impedance/pH monitoring (MII) on obese children, BMI 95%. Anti reflux medications were discontinued 5–7 days before study. We measured forearm vascular resistance (FVR) using strain gauge venous occlusion plethysmography (DE Hokanson Inc, Bellevue, WA). Changes in FVR >70% represented normal endothelial function.

Results: We evaluated 9 patients; 4 M/5F, age 9.6–18 yrs, mean 13.7 ± 3.2 yrs. Data revealed 40 non-acid (0–14, median 5) and 399 (18–99, median 34) acid GER, median reflux index 6.5 (1.1–15.9). Change in vascular resistance (CVR) ranged from 23.4%–84.7%, being abnormal in 5 (55.5%) patients who had more awakenings/hr (4.4 ± 2.4 vs 2.4 ± 1, P = 0.08), and lower sleep time (357.5 min ± 41.2 vs 449.1 ± 91.6, P = 0.08). Abnormal CVR was marginally associated with more acid GER/hr during sleep (1.3 ± 1.2 vs 0.5 ± 0.5, P = 0.08). Only 3 patients with abnormal CVR spent 0.02–0.1% time under 90% saturation during sleep, (P = 0.17). A positive SAP for awakening was more common in patients with normal CVR (3/4 vs 1/4, Fisher Exact Test P = 0.21), with higher SAPs median 98.8, IQR 95.4–99.9 vs 44.7 IQR 0–58.9, P = 0.04).

Conclusions: Endothelial dysfunction is associated with more frequent desaturations and reflux episodes in obese patients. CVR was inversely related to awakenings, what could suggest a higher threshold for sleep interruption in obese children. Data indicates further evaluation of the relationship between endothelial dysfunction and upper GI motility.

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COST OF TREATMENT OF CONSTIPATED PATIENTS WITH FECAL INCONTINENCE
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Background: Chronic functional constipation (CFC) is a prevalent disease in the pediatric population. The treatment of many chronic diseases has a high economic impact on patients and their families. The aim was to evaluate the monthly cost of the drug treatment of children with CFC.

Methods: Prospective 1-year follow-up of low income constipated patients at the tertiary ambulatory of the Federal University of Minas Gerais. The following parameters were analyzed from the patient’s protocol: number of appointments, dosage of medicine (mineral oil, milk of magnesiu,
polyethylene glycol without electrolytes and/or lactulose); monthly cost of the treatment, and presence of fecal incontinence.

**Results:** 51 patients were analyzed during 12 months of treatment. The average patient’s age was 5.8 years and 56.9% (29) were male. The average cost of the drug treatment was US$72.89 per month for patients who showed clinical improvement (n = 16) and US$82.84 for those who did not (n = 15). The average number of appointments for incontinent patients was 6.71 per year and 6.67 for continent patients. The introduction of drugs into the CFC treatment was necessary for 12 patients (8 were incontinent and had an average of 7.25 appointments).

**Conclusions:** Children with fecal incontinence had the worse clinical scenario. This finding is consistent with Rome III (just one episode of fecal incontinence is a serious problem and it is related to worse clinical evolution). The difference between the number of appointments for the groups with or without fecal incontinence was not significant. However, the cost of the drug treatment for incontinent patients was higher, and represented 16% (US$45.19) of the average monthly income of the patient’s family (US$281.77). This finding could be related to worse adherence to treatment. Some patients, for example, had to change drugs during treatment due to financial considerations.

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A LARGE PROSPECTIVE STUDY OF CHILDREN WITH CYCLIC VOMITING SYNDROME: SINGLE-CENTER EXPERIENCE

Ashley Keilman, Jonathan Moses, Sarah Worley, Sumit Parikh, David Rothner, Kadakkal Radhakrishnan. The Cleveland Clinic, Cleveland, OH.

**Background:** Cyclic Vomiting Syndrome (CVS) is a chronic disorder of unknown etiology characterized by repeated stereotypical vomiting episodes accompanied by debilitating nausea and/or headaches. Diagnosis is made by exclusion of other organic diseases. The aim of the study was to examine the presentation, evaluation and management of our CVS patients.

**Methods:** The study included 100 consecutive patients less than 21 years of age at diagnosis seen from January 2007 to April 2010. Information regarding data, anthropometrics, medical history, laboratory and radiological studies, medications and treatment outcomes was collected.

**Results:** The mean age at diagnosis was 8.9 ± 5.0 years. The patient population was 57% male and 77% Caucasian. Patients reported cycles with median duration of 24 hours, 18 vomiting episodes per cycle and a peak of 5 vomits per hour at 4-week intervals. Most patients (88%) reported complete symptom resolution between episodes. 10% of episodes required IV fluids. Warning symptoms occurred in 63%, typically abdominal pain and nausea (37%). Episode triggers were identified in 66%, with intercurrent illness in 35%; motion sickness triggered events in 16%. Autonomic symptoms were seen in 25%, including fever and hypertension. For prophylactic treatment, amitriptyline was effective in 23 of 40 patients (58%) and cyproheptadine was effective in 30 of 61 (49%). High dose oral ondansetron improved or resolved acute symptoms in 56 of 85 (66%). There was a family history of migraines in 71% of patients, and epilepsy in 10%. A personal history of migraine was noted in 26%. A subset of patients had abnormalities on metabolic testing, neuroimaging or GI studies.

**Conclusions:** These data are consistent with previous reports of CVS patients. Increased understanding of CVS will aid providers in making earlier diagnoses and instituting more effective treatment. Amitriptyline and high dose ondansetron were effective in most patients. Further results regarding evaluation and treatment outcomes are pending.

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NONACID REFLUX EPISODES ARE AS LIKELY AS ACID REFLUX EPISODES TO BE ASSOCIATED WITH SYMPTOMS IN INFANTS

Jose M. Garza, Cade Nylund, Ajay Kaul. Gastroenterology, Hepatology and Nutrition, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

**Background:** Symptoms of gastroesophageal reflux (GER) in infants are non specific and there is conflicting data on the association of specific symptoms with reflux episodes. Combined pH-impedance technology (ph-MII) provides an important modality to study this association. Our primary goal was to determine the association of reported symptoms in infants with GER episodes using pH-MII technology. The secondary goal was to determine if symptom association was more likely to occur with an acid or nonacid event.

**Methods:** A total of 186 pH-MII tracings of infants suspected of having GERD related symptoms were retrospectively analyzed. All reflux events were counted and characterized as acid or non acid. All symptoms reported during each study were recorded and Symptom Index (SI) calculated as the percentage of symptoms that were reflux related. A multivariate logistic regression model was generated with the presence or absence of a positive SI as the independent variable. Negative binomial distribution was used to analyze count data, analyzing the total related reflux episodes offsetting for the total number of symptoms.

**Results:** A total of 4159 symptoms were recorded on the 186 studies. Of these, only 1504 (36%) were associated with a reflux episode: 1135 (27%) with nonacid and 369 (9%) with acid reflux episodes. A non acid reflux episode was as likely to be associated with a symptom as an acid episode. Cough was the most frequently reported symptom with only 34% associated with a reflux episode. Regurgitation events had one of the highest associations with reflux events (52%), especially in younger infants. Interestingly, desaturations were not associated with reflux episodes and the perceived pain events were not associated with acid reflux episodes.

**Conclusions:** Most symptoms in infants that are attributed to GERD did not appear to be associated with reflux episodes.
In those infants who did show an association, non acid reflux episodes were just as likely as acid episodes to correlate with symptoms.

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**INTRAPYLORIC INJECTION OF BOTULINUM TOXIN A FOR THE TREATMENT OF GASTROPARESIS IN CHILDREN**

Leonel Rodriguez, Rachel Rosen, Samuel Nurko. Gastroenterology, Children's Hospital Boston, Boston, MA.

**Background:** Gastroparesis in children is poorly understood, and there are limited efficacious therapies. We present our experience using intrapyloric botulinum toxin A injection in the treatment of gastroparesis.

**Methods:** This is a retrospective review of records of patients undergoing endoscopic intrapyloric injection of botulinum toxin A for the treatment of gastroparesis. All patients failed medical management and underwent a gastric emptying study and/or an antroduodenal manometry study to document delayed gastric emptying and/or postprandial antral hypomotility respectively as indications for the injection.

**Results:** 54 injections of 100 u were given to 35 patients; 20 (57%) were female with a mean age of 10.7 ± 6.2 y. Most common presenting symptoms were vomiting, nausea and abdominal pain. Etiology of the gastroparesis was idiopathic in 30 (85%), diabetic in 2 (3.7%) and mitochondrial dysfunction in 3 (5.6%). Improvement after the injection was graded as failure (no response), good (improved with residual symptoms but no further interventions) and excellent (asymptomatic). Information on response was available in 29 subjects (42 injections). 20/29 or 69% of patients had a positive outcome after injection and 29/42 or 69% of injections yielded symptomatic improvement. The mean duration of response after injection was 4.5 months (range 1–22 months). We found no difference between the means gastric emptying in patients that responded (29% emptying at 1 h) or failed (36% emptying at 1 h) to the injection. Patients with a poor symptomatic response had a higher frequency of antral hypomotility (4/5) than those with a good response (6/9) but this difference did not reach statistical significance. There were no adverse events in any of the patients except one patient reported short-lived (<1 week) exacerbation of vomiting after injection followed by complete resolution of symptoms.

**Conclusions:** Intrapyloric injection of botulinum toxin A is safe and effective in the management of children with symptoms of gastroparesis. Prospective randomized trials in children are needed.

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**LAPAROSCOPIC ASSISTED PERCUTANEOUS ENDOSCOPIC CECOSTOMY: LAPEC**

Leonel Rodriguez, Alex Flores, Brian Gilchrist, Allan Goldstein. Gastroenterology, Children’s Hospital Boston, Boston, MA; Pediatrics, Massachusetts General Hospital, Boston, MA; Pediatrics, Floating Hospital for Children, Boston, MA; Surgery, Floating Hospital for Children, Boston, MA; Surgery, Massachusetts General Hospital, Boston, MA.

**Background:** Antegrade continence enema (ACE) has become widely used in the management of children with defecatory disorders. This procedure has undergone many technical modifications, we have developed a novel minimally invasive technique, the laparoscopic-assisted percutaneous endoscopic cecostomy (LAPEC).

**Methods:** Children with defecation disorders undergoing ACE procedure from January 2004 to January 2009 at two tertiary care centers. We also compare the length of stay and operative time between the LAPEC and the laparoscopic cecostomy without endoscopic assistance.

**Results:** 50 patients underwent the LAPEC procedure and 15 underwent laparoscopic cecostomy. Of the 50 LAPEC patients, 35 (70%) were male with a mean age of 12 ± 4.2 years and a mean weight of 42 kg (range 17–81 kg). For LAPEC, the mean surgical operative time was 100.1 ± 16.6 minutes (range 50–135 minutes) and the mean length of stay was 3.4 ± 1.4 days (range 1 to 7 days). The mean surgical operative time for laparoscopic cecostomy was 100.8 ± 19.1 minutes with a mean hospital stay of 3.8 ± 1.6 days. No statistical difference was found between the two groups. The single intraoperative complication during LAPEC was a cecal wall hematoma that required a small incision to place the needle. Postoperative complications included: 6 patients with low-grade fever that responded to antibiotics, 2 patients with tube dislodgement (1 required a repeat LAPEC and the other open surgery), 1 minor local skin erosion, and 1 case of significant local skin breakdown necessitating cecostomy tube removal. Of the 50 LAPEC patients and their families, 48 were satisfied with the outcome (determined by review of medical notes and discussion with subjects and their parents).

**Conclusions:** We recommend LAPEC as the procedure of choice for cecostomy placement in children with refractory constipation or fecal incontinence.

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**MEASURING OF GASTRIC EMPTYING IN EGYPTIAN PEDIATRIC PATIENTS WITH PORTAL HYPERTENSION AND NONULCER DYSPESIA BY USING REAL-TIME ULTRASOUND**

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**Background:** Using real-time ultrasound for the evaluation of gastric emptying is a non-invasive diagnostic tool. Defecatory disorders are common among Egyptian pediatric patients with portal hypertension and nonulcer dyspepsia. Antegrade continence enema (ACE) has become widely used in the management of children with defecatory disorders. This procedure has undergone many technical modifications, we have developed a novel minimally invasive technique, the laparoscopic-assisted percutaneous endoscopic cecostomy (LAPEC).

**Methods:** Children with defecation disorders undergoing ACE procedure from January 2004 to January 2009 at two tertiary care centers. We also compare the length of stay and operative time between the LAPEC and the laparoscopic cecostomy without endoscopic assistance.

**Results:** 50 patients underwent the LAPEC procedure and 15 underwent laparoscopic cecostomy. Of the 50 LAPEC patients, 35 (70%) were male with a mean age of 12 ± 4.2 years and a mean weight of 42 kg (range 17–81 kg). For LAPEC, the mean surgical operative time was 100.1 ± 16.6 minutes (range 50–135 minutes) and the mean length of stay was 3.4 ± 1.4 days (range 1 to 7 days). The mean surgical operative time for laparoscopic cecostomy was 100.8 ± 19.1 minutes with a mean hospital stay of 3.8 ± 1.6 days. No statistical difference was found between the two groups. The single intraoperative complication during LAPEC was a cecal wall hematoma that required a small incision to place the needle. Postoperative complications included: 6 patients with low-grade fever that responded to antibiotics, 2 patients with tube dislodgement (1 required a repeat LAPEC and the other open surgery), 1 minor local skin erosion, and 1 case of significant local skin breakdown necessitating cecostomy tube removal. Of the 50 LAPEC patients and their families, 48 were satisfied with the outcome (determined by review of medical notes and discussion with subjects and their parents).

**Conclusions:** We recommend LAPEC as the procedure of choice for cecostomy placement in children with refractory constipation or fecal incontinence.
Background: The aim of our work was to measure the gastric emptying (GE) in pediatric patients with portal hypertension (PH) and in patients with nonulcer dyspepsia (NUD) by using real-time ultrasound.

Methods: 40 patients with PH with mean age 7 ± 2.8 years and 30 patients with NUD with mean age of 8.3 ± 2.9 years as well as 20 matched control subjects underwent GE study by using real-time ultrasound. Upper gastrointestinal endoscopy was done for all patients with the exclusion of the control subjects. After an overnight fast, the fasting antral volume was taken. Each patient was allowed to drink tap water adjusted to provide 20 ml/kg, then re-measuring the antral volume every 15 minute for one hour. The GE was calculated by regression equation curve.

Results: The mean GE time was 27.1 ± 3.6 (range 21.4–36) minutes for the control subjects, 28.2 ± 2.7 (range 25.6–38) minutes for the NUD group and 40 ± 6.8 (range 21.7–54.7) minutes for the PH patients. It was significantly delayed in PH patients, when compared to NUD patients and control (P < 0.01), which may be attributed to previous sclerotherapy in all patients with PH. On the other hand, no statistical significant difference was noted between the control and the NUD groups. Endoscopic finding in patients with NUD revealed reflux esophagitis in 60%, incompetent cardia in 47% and mild to moderate gastritis in 83%. While in patients with PH revealed reflux esophagitis in 28%, incompetent cardia in 13% and esophageal varices in all patients.

Conclusions: Gastric emptying was significantly delayed in patients with chronic liver disease with evidence of PH. Ultrasound is a noninvasive and reliable method for measuring GE in Pediatric patients.

Results: Duodenum mast cell peak density was 22 ± 7.2, range 8–34, for the patient group. Sixteen of these patients (84%) were found to have eosinophilic duodenitis (ED) on biopsy (peak >20). The patient group had a L/M ratio of 0.0317 ± 0.0104 compared to 0.0340 ± 0.0129 for the control group (P = 0.6). The receiver operating characteristic (ROC) curve showed the L/M ratio performed no better than chance for predicting FD patient versus control group (AUC = 0.551.) Eliminating FD patients without ED from the L/M analyses did not change the ROC (AUC = 0.549.)

Conclusions: We found no significant difference in intestinal permeability, as measured by the L/M ratio, in patients with FD (with or without ED) compared to healthy controls. The L/M ratio has proven to be a useful marker for detecting large changes in barrier dysfunction such as that seen in celiac disease. A more sensitive test is needed to evaluate intestinal permeability and understand any potential role for barrier dysfunction in FD.

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CLINICAL OUTCOMES OF FORMER PEDIATRIC PATIENTS WITH HISTOLOGIC REFLUX ESOPHAGITIS
Sara W. Rippel1, Lynn Walker2.1Department of Pediatrics, Division of Pediatric Gastroenterology, Hepatology and Nutrition, Vanderbilt University, Nashville, TN; 2Department of Pediatrics, Division of Adolescent Medicine, Vanderbilt University, Nashville, TN.

Background: Assess clinical outcomes at follow up for former pediatric patients with histologic reflux esophagitis compared to those with normal endoscopy and healthy controls.

Methods: The prospective cohort included children aged 8–16 years referred to Vanderbilt Pediatric Gastroenterology Clinic for chronic abdominal pain (CAP) that underwent upper endoscopy and healthy controls. Histologic reflux was characterized by basal cell hyperplasia, spongiosis, and intraepithelial lymphocytes. All participants were seen for follow-up assessment 5–15 years later at ages 13–32 years. Measures administered at follow-up included the somatization inventory and health service utilization to help categorize symptoms, acid suppression use, and previous surgical history.

Results: See Table,* indicates statistical difference using chi-square analysis or Fisher exact test.

Conclusions: More than a third of the patients with histologic reflux esophagitis as children are on acid suppression at follow up which is statistically different than those with a previous normal endoscopy and healthy controls. Additionally, both those with reflux esophagitis and normal endoscopy had more abdominal pain and nausea compared to healthy controls at follow-up. There was not a statistically significant difference in chest pain, vomiting, dysphagia, or Nissen fundoplication.

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INTESTINAL PERMEABILITY IN FUNCTIONAL DYSPESIA: A CASE-CONTROL, SINGLE-BLIND, OBSERVATIONAL PILOT STUDY

Background: Intestinal barrier dysfunction is associated with most types of intestinal inflammation. In our clinic, duodenal mucosa inflammation is seen in about 75% of children with functional dyspepsia (FD). We hypothesized that children with FD would have increased barrier dysfunction related to mucosa inflammation. The aim was to determine if intestinal permeability is increased in children with FD compared to healthy controls.

Methods: We studied 19 children, aged 8–17 years (mean 13 ± 2.3; 5 M, 14 F) with FD unresponsive to acid reduction therapy that were scheduled for endoscopy with biopsies. Nineteen children aged 10–17 years (mean 13 ± 2.0; 8 M, 11 F) without history of chronic or current gastrointestinal symptoms, asthma or allergies were studied as a healthy control. Intestinal permeability was evaluated using the lactulose/mannitol (L/M) sugar absorption test.
Table. Percentage of clinical outcomes by group

<table>
<thead>
<tr>
<th></th>
<th>Histologic Reflux; n = 39 (of initial 121)</th>
<th>Normal Endoscopy; N = 39 (of initial 137)</th>
<th>Controls; n = 122 (of initial 350)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest Pain</td>
<td>28</td>
<td>31</td>
<td>20</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>64</td>
<td>67</td>
<td>34</td>
</tr>
<tr>
<td>Nausea*</td>
<td>79</td>
<td>67</td>
<td>35</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>5</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Acid Suppression</td>
<td>36</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Nissen fundoplication</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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GASTROESOPHAGEAL REFLUX IS ASSOCIATED WITH A DISTINCT PATTERN OF DENTAL EROSION

Yvette K. Wild1, Peter Rechmann2, Eric Vittinghoff3, Deepal Dalal1, Beate Rechmann2, Melvin B. Heyman1, 1Pediatrics, University of California, San Francisco, CA; 2Dentistry, University of California, San Francisco, CA; 3Biostatistics, University of California, San Francisco, CA.

Background: Untreated gastroesophageal reflux (GER) in children may lead to extraesophageal injury, including dental erosions. Details of the unique dental erosions characteristics remain to be systematically investigated. We performed an single-blinded cross-sectional study of the association and location of dental erosions in children with or without GER symptoms.

Methods: Subjects (9–17 yrs) were recruited from pediatric gastroenterology and general pediatric clinics and identified as symptomatic or asymptomatic with GER by self-administered questionnaires. Permanent teeth were examined for erosion into dentin, erosion location (upper, lower, anterior, posterior teeth), and affected tooth surface (facial, occlusal, lingual). Because numbers of total teeth per child varied, groups were analyzed by erosion per tooth in each child. Results were age adjusted. Descriptive data are expressed as mean ± SD. Wilcoxon rank sum and the sign test compared erosions between and within groups.

Results: 79 children were studied: 59 (13.8 ± 2.4 yrs; 24 male) with and 20 (12.4 ± 2.0 yrs; 10 male) without GER symptoms. Children with symptoms had more erosions per tooth (0.19 ± 0.18) compared with those without symptoms (0.11 ± 0.14; P = 0.03). In symptomatic children with facial surface erosions, posterior teeth were more often damaged than anterior teeth (P = 0.06). Furthermore, posterior facial erosions occurred more often on lower than upper teeth (P = 0.01). Overall, symptomatic children had more erosions on upper teeth (P = 0.03) and occlusal (P = 0.005) surfaces than asymptomatic children.

Conclusions: We confirm the association between GER symptoms and dental erosion, particularly in lower posterior facial surfaces, occlusal surfaces and upper teeth. Recognition of location-specific erosions may aid in patient referral for possible GER disease that precedes esophageal symptoms and injury. Further study is needed to determine the pathogenesis of GER-associated dental erosion.

Pancreas/Cystic Fibrosis

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AGE-SPECIFIC COMPLICATIONS OF ACUTE PANCREATITIS IN CHILDREN

Sona Sehgal, Jason Goldberg, John Snyder. Pediatric GI, Children’s National Medical Center, Washington, DC.

Background: Previous studies of acute pancreatitis (AP) in children have reported that complications are infrequent. The most frequently reported local complications include peri-pancreatic fluid collections, pseudocysts, necrosis and hemorrhage. Systemic complications can involve sepsis, shock and respiratory failure. We evaluated the age-specific outcomes of AP from our predominantly urban population.

Methods: We conducted a retrospective chart review of patients less than 21 years old from January, 2003-December, 2008. Patients were diagnosed with AP if they had 2 of the following 3 criteria: (1) Acute onset of abdominal pain, back pain, irritability, nausea, vomiting or ileus; (2) Elevation of the serum amylase or lipase three times the upper limit of normal; and (3) Imaging suggesting pancreatitis.

Results: 24 complications developed in 18 of 267 (7%) patients with AP (Table). The most common complication was the development of chronic pancreatitis (CP; 13/18, 72%). The most common cause of chronic pancreatitis was HIV infection (4/13). The rate of complications was similar in children with an associated illness (7%) and those with no associated illness (5%).

Conclusions: The complication rate for acute pancreatitis in our population was low for children with and without an associated illness. The percentages of those with any complication and for those with chronic pancreatitis were similar in all age groups. Life-threatening complications were rare and no deaths occurred from acute pancreatitis.

Table. Age-specific complications of acute pancreatitis

<table>
<thead>
<tr>
<th>Age, y</th>
<th>AP</th>
<th>Patients with complications</th>
<th>CP</th>
<th>Pseudocyst</th>
<th>Necrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>44</td>
<td>2 (4%)</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5–9</td>
<td>51</td>
<td>5 (10%)</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>10–14</td>
<td>95</td>
<td>8 (8%)</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>15–20</td>
<td>77</td>
<td>3 (4%)</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>267</td>
<td>18 (7%)</td>
<td>13</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>
AGE-SPECIFIC IMPACT OF OBESITY ON ACUTE PANCREATITIS AND GALLSTONE PANCREATITIS IN CHILDREN
Sona Sehgal, Jason Goldberg, John Snyder. Pediatric GI, Children’s National Medical Center, Washington, DC.

Background: Earlier pediatric studies have reported that up to a third of children with acute pancreatitis (AP) are overweight and that the prevalence of acute pancreatitis caused by gallstones ranges from 10–30%. We evaluated the age-specific prevalence of AP and gall-stone pancreatitis (GSP) and the association with obesity in our predominantly urban population of Washington, DC.

Methods: A retrospective chart review was conducted from Jan 2003-Dec 2008. Patients less than 21 yrs old were included if they met the diagnostic criteria for acute pancreatitis (AP) of having 2 of the following 3 criteria: (1) Acute onset of abdominal pain, back pain, irritability, nausea, vomiting or ileus; (2) Elevation of the serum amylase or lipase three times the upper limit of normal; and (3) Imaging consistent with a diagnosis of pancreatitis.

Results: 267 patients met the criteria for AP. The prevalence of AP was nearly twice as high for the 10–20 year age group (64%) compared to the 0–9 year age group (36%, P < 0.01) (Table). The most common comorbidity for AP was obesity (67, 25%); 28 patients (10%) had no comorbidity. 40 patients (Table). The most common comorbidity for AP was obesity (64%) compared to the 0–9 year age group (36%, P < 0.01).

Obesity was the most common comorbidity associated with GSP (43%); 9 patients (22%) with no co-morbidity had GSP.

Conclusions: Our data indicate that the prevalence of AP and GSP are far more common in older children. Obesity was the most commonly associated comorbidity for all children with AP and accounted for almost half of the cases of GSP which had a comorbidity.

Table. Age-specific prevalence of AP and GSP and the association with obesity

<table>
<thead>
<tr>
<th>Age range, y</th>
<th>AP</th>
<th>Obesity</th>
<th>GSP</th>
<th>Obesity and GSP.&lt;B.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>44 (17%)</td>
<td>7 (16%)</td>
<td>2 (0.5%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>5–9</td>
<td>51 (19%)</td>
<td>13 (26%)</td>
<td>4 (2%)</td>
<td>0</td>
</tr>
<tr>
<td>10–14</td>
<td>95 (36%)</td>
<td>31 (33%)</td>
<td>15 (6%)</td>
<td>6 (40%)</td>
</tr>
<tr>
<td>15–20</td>
<td>77 (29%)</td>
<td>16 (21%)</td>
<td>18 (7%)</td>
<td>10 (56%)</td>
</tr>
<tr>
<td>Total</td>
<td>267</td>
<td>67 (25%)</td>
<td>40 (15%)</td>
<td>17 (43%)</td>
</tr>
</tbody>
</table>

CHRONIC AND RECURRENT ACUTE PANCREATITIS IN CHILDREN
Mutaz Sultan, Michael Jensen, Steven Werlin, Narayanan Venkatasubramani. Department of Pediatrics, Division of Pediatric Gastroenterology and Nutrition, Medical College of Wisconsin, Milwaukee, WI.

Background: Etiologies of chronic pancreatitis (CP) and recurrent acute pancreatitis (RAP) in children include anatomic abnormalities, hereditary, metabolic and autoimmune disorders with the majority of cases being labeled as idiopathic. Genetic pancreatitis (GP) may be caused by mutations of cationic trypsinogen (PRSS1) gene, serine protease inhibitor kazal type 1 (SPINK1), and cystic fibrosis transmembrane conductor regulator gene (CFTR). There is
Methods: We reviewed the charts of children younger than 18 years of age with RAP or CP diagnosed between 2000 and 2009 at Children’s Hospital of Wisconsin, who tested positive for any of the above mentioned genes.

Results: 23 RAP or CP were identified. The mean age of symptom onset was 6.7 years (range 9M-15 years) and age at diagnosis was 7.4 years (range 1–16 years). 21 were Caucasian; 14 were females. The most common presenting symptoms were abdominal pain (100%) and vomiting (74%). Patients with RAP had 2–8 episodes within 3.6 years mean follow-up. A family history was present in 5 patients (2 PRSS1 and 3 CFTR mutations). PRSS1, SPINK1 and CFTR mutations were seen in 8 (34%), 7 (30%) and 14 (60%), respectively. 8 CFTR mutations were homozygote and 6 heterozygote: 6 patients with CP had a combination of CFTR and SPINK1 or PRSS1 mutations. 10/23 (43%) patients met radiologic criteria for CP. All heterozygote patients for CFTR and SPINK1 mutations had chronic pancreatitis. 8 patients developed chronic pain syndrome and 2 developed exocrine pancreatic insufficiency.

Conclusions: CFTR mutations were most frequently seen in our patients with RAP and CP. Testing for PRSS1, SPINK1 and CFTR mutations is indicated after a second episode of pancreatitis. GP is associated with early and severe pancreatitis, and a high risk of CP, and chronic pain syndrome. Patients with combined CFTR and SPINK1 mutation might be at higher risk for CP.

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INFLAMMATION CONtributes TO THE PATHOGENESIS OF PancreATIC LEsIONS IN CYSTIC FIBROSIS

Maisam Abu el haija1, M. Sinkora2, S. Ramachandran1,3, P. Ludwig1, D. Meyerholz1,3, J. Butler1,3, M. Welsh1,3, P. McCray1, A. Uc1, 2University of Iowa Hospitals, Iowa City, IA; 3Academy of Sciences of the Czech Republic, Novy Hradek, Czech Republic; 4HHMI, Iowa City, IA; 5Carver College of Medicine, Iowa City, IA.

Background: Pancreatic disease begins in utero in the majority of patients with cystic fibrosis (CF) and progresses over time to complete destruction of the organ. Hypothesis: Inflammation plays a role in the progression of pancreatic disease in CF.

Methods: Pancreatic histopathology was studied. Microarray expression profiling was done using an Affymetrix Porcine Genechip on pancreas CF (4CFTR+/−) and WT (4CFTR+/+). Using four-color flow cytometry, the surface phenotype of leukocytes in the pancreas, blood and mesenteric lymph nodes (MLNs) of CF pigs (4CFTR+/−/1 CFTRΔF508/ΔF508) and WT and heterozygous pigs (3CFTR+/−/1 CFTRΔF508) were analyzed. Primary monoclonal antibodies against CD2, CD3, CD4, CD8, CD14, CD21, CD25, IgM, TCR γδ, SWC1, SWC7, SWC8 and MHC-II antigens were used. Measurements were made using a FACS Calibror flow cytometer.

Results: WT and heterozygous pigs had identical pancreatic histology, microarray gene expression and leukocyte cell populations. Histopathological tissue examination showed
Conclusions: duodenal erythema respectively were on acid suppressive 9/10 (90%) and 2/3 (66%) of patients with gastric and in the colon 0/1 (0) and correlated with mucosal erythema. in 4/10 (40%), but less in the esophagus (1/6) and not

13.5% and 3.75%, respectively. Histologic inflammation denal ulceration, edema or nodularity were found in 13.5%,

Both the innate and adaptive immune systems affect the GI tract, which may require endoscopic evaluation for various symptoms. Pediatric literature has sparse data on endoscopic findings. The aims were to review the demographics, indications and frequency of endoscopic findings in children with CF.

Methods: Chart review of all CF children who underwent upper (EGD) and/or lower endoscopy at a single center from 1 January 1998 to 31 July 2008. Results: 80 procedures (66-EGD, 12-colonoscopy, 2-flex sig) were performed on 49 patients (28 M, 21 F) mean age 9 y (median 7.75 y, range 1.5 mo-19.6 y). 26 (53%) were homozygote for F508del and 14 (29%) were heterozygote. (median 7.75 y, range 1.5 mo-19.6 y). 26 (53%) were sig) were performed on 49 patients (28 M, 21 F) mean age 9 y

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Erythema was the most common finding seen in 27/80 (33.7%) of procedures. Gastric, esophageal, or duodenal ulceration, edema or nodularity were found in 13.5%, 13.5% and 3.75%, respectively. Histologic inflammation was found in the duodenum in 3/3 (100%) and in the antrum in 4/10 (40%), but less in the esophagus (1/6) and not in the colon 0/1 (0) and correlated with mucosal erythema. 9/10 (90%) and 2/3 (66%) of patients with gastric and duodenal erythema respectively were on acid suppressive medications.

Conclusions: On average 8 endoscopies/year are performed on CF patients in our center. Erythema was only predictive of histologic inflammation in the antrum and duodenum. No medication changes were prompted based on these findings. In our center, nutritional indications predominated, as evidenced by the frequency of PEG placement. Endoscopy in CF patients is most valuable when done for PEG placement or when indicated for traditional diagnostic/therapeutic purposes.

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SWITCHING CF PATIENTS FROM PREVIOUS PANCREATIC ENzyme PRODUCTS TO ZENPEP (PANCeRILPASE) DELAYED-RELEASE CAPSULES IMPROVES SYMPTOM CONTROL OF EXOCRINE PANCREATIC INSUFFICIENCY WITHOUT USE OF PPIs/H2 ANTAGONISTS

James Heubi1, Cristina Straforini2, Delma Broussard2, Ruth Thieroff-Ekerdt2. 1Cincinnati Children’s Hospital, Cincinnati, OH; 2Eurand Pharmaceuticals, Inc, Yardley, PA.

Background: Zenpep (pancrelipase) Delayed-Release Capsules, an FDA-approved pancrelipase formulation with 100% labeled lipase content without overage, significantly improved steatorrhea in a randomized, double-blind, placebo-controlled, crossover study of 34 CF pts with exocrine pancreatic insufficiency (EPI). The aim was to assess symptom improvement with ZENPEP after switching pts from previous formulations of pancreatic enzyme products (PEPs) not meeting new FDA requirements (FDA-unapproved [eg, Creon, Ultrase, Pancrecarb]) in a post hoc analysis of 31 patients. In a subgroup analysis, symptom improvement was compared in those previously taking, or not taking, proton pump inhibitors (PPIs)/H2 receptor antagonists.

Methods: Patients discontinued PPIs/H2 antagonists and switched from FDA-unapproved PEPs to ZENPEP in a dose stabilization period based on symptom control of EPI for 6–9 days before randomization (ZENPEP or placebo). Total symptom score index (TSI) was calculated from stool consistency, bloating, flatulence, pain, and oil in stool.

Results: At comparable mean doses, a significant, rapid symptom improvement during the stabilization period was observed when switched from previous PEPs (5100 U lipase/kg/day) to ZENPEP (4600 U lipase/kg/day). TSI (mean ± SD) decreased significantly from 11.2 ± 15.8 on previous PEPs to 4.3 ± 4.0 after 7 days of ZENPEP treatment (P < 0.004). Symptom improvement was observed by day 2 [significant at day 4 (P = 0.017)]. Variability in symptom severity was markedly decreased with ZENPEP. There was no significant impact on symptom improvement in 20/34 (58%) previously exposed to PPIs/H2 antagonists.

Conclusions: ZENPEP as a single agent enhanced EPI symptom control after CF patients were switched from FDA-unapproved PEPs, without additional reliance on PPIs/H2 antagonists, suggesting a potential for reduction of costs and pill burden.
FREQUENCY OF THE MUTATIONS R122H AND N29I IN THE GENE PRSS1 AND THE MUTATION N34S IN THE GENE SPINK1 IN CHILDREN AND ADOLESCENTS WITH ACUTE AND RECURRENT PANCREATITIS

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Background: The prevalence of pancreatitis in children has increased in the last years and seems not to be a benign entity since some cases can become recurrent and can be associated to mutations in several genes. The genetic assessment may help to identify the risk of developing more recurrences and chronic pancreatitis in infancy or adult life. The aims were to describe the frequency of the R122H and N29I mutations in the PRSS1 gene and N34S mutation in the SPINK1 gene in Mexican children and adolescents with pancreatitis; and to assess an association between acute and recurrent pancreatitis and the presence of these mutations.

Methods: Genomic DNA was extracted from peripheral blood leucocyte of unrelated cases with pancreatitis and 144 healthy control individuals. By PCR-RFLP analysis the N34S mutation and one patient (1.8%) for the N29I mutation were detected and by allele specific-PCR the N29I mutation was identified ten times fold in acute pancreatitis than controls.

Results: n = 92. Acute pancreatitis (63%), recurrent pancreatitis (37%). Mean age 10.8 ± 3.4 years old. The distribution by gender was 48.8% female and 51.2% male. We found one mutated allele in 4/92 cases (4.3%) with pancreatitis and none in the control individuals. In the group of acute pancreatitis three patients (5.2%) were heterozygous for the N34S mutation and one patient (1.8%) for the N29I mutation. The R122H mutation was not identified in the group of patients with pancreatitis neither healthy controls. When comparing the frequency of mutations between the two groups (acute vs. recurrent) it was almost significant (P = 0.054) and was significant when comparing the group of pancreatitis with the control group (P = 0.023).

Conclusions: None of the mutations screened were found in the group of recurrent pancreatitis and the mutation N34S in the gene SPINK1 was identified ten times fold in acute pancreatitis than controls.

VITAMIN B12 STATUS IN CF


Background: Elevated vitamin B12 levels were found in a study of choline metabolism in subjects with CF. The objective was to describe predictors of serum vitamin B12 status in children with CF.

Methods: Baseline measurements were obtained in subjects with CF and PI (aged 5–17 y) participating in a nutrition intervention study. Fasting serum B12 (immunoassay), FEV1, liver enzymes, serum lipids, high sensitivity CRP (HS-CRP), genotype, current medications, PERT use, dietary and supplemental B12 intake were assessed. Height, weight, and BMI Z scores were calculated. Outcomes were compared for subjects with high serum B12 (HI-B12) to those within ref. range (NORM-B12); predictors of B12 status were determined.
Results: Mean serum vitamin B12 (n = 88; 50 males, 10.8 ± 3.0 μg/L) was 1228 ± 539 μg/mL (range 387–3455); 56% subjects were in the HI-B12 group. Dietary B12 intake was 6.9 ± 3.4 μg/d (~100% RDA). Supplemental B12 intake was 15.5 ± 18.6 μg/d (~900% RDA). Compared to subjects with NORM-B12, those with HI-B12 (P < 0.05) were older (11.5 ± 3.1 vs 9.9 ± 2.5), had greater supplemental B12 intake (19.2 ± 23.6 vs 10.8 ± 6.8), higher serum cholesterol (136 ± 21 vs 126 ± 23), lower FEV1 (88 ± 22 vs 103 ± 22), more likely to be on inhaled tobramycin (43 vs 21%) and antifungals (14 vs 0%). Best predictors of HI-B12 status were FEV1 (<), supplemental B12 intake (+) and serum cholesterol (+) (R² = 0.20, P < 0.001) in logistic regression models. Multiple regression models identified FEV1 (<), serum cholesterol (+), and HS-CRP (+) (R² = 0.21, P = 0.001) as significant predictors of serum B12.

Conclusions: >50% of subjects had elevated B12 levels; none were deficient. Elevated serum B12 levels were associated with greater B12 supplementation, higher serum cholesterol and poorer pulmonary function, suggesting B12 status is associated with excess intake and/or possibly better absorption. Elevated B12 may be a biomarker of poorer respiratory status, or reflective of an unknown mechanism.

IS PANCREATIC INSUFFICIENCY IN CELIAC DISEASE DUE TO TRANSIENT ENTEROKINASE DEFICIENCY?

Ari Dorros, Anjali Malkani, Samra Blanchard, Alessio Fasano, Anca Safa. Pediatric Gastroenterology, University of Maryland Medical Center, Baltimore, MD.

The aim of this study was to determine if the etiology of pancreatic insufficiency (PI) in celiac disease (CD) is due to transient enterokinase deficiency. This is a prospective study which included patients less than 21 years of age with suspected CD due to abnormal celiac serology who underwent endoscopy between 2009 and 2010. Biopsies were sent for enterokinase and disaccharidase analysis. In addition, secretin stimulation was performed and the duodenal fluid was sent for pancreatic and disaccharidase analysis. In addition, secretin stimulation was performed and the duodenal fluid was sent for pancreatic enzyme analysis. A total of 17 patients were identified and 8 patients were diagnosed with Marsh 3a to 3c CD. Signs and symptoms of these patients included failure to thrive, decreased appetite, abdominal pain, vomiting, headaches, constipation, diarrhea, and rashes. All patients had normal enterokinase levels in their duodenal mucosa. Three patients with CD did not have a generalized disaccharidase deficiency. One patient with CD had an isolated amylase deficiency, and one patient had an isolated lipase deficiency. Based on previous literature, the risk of PI appears to be increased in children with CD. In children who have partial or total villous atrophy, it would be expected that they have a generalized disaccharidase deficiency as well as a low enterokinase level, based on the co-localization theory of these brush border enzymes.

Surprisingly, all of our patients with 3a to 3c Marsh criteria CD had normal tissue enterokinase levels despite two thirds of the patients having a generalized disaccharidase deficiency. We would expect children with pancreatic enzyme deficiency to have low enterokinase levels, due to the activation cascade of pancreatic digestive zymogens. The 2 patients with isolated PI and CD had normal enterokinase levels. This may suggest enterokinase may not be directly related to PI in CD. Complete PI was not prevalent in our patients with CD. We postulate that complete PI might still be a result of enterokinase deficiency in CD; however, more patients must be enrolled in our study in order to understand the etiology of PI in children with CD.

ENTERAL NUTRITION IN CHILDREN WITH ACUTE PANCREATITIS: OPEN CLINICAL TRIAL

Mariana Gómez-Nájera1, Alfredo Larroso-Haro1,2, Carmen Bojorquez-Ramos1, Rocio Macías-Rosales1, Yolanda A. Castillo de León1, Osvaldo García-Salazar1, Gastroenterology and Nutrition, UMAE Hospital de Pediatría CMNO IMSS, Guadalajara, Mexico; Instituto de Nutrición Humana, Universidad de Guadalajara, Guadalajara, Mexico.

Background: To evaluate the efficacy of enteral nutrition (EN) with an elemental diet to prevent acute malnutrition in children with acute pancreatitis (AP).

Methods: Design: Open clinical trial. Setting: A pediatric referral hospital. Subjects: Pediatric patients with AP. Nutritional intervention: 24-hour naso-jejunal infusion of an elemental diet, 17.5–20 g/dL; EN was started once the ileum was resolved. Initial intake: 100% of DRIs; a daily increase of 15% led to ~130% by the 3rd day. Outcome variable: Nutritional status evaluated by weight/height, arm anthropometrics and serum albumin. Procedure: Total “pancreatic rest” time was 7 days in mild and 14 days in severe AP. Analyses: Wilcoxon and Friedman tests.

Results: Patients: Seventeen patients with AP were studied; 47.1% were edematous (mild AP) and 52.9% necrotic-hemorrhagic (severe AP). Median age: 126.5 months, 70.6% were females. At day 3, the mean intake was 129% of DRIs. Nutritional status: Initial/final weight/height z-score increased from 0.3 to 0.9, P = 0.007. Medium arm circumference, triceps skin fold and arm areas’ z-scores had no statistical difference along the trial. Median albumin on admission was 2.8 g/dL and at day 14th it was 3.4 g/dL, P = 0.003. Safety: There were no relapses of abdominal pain plus hyperamylasemia. No infectious nor metabolic complications were observed.

Conclusions: The current protocol was effective in preventing acute malnutrition in contrast with previous experience. The intervention was safe and as a part of an integral management protocol it supported a nice clinical outcome even in severe cases.
DOES G195R MUTATION OF ORNITHINE TRANSCARBAMYLASE DEFICIENCY PREDISPOSE TO PANCREATITIS?

Ala Shaikh Khalil, Steve Erdman, Dennis Bartholomew, Jaya Panati. Division of Gastroenterology, Nationwide Children’s Hospital/Ohio State University, Columbus, OH; Section of Molecular and Human Genetics, Nationwide Children’s Hospital/Ohio State University, Columbus, OH.

Ornithine transcarbamylase (OTC) deficiency is an X linked urea cycle defect not known to cause pancreatitis. We report two patients with OTC deficiency and recurrent pancreatitis. Our two patients (A and B) are females (3 and 8 years) who presented with abdominal pain and vomiting. Acute pancreatitis was diagnosed based on elevated lipase (3184 and 10,111 U/L) and evidence of pancreatic inflammation on computed tomography. Both needed total parenteral nutrition (TPN) due to severe pancreatitis. Within 48 hours of starting TPN (1.7 grams of protein/kilogram/day) both patients developed encephalopathy with elevated serum ammonia (240 and 216 μmol/L). Further evaluation with serum amino acids and urine orotic acid revealed deficient OTC activity. Genotype analysis showed both patients to be heterozygotes for a known mutation of OTC deficiency: G195R. Males with OTC deficiency present with severe hyperammonemia as neonates. Due to X chromosome inactivation, females have a different phenotype ranging from being asymptomatic to developing severe hyperammonemia at any age. Our patients were previously asymptomatic but had self restricted their oral protein intake. Both patients recovered, but later had recurrent pancreatitis despite medical therapy for OTC deficiency. Patient A developed chronic pancreatitis with evidence of structural disease on endoscopic retrograde cholangiopancreatography. Patient B developed a pancreatic pseudocyst. Genetic analysis showed that patient A was also a heterozygote for SPINK-1 mutation; patient B had no mutations on CFTR, PRSS1, or SPINK1 genes. Patient B had a male sibling with OTC deficiency. With more than 340 known mutations; it is interesting that patient A was also a heterozygote for SPINK-1 mutation; patient B had no mutations on CFTR, PRSS1, or SPINK1 genes. Patient B had a male sibling with OTC deficiency. With more than 340 known mutations; it is interesting that our patients share the same mutation for OTC deficiency, this suggests a possible link to pancreatitis. Careful metabolic monitoring during evaluation of acute pancreatitis may help identify more children with associated OTC deficiency.

INOSITOL 1,4,5-TRISPHOSPHATE RECEPTOR TYPE 2 DEFICIENCY LEADS TO ACCUMULATION OF ZYMOCEN GRANULES IN PANCREATIC ACINAR CELLS

Zahir M. Mannan, Abraham I. Orabi, Ahsan U. Shah, Sohail Z. Husain. Pediatrics, Yale University, New Haven, CT.

Calcium signals are critical to physiologic secretion of pancreatic enzymes from the pancreatic acinar cell. The primary calcium channel in the secretory, apical pole of the acinar cell is the intracellular ER-bound inositol 1,4,5-trisphosphate receptor, or IP3R. The type 2 isoform, or IP3R2, contributes about half of IP3R expression. In this study, we examined the role of IP3R2 in maintaining acinar cell secretion by using mice deficient in IP3R2. On hematoxylin and eosin staining as well as electron microscopy of pancreatic tissues, IP3R2-deficient acinar cells had a larger and greater number of zymogen granules (ZGs). They also appeared to occupy a larger cross-section of the acinar cell. By immunoblot, amylase was increased by 2 fold, compared to wildtype (P < 0.05), whereas insulin levels were unchanged. By activity measurement, amylase content was similarly increased in these cells. However, acinar cell amylase secretion after secretagogue stimulation (with either a CCK analog or an Ach analog) or at baseline within a one hour incubation period was unchanged between IP3R2-deficient and wildtype cells. Nevertheless, electron microscopy showed morphological evidence of basolateral exocytosis. Further, serum levels of amylase at baseline in the IP3R2 deficient mice were 40% higher than in wildtype mice (P < 0.05). In summary, we demonstrate that IP3R2 deficiency causes an accumulation of zymogen granules. The effect is likely a result of reduced exocytosis over a long-term period, but our short term secretion studies could not identify this defect. The defect results in pathologic basolateral exocytosis. In conclusion, these data implicate IP3R2 in calcium-dependent pancreatic enzyme secretion.

Concurrent Session III:
Upper Gastrointestinal Mucosal Disease
2:00 PM–3:30 PM

A NATURAL HISTORY OF EOSINOPHILIC ESOPHAGITIS (EOE) IN CHILDHOOD: WHAT HAPPENS WHEN THEY GROW UP?

James P. Franciosi, Charles W. DeBrosse, Eileen C. King, J.P. Abonia, Bridget Buckmeier Butz, Margaret H. Collins, Allison Greenberg, Alexandria Greenler, Michael D. Eby, Marc E. Rothenberg. Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; Division of Allergy and Immunology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; Division of Biostatistics and Epidemiology, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Background: The natural history of pediatric Eosinophilic Esophagitis (EoE) has not been fully characterized.
Methods: Esophageal biopsies between 1982–1999 were re-examined and re-classified as retrospective eosinophilic esophagitis (rEoE: ≥15 eos/hpf) or chronic esophagitis...
(CE: <15 eos/hpf). A relative age-matched cohort of 100 healthy subjects was identified. Subjects were then asked to complete questionnaires.

**Results:** 666 patients were identified as rEoE (198) or CE (468). Subjects had death records reviewed (rEoE, 11; CE 56; P < 0.01), contact information verified (rEoE 97, 49%; CE 187, 39%; P < 0.05), and were then asked to complete questionnaires (rEoE 30, 31%; CE 46, 25%; P = ns). History of dysphagia (rEoE 51%; CE 37%; control 6%; P < 0.001), food impaction (rEoE 39%; CE 16%; control 2%; P < 0.001), esophageal dilation (rEoE 19%; CE 7%; control 0%; P < 0.001), food allergy (rEoE 37%; CE 13%; control 12%; P < 0.01), rates of fundoplication (rEoE 38%; CE 22%; control 0%; P < 0.001), current PPI use (rEoE 39%; CE 31%; control 3%; P < 0.001) and current care by a gastroenterologist (rEoE 42%; CE 32%; control 3%; P < 0.001) were all significantly increased in the rEoE cohort. Reflux Disease Questionnaire mean scores (rEoE 8.8; CE 7.9; control 1.6; P < 0.001) and family history of Barrett’s esophagus (rEoE 7.9%; CE 7.7%; control 0%; P < 0.001) were similar among rEoE and CE cohorts, yet distinct from controls.

**Conclusions:** Pediatric rEoE patients are at increased risk of developing persistent disease characterized by dysphagia, food impaction, the need for esophageal dilation, and food allergy.

### 269 LUNG PEPSIN IS CORRELATED WITH NONACID REFLUX BURDEN BUT NOT LUNG DISEASE SEVERITY

Rachel L. Rosen1, Nikki Johnston2, Mary Warlaumont1, Kristen Hart1, Umakanth Khatwa1, Samuel Nurko1,1Children’s Hospital Boston, Boston, MA; 2Medical College of Wisconsin, Milwaukee, WI.

**Background:** Pepsin has been proposed as a marker of reflux-related lung disease but the relationship between reflux disease and pepsin in children is less certain. The aim of this study is to determine if pepsin in the lung is associated with a high reflux burden and more severe pulmonary disease.

**Methods:** We prospectively recruited 50 patients undergoing combined bronchoscopy, endoscopy and pH-MII testing off acid suppression therapy for the evaluation of cough or asthma. Patients completed quality of life questionnaires and baseline historical questionnaires. Bronchial lavage fluid was collected and pepsin, lipid laden macrophage indices, and cell counts were measured. Pepsin was measured by Western blot analysis for human pepsin.

**Results:** The mean patient age was 74 ± 46 months. 41% of patients had pepsin in the airway. The number of nonacid reflux events and the LLMI were associated with pepsin positivity (Table). There was no difference in the mean percentage of neutrophils between pepsin positive (13 ± 12%) and negative patients (12 ± 9%; P = 0.5) or the percentage of full column reflux events between pepsin positive (45 ± 20%) and negative patients (46 ± 21%).

**P = 0.8.** Using the pediatric quality of life score and steroid use as indicators of disease severity, pepsin positive did not have more severe disease than pepsin negative patients (P > 0.08). Pepsin positive patients did not have more ear or sinus infections, dental caries or pneumonias than patients who were pepsin negative (P > 0.1).

**Conclusions:** Patients with pepsin in the lung have a higher nonacid reflux burden but the presence of pepsin did not translate into more severe disease or extraintestinal manifestations of GERD.

**Table.**

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<thead>
<tr>
<th>Pepsin Negative</th>
<th>Pepsin Positive</th>
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<tbody>
<tr>
<td>Mean # Acid Events</td>
<td>28 ± 14</td>
<td>23 ± 15</td>
</tr>
<tr>
<td>Mean # Non-Acid Events</td>
<td>14 ± 10</td>
<td>23 ± 19</td>
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<tr>
<td>Mean no. Total Events</td>
<td>41 ± 20</td>
<td>46 ± 29</td>
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<tr>
<td>Mean no. pH-only Events</td>
<td>8 ± 5</td>
<td>7 ± 7</td>
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<tr>
<td>% time pH &lt; 4</td>
<td>3.7 ± 3.7</td>
<td>4.2 ± 5.9</td>
</tr>
<tr>
<td>Mean LLMI</td>
<td>47 ± 26</td>
<td>83 ± 54</td>
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### 270 ESOMEPRAZOLE TREATMENT FOR SIGNS/SYMPTOMS OF GASTROESOPHAGEAL REFLUX DISEASE IN NEONATES

Marta Illueca1, Michael Thomson2, Geoffrey Davidson3, Taher Omar1, Tobias G. Wenzl4, Peter Barker1, Per Lundborg5, Astrazeneca LP, Wilmington, DE; 2Sheffield Children’s Hospital, Sheffield, United Kingdom; 3Women’s and Children’s Hospital, North Adelaide, SA, Australia; 4Kinderklinik, Universitaetsklinikum Aachen, Aachen, Germany; 5AstraZeneca R&D, Mölndal, Sweden.

This multicenter, randomized, double-blind study (D9614C00004; NCT00427635) assessed esomeprazole (ESO) in neonates (premature to 1mo corrected age) with GERD signs/symptoms using novel integrated pH/impedance (measured using a probe placed prefeeding; data recorded for 18–24h), cardiorespiratory (recorded respiration rate, apnea, heart rate, O2 saturation levels for 8h), and video monitoring (recorded for 8h). Reflux episodes (acidic [pH < 4.0], weakly acidic [pH 4.0–6.9], nonacidic [pH ≥ 7.0]) were evaluated at baseline and final visit. Neonates received ESO 0.5 mg/kg or placebo (PBO) PO 30 min before AM feeding for ≤14 d. Changes from baseline (log-scale) in number of GERD signs/symptoms (vomiting, gagging, back arching, irritability/crying/fussing, bradycardia, O2 desaturation, or apnea) (primary endpoint), individual signs/symptoms, and signs/symptoms temporally associated with acidic reflux events (±2 min of acidic reflux onset) were analyzed via ANCOVA. LSMs were transformed and expressed as % change from baseline. At baseline, ~50% of events were irritability/crying/fussing and ~30% were O2 desaturation events. Decreases in number of GERD signs/symptoms was similar between treatments (ESO [n = 25], −14.7%; PBO [n = 26], −14.1%; P = 0.92) with no significant differences for individual signs/symptoms. A significant decrease was observed in number of
signs/symptoms temporally associated with acidic reflux episodes for ESO vs PBO ($P < 0.0001$) including back arching ($P < 0.01$) and irritability/crying/fussiness ($P < 0.0001$). No significant difference was seen in ESO vs PBO in overall symptom reduction, but a significant reduction was seen in neurobehavioral signs/symptoms—temporally associated with acidic reflux episodes, suggesting a limited role for empirical acid suppression in neonates with GERD signs/symptoms without diagnostically proven acid-related disease.

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PATIENTS WITH EOSINOPHILIC ESOPHAGITIS EXPRESS HIGH LEVELS OF IgE-RECEPTORS IN ESOPHAGEAL LESIONS AND CARRY IgE ON PERIPHERAL BLOOD CELLS, EVEN IN THE ABSENCE OF ELEVATED SERUM IgE

Eleonora Dehlink1,3, Peter Dwyer1, Elizabeth Yen1, Jason Hornick2, Kristen Hart1, LaRosa Jessica1, Edda Fiebiger1, Samuel Nurko1, 1Division Gastroenterology, Children’s Hospital Boston, Boston, MA; 2Department of Pathology, Brigham and Womens Hospital, Boston, MA; 3Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria.

**Background:** Eosinophilic esophagitis (EoE) is an allergic disease of the esophagus, marked by an eosinophil-rich inflammatory infiltrate of the esophageal mucosa. The majority of EoE patients, but not all, show elevated serum IgE levels. The aim was to characterize IgE receptors in the esophageal epithelium and on peripheral blood cells of patients with EoE, reflux esophagitis and healthy controls and to analyze associations of IgE receptors expression levels with serum IgE.

**Methods:** Immunohistochemical stainings for the high affinity IgE receptor FcεRI were performed on esophageal biopsies from EoE patients and age-matched controls (19 EoE, 22 reflux esophagitis, 21 normal controls). Whole blood samples were analyzed by flowcytometry for FcεRI, CD23, and cell-bound IgE on the surface of dendritic cells (CD11c+MHCI class II+), monocytes (CD14+), basophils (CD123+MHCI class II-) and neutrophils (myeloperoxidase+). Total serum IgE was measured by ELISA. Correlations were calculated using Spearman rank correlation test.

**Results:** Our data show that FcεRI is highly abundant on immune cells in inflammatory lesions in EoE patients of the allergic status of the patient. On FcεRI+ DCs, monocytes, and neutrophils, a positive correlation between cell-bound IgE and absolute total serum IgE was detected. We also show by flow cytometry that peripheral blood cells are loaded with IgE via FcεRI and to a lesser extent CD23. We found that numbers of IgE-positive cells did not significantly differ between children with elevated and normal serum IgE.

**Conclusions:** We conclude that immune cells in peripheral blood can carry cell surface bound IgE which makes them susceptible to IgE-mediated cell activation. This mechanism might be relevant for the elicitation of allergic symptoms even in EoE patients with low serum IgE levels.

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ALTERED ESOPHAGEAL EPITHELIAL INTERCELLULAR SPACE—A MARKER OF ESOPHAGEAL INJURY IN CHILDREN WITH REFLUX SYMPTOMS

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**Background:** Most children with gastroesophageal reflux, retrosternal, and epigastric pain have no identifiable erosions on endoscopy (NERD). Acid, pepsin, and bile reflux have been implicated in pathophysiology of NERD. Esophageal epithelial intercellular space (ICS) is considered reliable marker of mucosal permeability and electron microscopic evaluation of ICS is considered a “gold standard.” The aim was to evaluate ICS changes in children with NERD. To compare ICS measured using electron microscopy (EM) and light microscopy (LM).

**Methods:** Esophageal mucosal biopsies were obtained 3–5 cm proximal to the gastroesophageal junction in 25 subjects with NERD and 9 asymptomatic controls. Pathologist blinded to subject groups selected areas from basal epithelial layer for EM and LM evaluation. Photographs were digitized and average of 100 measurements was used for EM evaluation. At least 4 images at 200X magnification using Axial Cam and AXIO VISION software were evaluated by LM. Phase contrast was used to measure ICS percentage area. Groups were compared using a Mann-Whitney nonparametric test. Data are summarized as median (25th percentile, 75th percentile) because of outliers.

**Results:** The mean (SD) age for NERD group was 10.8 yr (±2.8 yr) and control group 10.2 yr (±3.1 yr) ($P$ value n.s.). The mean (25th-75th IQR) ICS measured by EM was 1.15 μm (1.01 μm-1.28 μm) and 0.90 μm (0.82 μm-1.03 μm) for NERD and controls, respectively ($P = 0.002$). The median (25th-75th IQR) ICS measured by LM was 14.4% (13.19%-15.22%) and 9.92% (8.78%-12.425%) for NERD and controls respectively ($P = 0.001$). An 11.65 μm cutoff value for LM ICS gives 96% sensitivity and 78% specificity. A 1.08-μm cutoff value for EM ICS gives 72% sensitivity and 65% specificity.

**Conclusions:** A group, NERD subjects had significantly increased ICS compared to asymptomatic controls. Increased in NERD subjects may allow the acid to permeate the mucosa and cause pain. LM evaluation of ICS has better sensitivity and specificity compared to EM.

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CD40 IS IMPLICATED IN THE PATHOGENESIS OF EOSINOPHILIC ESOPHAGITIS

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Eosinophilic esophagitis (EoE) is an emerging disease characterized by marked eosinophil infiltration into the esophageal epithelium. Recent studies show that Th2 lymphocytes play a key role in the development of EoE, however the molecular mechanism of Th2 cell activation in EoE remains to be fully studied. Of the various receptors and ligands that regulate T cell function, the co-stimulatory molecule CD40 expressed by antigen presenting cells is critical to lymphocyte activation. In this study, we aimed to define the role of CD40 in the pathogenesis of EoE. We developed a murine EoE model through a systemic sensitization of Balb/c mice with ovalbumin (OVA) followed by repeat intraesophageal OVA challenge. The severity of EoE between wild-type and CD40 knockout mice was compared histologically. Subsequently, the expression of CD40 and IL-9 in the draining lymph nodes was analyzed by flow cytometry and RT-PCR, respectively. In addition, serum IgE level was determined using ELISA. Additionally, immunohistochemistry was employed to examine CD40 expression in the esophageal biopsy specimens of human EoE patients. Wild-type mice developed esophageal eosinophilic infiltration in response to OVA challenge, whereas there was no eosinophilic inflammation observed in the esophagus of CD40 knockout mice. In addition, the wild-type animals displayed a marked increase of CD40, IL-9, and OVA-specific IgE expression. In contrast, OVA failed to elicit the Th2 response in the CD40 knockout mice. Finally to validate this experimental finding in human patients, we demonstrated substantial immunostaining of CD40 in the esophageal epithelium of 4 children with EoE. These results strongly suggest that CD40 is essential to the development of EoE. Our study demonstrates the clinical importance and relevance of CD40 research. It further provides a rationale to test the feasibility of a CD40-targeting therapy for treating EoE and other Th2-mediated diseases.

Background: Irritable Bowel Syndrome (IBS) is a common motility disorder that negatively impacts the quality of life of many children. IBS has been associated with alteration in the gut microbiome and adult subjects have distinctly different microbiome. The microbiome is a large contributor to the health of the colonocytes through the production of short chain fatty acids. The goal of this study is to characterize the gut microbiome with its metabolite profile in children with diarrhea-predominant IBS.

Methods: The microbiome was evaluated using microarray to identify 16S rRNA of 852 intestinal microbial phylotypes. Fecal samples were collected from 26 healthy controls and 36 children with diarrhea-predominant IBS. DNA extraction, PCR amplification of the 16S rRNA segment, hybridization of the microarray, and analysis of the signal strength was performed. In addition, the metabolite profile of the gut microbiome was investigated using nuclear magnetic resonance (NMR).

Results: Children with diarrhea-predominant IBS had 217 (26%) phylotypes that were significantly different from healthy children (corrected P value <0.05). Twenty phylotypes (10%) and 197 (90%) were increased. At the class level, Clostridia were reduced, while fusobacteria and gammaproteobacteria were increased. In addition, the short chain fatty acid (SCFA) profile in pediatric IBS was significantly reduced with an almost 2-fold decrease in total short chain fatty acid as well as a decrease in the individual SCFA such as acetate, butyrate and propionate.

Conclusions: This report suggests that children with diarrhea-predominant irritable bowel syndrome harbor a distinctly different gut microbial profile which produces significantly lower quantities of short chain fatty acids, thus reducing the colonic energy resources, which in turn, may contribute to the dysmotility seen in this disorder. The data can serve as the basis for future endeavors to modify the gut microbiome for therapeutic interventions.

Concurrent Session IV:
Motility/Functional Disease
3:45 PM–5:15 PM

Naspghan Neurogastroenterology and Motility Prize (Basic)

THE GUT MICROBIOME AND ITS METABOLITE PROFILE IN CHILDREN WITH DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME
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Naspghan Neurogastroenterology and Motility Prize (Clinical)

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MUCOSAL CFTR EXPRESSION IN THE DISTAL COLON IS UPREGULATED FOLLOWING FECAL IMPACTION RESULTING IN WATER SECRETION
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Background: Rectal fecal impaction is common in functional fecal retention, pelvic floor dyssynergia and anal achalasia and is associated with liquid fecal incontinence. The pathophysiology of fecal incontinence due to fecal...
impaction is poorly understood. Animal studies suggest that rectal balloon distension results in increased luminal water secretion and that increased luminal pressure stimulates chloride channels in rats in vitro. We hypothesized that colonic distension will upregulate cystic fibrosis transmembrane conductance regulator (CFTR), a cAMP-activated chloride channel expressed in colonic mucosa.

Methods: Under isoflurane anesthesia the anus was ligated to produce a 75% stenosis in rats. Control rats received ligation without inducing anal stenosis. One day after anal ligation, the proximal, mid and distal colon were removed. Mucosal short-circuit current (Isc) was measured by conventional Ussing chamber and Western blot analysis was used to detect CFTR expression in the colonic mucosa.

Results: 24 hours after anal ligation the rats failed to defecate, while control rats passed normal stool. The ligated colons were markedly dilated with retained solid and watery feces. Water content of the luminal feces was significantly increased to 60 ± 1.1% (P < 0.01, n = 12) in ligated rats, compared to control rats (49.5 ± 5.2%, n = 10). Ussing chamber analysis showed that baseline Isc was significantly increased in the distal colon (78.8 ± 7.4 µA/cm², n = 7, P < 0.05) of ligated rats, compared to control rats (21.5 ± 3.2 µA/cm², n = 6). CFTR expression in the distal colon was significantly increased in ligated rats by a mean 5.45 times that of controls (n = 4).

Conclusions: It is suggested that colonic distension due to fecal impaction resulting from anal ligation induces an up-regulation of colonic CFTR. This alters function from a net absorptive to a net secretory state. This could be an important compensatory mechanism to alleviate colonic distension due to fecal impaction.

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NEONATAL CYSTITIS INDUCED COLONIC HYPERSENSITIVITY IN ADULT RATS: A MODEL OF VISCERO-VISCERAL CONVERGENCE

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Background: The coexistence of interstitial cystitis and irritable bowel syndrome is well documented. The objective of the study was to determine if cystitis during the neonatal period alters colonic sensitivity later in life and to investigate the role of primary sensory afferents, spinal neurons, mast cells and eosinophils.

Methods: Female rat pups were treated (postnatal days 14–21) with intravesical zymosan, normal saline, or anesthesia. Zymosan-induced bladder hypersensitivity and the estrus cycle was documented in all rats. Sensitivity and the estrus cycle were recorded in all rats sensitized with zymosan. The hypersensitivity is maintained by sensitization of UBD-sensitive spinal neurons demonstrated a significant increase in response to bladder distension (0.2–0.8 m1) in cystitis rats (n = 4) compared to control (n = 4).

Conclusions: Neonatal cystitis results in colonic hypersensitivity in adult female rats that is independent of the estrus cycle. The hypersensitivity is maintained by sensitization of spinal neurons and not pelvic afferents. Mast cells and eosinophils do not contribute to the observed hypersensitivity.

THE ROLE OF GASTROESOPHAGEAL REFUX (GER) IN SLEEP-DISORDERED BREATHING IS AGE DEPENDENT

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Background: Obstructive sleep apnea (OSA) and cortical arousals affect up to 2–3% of school age children. The aims were to evaluate the relationship between GER and sleep disordered breathing in children and the role of age on this relationship.

Methods: We performed simultaneous sleep studies and multichannel intraluminal esophageal impedance/pH (MII/ pH) monitoring on children. MII/pH events were evaluated during sleep, wakefulness after sleep onset (WASO) and daytime. Arousal index: number of arousals/hr. An event is associated with GER if happened up to 2 min after GER and the SAP ≥95%.

Results: We evaluated 45 subjects; 24 infants 14 M/10F, age 4.8 mo ± 2.8 and 21 children age ≥1 yr. (14 M/7F, mean age 11.1 yrs SD 11.9). Patients presented 3942 GER episodes (87.6 ± 41.6), 10,957 desaturations (243.5 ± 368.7), 101 hypopneas (2.2 ± 4.7), and 109 apneas (2.4 ± 7.7). Only 1 child had positive SAP for hypopnea, while 2 (1 infant) were positive for apnea and 13 (5 infants, P = 0.2) were positive for desaturation. Arousal indices were higher in infants (8 ± 3.3 vs 5.6±±3.1, P = 0.01), and reflux-associated arousals were found in 7 (29.2%) infants and only in 1 child (4.8%, P = 0.05). Awakenings were more frequent in infants (4/hr ± 2.3 vs 2/hr ± 1.6, P < 0.01), as well as the frequency of GER-associated awakenings (9/24 vs 2/21, P = 0.04).
Infants had higher rates of nonacid reflux exposure during sleep (0.27% interquartile range (IQR) 0.06–1.12 vs 0 IQR 0–0.18, P < 0.01), and WASO (1.42% IQR 0.14–.49 vs 0 IQR 0–0.07, P < 0.01). Nonacid reflux time was significantly associated with arousals even after controlling for age (P < 0.01). The duration of sleep-time acid reflux events was associated with GER-related arousals (206.2 sec IQR 139.9–525.1 vs 70.6 IQR 37.9–123.6, P < 0.01).

Conclusions: Infants have more arousals and awakenings and more GER-related arousals and awakenings than children. Findings are related to the higher exposure to non-acid reflux episodes during sleep. GER should be considered a cause of poor sleep quality in infants.

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FIRST EPIDEMIOLOGICAL STUDY OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN SCHOOLCHILDREN OF COLOMBIA
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Background: Functional gastrointestinal disorders (FGIDs) are common in North-American and European children. Epidemiology of GI disorders may vary by region. Investigating regional epidemiology is important for clinical practice and funding allocation. There are no epidemiological studies of FGIDs in South-American children. The aim was to investigate the epidemiology of FGIDs in Colombian children.

Methods: The questionnaire (QPGS-Rome III) was translated from English to Spanish. Wording was adapted to local common children’s language by interviewing 24 schoolchildren in 2 Colombian cities (Pasto, Cali). 3 schools (948 students total) representing demographic and socio-economic composition of Pasto (population 400,000) were selected. Sample size (n = 355) calculated based on estimated prevalence of FGIDs, confidence level 95%, error margin 5%. 488 school children invited to participate to account for estimated 30% attrition rate. Children had instructional session on questionnaires completion. GI Family history (FHx) obtained. IRB approved.

Results: 82 parents refused. 406 children, mean age 9.96 (8–14 years) included. 373 children, 9–11 years (50.2 % girls), (58% mixed race, 38% Caucasian, 4% Black) from 1 public PU (n = 278) and 2 private PR schools (n = 95), completed translated/adapted QPGS III. 26.5% children met FGIDs Rome III criteria diagnosis (24% PU, 33% PR). Functional Constipation (14%), IBS (5.4%), Functional Abdominal Pain (2.7%), Functional Dyspepsia (1.7%), Nonretentive Fecal Incontinence (1.5%), Abdominal Migraine (1%), Cyclic Vomiting (0.2%). FGIDs more likely in girls (OR = 1.6, CI 95% 1.01–2.63, P = 0.04). 24 % children with FGIDs had FHx of FGIDs. School type, race, household size, and intact vs. broken families: no effect in FGIDs prevalence. Children with FGIDs were more likely than children with organic GI conditions to live with family members with FGIDs.

Conclusions: FGIDs are common in Colombian children. FGIDs more common in girls and families with FGIDs. This is the first epidemiological study of FGIDs (Rome III) in children of South America.