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Pediatric Gastroenterology, Hepatology and Nutrition
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Las Vegas, NV

Scientific Abstracts

POSTER SESSION I

Thursday, November 2

5:00pm – 7:00pm

*Posters of Distinction

ENDOSCOPY/QI/EDUCATION

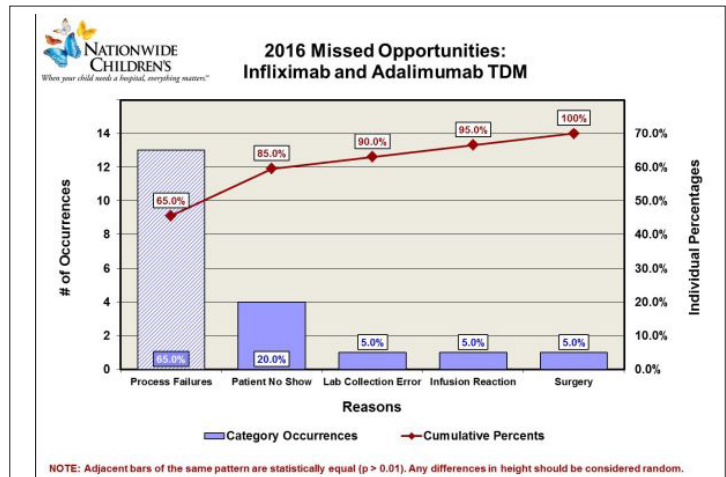
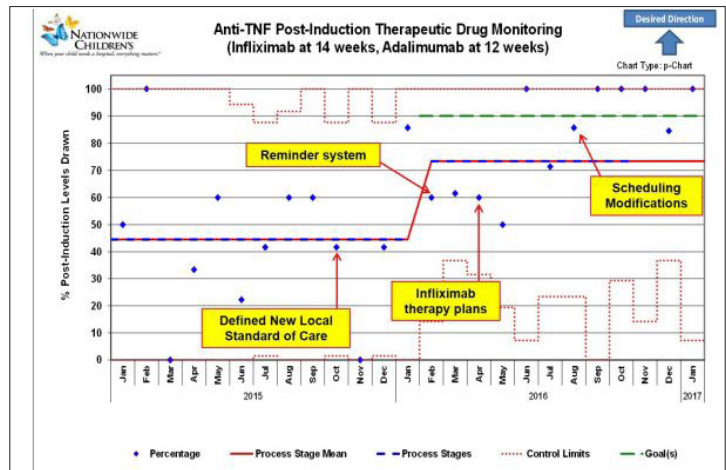
3 IMPROVING QUALITY AND UTILIZATION OF ANTI-TNF POST-INDUCTION THERAPEUTIC DRUG MONITORING. Amy Peasley, Emily Homan, Amy Donegan, Ross Maltz, Jennifer Dotson, Wallace Crandall, Brendan Boyle. Gastroenterology, Nationwide Children's Hospital, Columbus, OH

Background: Anti-tumor necrosis factor (TNF) therapy has revolutionized the care of pediatric patients with moderate to severe Crohn's disease and ulcerative colitis. However, an estimated 40% of patients who initially respond to an anti-TNF will lose response within the first 12 months of initiation. Loss of response can have significant clinical consequences as alternative medical therapies after failing an anti-TNF medication are limited. Because of the high rate of loss of response and the limited treatment options available to these patients, a focus upon individualized care and optimization of anti-TNF therapy through therapeutic drug monitoring (TDM) has continued to grow. TDM ensures adequate serum drug levels in order to minimize antibody formation and maintain disease control. Detectable serum drug levels have been associated with higher rates of clinical remission, lower C-reactive protein, and endoscopic healing. Proactive TDM has been associated with greater drug durability, reduced formation of antibodies, and reduced risk of IBD-related surgery and hospitalization. We aim to describe the quality improvement (QI) methods used at our institution to improve post-induction TDM in children initiating anti-TNF therapy, and to optimize our use of these medications through dose adjustments.

Methods: This QI initiative was started in February 2016. All patients initiating anti-TNF therapy were identified and tracked. We defined the post-induction period for infliximab as any level obtained within 15 weeks of the first dose.

We defined the post-induction period for adalimumab as any level drawn between 8-12 weeks of the first dose. PDSA cycles included the initiation of therapy plans for infliximab, modifications of electronic medical record (EMR) strategies for consistent ordering of labs, real-time reminders for practitioners, and scheduling modifications within 6-8 weeks after anti-TNF therapy initiation. Baseline data from prior to 2016 was compared to data after initiation of the QI project.

Results: In 2015, 85 patients began anti-TNF therapy (56 infliximab (66%) and 29 adalimumab (34%) within our IBD center. Among these patients, 35/85 (41%) had post-induction anti-TNF levels obtained. In 2015, 30/56 infliximab post-induction levels were obtained (54%) and 5/29 adalimumab post-induction levels were obtained (17%). In 2016, 89 patients began anti-TNF initiations (41 infliximab (46%) and 48 adalimumab (54%). Among those 89 new starts in 2016, 69 post-induction levels were obtained (78%). There were 30/41 post-induction infliximab levels obtained (73%) and 39/54 post-induction adalimumab levels obtained (81%). There were 20 missed opportunities due to process failures, patient no show, lab collection error, infusion reaction, and surgery.



Conclusions: Through quality improvement methodology, we have improved our use of post-induction anti-TNF TDM from a baseline of about 41% to almost 80% within 1 year. Monthly data indicate 85-100% compliance with post-induction TDM since August 2016. Future studies will compare clinical outcomes after project initiation with a historical cohort.

4 MULTIDISCIPLINARY CLINIC APPROACH FOR THE CARE OF CHILDREN WITH INTESTINAL FAILURE- MAINTAINING EFFICIENCY IN A HIGH VOLUME CLINIC

Andrea Martinez^{1,4}, Matthew Nelson², David During², Debra Harrison⁴, Karen Steinberg⁴, Glenda Courtney-Martin⁴, Christina Kosar⁴, Paul W. Wales^{4,3}, Yaron Avitzur^{1,4}. ¹Division of Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children, Toronto, ON, Canada; ²Process Improvement and Innovation Team, Hospital for Sick Children, Toronto, ON, Canada; ³Division of General Surgery, Hospital for Sick Children, Toronto, ON, Canada; ⁴Group for the Improvement of Intestinal Failure and Treatment, Hospital for Sick Children, Toronto, ON, Canada

Background: Children with intestinal failure benefit from multidisciplinary care. Since 2005, our intestinal rehabilitation (IR) clinic has fostered a multidisciplinary approach that includes a surgeon, gastroenterologist, nurse practitioners, dietitians, social worker, occupational therapist, physiotherapist and a speech pathologist. The team provides a simultaneous multidisciplinary assessment and care plan to the patient and family. This model is effective clinically, but time and resource consuming. With the growth in patient population, prolonged clinic wait times compromised the patient experience. We aimed to reorganize the IR clinic while maintaining the multidisciplinary model to improve clinic flow, efficiency and patient/family experience.

Methods: We determined outcome, process and balance measures, administered questionnaire and performed value stream mapping to understand current clinic status and identify areas of opportunity. Real-time measurement of the clinic process was completed. Through LEAN methodology, 8 wastes were identified and PDSA cycle was created and implemented in the clinic. After 6 months real-time measurement was performed to assess the impact of these changes.

Results: The patient survey demonstrated mean overall clinic satisfaction of 9.5/10; however, wait time score was 4.2. A new template for efficient multidisciplinary patient focused discussion and simultaneous follow up with re-organization of the clinic visit were created. Average appointment time before and after implementation were 114.28 min (SD 60.96 min) vs 65.10 min (SD 30.60 min) respectively. Before implementation, non-value added time (Amount of time that does not directly involve patient care), exceeded value added time (Amount of time involves patient interaction/care). After implementation value added time and team consult time increased from average 25.17 min to 27.44 min and 15.12 min to 18.05 min respectively. Measurement after implementing changes showed a reduction in clinic time by 44% and increased value added time by 9%.

Conclusions: As the number of children with IF grows, efficient structure of the IR multidisciplinary clinic is essential for optimal patient care. Our project demonstrates the feasibility of stream-lined care delivery without compromising the benefit of a multi-member, simultaneous assessment clinic and providing better care and more valuable time for the patients.

5 ESOPHAGEAL CAPSULE ENDOSCOPY (ECE) IN CHILDREN AND YOUNG ADULTS.

Anita Pai, Maureen Jonas, Victor Fox. Pediatric Gastroenterology, Hepatology, and Nutrition, Boston Children's Hospital, Boston, MA

Background: Variceal hemorrhage (VH) is a serious complication of portal hypertension (PH). Screening PH patients for varices and implementing prophylactic measures reduces VH risk. Data on ECE variceal detection in adults has been promising, but pediatric experience is limited.

Methods: A cohort of children and young adults with suspected PH referred for variceal screening or surveillance at Boston Children's Hospital (2005-2017) was offered ECE. A standard ingestion protocol was used. Clinical data, ECE performance, findings, and consequences of results were reviewed retrospectively.

Results: 141 ECE studies (30 serial cases) were performed in 94 patients (53 males, 56.4%) using 3 ECE devices (PillCam™ ESO: 65, ESO2: 67, and UGI Capsule: 9). Videos were interpreted by 3 readers (#1: 122, 88.4%, #2: 14, 10.1%, #3: 2, 1.4%). Median age was 16y (IQR 4.8). Primary diagnosis: cholestatic (n=42, 29.8%), hepatocellular (n=9, 6.4%), metabolic (14, 9.9%), cystic fibrosis (n=39, 27.6%), pre-hepatic vascular (14, 9.9%), post-hepatic vascular (17, 12.1%), cryptogenic (6, 4.3%). There were 15 congenital heart cases (median 18.1y, IQR 4.7y; median Fontan pressure: 17, IQR 7.3 mmHg). 29 cases had a prior history of GI bleeding (GIB), 6 in the preceding 12 months.

Median esophageal transit time (ETT) was 00m:20s (IQR 02m:20s) and study duration 31m:54s (IQR 11m:30s). 3 cases (ages 10.7, 11, 11.9y) were aborted due to difficulty swallowing capsules. Of the 138 ingested capsules, the final image was

in the esophagus (2, 1.4%), stomach (64, 46.4%), or post-pyloric (72, 52.2%). ECE detected varices in 62 cases (44.9%), including 57 esophageal, 17 gastric, and 6 duodenal. Small (49), medium (18), and large (5) varices were found in the distal (55), mid (4), and proximal (3) esophagus. Post-Fontan cases had median ETT of 05m:02s (IQR 09m:42s) and 3 “downhill”, 4 small distal, and 0 large varices. ECE also detected portal gastropathy (25, 18.1%), esophagitis (20, 14.5%), ulcers (5, 3.6%), erythema (26, 18.8%), erosions (31, 22.5%), heterotopic tissue (13, 9.4%), blood flecks (23, 16.7%), and mucosal scars from prior ligation (17, 12.3%). There were 2 transient capsule retentions and no major adverse events.

ECE results led to follow-up EGD in 10 (6 variceal banding) and medication initiation in 11 (4 proton-pump inhibitor, 6 non-selective beta blocker, 2 other) cases. 4 patients had GIB within 12 months of ECE attempt (1 after aborted ECE).

Conclusion: ECE is a feasible alternative to conventional endoscopy for screening and surveillance of esophageal varices in children and young adults, offering a less invasive approach for patients considered higher risk for anesthesia.

8 NOVEL INTERACTIVE PEDIATRIC GASTROENTEROLOGY FELLOWSHIP CURRICULUM

IMPROVES TRAINEE ENGAGEMENT. Arvind Srinath^{1,2}, Sandra Kim^{1,2}, J.B. McGee^{3,2}. ¹Pediatrics, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA; ²University of Pittsburgh School of Medicine, Pittsburgh, PA; ³Gastroenterology, University of Pittsburgh Medical Center, Pittsburgh, PA

Background: The ACGME recommends didactic, self-directed learning modalities for trainees in knowledge acquisition. Like most fellowship programs, we have used weekly didactics on general GI topics using a standard textbook; topics are chosen based on need by fellow evaluations. However, fellows have raised concerns over passive learning and potential for outdated information, author judgement, and clinical relevance from textbooks. This risks poor long-term medical knowledge retention due to lack of interest and engagement. We thus successfully piloted an innovative learning module employing the flipped classroom format aligning the fellow curriculum with the American Board of Pediatrics (ABP) content while accounting for fellow time limitations and lack of reinforcement for fellow preparedness. In this study, we implemented a module series utilizing the pilot module principles. We hypothesized this interactive learning module series would improve curricular satisfaction and facilitate fellow engagement in self-directed learning.

Methods: We created a web-based module based on an ABP content topic (10 multiple-choice questions along with links to sentinel articles). The module focused on current literature in a structured format and could be tracked by the creator for fellow completion, competency, and navigation patterns. If fellows answered a question correctly, they could move on to the next question. All answer explanations were linked to specific article texts. In the subsequent didactic a week later, the module author reviewed the questions and obtained accuracy-related feedback. Fellows could access the module later for reference (e.g. training exams). Outcomes were utilized to implement a four-month curriculum covering ten ABP objectives. Quality surveys were administered pre- and post- module completion.

Results: All fellows (n=7) completed the pilot module and quality surveys. The pilot module demonstrated statistically significant improvements in quality, delivery, active learning promotion, curricular satisfaction, use of discussion time, and self-directed learning promotion.

Fellow accuracy was 60±21% correct. Navigation pattern review on questions demonstrated fellows were not randomly selecting answers. This notion was furthered through statistically significant differences between question stem versus average time to read answers choices. Pilot module re-implementation 6 months later demonstrated learning sustainment. The subsequent module curriculum adjusted the number of questions per module (5-10) to better utilize fellow preparation time; 72.8% completed the modules. In addition to the pilot module improvements, the module curriculum showed statistically significant improvements in material datedness and appropriate preparation time use (Table 1). Module accuracy ranged from

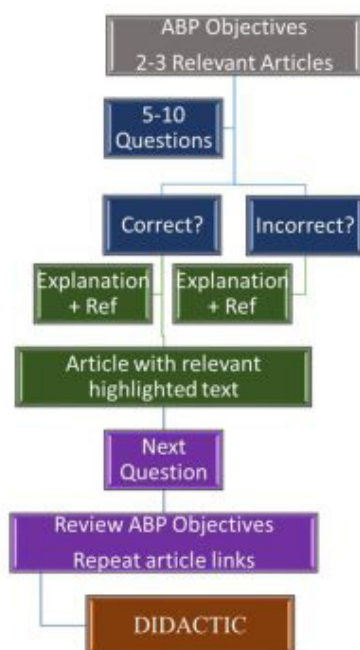
Question	Pilot	Series
I found the information valuable to my future profession		
I will use the knowledge acquired		
The material quality is excellent	•	
The material quality is up to date		•
The material is delivered effectively	•	•
The material promotes active learning	•	•
I am satisfied with this curriculum	•	•
The time I devote preparing is appropriate		•
Time is allowed for group discussion	•	•
This curriculum promotes self-directed learning	•	•

Areas where pilot module and module curriculum series showed significant (*p

30-80%. The navigation patterns mirrored that of the pilot module. Accuracy and navigation time trends did not wane over time.

Conclusion: Our unique web-based module format led to improved satisfaction and fellow engagement. The format was feasible, sustainable, innovative, and novel in pediatric GI trainee curricula. This format allows for fellow tracking and test-taking skill assessment, and could encompass trainee curricula across fields.
Evaluation of Module Pilot and Series

Fig 1. Curriculum Module Flowchart



- 13 **“WE AGREE, IT’S NOT IN YOUR HEAD!” THE SUCCESSES AND CHALLENGES OF INTEGRATING PSYCHOSOCIAL CARE: A REVIEW OF ONE YEAR WITH AN EMBEDDED PEDIATRIC PSYCHOLOGIST.** Bradley Jerson^{1,2,4}, Barbara Rzepski^{2,3}, Zev Davidovics^{1,4}, Karan Emerick^{1,4}, Melissa Fernandes^{1,4}, Franziska Mohr^{1,4}, Jasmeet Mokha^{1,4}, Kristin Philipp¹, Wael Sayej^{1,4}, Heidi Sweeney¹, Townsend Peter^{1,4}, Bella Zeisler^{1,4}, Jeffrey Hyams^{1,4}. ¹Digestive Diseases, Hepatology, & Nutrition, Connecticut Children’s Medical Center, Hartford, CT; ²Pediatric Psychology, Connecticut Children’s Medical Center, Hartford, CT; ³Psychiatry, Hartford Hospital Institute of Living, Hartford, CT; ⁴Pediatrics, University of Connecticut, Storrs, CT

Background: The pediatric GI community widely acknowledges the importance of utilizing a biopsychosocial lens for conceptualization and treatment planning (1). Thus, it is surprising that it is still rare for full integration of mental health providers into multidisciplinary GI teams (2). A nationwide survey of pediatric gastroenterologists indicated that psychological evaluation was included in “standard assessment” for only 5% of physicians. However, the importance of psychological treatment is well-recognized, as 65% of providers reported that they routinely referred patients to a mental health provider (3).

We conducted a retrospective chart review of one year of patient visits since our program fully embedded a pediatric psychologist into our multidisciplinary team. We evaluated trends in the referral process, diagnoses of patients being referred, and assessed changes in health care utilization. Preliminary results of this on-going study are presented.

Method: We utilized Abacus Analytics software to review all patient visits completed in the Division of Digestive Diseases, Hepatology, & Nutrition at Connecticut Children’s Medical Center between June 1, 2016 and May 31, 2017 (n = 12,177) and cross-referenced this with our electronic medical record to identify all referrals made by attending providers to the department psychologist (n = 331). We reviewed all completed visits during the above date range with the psychologist and analyzed by medical diagnosis, billing code, number of follow-up appointments for those families receiving ongoing psychological intervention.

Results: Our psychologist completed 231 new intake appointments during the date range, which indicates approximately 75% of referrals made by provider were completed by families. Of those who attended intakes, approximately 38% (n = 87) continued psychological treatment for at least 1 follow-up session. The psychologist completed a total of 484 patient visits (both new and follow-up) during the year, meeting with 252 unique patients (some of whom were established in ongoing psychological treatment from before the date range in this study. Medical diagnoses of the patients seen are summarized in Table 1. Most common reasons for referral were assessment of psychological factors associated with pain-predominant FGID (abdominal pain, IBS-D), coping with IBD (including adjustment to new diagnosis, depression and anxiety treatment, treatment adherence), vomiting (functional nausea, functional dyspepsia, or rumination), school avoidance secondary to medical symptoms or anxiety, weight loss or feeding difficulties, adherence to dietary treatments, and encopresis and fecal incontinence. Ongoing analysis is examining a more detailed breakdown of comorbid psychiatric diagnoses, treatment follow-up, insurance coverage and reimbursement for psychology services, and assessment of post-intervention changes in treatment utilization.

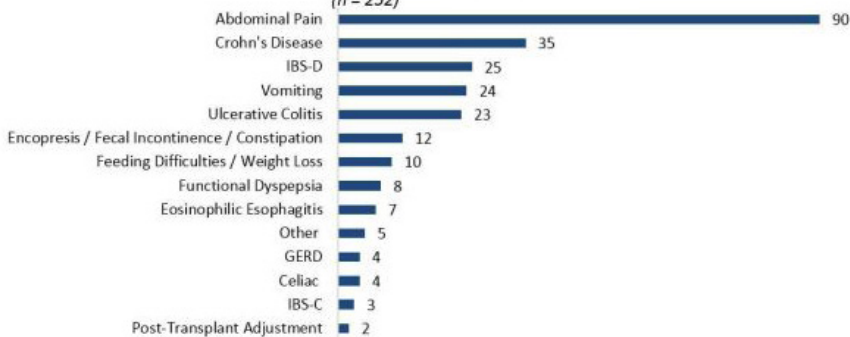
Discussion: Our results indicate that having an embedded psychologist within the medical team increases treatment availability and follow up on provider recommendations for psychological intervention compared to previously published experience. One possible explanation for greater completion of referrals from families is the opportunities for brief meetings with the psychologist when he was embedded in a clinic. The familiarity of space and environment and the uniformity of treatment planning indicate shared goals across team members, rather than following up with a referral to an outside mental health professional. This suggests that the integration of two hospital departments (GI and pediatric psychology), may encourage a systemic embrace of biopsychosocial conceptualization and treatment. Department-wide collaboration, including administrative support and the continuous opportunity for multidisciplinary treatment planning through “curbside consultation,” was essential. Additional challenges experienced during this implementation will also be reviewed.

(1) Mackner et al. Psychosocial Issues in Pediatric Inflammatory Bowel Disease: A Clinical Report of NASPGHAN. *JPGN*. 2013;56(4):449-458.

(2) Moser, et al. Integrating behavioral health services into pediatric gastroenterology: a model of an integrated health care program. *Clinical practice in pediatric psychology*, 2014, 2(1), 1.

(3) Schurman, et al. Conceptualization and treatment of chronic abdominal pain in pediatric gastroenterology practice. *JPGN*, (2010):50(1), 32-37.

Table 1:
Medical Diagnoses of Patients Seen by Psychologist
(n = 252)



14 THE ENDOSCOPIC AND HISTOLOGIC FINDINGS OF INFANTS WHO HAVE EXPERIENCED BRIEF RESOLVED UNEXPLAINED EVENTS.

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Introduction: A Brief Resolved Unexplained Event (BRUE) describes an event associated with a change in muscle tone, color, respiration and responsiveness that is unexplained after an appropriate examination. Some infants with higher risk BRUE may undergo endoscopy as part of their evaluation.

Objective: This retrospective study aimed to identify the endoscopic findings in infants who have experienced a BRUE. We also compared the characteristics, pre-natal, natal and post-natal risk factors between 23 endoscopic infants and 23 race/sex/term/preterm-matched non-endoscopic infants.

Results: Twenty-three infants (mean age 2.73 months) with higher risk BRUE underwent an esophagogastroduodenoscopy and flexible sigmoidoscopy from a total 119 infants with BRUE. Apnea (87%) was the most common presentation of BRUE. Most were female (57%) with a mean age at BRUE presentation of 2.73 months. We found 10 (43.5%) term infants and 13 (56.5%) preterm infants in our study. There were no significant differences in demographics, pre-natal, natal and post-natal risk factors between endoscopic and non-endoscopic group. Interestingly, we found only the electrocardiogram in non-endoscopic group was higher than endoscopic group significantly. The most common abnormal endoscopic finding

was lymphonodular hyperplasia (LNH) associated with eosinophilia in the rectosigmoid colon. Interestingly, we found the proportion of females in the LNH group was significantly higher than in non-LNH group.

Conclusion: Rectosigmoid LNH and eosinophilia, which are associated with milk soy protein intolerance (MSPI), were the most common findings attributed to endoscopic evaluation. Although there is no proof of causation between MSPI and BRUE, MSPI should be considered in the differential diagnosis for higher risk BRUE.

16 SAFETY AND EFFICACY OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY TUBE FEEDINGS IN MALNOURISHED PEDIATRIC CANCER PATIENTS. Claudia Phen¹, Devendra Amre³, Michael Wilsey². ¹Office of Medical Education, Johns Hopkins All Children's Hospital, St. Petersburg, FL; ²Pediatric Gastroenterology, Johns Hopkins All Children's Hospital, St. Petersburg, FL; ³Clinical and Translational Research Organization, Johns Hopkins All Children's Hospital, St. Petersburg, FL

Background: Malnutrition is a significant issue for pediatric cancer patients. Poor nutritional status adversely affects cancer patients resulting in impaired cell-mediated immunity, poor wound healing, increased risk of infection, chemotherapy intolerance, tumor relapse, and decreased survival. Most guidelines recommend that children with cancer be screened for malnutrition risk during therapy; however, guidelines for nutritional rehabilitation in this population are not well defined. Enteral nutrition using percutaneous endoscopic gastrostomy (PEG) feedings have long been used in the adult population in patients with head and neck cancer. The safety and efficacy of PEG tube feedings in pediatric cancer patients have not been widely investigated. PEG feedings may prevent or reverse malnutrition in this population. Our aim was to identify the efficacy of PEG feedings using Z-scores for weight. We hypothesized that PEG feedings would lead to an increase in Z-scores for weight in children with cancer.

Methods: After IRB approval, data was collected through retrospective chart review at Johns Hopkins All Children's Hospital from patients with cancer diagnoses between January 2000 and February 2016. Medical records of pediatric cancer patients with PEG were reviewed. All PEGs were placed at our institution. Variables analyzed included gender, age, diagnosis, length of procedure, G-tube device, duration of G-tube usage, and complications. Efficacy of enteral nutrition was evaluated by comparing pre- and post-PEG changes in weight z-scores. Changes were compared using paired t-tests. Statistical significance was set for P < 0.05.

Results: Six hundred and seventy-three patients with neoplasm and malnutrition were identified at our institution. Of the ninety-three that underwent PEG placement, sixty-three had complete pre- and post-PEG weight measures. Males (35, 55.6%) were more predominant as compared to females (28, 44.4%). The mean (± SD) age was 6.8 (± 6.2) years. Diagnoses included leukemia/lymphoma (n= 13/63, 20.6%), central nervous system tumor (n= 32/63, 50.8%), and solid tumor (n=18/63, 28.6%). Overall the average z-scores for weight in these patients were -1.38 (± 1.37) prior to PEG placement. Enteral nutrition showed improvement in weight z-scores in 59% (37/63) of patients, but the overall average change in z-score post-PEG was modest (-1.27 ± 1.37; p=0.07).

Table. Comparison of the differences in characteristics between lymphonodular hyperplasia and non-lymphonodular hyperplasia and between eosinophilia and non-eosinophilia.

Characteristics	Lymphonodular hyperplasia (13)	Non-lymphonodular hyperplasia (10)	P-value	Eosinophilia (20)	Non-eosinophilia (2)	P-value
Gender						
- Male	3 (23%)	7 (70%)		9 (45%)	0	
- Female	10 (77%)	3 (30%)	0.039	11 (55%)	2 (100%)	0.494
Age of study in months (mean ± SD)	1.90 ± 1.19	3.79 ± 3.85	0.257	2.34 ± 2.03	2.00 ± 1.41	1.000
Gestational age in weeks (mean ± SD)	35.33 ± 2.43	35.25 ± 3.77	1.0	35.49 ± 3.04	33.50 ± 0.71	0.337
Birth weight in kg (mean ± SD)	2.60 ± 0.87	2.11 ± 0.90	0.224	2.42 ± 0.95	2.08 ± 0	0.933
Weight at diagnosis in kg (mean ± SD)	4.10 ± 1.50	4.83 ± 2.59	0.733	4.282 ± 1.852	3.45 ± 0.92	0.776
Length at diagnosis in cm (mean ± SD)	50.43 ± 14.37	56.10 ± 12.47	0.901	53.67 ± 6.92	30.55 ± 35.99	0.607
Hospitalized duration in days (mean ± SD)	4.84 ± 3.65	3.80 ± 2.39	0.683	4.35 ± 3.15	5.50 ± 4.95	0.862
Number of preterm at birth	9 (70%)	4 (40%)		11 (55%)	2 (100%)	
Number of term at birth	4 (30%)	6 (60%)	0.222	9 (45%)	0	0.494
Formula						
-Hypoallergic formula	7 (53.8%)	4 (40%)		10 (50%)	1 (50%)	
- Non-hypoallergic formula	6 (46.2%)	6 (60%)	0.680	10 (50%)	1 (50%)	1

SD, standard deviation

Conclusions: A proportion of children showed improvement in their weight after institution of gastrostomy feeding. Gastrostomy tube feedings are a viable option to help treat chronic malnutrition in pediatric patients with cancer. Further analyses are needed to determine which factors contribute to continued malnutrition in children with cancer following PEG placement.

19 IMPROVING CELIAC SCREENING FOR CHILDREN WITH TYPE 1 DIABETES AND LESSONS FROM FALSE POSITIVE SEROLOGY. Daniel Mallon¹, Nancy Crimmins², Chijioke Ikomi², Farida Mostajabi³, Sarah Corathers², Dana Dykes¹, Jessica Gahl², Mary Jolly². ¹Pediatric Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ²Endocrinology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ³James M Anderson Center for Health Systems Excellence, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

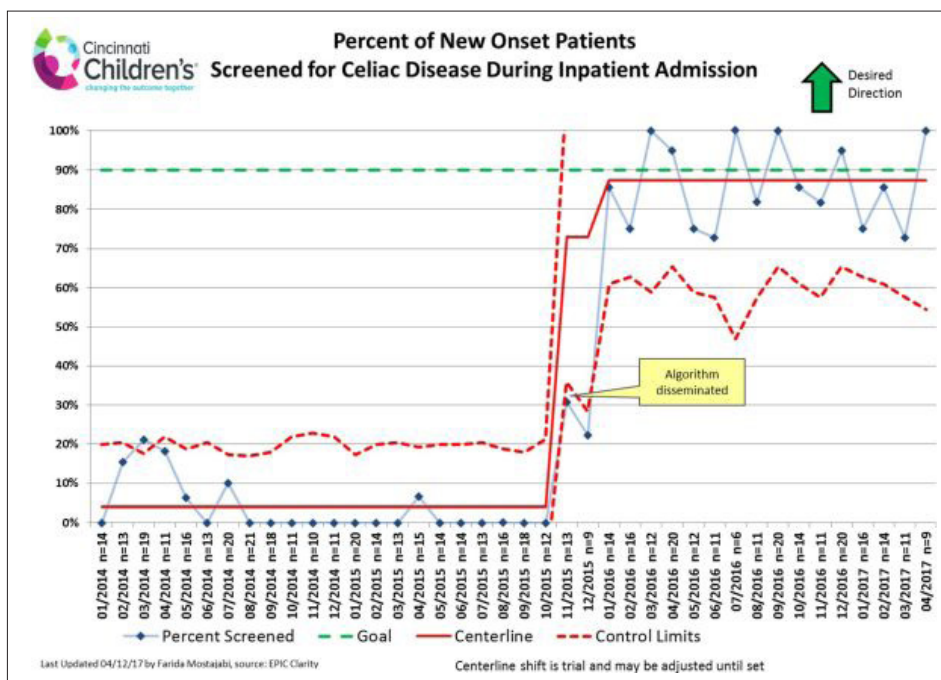
Background: Children with type 1 diabetes mellitus (T1D) have a 5-7 times higher risk of developing celiac disease (CD), and screening for CD is recommended. However, screening guidelines lack specificity regarding timing and the possibility of spontaneous normalization of elevations in celiac autoantibodies at the time of T1D diagnosis. There has been great variability in when and whether T1D patients were screened at our institution.

Methods: A quality improvement (QI) program was established to standardize screening of T1D patients for CD. Representatives from Endocrinology and Gastroenterology (GI) developed and implemented a screening algorithm based on published guidelines and completed iterative Plan-Do-Study-Act cycles to improve the following process measures: (1) increase proportion of patients with IgA anti-tissue transglutaminase (TTG) measured at T1D diagnosis; (2) increase proportion of established T1D patients who had TTG measured in the last 24 months; (3) increase proportion of T1D+CD patients who have seen a dietitian in the last 13 months. Electronic medical records were queried to provide dates and values of labs, dates of diagnosis of T1D, and frequency of dietitian visits. Process control run-charts were generated to track process measures. The algorithm guided referral to GI for TTG elevation that a) persisted > 12 months, b) was associated with symptoms, or c) was >10 times the upper limit of normal (ULN). Outcome measures included comparisons of tissue transglutaminase (TTG) levels, biannual standardized health related quality of life assessments, and hemoglobin A1c (HbA1c) in patients with T1D+CD and T1D alone. Control measures included false positive TTG tests, assessed as elevated TTG and a duodenal biopsy inconsistent with celiac disease.

In November 2015, the algorithm was approved by consensus by both divisions' faculty, presented at faculty meetings and disseminated to all clinicians via email. Screening tests were added to diabetes inpatient and outpatient order sets in the electronic medical record, and inpatient Endocrine unit charge nurses were engaged to remind clinicians to send screening labs prior to discharge. Subsequent actions included adding celiac screening to pre-visit planning forms for outpatients (May 2016), and presenting run-charts at Endocrine faculty meeting (January 2017).

Results: Screening rates for patients newly diagnosed with T1D surpassed the goal (90%) within 4 months have been maintained at 87% over 14 months. Screening rates for patients with established diagnosis of T1D improved from baseline of 38% to 68% as of April 2017. No statistically significant difference in mean HbA1c between the patients with T1D+CD and patients with T1D (8.89 vs. 8.8, p=0.97).

Twelve of 833 (14.4%) patients with new onset T1D had elevated TTG at time of diagnosis since Nov 2015. Eight patients with very elevated TTG and/or abdominal pain underwent duodenal biopsy.



Four of the 8 were confirmed to have CD, and 4 had biopsies inconsistent with celiac disease, including 3 with TTG levels >10 times the ULN, and 2 with positive IgA anti-endomysial antibody. Four patients have not been biopsied: one had TTG <2 times the ULN and no symptoms and normal TTG 6 months later, one had TTG >60X the ULN and is awaiting biopsy, and two had TTG <10 times the ULN, and have yet to have TTG rechecked.

Conclusions: Clinical algorithm and QI methodology resulted in increased fidelity to screening guidelines for CD amongst patients with new onset and established diagnosis of T1D. Screening is important to identify dual T1D+ CD, however, false positive TTG tests warrant investigation of more stringent criteria to prompt biopsy.

20 FOREIGN BODY INGESTIONS AMONG CHILDREN LESS THAN 6 YEARS OF AGE TREATED IN U.S. EMERGENCY DEPARTMENTS, 1995-2015. Danielle Orsagh-Yentis¹, Roxanne Clark², Kristi Roberts², Rebecca McAdams², Lara McKenzie². ¹Gastroenterology, Hepatology and Nutrition, Nationwide Children's Hospital, Columbus, OH; ²Center for Injury Research and Policy, The Research Institute at Nationwide Children's Hospital, Columbus, OH

Background: Whether due to curiosity, playfulness, or goading, children frequently pick objects up and place them in their mouths. While some of these ingested items are relatively innocuous and likely to pass through the gastrointestinal tract on their own, some can cause grievous harm. To our knowledge, this is the first study to describe foreign body ingestions treated in U.S. hospital emergency departments (EDs) over a two-decade period.

Objectives: To describe the epidemiology of foreign body ingestions of U.S. children < 6 years of age who were treated in hospital EDs from 1995 through 2015.

Methods: We performed a retrospective analysis by using data from the National Electronic Injury Surveillance System (NEISS) for children < 6 years of age who were treated due to concern of foreign body ingestion from 1995 through 2015. A total of 30,097 actual cases were reviewed. Cases were excluded (n=97) when the foreign body was not localized to the gastrointestinal tract. The included cases and weighting factors assigned by the U.S. Consumer Product Safety Commission were used to calculate national estimates of foreign body ingestions.

Results: An estimated 761,945 children < 6 years of age were treated for foreign body ingestions over the 21-year study period. Boys more frequently ingested foreign bodies (53.0%), as did children 1 year of age (21.3%). Most children were able to be discharged following their ingestion (89.7%). Among the types of objects ingested, coins were the most frequent (61.9%). Toys (10.6%); jewelry (7%); nails, screws, tacks and bolts (6.4%); and batteries (6.2%) followed thereafter. Across all age groups, the most frequently ingested coin was a penny (66.3%). Children 1 year of age were most frequently hospitalized following their ingestion (21.7%), followed by 2-year-olds (19.9%), and 3-year-olds (19.6%). Pennies remained the coin type most frequently ingested among those who had to be hospitalized (53.5%), followed by quarters (32.7%), and nickels (9.7%). Children who ingested a quarter were 2.5 times (95% CI: 2.18-2.97) as likely to be hospitalized when compared to children who ingested another type of coin.

Conclusion: Foreign body ingestions remain quite common in children < 6 years of age. Coins were the objects most frequently ingested by children in this age group. Most children were able to be discharged following their ingestions, but those who ingested quarters were more likely to be hospitalized than those who had ingested other coins. The high frequency of foreign body ingestions noted in this study highlights the need for more research to determine how best to prevent these injuries.

22 POST-ERCP PANCREATITIS IN CHILDREN - A REPORT FROM AN INTERNATIONAL MULTICENTER STUDY GROUP (PEDI DATABASE). David Troendle^{1,2}, Bradley Barth^{1,2}, Douglas Fishman^{3,4}, Quin Liu⁵, Yuhua Zheng^{6,8}, Matthew Gieffer^{7,9}, Kyung Mo Kim^{10,11}, Luigi Dall'Oglio¹², Giulia Angelino¹², Paola DeAngelis¹², Simona Faraci¹², Mercedes Martinez^{13,14}, Roberto Gugig¹⁵, Petar Mamula¹⁶, Samuel Bitton^{17,18}, Michael Wilsey¹⁹, Khalaf Racha¹⁹, Steven Werlin^{20,21}, Kulwinder Dua^{20,21}, J. Antonio Quiros²⁴, Amit Grover^{22,23}, Victor Fox^{22,23}. ¹Pediatrics, UT Southwestern, Dallas, TX; ²Children's Health Children's Medical Center, Dallas, TX; ³Baylor College of Medicine, Houston, TX; ⁴Texas Children's Hospital, Houston, TX; ⁵Cedars-Sinai Medical Center, Los Angeles, CA; ⁶Children's Hospital of Los Angeles, Los Angeles, CA; ⁷University of Washington, Seattle, WA; ⁸University of Southern California, Los Angeles, CA; ⁹Seattle Children's Hospital, Seattle, WA; ¹⁰University of Ulsan College of Medicine, Seoul, Korea (the Republic of); ¹¹Asan Medical Center Children's Hospital, Seoul, Korea (the Republic of); ¹²Bambino Gesù Children's Hospital, Rome, Italy; ¹³Columbia University, New York, NY; ¹⁴New York Presbyterian Morgan Stanley Children's Hospital of New York, New York, NY; ¹⁵Children's Hospital of Central California, Madera, CA; ¹⁶Children's Hospital of Philadelphia, Philadelphia, PA; ¹⁷Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY; ¹⁸Steven and Alexandra Cohen Children's Medical Center, New Hyde Park, NY; ¹⁹Johns Hopkins All Children's Hospital,

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Introduction: Risk factors for development of post-ERCP pancreatitis (PEP) remain poorly defined in the pediatric patients. It remains unclear what constitutes appropriate prophylaxis (PPx) in this patient population.

Aim: To identify factors associated with PEP in the pediatric population, and evaluate utility PEP PPx utilizing a prospective multicenter approach.

Methods: Consecutive ERCPs on children < 19 years from 13 IRB approved centers were entered into a REDCap database. Inclusion criteria for analysis included: ERCPs entered between 5/1/2014 to 11/29/2016 and pre-procedural form completed prospectively (before ERCP performed). Fischer's exact test was utilized to evaluate association of pre-procedural and procedural factors with development of PEP as well as effectiveness of PEP PPx. High risk patients were defined as those with PD injection. PEP and its severity was defined according to the ASGE lexicon.

Results: 707 ERCPs in 549 (78%) unique patients met inclusion criteria and were analyzed. Mean age was 12.1 years (IQR 9.2-15.7). 666 (94%) were performed for a therapeutic indication, 533 (75%) for a biliary indication, 200 (28%) for a pancreatic indication. PEP occurred in 33 (4.7%, 23 mild, 8 moderate, 2 severe). There were no deaths. Table 1 demonstrates factors associated with developing PEP and effectiveness of PEP PPx in all patients as well as those defined as "high risk" for PEP development.

Conclusion: Rates of PEP in the pediatric population mirror those reported in adult series. PD injection, PD cannulation, a history of recurrent acute pancreatitis, and ASGE procedural difficulty grade>2 were found to be associated with increased rates of PEP. Pancreatitis within the preceding week was associated with lower rates of PEP. Commonly implemented forms of PEP PPx in adult patients such as rectal indomethacin and PD stenting were not associated with lower rates of PEP in the pediatric population. In fact, strong trends towards increased rates of PEP were seen in high risk patients who received any form of PEP PPx. Clearly further study is needed to clarify what constitutes appropriate PEP PPx in the pediatric population.

EoE/GERD/AERODIGESTIVE

27 **THERAPY ASSOCIATED BACTERIAL AND FUNGAL DYBIOSIS IN EOSINOPHILIC**

ESOPHAGITIS. *Alain Benitez, Kyle Bittinger, Ceylon Tanes, Casey Hofstaedter, Dorothy Kim, Jonathan Gross, Jonathan Spergel, Amanda Muir. Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA*

Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease characterized by infiltration of inflammatory cells into the esophagus. Therapies associated with EoE include antacids, dietary interventions, and the use of swallowed steroids. Bacterial dysbiosis has been previously reported in active-EoE as well as bacterial disturbances during food trials using highly allergenic foods. Characterization of the fungi in the esophagus is limited in the field of esophageal inflammation, as are the effects of therapy on fungal communities. We characterized the bacterial and fungal communities in the esophageal mucosa of children with EoE in the presence and absence of esophageal inflammation during dietary or swallowed steroids therapy and compared these samples to non-EoE controls.

Methods: Esophageal biopsies were obtained from 70 patients with active or inactive EoE who were either on or off swallowed steroids, as well as ten non-EoE controls. Bacterial and fungal communities were profiled using 16S rRNA gene and ITS tag sequencing, respectively. Nine patients with active EoE were sampled at a later time point, following initiation of therapy with swallowed steroids and resolution of esophageal inflammation.

Results: The abundance of *Haemophilus* increased in a stepwise manner from inactive to active EoE subjects, relative to non-EoE controls, in the absence of swallowed steroid therapy (P=0.003). The increased abundance of *Haemophilus* was not observed for subjects on swallowed steroids. The abundance of *Actinobacillus* was lower in the presence of swallowed steroids, relative to active and inactive EoE subjects not on swallowed steroid therapy. In the fungal community, *Candida* was present in a greater proportion of control samples and EoE patients on swallowed steroids, relative to EoE patients not on swallowed steroids (P=0.006 and 0.0008, respectively). *Cladosporiaceae*, an environmental fungus, had higher abundance in patients on swallowed steroids than in patients without (P=0.004). For subjects sampled again after reduction in inflammation, the bacterial community composition was altered consistently, as evaluated by unweighted UniFrac distance between samples (P=0.004, PERMANOVA test). Following initiation of swallowed steroids, the abundance of *Actinobacillus* was decreased at the second time point, consistent with our results from the cross-sectional comparison.

Conclusions: Therapies commonly used in EoE are associated with disturbances in the bacterial and fungal communities of the esophagus. Candida species were found more often in the presence of swallowed steroid therapy, consistent with clinical reports.

ALL PATIENTS (N=707)	No PEP (n=674)	PEP (n=33)	P value
Pre-procedural factors			
Female	406 (60%)	19 (58%)	0.86
Recurrent acute pancreatitis	106 (16%)	11 (33%)	<0.05*
Chronic pancreatitis	99 (15%)	6 (18%)	0.61
Acute pancreatitis in prior week	124 (18%)	1 (3%)	<0.05**
Suspected SOD	11 (2%)	2 (6%)	0.12
Previous episode of PEP	24 (4%)	2 (6%)	0.34
Previous failed cannulation	21 (3%)	3 (9%)	0.10
ASGE difficulty grade>2	271 (40%)	20 (61%)	<0.05*
Therapeutic Indication	635 (94%)	31 (94%)	1.00
Pancreatic indication	187 (28%)	13 (39%)	0.17
Procedural factors			
Biliary sphincterotomy performed	358 (53%)	15 (45%)	0.48
Pancreatic sphinterotomy performed	54 (8%)	3 (9%)	0.74
Minor papillotomy performed	13 (2%)	1 (3%)	0.49
Attempt at PD cannulation via major papilla	260 (39%)	21 (64%)	<0.01*
Successful PD cannulation via major papilla	243 (36%)	19 (58%)	<0.05*
Attempt at PD cannulation via minor papilla	46 (7%)	2 (6%)	1.00
Successful PD cannulation via minor papilla	32 (5%)	1 (3%)	1.00
Pancreatic injection	225 (33%)	25 (76%)	<0.0001*
Trainee involved	253 (38%)	16 (48%)	0.27
PPx given (any form)	306 (45%)	24 (73%)	<0.005*
PPx indomethacin given only	167 (25%)	11 (33%)	0.30
PPx pancreatic stent only	25 (4%)	3 (9%)	0.14
Other PPX given alone	60 (9%)	6 (18%)	<0.05*
HIGH RISK PATIENTS (n=250)			
PPx given (any form)	129 (57%)	19 (76%)	0.06
PPx indomethacin only	69 (31%)	7 (28%)	1.00
PPx pancreatic stent only	21 (9%)	3 (12%)	0.72
Other PPx only	17 (8%)	5 (20%)	0.05

*statistically significant association with increased rates of PEP.

**statistically significant association with reduced rates of PEP.

28 **IGG4 STAINING IS AN UNRELIABLE DIAGNOSTIC MARKER IN EOSINOPHILIC**

ESOPHAGITIS. Amanda Pope¹, Bita Naini⁵, Maria Garcia-Lloret², Kevin Ghassemi³, Elizabeth Marcus^{1,4}, Martin Martin¹, Laura Wozniak¹ ¹Pediatric Gastroenterology, UCLA, Los Angeles, CA; ²Allergy and Immunology, UCLA, Los Angeles, CA; ³Gastroenterology, UCLA, Los Angeles, CA; ⁴VA GLAHS, Los Angeles, CA; ⁵Pathology and Laboratory Medicine, UCLA, Los Angeles, CA

Background: While known to be allergen-driven, the pathogenesis of eosinophilic esophagitis (EoE) remains poorly understood. Recent studies show increased serum and esophageal IgG4 in adult EoE patients compared to controls, suggesting a possible IgG4-mediated process. However, the role of IgG4 in EoE has not been extensively investigated. Our aim was to analyze IgG4 in esophageal tissue in children and adults with EoE compared to controls. Our hypothesis was that IgG4 staining would be prominent in the majority of children and adults with EoE.

Methods: In a retrospective IRB-approved study, we performed immunofluorescence analysis of IgG4 in esophageal mucosal biopsy specimens from 39 subjects: children with EoE (n=16), adults with EoE (n=15), children with reflux esophagitis (n=4), normal pediatric controls (n=4). Inclusion criteria included patients who underwent EGD for suspicion of EoE and EGDs in which biopsies were obtained from multiple levels of the esophagus. Exclusion criteria included pre-existing diagnosis of EoE or EoE treatment prior to EGD with dietary elimination or corticosteroid therapy. Diagnosis of EoE was based upon presence of ≥ 15 eosinophils per high powered field (hpf) and a lack of clinical or histologic response to proton pump inhibitor therapy. Diagnosis of reflux esophagitis was based upon presence of 1-14 eosinophils per hpf in the distal esophagus. Normal control patients had esophageal biopsy specimens that lacked eosinophils. Immunohistochemical staining for IgG4 was retrospectively performed and assessed by a blinded pathologist.

Results: Median (range) age of pediatric and adult EoE patients was 11.9 (6-17) and 38.2 (20-76) years, respectively. Pediatric EoE patients most often presented with weight loss/poor weight gain and emesis. Adult EoE patients typically presented with food impaction. Dysphagia was common in both pediatric and adult EoE patients. Fifty eight percent of pediatric EoE patients and 43% of adult EoE patients had peripheral eosinophilia. Patients with EoE were significantly more likely to stain positive for IgG4 compared to patients without EoE (p=0.012, chi-square test). Eight of 16 (50%) pediatric EoE cases and seven of 15 (47%) adult EoE cases stained positively for IgG4. Some cases had staining in both epithelium and submucosa, while some had staining only in submucosa. Most cases stained in the distal and mid esophageal levels, but 3 adult cases stained only at the mid or distal esophageal level. No identifiable clinical, gross, or histologic differences between the positive cases and the rest of the cohort were present. None of the reflux esophagitis or control cases stained positively for IgG4. Overall, IgG4 staining was found to have 48% sensitivity and 100% specificity.

Discussion: Our study suggests IgG4 is not a reliable marker of EoE at disease diagnosis. Although positive IgG4 staining was specific for EoE, it had a poor sensitivity with positive staining in only 48% of EoE patients. In addition, even when positive, IgG4 staining was not seen at all levels biopsied. Further studies are warranted to fully elucidate the role of IgG4 in EoE.

30 **THE IL-10/IL-5 RATIO AS A POTENTIAL TOOL FOR MONITORING THE INFLAMMATORY PROCESS IN EOSINOPHILIC ESOPHAGITIS.**

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Background: Eosinophilic esophagitis (EoE) is an allergic, antigen driven immunologic response that causes esophageal dysfunction. Studies have shown that the pathogenesis of EoE and asthma to be similar. IL-5 and IL-10 are prominent cytokines in the regulation of eosinophils in asthma and EoE. IL-10 is an anti-inflammatory cytokine that suppresses Th2 response to allergens. IL-5 contributes to the differentiation, activation and recruitment of eosinophils. The IL-10/IL-5 ratio has shown to be a possible tool in monitoring disease progression in asthma. A serum biomarker has yet to be found for diagnosis and monitoring of the disease activity in EoE.

Objectives: Evaluate the IL-10/IL-5 ratio in serum, plasma and tissue culture supernatant in patients with EoE vs. Controls. Determine whether the IL-10/IL-5 ratio can be used as a marker for monitoring disease activity in EoE. Demonstrate whether serum or plasma are superior in detecting cytokine levels.

Methods: Children between the ages of 4 and 17 years undergoing endoscopy were prospectively enrolled from December 2011 to August 2014. Patients were classified into 4 groups: EoE-Active (>15 eos hpf on treatment), EoE-New (>15 eos hpf), EoE-Remission (< 5 eos hpf), Controls (0 eos hpf). Serum and Plasma samples were collected at the time of endoscopy. The samples were spun and the serum and plasma were stored at -80C until analyzed. A single biopsy was placed in culture medium and incubated at 37C for 72 hours. The supernatant was collected and stored at -80C until analysis. We performed

ELISA using R&D Duoset kits for IL-10 and IL-5 on 68 serum and plasma samples. We also selected a cohort of 39 patients including EoE-New (n=9), EoE-Active (n=10), EoE-Remission (n=10) and Controls (n=10). They were analyzed via Millipore Milliplex 11-plex Human Cytokine Magnetic kit which included IL-10 and IL-5. ANOVA followed by the Bonferroni analysis was used for multiple comparison tests.

Results: By performing ELISA, IL-10 was detectable in 30/68 (44%) serum samples and 47/68 (69%) plasma samples. IL-5 was detectable in 27/68 (39.7%) serum samples and 60/68 (88%) plasma samples. The ELISA IL-10/IL-5 ratio was measurable in 17/68 (25%) paired serum samples and 43/68 (63%) paired plasma samples. Multiplex assays detected 21/39 (53.8%) IL-10 serum samples and 17/39 (43.5%) IL-10 plasma samples. IL-5 was detectable in 16/39 (41%) serum samples and 16/39 (41%) plasma samples. The Multiplex IL-10/IL-5 ratio was measurable in 12/39 (30.7%) of the serum samples and 11/39 (28%) of the plasma samples. While there were trends showing elevated IL-5 levels in EoE active and EoE- New groups, statistical significance was only achieved in the ELISA serum analysis. Serum IL-5 levels were significantly higher in EoE-Active vs. Controls (P = 0.0240). The IL-10 levels were higher in Controls and EoE-Remission compared to EoE-New and EoE-Active, however it was not statistically significant. The IL-10/IL-5 ratio was inconsistently higher in the Control patients and EoE-Remission patients compared to EoE-New and EoE-Active. Furthermore, IL-5 levels were only detectable in 1/39 (3%) tissue culture supernatant sample whereas IL-10 levels were detectable in 34/39 (87%) samples.

Conclusions: The overall analysis of both ELISA and Milliplex concluded that plasma better than serum in analyzing cytokine levels. The study also demonstrates IL-5 levels higher in EoE-New and EoE-Active patients compared to controls. IL-10 levels in EoE-Remission show a close association with the controls suggesting IL-10 levels increase or normalize with decreased inflammation. There was inconsistent IL-10/IL-5 ratio association secondary to elevated IL-5 levels in the remission group. It is unclear why the EoE-Remission group had high IL-5 levels compared to controls, which may be attributable to the majority of the IL-5 remission population having asthma. IL-5 was almost completely undetectable in the tissue culture supernatant which may suggest that IL-5 is not produced locally. Furthermore, with a larger sample size, analyzing IL-10 and IL-5 levels may be useful in the future to show a predictive value for diagnosis and monitoring of EoE.

31 **LOEYS-DIETZ SYNDROME: A MONOGENIC PRESENTATION OF EOSINOPHILIC**

ESOPHAGITIS. Anthony Guerrero¹, Karen Laky², Jessica Kinar², Harry Dietz^{3,4}, Pamela Frischmeyer-Guerrero². ¹Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD; ²National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD; ³Institute of Genetic Medicine, Johns Hopkins School of Medicine, Baltimore, MD; ⁴Howard Hughes Medical Institute, Baltimore, MD

Loeys-Dietz Syndrome (LDS) is a genetic disorder caused by mutations in genes essential to TGF β signaling including TGFBR1, which encodes a TGF β receptor subunit. LDS patients exhibit a high prevalence of allergic disease. A mouse model of LDS Type I (TGFBR1M318R^{+/-}) has been developed to further study this disease and its associated allergic conditions including eosinophilic esophagitis (EoE). EoE is characterized by the abnormal influx of eosinophils into esophageal tissue, basal cell hyperplasia, and smooth muscle dysfunction. Current dogma posits that EoE occurs when Th2 cells are stimulated by inhaled or ingested antigens to secrete cytokines that then recruit and stimulate eosinophils and mast cells. Thus we were surprised to find that RAG2^{-/-}R1 mice developed disease, illustrating that EoE associated with the TGFBR1M318R mutation was not lymphocyte-dependent. Bone marrow (BM) chimeras were made to confirm that altered TGF β signaling in radio-resistant cells was sufficient to cause EoE. Lethally irradiated R1 mice reconstituted with WT BM developed EoE. In contrast, eosinophils and IgE were not elevated in WT mice reconstituted with R1 BM. Further investigation has revealed increased numbers of type two innate lymphoid cells (ILC2s) in the esophagus of TGFBR1M318R^{+/-} mice compared to wild type (WT) littermates. These cells are lineage negative, ST2⁺, GATA3⁺, and produce large amounts of IL-5 and IL-13, and to a lesser extent IL-4, following in vitro stimulation.

32 **TH2 VS. TH1 IMMUNE POLARIZATION DISTINGUISHES EOSINOPHILIC ESOPHAGITIS FROM GASTROESOPHAGEAL REFLUX DISEASE.**

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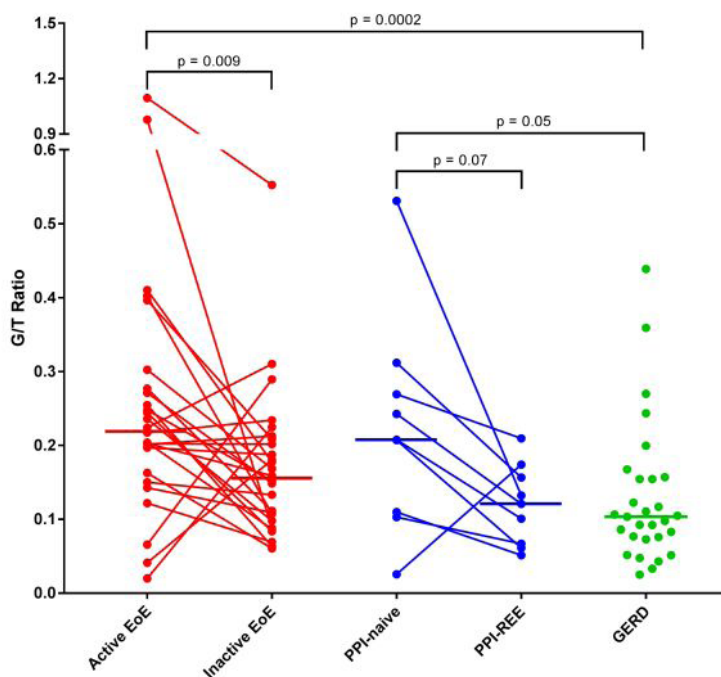
Background: The current diagnostic metric for eosinophilic esophagitis (EoE) of ≥ 15 eosinophils per high powered field (eos/hpf) distinguishes most subjects with EoE, however, some patients with severe gastroesophageal reflux disease (GERD) may have distal esophageal eosinophilia exceeding this histologic threshold. Recent evidence suggests that EoE and proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE) are phenotypically and genotypically indistinguishable. The local inflammatory responses in EoE have been classified as T_H2-predominant due to overexpression of T_H2-associated genes and increased mRNA expression of T_H2 cytokines (i.e. IL-5 and IL-13). In contrast, esophageal biopsies from patients

with GERD are more commonly associated with a Th1 phenotype. T-bet and GATA-3 are transcriptional regulators that drive differentiation of T_H0 $CD4^+$ lymphocytes to T_H1 and T_H2 lineages respectively. Given its role in Th2 inflammation, we hypothesized that GATA-3 expression would be increased in the esophageal epithelium of subjects with EoE and that the ratio of GATA-3/T-bet expression would differentiate these individuals from subjects with GERD.

Methods: We performed a retrospective case control study of pediatric subjects with EoE (defined by consensus guidelines), PPI-REE (≥ 15 eos/HPF prior to PPI) and GERD (symptoms of GERD defined by a gastroenterologist) using paraffin embedded esophageal tissue sections from the Children's Hospital of Colorado. All subjects with esophageal eosinophilia demonstrated histologic resolution (< 15 eos/hpf) after at least 6-8 weeks of dietary elimination, swallowed topical steroids or PPI therapy. Serial tissue sections from biopsies obtained at baseline and following treatment were assessed with nuclear stains for T-bet and GATA-3. Slides were digitized using an Aperio slide scanner and lymphocyte T-bet and GATA-3 expression profiles were quantified using ImageScope software. The number of pixels staining positive were divided by the total pixels comprising the area of esophageal epithelium for each slide to calculate the %T-bet+ and %GATA-3+ areas. The polarization of the immune microenvironment was assessed by the G/T ratio (%GATA-3+ area / %T-bet+ area).

Results: A total of 26 active EoE cases, 9 PPI-REE cases, and 29 GERD controls were analyzed. Paired samples from post-treatment biopsies were available for all EoE and PPI-REE subjects in addition to 5 cases of inactive EoE. The median G/T ratio was < 1 in all groups, however, G/T ratios were significantly elevated in both EoE and PPI-REE subjects when compared to GERD (median 0.22 vs. 0.1, $p = 0.0002$, 0.21 vs. 0.1, $p = 0.045$, respectively). Post-treatment biopsies showed significant decreases in the G/T ratio for EoE subjects ($p = 0.009$) with a similar trend for PPI-REE subjects.

Conclusion: The G/T ratio is elevated in subjects with EoE compared to GERD and declines in response to therapy. Our findings support the prevailing notion that EoE is a T_H2 -driven process. Assessment of immune polarization by the G/T ratio in conjunction with evaluation of tissue eosinophil activity may aid in discriminating subjects with EoE/PPI-REE and GERD.



The G/T ratio is significantly elevated in EoE/PPI-REE compared to GERD. In EoE subjects, the G/T ratio declines in response to therapy.

33 EVALUATION OF SECOND OPINION PATIENTS WITH ESOPHAGEAL EOSINOPHILIA:

A 5-YEAR REVIEW. Bridget Godwin¹, Chris Liacouras¹, Vijay Mehta², Josh Eisenberg³, Amanda Muir¹.

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Background and Aims: Eosinophilic Esophagitis (EoE) is a chronic, antigen and immune-mediated esophageal disease characterized by symptoms of esophageal dysfunction and > 15 eosinophils/high-powered field (eos/hpf) isolated to the esophagus. Proton pump inhibitor responsive esophageal eosinophilia (PPI-REE) is an entity of esophageal eosinophilia that responds to PPI therapy and is thought to be clinically and chemically similar to EoE. Current guidelines suggest therapy with PPI prior to endoscopy and use of PPI as first line for esophageal eosinophilia. In this study, we sought to evaluate the clinical presentations, treatment and final diagnoses for patients presenting to our institution for second opinions of esophageal eosinophilia over the past 5 years. We also aimed to identify similarities and differences between patients with EoE and PPI-REE.

Methods: An IRB-approved search of our electronic medical record yielded a list of patients presenting for a second opinion of esophageal eosinophilia. Included charts were reviewed for clinical information, including symptom history, therapies, endoscopic findings, treatments and diagnoses.

Results: A total of 193 charts were included for analysis. Patients ranged from 1-19 years old with 76% being male and 74% being Caucasian. Presenting clinical symptoms included: vomiting/regurgitation in 135, dysphagia in 47 (16 with stricture or food impaction), and FTT or other symptoms in 11. Data analysis revealed that of 175 patients who had documentation of medications at time of initial endoscopy, 122 (69.7%) were not on any PPI prior to their initial endoscopy, and 163 (93%) were on < 2mg/kg/day. Patients that had their initial endoscopy after publication of 2011 guidelines were significantly more likely to have been on PPI at time of initial endoscopy (34% vs. 17.6%, p=0.013). Of 163 patients given inadequate PPI prior to initial endoscopy, 112 (68.7%) were treated with diet, steroids, or both without first being trialed on PPI alone after diagnosis of esophageal eosinophilia – of these 22 (20%) had undiagnosed PPI-REE. After PPI trial, 122 (63%) kept their diagnosis of EoE; 22 (11%) were diagnosed with PPI-REE; 13 (7%) with another disorder (EoG, IBD, etc.) and 36 (19%) did not have final diagnoses at time of analysis. Patients with final diagnosis of EoE had significantly higher eos/hpf found on initial endoscopy compared to those with final diagnosis of PPI-REE vs. GERD (52.5±30.2 v. 28.8±19.7, p<0.001), as well as higher likelihood of having IgE-mediated food allergy (78% v. 59%) and reports of food impaction or stricture (9% v. 4.5%).

Conclusions: Diagnostic and therapeutic algorithms are needed for esophageal eosinophilia to prevent misdiagnosis and unnecessary therapies. Twenty percent of patients subjected to burdensome diet eliminations and steroid therapy had their diagnoses changed from EoE to PPI-REE after adequate PPI trial, a finding that illuminates the importance of practicing per the guidelines. Our data also highlights differences in populations that respond to PPIs compared to those who do not, suggesting that while the two groups may overlap in some characteristics, they may represent distinct disease entities.

34 UPPER GASTROINTESTINAL CONTRAST SERIES: THE BEST WAY TO DIAGNOSE MALROTATION? A RETROSPECTIVE REVIEW OF SYMPTOMS AND ABDOMINAL ULTRASOUND FOR SUSPICION OF OBSTRUCTION/MALROTATION. *Brigitte Moreau¹, Amelie Carbonneau-Cera². ¹Pediatric Gastroenterology, Sherbrooke University Health Center, Sherbrooke, QC, Canada; ²Sherbrooke University Health Center, Sherbrooke, QC, Canada*

Background: Intestinal malrotation arises as a result of an interruption of normal rotation and fixation of the embryonic gut. This anomaly can lead to clinical symptoms through volvulus, when the mesentery twists, or through acute intestinal obstruction, when the Ladd bands constrict the duodenum. Urgent Ladd procedure is need when patient are symptomatic. In the typical cases of malrotation, bilious emesis and other features of bowel obstruction manifest. With age, the symptoms and signs are variable, insidious and more chronic by nature. Upper gastrointestinal(GI) contrast series is the imaging of choice when malrotation is suspected; it remains the gold standard. Ultrasonography is being increasingly used, as an inversion of the mesenteric vessels frequently coexists with malrotation. However, literature tends to suggest its sensitivity is inadequate, since a normal ultrasound(US) does not exclude malrotation. The purposes of this study was to first review the symptoms of children who underwent an upper GI series for a clinical suspicion of malrotation to compare patients who were positive for malrotation with negative patients to see if their presentations differed and to try to elicit clinical predictors. Moreover, we aimed to ascertain if an abdominal US, when done, accurately identified the inversion of the mesenteric vessels in patients with confirmed malrotation.

Method: This study was a retrospective chart review conducted at the Sherbrooke University Health Center in Sherbrooke, Quebec, Canada. We revised all the charts in which an upper GI series was ordered from January 1, 2003 to December 31, 2014 to extract the ones who were evidently obtained to evaluate for malrotation. Those charts were then reviewed for signs and symptoms previously shown to be associated with malrotation. Logistic regression was done to find clinical predictor of malrotation. Secondly, among all the patients with a confirmed malrotation who had an abdominal US done as well, we assessed if the US had correctly identified the malrotation through the inversion of the mesenteric vessels.

Results: During this 12-year period, 1174 upper GI series were ordered. 16 patients were excluded because the charts were not available. Upper GI series were ordered for a suspicion of obstruction/possible malrotation in 334 cases. Only 4% (14) of upper GI series were positive for malrotation. After logistic regression and even with a small sample size, bilious emesis (OR 29,6 CI 3,5-248; p < 0,01) and feeding intolerance were positive predictive factors for finding malrotation (OR 13,4 CI 3,5-51,4; p < 0,01). A trend was seen in the duration of vomiting as a presentation of less than a week seemed to be associated with malrotation (OR 3,89 CI 0.98- 15,4; p= 0,053). Other symptoms such as non-bilious or chronic emesis/reflux, abdominal pain, nausea, bloating and change in bowel habits were not associated with malrotation. No signs were associated with malrotation.

During this 12-year period, 21 malrotations were confirmed after a surgical procedure. 12 of them were clinically suspected (including 5 patients with acute presentation and volvulus), 6 of them were fortuitous findings of inversion of mesenteric vessels at the US and 3 of them were fortuitous findings at the upper GI series initially ordered for another reason. The sensitivity of the upper GI series to detect malrotation was 90% and the sensitivity of the abdominal US to detect malrotation was 80%. Some abdominal US and upper GI series read negatively were repeated later and suspected of malrotation

thereafter. These findings reflect that these radiological techniques are operator-dependent. Unfortunately, of all the 334 patients suspected of malrotation, approximately a third of them never had an abdominal US done before the upper GI series and a third of them have had an abdominal US without identification of mesenteric vessel or was not able to see it.

Conclusion: Our retrospective review allowed us to observe that many upper GI series are requested to eliminate an obstruction/malrotation, but that only 4% of them are positive. This technique is more costly and generates more radiation than an abdominal ultrasound. Only a third of suspected malrotation had an adequate abdominal US done before the upper GI series. This finding let us conclude that clinician a not aware that sign of malrotation can be observed with an abdominal US and that radiologist doesn't report systematically the orientation of the mesenteric vessels. Despite the non-equivalence but good sensitivity of the abdominal US (80%), a large majority of patients with non-specific and chronic digestive symptoms might require only an abdominal US with the indication to look at the orientation of the mesenteric vessels as well as a longitudinal follow-up. Prospective study are need to evaluate the accuracy of US when malrotation are suspected.

37 THE CHARACTERISTICS OF ESOPHAGEAL MULTICHANNEL INTRALUMINAL IMPEDANCE-PH MEASUREMENTS IN INFANTS EXPERIENCING BRIEF RESOLVED UNEXPLAINED

EVENTS. Chaowapong Jarasvaraparn¹, Maria Belen Rojas Gallegos¹, Madhuri S. Mulekar², Bin Wang², David Gremse³, Karen Crissinger³ ¹Pediatrics, University of South Alabama, Mobile, AL; ²Department of Mathematics and Statistics, University of South Alabama, Mobile, AL; ³Division of Pediatric Gastroenterology, Hepatology and Nutrition, University of South Alabama, Mobile, AL

Introduction: A Brief Resolved Unexplained Event (BRUE) is defined as an event occurring in an infant younger than the age of one year when the observer reports a sudden, brief and now resolved episode of cyanosis or pallor, absent/decreased/irregular breathing, change in tone and altered level of responsiveness. Gastroesophageal reflux has been proposed as one of the causes of BRUE.

Objective: This study aims to identify the characteristics of Multichannel Intraluminal Impedance-pH (MII-pH) in infants who have experienced a BRUE.

Design: This was a retrospective descriptive study between October 2015 and February 2017.

Results: Fifty-three infants (preterm 25, term 28) were included in our study. The mean age at diagnosis of BRUE was 2.25 months. Apnea (41/53; 77.4%) was the most common manifestation of BRUE. During the MII-pH study, the non-acid reflux episode was the most common in this study (66%). The final result of MII-pH showed 18/53 (33.96%) negative reflux, 6/53 (11.32%) acid reflux, 17/53 (32.08%) non-acid reflux and 12/53 (22.64%) both acid/nonacid reflux. There were significant differences in longest acid episode and Reflux Symptom Sensitivity Index (RSSI) of cough/gag/choke between preterm and term infants. We found a significant correlation between number of acid reflux episode and all MII-pH parameters. There were significant correlations during

Table Correlation between pain/fussiness, cough/gag/choke, and vomiting symptoms and correlation between RSI, RSSI, and RSAP in BRUE (P value)

1. RSI	Pain/fussiness	Cough/gag/choke	Vomiting
Pain/fussiness	N/A	0.39 (P=0.004)	0.42 (P=0.002)
Cough/gag/choke	0.39 (P=0.004)	N/A	0.38 (P=0.005)
Vomiting	0.42 (P=0.001)	0.38 (P=0.005)	N/A
2. RSSI	Pain/fussiness	Cough/gag/choke	Vomiting
Pain/fussiness	N/A	0.5 (P=0.0004)	0.57 (P<0.0001)
Cough/gag/choke	0.5 (P=0.0004)	N/A	0.61 (P<0.0001)
Vomiting	0.57 (P<0.0001)	0.61 (P<0.0001)	N/A
3. RSAP	Pain/fussiness	Cough/gag/choke	Vomiting
Pain/fussiness	N/A	0.32 (P=0.02)	0.13 (P=0.36)
Cough/gag/choke	0.32 (P=0.02)	N/A	0.29 (P=0.035)
Vomiting	0.13 (P=0.36)	0.29 (P=0.035)	N/A
4. Pain/Fussiness	RSI	RSSI	RSAP
RSI	N/A	0.47 (P=0.0004)	0.67 (P<0.0001)
RSSI	0.47 (P=0.0004)	N/A	0.42 (P=0.0018)
RSAP	0.67 (P<0.0001)	0.42 (P=0.0018)	N/A
5. Cough/gag/choke	RSI	RSSI	RSAP
RSI	N/A	0.57 (P<0.0001)	0.79 (P<0.0001)
RSSI	0.57 (P<0.0001)	N/A	0.44 (P=0.001)
RSAP	0.79 (P<0.0001)	0.44 (P=0.001)	N/A
6. Vomiting	RSI	RSSI	RSAP
RSI	N/A	0.49 (P=0.0004)	0.86 (P<0.0001)
RSSI	0.49 (P=0.0004)	N/A	0.51 (P=0.0004)
RSAP	0.86 (P<0.0001)	0.51 (P=0.0004)	N/A

RSI, Reflux Symptom Index; RSSI, Reflux Symptom Sensitivity Index; RSAP, Reflux Symptom Association Probability

the pain/fussiness, cough/gag/choke and vomiting symptoms in terms of symptom association analysis (RSI, Reflux Symptom Index; RSSI, Reflux Symptom Sensitivity Index; and RSAP, Reflux Symptom Association Probability). RSI, RSSI and RSAP were significantly correlated with each other in all symptoms (pain/fussiness, cough/gag/choke and vomiting). However, the correlation was strongest between RSI and RSAP in all symptoms.

Conclusion: Among infants experiencing a BRUE, MII-pH monitoring revealed acid or nonacid reflux in 2/3 of patients in this small study.

39 **PROTON PUMP INHIBITORS WORSEN HOSPITALIZATION RISK IN PEDIATRIC PATIENTS WITH ASPIRATION.**

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Background: There is growing concern about the respiratory infection risks in children taking proton pump inhibitors (PPI). Despite this, PPIs are commonly prescribed to children with oropharyngeal dysphagia / aspiration. The aim of this study was to determine if there is increased risk of hospitalization in pediatric patients with aspiration who are treated with PPI.

Methods: We retrospectively reviewed the records of children under 2 years with evidence of aspiration and/or penetration on videofluoroscopic swallow study (VFSS) at Boston Children's Hospital from January to December 2015 to determine patient characteristics, including PPI exposure status, and the number, length and types of hospitalizations in the year following aspiration diagnosis. Univariate and multivariate analyses were performed using t-tests and ANOVA to adjust for comorbidities (enteral tubes, neurologic status, cardiac disease, metabolic disorders and prematurity). Survival analysis was used to evaluate time to first admission following aspiration diagnosis.

Results: We evaluated 292 subjects with a mean age of 8.8±0.4 months who were found to have aspiration or penetration on VFSS; 53% (n=156) had aspiration and 47% (n=137) had penetration on VFSS. 49% (n=143) of patients were on PPI and 51% (n=149) were not on PPI. PPI treated patients had double the number of total and gastrointestinal hospitalizations, even after adjustment for comorbidities, and more than double the number of total, pulmonary and gastrointestinal nights, as shown in tables 1 and 2. PPI treated patients also had significantly shorter time to their first overall, pulmonary, and gastrointestinal admission (p<0.05).

Conclusions: Children with aspiration who are treated with PPI have more than double the risk of hospitalization and significantly shorter time to their first admission than untreated patients. These results support growing concern about the risks of PPI use and suggest the need to reevaluate the use of pharmacologic acid suppression in children with aspiration.

Table 1: Patients Exposed to PPI Have More Admissions, Even After Adjustment for Comorbidities

Univariate Results			
	Patients on PPI	Patients not on PPI	p-value
Total Admissions	1.3±0.09	0.63±0.09	0.001
Pulmonary Admissions	0.36±0.05	0.18±0.05	0.05
Gastrointestinal Admissions	0.3±0.03	0.09±0.03	0.002
Multivariate Results			
	Patients on PPI	Patients not on PPI	p-value
Total Admissions	1.2±0.12	0.65±0.11	0.0001
Pulmonary Admissions	0.36±0.07	0.2±0.07	0.09
Gastrointestinal Admissions	0.28±0.04	0.11±0.04	0.006

Data are expressed as mean ± standard error

Table 2: Patients Exposed to PPI Have Longer Length of Stay, Even After Adjustment for Comorbidities

Univariate Results			
	Patients on PPI	Patients not on PPI	p-value
Total Admission Nights	5.67±0.85	2.28±0.85	0.04
Pulmonary Admission Nights	1.09±0.17	0.4±0.17	0.04
Gastrointestinal Admission Nights	1.27±0.18	0.38±0.18	0.01
Multivariate Results			
	Patients on PPI	Patients not on PPI	p-value
Total Admission Nights	5.76±1.1	2.3±1.13	0.03
Pulmonary Admission Nights	1.09±0.17	0.4±0.17	0.12
Gastrointestinal Admission Nights	1.21±0.24	0.45±0.24	0.03

Data are expressed as mean ± standard error

41 FECAL CALPROTECTIN AS A RELIABLE MAKER FOR DIFFERENTIATING EOSINOPHILIC GASTROINTESTINAL DISORDERS FROM INFLAMMATORY BOWEL DISEASE AND FUNCTIONAL ABDOMINAL PAIN IN CHILDREN. Do Hyun Kim¹, Jim Min Cho¹, Hye Ran Yang^{1,2}

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Background/Aims: Fecal calprotectin (FCal) is used as a noninvasive marker to rule out organic gastrointestinal diseases such as inflammatory bowel disease (IBD) from functional gastrointestinal disorders in children with chronic gastrointestinal symptoms. The aim of this study was to evaluate diagnostic accuracy of FCal for gastrointestinal inflammation and optimal cutoffs to differentiate IBD from eosinophilic gastrointestinal disorders (EoGD) and functional abdominal pain disorders (FAPD) in children with chronic gastrointestinal symptoms.

Method: Between August 2015 and March 2017, a total of 253 children (123 boys and 130 girls, aged 2.9-17.8 years) were recruited and divided into the 3 study groups; FAPD (n=187), EoGD (n=28), and IBD (n=38). FCal, WBC, ANC, ESR, and hsCRP were measured at initial diagnosis in all subjects. Spearman correlation analysis was performed to evaluate the correlation between FCal and other inflammatory markers. Receiver-operating characteristics plot analysis was used to evaluate optimal cutoff levels of FCal.

Results: Median FCal levels of FAPD, EoGD, and IBD in pediatric patients were 23.4 (11.5-1285.5) µg/g, 77.5 (11.5-2000) µg/g, and 2000.0 (60.4-2000) µg/g, respectively, which were significantly different among the 3 groups (p < 0.001). FCal correlated positively with ESR (r = 0.569, p < 0.001) and hsCRP (r = 0.480, p = 0.004) in the IBD group, and FCal correlated positively with ESR (r = 0.566, p = 0.004) in the EoGD group. A cutoff of FCal 90.3 µg/g distinguished EoGD from FAPD with a sensitivity of 54 % and a specificity of 83 %, and a cutoff of FCal 292.7 µg/g distinguished IBD from FAPD with a sensitivity of 92 % and a specificity of 95 %. A cutoff of FCal 677.4 µg/g distinguished EoGD from IBD in children with a sensitivity of 81 % and a specificity of 89 %.

Conclusion: FCal is a useful and reliable noninvasive marker in differentiating EoGD from either functional abdominal pain or IBD in children manifesting with chronic gastrointestinal symptoms, when optimal cutoffs are applied.

Key words: Fecal calprotectin, eosinophilic gastrointestinal disorder, inflammatory bowel disease, functional abdominal pain, cutoff, child

42 A NOVEL MOUSE MODEL OF PEDIATRIC EOSINOPHILIC ESOPHAGITIS THROUGH CONDITIONAL IL-13 OVEREXPRESSION. Dominique Bailey¹, Yongchun Zhang², Ming Jiang², Jianwen Que². ¹Division of Pediatric Gastroenterology, Hepatology and Nutrition, Columbia University Medical Center, Morgan Stanley Children's Hospital of New York Presbyterian, New York, NY; ²Division of Digestive and Liver Diseases and Center for Human Development, Department of Medicine, Columbia University Medical Center, New York, NY

Background: Eosinophilic Esophagitis (EoE), an allergen-associated disease, is thought to be one of the most prevalent causes of chronic esophageal symptoms among children and young adults. The major pathological changes of EoE include extensive infiltration of eosinophils and basal cell hyperplasia accompanied by increased levels of cytokines such as IL-5 and IL-13 in the esophageal epithelium of patients with EoE. Progress towards understanding the pathophysiology of EoE has mostly relied on adult animal models. We hypothesize that pediatric EoE is a subtype of EoE and the mechanism of disease differs from adult EoE. To understand the pathophysiology of pediatric EoE we sought to establish a pediatric mouse model.

Methods: We have previously shown that conditional overexpression of IL-13 in esophageal basal cells of an adult mouse leads to basal cell hyperplasia in the esophageal epithelium resembling EoE. We adapted our transgenic mouse model to generate Krt5-rtTA; tetO-IL13 compound mice pups. The Keratin 5 (Krt-5) promoter controls rtTA expression in basal cells. Water containing doxycycline was given to infant pups, which allows rtTA to bind to doxycycline and this complex can then bind to the tetO promoter to induce conditional overexpression of IL-13 in esophageal basal cells. **Results:** Krt5-rtTA; tetO-IL13 transgenic infant mice demonstrated IL-13 overexpression in basal cells at early postnatal age 10. Keratin 5 (Krt-5) and major basic protein (MBP) immunostaining confirmed proliferation of basal progenitor cells and eosinophils in the esophageal epithelium of infant mice. These mice weighed less than non-compound litter-mate controls; suggestive of a failure to thrive phenotype as seen in human infants with EoE. Transgenic infant mice also developed skin lesions likened to an atopic dermatitis.

Conclusions: Our preliminary results indicate that this transgenic mouse model can serve as a novel animal model of pediatric EoE. Future aims using this model will evaluate how IL-13 induces basal cell hyperplasia and eosinophilia within the esophageal epithelium. Additionally, we plan to carry out timed experiments to investigate the timepoint at which basal cell hyperplasia and eosinophilia resolves. Lastly, we plan to treat transgenic infant mice with oral viscous budesonide as well

as QAX576, a monoclonal antibody against IL-13, to investigate if treatment with these agents decrease eosinophilia and basal cell hyperplasia in the esophageal epithelium of infant mice.

Key words: eosinophilic esophagitis, IL-13, pediatric mouse model, basal cell hyperplasia, eosinophilic infiltration

43 **ORAL VISCOUS MOMETASONE TO TREAT EOSINOPHILIC ESOPHAGITIS IN CHILDREN.**

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Background: Children with eosinophilic esophagitis (EoE) are often treated with chronic oral topical steroids. Mometasone has low systemic bioavailability, yet high binding affinity for the glucocorticoid receptor making it ideal for long term therapy.

Specific Aim: To determine if oral viscous mometasone achieves mucosal healing in children with eosinophilic esophagitis.

Study Design: Boston Children's Hospital IRB approved retrospective analysis of histologic and endoscopic findings in children with EoE treated with viscous mometasone compounded to 750mcg/5mL with methylcellulose. Response to therapy was determined histologically by the number of eosinophils per high power field (eos/HPF). Patients were classified as responders (0-15 eos/HPF), partial responders(16-25 eos/HPF), and nonresponders(>25 eos/HPF). The Eosinophilic Esophagitis Endoscopic Reference Score (EREFS) was also used to compare data.

Results: In 11 children (mean age: 11.5 year, median age: 12 year), there were 9 responders (82%), 0 partial responders, and 2 non-responders (18%). The median peak eosinophil count was 63 eos/HPF before treatment (range 0-120) and 5 eos/HPF after treatment (range 0-100). None of the patients had an EREFS score higher than 3 prior to treatment with mometasone. None had strictures or rings before or after treatment. Five of the responders were started on mometasone due to treatment failure with budesonide, 3 due to diet failures. Two responders had been in remission on budesonide but were switched to mometasone due to short stature. One responder was changed to mometasone for behavioral changes attributed to budesonide - her EoE was responsive to mometasone and behavioral changes resolved. All non-responders had been changed to mometasone due to treatment failure with budesonide. No adverse events were reported on mometasone.

Conclusion: Topical viscous mometasone may be an effective therapy to treat uncomplicated eosinophilic esophagitis. However, further studies are required to optimize dosing.

*44 **EOSINOPHILIC ESOPHAGITIS REFERENCE SCORE ACCURATELY IDENTIFIES DISEASE ACTIVITY AND TREATMENT EFFECT IN CHILDREN.**

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Background: The EoE Endoscopic Reference Score (EREFS) assesses severity of five endoscopic findings: edema, rings, exudates, furrows and strictures and is based on the findings described and validated in adults. The relationship between endoscopic findings and histology as scored by the EREFS system in eosinophilic esophagitis (EoE) in children has not been previously explored. We aimed to determine the diagnostic utility of EREFS scoring and assess the relationship between endoscopic changes after treatment in children.

Methods: We performed a prospective study in children undergoing diagnostic or follow up upper endoscopy at Ann & Robert H. Lurie Children's Hospital of Chicago, IL USA from December 2012 to December 2016. Incident cases of EoE were diagnosed based on 2011 consensus guidelines and treated with either elimination diet or topical steroids. EREFS scores and receiver operating characteristic were determined for 1) incident EoE cases (N= 77) vs controls (N= 115), 2) post-treatment active (N =101) vs inactive (N=128) EoE cases, and 3) paired pre- and post-treatment EoE cases (N=85). Component and composite EREFS scores were correlated with eosinophil counts.

Results: 192 diagnostic (mean age 10, 54% male, 92% Caucasian) and 229 post-treatment (mean age 10, 79% male, 90% Caucasian) endoscopies were evaluated in 421 children. The sensitivity and specificity was determined for each finding. The mean EREFS inflammatory score was 2.6 for incident EoE patients compared to 0.1 in controls (p<0.001). Post-treatment EREFS inflammatory score for active disease decreased from a mean of 2.4 to 0.5 (p<0.001) for inactive disease. The EREFS inflammatory score strongly correlated with peak eosinophilia (p<0.001). Baseline and post-treatment longitudinal data from

85 patients demonstrated a significant reduction in the composite EREFS inflammatory score from 2.4 to 0.7, $p < 0.001$) for treatment responders, with 92% of responders demonstrating score reduction.

Conclusions: The EREFS scoring system accurately identifies children with EoE at diagnosis. Treatment responders had significantly lower EREFS scores than non-responders. EREFS scoring system can be used as biomarker to identify children with EoE and monitor outcome following treatment in conjunction with histology.

45 **MULTICHANNEL INTRALUMINAL IMPEDANCE WITH PH TESTING REDUCES PROTON PUMP INHIBITOR USAGE IN CHILDREN WITH NONEROSIVE REFLUX.**

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Introduction: Proton pump inhibitors (PPIs) are widely used in the diagnosis and management of pediatric gastroesophageal reflux disease (GERD). However, recent data in adults and children suggests that these medications are associated with significant adverse effects and should be used judiciously. The current gold standard for diagnosing GERD remains multichannel intraluminal impedance with pH (pH-MII) testing. However, little is known about whether pH-MII results change management and predict clinical outcomes. The aim of this study was to determine the prevalence of PPI therapy for different reflux phenotypes at follow-up after pH-MII testing.

Methods: Children ≥ 5 years who underwent upper endoscopy and pH-MII testing for evaluation of typical reflux symptoms (pain, heartburn, chest pain, reflux, or regurgitation) between 2004 and 2016 were included. All children underwent a minimum of an 8-week PPI trial prior to diagnostic studies, though all studies were performed off PPI therapy. Children with eosinophilic or erosive esophagitis, a history of thoracic or abdominal surgery and those who did not report symptoms during the pH-MII study were excluded. The results of pH-MII testing were used to categorize patients into nonerosive esophageal phenotypes: those with abnormal esophageal acid exposure (pH < 4 for $> 6\%$ of the study) were classified as having nonerosive reflux disease (NERD), those with normal acid exposure but a positive symptom index (SI) were classified as reflux hypersensitivity (RH) and those with normal acid exposure and negative SI were classified as functional heartburn (FH). PPI use at follow-up after pH-MII testing was determined from review of the medical record.

Results: A total of 45 children met inclusion criteria: 29% of patients were categorized as having NERD, 29% of children had RH and 42% had FH. 6 children were lost to follow-up after pH-MII testing (2 NERD, 1 RH and 3 FH). Follow-up medication data was available in 39 children. 79% of all patients remained on PPI at the time of the first follow-up visit after pH-MII testing. Patients were using PPIs at the first follow-up visit in 91% of NERD patients, 92% of those with RH and 63% with FH. Based on pH-MII results in patients with NERD, 46% continued PPI at the same dose, 27% increased dose, 18% changed brands and 9% discontinued PPI. In patients with RH, 42% continued PPI at the same dose, 17% increased dose, 25% decreased dose, 8% changed brands and 8% discontinued PPI. In patients with FH, 31% continued PPI at the same dose, 44% discontinued PPI, 13% changed brands, 6% increased dose and 6% decreased dose. In total, 33% of children either discontinued PPIs or decreased the total dose based on the results of pH-MII testing. Long-term, the total time that patients remained on PPI after pH-MII testing was 22 ± 18 months in the NERD group, 18 ± 19 months in the RH group and 8 ± 20 months in the FH group, though there were no significant differences between these groups ($p = 0.16$).

Conclusions: The majority of children remain on PPI therapy after pH-MII testing. However, the results of pH-MII testing led to decreasing the PPI dose or discontinuing the medication in one third of patients. Children with FH were most likely to have reduced PPI usage.

46 **THE EPIDEMIOLOGY AND COST OF INPATIENT CARE FOR PATIENTS WITH EOSINOPHILIC ESOPHAGITIS IN THE UNITED STATES.**

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Introduction: Although a rare chronic condition with increasing recognition, evidence suggests that eosinophilic esophagitis (EoE) contributes significantly to healthcare cost for commercially insured individuals in the United States. However, there is limited information on the direct cost of inpatient care for patients with EoE. This study describes the epidemiology and costs of care for the US population with EoE focusing on inpatient care.

Methods: This is a cross-sectional case-control design utilizing the National Inpatient Sample (NIS) database between 2010 and 2013 from the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). Cases of EoE were identified using ICD-9 code 530.13. For each year, three inpatient controls were randomly selected for each case of EoE, matched based on gender, age, race and presence of another chronic comorbidity. The procedures considered include Esophagogastroduodenoscopy (EGD) and allergy testing while chronic conditions comprised

Results: There were 16,518 admissions associated with EoE over the four-year period, with increasing admission rates over time. Most of the patients were below 19 years of age (41%) and were Caucasian (80%). The median length of stay (LOS) and total cost of EoE inpatient care was approximately 2 days (interquartile range (IQR) 1-5) and \$20,350 (IQR \$11,355-\$37,207) respectively per patient, compared to controls with median LOS of 3 days (IQR 1-5) and total cost of \$20,441 (\$10,572-\$41,417). EGD with closed biopsy in EoE patients accounted for about 91% of the procedures during admission with average and median cost of \$37,834 (+/- \$1699) and \$24,639 (IQR \$15,441 - \$41,286) respectively. The sources of payment among EoE patients were mostly private insurance (56%) and Medicaid (20%). The peak admission periods were between March to May and August to October.

Discussion: Increasingly, EoE is being shown to constitute a significant health burden, necessitating prompt attention. The severity of this disorder may demand inpatient admission and close monitoring. This study describes the characteristics and cost of inpatient care including LOS, cost of procedure and total hospital charge. Our study suggests there is a significant increase in inpatient cost per day for individuals with EoE compared to controls. Thus, development of non-invasive procedures for monitoring EoE disease progression will be critical to reduce the inpatient cost of care in this population.

47 **DIAGNOSIS AND MANAGEMENT OF EOSINOPHILIC ESOPHAGITIS WITH A THROAT**

SWAB. Shauna Schroeder^{1,2}, Kelly Shim^{1,3}, Sergei Ochkur³, Katie Galvin², James Lee³, Benjamin Wright^{1,2,3}. ¹Phoenix Children's Hospital, Phoenix, AZ; ²University of Arizona College of Medicine, Phoenix, AZ; ³Mayo Clinic, Scottsdale, AZ

Background: Currently diagnosis of eosinophilic esophagitis (EoE) can only be accomplished by an invasive endoscopic biopsy. While this procedure is safe overall, several down sides exist, including the potential complications of the procedure/ anesthesia, limited sampling of esophageal surface area (< 0.0001%), and cost. Collectively, observations suggest that there is a need for a non-invasive biomarker of EoE for diagnosis and monitoring response to therapy. We have developed a novel, high throughput ELISA for detection of the eosinophil secondary granule protein, eosinophil peroxidase (EPX). Unlike other granule proteins which may be expressed by other cell types, EPX is exclusively released by eosinophils. Noninvasive measurement of EPX has been successful in the past as demonstrated by the esophageal string test. However, limitations of this method include potential difficulty associated with swallowing a capsule in pediatric patients.

Hypothesis: We hypothesized that measurement of EPX from throat swabs of subjects undergoing upper endoscopy for symptoms of esophageal dysfunction would correlate with esophageal eosinophilia and serve as a surrogate biomarker for EoE.

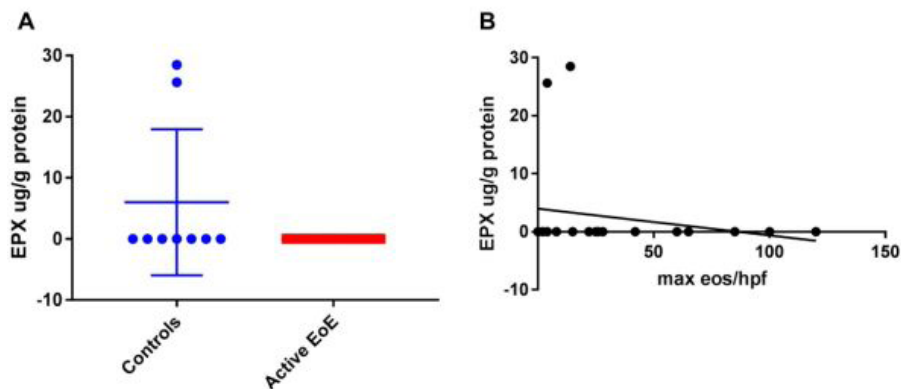
Methods: We performed a prospective case control study of consecutive pediatric patients undergoing endoscopy for surveillance of known EoE or symptoms of esophageal dysfunction. Cases of EoE were defined by consensus guidelines. Cases of active EoE had an esophageal biopsy with ≥ 15 eosinophils per high-power field (eos/hpf) after an eight week trial of a high dose proton pump inhibitor (PPI). Subjects with < 15 eos/hpf at the time of initial biopsy served as controls. Clinical data including demographics, symptoms, and relevant medical history were collected. Swabs of the posterior oropharynx and anterior nasal vestibule of each patient were performed prior to endoscopy. Esophageal biopsies were obtained during clinically indicated endoscopies and evaluated by a pediatric pathologist

	Atopic Controls/ Inactive EoE (n = 9)	EoE (n = 12)	P*
Mean age (\pm SD)	9.68 \pm 3.16	11.79 \pm 4.52	
Males (n, %)	4 (44)	11 (92)	
White (n, %)	7 (78)	12 (100)	
Symptoms at time of endoscopy			
Dysphagia	3 (33)	2 (17)	
Heartburn	0	1 (8)	
Poor weight gain	1 (11)	1 (8)	
Vomiting	0	0	
Abdominal pain	1 (11)	1 (8)	
None (surveillance endoscopy)	5 (56)	8 (66)	
Atopic conditions (n, %)			
Asthma	6 (60)	5 (45)	
Dermatitis	2 (20)	0	
Seasonal allergies	7 (70)	7 (64)	
Food allergies	0	8 (67)	
Tissue eosinophil counts (max eos/hpf \pm SD)	3.56 \pm 4.77	51.08 \pm 34.8	p < 0.001
Throat EPX (ug/g protein \pm SD)	6.01 \pm 11.95	0 \pm 0	
Nasal EPX (ug/g protein \pm SD)	5.44 \pm 8.89	5.45 \pm 8.64	

to quantify eosinophil density. Protein isolates from throat/nasal swabs eluents were analyzed for EPX content by ELISA and EPX levels were normalized for total protein content.

Results: Throat swabs were obtained from 21 subjects at the time of upper endoscopy and esophageal biopsy. A majority of subjects (13/21) were undergoing clinical surveillance endoscopies for changes in treatment modality of their EoE or confirmation of histologic remission. Eosinophilic inflammation in active EoE subjects (n = 12) was mostly localized to the distal and mid esophagus. Control subjects (n=9) were patients with atopy and gastrointestinal symptoms (abdominal pain or esophageal dysfunction) or inactive EoE (Table 1). Throat-derived EPX was undetectable in all EoE cases and did not distinguish EoE cases from controls. (Figure 1, panel A) Nasal EPX levels were higher in subjects with allergic rhinitis; however, this difference did not reach statistical significance. EPX from the throat swabs did not correlate with esophageal eosinophil counts (Figure 1, panel B).

Conclusion: We detected small quantities of EPX from the throat swabs of two of the control patients but did not see any correlation between eosinophil counts in the esophagus and EPX level. Consequently, EPX levels in the throat do not serve as a reliable marker of EoE. Esophageal biopsies remain the gold standard for assessment of disease activity.



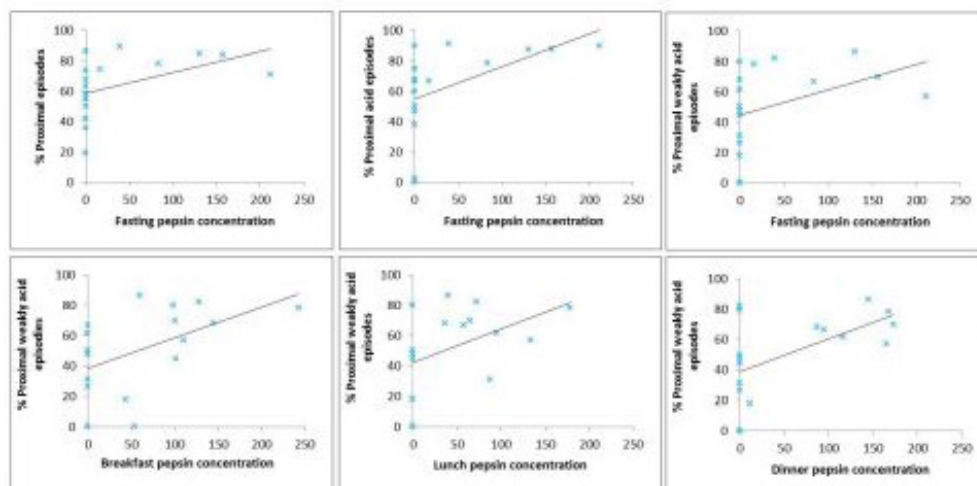
FUNCTIONAL/MOTILITY

49 SALIVARY PEPSIN DETECTION AS A GASTROESOPHAGEAL REFLUX DISEASE MARKER IN A PEDIATRIC POPULATION. Andres Bodas¹, Ana Garrido¹, Julio Perez de la Serna², Arantxa Recio¹, Raquel Vecino¹, Antonio Ruiz de Leon². ¹Pediatrics Gastroenterology, Hospital Clinico San Carlos, Madrid, Madrid, Spain; ²Gastroenterology, Hospital Clinico San Carlos, Madrid, Madrid, Spain

Background/Objectives: Current diagnostic methods for gastroesophageal reflux disease (GORD) are invasive. Peptest allows the detection of salivary pepsin, which is believed to be a GORD marker. The aim is to establish test sensitivity and specificity, predictive value and its validation in a pediatric population.

Material/Methods: 18 controls and 18 patients with suspected GORD were studied. Cut-off value for pepsin positivity was 16ng/mL. In addition, patients underwent MII-pH monitoring (multichannel intraluminal impedance ph monitoring) and were divided in two groups: normal and abnormal results in MII-pH monitoring. Results of peptest and MII-pH monitoring between the two populations were compared.

Results: Up to 1/3 of controls had pepsin in saliva at low concentrations. Symptomatic patients had higher pepsin prevalence and concentration than controls (98,7(21,75-144,85)ng/mL). Having at least one positive test had 88,9% sensitivity and 37,5% specificity and increased the likelihood of GORD from 52,9% to 61,53%. Moreover, there was a positive correlation between pepsin concentration and the episodes that reach the proximal esophagus.



Conclusions: According with the technique used in this study, peptest seems to have good sensitivity, albeit not enough specificity to avoid invasive tests. However, given the fact that peptest is related to episodes that reach proximal esophagus, it might be useful in the diagnosis of GORD with atypical symptoms.

50 **UPPER GASTROINTESTINAL SYMPTOMS IN ORTHOSTATIC INTOLERANCE/POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS) ARE RELATED TO FUNCTIONAL AND NOT ORGANIC ABNORMALITIES.**

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Objectives: Upper gastrointestinal (GI) symptoms of dysphagia, reflux, regurgitation, food impaction, and dyspepsia are common in children and young adults with Orthostatic Intolerance (OI) or Postural Orthostatic Tachycardia Syndrome (POTS), which is characterized by maladaptive hemodynamic changes to posture caused by autonomic instability. In the past, food allergy, such as cow's milk protein intolerance, has been thought to be the underlying basis for these symptoms in POTS and related conditions like chronic fatigue syndrome. We retrospectively reviewed the charts of OI/POTS patients who underwent upper GI investigations to assess for the underlying esophageal disease. We hypothesized that there would be a positive association between the presence of mucosal conditions such as eosinophilic esophagitis (EoE) and POTS.

Methods: We reviewed medical records of 103 consecutive children and young adults from Children's National Medical Center with POTS and upper GI symptoms. All subjects had tilt table tests (TTT) to establish diagnosis of OI/POTS). All subjects underwent upper GI endoscopies (esophagogastroduodenoscopy or EGD) with biopsies, and select subjects underwent barium swallow studies, pH impedance studies and high resolution esophageal manometry (HRM) based on their predominant presenting symptoms.

Results: The subjects with POTS included in this review ranged in age from 8 to 29 years, mean age (+/-SD)= 16.8 (+/-2.86) years. TTT was abnormal in all subjects and GI symptoms such as nausea and vomiting were reproduced in 99/103 (96.1%) subjects during their TTT. Abnormal findings in EGD were noted in 13/103 (12.6%) subjects, including 10 with chronic gastritis, 2 with esophagitis and 1 with EoE. For the subject with EoE, there were 50 eosinophils per high powered field. Abnormal findings were noted in 3/32 subjects (9.4%) who underwent barium swallow studies and 3/38 subjects (7.9%) who underwent pH impedance studies. In contrast, 15/25 (60%) subjects who had HRM studies had abnormal results. Abnormal findings in HRM included 12 with LES dysfunction, 1 with Type 2 Dysphagia, 1 with nutcracker esophagus, and 1 with diffuse esophageal spasm.

Conclusions: Despite clinical symptoms of dysphagia, reflux, regurgitation, and food impaction being common in OI/POTS patients, endoscopic/mucosal changes such as EoE, are not the predominant findings. Barium swallow studies and pH impedance monitoring did not lead to high diagnostic yields. Most subjects who underwent esophageal manometry however, did demonstrate abnormal esophageal motility. Upper GI symptoms in subjects with POTS appear to be more related to functional, rather than mucosal/organic conditions.

53 **CAN THE HIGH-RESOLUTION ELECTROGASTROGRAM SEPARATE ANTRAL AND PYLORIC ACTIVITY IN CHILDREN?**

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Introduction: Antroduodenal manometry (ADM) is a well-established diagnostic test that can guide the management of 15-20% of patients with upper GI symptoms. Placing the ADM catheter is an invasive procedure that requires sedation and is performed only in highly specialized motility centers. There is a need for a more accessible and easily-administered technique to provide this information. The electrogastrogram (EGG) is a noninvasive technique for measuring gastric myoelectric activity, however it has reported limitations. We have developed novel approaches using high-resolution cutaneous arrays with the hopes of improving the clinical utility of the EGG (Gharibans et al., 2016). We recently showed a correlation between manometry and the HR-EGG in children (Gharibans et al., 2017), and hypothesize the HR-EGG can be further used to separate antral and pyloric activity.

Methods: We enrolled 13 subjects (9F/4M) with average age of 13 years (range 7-17 years) who presented with postprandial vomiting and dyspepsia and underwent antroduodenal motility studies as part of their evaluation. ADM was performed with a flexible catheter comprised of 8 water-perfused channels. We positioned the catheter with 3 to 4 sensors in the antrum and one in the pylorus (1cm spacing), and the duration of the recordings were 6 to 8 hours (4 hours fasting, 2 hours postprandial, and occasionally an additional 2 hours after intravenous administration of erythromycin if an interdigestive Phase III MMC was not observed). HR-EGG was simultaneously recorded using 25 cutaneous electrodes (5x5 array with

2cm spacing). Blind source separation (Bell and Sejnowski, 1995) was applied to isolate the electrical activity from different regions of the stomach. Linear regression between the power of the HR-EGG sources and intragastric motility index across time was used to evaluate our hypothesis (p-value < 0.001 was considered significant).

Results: In 46% of the subjects (6/13) one of the extracted HR-EGG sources correlated significantly with an antral manometry channel, while another source correlated with the pylorus channel. Figure 1 is a plot of the results for a representative subject. In 31% of the subjects (4/13) only one of the HR-EGG sources correlated significantly with either an antral or pyloric manometry channel. In two of these subjects, the manometry readings were very similar in all channels and a distinct pyloric channel was not observed. In the remaining 23% of the subjects (3/13) we did not find a significant correlation, which we suspect was due to either inaccurate array or catheter positioning. For all subjects, the mean correlation coefficient was 0.58 ± 0.12 and 0.57 ± 0.18 in the antrum and pylorus, respectively (see Table 1). The study was well tolerated by patients and no side effects were noted.

Conclusion: We were able to extract both antral and pyloric activity noninvasively in nearly half of the subjects. We believe these results can be improved in future studies with high-resolution manometry and further refinement of the technique. HR-EGG is a safe and feasible test in the pediatric population.

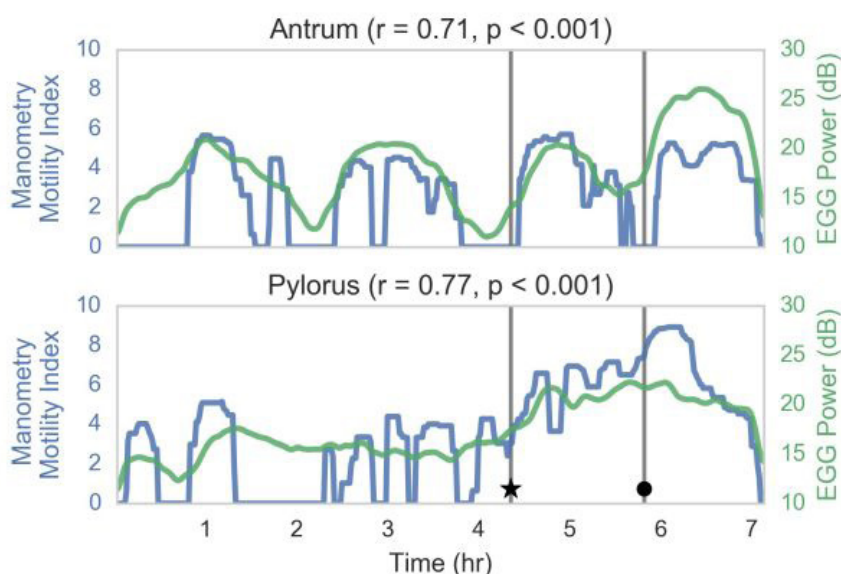


Figure 1: Motility index for antrum and pylorus manometry channels (blue) plotted with extracted EGG sources (green) for Subject 2. The black star indicates intravenous administration of erythromycin and the black circle indicates consumption of a meal.

SUBJECT	AGE (YEARS)	GENDER	HR-EGG / ADM CORRELATION (R-VALUE)	
			ANTRUM	PYLORUS
1	13	F	0.67*	0.75*
2	14	F	0.71*	0.77*
3	7	M	0.54*	0.33*
4	15	F	0.49*	ns
5	17	M	ns	ns
6	12	F	0.48*	0.45*
7	8	F	0.54*	0.44*
8	14	F	0.50*	ns
9	10	M	0.60*	ns
10	15	M	ns	ns
11	15	F	0.43*	0.65*
12	16	F	ns	ns
13	17	F	ns	0.80*
MEAN	13 ± 3		0.58 ± 0.12	0.57 ± 0.18

* p < 0.001 ns: not significant

Table 1: Correlation between HR-EGG and motility index of antrum and pylorus across subjects.

54 AN EPIDEMIOLOGICAL STUDY EXPLORING THE PREVALENCE OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN SOUTH AMERICAN INFANTS. Ashish Chogle¹, Carlos Velasco-Benitez¹, Ricardo Chanis², Milton Mejia³, Miguel Saps⁵. ¹Pediatric Gastroenterology, Children's Hospital of Orange County, Orange, CA; ²Hospital del Niño, Ciudad de Panamá, Panama; ³Hospital infantil de Nicaragua, Managua, Nicaragua; ⁴Universidad del Valle, Cali, Colombia; ⁵Nationwide Children's Hospital, Columbus, OH

Background: Functional gastrointestinal disorders (FGIDs) are commonly observed in children. Ethnic and cultural differences, parental beliefs and coping abilities may influence the parental report of the infant signs and symptoms and thus the prevalence of FGIDs. Infection patterns and health care delivery vary by region. The use of antibiotics in the first year of life, intestinal and extra-intestinal infections, gastrointestinal allergies, diet, length of breastfeeding and early adverse life events are likely to differ among countries. Presence of FGIDs at early stages of life may have long-term consequences

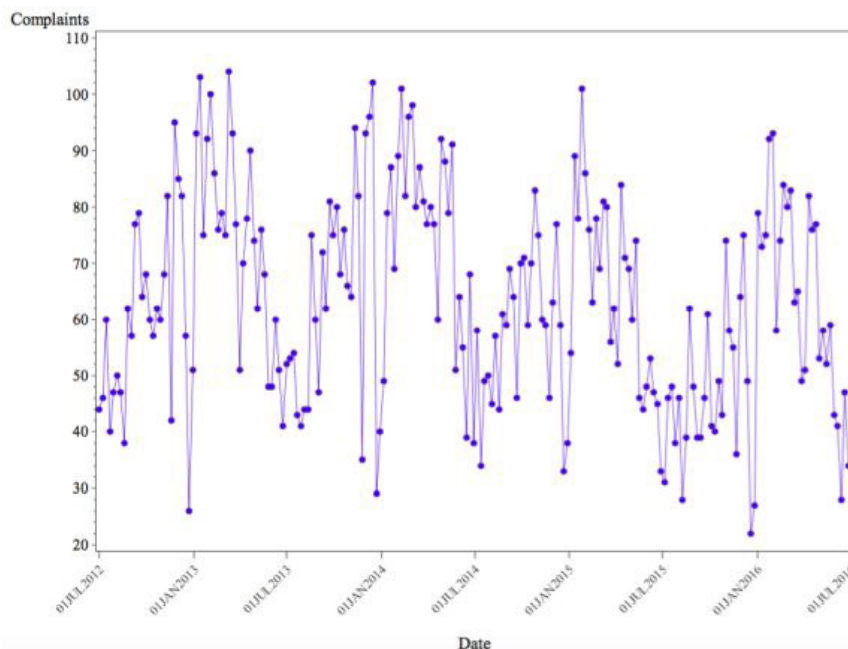
and influence the child's sick role in the family, perception of vulnerability, the family dynamics, parental quality of life and health care utilization. The impact of FGIDs on the child, family and the healthcare system underscore the need for large studies using standardized diagnostic criteria in children of different regions and ethnicity. We conducted the first international population based study to investigate the epidemiology of FGIDs in infants using the Rome III criteria. Due to the dearth of data on the epidemiology of FGIDs in infants and the potential long-term implications of FGIDs, our study has the potential to fill an important void in the literature.

Aim: Our aim is to perform a population-based study using Rome III criteria to describe the prevalence of FGIDs in infants in 3 countries in South America.

Methods: We conducted a multi-country cross-sectional study to investigate the epidemiology of FGIDs in children 0 to 12 months of age, using the Rome III criteria, in Colombia, Panama, and Nicaragua. Children with organic medical diseases were excluded. Parents provided demographic information and completed the Spanish version of the Questionnaire on Pediatric Gastrointestinal Symptoms for Infants & Toddlers (QPGS III IT- Spanish).

Results: Parents of 404 infants completed the questionnaires. Fifty-three infants were excluded due to presence of organic diseases. One hundred and forty one infants (40.2%) were diagnosed with at least one FGID according to the Rome III diagnostic criteria (43.9% female, median 5.2 months). Colic was the most commonly diagnosed disorder in infants (22.8%). Functional dyschezia, constipation and regurgitation were the next most common disorders (14.9%, 9.7% and 9.4% respectively) followed by rumination (6%). Twenty-six infants (7.4%) had more than one FGID diagnosis. Infants up to 6 months are included in Rome III criteria for functional dyschezia. On applying the Rome IV criteria for functional dyschezia (which includes infants up to 9 months), 13% infants qualified for the diagnosis that is almost same as the prevalence found with Rome III criteria. Marital status of the mother, number of siblings, birth order and prior history of diarrhea had no significant effect on the risk of FGIDs.

Conclusion: Current findings suggest that FGIDs are common in infants from South America. Colic and functional dyschezia were the most common FGIDs. The prevalence of FGIDs in infants from these South American countries was not significantly influenced by socio-demographic, familial, clinical, and environmental variables.



55 SEASONAL VARIATIONS IN PEDIATRIC ABDOMINAL PAIN CONSULTATIONS. Ashley Debeljak^{1,2}, Katherine Lamparyk^{2,3}, Lori Mahajan³. ¹Psychology, Wright State University School of Professional Psychology, Dayton, OH; ²Center for Pediatric Behavioral Health, Cleveland Clinic Children's Hospital, Cleveland, OH; ³Pediatric Gastroenterology, Cleveland Clinic Children's Hospital, Cleveland, OH

Background: While one prior study has demonstrated a seasonal pattern to pediatric abdominal pain consultations (Saps et al., 2010), specific factors contributing to this pattern have not been examined. Further, no studies have evaluated the pattern of abdominal pain consultations on a more robust and informative weekly frequency. Prior proposed contributing factors have included psychosocial stress, climate, and latitude. We hypothesized confirmation of a seasonal pattern of abdominal pain where consultations increase during periods of academic stressors and adverse weather conditions.

Patients/Methods: A retrospective study analyzed patient medical charts from children aged 6 - 18 seen for complaints of abdominal pain from 2012-2016. Variables retrieved included demographics of age and gender, date of physician office visit, and primary reason for visit. Patients with organic medical conditions related to symptoms of abdominal pain were excluded from analysis. State school testing, school schedules, and monthly weather data were extracted from public databases for predictor variables in linear regression analysis.

Results: A total of 13,232 pediatric office visits with the presenting problem of abdominal pain occurred within the five-year time period. Results confirmed a predictable seasonal pattern in the number of weekly visits for reason of abdominal pain. Linear regression analysis found that temperature and school calendar successfully predicted variations in consultation visits, with rates of abdominal pain visits being negatively related to school being in session and average temperature. Other variables did not significantly predict abdominal pain visits.

Conclusion: Abdominal pain is predictably variable over time, with more visits for this area of complaint during periods of colder weather and when school is in session. A possible role of psychosocial stress factors associated with school (i.e. workload, bullying, peer conflict) and the biological impact of cold temperature on the body are proposed to be underlying factors in the apparent seasonal variation in pediatric abdominal pain.

Variable	Label	DF	Parameter Estimate	Standard Error	T Value	P Value	Variance Inflation
Intercept	Intercept	1	55.62668	7.01325	7.93	<.0001	0
Ave. Temp	Ave. Temp	1	-0.33232	0.10593	-3.14	0.0020	4.19029
Ave. Precip	Ave. Precip	1	28.47812	19.36159	1.47	0.1429	1.41831
Ave. Snow	Ave. Snow	1	6.21577	6.60719	0.94	0.3480	3.60309
School	School In Session	1	19.44467	2.44831	7.94	<.0001	1.59436
Testing	Major Test	1	1.31597	2.24669	0.59	0.5587	1.44698
Year 2012		1	5.66071	3.15354	1.80	0.0742	1.43977
Year 2013		1	12.47718	2.51993	4.95	<.0001	1.52737
Year 2014		1	8.25258	2.57860	3.20	0.0016	1.59932
Year 2016		1	5.72327	3.09490	1.85	0.0659	1.34271

56 BASELINE CHARACTERISTICS AND OUTCOME PREDICTORS IN PEDIATRIC PATIENTS WITH PAIN-PREDOMINANT FUNCTIONAL GASTROINTESTINAL DISORDERS (FGID).

Beate Beinvog¹, Elizabeth Burch¹, Julie Snyder Christiana¹, Neil Schechter², Fiona Paul¹, Karen Warman¹, Yoshiko Okazaki¹, Amelia Sparrow¹, Samuel Nurko¹.¹Gastroenterology, Boston Children's Hospital, Boston, MA; ²Department of Anesthesiology, PerioperaCve and Pain Medicine, Boston Children's Hospital, Boston, MA

Children with functional gastrointestinal disorders (FGID) can have severe disability, can be difficult to treat and have variable outcomes. Predictors of outcome are unknown.

Aim: To describe baseline characteristics and outcome predictors in intractable Functional Abdominal Pain (FAP), Irritable Bowel Syndrome (IBS) and Functional Dyspepsia (FD) in pediatric patients.

Methods: A retrospective chart review was performed of 74 patients, seen for initial consultation and at least one follow-up. Patients were screened for severity before evaluation, and only severely disabled patients with intractable symptoms were seen. All were seen by a multidisciplinary team consisting of a gastroenterologist, psychologist, pain specialist, nurse practitioner, dietitian and social worker using the bio-psycho-social model of pain and disease. Patients with diagnoses FAP, IBS and FD, as defined by Rome III, were selected for this analysis. Baseline measures of pain (API), daily functioning (FDI), depression and anxiety (CDI, RCADS), somatization (CSI), pain response behaviors (PRI), psychosocial health, emotional functioning and degree of worry about stooling and abdominal pain (PedsQL GI) were obtained.

Primary outcome measure was subjective improvement in pain and/or functioning. ANOVA was used to analyze differences in baseline characteristics between the three FGID sub-groups (IBS, FAP and FD) as well as between responders and non-responders across all patients. A multivariate analysis was used to identify predictors of outcome.

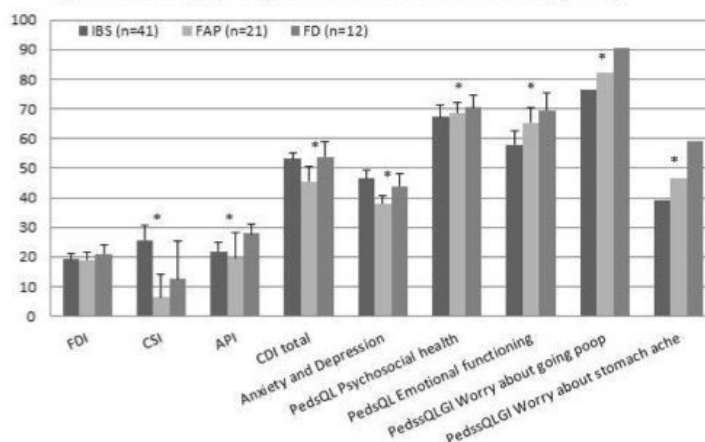
Results: Baseline characteristics (n=74): 75% female, 25% male with a mean age of 15.1 ± 3.1 years (10 to 21 years). All had a long-standing history of symptoms with a mean of 2.5 years (2 months – 12 years). 55% of patients met criteria for IBS, 28.4% FAP and 16.2% FD.

Baseline psychological measures: see Figure 1

Psychological measures among responders vs non-responders: see Figure 2

Predictors of response: Multivariate analysis, controlling for all pertinent variables, shows that the type of FGID (p=0.0019), Depressive Symptoms

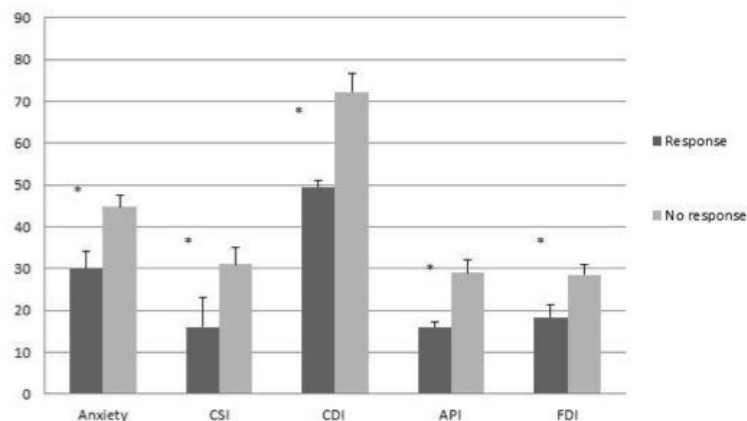
Figure 1: Baseline psychological measures across selected FGID (* p<0.05)



($p=0.004$), Somatization ($p=0.23$) and the Coping style ($p=0.009$) are predictors of improved outcome. Neither functional disability ($p=0.2$) nor Abdominal pain ($p=0.23$) were predictors of outcome.

Conclusion: Baseline psychological measures of pain severity, disability, anxiety, depression, somatization, coping, psychosocial health and emotional functioning differ significantly between different FGID. Additionally, the type of FGID, depressive symptoms, somatization and the coping style are predictors of response to therapy. Identifying baseline markers of treatment success or failure will provide better understanding of the natural history of FGID, success of treatment strategies and better targets for future therapies.

Figure 2: Baseline characteristics in responders and non-responders. (* $p < 0.05$)



60 RISK FACTORS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN AND ADOLESCENTS.

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Introduction: Functional gastrointestinal disorders (FGIDs) are common in children, Better knowledge of the risk factors associated with the development of FGIDs may help understand their pathophysiology and design treatment and prevention strategies.

Objective: To identify possible risk factors for FGIDs in a children and adolescents from Colombia.

Methods: Children and adolescents from public and private schools in four Colombian regions completed the Spanish version of the Questionnaire of Pediatric Gastrointestinal Symptoms (Rome Criteria III). Demographic, socioeconomic, family data (separated/divorced parents, single child, family history of FGIDs) and past medical history of dengue from children with and without FGIDs were compared. Uni and multivariate analyses and multiple logistic regression (ORs and 95% CI) were calculated. Significance was set at $p < 0.05$.

Results: 4218 school children ($n=2609$) and adolescents ($n=1609$) 80.5% public schools completed the surveys. Age 11.9 ± 2.3 years, 52.6% male. 23.0% of children were diagnosed with at least one FGID. FGIDs were significantly more common in children of prepuberal age (schoolchildren between 8 and 12 years) (OR = 1.30 CI 95% = 1.11-1.51 $p = 0.0006$), female gender (OR = 1.19 95% CI = 1.03-1.38 $p = 0.0155$), children attending private schools (OR = 1.54 CI 95% = 1.29-1.83 $p = 0.0000$), children of separated/divorced parents (OR = 1.19 95% CI = 1.02-1.39 $p = 0.0194$) and children with a previous history of dengue (OR = 2.95 95% CI = 1.54-2.59 $p = 0.0000$).

Conclusions: In children and adolescents of Colombia, prepuberal age, female gender, attending a private school, having separated/divorced parents and the antecedent of previous dengue infections are associated with the diagnoses of FGIDs. Large prospective studies should confirm our findings

63 GASTROINTESTINAL SYMPTOMS AND CONTINENCE IN PATIENTS WITH PHELAN MCDERMID SYNDROME.

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Objective: To characterize the nature and frequency of gastrointestinal issues and incontinence in a cohort of patients with Phelan McDermid Syndrome (PMS), a rare condition associated with genetic variants of chromosome 22q13 and SHANK3.

Methods: Seventeen patients (47% female, median age 11 years) participating in a natural history study of PMS at the National Institutes of Health completed a standardized evaluation, including detailed history related to toilet training and continence. Eleven participants completed a Sitz marker study to evaluate gastrointestinal motility and rectal outlet dysfunction. All participants also completed standardized neurocognitive testing and characterization of 22q13 deletion. In addition, patient data were obtained from the Phelan McDermid Syndrome Data Network (PMS_DN). Parents of 363 individuals with PMS answered multiple choice survey questions related to GI symptoms and toilet training.

Results: In the NIH cohort, GI symptoms were relatively common, with 76% reporting ever taking GI medication and 53% currently on GI related medication. Common current complaints were abdominal pain (50%), constipation (35%), difficulty swallowing (29%), choking or gagging (29%), gastroesophageal reflux (GERD) (24%), and vomiting (6%). Primary incontinence of urine and stool was present in 65%. Despite the high frequency of primary incontinence, toilet training was still a goal for 47% of parents at the time of consultation. Those with primary incontinence had a significantly larger deletion size (mean: 4743 kb vs. 1577 kb, $p=0.028$)*, a significantly lower mean Non-verbal Mental Age (NVMA) (13 vs. 35.6, $p=0.007$), and a lower mean Full-Scale IQ/Developmental Quotient (9.3 vs. 39.1 $p=0.004$) compared to those with continence of urine and stool. Two of the eleven participants who completed a Sitz marker study had abnormal retention of markers consistent with rectal outlet dysfunction, but without evidence of global dysmotility.

We found similar common conditions represented in the PMS data network. The most common symptoms reported were GERD (40%), difficulty swallowing (29%), constipation (25%) and gagging (23%). In addition, parents' reports of problems with vomiting (22%) and abdominal pain (17%) were common. Thirteen percent of participants in the network were toilet trained at night, and 11% were toilet trained during the day. An additional 13% reported partial toileting during the daytime.

Summary: GI symptoms and primary incontinence are common among patients with PMS. Ability to partially and/or reliably toilet train for urine and stool is closely associated with measures of verbal and cognitive function and may be related to size of 22q13 deletion. These data may offer healthcare providers and parents with information needed to optimize daily symptom management and guide appropriate goals for toileting.

*Comparisons with deletion size excluded two patients with nondeletion mutations of SHANK3

Acknowledgments:

Data used in the preparation of this abstract were obtained from the Phelan-McDermid Syndrome International Registry (PMSIR) version dated 3/1/17.

65 **PEDIATRIC OUTPATIENT INTENSIVE FEEDING THERAPY: A TERTIARY CENTER'S EXPERIENCE**

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Introduction: Feeding problems are common in childhood with up to 40% of toddlers and young children displaying some difficulty with meals. Usually these behaviors ultimately resolve, however 3% to 10% of children develop chronic feeding disorders, with texture aversion and sensory problems. This in turn may impact their developmental or medical outcome. Many of these children require alternative nutritional support, such as with gastric feeding tube (G-tube) placement. Studies have demonstrated the efficacy of inpatient and outpatient childhood feeding programs. Our study focused on identifying underlying gastrointestinal (GI) etiologies uncovered prior to enrollment in our outpatient feeding center. In addition, we also reviewed outcomes of children with G-tubes who were enrolled in the program.

Methods: We retrospectively reviewed medical records of 52 patients that completed a 4-week intense feeding program for feeding difficulties within the last 5 years. Children enrolled in the program met specific criteria, including total or significant food refusal, texture aversion, limited food selectivity, nutritional supplement dependence, and being nutritionally compromised, among other criteria. Our program is supervised by two pediatric gastroenterologists, and involves dietitians, occupational, behavioral, and speech therapists. Patients underwent a multidisciplinary evaluation and thorough pertinent investigation for underlying etiologies, including endoscopies, laboratory studies, allergy testing, gastric emptying scan, pH impedance study, oropharyngeal motility studies, and radiographic imaging. We report underlying GI conditions found in this cohort. We also reviewed medical records of 18 participants with G-tubes who completed the program. We identified two main categories: (1) Those who were weaned completely off G-tube feedings and (2) Those who were partially weaned from G-tube feedings. Weaning from G-tube feeding was considered successful based on adequate oral intake of calories versus the amount of calories needed from G-tube feedings.

Results: The majority of enrolled patients were males (79%). Average age was 4.78 ± 2.83 years. Thirty-nine children underwent esophagogastroduodenoscopy. Half (20) of them showed abnormal esophageal pathology with the majority showing changes suggestive of esophagitis and 2 (5%) had eosinophilic esophagitis. Gastric pathology was abnormal in 7/39, mainly with findings of inactive chronic gastritis. Duodenal biopsies were normal in 92% of the cases. Lactase deficiency was present in 17/39. Microbial overgrowth was found in 17 of 22 who had duodenal culture. Gastric emptying scan was done in 28 patients with 5 showing gastroparesis and 1 dumping syndrome. Eighty percent of the patients had constipation at enrollment. Forty underwent ImmunoCap testing and 21 were abnormal. Fourteen were on allergy medications. pH/impedance studies were done in 18 children and 13 showed abnormal reflux patterns (acidic and/or volume). Proton pump inhibitors were prescribed in 33 (63%) and H₂-blockers in 16 (30%). A prokinetic agent was used in 23 (44%) children.

18 children (35%) had G-tubes for nutritional support. Of this cohort, 15 of them (83%) were receiving > 50% of their required daily calories via G-tube feedings at the beginning of the program. By the end of the 4-week program, 11 children (61%) were consuming 100% of their caloric needs by mouth, and were off G-tube feedings. Every child with G-tube had improvement in their oral caloric intake by at least 20% by the end of the program.

Conclusion: Gastrointestinal organic etiologies are common in children with feeding difficulties and should always be considered prior to enrollment into an intense feeding program. Both inpatient and outpatient feeding programs are efficacious in treating children with chronic feeding problems. Our experience serves as further evidence that intensive outpatient feeding therapy is also highly successful in helping to wean children from nutritional support via G-tube.

66 **THE ROLE AND MECHANISM OF PROTEIN TYROSINE PHOSPHATASE RECEPTOR R (PTPRR) IN THE DEVELOPMENT OF ENTERIC NERVOUS SYSTEM AND ITS MULTIPOTENT PROGENITOR.**

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Background: Hirschsprung disease (HSCR) is the most common identifiable developmental disorder of the enteric nervous system (ENS). Recent efforts are to identify HSCR susceptibility genes as well as to unravel cellular and molecular events underlying ENS development. However, the specific mechanisms have not yet been fully elucidated.

Aim: To explore the role and mechanism of HSCR associated PTPRR (protein tyrosine phosphatase receptor-type R) in the development of ENS and its multipotent progenitor.

Methods: Genetic intervention technique was employed to explore the role of protein PTPRR in biological function of ENCCs (enteric neural crest cell) and the development of ENS.

Results: 1. After transfected, PTPRR mRNA and protein level were significantly increased in Adv-PTPRR Exp-RNA ENCCs in comparison to the control vector or blank control group; PTPRR mRNA and protein level of Adv-PTPRR shRNA ENCCs were significantly lower than that in control vector or blank control group. 2. The ENCCs remained undifferentiated in Adv-PTPRR Exp-RNA group, with significantly decreased TUJ1- or GFAP-positive immunofluorescence and increase EdU-positive immunofluorescence. In comparison in Adv-PTPRR shRNA group, apparently differentiated ENCCs had significantly increased TUJ1- or GFAP-positive immunofluorescence and decreased EdU-positive immunofluorescence 3. ENS development was stunted in Adv-PTPRR shRNA group but not affected in Adv-PTPRR Exp-RNA and control groups. 4. GDNF activated ERK1/2 expression was decreased significantly as reflected by western-blot or immunofluorescence analyses after genetic modulation in Adv-PTPRR Exp-RNA group while it was increased significantly in Adv-PTPRR shRNA group.

Conclusions: The differential expression of PTPRR was related to proliferation and differentiation of ENCCs. Our results confirmed the important role of PTPRR in maintaining multipotent ENS precursor cells, established the PTPRR proteins as negative regulators of MAPK/ERK1/2 signaling cascades in neuronal differentiation and demonstrated their involvement in pathophysiology of HSCR.

67 **NONINVASIVE DETECTION OF COLORECTAL ACTIVITY BY EMG AND ELECTRICAL BIOIMPEDANCE**

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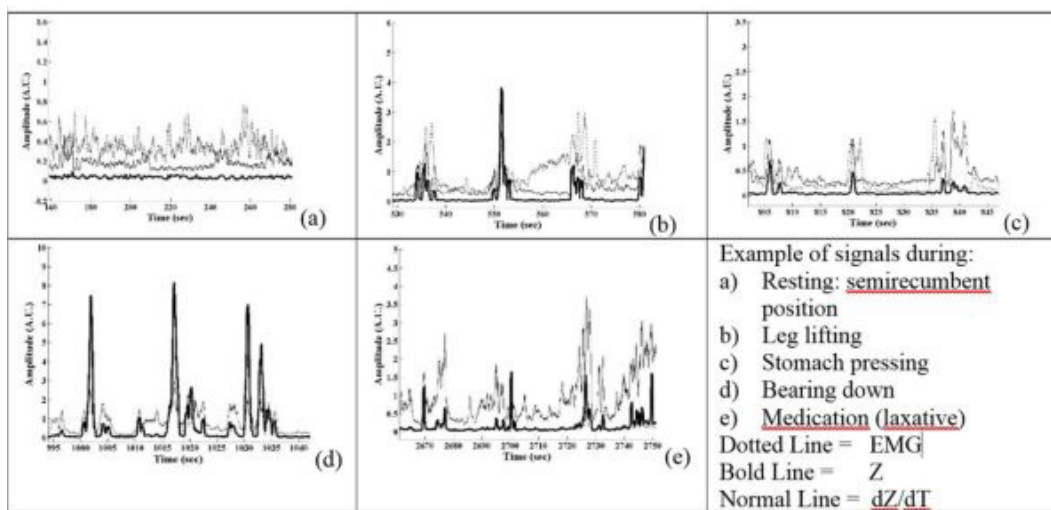
Electrical bio-impedance (EBI) technique measures internal resistance to the flow of electrical currents, specifically for the case of alternate currents. Any change in internal configuration of density, material content, fluid conductivity, or conformation is detected through the change in the impedance of that region. Surface (noninvasive) EBI technique is used in the measurement of cardiac output, body composition, respiratory monitoring, and gastric motility among other applications. We evaluated the use of EBI with surface electrodes in a non-invasive configuration to assess the distal colon and rectum in combination with EMG recordings.

Body movement artifacts are analyzed to discriminate from intrinsic bowel activity. Fixed alternating current of less than 1mA

	EMG vs. Z	EMG vs dZ/dT	Z vs dZ/dT
Resting	0.05	0.04	0.63
Leg lifting	0.24	0.44	0.59
Stomach pressure	0.34	0.24	0.58
Bearing down	0.84	0.51	0.62
Stimulant laxative	0.71	0.24	0.41

and of 50 KHz frequency was applied to the pelvic region in a configuration meant to maximize generation of equipotential line/electrical field across the rectum. This preliminary, preclinical study included measurements at rest in a semi-recumbent position, and during hip flexion, external stomach pressure, bearing down, and ingestion of a stimulant laxative medication. Analysis of the EMG signal, impedance (Z), and the derivation of the impedance (dZ/dT) was performed by filtering, averaging and variability analysis, considering averaging and standard deviation (SD) for discrete periods. Results support the conceptual framework

of colorectal electrical bioimpedance, and demonstrate differences between EMG and EBI activity under various conditions (see Table and Image). Further validation of these methods will be performed to improve event discrimination and maximize data acquisition and quality. Correlations among measured signals (mean)



68 ANTRAL MOTILITY IN IDIOPATHIC GASTROPARESIS. *Jacob Wang, Shazia Malik, Khalil El-Chammas, Ajay Kaul. Gastroenterology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH*

Background: Gastroparesis is a syndrome of objectively delayed gastric emptying in the absence of a mechanical obstruction. While pediatric case series have described postprandial antral hypomotility (PPAH) in diabetic and postviral gastroparesis, there is no data available regarding gastric motility in pediatric patients with idiopathic gastroparesis.

Objective: To evaluate antral motility (AM) in pediatric patients with idiopathic gastroparesis.

Methods: The database of a tertiary pediatric referral center was screened to identify all children with delayed gastric emptying of solids on scintigraphy without an identifiable cause and who had also underwent antro-duodenal manometry testing using a water perfused system performed according to published standard protocol.

Results: Of 33 patients identified, 66% were female with a mean (SD) age of 10.3 (+/- 5.2) years. Of these 33 patients, 22 (67%) had normal AM as evidenced by increased antral motor activity after feeds and IV erythromycin. PPAH (no increase in antral motor activity after feeds) was observed in 12 (36%) patients and all except one responded to erythromycin.

Conclusion: There is a female preponderance in children with idiopathic gastroparesis similar to adults. In contrast to published data in adults, AM is preserved in the majority of children with idiopathic gastroparesis and PPAH is seen in only a third. Our study highlights the virtue of providing targeted therapy by performing manometry to identify the subset of children with PPAH who respond to erythromycin.

69 SACRAL NERVE STIMULATION OR ANTEGRADE CONTINENCE ENEMA TREATMENT FOR CHILDREN WITH INTRACTABLE CONSTIPATION AND FECAL INCONTINENCE? *Mana Vriesman^{2,1}, Peter Lu², Karen Diefenbach³, Seth Alpert⁴, Marc Benninga¹, Karla Vaz², Desale Jacob², Carlo Di Lorenzo². ¹Department of Gastroenterology and Nutrition, Emma Children's Hospital / Academic Medical Center, Amsterdam, Netherlands; ²Division of Gastroenterology, Hepatology and Nutrition, Nationwide Children's Hospital, Columbus, OH; ³Department of Surgery, Nationwide Children's Hospital, Columbus, OH; ⁴Division of Urology, Nationwide Children's Hospital, Columbus, OH*

Background: Treatment options for children with intractable functional constipation (FC) and fecal incontinence (FI) are limited and include sacral nerve stimulation (SNS) and antegrade continence enema (ACE) treatment. No studies have compared these two treatments. The objective of this study was to compare the efficacy of SNS and ACE treatment for children with intractable FC and FI.

Methods: We performed a retrospective cohort study. We included children 6-18 years old with FC based on Rome IV criteria and FI who were treated with either SNS or ACE at our institution from 2012-2016. We excluded children with organic causes of constipation or with prior abdominal surgery. We recorded demographic information, medical history, and symptoms at baseline, 6 months, 12 months, 24 months, and at the most recent visit after starting SNS or ACE treatment. We compared improvement in FI, bowel movement (BM) frequency, abdominal pain, and oral laxative use at each follow up time point between patients treated with SNS and ACE. We also recorded complications.

Results: We included 19 patients treated with SNS (74% female, median age 10 years at initiation, range 7-16) and 23 patients treated with ACE (52% female, median age 10 years, range 6-17). The most recent visit was a median of 25 months (range 4-52) after treatment initiation. All patients had symptoms of FC for >12 months (median 66 months) and were treated with oral laxatives before SNS or ACE. Patients who received the ACE were more likely to have been treated with rectal enemas (87% vs. 5%, $p<0.001$). Patients who received the SNS were more likely to have urinary symptoms (95% vs. 30%, $p<0.001$). As shown in Table 1, improvement in FI was greater for patients treated with SNS than ACE at 12 months ($p=0.03$) and 24 months ($p=0.06$). Improvement in BM frequency was significantly greater for patients treated with ACE than SNS at all time points (all $p<0.05$). At the most recent visit, 82% of SNS patients had >2 BMs per week versus 100% of ACE patients ($p=0.04$). Improvement in abdominal pain was greater for patients treated with ACE than SNS at 24 months and at the most recent visit (both $p<0.05$). Patients treated with ACE were also more likely to be able to discontinue laxative use at all time points (all $p<0.01$). At the most recent visit, 84% of SNS patients remained on oral laxatives versus 48% of ACE patients ($p=0.01$). The number of patients who had complications requiring further surgery was similar between SNS and ACE groups (26% vs. 22%, NS), but overall complications were more common in the ACE group ($p<0.01$).

Conclusion: In the first comparison of SNS and ACE, we found that both SNS and ACE led to durable improvement in FC and FI symptoms. SNS was more effective in treating FI, but ACE led to greater improvement in BM frequency. Prospective studies are needed to determine the optimal treatment strategy for children with intractable FC and FI.

Table 1: Number of patients with >1 episode of FI per week at baseline and follow up.

	SNS (n= 19)	ACE (n= 23)	p-value
	n (%)	n (%)	
Baseline	19 (100%)	23 (100%)	1.00
6 months	7 (38.9%)	10 (43.5%)	0.77
12 months	1 (7.1%)	9 (42.9%)	0.03*
24 months	0 (0%)	6 (33.3%)	0.06
Most recent visit	2 (11.8%)	7 (30.4%)	0.26

*p

70 COLONIC MUCOSAL EOSINOPHILIA IN CHILDREN. Meenal Singh^{1,2}, Vivek Singh², Craig Friesen¹.

¹Gastroenterology, Children's Mercy Hospital, Overland Park, KS; ²Pathology, Children's Mercy Kansas City, Kansas City, MO

Background: Increased mucosal eosinophils (eos) in the colon is a finding that is increasingly encountered in biopsies of children undergoing endoscopic evaluation for common gastrointestinal complaints. We and others have previously reported the association of colonic mucosal eosinophilia (CME) in children who ultimately have inflammatory bowel disease (IBD). However, a significant proportion of children with CME do not develop IBD. The relative frequencies of various etiological factors and the clinical presentation of children with CME who do not develop IBD is not well known.

Objective: Our objective was to study children with CME who do not have IBD, in order to understand their clinical presentation, relative frequency of etiological associations and the distribution of eos in various regions of colon.

Methods: We undertook a retrospective analysis of histopathological, laboratory and clinical data of children who underwent endoscopic biopsies at our institution. Pathology records were searched using key words "colon," "mucosa" and "eos". We selected consecutively appearing cases if their laboratory and histopathology result did not indicate IBD. Laboratory data such as elevated ESR and CRP along with high fecal calprotectin; histopathology data such as architectural distortion, basal plasmacytosis, granulomata, neutrophilic cryptitis and neutrophilic crypt abscess were used to exclude cases from the study. We identified 79 patients who ranged in age from 1 to 17 years. Histology data, which reported the peak eos density as eos counts/high power field was used to identify the affected colonic regions from sampled sites.

Results: The frequency of abdominal (abd) pain, diarrhea, constipation and blood in stools in the study patients is shown in table. There were 20 patients (25.3%) who had allergies to different foods including milk, formula, fruits, nuts, vegetables and seafood. Lactase deficiency was present in 10 (12.7%), asthma in 8 (10.1%), autoimmune diseases in 3 (3.8%), pinworm infestation in 2 (2.5%), cystic fibrosis in 1 (1.3%) and celiac disease in 2 (2.5%) patients. Although hypereosinophilia syndrome was not seen, 7 (8.9%) patients had increased eos in their blood. Histologically, only two (2.5%) patients had eos in the crypt epithelium or crypt lumen, whereas all patients had increased eos in the lamina propria. There were 13 patients with eos elevated in only one region of colon, 32 showed elevated eos in 2 regions, 28 in 3 regions, and 6 patients in 4 regions. The patients with diarrhea and constipation were similar in that the proximal and distal colons were almost equally affected by increased eos.

Conclusion: Allergies and parasite infestation, the well-known etiological agents of mucosal eos accounted for only 38% of patients with CME in our study. Remarkably, lactase deficiency was noted in 12.7% patients. Management of patients with CME could pose a dilemma if known etiological agents are not present.

Table. Symptoms & Signs in 79 patients (%age)

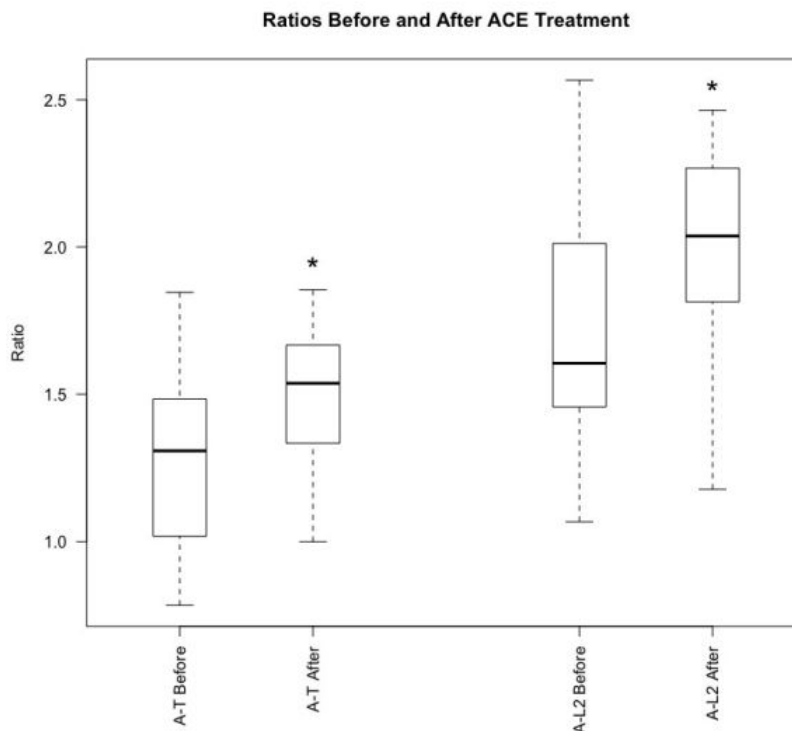
Abd Pain	63 (79.7)
Diarrhea	26 (32.9)
Blood in stool	20 (25.3)
Constipation	38 (48.1)
Abd pain + Diarrhea	20 (25.3)
Abd pain + Constipation	31 (39.2)

71 PROXIMAL COLONIC DILATION AFTER ANTEGRADE CONTINENCE ENEMA TREATMENT IN CHILDREN WITH SEVERE CONSTIPATION. Mhd Louai Manini^{1,4,5}, Peter Lu⁴, Benjamin Thompson², Ilan Koppen³, Karla Vaz⁴, Desale Yacob⁴, Carlo Di Lorenzo⁴. ¹Pediatric Gastroenterology, Hepatology, and Nutrition, Mayo Clinic, Rochester, MN; ²Pediatric Radiology, Nationwide Children's Hospital, Columbus, OH; ³Pediatric Gastroenterology and Nutrition, Emma Children's Hospital, Amsterdam, Netherlands; ⁴Pediatric Gastroenterology and Nutrition, Nationwide Children's Hospital, Columbus, OH; ⁵Center of Enteric Neuroscience Translational and Epidemiological Research (C.E.N.T.E.R.), Mayo Clinic, Rochester, MN

Background: Antegrade continence enemas (ACE) are an established treatment option for children with severe constipation refractory to conventional treatment. However, the physiologic effects of long-term ACE treatment are not well understood. The objective of this study is to evaluate whether ACE treatment leads to structural changes of the colon in children with severe constipation. We hypothesized that ACE treatment can lead to dilation of the proximal colon.

Methods: We performed a retrospective review. We included children up to 18 years of age with severe constipation who were treated with ACE and who had contrast enema studies performed before and after initiation of ACE treatment. We recorded information on demographics, medical history, and clinical symptoms before ACE treatment and at the time of follow up contrast enema studies. A pediatric radiologist and a gastroenterologist reviewed each contrast enema study. We recorded ratios of the width of the ascending colon to the widths of the transverse colon and L2 vertebra. We compared ratios and symptoms recorded before and after ACE treatment.

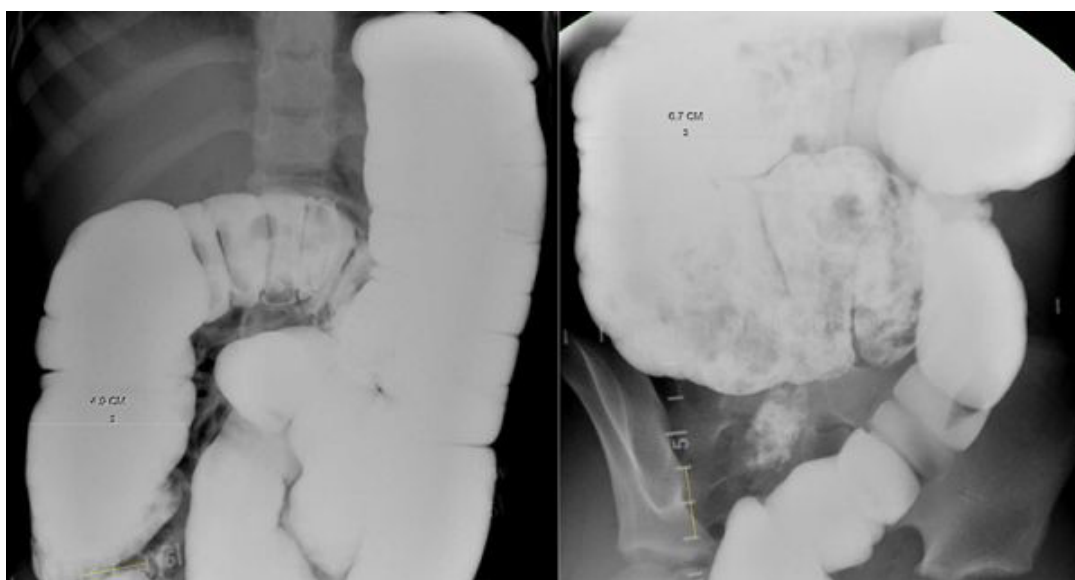
Results: We included 24 patients in our study (58% female, median age 7.5 years at time of ACE initiation, range 2-18 years): 5 had a history of anorectal malformation



Box and whiskers plot comparing ratios of ascending colon diameter to transverse colon diameter (A-T) and ascending colon diameter to L2 vertebral body diameter (A-L2) before and after ACE treatment. (*) indicate P<0.05

and 2 had a history of spinal cord abnormality. At baseline, patients had bowel movements 3 (IQR 2-6.25) times per week, and 95% (21/22) reported fecal incontinence, 67% (14/21) reported abdominal pain, and 43% (10/23) reported urinary incontinence. Twelve patients (50%) received cecostomy placement, 11 Malone appendicostomy, and 1 initial cecostomy and subsequent Malone appendicostomy. All patients were treated with daily ACE flushes consisting of saline and either bisacodyl or glycerine. The ratio of ascending colon to transverse colon width was 1.31 before ACE (IQR 1.04-1.48) and increased to 1.54 after ACE treatment (IQR 1.36-1.66, $p < 0.001$). The ratio of ascending colon to L2 vertebral width was 1.61 before ACE (IQR 1.48-1.99) and increased to 2.04 after ACE treatment (IQR 1.81-2.26, $p < 0.05$). Follow up contrast enema studies were performed a median of 26.5 months (IQR 15.5-32.5) after the baseline contrast enema and 17 months (IQR 12.75-28.25) after ACE initiation. At the time of follow up contrast enema, patients reported bowel movements 7 times per week (IQR 7-7, $p < 0.01$), and 38% (9/24) reported fecal incontinence ($p = < 0.05$), 42% (10/24) reported abdominal pain (NS), and 17% (4/24) reported urinary incontinence ($p < 0.001$).

Conclusion: In our study of children with severe constipation treated with ACE, we found a significant increase in ascending colon width after ACE treatment relative to both the transverse colon and L2 vertebra. Children experienced improvement in constipation symptoms after ACE treatment. Further studies are needed to understand the impact of proximal colon dilation on response to ACE treatment and clinical outcomes, particularly in the long term.



Barium contrast studies in a 7 year old patient before (left) and 14 months after ACE treatment (right). Note the increase in ascending colon diameter from 49 to 67 mm.

74 **ABDOMINAL MIGRAINES: ASSESSING STANDARDIZATION OF DIAGNOSIS AND TREATMENT.** Shivani Gupta, Kathryn Hawa, Miguel Saps. *Pediatrics, Nationwide Children's Hospital, Columbus, OH*

Background: Abdominal migraine (AM) is the least prevalent (<1%) of all functional abdominal pain disorders (FAPDs). Although the Rome criteria defines AM as a functional gastrointestinal disorder, neurologists may care for children with AM. There are no evidence-based guidelines for children with AM and there have not been any clinical trials for treatment in the last 20 years. Due to low prevalence of this disorder, lack of management guidelines and dearth of clinical trials, the management of AM is likely heterogeneous.

Aim: To review the diagnostic process and management of AM in a single institution.

Methods: The charts of all children 1-18 years of age seen at a major Midwest pediatric hospital with the diagnosis of AM (ICD-9 abdominal migraine, abdominal migraine intractable and abdominal migraine non-intractable, ICD-10 variants of migraine, not elsewhere classified, without mention of intractable migraine without mention of status migrainosus) seen between 2011-2017 were reviewed for accuracy of AM diagnosis, testing and treatment. 69 charts were identified.

Results: Mean age at diagnosis was 9.7 years, 48% females. 50/69 (72.4%) were seen by GI, 10/69 cases (14.5%) by neurology, 6/69 (8.7%) by GI but later referred to neurology who made the diagnosis, 2/69 (2.9%) were seen by neurology and GI but the diagnosis was made by GI and 1/69 (1.5%) was diagnosed by a pediatrician. Children diagnosed by neurology were younger (mean age 8 years, range 6-12 years) than those diagnosed by GI (mean age 10 years, range 6-14 years) (p -

0.0038, CI -3.14 to -0.63). 3/10 (30%) diagnosed by neurology did not have abdominal pain while all children diagnosed by GI did ($p=0.0035$). 16/50 (32%) of children diagnosed with AM by GI and 3/10 (30%) of children diagnosed by neurology met Rome III/IV criteria (compared with updated criteria at diagnosis) ($p=1.0$). 9/50 (18%) diagnosed by GI did not have documentation commenting on all criterions of the Rome III/IV criteria so no conclusion was made. 25/50 (50%) seen by GI did not meet the Rome criteria. 1/1 (100%) diagnosed by a pediatrician did not meet Rome criteria. All patients were treated. The most common drugs used by GI were Cyproheptadine and Promethazine. The most common used by neurology were Cyproheptadine, Amitriptyline and Sumatriptan. Treatment did not differ between those with/without abdominal pain. 8/16 (50%) seen by neurology showed improvements in symptoms while 33/52 (63.5%) diagnosed by GI improved. 6/16 (37.5%) neurology patients and 16/52 (30.8%) GI patients have not had follow up appointments. 2/16 (12.5%) neurology patients and 3/52 (5.8%) GI patients did not have improvements in their symptoms. GI physicians mentioned the Rome criteria in 5/50 charts, whereas no neurology charts mentioned it.

Conclusion: This study showed that a large number of diagnoses made by neurology did not have documented abdominal pain even though abdominal pain is a significant component of the Rome III/ IV criteria. In comparison, GI patients were all found to have abdominal pain charted. However, only a third of patients analyzed met criteria for Rome III/IV when diagnosed by GI or neurology. Even less mentioned the Rome criteria. Education on the diagnosis of AM using Rome criteria should be encouraged.

INFLAMMATORY BOWEL DISEASE

- 76 **PREVALENCE OF CHRONIC OPIOID USE AMONG ADOLESCENTS AND YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE.** Anava Wren¹, Rachel Bensen¹, Helen Yu¹, Jessie Wong², Donna MacIsaac^{1,3}, Zachary Sellers¹, Cindy Kin³, KT Park¹. ¹Department of Pediatrics, Stanford University, Palo Alto, CA; ²Department of Medicine, Stanford University, Palo Alto, CA; ³Department of Surgery, Stanford University, Palo Alto, CA

Background: Given the opioid epidemic in the United States (US), opioid use among individuals with Inflammatory Bowel Disease (IBD) has become a topic of increasing importance. In IBD management, opioids are typically prescribed for temporary pain relief (e.g., post-surgical pain). However, emerging evidence in tertiary care clinics has shown that a subset of patients with IBD are chronic opioid users, and that adolescent and young adult (AYA) populations are at particular risk. The prevalence of chronic opioid use among AYAs has not been examined over time in a nationally representative sample. The aim of this study was to examine trends in the prevalence of chronic opioid use in AYAs with IBD in the US.

Methods: A large private insurance claims database (Truven Health MarketScan Database) was analyzed from years 2007-2015. Study criteria included patients 15-29 years old with: 1) 2 or more IBD diagnoses (Crohn's – 555.xx/K50.xx, UC – 556.xx/K51.xxx); 2) 2-year minimum of continuous enrollment. A patient was classified as having chronic opioid use if s/he had at least 3 separate opioid drug claims within a 2-year rolling window. Opioid drug claims within 30 days of a major abdominal operation were excluded. To account for fluctuations in total Truven enrollment, chronic opioid use was represented using a standardized index score (total opioid drug claims per year divided by the total number of members in each year that met criteria for chronic opioid use). Analyses were performed using Stata. Multivariate logistic regression examined differences between patients with and without chronic opioid use.

Results: The study cohort consisted of 54,528 IBD patients; 23.78% (20.26% M, 27.00% F) met criteria for chronic opioid use from 2007-2015. The proportion of the sample meeting criteria for chronic opioid use increased from 6.8% in 2007 to 9.0% in 2015. Opioid prescriptions per patient per year increased from 5.78 in 2007 to 6.70 in 2015. Older age ([20-24]: OR, 1.26; 95% CI, 1.20, 1.34; [25-29]: OR, 1.46; 95% CI, 1.38, 1.54), and having a history of surgery (OR, 2.07; 95% CI, 1.93, 2.22) and chronic pain (OR, 10.45; 95% CI, 9.36, 11.67) were significantly associated with a higher risk for chronic opioid use. Being male (OR, 0.72; 95% CI, 0.69, 0.75) and having UC (OR, 0.74; 95% CI, 0.68, 0.80) were associated with a lower risk for chronic opioid use.

Conclusion: This study highlights that approximately one fourth of AYAs in a nationally distributed sample met criteria for chronic opioid use between 2007-2015. Results demonstrated an upward trend in opioid prescriptions per patient per year in the sample. In 2015, AYA patients with IBD received almost seven opioid prescriptions on average. Findings underscore the increasing prevalence of opioid use among AYAs with IBD. These results are noteworthy given the risks of long-term opioid use on addiction, IBD-related complications, and mortality. Research is needed to further explore risk factors of chronic opioid use among AYAs with IBD, as well as interventions to address this problem.

77 **YOGA FOR YOUTH WITH INFLAMMATORY BOWEL DISEASE: A PILOT FEASIBILITY STUDY.**

Jenna Arruda², Alyssa Bogetz², Anava Wren¹, Srisindu Vellanki², Ann Ming Yeh¹. ¹*Pediatric Gastroenterology, Stanford University, Stanford, CA;* ²*Department of Pediatrics, Stanford University, Stanford, CA*

Background: Current standard of care treatment for inflammatory bowel disease (IBD) addresses the inflammatory process of IBD. However, IBD patients identify stress as a disease-exacerbating factor, evidenced by psychosocial stressors triggering IBD flares, comorbid mood disorders, and irritable bowel symptoms concurrent with quiescent IBD. Thus, a need for further mind-body interventions for IBD treatment. Yoga has been shown to improve pain and quality of life in youth with irritable bowel syndrome, but no published studies to date have investigated yoga for youth with IBD. This study aimed to determine whether an 8-week yoga intervention is a feasible and beneficial adjunct therapy to the medical standard of care for adolescents with IBD.

Methods: Nine adolescents between the ages of 11-16 with IBD were enrolled in this pilot IRB-approved clinical trial. The intervention consisted of 3 1-hour in-person yoga classes and 3 30-minute online yoga videos per week for 8 weeks. At the study's start and conclusion, participants provided a stool sample for calprotectin measurement and completed the PROMIS-37 pediatric profile to measure well-being (e.g., pain interference, anxiety). Participants also completed a satisfaction survey and participated in a 1-hour focus group at the end of the study to explore their experiences and attitudes towards yoga as a therapeutic intervention for IBD. Focus group data were thematically analyzed through an iterative inductive approach using conventional content analysis.

Results: Nine adolescents participated in the study (M=14.1 years; SD = 2.1). Eight were female; 8 had Crohn's disease and 1 had Ulcerative Colitis. Eight participated in one or more yoga videos per week and all 9 attended at least 2 in-person yoga classes. Of the 8 who participated in the online classes, 7 reported the quality of the video instruction as "good" or "excellent." Eight reported the quality of the in-person yoga instruction as "good" or "excellent." Focus group themes revealed several benefits of participating in online and in-person yoga, including feeling less stressed and more relaxed and aware of one's body and physical needs. In-person yoga classes were preferred by most patients due to the benefit of having live feedback and distraction-free, protected time to participate in yoga. Given the small sample size, there was not enough power to detect statistical significance in calprotectin or PROMIS measures. However, preliminary data demonstrated an improved calprotectin value after the intervention, with a positive mean change score of 226. Pain interference also improved, with a positive mean change score of 2.74.

Conclusion: Yoga is a feasible and safe adjunct therapy for adolescents with IBD. Qualitative data demonstrated high acceptability of the intervention, and patients reported increased relaxation and less stress. A larger, randomized study is necessary to determine if the yoga protocol results in clinically and statistically significant improvements in inflammatory biomarkers and patient reported outcomes in adolescents with IBD.

78 **SELECTIVE LACTASE DEFICIENCY IS COMMON IN PEDIATRIC PATIENTS UNDERGOING UPPER ENDOSCOPY.** Annie Goodwin, Lina Karam, Gopal Gopalakrishna, Richard Kellermayer. *Pediatric Gastroenterology, Hematology, and Nutrition, Baylor College of Medicine, Houston, TX*

Background: Lactase deficiency can lead to significant symptoms in the pediatric population, which in the IBD (inflammatory bowel disease) patient can mimic a disease flare. To date, few studies have examined the prevalence of enzyme testing based lactase and other disaccharidase deficiencies (DDs) in pediatric patients undergoing upper endoscopic evaluation.

Aim: The primary objective of this study was to determine the prevalence of selective lactase and other DDs amongst a large cohort of pediatric patients with and without IBD.

Methods: A chart review was performed on 739 patients who underwent EGD between April 2010 and August 2016. Demographic data and presenting symptomatology were recorded along with mucosal enzyme testing results. Statistical analysis was performed comparing rates of lactase deficiency amongst various population groups including IBD vs. non-IBD patients.

Results: A total of 560 underwent mucosal enzyme testing at the time of their EGD. The overall rate of lactase deficiency was 39% (ages 1-18yrs). Lactase deficiency positively correlated with age ($p=0.00017$), but there was no significant difference between age matched IBD and non-IBD patients (45% vs. 42% $p=0.68$). Four patients (0.17%) were found to have selective maltase deficiency. No selective sucrase or palatinase deficiency was identified. Statistically significant differences occurred in lactase deficiency amongst patients of different races.

Conclusions: Lactase deficiency is a relatively common finding in pediatric patients undergoing EGD though at no increased rate amongst the IBD patient population. Routine testing for disaccharidases is recommended in pediatric gastroenterology practice, beginning at 1 year of age.

79 PATIENT ENGAGEMENT IN RESEARCH: USING THE JAMES LIND ALLIANCE PROCESS TO IDENTIFY THE TOP 10 UNANSWERED QUESTIONS IN PEDIATRIC IBD. Anthony Otley^{1,2}, Anne Griffiths³, Amanda Hood², Melissa Crane², Kate Murray⁴, Marie-Josée Trempe⁵, Muneet Maghera⁴, Malcolm Mann⁴, Cheryl Kluthe⁶, Melissa Mansi⁴, Andreas Laupacis⁷, Amy Grant². ¹Pediatrics, Dalhousie University, Halifax, NS, Canada; ²Pediatrics, IWK Health Centre, Halifax, NS, Canada; ³Pediatrics, SickKids, Toronto, ON, Canada; ⁴Canadian Children's IBD Network (CIDsCANN), Toronto, ON, Canada; ⁵Pediatrics, Montreal Children's Hospital, Montreal, QC, Canada; ⁶Pediatrics, Stollery Children's Hospital, Edmonton, AB, Canada; ⁷Medicine, St Michael's Hospital, Toronto, ON, Canada

Background: With increasing emphasis among health care providers and funders on patient-centered care, it follows that patients and their caregivers should be included when priorities for research are being established. This study sought to identify the most important unanswered uncertainties/questions about pediatric inflammatory bowel disease (IBD) from the perspective of pediatric patients, their caregivers, and the health care professionals who care for these patients.

Methods: The priority setting methodology, developed by the James Lind Alliance, involved four key stages: gathering research questions; checking these against existing evidence; interim prioritization; and a final consensus meeting during which the top ten unanswered research questions were agreed using modified nominal group methodology. The research was led by a national steering committee composed of clinicians, patients and parents of children with IBD. Research uncertainties were identified through an online national Canadian survey of pediatric IBD patients, their caregivers, and health care professionals.

Results: 366 participants completed an online survey, eliciting 1209 raw questions. Once similar questions were combined, 626 unique questions were identified. These were reduced to 388 after eliminating out of scope and already answered questions (according to the literature and content experts), and through a qualitative analysis delineated into 17 themes. From this list, 78 indicative questions were derived by the steering committee, together with 32 questions from clinical practice guidelines. After an online, national vote, a list of the 30 most highly ranked questions via weighted scores were tabulated. This list was further reduced to 19 questions and subsequently discussed at a priority setting workshop with patients, caregivers and professionals and reached consensus on the top 10. This final list included questions about the causes of IBD, the role of diet in the management of IBD and the role of novel biomarkers in assessment of disease.

Conclusions: Through meaningful engagement of patients, caregivers and clinicians we have identified their research priorities, which will be used to guide researchers in designing future studies and inform health care funders.

Top 10 Pediatric Research Questions

10	What is the optimal approach to diagnosis (education, psychological support, diagnostic tests) in pediatric patients with IBD?
9	What is the impact of access to psychological/mental health support in the management of pediatric IBD?
8	How does an early diagnosis of IBD in childhood/teenagers impact the lifelong course (prognosis) of the disease?
7	What are the long term effects of medications used to treat IBD?
6	How can we increase the knowledge and/or awareness around pediatric IBD so that diagnosis is not delayed?
5	How can we better define the role of, and improve access to, newer non-invasive, less costly, biomarkers of IBD endoscopic activity?
4	What triggers flare ups in IBD?
3	What role does diet have in the management of IBD?
2	Can IBD be prevented?
1	What are the causes of IBD (Crohn's disease, ulcerative colitis)?

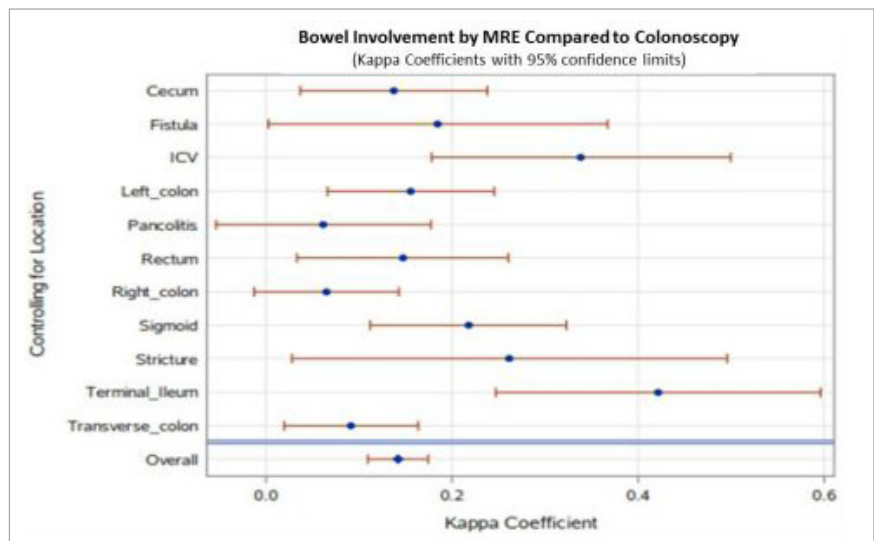
81 CORRELATION OF COLONOSCOPY WITH MAGNETIC RESONANCE ENTEROGRAPHY (MRE) AND FECAL CALPROTECTIN (FC) IN DIAGNOSIS OF PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD). Basavaraj Kerur¹, Navneetha Unnikrishnan¹, Alison Chambers², Carolina Cerezo¹, Jason Shapiro¹, Neal LeLeiko¹. ¹Pediatric Gastroenterology, Brown University, Providence, RI; ²Lifespan Biostatistics Core, Rhode Island Hospital, Providence, RI

Background: MRE enables the visualization of the whole spectrum of inflammatory lesions in intestine endoluminal, mural and extramural. MRE and colonoscopy are important to assess the small bowel in IBD. Fecal calprotectin (FC) is a non-invasive marker of intestinal inflammation. Pediatric literature looking at reliability/agreement between colonoscopy and MRE findings are scarce.

Aims: To determine if endoscopic assessment of bowel inflammation correlate with Magnetic resonance enterography. Determine if levels of fecal calprotectin assess disease burden or location of colonic inflammation.

Methods: 269 pediatric patients with IBD (CD 197, UC-72) diagnosed between 2011 and 2016 at Hasbro Children’s hospital were reviewed. Children who had MRE and endoscopy with in interval of 1-4 weeks were included in analysis. Clinical data, labs biopsies were collected. Bowel inflammation was assessed by reviewing ProVation records and MRE reports. Agreement between scope and MRE findings was estimated using the Kappa statistic and their 95% confidence intervals (CI). Results: 182 patients (UC 57, CD 125) had MRE within 30 days of colonoscopy, 109 patients with 1 week of scope. CRP was normal (<10mg/dl) in 50% of the children and ESR was normal (<20mm/hr) in 35% of the children at diagnosis of IBD. 49 patients had fecal calprotectin measured at the time of scope, 94% of the patients had elevated FC (>250mcg/g) at diagnosis of IBD. Pan colitis was seen by colonoscopy in 66/182 of patients (26% of UC, 38 % of CD) while MRE showed pancolitis in only 3/182 patients at the time of diagnosis. In children with crohns disease inflammation of terminal ileum (TI) by colonoscopy was seen in 91 patients, of these MRE detected inflammation in only 66 patients. However, in 6 patients TI involvement was detected by MRE but scope was normal. The kappa coefficients showing agreement between bowel inflammation by MRE and colonoscopy based on disease location is shown in fig 1. MRE provided additional information in 32 patients, abdomen abscess was detected in 8 patients, fistulas noted in 22 patients and entero-visceral fistulas in 2 patients. Fecal calprotectin correlated with disease location. Elevated fecal calprotectin (>250) was found in all the cases with pancolitis and proctitis

Conclusion: MRE had only moderate agreement (Kappa=0.4) with endoscopic findings in detection of small bowel inflammation in diagnosis of pediatric IBD. MRE failed to detect pancolitis or inflammation of segmental colon in majority of patients with IBD. At diagnosis of IBD, CRP was normal in 50% of patients and ESR were normal in 30 % of the patients. All the patients who had FC >250 had pancolitis.



83 VEDOLIZUMAB EFFECTIVENESS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE (IBD). Ana Ramirez¹, Glen Lewis¹, Laura Eshee², Olga Sherrod¹, Larry Saripkin¹, Steven Liu¹, Jose Garza¹, Clair Talmadge^{1,3}, Stanley Cohen¹, Seth Marcus¹, Jeffrey Blumenthal¹, William Meyers¹, Jeffery Lewis¹, Jay Hochman¹, Benjamin Gold¹. ¹Gastroenterology, Children’s Center for Digestive Healthcare, LLC, Atlanta, GA; ²GI Clinical Research, Children’s Health Care of Atlanta, Atlanta, GA; ³GI Physician Assistant, Children’s Health Care of Atlanta, Atlanta, GA

Introduction/Objective: Inflammatory Bowel Disease (IBD) (Crohn’s diseases, CD; ulcerative colitis, UC) is a chronic, autoimmune gastrointestinal disorder primarily diagnosed during childhood. A number of biological agents are available as first-line treatment of CD or UC in adults, 2 of these biologics are FDA-approved for children with IBD. Increasing numbers of children with UC fail initial biologic therapy and medical options remain limited for these patients prior to colectomy. Vedolizumab (Entyvio), the first gut-selective, a monoclonal antibody that targets $\alpha 4\beta 7$ -integrin, has been increasingly used as rescue or second-line biologic therapy “off-label” in pediatric patients with UC and CD. Several recent adult and a few, small

cohort pediatric studies demonstrated that Vedolizumab is tolerated and an effective therapy for induction and maintenance of both UC and to a lesser extent, CD. We describe the use and effectiveness of Vedolizumab in a single center cohort of pediatric patients with IBD.

Methods: This was a retrospective, observational study in which demographic, clinical and pharmacologic data was reviewed from the electronic medical records of children with IBD followed at our center from 2004-2017. Patients diagnosed with either UC or CD, who were treated with vedolizumab at a pediatric gastroenterology private practice that follows over 1,200 children and adolescents with IBD were included. Age, gender, race/ethnicity, CD or UC phenotype, as well as indications for treatment with Vedolizumab (i.e. previous biologic and/or standard therapies) and PUCAI/sPCDAI scores, were collected. Statistical analyses were done using Statistical Analysis Software (SAS).

Results: Forty-two patients received Vedolizumab in our practice as treatment for IBD; 38 of which had sufficient data for analysis. Patients were 9 and 24 years old; with a MEDIAN age of 16.2, 55% were male; 95% were non-Hispanic. 47% of children had UC, 40% CD and 13% IC; Furthermore, 93% of the cohort were exposed to other biologics before vedolizumab; of those 47% were exposed to Infliximab only and 50% received 2 or more biologics. The mean interval between vedolizumab infusions was 6.4 weeks (SD = 2). Mean PUCAI and sPCDAI score before vedolizumab infusion was 46.75 and 31.54 respectively. After infusion, PUCAI improved to 28.06 (p-value = 0.0197) and the sPCDAI improved to 22.33 (p-value = 0.01). Only 8% of the patients of the patients had adverse effects which were not reasons to discontinue treatment. Disease remission was observed in 39% of our cohort.

Conclusion: In our study, children with UC, CD, and IC receiving vedolizumab demonstrated a significant decrease in symptom severity and over a third (39%) achieved clinical remission. In our cohort of pediatric IBD patients, Vedolizumab was safe and effective in disease treatment, particularly those children who lost response to other biologics.

85 **IMPACT OF PHYSICAL EXERCISE ON HEALTH RELATED QUALITY OF LIFE AND DISEASE ACTIVITY IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE.** *Brian Maksimak, Katherine Lamparyk, Praveen Kumar Conjeevaram Selvakumar, Lori Mahajan. Peds GI, Cleveland Clinic, Cleveland, OH*

Background: Regular physical activity has been consistently shown to have a positive impact on multiple organ systems especially the cardiovascular system. Several studies have reported the anti-inflammatory role of exercise in humans by prohibiting the release of inflammatory mediators from visceral fats. Excess visceral adipose tissue has been associated with poorer outcomes in patients with Crohn's disease (CD). However, the impact of participation in exercise regimens on quality of life (QOL) or disease activity in pediatric CD has not been studied.

Objective: The primary aims are to determine if pediatric patients with CD, who participate in an exercise regimen/organized team sport, have overall improved quality of life and/or improved disease activity scores as compared to patients with CD who are not participating in an exercise regimen/organized team sport. Secondary aims included determining if there was any difference in infliximab doses and depression rates between the two groups.

Methods: Children (aged 12-18 years) with CD were randomly recruited from our infliximab infusion suite. Among the included children, disease activity was assessed using Pediatric CD Activity Index score (PCDAI) and QOL was determined using a validated questionnaire (IMPACT III). Patients were then stratified into 2 groups depending on self-reported current exercise regimen/sporting activity: exercise group or non-exercise group. We compared the groups using t test or Kruskal-Wallis test for continuous variables and Pearson's chi-square test or Fisher's exact test for categorical variables.

Results: A total of 42 patients, with 21 patients in each group, were included. There was no significant difference in age, gender, body mass index and location of disease between the two groups. The exercise group had a significantly lower mean PCDAI score compared to non-exercise group (0.0 vs. 7.5; p-value <0.001). Similarly, the exercise group had a significantly higher mean IMPACT III score (86.4 vs. 75.0; p-value <0.001). On a stratified analysis, the exercise group also had higher scores with regards to bowel/systemic symptoms, emotional/social functioning and response to treatment. There was no significant difference in the dose of infliximab or depression rates between the two groups.

Conclusions: This study found an improvement in QOL and disease activity in pediatric patients with CD who were involved in a routine exercise regimen, indicating the importance of physical activity in children with CD.

87 **INVESTIGATION OF THE PRESENCE OF MYCOBACTERIUM AVIUM SUBSP. PARATUBERCULOSIS IN CHILDREN WITH CROHN DISEASE USING QUANTITATIVE DNA SEQUENCE-BASED APPROACHES.** *Casey Hofstaedter¹, Máire Conrad¹, Ana Misic², Marie-Eve Fecteau³, Judith Kelsen¹, Kyle Bittinger¹, Daniel Beiting², Raymond Sweeney³, Robert Baldassano¹. ¹Division of Gastroenterology, Hepatology and Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA; ²Center for Host-Microbial*

Interactions, Department of Pathobiology, School of Veterinary Medicine of the University of Pennsylvania, Philadelphia, PA; ³New Bolton Center, School of Veterinary Medicine of the University of Pennsylvania, Kennett Square, PA

Background/Aim: *Mycobacterium avium* subsp. *paratuberculosis* (MAP) has been suspected to play a role in Crohn disease (CD) pathogenesis. Prior studies of MAP detection in dairy cows have been more extensively investigated, successfully detecting the organisms by culture and PCR. These studies have shown the organism to be the causative agent in Johne's disease, an enteritis in ruminants that is histopathologically similar to CD. We aim to use techniques which successfully detect MAP in cow feces and apply them to human feces and intestinal biopsy samples of patients with CD and healthy controls to see if MAP infection is correlated with active disease in children with CD.

Methods: Using feces and intestinal biopsy samples from known MAP-positive and negative calves, we performed several Mycobacterium-specific DNA extraction methods, aimed at lysing the thick and complex mycobacterial cell wall. To identify the presence of MAP in these samples, we used quantitative PCR and DNA-sequencing methods, both targeted and metagenomic. We applied these methods to samples from pediatric patients with CD and healthy controls. The intestinal samples were taken from eight patients, newly diagnosed with ileocolonic, granuloma-positive CD. Two samples were taken from each patient: one from the terminal ileum, and the other from either the cecum, left colon, or rectum. For half of the patients, tissue samples were obtained during endoscopy, and the other half were obtained during surgical resection. Five out of the eight patients were treatment naïve at the time of sample collection. The other three received antibiotics leading up to sample collection.

Results: We correctly identified the presence of MAP in intestinal biopsies from infected dairy calves using quantitative PCR, which aligned with culturing data from these biopsies. In our small subset of samples, we were unable to detect the presence of MAP in humans by any of these techniques.

Conclusion: While other groups have been able to identify the presence of this organism as being enriched in patients with CD compared to controls, we have not been able to see this enrichment in our patient population. The successful detection of MAP from intestinal biopsies in calves demonstrates that we can use these techniques to quantitatively identify the number of organisms in intestinal biopsies, without the use of culture-based methods. Here, we have confirmed the difficulty in detecting this organism in humans. Future work is ongoing to improve the sensitivity of our techniques and increase the number of patient samples tested for MAP presence, as only a small subcohort of CD patients may be affected by this organism.

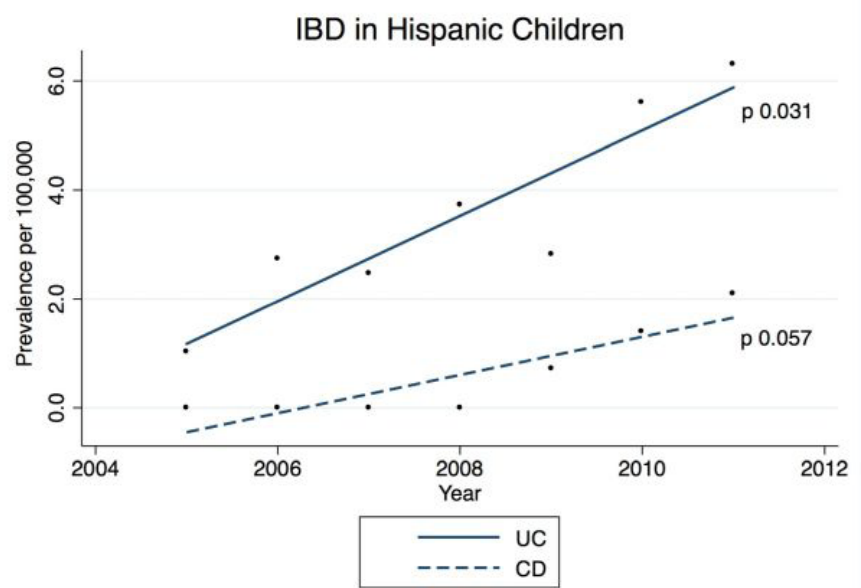
88 INFLAMMATORY BOWEL DISEASE IN HISPANIC CHILDREN: A POPULATION-BASED STUDY.

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Introduction: There is limited data regarding the incidence and prevalence of Inflammatory Bowel Disease (IBD) in Hispanic children. This study reports the incidence, prevalence and characteristics of IBD in this racial/ethnic minority in the state of Utah.

Methods: We reviewed medical records from the two major health systems that cover virtually all children in Utah in a population-based fashion. All inpatient, outpatient, and procedure encounters for patients who represented possible incident or prevalent cases of IBD born 1986-2011 with ICD-9 diagnostic codes for Crohn's disease (CD) or Ulcerative Colitis (UC) underwent a detailed records review. IBD diagnosis was confirmed based on chronicity of symptoms, exclusion of infections, and objective evidence of chronic inflammation on endoscopy and histopathology. Incidence and prevalence was calculated using US Census data.

Results: We identified 607 children with the diagnosis of IBD; CD in 52%, UC in 43%, and indeterminate colitis



in 5%. Hispanic children represented 4% of patients. The overall incidence and prevalence of IBD per 100,000 children was 5.7 and 22.3, respectively. In Hispanic children, the incidence and prevalence of IBD per 100,000 was 1.6 and 4.1, respectively. Caucasian children had an incidence and prevalence of IBD per 100,000 of 6.3 and 21.8, respectively. The mean age at diagnosis was similar in both populations. Hispanic children had UC more frequently while Caucasians had CD more frequently ($p=0.24$). Hispanic children had an increase in the incidence and prevalence of IBD of 0.2 per 100,000 per year ($p=0.133$) and 0.3 per 100,000 per year ($p=0.004$), respectively. Pancolitis was equally present in both groups. Primary Sclerosing Cholangitis occurred in 5% of Caucasians and 0% of Hispanics ($p=0.28$)

Conclusions: We calculated the incidence and prevalence of pediatric IBD in an important racial/ethnic minority in the largest such population-based study to date. IBD is less common in Hispanics relative to Caucasians, but the incidence and prevalence of IBD in Hispanics is increasing each year. Further study of the environmental and genetic factors that may explain this difference is warranted.

95 **THE ASSOCIATION OF CAESAREAN SECTION AND BREAST FEEDING WITH PEDIATRIC INFLAMMATORY BOWEL DISEASE.**

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Introduction: Mode of delivery and method of infant feeding are early exposures with the potential to alter development of the gastrointestinal microbiome. In altering the neonatal microbiome, birth by Caesarean section (CS) and formula feeding could both theoretically alter a child's risk of developing inflammatory bowel disease (IBD). Findings from previous studies on these exposures have been mixed, and there have been no cohort studies to examine this association in North America. We performed a retrospective cohort database-linkage study to determine whether there is a difference in the incidence of IBD amongst children born via vaginal delivery versus CS, and amongst those breastfed versus formula fed.

Methods: The current study was a cohort study using a linkage of the Nova Scotia Atlee Perinatal Database (NSAPD), which captures information on all births in the province, with a prospectively kept clinical registry of all children diagnosed with IBD at the province's only pediatric tertiary care hospital. All births between 1988 and 2014 were included (262,729 births). The primary outcome was a diagnosis of IBD (Crohn's disease [CD] and ulcerative colitis [UC]) before age 16 years. Information on the exposures CS and breast-feeding at hospital discharge was obtained from the NSAPD. Confounders of the association were identified a priori using a directed acyclic graph and included maternal age, parity, area-level income, rural residence, smoking, weight status, and birth weight for gestational age category. The association between CS and breast-feeding, respectively, and time to diagnosis of IBD was examined using multivariable-adjusted Cox proportional hazards regression models with robust standard errors to account for the clustering of infants in mothers. The analysis was stratified by type of IBD (CD, UC). Associations were reported as hazard ratios (HR) with 95% confidence intervals (CI).

Results: 319 cases of pediatric IBD (205 with CD and 114 with UC) were diagnosed in Nova Scotia in this cohort for a population incidence of 9.8 per 100,000 person-years. 77 and 23% of children were born by vaginal delivery and CS, respectively. There was no statistically significant association of CS (HR 1.07, 95% CI 0.82-1.42) or breast-feeding (HR 1.09, 95% CI 0.84-1.41) with IBD. There was no statistically significant difference in the risk of IBD between children who had CS before the 1st stage of labour (HR 1.09, 95% CI 0.83-1.44) and those who had CS during the 2nd stage of labour (HR 0.91, 95% CI 0.50-1.62) relative to children born vaginally. The HRs for CS and breast-feeding also did not differ between models for CD and UC.

Conclusion: The current study did not find an association between CS (compared to vaginal delivery) and later IBD. However, the study was not powered to detect effects with a HR < 1.25. There was also no association between breast-feeding (compared to formula feeding) at discharge and later IBD.

97 **WHOLE EXOME SEQUENCING OF OVER 1000 PEDIATRIC IBD PATIENTS FROM A SINGLE CENTRE IDENTIFIES MONOGENIC FORMS OF IBD.**

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Background: Inflammatory bowel disease (IBD) has a multifactorial aetiology, with complex interactions between genetic and environmental factors. Recent studies suggest an increasing spectrum of monogenic disease in the very young. The prevalence of these mutations in older children is unknown.

Objectives: To determine the prevalence of monogenic forms of IBD in pediatric patients and identify any phenotypic characteristics allowing for accurate diagnosis.

Methods: 2705 unique participants underwent whole exome sequencing (WES). This data was interrogated for a panel of 51 genes known to be associated with monogenic IBD. The Genome Analysis Toolkit (GATK) was used to identify highly penetrant rare variants of interest. Sanger sequencing verified variant genotypes. A clinical database was reviewed to ascertain phenotypic characteristics.

Results: A single centre retrospective study identified 1180 index cases, diagnosed over a 13 year period (2003-2015) who underwent WES. 2705 unique participants (556 trios, 31 quads, 34 affected siblings). Of sequenced affected cases, 56% CD, 26% UC, 11% IBD-U, 8% non-IBD. 21% < 6 years, 22% 7-10 years, 57% > 11 years. Across the 51 genes, 82 protein coding variants predicted to be deleterious were identified, which were high quality and rare (maf < 0.01). Disease causing mutations in XIAP, IL10R, SAP, TTC7A, LRBA, FOXP3, with rare damaging variants in NOX1, XIAP, DKC1 and FOXP3 over-represented in this cohort. Overall, approximately 1% of patients in a typical cohort of Pediatric IBD patients were found to have monogenic disease.

Conclusion: WES of this largest pediatric cohort to date confirms the highly varied phenotypic spectrum of IBD associated with monogenic disease. Most children with causal VEOIBD mutations were diagnosed < 1 year of age, yet a significant number of older children were identified. Characterising genotypic-phenotypic features may provoke earlier recognition which will allow novel therapeutic approaches in this paediatric IBD population.

101 EVALUATING THE ROLE OF DOCUMENTATION AND EDUCATION ON RATES OF INFLUENZA VACCINATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS AT AN URBAN TERTIARY CARE CENTER. Hillary Moore, Eve Thau, Melissa Shapiro, Philip Stein. *Section of Gastroenterology, Hepatology and Nutrition, St Christopher's Hospital for Children, Philadelphia, PA*

Background: Patients with inflammatory bowel disease (IBD) are at increased risk of vaccine-preventable illness due to underlying disease, malnutrition and immunosuppressive therapies. The safety and efficacy of influenza vaccination in IBD patients have been well established. Despite guidelines recommending annual influenza vaccination for IBD patients, rates remain suboptimal, ranging from 7.8 to 50%. Barriers to vaccination include concerns about safety and efficacy and unfamiliarity with guidelines. Given this disparity between guidelines and clinical practice, we hypothesized that an educational intervention targeting patients and providers would improve flu vaccination rates in pediatric IBD patients.

Methods: Chart review was performed of all IBD patient encounters in the GI clinic at our urban tertiary care facility in Philadelphia, Pennsylvania. Phase one of the study included encounters from September 2015-March 2016. Progress notes and vaccination data were reviewed. Phone calls were made to primary pediatricians when vaccine status was not documented. Following this season, IBD patients and their pediatricians received mailed letters stressing the importance of flu vaccination. Posters were hung in the GI waiting room and exam rooms. Gastroenterologists received education regarding the importance of discussing, counseling, and documenting the recommendation to receive the flu vaccine. Similar chart review was then performed for phase two of the study which included encounters from September 2016-March 2017. We noted whether patients received the flu vaccine during each season and whether discussion regarding the vaccine was documented in any GI note.

Results: During phase one, 95 patients met criteria. 40% received the flu vaccine during the 2015-2016 season. Gastroenterologist documentation regarding the flu vaccine was present in 39% of cases. During phase two, 88 patients met criteria. 51% received the flu vaccine during the 2016-2017 season. While not clinically significant, there seemed to be a trend of increased vaccination rate during the 2016-2017 season compared to the year prior (p=0.14). Gastroenterologist documentation was present in 49% of cases, which also showed a trend towards statistically significant increase (p=0.18). Of the patients with positive documentation, 67% actually received the vaccine. Of those without documentation, 36% received the vaccine (p=0.0032). Over both seasons, documentation regarding the flu vaccine was significantly associated with the likelihood of patients being immunized (p=0.0017).

Conclusions: Influenza vaccination rates in children with IBD continue to be suboptimal. Employing a multi-targeted educational intervention demonstrated improvement in vaccination rates in consecutive seasons as well as an increase in GI provider documentation. Perhaps a larger sample size would reveal a statistically significant improvement. Documentation regarding vaccination was significantly associated with increased likelihood of patients receiving the flu vaccine over both seasons. Thus, future interventions specifically stressing the importance of provider documentation may be especially valuable in improving vaccination rates. Documenting the recommendation to vaccinate may encourage GI providers to emphasize the advice and recruit primary care support. Consistent educational interventions for providers and patients alike will be necessary to achieve optimal vaccination rates in this vulnerable population.

102 CHARACTERISTICS OF 5 YEARS FOLLOW-UP DATA BASED ON PROSPECTIVE, NATIONWIDE INCEPTION COHORT: HUNGARIAN PEDIATRIC IBD REGISTRY (HUPIR).

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Objectives/Study: There is no nation-wide, 5 years follow-up epidemiological study of long-term disease course of pediatric inflammatory bowel disease (IBD), especially in the era of biologicals. The Hungarian Pediatric IBD Registry (HUPIR) is a nation-wide, prospective registry since 1st of January 2007.

Methods: Newly diagnosed pediatric patients with IBD (ages 0–18 years) are registered in this prospective, nation-wide registry (HUPIR), and followed-up yearly. The questionnaire at registration includes epidemiological data, disease extension, disease activity (PCDAI, PUCAI) and initial therapy. The follow-up questionnaire consists of questions about number of relapses, therapy (medication and surgery), extraintestinal manifestation, anthropometrical data.

Results: Between 1st January 2007 and 31st December 2014, 1168 new IBD cases were identified (729 Crohn's disease (CD), 365 ulcerative colitis (UC) and 74 IBD-unclassified). Incidence of IBD increased from 7.1/105 to 8.7/105 during 8 years. One hundred-forty-seven newly diagnosed IBD cases (Crohn disease: n=96, ulcerative colitis: n=37, IBD-U: n=14) were registered in 2010. Median age at diagnosis was 15 years in Crohn's disease, 13 years in UC and 12 years in IBD-U. In CD 21% of cases (17/82) had L1, 17% had L2 (14/82) and 61% had L3 (50/82) localization based on Paris Classification. Nine percent of UC patients (3/35) had proctitis, 31% of children had E2 localization (11/35), 11% of UC cases presented with extended colitis (4/35) and 49% of UC patients (17/35) had pancolitis (E4). Induction therapy in CD and UC were mainly steroid (CD: 64/96, [66%], UC: 19/37, [51%]) or mesalazine (CD: 87/96 [90%], UC: 31/37, [84%]) in Hungary.

By the end of the 5 years all data were available for 62 children (38 CD, 20 UC, 4 IBD-U). Reason for loss of patients (n=81) was mainly the transition to adult gastroenterologist (70%, 56/81). Relapse was detected in 46% of CD children (48/96), and in 50% of UC cases (18/37). Six percent of UC children (2/37) and 6% of CD patients (6/97) had steroid dependency, and 2 CD children were refractory to steroid therapy. Biologicals were applied in 22% of children with CD during the 5 years (21/96). Three children with UC received biological therapy. Bowel resection was performed in 9% of CD children during the 5 years, no colectomy was performed in UC (0/37).

Conclusion: Follow-up of pediatric IBD cases is difficult due to transition to adult health care. The management practice was different in Hungary from the international trends in 2010, however the disease course was similar to previous results.

103 EDUCATING PEDIATRIC RESIDENTS ON INFLAMMATORY BOWEL DISEASE (IBD) SCORING AND ITS APPLICATION.

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Background: Pediatric residents take care of IBD (inflammatory bowel disease) patients on inpatient floors, GI clinics, infusion centers and in the out-patient settings. However, not many residents were aware of IBD scoring and its clinical use. Pediatric IBD scoring consists of PUCAI (Pediatric Ulcerative Colitis Activity Index) and PCDAI (Pediatric Crohn's Disease Activity Index). The use of IBD scoring in clinical practice standardizes the gathering of clinical data at initial and follow-up visits, allows for an objective assessment of disease activity and of response to drug therapy (response versus remission), allows for prediction of clinically important outcomes and facilitates communication between physicians caring for the patient.

Objective: Our aim was to first evaluate residents' knowledge of IBD scoring and its clinical application. Our secondary aim was to assess the impact of self-directed learning combined with teaching and the use of modern technology in formulating an IBD score.

Design: Eighty pediatric residents at the SUNY Downstate program have participated in the pre-test questionnaire, which included a set of 14 questions. Three of those questions involved computing the IBD score. Information was obtained about their PGY level, whether the residents did a GI rotation and whether they were ever personally involved in the care of an IBD patient. A monograph describing the IBD scoring was sent to the residents via email prior to the lecture. A talk was given to teach the residents about the clinical use of IBD scoring. An online calculator and a digital app were introduced as part of the intervention. A post-test was conducted with the same set of questions. Seventy-four pediatric residents (92%) participated in the post test. The number of correct responses were measured in the pre-test and post-test. Pre-test and post test mean scores were compared to each other and pre-test mean scores were compared with variables such as having done a GI rotation or participating in IBD patient direct clinical care. Pre and post test responses were compared with and without the use of an IBD scoring app or an online calculator.

Results: A paired t-test was used to compare the mean score between various groups. A significant difference was found between the pre-test and post-test for the entire cohort and within each cohort of PGY level ($p < 0.0001$). A significant difference was also found with the use of a digital IBD app or an online calculator ($p < 0.001$). Taking care of an IBD patient made a significant difference ($p < 0.0025$), as well. Having done a GI rotation did not make a difference ($p = 1.2$) in the pre-test versus post-test results.

Discussion: The combination of the use of technology, teaching and self directed learning assisted in educating our pediatrics residents about IBD scoring and its use in objectively assessing pediatric patients suffering from IBD.

There is no literature found on IBD scoring and resident education. Our project, with a large sample size and significant statistical results, demonstrates that innovative methods can be employed for resident education.

104 INFUSION COST SAVINGS ATTRIBUTED TO ELIMINATING INFLIXIMAB PREMEDICATIONS FOR CHILDREN WITH INFLAMMATORY BOWEL DISEASE. Amanda Bradshaw, Teresa Wachs, David Suskind, Dale Lee, Stephanie Lammers, Rachelle Foreman, Sarah Mbonde, Ghassan Wahbeh. Seattle Children's, University of Washington, Seattle, WA

Background: Pre infusion medications (corticosteroids, diphenhydramine, acetaminophen) were thought to prevent infliximab (IFX) infusion reaction and antibodies to IFX, particularly with episodic dosing in inflammatory bowel disease (IBD). There is paucity of data to support the practice of premedicating in the setting of scheduled IFX dosing, which adds time and cost.

Aim: to demonstrate cost savings and outcomes for IBD patients on scheduled IFX who had their pre-infusion medications discontinued.

Methods: we embarked on discontinuing premedication for patients who have been stable on IFX >4 months without infusion reactions from June 2015 onwards. This was conducted on a case to case basis after discussion with the family. We retrospectively reviewed the clinical demographics, cost savings and clinical outcomes after our intervention for children with IBD on IFX at our IBD center from June 2015-Dec 2016.

Results: 23 patients were identified, 16 CD, 6 UC, 1 IBDU. 12 M and 11 females. Median age at diagnosis was 12 years (9-17). Median disease duration before IFX initiation was 7 months (<30 days to 85 months). Median time on IFX before discontinuing premedications was 17 months (4-239). For the 23 patients over the last 2 years, a total of 164 infusions were given without premedications, reflecting a total cost saving of \$80139, \$1742/patient/year. No patient in our cohort developed an infusion related reaction since the premedications were discontinued.

Conclusion: Discontinuing infliximab infusion premedications was cost effective with no noted infusion reaction in patients with IBD who are stable on infliximab after the induction phase.

107 EFFICACY AND SAFETY OF GOLIMUMAB FROM THE PURSUIT PEDS PK STUDY LONG-TERM EXTENSION. Jeffrey Hyams¹, Christopher D O'Brien², Lakshmi Padgett², Rawan Shraim², Joel Rosh³, Dan Turner⁴, Genevieve Veereman⁵, Anne Griffiths⁸, Melvin B Heyman⁶, Ghassan Wahbeh⁷, Joseph Adedokun², Richard Strauss², Daphne Chan². ¹Connecticut Children's Medical Center, Hartford, CT; ²Janssen Research & Development, LLC, Spring House, PA; ³Pediatric Gastroenterology, Clinical Development and Research Affairs, Goryeb Children's Hospital/ Atlantic Health, Morristown, NJ; ⁴The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Shaare Zedek Medical Center, The Hebrew University of Jerusalem, Jerusalem, Israel; ⁵UZ Brussels, Free University Brussels, Brussels, Belgium; ⁶Department of Pediatrics, University of California, San Francisco, San Francisco, CA; ⁷Seattle Children's Hospital, Seattle, WA; ⁸The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Objective: To evaluate the efficacy and safety of golimumab (GLM) in children with ulcerative colitis (UC) from the PURSUIT PEDS PK study long-term extension.

Methods: This multicenter, open-label study assessed the PK, efficacy, and safety of GLM in children 2-17yrs with moderate-to-severe UC (Mayo score 6-12, endoscopy subscore ≥ 2), unresponsive to prior treatments with corticosteroids or thiopurines (naïve to anti-TNF). The PK levels during the LTE (wk14-126) were determined. At wk6, Mayo responders continued GLM maintenance ($<45\text{kg}$ [$45\text{mg}/\text{m}^2$, $N=9$ {3 were $<30\text{kg}$ }]; $\geq 45\text{kg}$ [100mg], $N=11$) every-4-wks (q4w). Efficacy (PUCAI remission [<10 points], clinically meaningful change [decrease ≥ 20 points from baseline in the PUCAI score]) and safety were evaluated through wk110 & 126, respectively.

Results: Of the 35 children enrolled at wk0, 21 (60%) achieved Mayo response at wk6, and 20 entered the LTE follow-up at wk14. Of these, 9 (45%), 11 (55%), and 10 (50%) were in PUCAI remission at wks30, 54, & 110, respectively (Figure 1a).

Similarly, 11 (55%), 12 (60%), and 10 (50%) of patients had a clinically meaningful change at wks30, 54, & 110, respectively, (Figure 1b). Similar results were observed in subgroup analysis by baseline weight (Figure 1a and 1b).

Through wk126, 19 (95%) reported ≥ 1 AE; 3 (15%) had an AE leading to drug discontinuation (2 UC, 1 hemorrhagic diarrhea); 15 (75%) reported infections; 5 (25%) reported SAEs (3 had worsening UC), and 4 (20%) reported mild injection site reactions. Five children were positive for antibodies to GLM through wk126 using a drug tolerant enzyme immunoassay; titers were $\leq 1:96$. No anaphylactic or serum sickness-like reactions, opportunistic infections, malignancies or deaths were reported.

Conclusions: Continued clinical benefit was observed in children with UC who received GLM q4w maintenance through wk110 in this open-label study. No new safety signals were observed through wk126, and the safety profile was similar to that observed during the 14wk PK portion previously reported. These findings are consistent with the established clinical benefit and safety profile in the adult UC population.

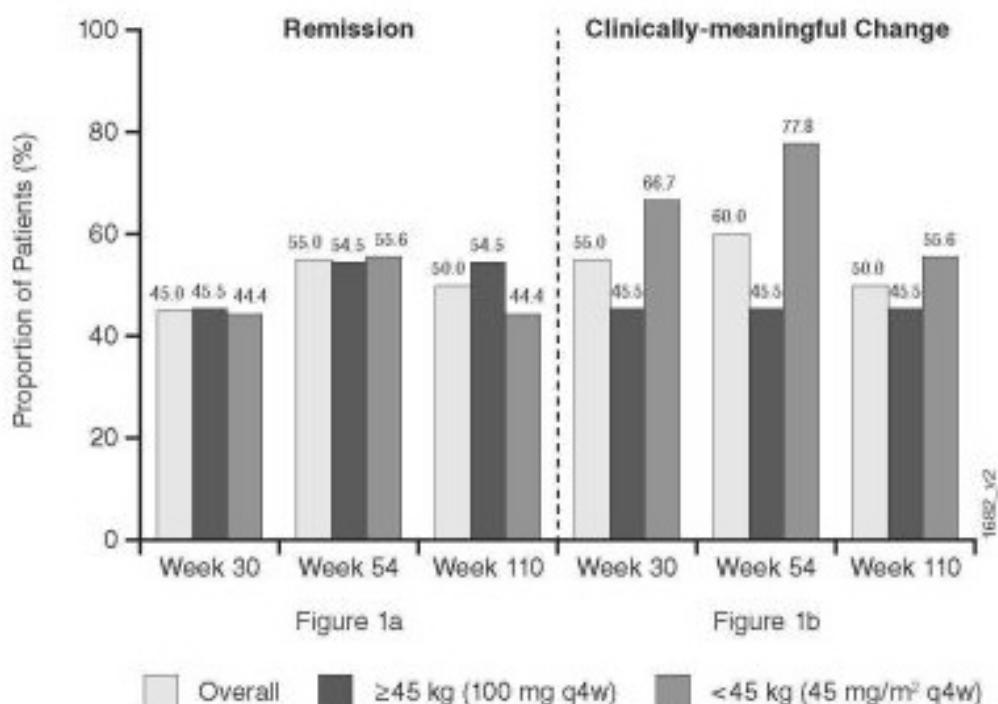
111 IL-33 INDIRECTLY INDUCES GOBLET CELL HYPERPLASIA IN THE MURINE INTESTINE THROUGH IL-13 PRODUCTION BY GROUP 2 INNATE LYMPHOID CELLS.

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Background: The intestinal mucus layer is critical to maintaining epithelial barrier function. IL-33 is a member of the IL-1 family of cytokines that signals through the receptor ST2, which is expressed on many cell types, including immune cells, epithelial cells and stromal cells. We have reported that deficiency of IL-33 or ST2 worsens histopathologic severity and goblet cell depletion in oxazolone-induced colitis in mice. IL-33 induces goblet cell hyperplasia in mice but the mechanism remains unclear. Our current study aims to determine how IL-33 affects goblet cell differentiation in vivo and in vitro, in primary murine epithelial enteroids.

Methods: Primary murine small intestinal crypt-derived enteroids were treated with IL-33 or IL-13 for up to 5 days and examined for *Atoh1*, *Spdef*, and *Muc2* expression and UEA-1 (a mucus-binding lectin) immunofluorescence. Enteroids were co-cultured with a primary intestinal fibroblast cell line (WEHI) or FACS sorted CD45⁺CD90⁺ mesenteric lymph node (MLN) cells from IL-33-treated mice to determine indirect effects of IL-33, and IL-13 production was measured by ELISA. Flow cytometry was performed to determine the IL-13 producing cell in the co-cultures with MLN cells. *Ilr4*^{-/-} enteroids were used to determine whether IL-13 from MLN cells was required for goblet cell differentiation. WT and IL-13^{-/-} mice were given IL-33 i.p. for 4 days and intestinal goblet cells were assessed by periodic acid Schiff (PAS) staining and mucosal *Muc2* and *Spdef* by RT-qPCR.

Results: While IL-33 did not affect *Muc2* expression in enteroids cultured alone or co-cultured with WEHI cells, IL-33 did induce a 3.6-fold ($p < 0.01$) increase in *Muc2* in enteroids co-cultured with MLN cells. Concurrently, IL-33 induced IL-13 protein secretion in enteroid-MLN cell co-cultures (4.6 vs. 0.01 ng/ml in treated vs. untreated, $p < 0.001$). Flow cytometry identified group 2 innate lymphoid cells (ILC2s, CD3⁺CD90⁺ST2⁺) as the IL-13 producing cell type in MLN cell co-culture experiments. IL-



13 alone increased enteroid *Muc2* expression 3.5-fold ($p < 0.001$), and UEA-1 staining confirmed the increase in goblet cells and mucus in IL-13-treated enteroids. *Atoh1*, *Spdef* and *Muc2* were not induced by IL-33 in *Il4r^{-/-}* enteroids co-cultured with CD90⁺ MLN cells indicating a requirement for IL-13 signaling in the epithelium. In WT mice, IL-33 induced *Muc2* 4.8-fold ($p < 0.001$) and *Spdef* 2.3-fold ($p < 0.01$) in the colon and increased PAS⁺ cells 3.1-fold in the colon ($p < 0.001$) and 2.5-fold in the small intestine ($p < 0.01$) compared to no treatment. However, IL-33 had no effect on these parameters in IL-13^{-/-} mice.

Conclusions: The presence of MLN immune cells was required for IL-33 to induce *Muc2* expression *in vitro* in primary murine enteroid cultures. MLN-derived ILC2s stimulated with IL-33 produced IL-13 in co-cultures with murine enteroids, and IL-13 alone was sufficient to induce *Muc2* expression. Goblet cells were not induced by IL-33 in *Il4r^{-/-}* enteroids co-cultured with MLN cells. IL-33-induced goblet cell hyperplasia was dependent on IL-13 *in vivo*. These studies indicate that IL-33 induces goblet cell hyperplasia in the intestine not through direct action on epithelial cells, but rather indirectly through IL-13 production by ILC2s. These findings may have important implications for treatments aimed at maintaining epithelial homeostasis in inflammatory bowel disease.

113 INFLIXIMAB DOSE DE-ESCALATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: A SINGLE-CENTER EXPERIENCE. Steven Fusillo¹, Taylor Olson¹, Máire Conrad^{1,2}, Robert Baldassano^{1,2}, Andrew Grossman^{1,2}, Judith Kelsen^{1,2}. ¹Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; ²Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

Background: Therapeutic drug monitoring has improved the efficacy and durability of IFX in inflammatory bowel disease (IBD). While dose escalation in the setting of low serum infliximab (s-IFX) levels has been extensively examined, few studies to date (and no pediatric studies) have evaluated the safety or efficacy of de-escalating IFX therapy based on supratherapeutic s-IFX.

Aims: To evaluate whether pediatric IBD patients on a stable maintenance IFX regimen with supratherapeutic s-IFX were able to tolerate de-escalation of IFX dosing, as assessed by IFX durability, clinical disease activity, CRP, and concurrent steroid exposure.

Methods: We performed a retrospective review of pediatric IBD patients on maintenance IFX at Children's Hospital of Philadelphia who, between June 2014 and September 2016, had s-IFX greater than 10 ug/mL and had subsequent IFX dose and/or frequency reduction within the next two IFX cycles. Outcomes measured included IFX durability at 52 weeks and disease activity (measured by Pediatric Crohn's Disease Activity Index and Pediatric Ulcerative Colitis Activity Index), CRP, and systemic steroid exposure at baseline (time of supratherapeutic s-IFX), 16 weeks, and 52 weeks.

Results: Seventy three patients with IBD (48 with Crohn disease, 14 with ulcerative colitis, 11 with indeterminate colitis) who underwent IFX dose de-escalation following supratherapeutic s-IFX (median 16.5 ug/mL, IQR 13.0-20.6) were included. Median duration of IFX therapy prior to de-escalation was 72 weeks (range 24-204). Dose reduction occurred in 16/73 (22%), ranging from 2.5mg/kg to 5mg/kg, and 62/73 (85%) had reduction in frequency of infusions (mean decrease 1.5 weeks, range 1-3); 5 patients (7%) had reductions in both dose and frequency. Mean dosing regimen was reduced from 9.2mg/kg q5.5 weeks to 8.6mg/kg q6.8 weeks following de-escalation. At one year, 70/71 patients with 52-week follow up remained on IFX (99% durability). Repeat s-IFX was obtained in 63 patients at median of 33 weeks, with median s-IFX of 9.2ug/mL (4.5-12.6). Re-escalation occurred in 8/71 patients (11%) prior to 52 weeks (median time-to-escalation: 26 weeks). In these patients, median s-IFX trough prior to dose escalation was 2.5ug/mL (1.2-5.8).

Disease activity was measured in 44 patients (60% of total sample) who had sufficient clinical data at both baseline and 16 weeks post de-escalation. Rates of clinical remission (PCDAI or PUCAI ≤ 10) for baseline and week 16 were 39/44 (89%) and 40/44 (91%), respectively. At 52 weeks, clinical data was available in 33 patients, with 30 (91%) remaining in clinical remission. Of note, 3 of the 5 patients with active disease at baseline also had active disease at one or both follow up assessments. Rates of CRP elevation (>0.9 ug/dL) at baseline, week 16, and week 52 were 10%, 16% and 21%, respectively. Rates of concurrent systemic steroid use at baseline, 16 weeks, and 52 weeks were 5%, 2%, and 0%, respectively.

Conclusions: This retrospective study is the first to evaluate IFX dose de-escalation in the setting of supratherapeutic s-IFX in pediatric IBD. IFX de-escalation in patients with s-IFX >10 ug/mL did not appear to adversely affect clinical outcomes, with remission rates remaining stable over 52 weeks. While 8 patients (11%) required re-escalation to initial IFX dosing, 99% of all patients remained on IFX at 52 weeks. IFX dose de-escalation appears to be a viable option for patients with supratherapeutic s-IFX, particularly those already in clinical remission. However, larger prospective studies are necessary to confirm the safety and efficacy of IFX dose de-escalation and to create more precise IFX dosing strategies.

114 MATERNAL SMOKING DURING PREGNANCY IS ASSOCIATED WITH COMPLICATED DISEASE IN OFFSPRING WITH NEWLY DIAGNOSED CROHN'S DISEASE.

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Background: Both genetic and environmental factors play pivotal role in the pathogenesis of Crohn's disease (CD). Early life environmental influences such as breast-feeding and exposures such as passive smoking have been investigated in the context of early disease. However, prior studies have not robustly conducted a prospective examination of their effect on disease phenotype and natural history in pediatric CD.

Methods/Aim: We used environmental exposure data from a large, multi-center, inception cohort of pediatric CD (RISK cohort) to examine the effect of early life exposures on phenotype and outcomes in pediatric CD. Exposures were ascertained using detailed questionnaires at enrolment and included mode of childbirth, breast-feeding, cigarette smoking using three measures – personal history of smoking in the index patient, exposure to passive smoke, and maternal smoking during pregnancy. Our primary outcomes were development of complicated phenotype (stricturing - B2/ internal penetrating - B3 = Montreal classification) and need for CD-related surgery and hospitalization at 1 year after diagnosis. We hypothesized that one-year outcome will be more reflective of environmental / perinatal factors still influencing the outcome in contrast to long term outcome where treatment effect could be confounding. Secondary outcomes included need for biologic therapy. Univariate and multivariable logistic regression models were developed, adjusting for potential confounders.

Results: Out of 1127 newly diagnosed CD cases, 1,055 had non-complicated inflammatory disease (B1) status, 28 B2 and 8 B3 at diagnosis. At one year follow up, additional 34 developed B2 and 7 developed B3. The mean age at diagnosis was 11.72 years (range 1 – 17). 70% of patients reported a history of breastfeeding, 23.7% C-section delivery, 1.5% had personal history of smoking, 18.5% had exposure to passive smoke, and 6.7% had a history of maternal smoking during pregnancy respectively. On multivariable analysis, maternal smoking during pregnancy was associated with a significantly higher likelihood of B2/B3 disease at diagnosis or 1 year follow up (OR 2.52, 95% CI 1.12 – 5.66) (see Table 1). Restricting analysis to B1 disease at diagnosis, maternal smoking during pregnancy remained associated with an increased risk of progression to B2/B3 disease at 1 year (OR 3.32, 95% CI 1.07 – 10.29). On univariate analysis, maternal smoking during pregnancy was also associated with higher likelihood of needing biologics and IBD-related hospitalization. In contrast, breast-feeding was independently associated with a lower likelihood of needing surgery at 1 year (OR 0.31, 95% CI 0.09 – 0.98).

Conclusion: Our study demonstrates for the first time that maternal smoking during pregnancy is associated with more complicated phenotype in the offspring with CD, suggesting that such exposure may result in epigenetic imprinting that modifies disease behavior. In contrast, breast-feeding appears associated with a lower need for surgery in newly diagnosed CD patients.

Association between maternal smoke exposure, history of breastfeeding and study outcomes in newly diagnosed Crohn's disease

	Maternal smoke exposure				History of breastfeeding			
	Univariate analysis		Multivariable analysis †		Univariate analysis		Multivariable analysis †	
	OR (95%)	P-value	OR (95%)	P-value	OR (95%)	P-value	OR (95%)	P-value
Disease phenotype								
B2/B3 disease at diagnosis or 1 year follow-up (N:B2-62, B3-15)	2.37 (1.08-5.22)	0.027	2.52 (1.12-5.66)	0.032	NS	NS	NS	NS
B2/B3 disease at follow-up among those with B1 at diagnosis (N:B2-34, B3:7)	2.48 (1.12-5.47)	0.025	3.32 (1.07-10.29)	0.050	NS	NS	NS	NS
Outcomes								
Immunomodulator use	NS	NS	NS	NS	NS	NS	NS	NS
Biologics use*	1.63 (1.02-2.61)	0.041	NS	NS	NS	NS	NS	NS
CD-related surgery	NS	NS	NS	NS	0.31 (0.10-0.98)	0.035	0.31 (0.09-0.98)	0.046

† - Variables included in the stepwise multivariable model includes age at diagnosis, gender, race (white or non-white), disease location, perianal involvement, breast-feeding, maternal smoking during pregnancy, passive smoke exposure, and personal history of smoking * At diagnosis or follow-up. NS - not significant

LIVER

118 **INCIDENCE OF INFECTIONS AND ASSOCIATIONS WITH IMMUNOSUPPRESSION IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS.** Lauren Klein², Bryce Russo³, David Cousino³, Deepak Vikraman-Sushama³, Alisha Mavis¹. ¹Pediatric Gastroenterology, Hepatology, and Nutrition, Duke University, Menomonee Falls, WI; ²Pediatrics, Duke University Medical Center, Durham, NC; ³Abdominal Transplant Surgery, Duke University Medical Center, Durham, NC

Background: Advances in immunosuppressive therapy have decreased the rates of acute graft rejection and graft failure in pediatric liver transplantation. However, infection is a permanent and serious risk in all patients receiving immunosuppressive therapy and is increasingly recognized as a risk factor for chronic graft rejection in solid organ transplant. The risk of infection is a combination of exposures, immune deficits, and cumulative immunosuppressed status. The most likely cause for hospitalization in the first two years post-pediatric kidney transplantation is now infection. Data regarding infection risk in children post-liver transplantation is lacking. Furthermore, few studies have examined the relationship between specific immunosuppression regimens and risk of infection. The aim of our study was to define the incidence of infection and associations between infection, immunosuppression, and related complications in pediatric liver transplant recipients.

Methods: We conducted a single-center, retrospective study of pediatric transplant recipients followed at the Duke Pediatric Liver Transplant Program between January 2010 and December 2016 at Duke University Medical Center. We collected clinical data, labs, imaging, and pathology reports. Data were summarized descriptively. We assessed the incidence of infection and association with post-transplant complications and cumulative immunosuppression.

Results: We identified 74 pediatric patients (42 (57%) male) who had a total of 79 liver transplants. Three patients had 2 liver transplants and one patient had 3 transplants. The median age at the time of transplant was 4.51 yrs (IQR: 0.04 – 18.11 yrs). The most common diagnoses at transplant: 1) biliary atresia, 2) Alagille syndrome, 3) hepatoblastoma. The average length of follow up was 3.81 yrs (IQR: 0.39 – 6.98 yrs). Maintenance immunosuppression consisted of monotherapy (tacrolimus or sirolimus alone), double therapy (tacrolimus with antimetabolite or prednisone), and triple therapy (tacrolimus,

antimetabolite, and prednisone) in 70% (n=52), 22% (n=16), and 8% (n=6) respectively. 62 patients (84%) had at least one notable infection and 34 patients (46%) had two or more significant infections requiring treatment. 13 (59%) of the patients on double or triple immunotherapy had >1 major infection. 17 (23%) patients had acute cellular rejection necessitating increased immunosuppression and 3 (4%) patients had post-transplant lymphoproliferative disorder (PTLD). 2 of the 4 patients who received multiple transplants had only one major infection but the other 2 had multiple infections. There were no deaths.

Conclusions: The incidence of significant infections in our pediatric liver transplant recipients is high. The cumulative immunosuppression received by these patients places them at high risk for serious infections consequently increasing the risk of chronic graft rejection and other transplant related complications. More studies are needed to guide the development of patient specific immunosuppressive regimens in order to balance rejection and the risk of infection, thus improving both patient and graft outcomes.

119 BILIATRESONE, A TOXIN CAUSING BILIARY ATRESIA, LEADS TO INCREASED MRNA AND PROTEIN EXPRESSION OF CX3CL1 (FRACTALKINE), A LEUKOCYTE ADHESION LIGAND, IN MOUSE CHOLANGIOCYTES AND ORGANIDS. Alyssa Kriegermeier¹, Orith Waisbourd-Zinman², Pierre-Marie Lavrut³, Rebecca Wells³. ¹Gastroenterology, Hepatology & Nutrition, The Children's Hospital of Philadelphia, Philadelphia, PA; ²Schneider Children's Medical Center of Israel, Tel-Aviv, Israel; ³Department of Medicine, University of Pennsylvania, Philadelphia, PA

Background/Aims: Biliary atresia (BA) is a progressive fibrosing cholangiopathy of unknown etiology affecting the extra-hepatic bile ducts (EHBD) of infants. Our group previously isolated a novel isoflavonoid, biliatresone, from plants responsible for outbreaks of a BA-like disease in Australian livestock. We showed that biliatresone causes luminal obstruction in cholangiocytes in 3D and mouse EHBD explants. In our current study, we aimed to identify changes in pro-inflammatory cytokines and receptors triggered by biliatresone that are potentially relevant to the progressive inflammatory bile duct injury seen in BA.

Methods: Cultured mouse cholangiocytes were exposed to either biliatresone or DMSO (control) for 24h and gene expression was evaluated using a Qiagen PCR array for 84 pro-inflammatory cytokines and receptors. qRT-PCR testing was done to evaluate and confirm changes in expression of CX3CL1 specifically. Enzyme-linked immunosorbent assay (ELISA) for CX3CL1 was performed on conditioned media. Cholangiocyte organoids with open lumens were generated by growth in 3D culture and then treated with DMSO or biliatresone for 24h. Organoids were fixed and stained with anti-CX3CL1 antibody and DAPI and imaged with confocal microscopy. CX3CL1 staining intensity was quantified via ImageJ software.

Results: The initial PCR array reported an increase in 10 cytokines/receptors in cholangiocytes treated with biliatresone compared to control: CX3CL1 (known as fractalkine), CXCL10, CSF1, CSF3, IL15, IL17a/f, IL1r1, IL6ra, and Tnfsf13. The increased expression of CX3CL1 was confirmed by qRT-PCR, which showed an 11.8±0.644 (mean±SEM)-fold increase in biliatresone-treated cholangiocytes. CX3CL1 exists in both soluble and membrane-bound forms. An ELISA for CX3CL1 showed no increase in soluble CX3CL1 in biliatresone treated media compared to DMSO treated media; however, organoids treated with biliatresone had a 6 fold increase in CX3CL1 staining compared to DMSO-treated organoids which was statistically significant (P<.001).

Conclusions: Biliatresone induces increased CX3CL1 expression in cholangiocytes at both the mRNA and protein levels. This increase appears to be in the membrane-bound form of CX3CL1, which is known to be expressed on epithelial cells and promotes the adhesion and transmigration of leukocytes. Our data using mouse cholangiocytes are consistent with the dramatically increased CX3CL1 expression observed in human BA livers (Okamura et al., Participation of natural killer cells in the pathogenesis of bile duct lesions in biliary atresia. *J. Clin. Pathol.* 2013;66(2):99–108) and could explain the inflammatory response in the extra-hepatic biliary tree and liver parenchyma that occurs in BA after an initial insult. This work suggests that biliatresone will be a useful tool to induce relevant injury in cholangiocytes. Further studies are currently in process to validate other cytokine changes and to demonstrate their functional relevance in propagation of bile duct injury.

***120 A COMPARISON OF PRIMARY SCLEROSING CHOLANGITIS WITH AND WITHOUT ASSOCIATED INFLAMMATORY BOWEL DISEASE: DATA FROM THE PEDIATRIC PSC CONSORTIUM.** Amanda Ricciuto¹, Binita Kamath¹, Reham Abdou², Khaled Alqoer³, Mansi Amin⁴, Achiya Amir⁵, Marcus Auth⁶, Fateh Bazerbach⁷, Annemarie Broderick⁸, Albert Chan⁹, Jillian Cotter¹⁰, Syliva Doan¹¹, Wael El-Matary¹², Mounif El-Youssef¹³, Federica Ferrari¹⁴, Katryn Furuya⁷, Madeleine Gottrand¹⁵, Frederic Gottrand¹⁵, Nitika Gupta¹⁶, Matjaz Homan¹⁷, Kyle Jensen¹¹, Kyung Mo Kim¹⁸, Kaija-Leena Kolho¹⁹, Anastasia Konidari²⁰, Bart Koot²¹, Raffaele Iorio²², Oren Ledder²³, Cara Mack¹⁰, Mercedes Martinez²⁴, Tamir Miloh^{25,26}, Parvathi Mohan²⁷, Niamh O'Cathain⁸, Alexandra Papadopoulou²⁸, Pushpa Sathya²⁹, Mark Deneau¹¹. ¹Gastroenterology, Hospital for Sick Children, Toronto, ON,

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Background: Primary sclerosing cholangitis (PSC) frequently co-exists with inflammatory bowel disease (IBD). Data comparing IBD-associated PSC and isolated PSC in children are sparse. We aimed to evaluate disease characteristics and long-term outcomes of PSC in children with and without IBD in a large, multicenter pediatric cohort.

Methods: We examined data from the Pediatric PSC Consortium, a collaboration of 36 centers. We performed survival analysis from time of PSC diagnosis to any of: 1) a portal hypertensive complication (ascites, encephalopathy, esophageal varices), 2) dominant biliary stricture requiring stent, dilation or drainage, 3) liver transplantation, 4) cholangiocarcinoma and/or 5) liver-related death. Multivariate Cox regression was used to examine the association between IBD and the risk of progression to adverse liver outcomes, adjusting for age, gender, ductal involvement, autoimmune hepatitis (AIH) overlap, ursodiol use, and baseline MELD and AST to Platelet Ratio Index (APRI).

Results: 571/751 PSC patients (76%) had IBD (83% ulcerative colitis (UC), 17% Crohn disease (CD)). PSC without IBD was characterized by more females, a greater proportion of AIH overlap (51 vs. 28%) and higher baseline MELD (4 vs. 0), APRI (1.57 vs. 0.68) and ALT (286 vs. 176), all p<0.001. Small vs. large duct involvement and GGT were similar in both groups. The probability of portal hypertensive and biliary complications within 5 years of diagnosis in the PSC vs. PSC-IBD groups was 31 vs. 21%, and 24 vs. 12%, respectively (p<0.01), despite a 5% baseline prevalence in both groups. Event-free survival at 5 years was worse in PSC vs. PSC-IBD (58% vs 73%, p<0.001). In univariate analysis, IBD, small duct disease and lower baseline MELD were associated with a higher probability of event-free survival. In multivariate analysis, only MELD was associated with outcome (HR 1.09 [95% CI 1.05-1.13]). Event-free survival did not differ between UC and CD phenotypes.

Conclusions: PSC-IBD patients experienced fewer adverse liver outcomes during follow-up compared to patients with no IBD. Concomitant IBD and a small duct phenotype appeared to be protective in univariate analysis. However, this association was lost when controlling for baseline disease severity in multivariate analysis. PSC-IBD patients had lower MELD scores and surrogate markers of fibrosis at baseline. It is unclear if this difference in baseline characteristics reflects a lead-time bias (due to routine liver enzyme monitoring in IBD patients and earlier diagnosis of PSC), or an intrinsically more aggressive cholangiopathy in patients without IBD. Further analysis of IBD activity and colectomy rates in this cohort is underway.

NB: authors missing due to space limitations

Univariate and multivariate analyses examining event-free survival in pediatric PSC

	Univariate Hazard Ratio (95% CI)	p-value	Multivariate Hazard ratio (95% CI)	p-value
IBD	0.66 (0.49-0.88)	0.006	0.88 (0.56-1.37)	0.577
Large duct disease	1.40 (1.01-1.92)	0.042	1.40 (0.87-2.24)	0.167
AIH overlap	0.99 (0.75-1.32)	0.990	1.01 (0.68-1.49)	0.971
Male gender	0.88 (0.67-1.14)	0.342	1.02 (0.69-1.49)	0.937
Ursodiol therapy	0.99 (0.68-1.44)	0.940	0.81 (0.50-1.32)	0.403
Age at PSC diagnosis	1.00 (0.97-1.03)	0.868	0.97 (0.93-1.02)	0.239
APRI	1.02 (0.99-1.05)	0.280	0.99 (0.95-1.02)	0.472
MELD	1.07 (1.05-1.10)	<0.001	1.09 (1.05-1.13)	<0.001

121 RAPID WHOLE GENOME SEQUENCING IMPROVES DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH NEONATAL CHOLESTASIS. Amber Hildreth^{1,2}, Shareef Nahas², Shimul Chowdhury², David Dimmock², Stephen Kingsmore². ¹Pediatric Gastroenterology, UCSD/ Rady Children's Hospital, San Diego, CA; ²Rady Children's Institute for Genomic Medicine, San Diego, CA

Background: Neonatal cholestasis is caused by either a defect in the intrahepatic production or transmembrane transport of bile, or by a functional or mechanical obstruction of bile flow. The most commonly identified causes are extrahepatic biliary atresia (EHBA) (25-40%) and monogenic disorders (25%), with the remaining fraction including prematurity, TPN related disease, or unknown causes. Those patients being labeled "idiopathic neonatal hepatitis" continues to decline with the advancement of diagnostic tools and discovery of new genetic etiologies. Next Generation Sequencing technologies provide high-throughput sequencing in order to rapidly evaluate a patient's genome. The speed of diagnosis under rapid sequencing protocols have been as fast as 26 hours. We hypothesize that utilization of this technology in patients with neonatal cholestasis will provide a specific genetic diagnosis faster than standard clinical work up, enabling more specific care, sparing invasive diagnostic tests and surgeries.

Methods: Prospective single arm pilot of all cases <6 months of age with gestational age >34 weeks presenting to Rady Children's Hospital San Diego with neonatal cholestasis (direct bilirubin >1mg/dL). Eligible patients were enrolled in the Rady Children's Institute for Genomic Medicine's Biorepository and underwent rapid whole genome sequencing (rWGS) as either proband only, parent-child duo, or parent-child trio. Variants determined to be likely disease causing were scored based on the American College of Medical Genetics guidelines for interpretation with supporting evidence from available literature. The US FDA allowed for provisional reporting of results to the primary medical team if such information had significance potential to avoid morbidity or mortality. All pathogenic or likely pathogenic variants were confirmed by medically accepted orthologous techniques.

Results: A total of seven patients were enrolled between Sep 2016 and May 2017. Average age at enrollment was 57 days (range 26-81, median 59). A genetic diagnosis was made by rapid WGS in 2 cases (Niemann-Pick Type C1 (NPC1) disease (homozygous NPC1 c.2713C>T; p.Gln905Ter), and Alagille Syndrome (heterozygous 3Mb deletion chr20:10471400-13459333- region includes JAG1) and a partial explanation in 1 heterozygous SERPIN1A (c.1096G>A; p.Glu366Lys). The remaining diagnoses included EHBA (3 cases) and idiopathic neonatal hepatitis (1 case). The fastest genetic diagnosis was made in just 68 hours. Both cases with a genetic diagnosis received an immediate change in clinical management. Patient 2, who was diagnosed with NPC1, received results 16 days prior to standard gene panel testing (with expected results 39 days early if the Spanish consent forms had been approved at the time of nomination). This child was started on targeted therapy with Miglustat prior to onset of neurologic symptoms. Patient 4 was diagnosed with Alagille Syndrome minutes before undergoing intraoperative cholangiogram with reflex to Kasai. The rWGS diagnosis meant that this procedure was cancelled. Results were reported 6 days before confirmatory microarray. The cost saving in this case alone would cover the rWGS costs for all 7 cases.

Discussion: Rapid WGS has the ability to make a genetic diagnosis in patients with neonatal cholestasis much faster than standard clinical work up. Providing an early diagnosis in this population is crucial to ensure timely targeted therapy for the myriad of rare treatable genetic causes of cholestasis. In addition standard invasive procedures such as a liver biopsy or intraoperative cholangiogram may be avoided if a timely genetic diagnosis can be made.

***124 SEX DEPENDENT INTESTINAL EXPRESSION OF ASBT DETERMINES THE SCLEROSING CHOLANGITIS PHENOTYPE AND THE RESPONSE TO PHARMACOLOGICAL INTERRUPTION OF ENTEROHEPATIC CIRCULATION OF BILE ACIDS IN MDR2^{-/-} MICE.** Ana Catalina Arce-Clachar¹, Tiffany Shi¹, Ramesh Kudira¹, Mary Mullen¹, Celine S. Lages¹, Amy Taylor¹, Wujuan Zhang², Julia Simmons¹, Rebekah Karns¹, Kumar Shanmukhappa¹, Kenneth Setchell², Alexander Miethke¹. ¹Gastroenterology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ²Pathology and Laboratory Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background/Aims: In humans, Primary Biliary Cirrhosis and Primary Sclerosing Cholangitis, exhibit sex variability in incidence, onset and progression. Here we examine the sex bias for liver disease phenotype and response to anti-cholestatic therapy in Mdr2^{-/-} mice, a model of defective canalicular excretion of phospholipids which leads to biliary precipitation of bile acids (BA) and cholesterols, cholangiocyte injury, sterile inflammation and fibrosis.

Methods: Male and female Mdr2^{-/-} (BALB/cJ) were single housed at day 30 and fed high-fat chow for 14 days until harvest. Plasma and serum biochemistries were measured with colorimetric assays at 45-days and liver histology was assessed by blinded review of H&E and Sirius red staining. Fractions of hepatic mononuclear cells (MNCs) were analyzed by flow cytometry. Hepatic, biliary and serum BA profiles were determined by mass spectrometry. Purified total RNAs from liver and

terminal ileum was used for RNAseq and Taqman-based qPCR studies. To examine whether sex-dependent intestinal ASBT expression was associated with response to ASBT directed anti-cholestatic therapy, MDR2^{-/-} mice were treated with SC-435 (10mg/kg/day), a minimally absorbed apical sodium-dependent bile acid transporter (ASBT) inhibitor, admixed to the chow for 14 days beginning at day 30.

Results: Mdr2^{-/-} female mice displayed higher serum levels of alkaline phosphatase (ALP: mean of 327±38 vs 194±23 IU/L in female vs male, n≥7 per group; p=0.01), total bilirubin (TB: 5.8±0.6 vs 0.95±0.3 mg/dL; p=0.0003) and alanine aminotransferase (ALT: 1326±188 vs 642±55 IU/L; p=0.01). Review of liver histopathology revealed higher scores for bile duct proliferation on a 1 to 4+ scale for sclerosing cholangitis (mean score of 3.6±0.2 vs 1.8±0.2; p<0.0001), necrosis of hepatocytes (1.75±0.16 vs 2.33±0.21; p=0.04) and fibrosis (3.8±0.2 vs 3.1±0.2; p=0.04). The latter was confirmed by image analysis of collagen deposition on Sirius Red-stained sections (mean % fibrosis of 11.1±2.9 vs 2.0±0.48; p=0.02). Biochemical and histological findings of aggravated inflammatory hepatobiliary injury were corroborated by flow cytometry: Mdr2^{-/-} females showed increased frequency of Kupffer cells (mean % 10.13±0.99 vs 0.68±0.21 of CD45⁺ hepatic MNCs; p<0.0001) and monocyte-derived macrophages (14.73±1.52 vs 6.04±1.93; p=0.004) compared to males. To further investigate factors regulating a potential sex-dependent bias of murine sclerosing cholangitis, we assessed BA in various compartments: although serum concentrations of total and specific hydrophilic and hydrophobic BA did not differ between both sexes (mean of 3900±700 vs 4400±2100 uM in female vs male; p=0.78), the amount of hepatic BA was higher in females than males (81±16 vs 57±11 pmole/gram body weight; p=0.09) and biliary concentrations were significantly elevated in female mice (162±29 vs 19±11 mM; p=0.002). Surprisingly, global liver RNAseq and candidate qPCR studies showed downregulation of genes associated with pathways of BA metabolism and cholesterol synthesis in females (p<0.0001). Specifically, hepatic expression of Cyp8b1 and Cyp27a1 which encode key enzymes of de novo BA synthesis, were reduced by 66-fold (p=0.03) and 128-fold (p=0.03), respectively. However, intestinal mRNA expression for ASBT, a facilitator of enteral BA re-uptake, was upregulated in female compared with male Mdr2^{-/-} mice (11-fold; p=0.09). This corresponded with decreased fecal BA excretion (mean 0.43±0.08 vs 1.43±0.39 umole/gram body weight/day; p=0.01). Collectively, those data suggest that enhanced BA re-absorption in the ileum via ASBT expands the BA pool size in female mice which subsequently results in higher biliary BA concentrations exerting epithelial injury. The ASBT inhibitor SC-435 increased fecal BA excretion in females by 7-fold and in males by 5-fold. Importantly, SC-435 treatment was associated with greater reduction of ALP, TB and ALT in females than in males compared with untreated sex-matched Mdr2^{-/-} control mice (% decreased ALP of 60±3.74 vs 13±7.59; p=0.0003, TB of 93±0.6 vs 45±8.76; p<0.0001, and ALT of 86±1.66 vs 72±13.75; p=0.09). Treated female Mdr2^{-/-} mice had a 29% weight gain compared to 12.5% in male mice (p=0.02).

Conclusion: Female Mdr2^{-/-} mice display an aggravated sclerosing cholangitis phenotype with worse cholestasis, liver fibrosis and prominent hepatic infiltration of macrophages. We propose that increased ASBT-mediated BA reabsorption in female mice leads to increased BA pool size and subsequently higher biliary BA concentrations, which (in the absence of phospholipid) may exert greater injury to cholangiocytes. Intriguingly, decreased intestinal ASBT expression, less efficient intestinal BA reabsorption, and subsequently increased hepatic BA and cholesterol metabolism in male mice is associated with decreased biochemical response to ASBT inhibitor. Whether these pathways are directly controlled by sex hormones requires further investigations.

125 CHALLENGES IN SCREENING FOR PEDIATRIC NONALCOHOLIC FATTY LIVER DISEASE. *Anna Ferguson¹, Stavra Xanthakos¹, Robert Siegel². ¹Gastroenterology, Cincinnati Children's Hospital, Cincinnati, OH; ²Center for Better Health and Nutrition, The Heart Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, OH*

Background: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of elevated liver enzymes in children in the United States. Screening for NAFLD in children with obesity is controversial and not recommended by all published guidelines. Further, the outcomes of screening for NAFLD in a pediatric weight management program are unknown.

Objective: Our study aimed to describe the screening practices for NAFLD in a large pediatric weight management program during a one year time period and the outcomes of those identified to have elevated liver enzymes.

Design/Methods: Diagnostic testing performed for the evaluation of NAFLD was extracted from electronic medical records on all children seen at the Center for Better Health and Nutrition (CBHN) at Cincinnati Children's from 1/1/14- 12/31/14. Descriptive statistics were used to calculate frequency of laboratory and imaging testing and diagnoses. Results: During 2014, 1312 patients were seen, with a liver enzyme panel obtained in 847 (64.5%). Only 47/847 (5.5%) had an elevated liver enzyme (AST, ALT, or GGT). Of the 47, 33 (70%) patients had persistently elevated liver enzymes. Of those 33, 22 (67%) had further exclusionary lab testing, with 9 (27%) having test results suggesting potential alternative diagnoses. Abdominal ultrasound was performed in 17 (52%) of which 2 were normal and 14 were abnormal. There was increased echogenicity consistent with NAFLD in 12. Two patients had ultrasound findings suggestive of gallbladder disease and both patients had abdominal pain.

Conclusion(s): In summary, recommended screening and evaluation for NAFLD was not universally implemented in our large well-established pediatric weight management program, despite an established protocol that was well aligned with published guidelines for screening of NAFLD in overweight and obese children. In our experience, in the absence of physical findings, abdominal ultrasound did not add any value to the diagnostic evaluation of children with obesity and increased liver enzymes. As obesity continues to rise and NAFLD is projected to become the leading cause of liver transplantation in adults in the next 5 years, barriers to care and the challenges of screening for NAFLD need to be addressed.

130 EVALUATING FOR HUMAN HERPESVIRUS-6 IN CHILDREN WITH LIVER FAILURE OF UNKNOWN ETIOLOGY.

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Background: Liver failure of unknown etiology (LFUE) presents more frequently in children compared to adults, and transplant-free survival is <25%. LFUE is suspected to have a viral etiology, but commonly evaluated viruses are negative in LFUE. Human herpesvirus-6 (HHV-6) may be associated with LFUE in children, but studies in the literature are limited by small sample size. We present the largest study thus far, in which we evaluate 102 patients for HHV-6 in liver tissue.

Methods: All children who underwent liver transplant for LFUE at a single quaternary children's hospital over the past 20 years were identified. Controls were children who underwent liver transplant for metabolic liver disease at the same institution. Cases and controls were age-matched to be within 6 months of each other in age at time of transplant. Sixty-five cases of LFUE were identified, and 51 had age-matched controls available. DNA from formalin-fixed paraffin-embedded tissue from the explants of all cases (n=51) and controls (n=51) was extracted, and quantitative PCR for HHV-6 was done. Fisher's exact test was used to evaluate whether HHV-6 was present significantly more often in cases compared to controls, and Mann Whitney U test was used to evaluate for significant differences in viral load between cases and controls, with p<0.05 being statistically significant. The HHV-6/b-globin ratio was used to quantitate viral load against a standard curve.

Results: HHV-6 was present in 34/51 cases (66.7%), and 19/51 controls (37.3%) (p=0.005). Average viral load in patients with HHV-6 was 213,207 copies/10⁶ cells in cases (range: 7,293-1,102,030), and 38,115 copies/10⁶ cells in controls (range: 1,382-122,375) (p=0.0008). When stratifying patients by age, HHV-6 was present significantly more often in cases compared to controls up to patients <6 years in age; in particular, in patients <3 years in age, HHV-6 was present in 13/27 cases (48.1%), and 2/27 controls (7.4%) (p=0.0009).

Average age of cases and controls was 4 years (range: 2 months-15 years 5 months for cases, 3 months-15 years 5 months for controls).

Conclusions: HHV-6 was present in the liver significantly more often and in higher quantities in children transplanted for LFUE compared to controls, and this was particularly evident in children <3 years in age. Our data suggest HHV-6 should be evaluated for in young children who present with LFUE. Treatment for HHV-6 exists, and early initiation of therapy may prevent the need for liver transplant. Current studies include in situ hybridization to localize HHV-6 in the explants, and analysis of all samples for 16 other viruses to identify other viral etiologies for further investigation.

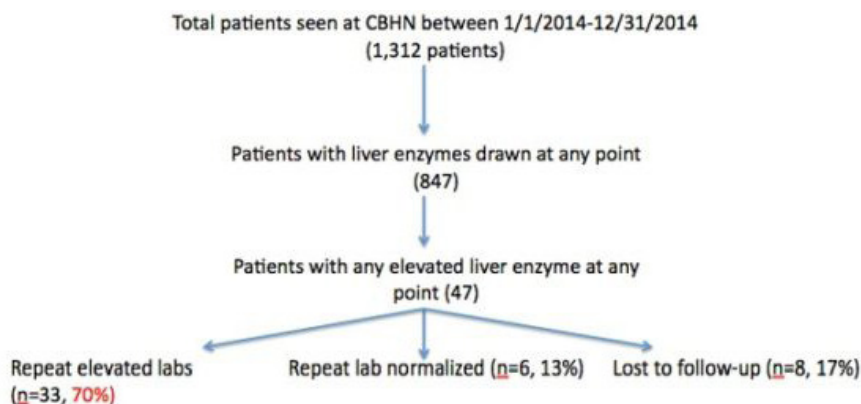


Figure 1: Flow chart describing workup of 1312 patients seen in 2014 at CBHN

Table 3: Outcome of patients with persistent serum aminotransferase levels ≥ 50 U/L

Lost to follow-up without further testing	3 (9%)
Laboratory testing obtained for other causes of hepatitis	22 (67%)
Abdominal ultrasound obtained	16 (46%)
Referral to Gastroenterology	23 (70%)

132 HEPATIC DISEASE IN CYSTIC FIBROSIS. A LOOK AT HISTOLOGY PREVIOUS LIVER TRANSPLANTATION.

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The hepatic complication in Cystic Fibrosis (CF) cause important morbidity and mortality and the hepatic transplantation arises as a therapeutic alternative. The pre transplantation Histological pattern has not been clearly described.

Aim: describing liver histology in the whole liver of transplanted patients with CF.

Methods and Material: a descriptive, retrospective, observational study. On a transplant list from a multicenter of 1,253 hepatic pediatric patients who were transplanted from 1990 to 2016. 10 CF patients were transplanted (0, 7 %) median age for transplant was 10.6 years (IQR 6-18 years). Six explanted were studied in a single center. After weighing, recording the external surface appearance and measuring the liver, at least four different sections were taken from the porta hepatis. Three different sections were submitted from the right and left lobes as well as caudate, quadrate and gallbladder.

Results: All explants showed macronodules with irregular patterns of fibrosis, coarsely nodular liver regeneration and areas of nodular hyperplasia-like nodules without cirrhosis. Most remarkable findings were portal fibrosis; forming sclerosis and obliteration of small-sized portal vein. Some portal tracts showed clusters of small vessels like angiomas. Scarce, large hepatic veins had segmental sclerotic changes. Vascular lesion was associated with areas of macronodules and septal fibrosis.

Three explants had Portal expansion with proliferating bile ducts containing bile plugs and mild inflammatory infiltration-

Conclusion: The liver explants showed regenerative macronodules associated with severe fibrosis and different types of vascular lesions like obliterative portal venopathy. This findings could be the most important cause of portal hypertension.

***133 PIOGLITAZONE INCREASES RXR-DNA BINDING TO AND EXPRESSION OF MITOCHONDRIAL RESPIRATION GENES IN THE LIVERS OF MICE WITH DIET-INDUCED NAFLD.** Sakil Kulkarni¹,

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Introduction: Pioglitazone (PIO) is a PPAR γ -activating thiazolidinedione that exerts beneficial effects in a subset of human subjects with non-alcoholic fatty liver disease (NAFLD). Obeticholic acid (OBE) activates another nuclear hormone receptor (NHR), the farnesoid X receptor, and also improves NAFLD in some subjects. Retinoic acid X receptor (RXR) is an obligate binding partner of PPAR γ , FXR and other NHRs. The specific goal of this study was to define the influence of PIO on hepatic genome-wide patterns of RXR-DNA binding and the liver transcriptome in a mouse model of diet-induced NAFLD. The longer-term goal is to elucidate the genomic mechanisms that mediate differences in efficacies of PIO and other NHR ligands in human NAFLD.

Methods: Wildtype male C57BL6/J mice were given ad lib access to high fat (HFD) or control diets with or without PIO supplementation (0.01% w/w; n=5 mice/group) beginning at age 2 months and continued until age 5 months, then euthanized for tissue harvest and analysis. Genome-wide interrogation of RXR binding was conducted by chromatin immunoprecipitation combined with next generation DNA sequencing (ChIP-Seq). The effect of HFD and PIO on the hepatic transcriptome was investigated by RNA-Seq. Binding and Expression Target Analyses (BETA) software was used to integrate ChIP- and RNA-Seq datasets and thereby predict RXR-DNA binding-dependent genomic targets of PIO. Gene set enrichment analyses (GSEA) were conducted with DAVID.

Results: HFD-treated mice showed expected increases in weight gain, serum free fatty acids, and hepatic triglyceride content vs. those on control diet (p<0.05). Mice on PIO-supplemented HFD showed significantly greater weight gain (p<0.05), but comparable hepatic triglyceride content when compared to mice on PIO-supplemented control diet. PIO treated mice on control or HFD showed increased hepatic steatosis compared to mice not treated with PIO. Surprisingly, ChIP-Seq analyses showed that HFD did not have dramatic effects on liver RXR DNA binding (whether or not the animal was treated with PIO) in this model. In contrast, RXR ChIP-Seq also showed that PIO increases liver RXR DNA binding to 275 gene targets in mice on control diet and 583 targets in mice on HFD (using a false discovery rate threshold (FDR) of q<0.05). Almost all genes identified as RXR bound in PIO treated mice on control diet were also detected in PIO-treated mice on HFD. Similar to the results of the RXR ChIP-Seq analyses, RNA-Seq showed a high degree of concordance between genes whose hepatic expression is induced by PIO in the absence or presence of HFD (p<0.001). Finally BETA was used to identify genes whose PIO-induced changes in expression were likely to be regulated by RXR. The highest scoring genes were subjected to GSEA, with the results showing enrichment of RXR-dependent, PIO-induction of genes associated with cellular metabolism and neurodegenerative diseases (q<0.05). The majority of these are nuclear genes that encode mitochondrial proteins involved in oxidative phosphorylation.

Conclusion: These data show that PIO induces hepatic RXR binding to and expression of genes encoding proteins involved in mitochondrial respiration, and that this effect is independent of HFD exposure in this model. Several of the genetic targets identified here were previously implicated as modifiers of Alzheimer's and Parkinson's disease, raising the provocative possibility that these genes modify NAFLD by similar mechanisms. Only c.a. half of the subjects in the human PIO and OBE

intervention trials, mentioned above, showed drug-induced improvements in NAFLD. Our data suggest the possibility that variations in responses to these or other NHR-based candidate NAFLD therapies may be determined by effects on RXR-regulated changes in hepatic expression of genes that affect mitochondrial function. Studies are currently underway to test the effects of PIO on RXR-regulated hepatic gene expression in liver-specific PPAR γ mice. Future studies should compare the effects of PIO, OBE, their combination, and perhaps other NHR ligands on RXR-DNA binding and NAFLD in this and other models. The results could inform rational consideration of future human intervention trials.

137 APPROACH TO PROPHYLAXIS AND TREATMENT OF VARICEAL BLEEDING IN PEDIATRIC PATIENTS: THE UNITED STATES EXPERIENCE. *Einar Hafberg, Lee Bass, Gastroenterology and Hepatology, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL*

Background: Upper GI bleeding (UGIB) from esophageal or gastric varices is one of the most severe complications of portal hypertension (PHT) in children and adults. The Baveno V conference offered recommendations for treatment of UGIB secondary to PHT. In pediatrics there is little consensus on the approach to the acute treatment of UGIB from PHT and less regarding long term management approach to prevention of the first episode of bleeding or prophylaxis. To achieve consensus, objective analysis of current centers practices is required.

Aim: To survey the practices of physicians at large hepatology centers of prevention and treatment of variceal hemorrhage in Pediatrics.

Methods: Online questionnaire to pediatric gastroenterologists and hepatologists to query their practice in managing children with portal hypertension and their complications. The institutional review board at the Ann & Robert H. Lurie Children's Hospital of Chicago approved this study.

Results: Pediatric gastroenterologists and hepatologists from academic centers performing liver transplants were queried. 22 responses were received. Geographically, 52% of responses were from the Midwest, 10 % south, 14% west and 24 % from North east region of the US. In the respondents' practices, 70% of patients were on public aid. 57 % cared for > 30 patients with portal hypertension. Etiologies of portal hypertension were multifactorial with biliary atresia, other cholestatic liver disease, and portal vein thrombosis accounting for the majority of causes. 55% of responders performed primary screening for varices. 42%, of those who did, used any evidence for PHTN as indication for screening EGD. 50% of those who did screening performed primary prophylaxis. No one intervened in small varices, 10% did so when they did not flatten with insufflation and were <25% of the lumen. 40 % engaged all varices if continuous with gastric varix. All used banding and 63.5% sclerotherapy depending on patient's size. Non selective beta blockers (NSBB) are used by 57% of responders as primary prophylaxis, of which 30% used them for any size varices. Majority used heart rate decrease as a clinical endpoint while 18% did not monitor. The number of patients that each responder treated with variceal bleeding was equally distributed 1-5(n=6); 5-10(n=7) or >10(n=8) per year. 90% of responders prescribed antibiotics when patient presented with upper GI bleeding with Piperacillin/Tazobactam or 3rd generation cephalosporin being the antibiotics used in 61.1% and 38.9 % of cases respectively. Hemoglobin level for transfusion was <7 gr/dl for 52.4 % and <8 gr/dl for 47.8%. Secondary prophylaxis was performed by all that answered with 2-4 weeks interval being the most common frequency in 61%, 17% did that in 0-2 weeks and 22 % 4-6 weeks. After obliteration of varices 47% did yearly surveillance while 33% did so every 6 months.

Conclusions: There remains a wide range of practice when managing UGIB secondary to PHT. Many practitioners have begun to use NSBB despite a lack of consensus recommendations for their use in pediatrics. This study highlights the need for greater consensus guidelines in the treatment of these patients.

138 PREDISPOSING CONDITIONS TO PEDIATRIC HEPATOCELLULAR CARCINOMA. *Elizabeth Cowell¹, Kalyani Patel², Hao Wu², Andras Heczey¹, Rajkumar Venkatramani¹, Milton Finegold², Tamir Miloh¹.* ¹Pediatrics, Baylor College of Medicine, Houston, TX; ²Pathology, Baylor College of Medicine, Houston, TX

Background: Hepatocellular carcinoma (HCC), the second most common malignant liver tumor in children, has been linked to chronic viral, metabolic, or genetic liver disease and other systemic conditions. This retrospective review describes the underlying medical conditions of children with HCC.

Methods: Following institutional review board approval, patients \leq 21 years old with HCC were identified from our pathology database, including those managed at our institution and through external consultation. Data collection included demographics, history, and pathology, and for consult patients was limited to age and medical condition as described in pathology reports or evidenced by non-cancerous liver pathology.

Results: 61 cases of HCC diagnosed between 1996 and 2016 were identified: 16 at our institution (56% male, median 9.5 years) and 45 in consultation (66% male, median 8 years). The most common presenting complaints included abdominal pain,

distension, and vomiting/hematemesis. Within our institution, 7 patients (44%) had underlying liver or associated disease: cryptogenic cirrhosis (2), tyrosinemia (1), Hepatitis B (1), progressive familial intrahepatic cholestasis (PFIC) Type 3 (1), and idiopathic aplastic anemia (1). Among consult patients, medical history was available for 36 patients; 18 had an underlying condition: cryptogenic cirrhosis/fibrosis (6), steatosis (3), Alagille syndrome (3), PFIC type unknown (2), biliary atresia (1), and Fanconi anemia (1). Average age at diagnosis was 7.2 years for those with, compared to 9.6 years for those without underlying disease. Within our institution, metastatic disease at presentation was seen in 15% (1/7) of patients with underlying disease, compared to 44% (4/9) of those without an underlying condition. Alpha fetoprotein (AFP) was elevated at diagnosis in 80% (4/5) of patients with and 71% (5/7) without underlying disease (median 2,050 ng/ml, range 0.7-1 million). Thirty-three percent (3/9) of patients without an underlying condition had moderate-poorly differentiated HCC and another 44% (4/9) were fibrolamellar, compared to well-differentiated HCC in 57% (4/7) of patients with underlying disease. None of the patients with fibrolamellar HCC had an underlying condition, and 3 had normal AFP at diagnosis (median 2.3 ng/ml, unavailable in 1).

Conclusion: Approximately one-half of pediatric patients with HCC did not have underlying liver or associated disease. These patients were diagnosed at a later age with a higher rate of metastatic disease and worse histopathologic differentiation compared to those with underlying disease. Fibrolamellar histology was seen exclusively in cases of *de novo* HCC. These findings contribute to our understanding of the epidemiology of pediatric HCC and challenge the development of surveillance guidelines for this diverse patient population.

140 PREVALENCE OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN CHILDREN WITH OBESITY. Elizabeth Yu^{4,2}, John Fontanesi³, Kathryn Harlow^{4,2}, Jorge Angeles¹, Janis Durelle⁴, Nidhi Goyal^{4,2}, Kimberly Newton^{4,2}, Jonathan Hooker^{5,6}, Ethan Sy^{5,6}, Claude Sirlin^{5,6}, Jeffrey Schwimmer^{4,2}. ¹University of California San Diego, San Diego, CA; ²Division of Pediatric Gastroenterology, Hepatology and Nutrition, Rady Children's Hospital San Diego, San Diego, CA; ³School of Medicine, University of California San Diego, La Jolla, CA; ⁴Department of Pediatrics, University of California San Diego, San Diego, CA; ⁵Department of Radiology, University of California San Diego, San Diego, CA; ⁶Altman Clinical Translational Research Institute, University of California San Diego, San Diego, CA

Background: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children. The biggest risk factor for NAFLD is obesity and guidelines from NASPGHAN recommend screening for NAFLD in children with obesity ≥ 9 years of age. Public health efforts require accurate estimates of disease prevalence. However, due to numerous methodological issues, the current estimate of the prevalence of NAFLD in children with obesity ranges from 11% to 85% and therefore, is too broad to be useful. To improve guidelines and inform health care policy, an accurate estimate of the prevalence of NAFLD in children with obesity is needed. Therefore, the primary aim of our study was to estimate the prevalence of NAFLD in children with obesity. A secondary aim was to evaluate the accuracy of serum alanine aminotransferase (ALT) for detecting NAFLD.

Methods: We evaluated children in San Diego County ages 9 to 17 years with obesity (BMI $\geq 95^{\text{th}}$ percentile) for the presence of NAFLD. Diseases other than NAFLD were excluded based upon a combination of history and laboratories. Whole liver MRI was performed at 3.0 T for the measurement of proton density fat fraction (PDFF). Fatty liver was defined as MRI PDFF $\geq 5.0\%$. The biology-based upper limit of normal (ULN) for ALT derived from the SAFETY study was 26 U/L for boys and 22 U/L for girls. We evaluated the diagnostic accuracy of two times this ULN for ALT (ALT > 52 U/L boys; ALT > 44 U/L girls) for detecting NAFLD in children with obesity.

Results: There were 408 study participants (M=217, F=191) with mean age of 13.2 years (+/- 4.0). The majority (77%) were Hispanic. The mean BMI was 31.3 (+/- 4.9) kg/m² and the mean ALT was 32 (+/- 32) U/L. The estimated prevalence of NAFLD was 28.7% (95% CI 26.7 – 30.6). NAFLD was more prevalent in boys (31.8%; CI 28.1 – 35.4%) than girls (25.1%; CI 17.8 – 32.4%). For detecting NAFLD, ALT provided 34.2% sensitivity; 95.9% specificity; and 78.2% overall accuracy.

Conclusions: NAFLD was common but not ubiquitous among children with obesity drawn from a community sample. The overall estimated prevalence of NAFLD in children with obesity was 28.7%. Commonly used thresholds for ALT offer high specificity but low sensitivity for NAFLD. In order to optimally identify children with NAFLD, further refinements in the current screening recommendations are needed.

141 HEPATIC PARENCHYMAL INJURY IN CRIGLER-NAJJAR SYNDROME. Ellen Mitchell¹, Sarangarajan Ranganathan², George Mazariegos³, Patrick McKiernan¹, Kyle Soltys³, Robert Squires¹, Kevin Strauss⁴, James Squires¹ ¹Pediatric Gastroenterology, Children's Hospital of Pittsburgh of UPMC, Swarthmore, PA; ²Pathology, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA; ³Pediatric Transplant, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA; ⁴Pediatrics, Clinic for Special Children, Strasburg, PA

Background: Crigler-Najjar syndrome (CN) arises from biallelic variants of UGT1A1 that abrogate UGT1A1 activity and result in unconjugated hyperbilirubinemia. Historically, liver parenchyma in CN was considered structurally and histologically normal. However, recent review of CN explants obtained at the time of liver transplant (LT) revealed fibrosis. Our aim was to investigate the association between hepatic histology and disease phenotype among subjects with CN.

Methods: We included 22 patients with a confirmed diagnosis of CN who were transplanted at the Children’s Hospital of Pittsburgh of UPMC. We extracted data from the medical record at the time of transplant and reviewed liver explant histology for the presence of fibrosis. Continuous data were normally distributed, presented as mean (\pm 1SD), and analyzed using two-tailed Student’s t-test. Categorical data were analyzed using the chi-square test.

Results: Mild elevations of both alanine transaminase (ALT; mean 87.4 IU/L) and aspartate transaminase (AST; mean 54.6 IU/L) were noted. Nine (41%) of 22 explants had pericentral and periportal fibrosis that was grades ≥ 2 and/or ≥ 2 , respectively. We observed pericentral (n=5), periportal (n=2), and mixed (n=2) patterns of fibrosis, and a significant difference in mean age of subjects with fibrotic versus non-fibrotic livers (mean 16.1 vs 10.5 yrs; p=0.02). There were no indices of synthetic liver dysfunction or portal hypertension (Table 1). Neither a history of gallstone disease nor excess weight appeared to contribute to the development of fibrosis.

Conclusion: For the first time, we report a 41% prevalence of clinically silent, yet histologically significant fibrosis among subjects with UGT1A1 deficiency. Risk for fibrosis appears to accrue with time, indicating that earlier intervention may be prudent when considering alternative treatments such as hepatocyte transplant, auxiliary liver transplant, or viral gene therapy.

Table 1. CN Disease Phenotype

		All (n=22)	No Fibrosis (n=13)	Fibrosis (n=9)	p-value
Demographics	Age at transplant, yrs	12.8 (5.7)	10.5 (5.5)	16.1 (4.2)	0.02
	BMI Percentile	51.8 (24.1)	49.1 (27.5)	55.8 (19.1)	0.5
Hepatobiliary Markers	Total Bilirubin	18.8 (5.5)	17.5 (6.4)	20.7 (3.1)	0.2
	Direct/ Conjugated Bilirubin	0.9 (1.7)	1.1 (2.0)	0.3 (0.1)	0.5
	ALT	87.4 (59.4)	83.4 (41.3)	93.1 (81.4)	0.7
	GGT	32.3 (24)	29.8 (26)	35.9 (21.7)	0.6
Synthetic Liver Function Markers	INR	1.03 (0.07)	1.05 (0.07)	1.02 (0.07)	0.4
	Albumin	32.3 (24)	29.8 (26)	35.9 (21.7)	0.6
Portal Hypertension Markers	Platelets	275.5 (82.7)	285.2 (78.2)	261.6 (91.7)	0.6
	WBC	7.4 (1.8)	7.9 (2)	6.6 (1.3)	0.12
	APRI Score	0.4 (0.2)	0.4 (0.2)	0.4 (0.2)	0.8
History of Gallstones	% yes	62	50	78	0.2
Fibrosis-4 (FIB-4) Index		0.32 (0.2)	0.27 (0.2)	0.39 (0.2)	0.19

***142 CHARACTERISTICS AND OUTCOMES OF PEDIATRIC CHOLESTASIS IN ALAGILLE SYNDROME IN THE MODERN ERA: RESULTS OF A MULTI-CENTRE PROSPECTIVE OBSERVATIONAL STUDY.** *Binita Kamath¹, Wen Ye², Nathan Goodrich³, Kathleen Loomes⁷, Rene Romero⁴, James Heubi⁵, Daniel Leung⁶, Nancy Spinner⁷, David Piccoli⁷, Saul Karpen⁴, Jean Molleston⁸, Karen Murray⁹, Philip Rosenthal¹⁰, Jeffrey Teckman¹¹, Kasper Wang¹², Averell Sherker¹³, John Magee¹⁴.* ¹Division of Gastroenterology, Hospital for Sick Children and University of Toronto, Toronto, ON, Canada; ²Department of Biostatistics, University of Michigan, Ann Arbor, MI; ³Arbor Research Collaborative for Health, Ann Arbor, MI; ⁴Division of Pediatric Gastroenterology, Emory

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Background: Alagille syndrome (ALGS) is an autosomal dominant, multisystem disorder with substantial variation in the penetrance of clinical features. To date, only retrospective cohort studies from the 1990's and earlier, each with heterogeneous inclusion criteria, exist. The lack of prospective data describing current characteristics and outcomes of cholestasis in ALGS undermines clinical management, prognostic capabilities and evaluation of novel therapies.

Methods: We ascertained a cohort of children with ALGS (clinically +/- genetically defined) and native liver, from a multi-center prospective observational study within the Childhood Liver Disease Research Network (ChiLDRen). All patients had documented cholestasis, or a history of cholestasis, as defined by at least one of the following: total bilirubin > 2mg/dl, serum bile acids or GGT > 3x ULN for age, fat soluble vitamin deficiency or intractable pruritus. Survival analysis and competing risk analysis were used to calculate cumulative incidence rate over time for complications with native liver, liver transplant and death.

Results: 272 cholestatic ALGS subjects (2 months-25 years) with a median follow-up of 2.3 years (0-8.5yrs) were included. Genetic data are currently available for 157 subjects. In this group 135/157 (86%) had JAGGED1 mutations, 5/157 (3%) had NOTCH2 mutations and 17/157 had no mutations detected in either JAGGED1 or NOTCH2. Mean (SD) total bilirubin, ALT and GGT at baseline were 5.7mg/dL (6.6), 175U/L (136), and 526U/L (606) respectively. Growth at baseline was significantly delayed compared to norms, with median height Z-score -1.9 (interquartile range [IQR] -2.7, -1.0) and weight Z-scores -1.8 (IQR -2.9, -0.8). Amongst cholestatic ALGS subjects, 50% reported ascites and almost 25% had one or more episode of variceal bleeding by the age of 25 years. 38% experienced bone fractures with the majority of these occurring before the age of 13 years. 70% of cholestatic ALGS children had undergone liver transplantation by 17 years of age and 10% had died (multiple causes, only 3 clearly liver-related).

Conclusions: This study represents a comprehensive assessment of ALGS children with cholestasis in the largest prospective cohort ever described. Survival to early adulthood with native liver is only 20% with a high rate of liver-related complications. The burden of hepatic disease in ALGS is substantial and underpins the need for close medical monitoring and novel therapies.

143 UNRAVELING THE RELATIONSHIP BETWEEN ITCHING, SCRATCH SCALES AND BIOMARKERS IN CHILDREN WITH ALAGILLE SYNDROME.

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Background: Pruritus is a debilitating symptom for patients with cholestasis related to Alagille syndrome (ALGS) and a management challenge for physicians. The pathophysiology and biochemical correlates of cholestasis-induced pruritus have not been elucidated resulting in difficulties in selecting appropriate endpoints for the evaluation of novel therapies for pruritus. We intended to characterize pruritus and associated markers in ALGS subjects who were part of a randomized double-blind placebo-controlled trial (ITCH) of maralixibat (previously LUM001; SHP625), an Apical Sodium-dependent Bile Acid Transporter (ASBT) inhibitor, for cholestasis-induced pruritus.

Methods: Clinical features of ALGS were recorded at baseline and itching was assessed using a novel patient-derived digital diary based on twice-daily caregiver observation of itching severity (Itch Reported Outcome, ItchRO™[Obs], range 0-4[severe]) and the Clinician Scratch Scale (CSS), (range 0-4[severe]). Subjects were eligible for the trial if they had an average daily ItchRO score of ≥ 2 over a 2-week period. Serum biomarkers considered to be associated with pruritus were assessed. Correlations were calculated to compare baseline itching scores with biomarkers.

Results: 37 subjects with median age of 6yrs (1-17) were enrolled [Table 1]. 35 had mutations in *JAGGED1* and 2 in *NOTCH2*. No association was identified between either CSS or ItchRO scores and serum bile acids ($r=-0.08$; $p=0.6$ for both) or autotaxin levels ($r=0.22$; $p=0.2$ for CSS and $r=0.28$; $p=0.3$ for ItchRO). No association was identified between CSS and ItchRO scores ($r=0.22$; $p=0.2$). QOL was markedly reduced as measured by PedsQL (Parent) total score, however there was no significant association between these scores and CSS or ItchRO scores ($r=-0.23$; $p=0.2$ for CSS and $r=-0.16$; $p=0.36$ for ItchRO).

Conclusions: This study highlights the complexity of assessing pruritus in children with ALGS. Clinician and caregiver observations of itching do not correlate with each other, or with putative serum biomarkers of pruritus. The severity of pruritus, measured with either a novel or known disease-specific instrument, did not correlate with QOL, assessed with a generic tool. It should be noted that only patients with moderate to severe pruritus were studied. These observations need to be taken into account when assessing surrogate endpoints for clinical trials of therapies for pruritus.

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Baseline Characteristics of 37 ALGS subjects

	Total Bilirubin mg/dL	ALT U/L	GGT U/L	Total Cholesterol mg/dL	Bile Acids μ M	C4* ng/mL	Autotaxin** ng/mL	CSS	ItchRO™	PedsQL Total Score
Median (IQR)	2.1 (0.9,7.2)	137 (91,214)	329 (203,834)	320 (231,443)	155 (57,310)	4.0 (1.5, 12.8)	2114 (1574, 3264)	3 (2, 4)	2.9 (2.6, 3.1)	67 (52, 80)

*7-alpha-hydroxy-4-cholesten-3-one; biomarker of bile acid biosynthesis

**Enzyme synthesizing lysophosphatidic acid; suspected pruritogen

***144 A CROSS-SECTIONAL MULTI-CENTER ANALYSIS OF CLINICAL FEATURES OF PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS (PFIC) – INITIAL RESULTS OF THE CHILDREN LOGIC PROTOCOL.** Paula Hertel¹, Nathan Goodrich², Richard Thompson³, Laura Bull⁴, Wen Ye⁵, Lee Bass⁶, Molly Bozic⁷, James Heubi⁸, Karen Murray⁹, Grace Kim¹⁰, Sarangarajan Ranganathan¹¹, Robert Squires¹², Frederick Suchy¹³, Riccardo Superina¹⁴, Jeffrey Teckman¹⁵, Kasper Wang¹⁶, Kathleen Loomes¹⁷, Binita Kamath¹⁸, Rene Romero¹⁹, Saul Karpen¹⁹, John Magee²⁰, Averell Sherker²¹, Ronald Sokol²², Benjamin Shneider^{1,23}. ¹Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX; ²Arbor Research Collaborative for Health, Ann Arbor, MI; ³Genetics Core Lab, Institute of Liver Studies, London, United Kingdom; ⁴Liver Center and Institute for Human Genetics, University of California, San Francisco, San Francisco, CA; ⁵Department of Biostatistics, University of Michigan, Ann Arbor, MI; ⁶Division of Pediatric Gastroenterology, Hepatology and Nutrition, Ann & Robert H. Lurie Children's Hospital, Chicago, IL; ⁷Pediatric Gastroenterology, Indiana University School of Medicine /Riley Hospital for Children, Indianapolis, IN; ⁸Division of Pediatric Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ⁹Division of Gastroenterology and Hepatology, University of Washington School of Medicine, Seattle Children's Hospital, Seattle, WA; ¹⁰Department of Pathology, University of California, San Francisco, San Francisco, CA; ¹¹Department of Pathology, Children's Hospital of Pittsburgh, Pittsburgh, PA; ¹²Department of Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital of Pittsburgh, Pittsburgh, PA;

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Background: Limited prospectively collected multi-center data exist regarding the clinical features of PFIC. The **Childhood Liver Disease Research Network (ChiLDReN)** established the Longitudinal Study of Genetic Causes of Intrahepatic Cholestasis (LOGIC – NCT00571272) to fill this knowledge gap.

Methods: We analyzed baseline data from participants with PFIC (as defined in ChiLDReN) prospectively enrolled in LOGIC from 1/2008 – 12/2013. Genomic DNA was sequenced and further analyses were performed exclusively for those with pathogenic bi-allelic mutations in ABCB11 (BSEP) or ATP8B1 (FIC1), or on at least one allele in ABCB4 (MDR3). Baseline demographics, medical and surgical history, disease-related complications, laboratory values, and physical examination findings were analyzed. Subanalyses included those with surgical interruption of the enterohepatic circulation (sEHC), liver transplant (LT) and/or type of ABCB11 mutation.

Results: 238 enrolled participants had genomic sequencing of ATP8B1, ABCB11 and/or ABCB4. Of these, 101 revealing FIC1 (26), BSEP (54 including 8 with two protein truncating mutations [severe] and 9 with p.E297G or p.D482G [mild]), or MDR3 (21 including 5 monoallelic), were analyzed. 35 had sEHC including 10/22 who had undergone LT after sEHC. MDR3 participants were slightly older (table). Onset of symptoms was under 12 mo for ≥80% FIC1 and BSEP. History of pruritus was nearly universal in FIC1 and BSEP but also common in MDR3 disease. In participants with their native liver, thrombocytopenia (plt < 150) was most common in MDR3, and ALT was highest in BSEP, particularly before the age of 24 mo (<24 mo mean 223 IU/L). Failure to thrive was most common in FIC1. In FIC1 and BSEP with sEHC for ≥1 year (n=19; mean 7.2, SD 4.3 yr), 5/10 FIC1 and 4/9 BSEP reported pruritus with active scratching or cutaneous mutilation, and 2/10 FIC1 and 3/9 BSEP had thrombocytopenia suggestive of portal hypertension. The 8 with severe BSEP mutations had either undergone LT (n=4) or were < 24 mo of age (n=4), while 5/9 with mild BSEP mutations had also undergone LT.

Conclusions: We found early disease onset and pruritus predominant in FIC1 and BSEP disease, thrombocytopenia (reflective of portal hypertension) predominant in MDR3, and failure to thrive in FIC1. LT was most common in BSEP, consistent with previous reports. sEHC was commonly followed by persistent pruritus, thrombocytopenia, and/or LT, indicating that these procedures may be of modest success or only in select patients. All BSEP participants > 24 mo old with severe mutation type had undergone LT. Cross-sectional baseline analysis of this heterogeneous cohort is complex but provides insight into the natural history of these disorders.

	FIC1 (n = 26)	BSEP (n = 54)	MDR3 (n=21)
All sEHC : sEHC then LT	14 : 2	19 : 8	2 : 0
Participants enrolled post-LT	2	19	1
Age (mo) median (Q1, Q3)*	51 (14, 160)	60 (16, 123)	122 (59, 139)
Symptom onset	24 (92%)	43 (80%)	8 (38%)
History of pruritus	26 (100%)	51 (94%)	15 (71%)
Weight z-score < -2*	11 (48%)	2 (6%)	0 (0%)
Platelets < 150 (x 103/mm3)*	2 (10%)	5 (17%)	10 (53%)
ALT (IU/L) median (Q1, Q3)*	55 (30, 121)	104 (50, 217)	77 (40, 158)
Tbili (mg/dL) median (Q1, Q3)*	0.9 (0.4, 5.8)	1.1 (0.5, 4.3)	1.0 (0.6, 1.2)

* data reflects participants with native liver at enrollment

146 NOVEL HISTOLOGIC SCORING FOR CONGENITAL HEPATIC FIBROSIS. *Gihan Naguib^{1,2}, David Kleiner³, Karen Murray⁴, Ronen Arnon⁵, Jacqueline Jossen⁵, Kathleen Schwarz², Pallavi Surana¹, Sina Ogholikhan², Daniel Doherty⁷, Meral Gunay-Aygun⁶, Theo Heller¹. ¹Liver Diseases Branch, National Institutes of Health, Bethesda, MD; ²Pediatric Gastroenterology, Hepatology and Nutrition, Johns Hopkins, Baltimore, MD; ³Center for Cancer Research, National Cancer Institute, Bethesda, MD; ⁴Pediatric Gastroenterology and Hepatology, Seattle Children's Hospital, Seattle, WA; ⁵Pediatric Hepatology and Liver transplant, Mount Sinai School of Medicine, New York, NY; ⁶Institute of Genetic Medicine, Johns Hopkins, Baltimore, MD; ⁷Developmental Pediatrics, Seattle Children's Hospital, Seattle, WA*

Introduction: Autosomal recessive polycystic kidney disease (ARPKD), the most common ciliopathy of childhood, is characterized by congenital hepatic fibrosis (CHF) and cystic degeneration of the kidneys. The purpose of this study is to develop a scoring system for CHF and suggest semi-quantification of histologic features to provide a numerical index of histologic features and severity. Currently no histological evaluation system exists and pathology interpretation of disease extent is not standardized.

Methods: A multicenter study that included 38 patients with CHF from 4 centers were evaluated using a novel set of hepatic histologic features. Histologic parameters included scores for lobular inflammation (0-2), interface hepatitis (0 – 2), bile duct inflammation (0 – 1), portal venopathy (0 – 2), sinusoidal dilation (0-1), bile inspissation (0 – 1), ductular regeneration (0-2), duct dilation (0 – 2), ductular reaction distinct from the ductal plate malformation (0 – 3), sinusoid fibrosis (0-1), central vein fibrosis (CVF) (0-1), and fibrosis (0 – 3).

Results: Subject ages ranged from 2 days to 84 years (median 12 years), and 47% (18) of subjects were male. Association of the CHF with autosomal recessive polycystic kidney disease was present in 29% of subjects. Lobular inflammatory scores were in general low: 6 % of patients had a score of 2, 69% of patients had no lobular inflammation receiving a score of 0, and 25% had mild lobular inflammation (score of 1). Interface hepatitis was also not pronounced with only 3% scoring a 2, 30% scoring 1, and 67% of subjects scoring 0. Acute inflammation in the ducts was uncommon with only 14% scoring 1, the remainder 0. Portal venopathy was common with 80% scoring 2, 20 % scoring 1, and no subjects scoring 0. Inspissation of bile was noted in 61%. Duct dilation was noted in 61% (1), 30% with a score of 0 and 9% with a score of 2. Fifty percent had no ductular reaction. 33% of patients had CVF, but sinusoidal fibrosis was only found in 9%.

Fibrosis correlated with ductular reaction (R=0.33, p=0.04), bile inspissation (R=0.44, p=0.006) and bile duct inflammation (R=0.38, p=0.02). Ductular reaction correlated with lobular inflammation (R=0.33, p=0.04). CVF (R=0.53, p=0.001) and regeneration (R=0.48, p=0.01). CVF correlated with regeneration (R=0.47, p=0.01), fibrosis (R=0.69, p<0.001), and interface hepatitis (R=0.34, p=0.04). No correlations were found with portal venopathy.

A subset of subjects (n=25) had keratin (K7) stains. Presence of K7 stain in the periportal area correlated with ductular regeneration (R=0.56, p=0.006), but inversely with duct dilation (R=-0.53, p=0.006). K7 central zone stain correlated with interface hepatitis (R=0.44, p=0.02), but inversely with bile inspissation (R=-0.47, p=0.01).

Conclusion: Developing a pathologic scoring system will standardize the reporting of histological features and their severity in CHF. Standardized histological review and reporting could help elucidate aspects of the pathophysiology of the disease, and serve as a foundation on which clinical correlations can be made. Validation of the scoring system will be performed with a larger sample size.

Score	0	1	2	3
Lobular Inflammation	69	25	6	NA
Interface Hepatitis	67	30	3	NA
Bile duct inflammation	86	14	NA	NA
Portal venopathy	0	20	80	NA
Bile inspissation	39	61	NA	NA
Ductular regeneration	35	46	19	NA
Duct dilation	30	61	9	NA
Ductular reaction	50	36	11	3
Central vein fibrosis	67	33	NA	NA
Sinusoid fibrosis	91	9	NA	NA
Sinusoid dilation	86	14	NA	NA
Fibrosis	3	11	36	50

Results given in percent of subjects for each score N=38

147 **CARDIOMEGALY ASSOCIATED WITH TACROLIMUS USE IN PEDIATRIC LIVER**

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Introduction: There have been multiple case reports and autopsy studies associating the use of tacrolimus in organ transplant recipients with the development of cardiomegaly and left ventricular hypertrophy. There has been one prospective study reporting two cases of cardiac toxicity associated with tacrolimus; however, both the cases occurred in patients whose tacrolimus levels were above 30 ng/ml. Further studies are required to evaluate the association between tacrolimus use and cardiotoxicity. We aim to evaluate the association between tacrolimus use within therapeutic drug level goal of 8-12 ng/ml with cardiomegaly in pediatric liver transplant recipients at our institution.

Methods: This is a retrospective study involving pediatric liver transplant recipients, with no prior cardiomegaly, who received tacrolimus for maintenance immunosuppression. All patients between the ages of 0-19 years, who were transplanted between January, 2007 to December, 2016, were included in the study. Patients with previous history of cardiomegaly were excluded from the study. We reviewed their electronic medical records for findings of cardiomegaly or ventricular hypertrophy on chest x-ray, EKG, echocardiogram and CT chest. Patients with positive findings on either of these were evaluated for clinically significant cardiac disease based on change in medication or cardiology consultation.

Results: Total 63 patients were included in this study. Two patients who died in the immediate post-operative period were excluded from the study. Out of 61 patients, 8 patients (13%) had chest x-ray findings of cardiomegaly or enlargement of cardiac silhouette and 7 patients (11%) had EKG findings of ventricular hypertrophy. Only 2 patients (3%) had positive echocardiogram. None of these patients had any clinical implications of cardiomegaly as evidenced by the absence of cardiology consultation, tacrolimus dose modification or discontinuation.

Discussion: Tacrolimus-related cardiomegaly seems to be associated with higher drug levels. Tacrolimus drug level required for maintenance immunosuppression in liver transplant patients does not seem to be associated with tacrolimus-related cardiomegaly. Thus, tacrolimus can be safely used for long-term immunosuppression in liver transplant patients as long as there is close drug level monitoring.

148 **TRANSCATHETER RECANALIZATION WITH ANGIOPLASTY AND/OR STENTING: A NOVEL, MINIMALLY-INVASIVE TREATMENT FOR CHRONIC PORTAL VEIN THROMBOSIS WITH CAVERNOUS TRANSFORMATION IN CHILDREN.**

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Background: Chronic portal vein thrombosis (CPVT) with cavernous transformation of the portal vein (PV) is a common cause of noncirrhotic portal hypertension, and a leading cause of major gastrointestinal (GI) bleeding in children. A meso-Rex bypass is feasible in patients with confluent left and right intrahepatic PVs and a patent Rex segment of the left PV. We sought to evaluate the feasibility of performing transcatheter recanalization of CPVT with balloon angioplasty and/or stenting as an alternate means of therapy for patients with CPVT.

Methods: We performed a retrospective study of patients taken to catheterization (cath) for possible transcatheter recanalization of CPVT at a single tertiary children's hospital from 4/2014-6/2017.

Results: A total of 13 children (7 female) underwent 17 cath, with median weight of 13.9 kg (range 7.5-88) and age of 4.1 years (1-15.3). Pre-procedural imaging included MRI and Doppler ultrasound in all, with CPVT and cavernous transformation of the portal vein diagnosed in 11 patients, and 2 initially misdiagnosed as Abernethy malformation. Four patients had history of prematurity and prior umbilical venous catheterization. CPVT manifestations included GI bleeding (10 patients), hyperammonemia (3), thrombocytopenia (11) and splenomegaly (11). Complete right heart catheterization and hepatic vein wedge angiography were performed, followed by percutaneous trans-splenic and/or direct puncture of intrahepatic portal veins. Additional findings at cath included mild pulmonary hypertension (1 patient) and mild hepatopulmonary syndrome (1). Median cath time was 7.2 hours (range 2-11.5). Recanalization of CPVT was successful in 4 patients (single cath in 3 patients, 3 cath in 1 patient), unsuccessful in 7, and not attempted in 2. Successful procedures entailed balloon angioplasty of main and right PV with rheolytic thrombectomy in left PV in one case, balloon angioplasty of main PV and 4 branches of right PV with rheolytic thrombectomy in another case, balloon angioplasty of main, right and left PV in another case, and balloon angioplasty of main PV and 6 intrahepatic PV branches followed by reocclusion requiring re-angioplasty of 4 intrahepatic PV branches and placement of 3 stents during 2 subsequent procedures in fourth case. Diffuse intrahepatic PV

occlusion with non-confluent left and right PVs was found in 2 of 4 successful cases. There were no major complications such as urgent surgical exploration or mortality. Minor complications consisted of intra-abdominal bleeding from splenic puncture site requiring transfusion in 3 cath (2 among unsuccessful cases). All 4 successful cases were subsequently treated with low molecular weight heparin, with additional dual antiplatelet therapy in 1. At most recent follow-up from final cath (range 1 day - 20 months), the 4 patients with successful CPVT recanalization have maintained patency of PVs on ultrasound, with no recurrence of GI bleed and improvement in platelet count and spleen size.

Conclusion: Transcatheter recanalization of CPVT is feasible in a subset of patients, including those with diffuse intrahepatic PV occlusion that would not otherwise be candidates for meso-Rex shunting. In case of failure of balloon angioplasty due to reocclusion, stent implantation may be a viable option. At medium term follow-up, all successful recanalization cases continued to maintain patency with improved manifestations of hypersplenism. Although transcatheter recanalization is lengthy and technically challenging, it can be attempted with low risk. Further research is needed to determine the most suitable candidates for this procedure, and whether this approach should be considered as a viable first-line therapeutic option for children with CPVT.

Figure 1. Figure 1. (a) Early phase of initial venography revealed a portal cavernoma (*), but late phase of the same angiogram (b) disclosed a hypoplastic and nearly occluded main portal vein (arrow) with demonstration of small intrahepatic portal veins (arrowheads)

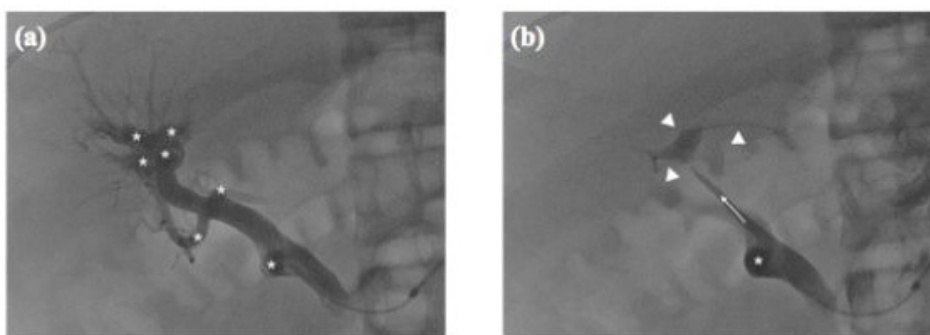
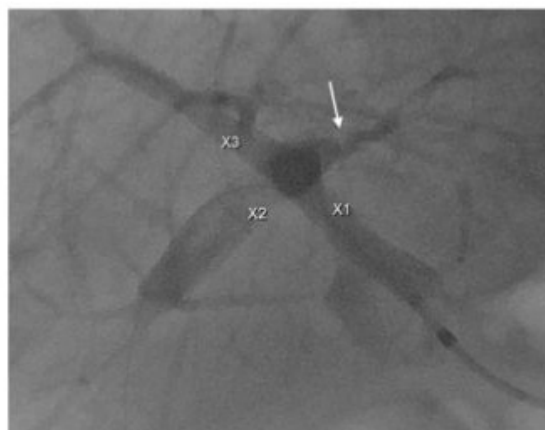


Figure 2. Post-intervention venography shows increased main portal vein caliber (x1) with filling of the right anterior (x2) and posterior (x3) portal veins and a persistent non-occlusive thrombus in the left portal vein (arrow)



151 HEPATOVENOCAVAL SYNDROME A DIFFERENT ENTITY FROM BUDD CHIARI SYNDROME IN CHILDREN. Huma Cheema. *Pediatric Gastroenterology Hepatology, Children's Hospital lahore, Lahore, Punjab, Pakistan*

Background: Hepatovenocaval syndrome (HVCS) is the obliteration of hepatic portion of inferior vena cava with or without involvement of hepatic veins (HV) and development of cavo-caval collaterals. Experts differ in opinion whether it is a variant

of classic Budd Chiari Syndrome or a separate entity in Asian population. We studied demographic, clinical, laboratory and outcome data in Hepatovenocaval Syndrome (HVCS) and Budd Chiari Syndrome (BCS) to evaluate for similarities and differences.

Methods: Children under 16 years of age having ascites, prominent veins over abdomen and obstruction or thrombosis of hepatic part of inferior vena cava and /or hepatic veins on Doppler ultrasound were studied over a period of 3 years from Jan: 2014 to Jan: 2017. HVCS was defined as obliteration of hepatic portion of IVC with or without involvement of hepatic veins and BCS was defined as obliteration of hepatic veins with or without involvement of supra hepatic portion of IVC. Data including age sex, caste, duration of symptoms, socioeconomic status detailed examination including height, weight, z-score and stigmata of chronic liver disease were recorded. Diagnostic paracentesis was performed to calculate SAAG gradient and ascetic fluid analysis. Gadoliniums enhanced Multiphasic Magnetic Resonance (MR) scans were performed in all children to confirm diagnosis. Liver biopsy was performed in children where coagulation profile was normal and Venocavography was performed in some children where diagnosis was in doubt.

Results: 58 out of 92 children fulfilled our inclusion criteria. Out of them 67% (39) were HVCS and 33% (19) were Budd Chiari Syndrome. Mean age of presentation in BCS was 9.5 ± 2.58 years and in HVCS it was 4.12 ± 0.977 years. Male to female ratio in BCS was 1:1 while female were little more affected in HVCS with a ratio of 1:1.8. All (100%) of our HVCS presented with chronic liver disease as compared to BCS (33%). Consanguinity was more prevalent in BCS as compared to HVCS (84% Vs 10%). 85% children belonged to poor socioeconomic status in HVCS as compared to 35% in BCS. All children with HVCS had acute exacerbation of their symptoms that responded to antibiotics. Procoagulant disorder was found in 47% children with BCS most common of them was deficiency of anti-thrombin III (26%) followed by protein S (11%) then protein C (5%) and Factor V mutation (5%) No Procoagulant disorder was found for Hepatovenocaval syndrome. Radiological parameters were also quite different in both, caudate hypertrophy, intrahepatic and sub capsular collaterals were found in BCS while cavo-caval collaterals were found in HVCS. In HVCS histopathology showed periportal inflammation with fibrous expansion of portal tracts, some of them were having cirrhotic nodule formation while in BCS histopathology revealed open sinusoids, peri-venular inflammation and ballooning degeneration of hepatocytes. 7 Children with Hepatovenocaval Syndrome developed chronic liver disease Child Pugh C. Three of them underwent successful orthotropic liver transplant, four of them expired because of non-affordability of liver transplant. Remainder has stable chronic liver disease requiring supportive treatment and antibiotics during acute exacerbation. One child with Budd Chiari Syndrome who presented with Fulminant form expired, three with chronic liver disease child Pugh C underwent orthotropic liver transplant. Nine of them presented with sub-acute form having pro-coagulant disorder were started on anti-coagulant therapy and doing well.

Conclusion: Hepatovenocaval Syndrome is a different entity from Budd Chiari Syndrome in etiopathogenesis, clinical presentation, radiological and histopathological findings and outcome. It affects young children with female preponderance. It is more common in the lower socioeconomic strata in developing countries and it is postulated that it probably has a similar etiopathogenesis to portal vein thrombosis with phlebitis involving the intrahepatic part of IVC. It has slow insidious course with acute exacerbation. Acute exacerbations may be related to recurrent gastrointestinal infections in the poor socioeconomic strata. If acute exacerbations are treated well subsequent ischemic injury to the liver can be halted slowing progress to liver cirrhosis.

152 **NONALCOHOLIC FATTY LIVER DISEASE IS ASSOCIATED WITH ABNORMAL PURINERGIC SIGNALING.** *Huyen Nguyen, Charles Kresge, Qin Li, Andrew Feranchak. University of Texas Southwestern, Dallas, TX*

Background: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in children and adults, however the cellular mechanism of liver injury is not completely understood. Cell volume regulation, linked to liver metabolism and insulin signaling, is a critical function of hepatocytes. Under normal conditions, hepatocyte cell volume is tightly regulated by the purinergic signaling pathway, involving ATP release and stimulation of cell surface purinergic P2Y2 receptors. Increase in cell size, ballooning degeneration, and apoptotic cell death are hallmarks of NAFLD and suggest abnormalities in cell volume regulation and purinergic signaling. Therefore, the aim of the present studies was to determine the role of purinergic signaling in the cellular response to fat accumulation as occurs during NAFLD.

Methods: Studies were performed in HTC rat hepatoma cells incubated in the presence or absence of free fatty acid. Fat accumulation was assessed by oil red staining. Cell volume was measured by Coulter-Multisizer; ATP release was measured by luciferin-luciferase assay; purinergic (P2) receptor expression was determined by RT-PCR and Western blot.

Results: Incubation with oleic acid, palmitic acid, and a combination of oleic acid/palmitic acid (2:1) all resulted in fat accumulation, though oleic acid caused the greatest increase in intracellular fat. In all cases, fat accumulation resulted in large cells which demonstrated abnormal regulatory volume decrease (RVD) when exposed to hypotonic conditions or

insulin. As normal RVD requires a coordinated response including ATP release and activation of membrane P2 receptors, we sought to determine effects of fat accumulation on ATP release and P2 receptor expression. Cells incubated with oleic acid or oleic/palmitic acid had significantly less ATP release than control cells in response to either insulin or hypotonic exposure. Additionally, while P2Y2 and P2X4 expression was unaffected by fat accumulation, P2X7 receptor expression increased by 4-fold. The increase in membrane P2X7 receptor expression was associated with an increase in apoptosis when fatty cells were exposed to exogenous ATP. The increase in P2X7 expression and the percent of apoptotic cells was greatest with palmitic acid.

Conclusion: Hepatocyte fat accumulation results in altered ATP release and cell volume regulation in NAFLD. Additionally, accumulation of free fatty acids was associated with altered expression of P2 receptors with an increase in the expression of the pro-apoptotic P2X7 receptor. Understanding the role of P2X7 receptor signaling in NAFLD may suggest a therapeutic target to modulate the cellular injury associated with fat accumulation during NAFLD.

153 DIFFERENCES BETWEEN NON-OBESE AND OBESE PEDIATRIC NONALCOHOLIC FATTY LIVER DISEASE PATIENTS: A SINGLE CENTER EXPERIENCE. *Hyun Jin Kim. Pediatrics, Inje University, Busan Paik Hospital, Busan, Korea (the Republic of)*

Introduction: Nonalcoholic fatty liver disease (NAFLD) is common in obesity and its incidence is increasing parallel with that. However, non-obese patients are also increasing susceptible to have NAFLD. The aim of this study was to compare the clinical characteristics of obese and non-obese pediatric patients with NAFLD.

Methods: We retrospectively analyzed 68 NAFLD patients who diagnosed at 10-18 years old between January 2010 and October 2016. Other diseases were excluded in all patients. Obesity was defined as a body mass index (BMI) \geq 95th percentile for age and gender or BMI \geq 25kg/m². A laboratory, anthropometrics study and abdominal ultrasonography were evaluated.

Results: Of 68 cases, 26 (38.2%) were non-obese. The male-to-female ratio was 5.8:1 and the median age at diagnosis was 13 years (range, 10-17 years) in all patients. Non-obese had significantly higher triglyceride (223.0 vs 145.9, $p = 0.047$) and total cholesterol (211.6 vs 173.2, $p = 0.011$) levels than obese patients. In univariate analysis, (high-density lipoprotein) HDL-cholesterol level of <40 mg/dl (HR: 6.5, 95% CI = 2.13-7.10, $p = 0.048$) and total cholesterol level of >200 mg/dl (HR: 5.6, 95% CI = 1.23-15.31, $p = 0.038$) were associated with increased risk of NAFLD.

Conclusion: Non-obese patients occupy large proportion of NAFLD. Similar to adult, NAFLD should be considered in lean patients, especially, who have metabolic disturbances.

155 SURVIVAL OF INFANTS WITH RAPIDLY PROGRESSIVE LYSOSOMAL ACID LIPASE DEFICIENCY TREATED WITH SEBELIPASE ALFA. *Simon Jones¹, Suresh Vijay², Simona Fecarotta³, Arunabha Ghosh¹, Kerstin Allen⁴, Mark Friedman⁴. ¹Manchester Centre for Genomic Medicine, Central Manchester University Hospitals NHS Foundation Trust, St. Mary's Hospital, Manchester, United Kingdom; ²Birmingham Children's Hospital, Birmingham, United Kingdom; ³Federico II University, Naples, Italy; ⁴Alexion Pharmaceuticals, Inc., New Haven, CT*

Lysosomal acid lipase deficiency (LAL-D) patients treated with sebelipase alfa (SA) have shown prolonged survival compared with historical controls, in whom median survival has been observed to be 3.7 months. In the current ongoing, open-label, phase 2 study of SA treatment in infants with rapidly progressive LAL-D, we evaluated patient survival and the clinical profile of infants surviving to >12 months of age. Typical presenting features included hepatosplenomegaly (9/10 patients), failure to thrive (8/10), severe anemia/thrombocytopenia (7/10), and adrenal calcification (5/10). All patients started on SA 1 mg/kg infused intravenously once weekly, and with the exception of 1 patient who died after 4 infusions, all other patients were dose escalated to at least 3 mg/kg once weekly following protocol-defined criteria. Median (range) age at SA treatment initiation was 2.8 (0.5 to 4.1) months. As of March 23, 2017, 8 patients remain in the study, and all but one is >12 months of age (median [range], 25.1 [11.4 to 37.5] months), with a mean time in the study of 21.7 months; all 8 patients continue to receive SA. The oldest patient has been receiving SA for 35.4 months. There have been 2 deaths (in infants ages 4.9 and 13.8 months), 1 due to a device malfunction and the other due to disease progression; both were considered unrelated to the study drug. Surviving patients who are older than 12 months demonstrated improvements at week 48 (Table). Patients' weight-for-age z scores at week 48 ranged from -1.4 to 0.7 with a median z score increase of 2.1. Investigators and patients' families reported satisfactory age-appropriate developmental progress for all subjects. All surviving patients continue to receive sebelipase alfa. Six of 10 patients have had detectable anti-drug antibody titers at ≥ 1 visit; all 6 developed neutralizing antibodies. However, there has been no association between the presence of antibodies and safety or efficacy outcomes. In conclusion, treatment with SA is associated with a considerable survival advantage and improvement in disease activity parameters in these infants with rapidly progressive LAL-D.

Patient		ALT (U/L)	AST (U/L)	Albumin (g/L)	Hb (g/L)	Platelet Count (/μL)	LDL-C (mg/dL)	Weight Percentile
2001-001	Observed Change from BL	73 -175	119 -322	33 13	123 42	309 74	89 -54	BL 0.1 Wk 48 28.4
2001-002	Observed Change from BL	148 --	232 --	26 --	118 --	145 --	42 --	BL 2.0 Wk 48 29.1
2001-006	Observed Change from BL	70 38	36 -22	26 -3	110 --	494 --	72* --	BL 28.4 Wk 48 77.0
2001-008	Observed Change from BL	30 -3	43 -58	26 6	110 --	206 --	124 --	BL 0 Wk 48 46.4
2002-005	Observed Change from BL	50 -17	93 -45	41 17	103 19	367 221	-- --	BL 0 Wk 48 20.9
2103-009	Observed Change from BL	103 66	88 -10	26 6	112 20	268 146	51 -68	BL 3.1 Wk 48 7.6
2401-007	Observed Change from BL	58 --	130* --	20 --	98 --	320 --	58 --	BL 28.1 Wk 48 75.8

*Collected 7 to 8 weeks early. BL= baseline.

156 **MDR3 DEFICIENCY MIMICKING WILSON DISEASE: THE IMPORTANCE OF NEXT GENERATION SEQUENCING BASED MULTI-GENE PANEL ANALYSIS FOR DEFINITIVE**

DIAGNOSIS. Kishwer Kumar, Ali Syed Akhaturl Hassan, Dieter Broering, Mohammad Shagrani. *Pediatric Transplant Hepatology, Organ Transplant Centre, King Faisal Specialist Hospital and Research Centre, Riyadh, Riyadh, Saudi Arabia*

Objectives and study: An autosomal recessive defect in the gene ABCB4 located on chromosome 7 that encodes for the Multidrug resistance class III P-glycoprotein (MDR3) results in clinical entity called Progressive Familial Intra-hepatic Cholestasis type 3 (PFIC3). Those affected usually present with high gamma glutamyl-transferase (GGT). The age at presentation varies from infancy to adulthood.

Wilson disease on the other hand is also an autosomal recessive disorder due to a mutation in the ATP7B gene that encodes for the copper-transporting P-type ATPase. A defect in this protein leads to excessive Copper accumulation in hepatocytes, also evidenced is low serum Ceruloplasmin level and high urinary copper excretion.

However, in cholestatic diseases such as MDR3 deficiency, primary sclerosing cholangitis and primary biliary cirrhosis we also find elevated hepatic copper content and biochemical profile similar to that found in Wilson disease. Hence making the diagnosis of these cholestatic disorders challenging. Here we present three such cases which were initially labeled as Wilson disease based on liver biopsy and biochemical profile but were later confirmed to have MDR3 deficiency based on genetic studies.

Methods/Results: Using next generation sequencing-based multi-gene panel for the first time to diagnose familial cholestatic diseases, in our retrospective cohort there were six (post liver transplant) out of 98 patients with clinical and biochemical diagnosis of Wilson disease. Three of them were found to be negative for Wilson disease gene and instead had a homozygous ABCB4 gene mutation. These three patients were previously misdiagnosed as Wilson disease based on low serum Ceruloplasmin, high serum Copper and high Copper content on liver biopsy.

Conclusion: There are scattered case reports of patients with PFIC3 mimicking the biochemical profile similar to that found in patients in Wilson disease. Labeling such patients erroneously as Wilson disease exposes them to wrong management. Since the administration of chelation therapy has its own adverse effects, the correct diagnosis of PFIC3 is imperative to avoid the toxicities attributed to chelation therapy. Early diagnosis and timely intervention in patients with PFIC3 helps reverse the disease. Patients with PFIC3 are known to be at risk of hepatocellular carcinoma (HCC) which may be averted by early initiation of Ursodeoxycholic acid thus further increasing the need for timely correct diagnosis.

Studies have showed that patients with MDR3 deficiency have altered metabolism of Copper in the hepatocytes. Thus they have an overlap in the presentation with Wilson disease patients due to this alteration of Copper metabolism. MDR3 protein is

predominantly expressed in the canalicular membrane of hepatocytes & is essential in transporting biliary phospholipids. Its dysfunction leads to exposure of the biliary epithelium to toxic bile salts which subsequently result in cholestasis, cholangitis and biliary cirrhosis.

Biochemical profile of low Ceruloplasmin, high urinary Copper and high Copper content on liver biopsy cannot be relied upon when making a definitive diagnosis of Wilson disease, doing so may lead to misdiagnosis which affects patient management. We emphasize the importance of confirming the diagnosis of Wilson disease and PFIC3 by genetic studies wherever possible since there is an overlap in the biochemical profile.

157 HUMAN STEM CELL-DERIVED ENCAPSULATED LIVER TISSUE AS AN EFFECTIVE, CONSISTENT AND LONG-LASTING IN VITRO TOOL FOR DRUG TESTING AND DEVELOPMENT.

Claudia Raggi¹, Marie-Agnès M'Callum², Chenicka-Lyn Mangahas², Anu David³, Zachary Cohen², Ariella Shikanov³, Massimiliano Paganelli^{1,2}. ¹Gastroenterology, Hepatology and Nutrition, Sainte-Justine Hospital, Université de Montréal, Montreal, QC, Canada; ²Hepatology and Cell Therapy Lab, Sainte-Justine Hospital, Université de Montréal, Montreal, QC, Canada; ³Biomedical Engineering, University of Michigan, Ann Arbor, MI

Background/Aim: Hepatocytes obtained through in vitro differentiation of induced pluripotent stem cells (iPSCs) are mostly immature as compared to primary hepatocytes and do not last long in culture. This limits their use for in vitro drug testing and development, as well as their potential for regenerative medicine. The aim of this project was to develop an innovative stem cell-based product able to perform mature liver functions in vitro, to be used for drug testing and stem cell therapy.

Methods: We used thoroughly-characterized human iPSCs, cultured in strict feeder-free and xeno-free conditions, to generate posterior foregut cells and endothelial and mesenchymal progenitor cells using in vitro differentiation protocols mimicking liver organogenesis. After full characterization, the 3 cell types were seeded at a fixed ratio and cultured for 5 days in suspension within custom-made low-attachment micropatterned plates (500mm-diameter microcavities), in a defined medium supplemented with growth factors to support liver development. At day 10 the obtained microaggregated (liver organoids) were characterized for liver-specific markers and functions, and then encapsulated in a finely-tuned PEG-based hydrogel. The obtained Encapsulated Liver Tissues, each containing tens-to-hundreds of organoids, were characterized (n=7) and compared to primary human hepatocytes.

Results: After 72h from seeding the 3 co-cultured, iPSC-derived cell types undergo condensation to form organoids measuring 194.3 ± 41.5 μ m in diameter. At day 10 they show a complex 3D structure consisting in a core composed of endothelial and mesenchymal cells, with extracellular matrix deposition, and an outer layer of hepatocyte-like cells. These hepatocytes express markers typical of fetal human hepatocytes (such as albumin, alpha-fetoprotein, CK-19 and EpCam). Maturation of posterior foregut-derived cells into hepatocytes (a portion of which comparable to adult hepatocytes), as well as the development of biliary and stellate cells within the organoids was confirmed at single-cell mRNA-Seq (Drop-Seq). Nevertheless, such **liver organoids** start synthesizing and secreting human albumin and urea at day 4 post-seeding, and at day 10 show a synthetic function comparable to that of thawed primary human hepatocytes (19.6 ± 4.6 mg albumin/24h/ 10^6 liver cells and 30.9 ± 4 mg urea/24h/ 10^6 liver cells). The activity of cytochrome P450 3A4 was detected in our liver organoids at day 10 (as compared to standard iPSC-derived hepatocyte-like cells that acquire Cyp3A4 function only after 25 days). Organoids were encapsulated within a PEG-based hydrogel to stimulate maturation (20 or 100 organoids/gel). We used 5% photopolymerized 4-arm PEG-vinyl sulfone (PEG-VS) to allow optimal diffusion of culture medium and growth factors while conferring physical properties that permit manipulation with surgical instruments. Full polymerization of the organoid-containing hydrogel was obtained in 4 minutes with a very low UVA radiation exposure (115.6 mW/cm²). Calculated mesh size (Flory-Rehner equation) of such a hydrogel was 17.7 ± 0.8 nm. Within the biomaterial, organoids' condensation and size increased, while no significant cell death was observed. Encapsulated organoids (**Encapsulated Liver Tissue**, or ELT) showed significantly higher Cyp3A4 activity and urea production capabilities than non-encapsulated organoids after only 10 days. RNA-Seq analysis confirmed the significant maturation of the organoids within the hydrogel. Albumin synthesis increased over the first 12 days within the hydrogel to reach levels comparable to freshly isolated primary human hepatocytes (1.2 mg/24h/ 10^6 liver cells). Such a function was maintained stably for at least 28 days. The ELT expressed phase I, II and III drug metabolizing enzyme and was able to efficiently metabolize ammonia and tacrolimus. The ELT could easily be generated in a 96-well format and was resistant to cryopreservation (showing no reduction in its metabolic functions upon freeze/thawing cycles).

Conclusions: To our knowledge, these are the first complex liver organoids generated using 3 cell types all derived from a single iPSC population. And the ELT is the first stem cell-derived product to show in vitro functions comparable to freshly-isolated primary human hepatocytes, with the added advantages of unlimited supply, consistent and long-lasting efficacy, and resistance to cryopreservation. All such features make the ELT a promising product for *in vitro* drug testing and development.

The hydrogel's mesh size allows urea and albumin to diffuse freely, while it block IgG. This, together with the hydrogel's non-degradability, support published data on immune-isolation provided by encapsulation, and open the way for the use of the ELT for heterologous cell therapy of liver disease, without immunosuppression. Its use for cell therapy applied to acute and chronic liver failure is currently being assessed.

158 THE ROLE OF INFECTION IN MORTALITY AFTER PEDIATRIC LIVER TRANSPLANT. Mohamed Barr^{1,2}, Kishwer Kumar¹, Ali Syed Akhtarul Hassan¹, Laszlo Szonyi¹. ¹Pediatric Liver Transplant, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia; ²Department of Pediatrics, Tanta University, Tanta, Tanta, Egypt

Background: Since the evolution of pediatric liver transplantation, early- and late-onset infections have been documented as etiologic factors contributing to recipient morbidity and mortality. The nature of the primary disease, post-transplant immunosuppressed state, possible post-transplant complications, co-morbid conditions, and invasive interventions, all might have variable implications on the recipient's response to a variety of infectious agents. There is scarcity of data describing the impact of infection as a direct etiology, or as a contributing factor, in limiting the life of recipient children after liver transplantation.

Aim: To estimate the role of infection in pediatric liver transplant mortality in a high volume pediatric liver transplant center.

Methods: We collected the documented mortalities, related to various infectious agents after pediatric liver transplantation, between January 2011 and June 2017, in King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.

Results: Out of 269 pediatric liver transplants, between January 2011 and June 2017, we reported (n=6; 2.2%) infection-related mortalities. All cases were females, and their ages at transplantation ranged from 7 months to 15^{6/12} years, with a mean of 63.2 months. Their primary diseases were; biliary atresia (n=2; 33.3%) -one of them was syndromic biliary atresia, with polysplenia-, sclerosing cholangitis (n=2; 33.3%), acute liver failure secondary to autoimmune hepatitis (n=1; 16.7%), and one case had autosomal recessive polycystic kidney disease with liver fibrosis (n=1; 16.7%). Four cases were transplanted once. Two cases were retransplanted; one of them after 24 days, secondary to hepatic artery thrombosis, then died 41 days post-second transplant. The other case was re-transplanted after 274 days, secondary to vanishing bile duct syndrome, however, her death was secondary to post-cardiac surgical infection (after repair of left ventricular outflow tract obstruction), and she died 211 days after re-transplant. The mean post transplant duration at death for all patients, was 345.8 days (considering the last transplant for re-transplanted patients). Regarding the causes of death; two cases had acute on top of chronic rejections complicated with sepsis, one of them had respiratory *Candida albicans*, in addition to urinary *Escherichia coli* (died 851 days post-transplant), and the other case had bloodstream *Candida dubliniensis* (died 647 days post-transplant). Of note, that the child transplanted secondary to syndromic biliary atresia (with polysplenia) developed severe CMV viremia, which responded to foscarnet, and then, she had bocavirus pneumonia ended with bronchiolitis obliterans, and downhill respiratory failure (died 108 days post-transplant). The other three cases had bacterial infections; one case had *Pseudomonas aeruginosa*, another case had *Escherichia coli*, and the third had vancomycin resistant-*Enterococcus*; all of them ended with sepsis with eventual multi-organ system failure (died 211, 217, and 41 days post-transplant, respectively).

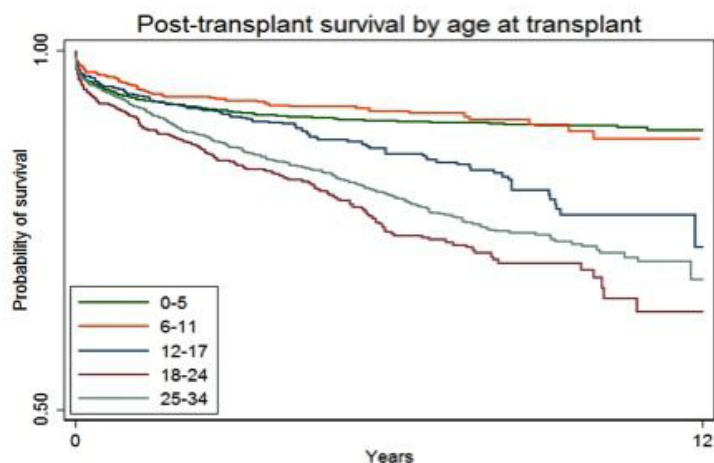
Conclusion: Over six years, and out of 269 pediatric liver transplants, infection related mortality was estimated as 2.2% in our data. Infections occurred at variable durations post-transplant, with a mean of 345.8 days. Several factors contributed to the life limiting infections; included the primary disease, post-transplant complications, re-transplantation, co-morbid states, and major surgical interventions. Adding to the few case reports in the literature, we described bocavirus pneumonia and bloodstream *Candida dubliniensis* as possible factors contributing to mortality after pediatric liver transplant.

160 WAITLIST AND POST-TRANSPLANTATION OUTCOMES IN LIVER TRANSPLANT REGISTRANTS AND RECIPIENTS AGES 18-24 YEARS OLD: ANALYSIS OF THE UNOS

DATABASE. Noelle Ebel¹, Evelyn Hsu^{1,2}, Kristin Berry³, Simon Horslen^{1,2}, George Ioannou^{4,5}. ¹Pediatrics, University of Washington, Seattle, WA; ²Center for Clinical and Translational Research, Seattle Children's Research Institute, Seattle, WA; ³Research and Development, Veterans Affairs Puget Sound Healthcare System, Seattle, WA; ⁴Medicine, University of Washington, Seattle, WA; ⁵Medicine, Veterans Affairs Puget Sound Healthcare System, Seattle, WA

We aimed to describe liver transplantation waitlist and post-transplantation outcomes in 18-24 year olds compared to both younger (0-17 year old) and older (25-34 year old) registrants (n=13,979) and recipients (n=8,718) utilizing national data from the United Network for Organ Sharing from February 2002 to March 2015. We used competing risks analysis to examine the association between age at listing and the competing waitlist outcomes of transplantation, death or drop-out and used a Cox proportional hazards regression model to study the association between age at transplantation and post-transplantation graft and patient survival. Among non-Status 1A registrants, both 0-17 and 25-34 year olds were less likely to experience drop-out from the waiting list compared to 18-24 year olds (adjusted sub-hazard ratio [ASHR] 0-5 years old=0.36, 6-11=0.29,

12-17=0.48, 18-24=1.00, 25-34=0.82) and 0-17 year olds were more likely to be transplanted compared to 18-24 year old registrants (ASHR 0-5 years old=1.94, 6-11=2.04, 12-17=1.49, 18-24=1.00, 25-34=1.05). While recipients aged 18-24 years had a similar risk of graft failure compared to all other age groups, late graft loss (>365 days after transplantation) was more likely to occur in adolescents and adults compared to children 0-11 years old (proportion 0-5 years old=0.23, 6-11=0.36, 12-17=0.67, 18-24=0.62, 25-34=0.53). Most strikingly, younger and older age groups had significantly lower post-transplant mortality compared to 18-24 year olds (adjusted hazard ratio 0-5 years olds=0.53, 6-11=0.48, 12-17=0.70, 18-24=1.00, 25-34=0.77). This may be related to lower likelihood of re-transplantation after graft failure in 18-24 year olds (odds ratio 0-5 years old=2.53, 6-11=2.78, 12-17=2.00, 18-24=1.00, 25-34=1.34). We describe for the first time worse waitlist and post-transplant outcomes in 18-24 year olds compared to both younger and older age groups among liver transplant registrants and recipients in the United States from 2002-2015.



MICROBIOLOGY/INFECTIONS/PROBIOTICS

162 DIFFERENCES IN THE STOOL AND SKIN MICROBIOME, VIRULENCE FACTOR AND ANTIMICROBIAL RESISTANCE GENES IN A PRIVATE ROOM VERSUS A SHARED SPACE NEONATAL INTENSIVE CARE UNIT. Allison Ta¹, Suchitra Hourigan^{1,2}, Elisabeth Klein¹, Rajiv Baveja¹, Nassim Chettout¹, Nicole Clemency¹, Colin Heberling³, Poorani Subramanian³, Nur Hasan³, Rita Colwell³. ¹Pediatrics, Inova Fairfax Hospital, Fairfax, VA; ²Pediatric Specialists of Virginia, Falls Church, VA; ³Cosmos ID, Baltimore, MD

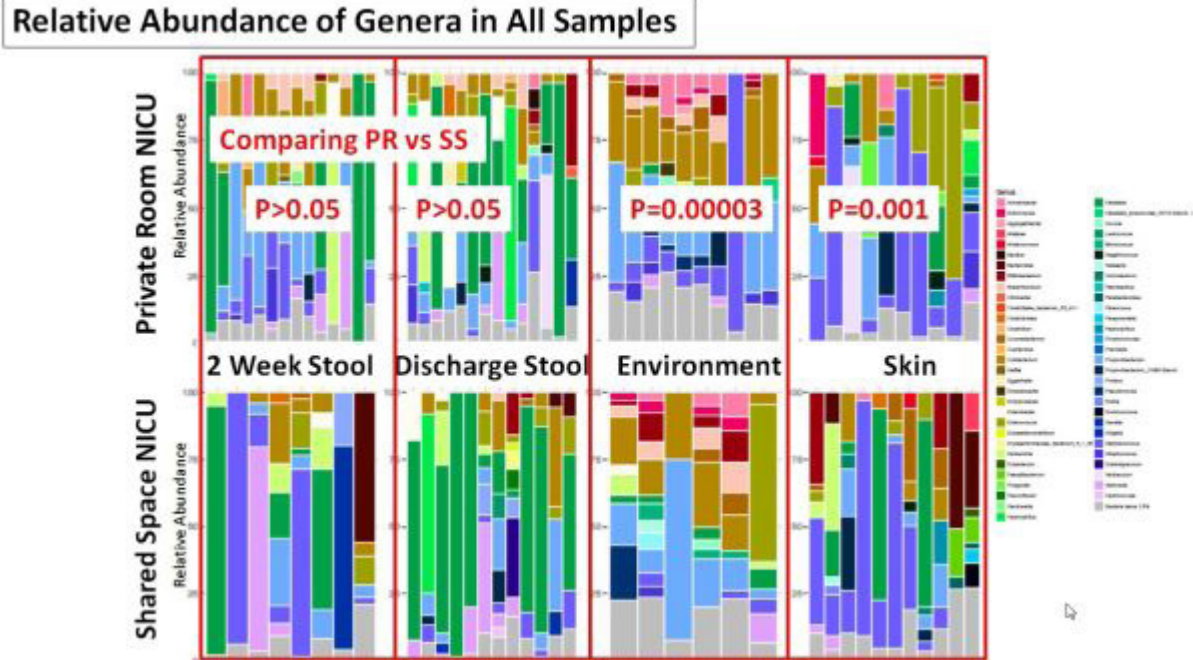
Background: Critical microbiome development occurs early in life impacting future health. It is unknown whether there is differential microbiome development in infants in the neonatal intensive care unit (NICU) cared for in private rooms (PRs) vs. a shared space (SS) with other infants. Aims: To identify differences in the skin, stool and environmental microbiome, virulence factor and antimicrobial resistance genes in neonates in a PR vs. a SS NICU.

Methods: As part of a longitudinal NICU microbiome study, stool was collected at 2 weeks and discharge along with a skin swab from the groin. 18 neonates from a PR NICU and 14 from a SS NICU were compared. Infants from each NICU were matched for gestational age, delivery mode and length of stay. Environmental swabs e.g. from sinks and isolettes were obtained. DNA was extracted from samples and underwent shotgun metagenomic sequencing. Libraries were sequenced using Illumina HiSeqv3 chemistry for 100bp single end reads with the aim to generate 40M reads per sample. Metagenomic sequencing reads were directly analyzed by CosmosID bioinformatics software (CosmosID Inc, Rockville, MD) to achieve bacterial identification at the species, subspecies, and/or strain level and quantification of relative abundance; similarly community resistome, virulence factors, viruses, fungi and parasites were identified.

Results: The likelihood ratio test comparing the 2 NICU cohorts (chi-squared) showed that the overall microbiome at genus level was significantly different for skin (p= 0.001) and environmental swabs (p=0.00003), but not for the 2 week and discharge stool (Figure 1). Several potential pathogen and virulence factor genes were found in all sample types from both NICUs including respiratory syncytial virus, clostridium difficile, Methicillin-resistant Staphylococcus aureus and the parasite Acanthamoeba polyphaga although none resulted in clinical disease. STL polyomavirus and MW polyomavirus were significantly higher in the SS NICU environmental samples (Kruskal-Wallis, p=0.017) and papillomavirus trended towards significance in these samples (p=0.05). Virulence factor genes associated with Clostridium perfringens were significantly higher in the PR discharge stool; however the prevalence of Clostridium difficile was higher in the SS stool. Several antibiotic resistance genes were present in both cohorts. A greater number of antibiotic resistance genes with over a log 2 difference in abundance between the 2 cohorts was seen in PR NICU, with the largest difference in beta lactamase resistance genes in the PR NICU compared with SS NICU.

Conclusions: Using shotgun metagenomic sequencing give a unique view of the infant microbiome, this pilot study shows that differences exist in the microbiome and possibly microorganisms with pathogenic potential and antibiotic resistance genes between a SS and PR NICU. Whether these confer differences in long term microbiome development or health outcomes will be examined in the extension of this study.

Figure1: Evaluation of relative abundance of genera in all samples. Shows comparison between private room(PR) NICU and Shared Space(SS) NICU in which there is no difference between the stool samples.



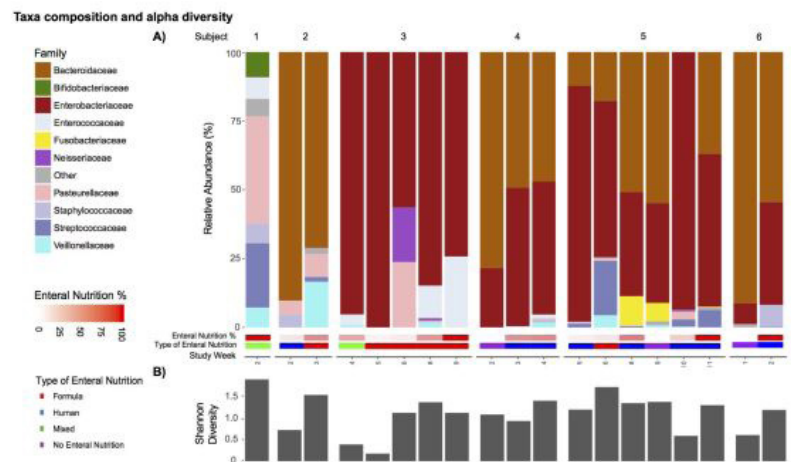
163 THE IMPACT OF NUTRITIONAL PRACTICES ON THE INTESTINAL MICROBIOME IN GASTROSCHISIS INFANTS. Allison Wu¹, Smruthi Murthy², David Lee², Nicole Tobin², Kara Calkins^{1,2}. ¹Pediatrics, UCLA Mattel Children’s Hospital, Los Angeles, CA; ²Pediatrics, David Geffen School of Medicine, Los Angeles, CA

Background: Survival rates for infants with gastroschisis are > 90%. However, because of intestinal dysmotility, gastroschisis infants require prolonged parenteral nutrition (PN), which is associated with infections and liver injury. The gut microbiome plays a major role in modulating motility, infections, and liver diseases. To date, little is known about the microbiome in gastroschisis infants, and how different types of nutrition influence the microbiome.

Objective: In gastroschisis infants, we aimed to: 1) characterize the evolution of the gut microbiome and 2) correlate nutritional practices with changes in the microbiome. We hypothesized: 1) prolonged PN would be associated with increased dysbiosis (increased pathogenic bacteria, decreased bacterial diversity) and 2) enteral nutrition, particularly breast milk, would restore commensal bacteria and increase bacterial diversity.

Methods: Inclusion criteria: infants with gastroschisis, <14 days of age, and projected PN requirement >14 days. Exclusion criteria: unlikely to survive and inborn errors of metabolism, congenital infections and liver disease. Fecal specimens were collected weekly while on PN and post-PN. 16S ribosomal sequencing was performed using DADA2 sequence inference, and data was analyzed via taxa distribution, alpha diversity indices, and principal coordinate analysis (PCoA) plots.

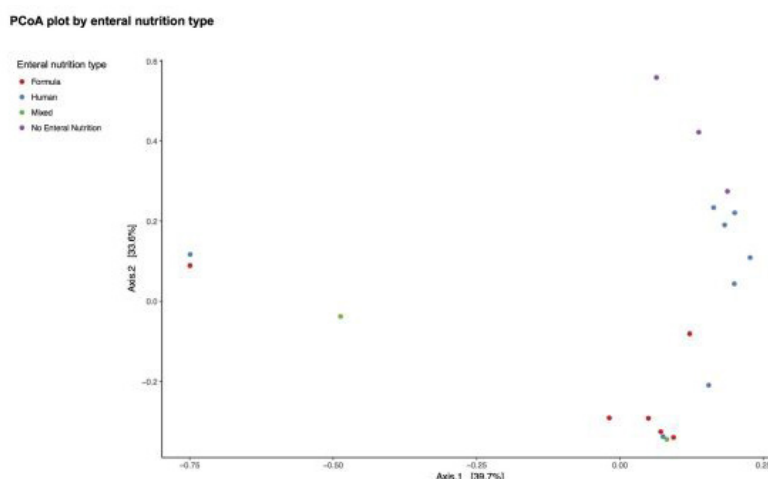
Results: Six male, gastroschisis subjects, born via vaginal delivery, were enrolled from May 2016-November 2016. The mean (± SD) gestational age and first day of enteral nutrition was 37 ± 2 weeks and 15 ± 9 days, respectively. PN duration was 34 ± 23 days. In 19 samples,



A) Taxa distribution by % relative abundance at family level, % enteral nutrition, enteral nutrition type (formula, human milk, mixed, or none), and study week at time of sample collection **B)** Shannon diversity index

compositional changes and fluctuations in bacterial diversity were observed over time. Bacteroidaceae and Enterobacteriaceae were the most predominate families throughout study weeks. In contrast, Bifidobacteriaceae was observed in only one subject (Image 1). When assessing variance between microbiota by PERMANOVA, the effect of the host was greatest ($R^2=0.77$, $P<0.05$), followed by enteral nutrition type ($R^2=0.08$, $p=0.12$). Alpha diversity varied in individuals over study week, with trends toward increased diversity while off PN. PCoA demonstrated segregation by enteral nutrition type (Image 2).

Conclusions: In a small group of gastroschisis infants, we observed a Bacteroidaceae and Enterobacteriaceae predominance. Bacteroidaceae are typically commensal bacteria in full term, healthy infants delivered vaginally, while Enterobacteriaceae have been associated with dysbiosis and neonatal diseases, such as necrotizing enterocolitis. In this study, bacterial diversity increased, but pathogenic bacteria persisted despite PN weaning. While enteral nutrition type appears to play a role in shaping the microbiome, more data is warranted to determine the influence of a human milk diet in this population. Subject recruitment continues, and future analyses will include healthy controls and the impact of other confounding factors.



PCoA plot with Bray-Curtis dissimilarity by enteral nutrition type

165 PEDIATRIC RECURRENT *C. DIFFICILE* INFECTIONS – A SIGN OF UNDIAGNOSED GI DISEASE.

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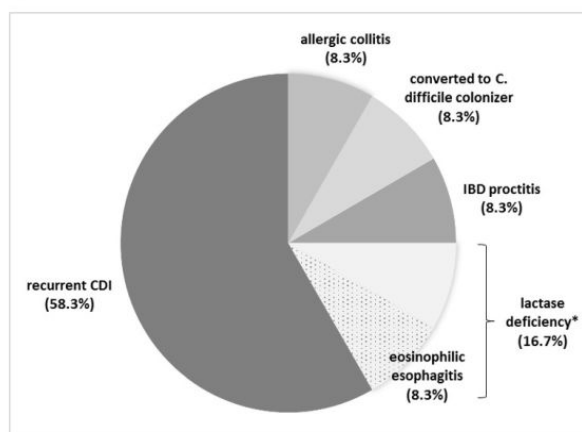
Background: Recurrent *Clostridium difficile* infection (CDI) in children can be difficult to manage and may represent an unidentified underlying pathology. Recurrence can be frequently encountered in immunodeficiency disorders and inflammatory bowel disease. The aim of this study is to describe a select population of children with recurrent CDI who have no identified risk of recurrence in the pediatric population and examine the potential for any underlying risk factors, disease course and disease outcome.

Methods: Patients aged 1-21 years with recurrent CDI were selected for a prospective study. All subjects with known immunosuppression or inflammatory bowel disease were excluded.

Results: Twelve children were identified. All patients were initially treated with antibiotic courses. There were 9 patients that failed antibiotic treatment of CDI and required fecal microbiome transplant (FMT), which prevented recurrence in all subjects. Four out of 12 patients had underlying pathology that was not previously identified, including allergic colitis and inflammatory bowel disease. CDI symptoms resolved after treatment of underlying colitis.

Conclusions: Pediatric patients with frequent recurrence of CDI have an increased likelihood of underlying GI pathology that should be investigated so that proper treatment can be initiated. Fecal microbial transplant appears to be a safe and highly effective therapy in this subpopulation of children.

Figure 1 - Ultimate Diagnosis



Abbreviations: CDI – Clostridium difficile infection, IBD – inflammatory bowel disease
*One patient was diagnosed with both eosinophilic esophagitis and lactase deficiency.

167 CORRELATIONS OF SYMPTOMS, STOOL *H.PYLORI* VS ENDOSCOPIC BIOPSY FOR *H.PYLORI*.

Ayesha Baig, Fernanda Kupferman, Mohamed Hamza, Sharef Al-Mulaabed, Radha Nathan. Pediatrics, Brookdale University Hospital and Medical Center, Brooklyn, NY

Background: Helicobacter pylori is a gram-negative, helical bacilli that lives in the gastric epithelium. It is able to thrive in the gastric environment due to urease, motility, and adherence to gastric epithelium [1], which allows it to neutralize gastric

acid, penetrate through the mucus layer to the gastric epithelium, and colonize. H.Pylori (HP) gastritis is prevalent in the pediatric and adolescent population. Diagnosing H.Pylori on the basis of symptomatology is a debated controversy. Studies done in the past do not show any specific clinical findings pertinent to HP gastritis [2].

Objectives: To assess whether there is any predominant symptom associated with stool or biopsy proven HP gastritis.

- To assess if there is any relationship between clinical symptoms and positivity for stool HP antigen and/or endoscopic biopsy(EB) results.
- To find out if there is any difference in symptoms with reference to age.

Design / Methods:

Study Design: Retrospective, case-control study

Inclusion Criteria: Patients aged 2 to 18 years

- Referred to the gastrointestinal clinic with chronic abdominal pain from November 2013 to September 2016
- Clinical diagnosis of gastritis and had undergone an upper GI endoscopy with biopsy

Exclusion Criteria: Children with complex syndromes or any associated GI disorder were excluded from the study.

Methods: A retrospective review of subjects was done who were referred to the gastrointestinal (GI) clinic with chronic abdominal pain [aged 2 to 18 years] from 11/13 to 9/16 with a clinical diagnosis of gastritis and had undergone an upper GI endoscopy with biopsy. Children with complex syndromes or any associated GI disorder were excluded.

Subjects were divided in two groups:

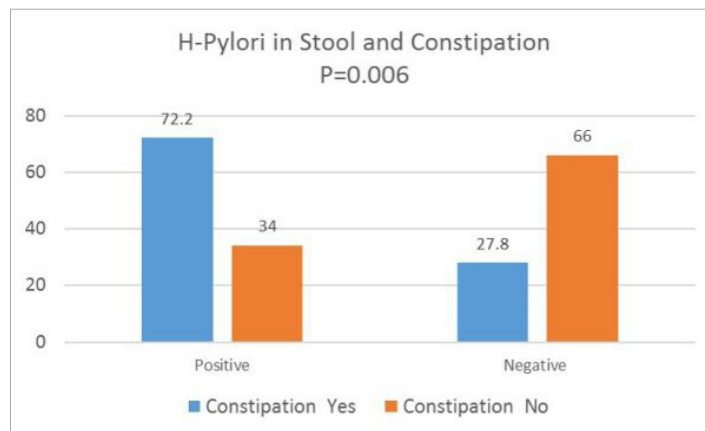
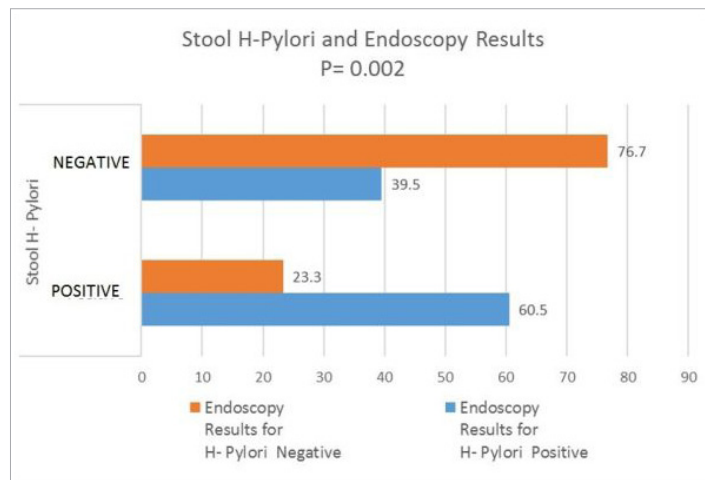
1. HP1 (positive for HP with stool antigen and/ or biopsy)
2. HP0 (negative for HP with stool antigen and/ or biopsy)

We compared the presence of nausea, vomiting, diarrhea, constipation, blood in stool as well as past history of proton pump inhibitors (PPI) use between groups.

Results: Of 91 subjects reviewed, 51% were males that tested positive on biopsy as compared to 58.6% for HP stool antigen (mean age 10-12 years, mostly African-American population). Significant relationship was found between constipation and stool HP test. In HP1, 72.2% patients who were constipated, tested positive for stool HP vs. 28.3% were positive on EB [X2(1,N=68)=7.8, P=.006]. Of all the subjects that were tested positive on endoscopy, 60.5% also had HP in stool as compared to 23.3% of the subjects who were positive for stool antigen but were negative for endoscopy (P=.002). There was no difference based on age groups in which endoscopy was performed and no difference in symptomatology with reference to age (p > 0.05).

Conclusion:

Our study highlights that a proportion of patients who tested positive for HP stool antigen tested negative for EB (a higher specificity method) for HP which indicates that stool antigen alone is not a definitive indicator for treating HP. Further investigation is warranted if symptoms persist despite empiric treatment. Also, a higher correlation between constipation and stool for HP was found. No statistical significance was found for other symptoms.



References:

3. Perry S, de la Luz Sanchez M, Yang S, Haggerty TD, Hurst P, et al. (2006) Gastroenteritis and transmission of *Helicobacter pylori* infection in households. *Emerg Infect Dis* 12: 1701-1708.
4. T.Sabbi. Short review about *H. Pylori* infection in pediatric age: epidemiological and clinical findings, diagnosis, therapy and role of probiotics. *Ped. Med. Chir. (Med. Surg. Ped)* 2011, 33 :221-226

168 ANALYSIS OF MICROBIAL COMMUNITIES IN THE DUEDENUM BRUSHING SAMPLES USING A COMBINATION OF METAGENOMICS AND BIOINFORMATICS TOOLS.

Bassam Abomoelak, Chirajyoti Deb, Karoly Horvath, Devendra Mehta. *GI, Orlando Health, Orlando, FL*

Background: The gut harbors several bacterial species that play a role in host nutrient acquisition, modulation of host gene expression, and regulation of host immune system. The conventional culture method detects only the cultivable microorganisms and it can be misleading or incomplete as most of the microorganisms are refractory to *in vitro* cultivation. In recent years, the use of high-throughput next generation sequencing (NGS) technologies to sequence microbial metagenomes has revealed the abundant presence of microflora in the human gastrointestinal tract and it is exploring the possible role of such microorganisms in health and disease. Our laboratory developed a novel technique for the sampling and identification of duodenal microflora by brushing during endoscopy. In an attempt to explore the microbial community in such samples, we used a combination of metagenomics and bioinformatics tools.

Methodology: The total purified DNA was used to amplify a conserved region of bacterial 16S rRNA gene using primer pairs that covered both the conserved and variable regions in the amplified 16S rRNA gene target. The designed primers amplified the total bacterial communities present in the sample. Genomic DNA was extracted from the brushing sample lysates, and subjected to metagenomics 16S rRNA analysis. Briefly, the V4 region was amplified by PCR and subsequently subjected to MiSeq Illumina platform pyrosequencing and bioinformatics analysis by Qiime 1.9.

Results: In this study, 25 brushing samples were selected for microbiome analysis. 11 patient samples showed *in vitro* growth on selective media plates, while 14 samples didn't show any visible growth on solid media. A total of 395,632 raw sequences passed the quality control parameters and yielded 2132 observation (OTUs). The average sample yield ranged from 3403 reads/sample to 27249 reads/sample (median 17387, mean 15825.3, and Std. Dev. of 6198.6). On the phylum level, firmicutes, proteobacteria, actinobacteria, bacteroidetes, and fusobacteria were the main phyla present in the brushing samples. Minor presence was reported for TM7 and Thermi, while 0.2% of the total reads were unassigned to any bacterial species. Proteobacteria was the predominant bacterial phylum (80%) compared to actinobacteria (5%), firmicutes (13%), and bacteroidetes (6%) in all the tested brushing samples. In-depth analysis revealed significant differences among the samples at the genus and species levels. Intra-sample statistics (alpha diversity) was performed using different metrics such as Choa1, Observed_otu, Shannon, and biodiversity (PD).

Conclusion: Correlations among the 25 samples were measured using beta diversity metrics (weighted and unweighted unifracs). The bacterial taxonomy revealed a perfect correlation with the culturing methods. In addition, a clear link was established between the patients' clinical symptoms and the microbiome.

170 THE EFFECT OF PROTON PUMP INHIBITOR THERAPY ON THE INFANT FECAL

MICROBIOME. Denease Francis¹, Grace Gathungu¹, Daniel Frank², Anupama Chawla¹. ¹*Pediatric Gastroenterology, Stony Brook Children's Hospital, South Setauket, NY;* ²*Infectious Disease, University of Colorado Denver, Denver, CO*

Background: Gastroesophageal reflux (GER) is a normal process that happens daily in healthy individuals when there is movement of gastric contents into the esophagus with or without vomiting. Gastroesophageal reflux disease (GERD) is defined as reflux producing bothersome symptoms and/or complications. Patients with GERD who fail therapy with dietary measures are placed on anti-reflux therapy to maintain intragastric pH at or above 4 for long periods of time and to inhibit meal-induced acid secretion. In recent years there has been an increase in the use of PPI therapy in neonates and infants diagnosed with GERD. There is also increasing evidence that alterations in the gastric pH, such as that induced by use of PPIs, may influence the bacterial profile and affect overall health. Gupta et al examined the effect of H-2 antagonists on the fecal microbiota of premature infants and noted a decrease in gut microbial diversity leading to a predominance of *Proteobacteria* which has been associated with cases of necrotizing enterocolitis (NEC). The objective of our study was to determine the effect on the fecal microbiota in infants on PPI therapy. To our knowledge there has been no previous pediatric study examining the association of PPI therapy and the fecal microbiota.

Objective: To determine the effect of proton pump inhibitors on composition of fecal microbiota in infants.

Design: A case controlled study was performed among patients between 0.5 to 6 months old. Subjects were on PPI therapy for at least 4 weeks prior to inclusion. However, controls as young as 2 weeks were included. Patients were excluded if they

had anatomical gastrointestinal disorders, were on antimicrobials within 30 days of enrollment, or if parents were unable to give informed consent. Stool was collected and DNA extracted using Zymo Research Fecal DNA Mini Prep kit. DNA was subjected to broad-range PCR amplification of the V3-V4 regions of the bacterial 16S ribosomal RNA (rRNA) gene, followed by next-generation sequencing. Sequences were sorted by sample barcodes and classified using the SILVA reference database. The 16S rRNA sequences were grouped into operational taxonomic units (OTUs) representing identified bacterial taxa.

Results: Although the overall microbiome composition of infants with reflux on PPI therapy did not differ significantly from controls (p 0.98), their microbiota were significantly less complex than those of controls (p <0.001 for Shannon diversity index). By one way ANOVA, each taxon [genus] was analyzed for differences in relative abundance between cases and controls. Findings revealed that controls had increased abundance of the *Proteobacterial* genera *Enterobacter* (p 0.04) and *B38* (p 0.03). Conversely, the infants on PPI therapy had greater abundances of the *Lactobacillales* genera *RS-D42* (p 0.05) and *Granulicatella* (p 0.04). This has clinical significance as *Granulicatella* has been associated with cases of endocarditis. No statistically significant difference in overall microbiome composition were noted by mode of birth (p 0.22). As expected, we observed a statistically significant difference by age in months (p < 0.001). It is known that the complexity of the microbiome increases with age due to environmental exposures. Our study suggests that this increase in complexity begins within the first few weeks of life.

Conclusions: Our data suggest that acid suppression impacted the diversity of the microbiome in infants with a trend towards increased pathogenic bacteria in those on PPI therapy. One of the limitations of the study is the small sample size. With an increase in the sample size, a statistically significant difference in the composition of the fecal microbiome in infants treated with PPI and controls may be observed.

171 LACTOSE INTOLERANCE IN CHILDREN WITH NONTYPHOIDAL SALMONELLA GASTROENTERITIS IN A TERTIARY CHILDREN'S HOSPITAL IN SOUTHERN CHINA.

Min Yang², Lu Ren², Sitang Gong², Ding-You Li¹

¹Pediatrics, Children's Mercy Hospital Kansas City, Leawood, KS; ²Gastroenterology, Guangzhou Women and Children's Medical Center, Guangzhou, Guangdong, China

Background: Nontyphoidal *Salmonella* infection is a common cause for acute bacterial gastroenteritis in children in China. Early studies suggest that secondary lactose intolerance occurs in children with acute infectious gastroenteritis. However there have been no reports of the prevalence of lactose intolerance in children with nontyphoidal *Salmonella* infection.

Aim: to characterize nontyphoidal *Salmonella* gastroenteritis in a tertiary children's hospital and evaluate lactose intolerance in children with prolonged nontyphoidal *Salmonella* gastroenteritis.

Methods: A retrospective case-series analysis was carried out in a tertiary children's hospital in Guangzhou, China. We included all infants and children who were diagnosed with nontyphoidal *Salmonella* gastroenteritis between 1 January 2014 and 31 December 2016. Patients' clinical features, feeding patterns, laboratory tests, and treatment outcomes were reviewed.

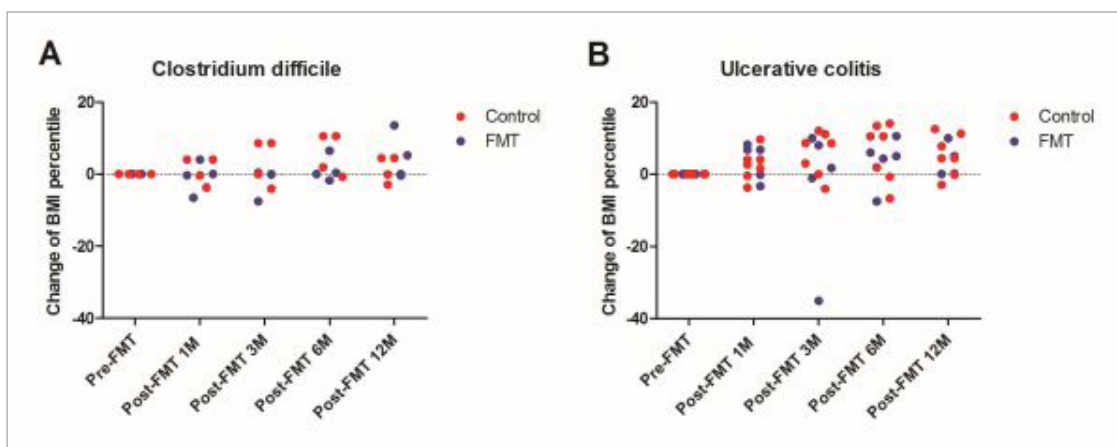
Results: A total of 142 infants and children were diagnosed with nontyphoidal *Salmonella* gastroenteritis. 52.1% of cases occurred in infants ≤12 months of age and the majority (89.4%) in children younger than 3 years old. The most common symptoms were diarrhea (100%), fever (62%) and vomiting (18.3%). Laboratory tests showed that most patients (89.4%) had elevated CRP. Leukocytosis, thrombocytosis and anemia occurred in 42.3%, 40.8% and 36.6% of children, respectively. *Salmonella* Typhimurium was the predominant serotype, accounting for 82.4%. 91.5% of patients were treated with antibiotics. Forty-one (28.9%) of children improved with a lactose-free formula or diet when diarrhea persisted for more than a week and stool testing was positive for carbohydrate malabsorption.

Conclusions: Most patients with nontyphoidal *Salmonella* gastroenteritis were younger than 3 years old and main symptoms were diarrhea, fever and vomiting. *Salmonella* Typhimurium was the predominant serotype. Lactose intolerance occurred frequently in children with nontyphoidal *Salmonella* gastroenteritis and dietary modification should be considered when diarrhea is persistent and prolonged

172 FECAL MICROBIOTA TRANSPLANTATION IN CHILDREN DOES NOT SIGNIFICANTLY ALTER BODY MASS INDEX. Dong Xi, Sonia Michail. Gastroenterology, Hepatology and Nutrition, Children's Hospital Los Angeles, Los Angeles, CA

Fecal microbiota transplantation (FMT) is nowadays a promising therapy for *Clostridium difficile* infection and a potential treatment for ulcerative colitis. Limited data suggests that FMT donated from healthy individuals is a safe therapy which is not associated with the development of new infections or diseases. However, it is still unclear whether the changes in intestinal microbiome will affect energy homeostasis or metabolism. A recent study demonstrated obese microbiome can be transmitted in animal models. FMT from nonideal donor was found to induce excessive weight gain in a case report. **This**

brings an intriguing question whether FMT from healthy donors affects recipient's body mass index (BMI). In our randomized placebo-controlled pilot study children patients with *Clostridium difficile* infection (n=8) or ulcerative colitis (n=12) were randomly divided into control and FMT groups. The BMI of both control and FMT groups was recorded at different time points, including pre-transplantation and 1 month, 3 months, 6 months, 12 months post-transplantation. The change in post-FMT BMI percentile compared to pre-FMT was calculated and graphed (Figure). The age range of *Clostridium difficile* infection cohort was 1 year to 17 years with the average of 8.5 years, while the range was 8 years to 21 years for ulcerative colitis cohort with the average of 15.2 years. Though the sample size was limited for both groups in our study, we successfully found that the BMI percentile was changed by (-0.7), (-1.8), 1.3, 4.6 (%tile) in *Clostridium difficile* infection, while by 3.6, (-3.3), 3.7, 7.1 (%tile) in ulcerative colitis at 1 month, 3 months, 6 months, 12 months after FMT (“-“ means decrease). These changes were confirmed to be not significant compared to control groups (p> 0.05). **CONCLUSION: From this randomized pilot study we concluded that FMT from healthy donors does not significantly alter body mass index in children with *Clostridium difficile* infection and ulcerative colitis over 12 months.** Future research will focus on enhancing the study by increasing the cohort size, and minimizing the effects of confounding variables including the medications or the severity of disease.



173 SINGLE CENTER EXPERIENCE IN MANAGING CLOSTRIDIUM DIFICILE IN CHILDREN.

Erin Alexander¹, Imad Absah², Mark Bartlett². ¹Pediatrics, Mayo Clinic, Rochester, MN; ²Pediatric Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN

Background: *Clostridium difficile* infection (CDI) is a common cause for infectious diarrhea in children. Recent reports suggest that both incidence and severity of CDI in children are increasing. There is a paucity of data regarding CDI in children younger than 3 years of age, resulting in variable testing and treatment practices for children in this age group. AAP guidelines recommend against testing children under the age of 1 year, and state that positive results in children aged 2 to 3 years are “difficult to interpret” since there are high rates of colonization in healthy children. We aim to review our experience in managing CDI cases in children less than 3 years of age.

Methods: We performed a retrospective review of the Mayo Clinic electronic records between 1997 and 2016. Children <3 years, with documented CDI diagnosis were included. Presence of CDI was confirmed by PCR or ELISA stool studies. Data abstraction included demographics, age at CDI diagnosis, comorbidities, antibiotic therapy, and risk factors (antibiotic use, gastric acid suppression, and hospitalization). This study was approved by the Mayo Clinic IRB.

Results: We identified 379 children who were diagnosed with CDI before 3 years of age. One hundred and fifty nine (42%) children were < 1 year of age at the time of diagnosis. The most common reported symptom was diarrhea in 326 (86%) of children. Of the 379 children, 298 (78%) had at least one risk factor for CDI. The most common risk factor was the use of antibiotics in the previous 3 months, seen in 251 (66%) of patients. Eighty four (22%) had no risk factor. Of those children, 348 (91%), were treated with antibiotics, 291 were initially treated with metronidazole (83%), and 57 were treated with vancomycin (16%) as first therapy. Of the treated children, 123 had recurrence (32%). Outcomes were assessed as improved, not improved, or unknown based on documentation of diarrhea in follow up. 272 (72%) had resolution of diarrhea at the follow up visit, 34 (9%) were not improved, and 73 (19%) had no documented follow up. When data was compared between children <1 and children 1-3, there were no significant differences in risk factors, antibiotic treatment choices, or in resolution of diarrhea, although the rate of recurrence was higher in the older group (40% versus 23%) - see table 1.

Conclusion: In this cohort of children under age 3, testing for CDI and treating symptomatic children appeared beneficial, as there was a 71% improvement in diarrhea with antibiotic treatment. There was no significant difference in improvement between children <1 and 1 to 3 years of age. Large prospective epidemiologic studies are needed to assess the true rate of colonization and CDI in young children and to clarify the role of treating positive results in this age group.

Table 1

Age at diagnosis in years	<1	1-3
a. Number of patients	157 (42%)	222 (58%)
b. Diarrhea	84%	87%
c. Risk factor(s)	82%	75%
d. Treated	84%	96%
- Flagyl, first treatment	73%	79%
- Vancomycin, first treatment	11%	17%
e. Recurrence	23%	40%
f. Diarrhea resolution	75%	70%

174 THE ASSOCIATION BETWEEN HELICOBACTER PYLORI INFECTION AND UNDERWEIGHT IN CHILDREN AND ADOLESCENTS. *Asha Sukumaran Nair, Sharef Al-Mulaabed, Fernanda Kupferman, Radha Nathan. Pediatrics, Brookdale University Hospital, Howard Beach, NY*

Background: Helicobacter pylori (HP) is the most common chronic bacterial infection in humans. HP infection can be acquired during childhood. There is controversy regarding the effect of HP infection on growth. Some studies have shown that treatment of HP improves dietary intake and weight gain in children.

Objective: The aim of this study was to determine whether HP infection is associated with underweight and short stature in children and adolescents.

Methods: This is a retrospective case control study. We assessed all patients (age 1-21 years) seen in pediatric gastroenterology clinic at Brookdale Hospital, New York, during the period September 2013 to December 2015. Patients who underwent testing for HP by stool antigen were included in the study. Patients were considered HP infected if they had positive stool antigen using laboratory-based monoclonal enzyme immunoassay. Based on CDC definition and growth charts, underweight was considered as BMI below 5th percentile, and short stature was defined as height below 5th percentile. We used SSPS (statistical package for social sciences) program for analysis. Differences in growth parameters and clinical characteristics between HP infection group and control group (no HP infection) were tested for significance by Fisher's exact test and/or chi-squared (χ^2) analysis, as appropriate. An a priori two-tailed level (p value) of significance was set at 0.05.

Results: A total of 177 patients were tested for HP infection and included in the study: mean (\pm SD) age was 9.8 (\pm 5.2) years, and male gender was 92/177 (52%). Out of 177 patients, 54 (30.5%) had positive HP stool antigen compared to 123 (69.5%) who were negative. Patients with HP infection were significantly more likely to have underweight [BMI less than 5th percentile] (12/54=22%) compared to (8/123=6.5%) in patients with no HP infection (p=0.002), table 1. Weight below 5th percentile was also significantly more prevalent in patients with HP infection (21/54=39%) vs those with no HP infection (10/123=8%); p<0.001). Height percentile was normal in 98% of HP infected patients and 99% of non-infected patients, with no significant difference between the two groups (p=0.518). Worth mentioning that patients with HP infection were significantly more likely to report history of weight loss than patients with no HP (37% and 9% in patients with HP infection and no HP infection, respectively, p<0.001), as well as history of inadequate dietary intake (18% and 6% in patients with HP and no HP, respectively, p=0.015).

Comparison between patients with HP infection and no HP infection revealed no significant differences in age, gender, history of abdominal pain, or history of diarrhea, as shown in table 1.

Conclusions: In our study, *Helicobacter pylori* infection seems to have significant association with history of weight loss as well as documented underweight. Height does not seem to be affected by HP infection. Therefore, in children with suspected HP infection, history of weight loss and underweight should prompt testing as well as treatment. Comparison between patients with *H. pylori* infection and no *H. pylori* infection (n=177)

Data	Patients with <i>H. pylori</i> (n=54)	Patients with no <i>H. pylori</i> (n=123)	P value
Age, Mean ± SD; years	10 ± 5.2	9.7 ± 5.3	0.764
Male, n (%)	26 (48%)	66 (54%)	0.499
History of weight loss, n (%)	20 (37%)	11 (9%)	<0.001*
Weight < 5th percentile, n (%)	21 (39%)	10 (8%)	<0.001*
BMI < 5th percentile (underweight), n (%)	12 (22%)	8 (6.5%)	0.002*
Height < 5th percentile, n (%)	53 (98%)	122 (99%)	0.518
History of inadequate dietary intake, n (%)	10 (18%)	8 (6%)	0.015*
History of abdominal pain, n (%)	50 (93%)	108 (88%)	0.343
History of diarrhea, n (%)	7 (13%)	18 (15%)	0.769

H. pylori = *Helicobacter pylori*, n = number, SD = standard deviation, * = statistically significant difference.

NUTRITION

177 FIRMICUTES DOMINANCE IS ASSOCIATED WITH LOWER SERUM BILIRUBIN LEVEL IN A NOVEL AMBULATORY MODEL OF PARENTERAL NUTRITION INDUCED LIVER INJURY AND GUT ATROPHY. Puneet Puri², Amber Price¹, Patrick Gillevet³, Keith Blomenkamp¹, Masoumeh Sikaroodi³, Nicole Heafner¹, Matthew Westrich¹, Shruthika Pochampally¹, Vindhya Kakarla¹, Jose Greenspon¹, Gustavo Villalona¹, Miguel Guzman¹, John Long¹, Brent Tetri¹, Jeffrey Teckman¹, Ajay Jain¹. ¹Saint Louis University, Saint Louis, MO; ²Virginia Commonwealth University, Richmond, VA; ³George Mason University, Manassas, VA

Background: Total Parenteral Nutrition (TPN), is a life-saving therapy however, its benefits come at the cost of gut atrophy and cholestasis. The etiology of TPN associated injury is likely multifactorial. We hypothesized that an altered enterohepatic circulation secondary to the absence of gut luminal nutrient contents during TPN therapy will result in a major shift in gut microbial ecology, thus altering the gut-liver cross talk and associated cholestasis, a marker for liver injury during TPN therapy.

Methods: We used our previously described novel ambulatory TPN piglet model for this study. Two groups of piglets, enteral nutrition (EN) or TPN were studied. Using Ion Torrent PGM 16S rRNA sequencing of the V1-V2 region, we performed the linear discriminant analysis (LDA) effect size (LEfSe) to determine across-group gut microbiota differences. First, the nonparametric factorial Kruskal-Wallis (KW) rank sum test was used to detect taxa with significant differential abundances. Biological consistencies were subsequently investigated with a set of pairwise tests among subclasses using the (unpaired) Wilcoxon rank sum test. Finally, LDA was used to estimate the effect size of each differentially abundant trait. Alpha values of 0.05 were used for the KW rank sum test, and a threshold of 2.0 was chosen for logarithmic LDA scores. Higher LDA scores indicated more differentially enriched taxa in that group. Additionally descriptive statistics on the outcomes were calculated as median and interquartile range (IQR). Serum bilirubin was used as a surrogate for hepatic cholestasis. A pairwise Mann Whitney U test was utilized to determine if there was an intergroup difference with a significance level < 0.05.

Results: A total of 16 piglets were included in the study spanning approximately 3 weeks. The EN group was significantly enriched with a healthy microbiome of Firmicutes phyla including Lactobacillaceae, Lachnospiraceae, and Ruminococcaceae family clades (LDA scores: 3.6 to 4.8). In contrast, the TPN group was significantly enriched with potent lipopolysaccharide and biofilm forming pathogens of the phylum Fusobacteria and several taxa in this clade (LDA scores: 3.8 to 4.8). A lower serum bilirubin value was associated with a clonal dominance of the Firmicutes phylum. Higher bilirubin strongly associated with higher Fusobacterium phyla. The median (IQR) for serum bilirubin was EN 0.12 (0.1-0.19) vs TPN 0.21 (0.17-0.22). A p value of 0.046 (Z value -1.71) was noted on Mann Whitney U analysis. Within the TPN group the Pearson correlation for a bilirubin >0.16mg/dL and Firmicutes content was, r=-0.81, (p=0.05).

Conclusion: Significant alterations of gut microbial ecology occur with TPN therapy. There is clonal degradation and loss of the gut protective, gram positive Firmicutes phyla and its clades and concomitant enrichment in LPS and biofilm forming obligate anaerobic gram-negative bacteria with TPN therapy. This ecological shift is associated with a higher serum bilirubin value indicative of hepatic cholestatic injury. We demonstrate a novel relationship between clonal shifts in the gut microbiota and cholestasis and this study supports the potential for therapeutic targeting of the gut microbiota to influence hepatic injury with TPN therapy.

178 DEVELOPMENT AND PILOT IMPLEMENTATION OF A NUTRITION CURRICULUM AND ROTATION IN PEDIATRIC GASTROENTEROLOGY FELLOWSHIPS.

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Background: Despite the well-recognized need for nutrition education in pediatric gastroenterology fellowships, structured nutrition rotations are rarely offered. The NASPGHAN Nutrition Committee developed a curriculum to serve as the basis for a rotation in clinical nutrition with the ability to customize to individual fellowship programs. Our initial aim was to develop and test this curriculum in a small pilot project.

Methods: The goals and objectives were adopted from core curricula and knowledge requirements published by national organizations and involved content areas that spanned the breadth of pediatric nutrition. To each content area, we linked a set of resources comprised of a reading list and corresponding clinical experiences (e.g. attending cystic fibrosis (CF) clinic, working with nutrition support services).

As part of the implementation, we worked with each program to customize implementation through locally available resources. We devised an outline for a rotation that included clinical experiences and self-study. Fellows completed a fifteen question pretest and a pre-rotation self-assessment where they ranked comfort with twenty-five nutrition topics.

Results: Five fellowship programs participated and developed a nutrition rotation. Twenty fellows took the baseline self-assessment. Using a Likert scale of 1-5 with 1 being not all comfortable, 3 being somewhat comfortable, and 5 being extremely comfortable, fellows felt least comfortable with the interpretation of calorimetry (average comfort level 1.95) and use of specialized anthropometrics (2.4). Fellows felt most comfortable with use of growth charts (4.05) and calculation of daily nutrition and fluid requirements (3.65). Notably, examples of topics where fellows felt only "slightly" to "somewhat" comfortable included nutrition management of CF (2.5) and short bowel syndrome (2.7), and enteral devices (2.75). Twenty-one fellows took the knowledge pretest with an average score of 69.9% (± 19.1). The pre-test topics that were most commonly answered incorrectly (50% incorrect) were growth charts, complications of PN, and formula additives. The pre-test topics that were most commonly answered correctly (95% correct) were refeeding, gastrostomy/central line, and gastrointestinal physiology.

Conclusions: A comprehensive nutrition curriculum with corresponding reading resources and clinical experiences can be developed, customized for each institution, and distributed on a national level among fellowship programs. Our pre-test and pre-rotation self-assessment give insight to which topics should be made a priority during a structured nutrition curriculum. Post-rotation data will be collected and analyzed for trends in fellows' comfort with topics and knowledge attainment. Our ultimate aim is to expand our curriculum to a broader audience while taking objective measures of knowledge attainment and using programmatic feedback to continuously improve the learner's experience.

179 PSYCHOSOCIAL OUTCOMES OF CHILDREN COMPLETING AN INTENSIVE OUTPATIENT BEHAVIORAL FEEDING PROGRAM.

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Introduction: Intensive outpatient behavioral feeding programs are frequently used in the treatment of severe feeding disorders to decrease negative mealtime behaviors of affected children and improve caregiver-child mealtime interactions. Yet, there are very few descriptions of these clinical practices and their effectiveness. The purpose of this study is to describe an intensive outpatient feeding treatment protocol and to evaluate the clinical outcomes of the program.

Method: This study utilizes a pre-post treatment assessment in patients completing a 5-day intensive outpatient parent training protocol. Treatment is divided into three distinct phases. Patients are fed three therapeutic meals each day. During the initial phase of treatment, all meals are fed by a team of 4 psychologists who alternate sessions. Caregivers observe the meals behind a one-way-mirror. During the second phase of treatment, caregivers transition into the feeding environment,

with psychology coaching directly in the room, gradually assuming the role of feeder. In the final phase, psychologists coach caregivers remotely via an earpiece to allow the feeding relationship to solidify between caregiver and child in the absence of the psychologist. Children complete the program when their parents are consistently able to demonstrate an ability to maintain the feeding intervention. The following measures were collected pre-/post treatment: (1) Mealtime Behavior Questionnaire assessing maladaptive feeding behaviors; (2) About Your Child's Eating Questionnaire assessing negative mealtime interactions; and (3) Feeding Strategies Questionnaire assessing rates of appropriate use of behavioral strategies. Comparisons of pre-post treatment effects on psychological measures were assessed by repeated measures one-way MANOVA. Percent change between the numbers of subjects scoring in clinical ranges pre to post-treatment were also reported.

Results: Findings from this study showed improved interactions between caregivers and children within a mealtime context (Child Resistance to Eating, $F=35.13$, $p<0.001$; Positive Mealtime Environment, $F=9.10$, $p=0.005$; Parent Aversion to Mealtime, $F=14.34$, $p=0.001$), decreased problematic mealtime behaviors (Distraction Avoidance, $F=61.48$, $p<0.001$; Food Manipulation $F=6.12$, $p=0.018$; Mealtime Aggression, $F=8.84$, $p=0.005$, Total MBQ $F=22.99$, $p<0.001$) and improved caregiver use of effective mealtime strategies (Schedule Structure, $F=35.88$, $p<0.001$; Setting Structure, $F=14.81$, $p<0.001$; Parent Control of Intake, $F=28.83$, $p<0.001$; Laissez-Faire, $F=10.19$, $p=0.003$; Coercive Interactions, $F=30.87$, $p<0.001$). Decreases in caregiver distress (Parent Distress $F=6.24$, $p=0.018$) and caregiver perceptions of their child as "difficult" (Difficult Child $F=6.58$, $p=0.015$) were also found.

Conclusion: The intensive outpatient treatment program helps caregivers to use effective strategies to facilitate appropriate interactions between caregivers and children within a feeding context. As caregivers gain skills and confidence children show markedly improved feeding behaviors. This is a program option that should be considered for failures of traditional outpatient care models.

***180 MEASUREMENT OF BODY COMPOSITION BY AIR DISPLACEMENT PLETHYSMOGRAPHY IN PEDIATRIC INTESTINAL FAILURE PATIENTS.** *Alexandra Carey^{1,2}, Paul Mitchell³, Daniel Elman³, Christopher Duggan^{1,2}.* ¹Gastroenterology and Nutrition, Boston Children's Hospital, Boston, MA; ²Harvard Medical School, Boston, MA; ³Institutional Centers for Clinical and Translational Research, Boston Children's Hospital, Boston, MA

Background: The nutritional status of children with intestinal failure (IF) on parenteral nutrition (PN) can be difficult to determine using currently available anthropometric techniques. Accurate body composition analysis allows for the determination of lean body mass (LBM). The accrual and preservation of LBM is important during intestinal rehabilitation as the child advances towards enteral autonomy. Implementation of a valid modality for calculating LBM in the IF population is therefore necessary. Air displacement plethysmography (ADP) is a non-invasive measure of whole body composition that measures body mass and volume, with a calculation of percent body fat (%BF) and LBM using age- and sex-specific equations.

Objective: To determine the agreement of %BF measurements in children with IF using ADP, bioelectrical impedance analysis (BIA), and bedside anthropometric methods (sum of four-site skinfolds).

Methods: We conducted a prospective cohort study of 17 children (20 planned) recruited through the Center for Advanced Intestinal Rehabilitation (CAIR) program at Boston Children's Hospital. Patients 2-17 years of age with IF dependent on PN for more than 90 days were included. Spearman rank correlation and the method of Bland and Altman were used to compare ADP to both BIA and four-site skinfold anthropometry for %BF calculation. This study is part of a larger validation study correlating ADP with the gold standard technique of deuterium isotope dilution.

Results: Seventeen children with IF, median (IQR) age 6.8 (5.1 – 9.1) years, 9 (53%) female, were studied. Subjects had a median (IQR) residual bowel length of 31 (11 – 85) cm with all but one in continuity with their colon. Thirteen subjects had their ileocecal valve (ICV) resected, three with unknown ICV status. Median (IQR) energy intake was 98 (88 – 116) kcal/kg/day with 45% (34 - 55) of total calories provided by PN. Total energy intake was negatively correlated with %BF based on BIA calculation ($r = -0.16$) and even more so by ADP ($r = -0.31$). Median %BF by sum of four-site skinfolds, BIA and ADP was 15.3%, 26.0%, and 18.8%, respectively. %BF by ADP was unbiased in comparison to skinfold anthropometry (mean difference = 0.2%), and negatively biased in comparison to BIA (mean difference = -8.8%).

Conclusion: In this study, %BF by ADP was unbiased in comparison to skinfold anthropometry and negatively biased in comparison to BIA. Future work will include validation of ADP via deuterium dilution, and estimation of 95% limits of agreement. If the feasibility and accuracy of ADP for body composition analysis can be demonstrated in our full cohort this technique holds promise as a measure of nutritional status in children with intestinal failure.

181 OBSERVATIONAL STUDY OF THE DIETARY MANAGEMENT OF CONSTIPATION IN INFANTS BETWEEN THE AGE OF 1 AND 2. Alexis Mosca¹, Christian Kempf², Jerome Valleteau de Moulliac³, Nastassja Augé⁵, Geraldine Gerardi-Temporel⁴, Louis-Dominique Van Egroo⁴. ¹Pediatric Gastroenterology, Robert Debré Hospital (APHP), Paris, France; ²CKConsulting, Ottrott, France; ³Pediatrician, Paris, France; ⁴Medical Affairs, Gallia, Villefranche-sur-Saône, France; ⁵Research and Development, Blédina, Villefranche-sur-Saône, France

Background: Little data is available on daily dietary management of constipation in infants, a condition affecting about 10% of them.

Objective: To describe the dietary management of constipated children between the age of one and two and to assess the impact of fiber enriched formula (FEF) on constipation at the age of two in real life settings.

Methodology: Prospective cohort study of one year old children requiring dietary management of constipation according to their pediatrician. Two cohorts (FEF and control) were followed-up to the age of two.

Results: Ninety-two pediatricians recruited 494 patients (314 FEF,180 control), 366 assessed at the age of 2. Both cohorts were similar in terms of characteristics at birth and at inclusion. Constipation (ROME IV) was confirmed at inclusion in 60% FEF and 64% control patients. At the age of two, only 5% of FEF and 7% of Control patients still had ROME IV constipation (NS). Significant differences ($p < 0.001$) in favor of FEF were found for the improvement of stools consistency according to the Bristol score (85% vs 64%), fear of defecation (28% vs 59%), pain at defecation (27% vs 47%), abdominal pain (29% vs 60%), bulky stools (49% vs 71%) and bloating (42% vs 57%). Similar proportions of patients had changed their formula during the year of follow-up (14% vs 12%, NS) and quality of life (QUALIN) improved (+8.7 vs +6.4 points, NS) in both cohorts.

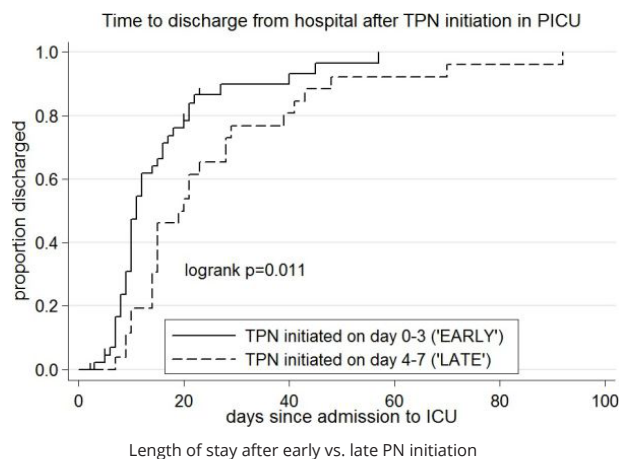
Conclusion: Constipation at the age of one is improved by dietary measures. The use of FEF significantly improved constipation related digestive symptoms at the age of two compared to control patients.

183 EARLY VS. LATE INITIATION OF PARENTAL NUTRITION IN A PEDIATRIC ICU: A QUALITY IMPROVEMENT INITIATIVE. Amber McClain¹, Collin Anderson², Jennie Lueckler³, Mark Deneau¹. ¹Pediatric Gastroenterology, Hepatology and Nutrition, University of Utah, Salt Lake City, UT; ²Pharmacy, Intermountain Medical Center, Salt Lake City, UT; ³Nutrition Support Services, Intermountain Medical Center, Salt Lake City, UT

Background: A landmark randomized controlled trial in over 1,400 children, published in the New England Journal of Medicine, by T. Fivez, demonstrated earlier discharge and lower mortality when parental nutrition [PN] was delayed for 7 days in the pediatric intensive care unit (PICU). After this publication, we evaluated the effects of a quality improvement (QI) effort to delay the start day of PN in our PICU to day 4 or later.

Methods: The QI was directed by a PICU dietician who rounded with physician teams on weekdays and advocated for a delay in PN initiation, held a monthly education seminar on benefits of delayed PN initiation, and documented a goal delayed PN start date in the medical record. To measure effects, we identified all patients who received PN in the PICU Jul-Dec 2015 and during the ongoing intervention Jul-Dec 2016, excluding patients on PN prior to PICU transfer. We created a retrospective cohort, starting the day of PICU admission, ending at hospital discharge. We compared length of stay (LOS) and total PN duration pre-intervention (2015) and during intervention (2016). To analyze the effects of delayed PN, we separately analyzed these outcomes in all patients stratified by PN start date, defining “early” as days 0-3 and “late” as days 4-9.

Results: PN was initiated in 35/749 (4.7%) PICU admissions in 2015, and 36/805 (4.5%) in 2016 ($p=0.87$). Patient ages and admitting diagnoses were similar in both groups. The median day of PN initiation was day 2 in both groups. The proportion of patients who started and stopped PN before day 5 was 17% in 2015 and 8% in 2016 ($p=0.22$). LOS was similar between groups: 15 vs. 14 days ($p=0.88$), and death occurred in 3 vs. 2 patients in 2015 and 2016, respectively. Comparing patients in whom PN was initiated on days 0-3 (“early”) vs. 4-9 (“late”), regardless of study year: PN duration was 7 vs. 5 days ($p=0.91$), median time to discharge was 11 vs. 19 days ($p=0.01$), proportion discharged home (instead of to chronic care facilities) was 62% vs. 36% ($p=0.046$), and mortality rate was 11% vs. 0% ($p=0.08$).



Conclusions: Our QI to delay the initiation of PN in PICU patients was ultimately ineffective and failed to shift the PN start day. There was a small effect on eliminating short-duration PN. LOS and mortality rate were unaffected. Post-hoc analysis showed that initiation of PN on or after PICU day 4 was associated with longer LOS, fewer discharges home, but a lower mortality rate compared to initiation of PN on or before day 3, an association that requires further study.

184 IMPACT OF BEHAVIORAL FEEDING INTERVENTION ON CHILD EMOTIONAL AND BEHAVIORAL FUNCTIONING, MATERNAL PARENTING STRESS, AND MOTHER-CHILD RELATIONSHIPS.

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Rationale: Behavioral intervention is the only empirically-supported treatment for pediatric feeding problems (Sharp, Jacques, Morton, & Herzinger, 2010). However, many parents may be hesitant to pursue behavioral intervention due to concerns regarding side effects of treatment that might negatively impact the parent-child relationship and/or child emotional and behavioral functioning (e.g. anxiety, aggression) given that treatment often requires parents to consistently ignore their young child’s indications that he/she does not wish to eat (Larue et al., 2011; Piazza, Patel, Gulotta, Sevin, & Layer, 2003). Despite these concerns, current research indicates that behavioral feeding intervention results in significantly decreased parental stress (Greer, Gulotta, Masler, & Laud, 2008) and more consistent parental responses to the child’s behavior during feedings (Mueller et al., 2013), which evidence suggests could increase the likelihood of secure attachment (Ainsworth et al., 1978; Atkinson et al., 2000).

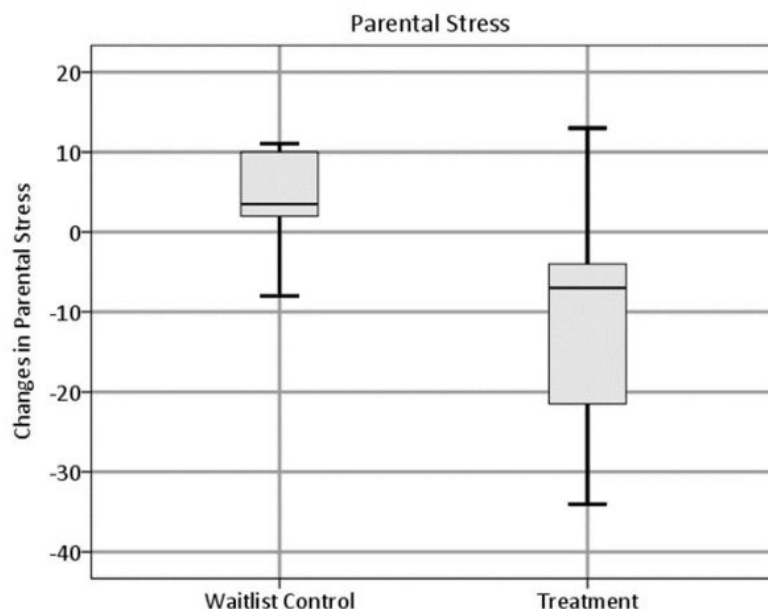
Objectives: This study investigated potential side effects of behavioral feeding treatment, including maternal parenting stress, internalizing (e.g. emotional reactivity, anxiety, mood issues) and externalizing (e.g. aggression, attention problems) problems in young children, and mother-child relationships.

Method: Participants in this study included 19 mother-child dyads from a behavioral feeding clinic waitlist at a Midwestern university medical center. Children were between the ages of 12 and 45 months (adjusted) at baseline. Participants were randomly assigned to the treatment or control group and completed the Brief Infant Toddler Social Emotional Assessment (BITSEA) or Child Behavior Checklist for Ages 1.5-5 (CBCL/1.5-5), Parenting Stress Index, 3rd Edition Short Form (PSI/SF), Behavioral Pediatrics Feeding Assessment Scale (BPFAS), the Strange Situation, and 10 minutes of mother-child free play that was analyzed using a coding system to examine the quality of mother-child interactions at baseline and again after 6 months. The treatment group began outpatient behavioral feeding intervention following the first evaluation, while the control group continued to remain on the clinic waitlist.

Results: A significant decrease was found in externalizing behavior problems for the treatment group compared to the control group. Although there was no significant difference between groups for internalizing problems, the effect size was moderate to large (0.65), suggesting that statistical significance could be reached with a larger sample size. The PSI/SF results revealed a significantly greater decrease in parenting stress for the intervention group. No significant differences between groups were found in parent-child attachment ratings based on the Strange Situation. The free play condition has been coded but not yet analyzed. The data will be analyzed prior to the NASPGHAN Annual Meeting.

Table 1. Group differences in changes in externalizing & internalizing problems over 6 months

	Mean	SD	Mean Difference	S.E. Difference	t	df	p	Cohen's d
Externalizing Problems								
Treatment group	-5.50	6.26	7.13	2.46	2.90	10.10	0.02	1.45
Control group	1.63	3.02						
Internalizing Problems								
Treatment group	-4.88	9.51	5.13	3.96	1.29	11.75	0.22	0.65
Control group	0.25	5.95						



188 OUTREACH PARENTERAL NUTRITION PROGRAM: 9 YEAR EXPERIENCE OF THE FIRST PROGRAM IN SAUDI ARABIA.

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Background: Parenteral nutrition (PN) is a lifesaving therapy for patients with intestinal failure, but is associated with numerous complications which increase morbidity and mortality. Long hospital stay and cost are major challenges. Nine years ago King Fahad Medical City, Riyadh, Saudi Arabia started an outreach parenteral nutrition (OPN) program by creating a multidisciplinary team to provide PN at home all over the Saudi Arabia.

Objectives: To report on the impact of OPN program on hospital stay, cost and outcome.

Methods: Retrospective chart review of patients with intestinal failure over a 14-year period was performed. Outcomes of patients followed up by OPN program (2008-2017) were compared to a historical data (2004-2007). Demographic, length of therapy, diagnosis, re-hospitalization, catheter related infection, hospital stay and cost were compared.

Results: Twenty-five patients with intestinal failure were enrolled in the OPN program and were compared to historical data from 15 patients treated prior to the OPN program. Sixty-five percent of patients were female. The mean (\pm SD) age was 5 ± 4 years. The primary indication for OPN was congenital tufting enteropathy which is 44 %. The average hospital stay decreased from 870 days to 130 days. The cost per patient, per year for patients on OPN has decreased from about \$400,000 USD to about \$121,000 USD. Patients followed up by OPN program had a lower rate of catheter related infections, 0.4-0.6 per 1000 catheter day compare to 8.1 per 1000 day prior to OPN program.

Conclusion: Team approach to provide nutrition support resulted in improvement in many aspects of patient care, significantly reduced cost and rate of infections in The Kingdom of Saudi Arabia.

190 A SCHOOL BASED CROSSECTIONAL STUDY ON THE RELATION OF FUNCTIONAL GASTROINTESTINAL DISORDERS AND NUTRITIONAL STATUS IN CHILDREN AND ADOLESCENTS FROM EL SALVADOR.

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The relation between obesity and functional gastrointestinal disorders (FGIDs) is controversial with some studies showing a positive association between them and other studies showing no association. No studies have investigated the relation between FGIDs and malnutrition as a whole (undernutrition/severe undernutrition and overweight/obesity) or between FGIDs and undernutrition in Latin America.

Objectives:

1. To assess the prevalence of FGIDS in children of El Salvador.
2. To investigate the relation between FGIDS and nutritional status.

Methods: Children and adolescents (8 to 15 years of age) from El Salvador were given the Questionnaire of Pediatric Gastrointestinal Symptoms (QPGS) Spanish version, a validated tool to diagnose FGIDs per the Rome III criteria. Weight and height were measured and data was plotted into World Health Organization (WHO) tables to establish their nutritional status. Nutritional status was defined by their BMI according to WHO criteria: undernutrition = -2 to -3 standard deviations (SD), severe undernutrition = ≥ -3 SD; overweight = +1 to +2 SD, obese = ≥ 2 SD. Children with BMI between -2 SD and +1 SD were considered well-nourished. Uni and multivariate analyses were performed (ORs with 95% CI). Significance was set at $p < 0.05$.

Results: 20.3% of children were diagnosed with one or more FGIDs (10.3% functional constipation, 3.8% irritable bowel syndrome, 2.5% functional abdominal pain, 0.5% functional abdominal pain syndrome, 1.8% functional dyspepsia, 0.8% abdominal migraine, 0.5% aerophagia and 0.3% rumination syndrome). Nutritional status- 77.4% of children were considered well-nourished, 2.0% of children had undernutrition, 0.5% severe undernutrition, 17.3% were overweight and 2.8% obese. There was no association between FGIDs and malnutrition as a whole (undernutrition, severe undernutrition, overweight and obesity) (OR = 1.06 95% CI = 0.56-1.95 $p = 0.82$) or between FGIDs and undernutrition/severe undernutrition combined or between FGIDs and overweight/obesity combined. There was also lack of association between the 2 most common FGIDs and nutritional state: functional constipation (malnutrition: OR = 1.27, 95% CI = 0.54-2.77 $p = 0.51$); irritable bowel syndrome (malnutrition: OR = 0.24 95% CI = 0.005-1.69 $p = 0.14$).

Conclusions: We found a high prevalence of FGDS and malnutrition. There was no association between FGIDs and abnormalities in nutritional status.

191 DAILY CONSUMPTION OF CHOLESTEROL, SATURATED, MONO-UNSATURATED AND POLYUNSATURATED FATTY ACIDS IN DIABETIC CHILDREN OF THE HOSPITAL UNIVERSITARIO DEL VALLE “EVARISTO GARCIA” OF CALI, COLOMBIA.

Carlos Velasco-Benitez, Audrey Mary Matallana, Claudia Ortiz. Pediatría, Universidad del Valle, Cali, Colombia

Introduction: Intake of saturated fat and cholesterol in diabetic children should be limited by their predisposition to hyperlipoproteinemias and atherosclerotic vascular disease.

Objective: To determine the daily consumption of cholesterol (Cholest), saturated fatty acids (SFA), mono-unsaturated fatty acids (MSFA) and polyunsaturated fatty acids (PUFA) through a 24-hour reminder in diabetic children of the Hospital Universitario del Valle HUV “Evaristo García” of Cali, Colombia, according to the Program for the Evaluation of Diets and Food Data Management (DIAL).

Methodology: Prevalence study of diabetic children between 2-17 years of age who consulted the HUV of Cali, Colombia between August 2, 2013 and February 23, 2017, who were given sociodemographic (age, sex), anthropometrics (weight, height, waist circumference) variables and were diagnosed of malnutrition by body mass index, low height by height/age and abdominal obesity by waist circumference. Normal daily intake of Cholest = 300 mg/d, SFA = $\leq 10\%$ total caloric value (TCV), MSFA = $\leq 15\%$ TCV and PUFA = $< 10\%$ TCV were considered according to age and sex.

Results: 144 children were included; 54.2% female, 10.9 ± 3.5 years of age, with kcal = 1150.1 ± 296.7 kcal/m²/d, Cholest = 322.7 ± 134.2 mg/d, SFA = 188.4 ± 85.6 mg/d, MSFA = 241.9 ± 120.1 mg/d and PUFA = 71.7 ± 31.6 mg/d, with malnutrition = 30.8%, low height = 11.1% and none with abdominal obesity. They presented a high daily consumption in Cholest = 57.6%, SFA = 77.1%, MSFA = 67.4% and PUFA = 5.6%; without possible risk factors.

Conclusion: Considering that for these diabetic children we recommend the intake of SFA and MSFA between 6-7% and PUFA $< 10\%$ of the total caloric value, the daily consumption of these diabetic children of the HUV from Cali, Colombia to Cholest, SFA and MSFA was altered above 57.6% and for PUFA in 5.6%, which necessitates an early and timely nutritional and dietary intervention in this group of children

192 METABOLIC STATUS AFTER 8 WEEKS OF PHYSICAL ACTIVITY IN CHEERLEADERS IN CALI, COLOMBIA. *Carlos Velasco-Benitez¹, Katherine Arias². ¹Pediatría, Universidad del Valle, Cali, Colombia; ²Grupo de Investigación Gastrohnp Univalle, Cali, Colombia*

Introduction: It has been demonstrated in children that at least 12 weeks of physical activity can reduce insulin resistance and some biochemical parameters related to cardiovascular risk factors.

Objective: To determine if an intervention during 8 weeks of physical activity developed in a group of cheerleaders can reduce insulin resistance and lipid profile.

Methods: 13 girls (mean age 15.5 ± 2.4 years) participated voluntarily in the study (descriptive-transversal). The girls performed strength/resistance and aerobic tests 6h/week for 8 weeks. The sociodemographic (age, sex) and biochemistry (glycemia, insulin, lipid profile) characteristics were determined at weeks 0 and 8. Statistical analysis included measures of central tendency and comparison of averages according to student t, with a significant $p < 0.05$

Results: After 6h/week for 8 weeks of strength/endurance and aerobic tests, there was a decrease in triglycerides (81.0 ± 22.4 mg/dl vs 68.9 ± 20.6 mg/dl $p = 0.0371$), VLDL-c (16.2 ± 4.4 mg/dl vs 13.8 ± 4.1 mg/dl $p = 0.0424$), HDL-c (49.8 ± 9.0 mg/dl vs 48.0 ± 9.2 mg/dl $p = 0.0462$) and the arterial index (3.0 ± 0.5 vs 3.1 ± 0.6 $p = 0.0340$), but not total cholesterol, LDL-c, Glucose, insulin and homeostatic index assessment (HOMA) index ($p > 0.05$).

Conclusions: Physical activity (strength/endurance and aerobic tests) after 6h/week for 8 weeks in this group of cheerleaders from Cali, Colombia, decreased some biochemical parameters related to cardiovascular risk factors (triglycerides, VLDL-c, HDL-c and arterial index), essential for maintaining good metabolic health status

195 OUTCOMES AND SAFETY OF BLENDERIZED TUBE FEEDINGS IN PEDIATRIC PATIENTS: A SINGLE CENTER’S EXPERIENCE. *Daphney Kernizan, Daria Mintz, Michele Colin, Lee Melanie, Lindsay Yoakam, Yen Chen, Elizaveta Iofel, Soula Koniaris, Melissa Weidner. Pediatrics, Rutgers Robert Wood Johnson University Hospital, Iselin, NJ*

Introduction: Recently there has been significant interest from families and health care providers to use blenderized tube feedings (BTF) in place of standard commercial formulas in children with gastrostomy tubes (G-tubes). Although many institutions are providing this nutritional option, there is a paucity of literature regarding outcomes and safety.

Objectives: To describe pediatric patients who are being treated with BTF at our institution and gain a better understanding of the reasons providers are initiating BTF. To study if there is any improvement in gastroesophageal reflux disease (GERD), constipation or gastrointestinal (GI) dysmotility symptoms after initiation of BTF. To determine if oral intake is impacted by the introduction of BTF. To evaluate adverse events related to BTF.

Methods: A retrospective chart review was performed on pediatric patients receiving BTF followed by the pediatric gastroenterology group at Rutgers-Robert Wood Johnson between January 2013 and April 2017. Demographic data, as well as dietary information prior to and after BTF were collected. Clinical data including, the reason for diet initiation, GI symptoms and growth measures, were recorded. Adverse effects if any, and symptom outcomes were assessed through physician documentation in clinic visits and through relevant medication changes.

Results: Thirty-five patients received BTF during the study period (24 male, 11 female). Ages ranged from 1-21 years, mean age of 8.3 years +/- SD of 5.8 years. Mean age at BTF initiation was 6.8 years +/- SD of 5.8 years. The most common reason for starting BTF was GERD (N=32). Almost all patients were on medications for GERD, constipation or GI dysmotility prior to starting BTF (N=33). The majority of patients had improvement in relevant GI symptoms (N=18, 52%) and 17 of 33 patients on relevant GI medications were able to wean or stop medication(s) (52%). Additionally, 2 patients were able to transition from gastrojejunostomy (GJ) tubes to G-tubes due to improvement in GERD and/or GI dysmotility. Finally, 3 patients had significant improvement in oral intake and were able to be weaned from G-tube feedings. There was no statistically significant difference in BMI or weight for length z scores prior to or after BTF diet initiation (p= 0.558). Mild adverse events were reported in 14% of patients (N=5), which included abdominal pain, rash, and diarrhea. Only 3 patients (9%) stopped the BTF diet due to adverse events or worsening GI symptoms. There were no serious life-threatening adverse events.

Conclusion: Our data suggests that BTF is a safe dietary intervention that may improve GI symptoms such as GERD, constipation and GI dysmotility in pediatric patients. Other potential therapeutic benefits may include improved oral intake and ability to transition from GJ tube feedings to G tube feedings. Further prospective studies are needed to compare safety and efficacy of BTF and standard commercial formula diets in pediatric patients receiving G-tube feedings.

PANCREAS/CELIAC/MALABSORPTION

197 **VITAMIN D AND MALNUTRITION STATUS OF NEWLY DIAGNOSED PEDIATRIC CELIAC PATIENTS.** Kara Feigenbaum, Lisa Fahey, Nancy Sacks, Ritu Verma. *The Children's Hospital of Philadelphia, Philadelphia, PA*

Background: Untreated celiac disease (CD) is associated with intestinal inflammation and malabsorption, which can lead to micronutrient deficiencies, poor weight gain and suboptimal growth. It is unknown whether the coexistence of malnutrition at diagnosis of celiac disease increases the risk for vitamin D deficiency.

Objective: To assess the prevalence of vitamin D deficiency and vitamin D insufficiency in children with newly diagnosed celiac disease and to identify correlation between malnutrition and vitamin D status.

Method: A retrospective chart review of children between the ages of two to 20 years with a confirmed diagnosis of CD between 2009-2014. Data collected included patient demographics, vitamin D 25-OH levels, and anthropometrics. Malnutrition criteria was assessed using BMI z-scores established by the World Health Organization and American Society for Parenteral and Enteral Nutrition. Definitions for vitamin D deficiency, vitamin D insufficiency, and vitamin D sufficiency were <20 ng/mL, 20-29 ng/mL, and 30-100 ng/mL respectively.

Results: Seven hundred-one patients were included in the final result analysis. Four hundred fifty-one (64%) were female and 250 (36%) were male with the average age at diagnosis of 10 years +/- 5. Average BMI z-score was 0.04 +/-1.07. Five hundred seventy-one (81%) were not malnourished, 103 (15%) were mildly malnourished, 26 (4%) were moderately malnourished, and 1 (<1%) was severely malnourished. Most had sufficient levels of vitamin D (33.2 +/-11.1) (60%), 32% were vitamin D insufficient (25.3 +/-3) and 8% (15.9 +/-3.3) were vitamin D deficient. There was no association between low vitamin D and malnutrition status, gender or race.

Conclusion: We found no support for the hypothesis that malnutrition at diagnosis of celiac disease is related to low vitamin D.

198 ZONULIN TRANSGENIC MOUSE AS A MODEL OF GUT-BRAIN AXIS CROSSTALK

INFLUENCING BEHAVIOR. Alba Miranda-Ribera^{1,2}, Phillip Daniel Rivera^{3,4}, Phuong Kim Tran^{3,4}, Jिंगgang Lan^{1,2}, Staci Bilbo^{3,4}, Alessio Fasano^{1,2}, Maria Rosaria Fiorentino^{1,2}. ¹Mucosal Immunology and Biology Research Center, Massachusetts General Hospital, Charlestown, MA; ²Division of Pediatric Gastroenterology and Nutrition, Harvard Medical School, Boston, MA; ³Lurie Center for Autism, MassGeneral Hospital for Children, Boston, MA; ⁴Program in Neuroscience Harvard Medical School, Massachusetts General Hospital for Children, Boston, MA

Background: Recent studies have shown that the intestine has a relevant role in providing a dynamic barrier to regulate the trafficking of environmental antigens across the host mucosa and in controlling the balance between tolerance and immunity to non-self antigens. The integrity of the intestinal barrier appears to be a key element in preventing uncontrolled passage of antigens and the onset of immune responses. Increased intestinal permeability has been correlated to chronic inflammatory diseases, including autoimmune disorders. Further, neuroinflammation and a leaky blood brain barrier (BBB) have been associated with microbiota-driven increased intestinal permeability. Several studies point to a gut-brain connection associating an impaired intestinal barrier to neurological diseases involving neuroinflammation. Zonulin [human prehaptoglobin-(HP)-2] has been identified as the principal and so far, only, endogenous regulator of epithelial and endothelial tight junctions.

Aim: Characterizing the zonulin transgenic mouse (Ztm) to understand whether it can be used as a model to study gut-brain axis dysfunctions leading to abnormal behavioral manifestations typical of neurobehavioral disorders such as ASD.

Methods: In our study, we used a zonulin transgenic mouse model expressing two copies of the zonulin gene [human prehaptoglobin-(HP)-2]. TJ proteins gene expression were evaluated by qPCR both at the intestinal and at the BBB level. Mice were also tested for repetitive behavior (marble burying), low anxiety activity (open field), and behavior in a mild anxiogenic setting (elevated zero maze).

Results: Zonulin transgenic mice had increased small intestinal permeability at baseline compared to wt (C57BL/6J) ($p < 0.01$). These changes were associated with a downregulation of claudin 3 (CLDN-3), CLDN-15 and membrane palmitoylated protein 5 (MPP5). To test vascular brain permeability, we evaluated the expression level of major components of the brain endothelial tight junctions (CLDN-1, -3, -5, -12, occludin) along with known markers of neuroinflammation (TSPO, IBA-1) by qPCR. We did not observe any significant difference between wt and zonulin transgenic mice, suggesting an unaltered BBB gene expression profile, but we did observe an increased CLDN-5 protein expression (by western blot) in the cortex of the transgenic male mice. Our behavioral tests show differences between males and females, with transgenic females showing more repetitive behavior (marble burying), while transgenic males appeared less anxious (open field). When evaluated in a mild anxiety setting (elevated zero maze) zonulin transgenic mice appear to be more anxious than wt mice.

Conclusions: Our results suggest zonulin transgenic mice have an impaired gut epithelial barrier associated with increased intestinal zonulin gene expression levels and altered tight junction gene expression, compared to wt mice. Although we did not see changes in gene expression level of BBB components, we observed increased CLDN-5 in the cortex of transgenic mice, suggesting an altered BBB. When tested for behavior zonulin transgenic mice showed sex-dependent differences: females displayed more repetitive/obsessive behavior, while males were less anxious (in a low anxiety setting). In a mild anxiety setting (elevated zero maze) transgenic mice showed a more anxious phenotype compared to wt mice. Combined, our data suggest that the zonulin transgenic mouse model could be a useful tool to study the gut-brain crosstalk in health and disease.

199 CHRONIC PANCREATITIS IS A DEVASTATING DISEASE ACROSS ALL AGES: COMPARISON OF TWO LARGE PEDIATRIC AND ADULT MULTICENTER COHORTS.

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Background: Chronic pancreatitis (CP), well-characterized in adults, is increasingly recognized in children. No study has compared CP patients who presented in childhood with those who presented as adults to identify unique differences between the groups.

Objective: We compared demographics, clinical presentation, risk factors and disease burden of pediatric and adult CP using two large multicenter cohorts.

Methods: We performed a cross-sectional study of data from INSPPIRE (International Study Group of Pediatric Pancreatitis: In search for a cure), a registry of children with acute recurrent pancreatitis and CP; and NAPS2 (North American Pancreatitis Study II), the largest multicenter cohort of US adults with CP. Values were reported as mean \pm SD. Between-group differences were compared using Pearson Chi-Square test. Wilcoxon rank sum test was used to compare pain patterns.

Results: Age of CP diagnosis was 9.8 ± 4.1 for children ($n=189$) and 47.3 ± 15.3 for adults ($n=1,195$). The majority were Caucasian (82% of children vs 76% of adults, $p=0.13$), female sex was predominant in children (57% vs 46%, $p=0.004$). Alcohol etiology and smoking exposure (active or passive) were found exclusively in adults (51% vs 1% and 49% vs 8% respectively, $p<0.0001$ for both); autoimmune pancreatitis and obstructive risk factors were more common in children (7% vs 2% and 30% vs 19% respectively, $p<0.001$ for both). Pancreatitis-predisposing genetic mutations were more frequently reported in children (77% of children with at least 1 genetic variant, vs 25% of adults, $p<0.0001$). Pancreatic calcifications on imaging were more common in adults (57% vs 16%, $p<0.0001$), pancreatic duct stricture was more common in children (38% vs 27%, $p=0.006$). Compared to children, adults with CP were more likely to suffer from exocrine pancreatic insufficiency (EPI) and diabetes (37% vs 25% $p=0.004$; and 32% vs 5% respectively, $p<0.0001$ for both). Eighty-seven percent of adults and children reported abdominal pain within the previous year, with constant pain reported more often in adults (56 vs. 43%, $p=0.05$). Pain medication and narcotic use were more commonly reported in adults (57% vs 70% and 41% vs 63% respectively, $p<0.001$ for both). Pancreatic sphincterotomy and stone removal were more commonly performed in children compared to adults (48% vs 31% and 25% vs 13% respectively, $p<0.0001$ for both).

Conclusions: Pediatric and adult onset CP have distinct risk factors and disease characteristics with advancing organ failure over time and burden in children approaching that of adults. The high rate of EPI in adults may suggest earlier onset that is not appreciated clinically. Children may be undertreated with respect to pain.

201 CISAPRIDE® USE IN PEDIATRIC PATIENTS WITH INTESTINAL FAILURE AND ITS IMPACT ON PROGRESSION OF ENTERAL NUTRITION.

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Background: Gastrointestinal dysmotility is common in pediatric intestinal failure patients (PIF), leading to delays in advancement of enteral nutrition (EN) and ability to wean parenteral nutrition (PN). Data on the safety and efficacy of Cisapride® for this purpose is scarce.

Objectives: Describe a single center experience with Cisapride® and its impact on enteral nutrition progression in patients with IF.

Study Design: Retrospective cohort study of PIF patients managed in an intestinal rehabilitation program between 2008-2015. Percentage of EN tolerance (proportion of overall kcal/kg being delivered enterally) prior to initiation of Cisapride®, progression of EN percentage at 3 and 6 months and ability to wean PN were calculated. Side effects were recorded to characterize safety of Cisapride® use.

Results: Use of any prokinetic was identified in 60/106 patients (56.6%), 29/60 patients (48.3%) failed to advance EN tolerance on other prokinetics and started on Cisapride®. Prior to Cisapride® the progress of EN had plateaued for a mean of 42.3 ± 60.2 days. The EN progression rate before and after initiation of Cisapride® was $0.14\%/day \pm 0.19\%/day$ vs $0.69\%/day \pm 0.31\%/day$ ($p < 0.001$). Percentage of EN tolerance 3 months after initiation of Cisapride® significantly improved compared to baseline (23.1% vs 79.4 % respectively; $p < 0.001$). Cisapride® was discontinued in 2/29 (6.8%) patients (1 prolonged QTc and 1 as a precaution due to cardiomegaly secondary to selenium deficiency).

Conclusion: Cisapride® can be beneficial in PIF patients who have failed to progress EN using other first line prokinetics. Cardiac side effects in our cohort were low, however cardiac monitoring is still recommended.

***202 ANALYSIS OF PEDIATRIC PANCREATITIS (APPLE STUDY). MULTRICENTRE PROSPECTIVE DATA COLLECTION AND ANALYSIS BY THE HUNGARIAN PANCREATIC STUDY GROUP.** *Andrea Parniczky^{1,2}, Balázs Csaba Németh³, Dóra Mosztbacher^{1,4}, Anna Zsófia Tóth⁵, Natália Lásztity², Alexandra Demcsák⁵, Andrea Szentesi¹, Corina Pienar¹⁰, István Tokodi⁶, Ibolya Vass⁷, Orsolya Kadenczki⁸, Judit Czelecz¹¹, Gábor Veres⁴, Miklós Sahin-Tóth⁹, Péter Hegyi¹. ¹Institute for Translational Medicine, University of Pécs, Pécs, Hungary; ²Heim Pal Children's Hospital, Budapest, Hungary; ³Department of Medicine, University of Szeged, Szeged, Hungary; ⁴First Department of Pediatrics, University of Semmelweis, Budapest, Hungary; ⁵First Department of Pediatrics, University of Szeged, Szeged, Hungary; ⁶Department of Pediatrics, St. George Teaching Hospital County Fejér, Székesfehérvár, Hungary; ⁷Department of Pediatrics, University of Pécs, Pécs, Hungary; ⁸Department of Pediatrics, University of Debrecen, Debrecen, Hungary; ⁹Boston University Henry M. Goldman School of Denatal Medicine, Boston, MA; ¹⁰Department of Pediatrics, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania; ¹¹Bethesda Children's Hospital, Budapest, Hungary*

Introduction: Despite of the rising incidence of pediatric pancreatitis(PP) in the last decade, there is still lack of information concerning the management of childhood onset pancreatitis.

Aims: The Pediatric Section of the Hungarian Pancreatic Study Group aimed to initiate a prospective international observational clinical trial (APPLE - Analysis of Pediatric Pancreatitis) to understand the genetic factors of all forms of pancreatitis occurred under 18(APPLE-R), and to collect a critical mass of clinical data and biomedical research samples from children suffering from PP(APPLE-P).

Methods/Design: The study has (i) been discussed and agreed in our latest international meeting, received the relevant ethical permission, been registered (ISRCTN89664974). The study is open for all centres.

Results:/APPLE-R: 75 acute, 32 recurrent acute and 14 chronic pancreatitis cases were enrolled yet. Concerning the etiology, biliary and drug-induced 9-9%, trauma, alcohol 2-2 %, postERCP and anatomic 5-5%, other 14% were identified however 54% of the cases still remained idiopathic. In 121 cases, genetic analyses of PRSS1, SPINK1, CFTR and CTRC genes have been completed. 48,8% (59/121) of the patients have pathogenic variants. Genetic alterations in PRSS1 were found in 4 cases, SPINK1 in 13 cases, CPA1 in 2 cases, CFTR in 15 case and CTRC in 51 cases. Pathogenic variants in two genes were observed: 2 PRSS1-CTRC, 1 PRSS1-SPINK1, 6 SPINK1-CTRC, 1 SPINK1-CFTR, 7 CTRC-CFTR, 1 CPA1-CFTR. There were no pathogenic variants in 62 cases. **APPLE-P:** We have already enrolled 18 patients.

Conclusion: Positive genetic alteration was found in 65% of the idiopathic and 30% of the non-idiopathic groups. Our results suggest that genetic testing should be performed in all children suffering from pancreatitis. The study is still ongoing, more patients are crucially needed.

203 **RESPONSE TO HEPATITIS B REVACCINATION IN CHILDREN WITH CELIAC DISEASE.**

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Introduction: Celiac disease is an immune-mediated disorder. Studies in children with celiac disease have previously reported a low response to the primary vaccine series for hepatitis B. One study in Turkish children with celiac disease suggested that these children demonstrated high response rates to revaccination with hepatitis B following initiation of a gluten free diet. However, these results have not been confirmed for children living in the United States. We performed a retrospective chart review to assess hepatitis B titers in children with celiac disease and whether baseline titers were affected by the presence of other autoimmune diseases, gender or vitamin D levels. We also assessed the response to an additional hepatitis B vaccine in children who were found to have negative titers.

Methods: A retrospective review of medical records at our institution was performed on 79 children with biopsy confirmed celiac disease or serology based on European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines. Information including age of diagnosis, gender, presence of other autoimmune disease, including type I diabetes and hypothyroidism, vitamin D levels and hepatitis B status were collected for each patient. A positive titer was considered a level of greater than 12 mIU. 25-hydroxy-vitamin D (D-25) levels were considered low if < 30 ng/ml and normal if 30 ng/mL or greater.

Results: Of the 79 children, 67 had a baseline hepatitis B titer. The average age of diagnosis was 6.74 years. The majority (60/67) were diagnosed via endoscopic biopsy (89.6%) while 10.4% (7/67) were diagnosed via serology based on ESPGHAN guidelines. Thirty-six (53.7%) were male and 31 (46.3%) were female. 60.6% of children (40/66) had normal vitamin D-25 levels.

Of the 67 children, 25 (37.3%) had positive hepatitis B surface antibody levels and 42 (62.7%) had negative hepatitis B surface antibody levels. There was no difference in response to the initial primary vaccine series based on gender. Twenty-three percent of children (6/26) with vitamin D levels <30 ng/mL and 45% of children (18/40) with vitamin D levels greater or equal to 30 ng/mL, had positive hepatitis titers (p=0.07). Twenty-one percent of children (3/14) with an additional autoimmune disease and 42% in children (22/53) without presence of an additional autoimmune disease, demonstrated hepatitis B immunity following primary vaccination (p=0.22).

Of the 42 with a negative baseline hepatitis B titer, 20 were revaccinated with one additional hepatitis B vaccine. One hundred percent (20/20) showed a positive titer following revaccination. Reasons for failure to revaccinate (22/42) included lack of pediatrician awareness for need of vaccine as child already completed primary vaccine series, parents not making an appointment to get vaccine, and recent awareness of hepatitis B titer status.

Conclusion: Our study confirms a lower rate of response to the hepatitis B vaccine in children with celiac disease. However, our rate of response is slightly lower (37.3% vs 46%) than previously published. Presence of additional autoimmune diseases, baseline vitamin D levels and gender did not play a role in response to the primary hepatitis B vaccine series. Our study

demonstrates that revaccination in US children with celiac disease with an additional Hepatitis B vaccine after initiation of a gluten free diet leads to a high response rate for hepatitis B immunity.

Larger studies would be helpful to confirm whether there is a small percentage of children who do not respond to revaccination as is seen in the general population and whether this small percentage of children would benefit from repeating the three hepatitis B vaccine series. In addition, future studies should include older children and adolescents and children from other medical centers to assess whether these children also demonstrate a similar response to revaccination.

Discussion: Children with celiac disease should have a hepatitis B surface antibody checked as part of health care maintenance. Children in the United States with celiac disease benefit from revaccination for hepatitis B.

Barriers to revaccination may be overcome through improved communication with pediatrician and pediatrician education regarding lack of initial response and need of vaccine in children with celiac disease and, if possible, administration of the vaccine at the time of visit with the pediatric gastroenterologist.

204 COMPARING THE THERAPEUTIC RESPONSE IN EOSINOPHILIC ESOPHAGITIS BETWEEN CHILDREN WITH AND WITHOUT CELIAC DISEASE.

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Celiac disease (CD) and eosinophilic esophagitis (EoE) share a commonality of disordered immune regulation and food antigen triggers. However, treatment responses of children affected by both conditions as compared to those with EoE alone have not been studied. The aim of this study was to determine whether children with both CD and EoE more frequently achieve esophageal histologic resolution with dietary therapy than children with EoE alone.

Methods: We conducted a retrospective study of electronic medical records of patients aged 0-18 years evaluated between January 1, 2010 and October 1, 2016, comparing those with EoE only versus those with EoE and CD (EoE-CD) using an institution-wide patient registry. Only cases with a histologic diagnosis of EoE or EoE-CD and ≥ 1 follow up esophageal biopsy after EoE diagnosis met inclusion criteria and were included. We collected demographics, clinical symptoms, results of allergy testing (ImmunoCAP and skin), treatment interventions (e.g. proton-pump inhibitor, dietary elimination, and/or swallowed corticosteroids) and esophageal biopsy results to determine attainment of histologic resolution. Logistic regression and Wilcoxon rank-sum test were used to analyze categorical and nonparametric variables, respectively.

Results: In this cohort study, 128 EoE and 17 EoE-CD patients met the inclusion criteria. Both groups showed a comparable median age at diagnosis (7.1 years in EoE vs. 8.8 in EoE-CD, $p=0.1$) and were similarly male-predominant (72.7% EoE vs. 58.8% EoE-CD, $p=0.2$). The majority of patients in both groups underwent objective allergy testing (79.7% EoE versus 88.2% EoE-CD, $p=0.4$). There were no significant differences in individual food allergy testing results between the two groups, including wheat allergy (44.2% EoE versus 41.7% EoE-CD, $p=0.9$). There was no significant difference in esophageal mucosal healing rates between the two groups by the end of the follow up period (68.8% of EoE vs 88.2% of EoE-CD, $p=0.1$). There were no significant differences in resolution rates with dietary elimination, corticosteroid treatment, or proton pump inhibitor therapy between the two groups, nor were there differences in the number of endoscopies required prior to achieving EoE remission ($p=0.5$).

Discussion: Children with EoE and CD show similar responses to therapy as those with EoE alone. Although limitations such as the sample size of the CD-EoE cohort may affect comparative analyses, our study shows no evidence that those with EoE and CD are more likely to respond to dietary eliminations, or that those with CD attain mucosal healing of the esophagus more quickly than those with EoE alone. Hence, treatment for EoE should proceed according to evidence-based guidelines for EoE independent of CD diagnosis.

205 ARE WE OVERLOOKING CELIAC DISEASE IN THE PEDIATRIC OUTPATIENT DEPARTMENT.

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Background: US population based studies have shown that celiac disease (CD) is largely underdiagnosed among all ethnic and racial groups. Presently, the prevalence of CD ranges from 0.4- 0.95%. The screening for CD now incorporates additional symptoms which relates to a higher prevalence of CD diagnoses. We are unaware of the local prevalence of the disease within our mostly African American population in Southern Alabama, including in those patients that present with symptoms characteristic of CD.

Aim: We aim to estimate the prevalence of CD among the mostly African American patients presenting to a primary care setting with symptoms that are suggestive of CD.

Methods: We retrospectively reviewed medical records of children who met the following criteria: children ages 1-18 who visited the primary care services at the University of South Alabama Children's and Women's Hospital from July 2015 – June 2017. We focused on an increased list of symptoms or diagnosis (ICD10) associated with an increased CD prevalence: constipation, diarrhea, iron deficiency anemia, abdominal pain, weight loss and failure to thrive. We recorded demographics and data using a clinical abstraction form. We collected all tissue transglutaminase (TTG- IgA) screening tests and the number of CD in that period. We looked specifically at symptom directed testing. We used descriptive statistics when applicable.

Results: We collected data on 11934 unique patients 7153(60%) were under 13years old. 64% were African American, 64% female; 2570 (22%) patients exhibited symptoms suggestive of celiac disease and 83 (3%) were screened with TTG-IgA . No patients were diagnosed with CD. Sixty-five percent of these tests were ordered among African American patients and 16% among whites. Forty-six percent were males and 46% of these tests were ordered in children over 13 years of age.

Conclusion: Despite the high national prevalence of CD, no cases were identified in our local population during the two-year period of the study. The screening for CD occurred only when symptoms directed. This conclusion either portrays an extremely low clinical prevalence of CD or lack of clinical knowledge in screening of the disease.

206 24 CASES OF CONGENITAL TUFTING ENTEROPATHY, THE CLINICAL FEATURES AND

OUTCOME, THE LARGEST SERIES. *Badr Alsaleem¹, Ali Asery¹, Musa Faqeeh², Nurah Albanyan³, Abdulrahman Al-Hussaini¹, Khurram Lone¹, Amna Ahmed¹. ¹Pediatric Gastroenterology, King Fahad Medical City, Faculty of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia; ²Pathology & Clinical Laboratory Medicine, King Fahad Medical City, Riyadh, Saudi Arabia; ³Pharmacy Administration, King Fahad Medical City, Riyadh, Saudi Arabia*

Objectives/Study: Tufting enteropathy (TE), also known as intestinal epithelial cell dysplasia is a rare autosomal disease that presents with intractable diarrhea in the neonatal period and requires parenteral nutrition (PN). There is villous atrophy and intestinal epithelial cells, are characterized by dysplasia and often there is tufting without inflammation.

Aim: The aim of this study is to describe the characteristics of clinical and laboratory features and outcome of patients with TE at tertiary care institution in Saudi Arabia (SA).

Methods: This is a retrospective study, reviewing the TE patient's files who are diagnosed by Epithelial cell adhesion molecule gene test (EPCAM) or has characteristic histopathology features and family history of TE at King Fahd Medical City, Riyadh, SA in the period, from May 2004 until May 2016.

Results: Twenty-four patients with TE have been identified. The median age at the onset of the diarrhea 7 days and median age at presentation 3.6 months. Fifteen (63%) were female, all were Saudi, all full term except one, and Twenty One (89%) Normal birth weight. All presented with severe failure to thrive, metabolic acidosis and normal serum albumin. Three refused admission and discharged against medical advises and died. Twenty one have been followed. One went for bowel transplant and died and two refused parenteral nutrition(PN). Eighteen (86%) still survived. The median follow up was 4.5 years (8.0 month-10.5 year).

Conclusion: TE should be considered in the preferable diagnosis of infants presenting with neonatal intractable diarrhea, severe failure to thrive and metabolic acidosis. Favorable outcome is possible with PN. To the best of our knowledge, this is the largest series about TE patients.

209 CELIAC DISEASE IN HEALTHY COLOMBIAN CHILDREN BY ANTI-TRANSGLUTAMINASE AND ANTIGENIC HISTOCOMPATILITY ANTIGENS.

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Introduction: The prevalence of celiac disease (CD) in healthy Colombian children is unknown.

Objective: To determine the prevalence of CD in healthy Colombian children using IgA anti-transglutaminase (tTG) and HLA DQ2/DQ8.

Materials/Methods: Were included 517 healthy children from La Unión (n = 324), Cali (n = 105) and San Andrés de Sotavento (n = 88), Colombia; 56.9% girls; 13.5 ± 3.6 years (8 infants, 7 preschoolers, 156 schoolchildren and 346 adolescents); 57.6% mestizos. Were taken tTG by digital puncture; and being positive, HLA DQ2/DQ8 was performed. Statistical analysis included chi2 and the McNemar test, as well as univariate, bivariate and association analyzes with the OR calculation and their corresponding 95% CI.

Results: The tTG was positive in 15 children (2.9%) (12 girls, 10 mestiza race, 9.9 ± 4.4 years) and HLA DQ2/DQ8 was positive in seven children (1.4%) (5 girls, 5 mestiza race, 10.4 ± 0.6 years): 3 HLA DQ2, 2 HLA DQ8 and 2 HLA DQ2/DQ8. There was a greater opportunity to present digestive symptoms in children with positive tTG (OR = 3.2 95% CI = 0.9-13.9 p = 0.0381) and HLA DQ2/DQ8 positive but no significant difference (OR = 2.9 95% CI = 0.4-30.7 p = 0.18).

Conclusion: 1.4:100 healthy Colombian children studied present CD, with HLA DQ2 being more prevalent, and with a greater opportunity to present digestive symptoms in tTG positive, which should force Colombian health policies to be aimed at early detection and timely management of this entity.

210 A FOCUS ON STENOSIS: PATIENT WITH CHRONIC PANCREATITIS AND PANCREATICOPLEURAL FISTULA WITH PANCREATIC DUCT STENOSIS.

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Background: Chronic pancreatitis is increasingly becoming a recognized disorder in the pediatric population. Although pleural effusion may occur in 3-17% of patients with acute pancreatitis, it is unusual in chronic pancreatitis, and may represent pancreaticopleural fistula (PPF). PPF occurs in only 0.4% of patients with pancreatitis and 4.5% of cases with pancreatic pseudocyst. The pathogenesis of PPF is typically from rupture of a mature pseudocyst or posterior leakage from an immature one. Leakage of pancreatic drainage is often associated with pancreatic duct obstruction or disruption. We report a 16 year old female with chronic pancreatitis and pancreatic pseudocyst without pancreatic duct dilatation, who developed PPF requiring partial pancreatectomy and fistulectomy. In contrast, PPF most often occurs with presence of pancreatic ductal dilation.

Case Report: Patient is a 16 year old Caucasian female with Factor V Leiden deficiency, and family history of pancreatitis and cystic fibrosis who presented with symptoms of abdominal pain, decreased appetite and a 19 kg weight loss over four months. Laboratory evaluation demonstrated elevated serum amylase and lipase concentrations of 4336 U/L, and 459 U/L, respectively. Her father died of pancreatic cancer at age 37 years. However, her pancreatic genetic mutation panel was negative for SPINK1, PRSS1, CTSC, or CFTR mutations. Serial abdominal ultrasound eventually revealed mild pleural effusion of the left lung with increase in size of the pancreatic pseudocyst to 6.1 cm x 4.5 cm x 3.2 cm, hepatomegaly in the presence of normal liver enzymes, and gallbladder sludge. Conservative management included analgesics, pancreatic enzyme supplementation, subcutaneous octreotide, and ursodeoxycholic acid. The pancreatic pseudocyst partially responded to conservative therapy and CXR revealed intermittent improvement of pleural effusion. In subsequent hospitalization, abdominal ultrasound revealed gallstones with bilirubin <0.2 mg/dL associated with right upper quadrant pain and biliary colic leading to laparoscopic cholecystectomy with interoperative cholangiogram. Due to presence of 500 mL of pleural fluid at the left lower lobe, a chest tube was placed to drain effusion that yielded an elevated pleural fluid amylase concentration. Post-op MRCP revealed slight interval decrease in size of the cystic collection at the tail of the pancreas. Ursodeoxycholic acid was discontinued and octreotide was decreased. Patient was symptom free for approximately one month when she returned with right upper quadrant abdominal pain, nausea, and shortness of breath. MRCP performed during admission demonstrated pseudocyst at the tail of the pancreas with fistulous to the left pleural cavity. There was no evidence of pancreatic duct enlargement. Pulmonary function test revealed a normal exam on spirometry. At this time, due to presence of PPF, surgery was performed 11 months after the onset of pancreatitis. Patient underwent laparoscopic distal pancreatectomy with splenectomy and resection of pseudocyst with repair of diaphragm and chest tube placement. Operative report revealed significant inflammation around the tail of the pancreas under the hilum of the spleen with some splenic artery and vein involvement in the phlegmon. Lesion was noted to be 2 cm in size; excision included inflammatory region located 2 cm from fistulous tract. Specimen collected resulted with no pancreatic atypia nor malignancy but with presence of eosinophilic material; hemosiderin and evidence of hemorrhage was noted with fibrous changes to lung tissue. Post-operative MRCP revealed resolved left pleural effusion with residual hyperintensity at the left diaphragm indication surgical changes. Laboratory workup following surgery revealed acute increase in lipase at 952 mg/dL to resolution at 136 mg/dL and persistent normalization in routine clinic visits up to 5 months post operatively.

Conclusion: PPF is a rare cause of pleural effusion. We conclude that PPF should be considered in patients with chronic pleural effusion and pancreatic pseudocyst. As in our patient, this PPF may occur without pancreatic ductal dilatation.

211 HIGH CARRIER FREQUENCY OF THE FOUR MOST COMMON CONGENITAL SUCRASE-ISOMALTASE DEFICIENCY PATHOGENIC VARIANTS DETECTED IN PEDIATRIC CASES WITH SYMPTOMS AND LOW SUCRASE VERSUS CONTROLS WITH NORMAL SUCRASE.

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Background: Congenital Sucrase-Isomaltase Deficiency (CSID) impairs sucrase-isomaltase (SI) activity resulting in carbohydrate malabsorption, colonic fermentation, symptoms of chronic diarrhea (CD), gassiness, and/or abdominal pain (AP). CSID can be diagnosed via disaccharidase assay with no/reduced sucrase and isomaltase, reduced maltase, normal lactase, and normal histology (NH). The frequency of the top 4 known pathogenic sucrase-isomaltase (SI) gene variants in subjects with low sucrase activity with and without normal lactase is unknown. We used a novel approach of analyzing variants using Next Generation Sequencing (NGS) of DNA from retrospectively available formalin fixed paraffin embedded (FFPE) tissue samples of CSID cases and controls.

Methods: An IRB approved retrospective case-control study was conducted to detect the frequency of SI-exon variants in DNA from FFPE tissue samples of Caucasian patients with low and high sucrase activities (Table 1). The NGS method was optimized with FFPE DNA for Illumina's MiSeq platform using custom amplicon design targeting the SI-exons. Cases (n=125) were Caucasian patients with a symptom complex including CD and/or AP, NH, low sucrase ($\leq 25U$), no known organic GI disorder, and with or without low lactase ($\leq 15U$). Controls (n=250) were Caucasian patients with high sucrase ($\geq 55U$), NH, no organic GI disorder, and without diarrhea. Presence of any pathogenic CSID variant was counted as a frequency of 1. The primary analysis was a one-sided Pearson's exact test.

Results: Age and gender were similar in both groups; the average disaccharidase activities were low in cases (Table 1). Three of the top 4 known CSID pathogenic variants were detected in 20 cases (all heterozygous) and 0 controls (Table 2). The top 4 known pathogenic CSID variant carrier frequency in cases was significantly greater (p-value < 0.001) than controls. Cases with GI symptoms and sucrase deficiency were 14.1 times (95% CI 23.0, 8.7) more likely to have top 4 known pathogenic CSID variants than the Exome Aggregation Consortium (ExAC) general population database. Cases with both normal lactase (p-value < 0.001) and abnormal lactase (p-value < 0.001) had statistically significantly higher CSID carrier frequencies.

Conclusion: This is the first report of SI-exon variant detection with FFPE samples using NGS. Three of the known top 4 CSID pathogenic variants were detected at a much higher frequency in cases vs. controls and in all case subsets including diarrhea, abdominal pain, and with or without normal lactase. Low sucrase activity with normal histology in symptomatic Caucasian patients may be explained by known SI variants in up to 15% of symptomatic patients with deficient sucrase, regardless of lactase activity. Using this novel approach we plan to explore further relationships between CSID heterozygosity and disease phenotypes. These results suggest that a genetic test would be valuable for suspected disaccharide malabsorption irrespective of lactase in Caucasians.

Table 1: Demographics and Clinical Characteristics of Patients

Demographics	FFPE Sample Types	
	Cases [N (%)]	Controls [N (%)]
N	125	250
Male	63 (50.4%)	127 (50.8%)
Female	62 (49.6%)	123 (49.2%)
Avg. Age Years (Min/Max)	13.1 (0.3/23.0)	10.8 (0.8/24.0)
Diarrhea	11 (8.8%)	0 (0.0%)
Abdominal Pain	87 (69.6%)	177 (70.8%)
D and AP	27 (21.6%)	0 (0.0%)
Without D or AP	0 (0.0%)	73 (29.2%)
Disaccharidase Activity	Average U (Min/Max)	Average U (Min/Max)
Lactase	10.3 (1.0/51.6)	29.9 (0.8/84.5)
Maltase	86.7 (25.7/201.0)	303.4 (120.4/729.9)
Sucrase	18.9 (1.3/25.8)	77.8 (55.0/171.2)
Palatinase	7.9 (0.4/14.4)	22.8 (12.0/44.8)
Glucoamylase	19.2 (7.3/44.7)	63.2 (32.3/115.0)
Top 4 CSID Variants	Cases (N)	Controls (N)
V577G	8	0
G1073D	5	0
F1745C	7	0
R1124X	0	0
Total	20	0

Abbreviations: N, Number of patients; D, Diarrhea; AP, Abdominal pain; U, Enzyme activity unit = $\mu M/min/gram$ protein

Table 2: Descriptive Statistics of Cases vs. Control

Sample Cohort	N	Top 4 CSID SNPs	Frequency	p-Value vs:		Odds Ratio vs. ExAC		
				Controls	ExAC	OR	Upper C.I.	Lower C.I.
Controls	250	0	0.0%					
Cases - Total	125	20	16.0%	<0.001	<0.001	14.1	23.0	8.7
Cases - Diarrhea Only	11	2	18.2%	<0.001	<0.001	16.5	76.6	3.6
Cases - Abdominal Pain Only	87	14	16.1%	<0.001	<0.001	14.2	25.4	8.0
Cases - Diarrhea & AP	27	4	14.8%	<0.001	<0.001	12.9	37.5	4.4
Cases - Normal Lactase	19	5	26.3%	<0.001	<0.001	26.5	73.9	9.5
Cases - Abnormal Lactase	90	12	13.3%	<0.001	<0.001	11.4	21.1	6.2
ExAC database	32,357	430	1.3%					

ExAC: Exome Aggregation Consortium, Broad Institute, USA.

213 PREVALENCE OF SPLANCHNIC VEIN THROMBOSIS IN PEDIATRIC PANCREATITIS – A SINGLE CENTER EXPERIENCE. Craig McKinney¹, Jeremy Middleton². ¹Pediatrics, University of Virginia Children's Hospital, Charlottesville, VA; ²Pediatric Gastroenterology, Hepatology, and Nutrition, University of Virginia Children's Hospital, Charlottesville, VA

Background/Objective: Splanchnic vein thrombosis (SVT) is a severe complication of pancreatitis that can lead to potential sequelae of portal hypertension and variceal bleeding. It is a well described in adult pancreatitis with estimated prevalence of

13.6%. However, the prevalence of SVT in pediatric patients with acute pancreatitis is unknown. The aim of this single center, retrospective study was to establish the prevalence of SVT in our pediatric population.

Methods: We reviewed 207 pediatric admissions for acute and chronic pancreatitis from January 1996 through December 2016. Data collected included patient demographics, etiology of pancreatitis, laboratory values, complications, and procedures/interventions. Imaging results were reviewed to identify the frequency and location of thrombosis.

Results: SVT was detected in 8/207 patients (3.8%). The mean patient age was 14.75 yrs and patients presented with thrombosis in the setting of both acute and chronic pancreatitis. The causes of pancreatitis were from medication (3/8 [37.5%]), idiopathic (2/8 [25%]), chronic hereditary (2/8 [25%]) and gallstone (1/8 [12.5%]). Although there were thrombi in the superior mesenteric vein (2/8 [25%]) and portal vein (2/8 [25%]), the majority of patients had isolated splenic vein thrombus (5/8 [62.5%]). One child had thrombosis of the splenic, SMV, and portal vein (1/8 [12.5%]). Patients with SVT had LOS of 23.5 days compared to 12.1 days for those without (P 0.24). Patients with SVT more commonly had more severe disease with complications including necrotizing disease (P=.056) and pseudocyst formation (P = .002). Ultrasound failed to identify a thrombus in 4 out of 8 patients who were ultimately identified with MRI or CT. Only 2 patients had complete resolution of thrombus, and 1 patient developed variceal bleeding as a sequelae of thrombosis.

Conclusion: Although pancreatitis-induced thrombosis in children occurs less often than in adults, SVT does appear in almost 4% of pediatric patients with acute pancreatitis. Severe disease course with necrotizing pancreatitis and pseudocyst formation may be risk factors for SVT. Advanced imaging with MRI or CT seems to be more sensitive in identifying patients with SVT.

214 HIGHER PREVALENCE OF MICROALBUMINURIA IN CHILDREN WITH DUAL DIAGNOSIS OF TYPE 1 DIABETES AND CELIAC DISEASE DESPITE NO DIFFERENCE IN CARDIOVASCULAR RISK FACTORS.

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Background: Celiac disease (CD) is a risk factor for development of retinopathy and nephropathy in adults with type 1 diabetes (T1D). Limited data in children exist.

Aims/Objective: Compare cardiovascular risk factors and diabetes complications in children with both T1D and CD compared to children with T1D alone.

Methods: Retrospective chart review of 90 children and adolescents with T1D and biopsy confirmed CD (from 2011-2015) was matched to controls with T1D alone for age, sex, race and duration of diabetes. BMI percentile, systolic/diastolic blood pressure percentiles, lipids (cholesterol, LDL, HDL, triglycerides), hemoglobin A1c and microalbuminuria (first morning urine specimen with albumin/creatinine ratio >30) were compared by Wilcoxon signed-rank tests and McNemar's tests for paired data between the two groups.

Results: 54% were male; 94% of patients were non-Hispanic white. Mean age of diagnosis of T1D was 7.5 ± 4.2 years; mean age of CD diagnosis was 12.8 ± 4.2 years. 59% (53/90) of children developed CD within the first 5 years of T1D diagnosis. Blood pressure and lipid profiles were not statistically different in those with CD+T1D compared to those with T1D alone. BMI percentile was lower in the CD+T1D group at diagnosis of CD (71.5 vs. 80.4; ns). Median HbA1c was 7.5% (IQR: 6.7-8.6) in those with CD+T1D vs. 7.7% (6.7-8.1) in those with T1D (ns). Microalbuminuria was found in 11% (10/90) of the CD+T1D group vs. 1/90 in T1D alone (p=0.01). 9 of the 10 CD+T1D patients with microalbuminuria were on ACE inhibitors.

Conclusion: Higher prevalence of microalbuminuria was found in children with T1D and CD despite no differences in cardiovascular risk factors when compared to matched controls with T1D alone. Further studies are needed to determine the factors contributing to the development of microalbuminuria in children with T1D and CD.

215 USE OF REMNANT SERUM FOR FATTY ACID BINDING PROTEIN TESTING IN INFANTS.

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Background: Necrotizing enterocolitis (NEC) is a highly morbid and potentially fatal condition for infants. Early detection continues to be challenging. Fatty acid binding protein (FABP), a biomarker of intestinal injury, shows promise in distinguishing NEC from benign conditions. An additional challenge for identifying new serum markers in infants is the limitation of blood volume that can be drawn at any one time.

Objectives: To determine if remnant serum specimens can be used to detect FABP, and to compare differences in serum concentration between infants with NEC, other surgical intestinal disorders, and "healthy" preterm infants.

Methods: Remnant specimens from routine blood draws within the first 3 days of diagnosis or surgery were collected from infants with Stage 2 and 3 NEC, spontaneous intestinal perforation, and intestinal surgical infants without perforation (gastroschisis or Hirschsprung's disease). Remnant specimens were also collected from fed preterm non-surgical control infants. Remnant blood was processed within 2-5 days and frozen at -80°C until assays were performed. A commercial intestinal FABP assay was used (Hycult Biotech, #HK406-01), requiring 10 microliters of serum. Values were log-transformed. Descriptive statistics and mixed effects multiple linear regression equations for longitudinal samples were used to compare results between groups.

Results: The following remnant samples were analyzed: 16 samples from 11 subjects with Stage 2 NEC, 10 samples from 9 subjects with Stage 3 NEC, 4 samples from 3 infants with SIP, 9 samples from 8 subjects with other surgery, and 35 samples from 31 control subjects. The mean gestational age was 28 weeks. Results for Stage 2 and Stage 3 NEC were similar, so the groups were combined. The median concentration within the first 3 days of diagnosis was 2,370 pg/ml (IQR 475-33,938) for stage 2&3 NEC, 313 pg/ml (IQR 226 – 1,169) for SIP, and 146 pg/ml (0-1,901) for other surgical infants. The median concentration for non-surgical controls was 1,104 pg/ml (IQR 661 – 2,201). There was not a statistical difference between any of the groups. However, only infants with NEC had concentrations >30,000 pg/dl (6 infants had concentrations ranging from 38,476 – 490,340 pg/dl). 8 NEC infants had undetectable FABP. The highest concentration in control infants was 14,459 pg/dl. 3 control subjects had undetectable levels.

Conclusions: Remnant serum samples are feasible to use for FABP testing, requiring only 10 microliters of serum. We did not detect a significant difference between NEC and various control groups. Variability in non-surgical controls is higher than previously reported. FABP may have high specificity for NEC at very high concentrations, but has poor sensitivity as a screening marker. Further testing with a larger sample size is required.

218 PROOF OF CONCEPT: COMPARISON OF THE BLOOD MICROBIOME BETWEEN CELIAC DISEASE PATIENTS AND HEALTHY DONORS. *Camron Davies, Gloria Serena, Alessio Fasano. Pediatrics, Massachusetts General Hospital, Boston, MA*

Typically, the blood is considered to be a sterile environment, but recent studies have revealed the existence of a blood microbiome that is derived primarily from the gut microbiome.

Seen in the context of celiac disease (CD), which is characterized by an increased intestinal permeability via the opening of tight junctions in response to gluten, this presents the possibility of increased bacterial translocation in the gut. In turn, chronic bacterial translocation into the blood through the gut has the potential to cause systemic low-grade inflammation, thereby priming the body's immune response for autoreactivity and activating a chronic stress response.

This study sought to determine, as a proof of concept, if it is possible to identify and characterize a blood microbiome associated with both active and inactive CD as compared to healthy controls. After isolating DNA from patients' whole blood (n=22), the V4 hypervariable region of the 16S rRNA gene was amplified and sequenced by Illumina.

Rarefaction curves show that the samples were sequenced with sufficient depth to be representative of their respective biomes, therefore confirming the reproducibility of the experiment.

Although this study failed (probably due to the small samples' size) to show significant differences among the three groups, it allowed us to see some interesting trends. Active CD samples appear to have the highest alpha diversity (Chao and PD indices), while CD patients in remission had the lowest one. Taxonomic analysis shows that CD group has the lowest level of *Actinobacteria Phylum*, CDGF the middle and HC the highest. Furthermore the active CD group lacks important bacteria genus such as *Clostridium* and *Bifidobacterium*.

The differences in alpha diversity found between active and inactive CD sustains the hypothesis that the gut barrier dysfunction triggered by gluten would increase the biodiversity of the blood by increasing intestinal translocation. The reduction of *Actinobacteria* and the absence of *Bifidobacterium* in active CD is compelling given the role that these microbes have in producing short chain fatty acids and regulating the intestinal immune homeostasis.

Overall each group blood microbiome compositions mirrored the previously described gut microbiome in its respective disease state. This experiment offers promising results for future explorations into the blood microbiome for CD and other diseases characterized by increased intestinal permeability. Future endeavors would particularly benefit from a larger sample size to help elucidate the specific differences in microbial compositions among groups and how these may play a difference in the final outcome of the disease.

219 THE PREVALENCE OF HELICOBACTER PYLORI IN CELIAC CASES AND ITS EFFECT ON CLINIC, HISTOPATHOLOGY AND LABORATORY PARAMETERS. Gokhan Tumgor¹, Mehmet Agin¹, Inci Batun², Semine Ozdemir², Figen Doran³. ¹Pediatric Gastroenterology, Cukurova University Medical Faculty, Adana, Turkey; ²Pediatrics, Cukurova University Medical Faculty, Adana, Turkey; ³Pathology, Cukurova University Medical Faculty, Adana, Turkey

Background: We have studied the prevalence of Helicobacter Pylori in children with Celiac Disease (CD) and the relations of HP with clinic, histopathology and laboratory parameters.

Methods: 256 patients who were serologically and histopathologically diagnosed celiac disease at Cukurova University, Medical Faculty, and Pediatric Gastroenterology Department between the dates of January 2012 - March 2016 were taken to the study. Besides obtaining duodenum biopsy through upper GIS endoscopy, antrum biopsy was also taken and histopathological HP existence and histological damage level were studied.

Results: 70 (27.4%) of 256 cases in the study were detected HP (+). There was no significant difference between HP (+) and HP (-) cases according to their gender and age. In HP (+) cases while the diagnose age was older, the complaints for diarrhea and abdominal distension were significantly higher. In the stomach biopsy of HP (+) cases with CD, activity and chronicity was significantly higher than the HP (-) cases with CD. Although hemoglobin, ferritin, vitamin B12 and transfer saturation were lower in HP (+) cases comparing to HP (-) ones, the differences were not statistically significant. Serum folate level in HP (+) group was significantly low ($p < 0.05$).

Conclusion: The prevalence of HP does not increase in cases with celiac disease, CD is lately diagnosed in HP (+) cases, distension and diarrhea complaints are more frequent, and folate deficiency is significantly higher. We think the reason for late diagnosis in HP (+) CD cases is caused by not considering CD since the HP was already diagnosed. We believe that for HP (+) cases, in presence of the distension and diarrhea complaints in advanced childhood period, physicians should consider Celiac disease.

220 HEREDITARY PANCREATITIS IN CHILDREN - REPORT OF 62 CASES.

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Objectives/Study: Hereditary Pancreatitis (HP) is a rare inherited condition. We reviewed our experience over the last 25 years. The aim of our study was to evaluate the clinical course of HP in children.

Methods: 369 children with chronic pancreatitis, hospitalized since 1988 to 2016, were enrolled into the study. The medical records of these patients were reviewed for data on the presentation, diagnostic findings and endoscopic treatment. All children were screened for the *PRSS1* gene mutations.

Results: Hereditary pancreatitis was diagnosed in 62 patients (16.8%) (39 girls and 23 boys; aged 0.8-17; mean-9.8 years). *PRSS1* gene mutations were found in 45 patients. We detected R122H/- in 18, R122C/- in 15, N29I/- in 5, E79K/- in 3, R116C/- in 2 and A16V/- in 2 patients. Family history was positive in 56 children with HP (90.1%). In 17 patients without mutations diagnosis of HP was made when the patients satisfied the requirements of the family history. In 7 patients we found *SPINK1* mutation (N34S/-), in 7 *CTRC* (G60G/-), in 1 *CFTR* mutation (delF508/-). There was no difference in age of the disease onset between HP group and non-HP group (8 vs. 9.1 years; NS). In children with *PRSS1* mutation ERCP had mean 2^o Cambridge grade, vs. 1.6^o, $p < 0.05$. Therapeutic intervention, including both surgical and endoscopic intervention, was more frequent in the HP group (75% vs. 35%; $p < 0.05$). Pancreatic duct stenting was done in 22 children with HP (35% vs. 26%; $p < 0.05$). ESWL was performed more frequent in HP group (10% vs. 3%; $p < 0.05$).

Conclusions: Hereditary pancreatitis in children has worse clinical course than CP in children without *PRSS1* mutations.

221 INCREASED ANTIDEPRESSANT AND STIMULANT USE IN CHILDREN WITH CELIAC DISEASE. Haley Zylberberg¹, Jonas Ludvigsson^{2,3}, Peter Green¹, Norelle Reilly¹. ¹Celiac Disease Center, Columbia University Medical Center, New York, NY; ²Medical Epidemiology and Biostatistics, Karolinska University Hospital and Karolinska Institute, Stockholm, Sweden; ³Pediatrics, Örebro University Hospital, Örebro, Sweden

Background: There is uncertainty regarding the association between Attention-Deficit/ Hyperactivity Disorder (ADHD) and other psychiatric illnesses in children with celiac disease (CD). We therefore assessed the prevalence of medication use to treat ADHD and other psychiatric disorders among children with CD.

Methods: Our study included 4,974 patients, aged 0-18 years, seen over a 10-year period from Jan 1 2007 to Dec 31 2016 at a tertiary care center. Using data derived from a center-based electronic medical record system, the prevalence of psychotropic

medication use among patients with CD (n=758) was compared to a control group (n=4216) with gastrointestinal symptoms of abdominal pain or reflux. Patients with a history of ulcerative colitis, Crohn's disease, eosinophilic esophagitis, and *Helicobacter pylori* gastritis were excluded. Multivariate analysis, adjusted for sex, was used to assess for independent associations between CD and medication use.

Results: Among our sample, 6.1% used any psychotropic medication, 2.8% use antidepressants, and 2.8% used stimulants. Patients with CD were more likely than controls to use any psychotropic medication (8.3% vs 5.7%, p=0.006), antidepressants (4.2% vs 2.6%, p=0.01), and stimulants (4.4% vs 2.5%, p=0.004). These results remained significant when adjusted for sex on multivariate analysis: children with CD had higher odds of being prescribed any psychotropic medication (OR: 1.53, 95% CI: 1.14-2.04) antidepressants (OR 1.58, 95% CI: 1.05-2.36) and stimulants (OR: 1.97, 95% CI: 1.32-2.95). Other medication categories, such as mood stabilizers, sleep aids, antipsychotics, and anxiolytics showed no differences between CD patients and controls.

Conclusions: Children with CD are prescribed psychotropic medications, specifically antidepressants and stimulants, at higher rates than children with other gastrointestinal symptoms. This data suggests that children with CD may be at greater risk of suffering from ADHD and depression.

Table 1: Comparison of Psychotropic Medication Use in Celiac Disease and Controls

Clinical Characteristics	Patient Total (n = 4974) (%)	Celiac Disease (n = 758) (%)	Control (n = 4216) (%)	P Values	Multivariate* OR (95% CI)
Sex					
Males	2394 (48.13)	284 (37.47)	2110 (50.05)	<0.0001	
Females	2580 (51.87)	474 (62.53)	2106 (49.95)		
Psychotropic					
Medications	4670 (93.89)	695 (91.69)	3975 (94.28)	0.006	
None	304 (6.11)	63 (8.31)	241 (5.72)		1.53 (1.14 – 2.04)
Any	140 (2.81)	32 (4.22)	108 (2.56)	0.01	1.48 (1.05 – 2.36)
Antidepressants	39 (0.78)	5 (0.66)	34 (0.81)	0.82	0.81 (0.32 – 2.08)
Antipsychotics	45 (0.90)	3 (0.40)	42 (1.00)	0.14	0.40 (0.12 – 1.30)
Anxiolytics	6 (0.12)	1 (0.13)	5 (0.12)	1.0	1.23 (0.14 – 10.83)
Mood Stabilizer	38 (0.76)	5 (0.66)	33 (0.78)	1.0	0.88 (0.34 – 2.28)
Sleep Aid	138 (2.77)	33 (4.35)	105 (2.49)	0.004	1.97 (1.32 – 2.95)
Stimulants	138 (2.77)	33 (4.35)	105 (2.49)	0.004	1.97 (1.32 – 2.95)

* Adjusted for sex

222 SPECTRUM OF CHRONIC PANCREATITIS IN PAKISTANI CHILDREN.

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Background: Chronic pancreatitis is characterized by inflammation of the pancreas, epigastric abdominal pain, elevated serum lipase or amylase and evidence of radiological pancreatic inflammation. Chronic pancreatitis is not commonly diagnosed in children. No pediatric-specific epidemiology is available in Pakistan. Though uncommon in pediatric age group it is associated with significant morbidity and mortality.

This study was conducted, to determine various clinical presentations, diverse etiological factors, complications & outcome, of chronic pancreatitis, in Pakistani children. To the best of our knowledge, this is first study done on chronic pancreatitis in children in this region. Study was conducted in Department of Pediatric Gastroenterology, Hepatology of The Children's Hospital & the Institute of Child Health Lahore.

Materials/ Methods: 42 patients aged 3 to 19 years having one of the following: Abdominal pain of pancreatic origin, evidence of exocrine pancreatic insufficiency, elevated serum lipase supported by imaging study suggesting pancreatic

damage were included in the study. Patients were selected by purposive consecutive sampling. Data was collected from all patients on an especially designed proforma including history, clinical examination, and laboratory and imaging investigations. 42 patients 15 males (35.7%) 27 females (64.2%) were included. Commonest features were abdominal pain, nausea & vomiting. Most common cause was familial in 14 children (33.3%). These patients had more than one family member afflicted with chronic pancreatitis. This was followed by idiopathic 10(23.8%), choledochal cyst in 5(11.9%), hyperlipidaemia in 3(7.1%), biliary tract stones/sludge 3(7.1%), pancreatic divisium in 2(4.7%), long channel defect in 1(2.38%), annular pancreas in 1(2.38%), autoimmune in 2(4.7%), drug induced (L- asparaginase) 1 (2.38%). 4(9.5%) patients had exocrine pancreatic insufficiency with faecal elastase less than 100. Abdominal ultrasound, CECT, MRI, MRCP & echocardiography was done in different patients as per need. MRI showed Calcification in 12(28.5%). All 4 patients with exocrine pancreatic insufficiency had calcifications in the pancreas and familial etiology. Abdominal ultrasound was a very useful initial imaging showing heterogeneous texture of pancreas, dilated Pancreatic duct, pancreatic ascites or an associated Choledochal cyst. MRCP was done in all patients. Most common findings were dilated pancreatic duct or beaded and dilated duct; MRCP also confirmed, pancreatic divisium in 2. In two patients enlarged head of pancreas with a query of mass led to screening of IgG4 blood levels, which were found to be considerably elevated. Complications observed in 13(30.9%) included Pseudopancreatic cyst 5(16.6%), haemorrhagic ascites 5(10%), haemorrhagic pleural effusion 4(6.6%), pericardial effusion in 1(3.3%) & Peripancreatic pseudo aneurysm in 1 (2.38%). 2(4.7%) developed diabetes mellitus by 18 years of age, 14 (33.3%) patients under went Peustow procedure. 3 patients (7.1%) showing a beaded and dilated pancreatic duct with stones underwent a therapeutic ERCP and stent was placed. These stents required replacement in all in 5 months .3(7.1%) pseudopancreatic cysts required drainage. Drainage was done in 3 cases each of Ascites & pleural effusion & 1 of pericardial effusion. Control of pain, Dietary restriction, proton pump inhibitors and pancreatic enzyme replacement where needed along with correction of underlying defect was the main stay of treatment in most of patients. Unfortunately 2 patients died, one due to overwhelming sepsis while 1 expired secondary to neuroendocrine tumour.

Conclusion: Pancreatitis is being increasingly recognized as an important and not uncommon disease entity in children. Chronic pancreatitis may have protean clinical manifestations and complications. It can mimic abdominal tuberculosis; can come with massive ascites and severe abdominal pain leading to undue laparotomies and interventions. High percentage of familial cases highlights the importance of genetic causes in our population. Patients with familial calcific pancreatitis were more likely to have early exocrine pancreatic insufficiency. A significant number of cases needed a Peustow procedure for relief of pain. Patients who underwent therapeutic ERCP with stent placement had a good temporary pain relief but all required repeat interventions for stent replacement.

223 **ASSESSING THE RISK OF CELIAC DISEASE IN FIRST DEGREE RELATIVES WITH POSITIVE CELIAC SEROLOGY.** *Shilpa Nellikkal¹, Yamen Hafed¹, Joseph Larson², Imad Absah¹. ¹Pediatric Gastroenterology and Hepatology, Mayo clinic, Rochester, MN; ²Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN*

The incidence of Celiac Disease (CD) which is one of the most common immune mediated disorders is continuing to increase. CD is changing with fewer patients presenting with classic symptoms and the majority presenting with atypical symptoms or no symptoms. Hence, many cases of CD remain undiagnosed and can be identified only through screening patients at higher risk for CD. First degree relatives (FDR) of CD patients are at increased risk of developing CD, but there is no clear agreement on FDR screening. Some experts recommend screening symptomatic FDR's only, while others recommend screening all FDR regardless of symptoms.

Methods: We performed a retrospective review of the Mayo clinic electronic medical records and the celiac registry between 1990 and 2015 to identify all patients (age < 80 years) who were diagnosed with CD (index group) during the study period. All CD patients who were screened and diagnosed only due to recent identification of first degree relative with CD were included (FDR group). We included all the FDR cases that were screened due to family history as a denominator. CD diagnosis was made based on NASPGHAN or ACG guidelines. Various demographic, clinical, serological and histological variables were recorded. This study was approved by the Mayo Clinic institutional review board (IRB)

Results: We identified a total of 365 FDR's who were screened due to a recent diagnosis of CD index case in their family. In this cohort the median percentage of FDRs in a family of index CD case to be screened is 67%. Of these screened FDR 123 (34%) were diagnosed with CD. Mean age at time of diagnosis was 26.6y ±20.5 with 74 (60%) being females. FDRs relation to the index case consisted of 53 (43%) siblings, 47 (38.2%) children and 23 (19%) parents. All FDRs were screened due high risk, records were available to review in 99 (80%) cases, reporting classic symptoms in 9 (9%), atypical symptoms in 56 (57%) and asymptomatic in 34 (33%). All FDR cases with CD had positive serology, of these 61 (66%) had anti TTG level >3ULN and 31 (34%) had anti TTG level >10ULN. The PPV highly positive of anti TTG level > 3 UNL was 97% (sensitivity 69.6% and specificity 98.6%) in predicting villous atrophy and confirming CD diagnosis.

Conclusion: One third of the screened FDRs in this cohort were diagnosed with CD. These results support the need for CD screening in FDRs regardless of symptoms, with siblings carrying the highest risk. In this cohort highly positive anti TTG levels accurately predicted the presence of villous atrophy in the FDR cases.

224 PEDIATRIC H.PYLORI – AN EMERGING ASSOCIATION WITH PANCREATITIS?

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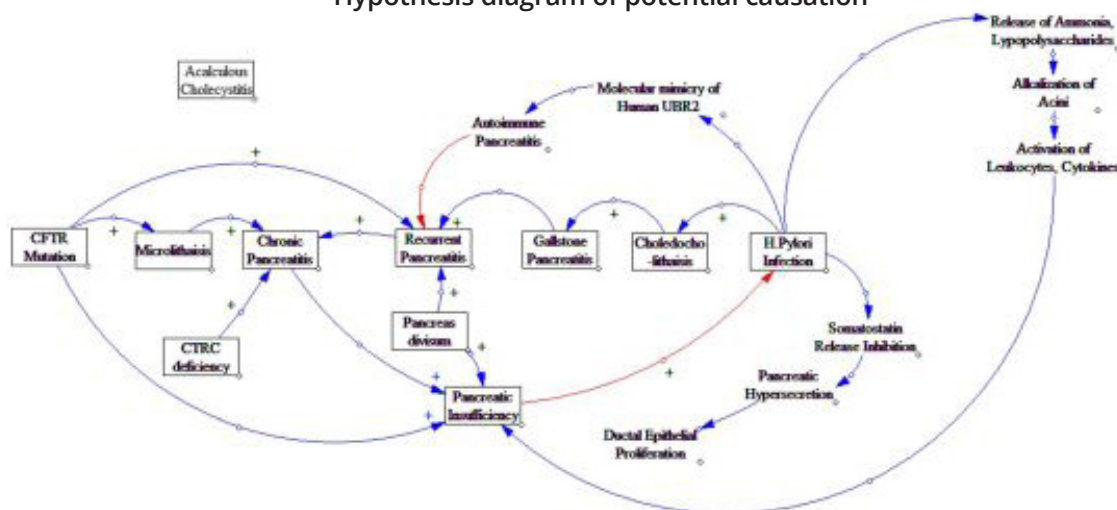
Introduction: Helicobacter pylori bacterial infection remains one of the most common diseases in the modern era, affecting more than 50% of the worldwide population. The prevalence of H. pylori has changed in the last decades in Europe and North America for the pediatric population. Prevalence as low as below 10% are found in the northern and western European countries. In a study conducted in a large urban children’s hospital in Texas the overall seroprevalence of H. pylori was 12.2% and increased with age (e.g., 8.3% at 6–11.9 months and 17.9% at 13 years). The disease has a well-understood association with gastrointestinal disorders including gastric and duodenal ulcers, gastritis, and an increased risk of developing gastric cancer. Though early childhood acquisition is suspected for nearly half of infections, the management and association of H. pylori with other diseases in the pediatric GI setting is still being investigated. A relationship between choledocholithiasis, pancreatitis and H. Pylori has been hypothesized in literature but not explored in the pediatric population. We reviewed a cohort of 42 pediatric patients who underwent treatment for gallstones or pancreatitis to determine the prevalence of concomitant H. pylori infection.

Materials/Methods: A retrospective chart review was conducted for all patients age 0 to 18 who underwent EUS, ERCP, or cholecystectomy with gastric, or duodenal, biopsy from January 2015 to May 2017 at The Children’s Hospital of San Antonio. 42 patients were identified, and 7 parameters were evaluated for trends including patient age, sex, diagnosis, BMI, ethnicity, procedure, and related family history. A subset of 11 patients diagnosed with H. Pylori via biopsy (n=9) or stool antigen (n=2) was identified and analyzed separately for any associations between variables.

Results and Discussion: Subgroup and population distributions for age and BMI were compared using two-sample t-tests assuming unequal variances and no significant differences were found (age t=0.66, BMI t=0.63). Hispanic patients had two times the risk of h. Pylori infection than non-Hispanic (OR=2.14, 95% CI 0.39-11.8, p=0.38) for all patients analyzed. Male patients had a slightly higher risk of infection than female (OR=1.08, 95% CI 0.22-5.09, p=0.92). Gallstones were not associated with increased occurrence of H. pylori (OR=0.24, 95% CI 0.05-0.99, p=0.049). Non gallstone-induced pancreatitis was the diagnosis most associated with a finding of H. pylori (OR=3.47, 95% CI 0.79-15.3, p=0.10).

Conclusions: A diagnosis of chronic or recurrent pancreatitis appears to be more strongly correlated with the presence of H. Pylori than other conditions, such as gallstones or gallstone-induced pancreatitis. This finding presents a new research opportunity to determine potential cause-effect relationships between these two conditions. Possible hypotheses involve pancreatic dysfunction leading to the creation of a more acidic duodenal environment where H. Pylori can flourish or resultant pathophysiological changes in the gastrointestinal tract such as reflux and indigestion which create an imbalanced environment that can lead to greater distribution of the bacteria.

Hypothesis diagram of potential causation



226 CLINICAL CHARACTERISTICS IN A CASE CONTROL STUDY OF CHILDREN WITH NECROTIZING PANCREATITIS.

Joshua Carroll, David Troendle, Shellie Josephs, Luis Sifuentes-Dominguez, Edaire Cheng, Bradley Barth. *Pediatrics, UT Southwestern, Dallas, TX*

Introduction: Necrotizing pancreatitis (NP) is a rare complication of acute pancreatitis (AP) in the pediatric population. Studies show rising incidence of AP in children. However, a dearth of knowledge remains with regards to the characterization of necrotizing pancreatitis in children. This goal of this study is to examine potential risk factors, comorbidities, clinical course, outcomes and differences between children with NP and those with AP.

Methods: A retrospective chart review examining children with a radiologic diagnosis of NP compared to those with AP. The radiology database at Children's Health Dallas was queried from January 1, 2005 to March 1, 2016 for search terms "pancreatitis", "necrotizing pancreatitis" and "pancreas necrosis". Cases identified as NP were reviewed by a radiologist and graded according to the CT Severity Index. An age and sex matched control group of patients with AP was identified using ICD 9 code for AP. Charts of NP and AP patients were reviewed and demographic information, medical history, presenting features, laboratory data, clinical course and complications were recorded.

Results: 31 patients with 32 episodes (18 female and 14 male) of NP over the last 11 years with pancreatic necrosis on CT were identified. One patient had 2 discreet episodes of NP 18 months apart. Over the same period, thirty two patients (age and sex matched) were identified with AP.

Mean BMI and BMI %ile was 27.3 kg/m² (range 14.5 to 48.4 kg/m²) and 85.2% (range 3 – 99.7%) in the NP group compared to 22.7 kg/m² (range 13.2 – 39.5 kg/m²) and 62.4% (range 2 – 99%) in the AP group. BMI and BMI %ile were significantly higher in the NP group compared to the AP group (p = 0.0277 and p = 0.0041).

The most common etiology of NP was choledocholithiasis at 28.1% (n=9) followed by medication induced at 18.8% (n=6, PEG Asparaginase = 3, Valproic Acid = 3). Of the remaining 16 cases, 1 was attributed to viral infection, 1 to alcohol and the remainder idiopathic. In the AP group the most common etiology was medication at 12.5% (n=4), choledocholithiasis 9.4% (n=3), genetic 9.4%(n=3), hypertriglyceridemia 6.3% (n=2), hypercalcemia 3.2% (n=1) and the remainder 59.3% (n=19) idiopathic. Genetic studies were sent on only four of the patients with NP and were all negative.

Patients in both groups had significant elevations in amylase and or lipase greater than 3 times the upper limit of normal. Mean peak amylase in the NP group was 908 (u/L) (85 – 4882) versus the AP group 565 (u/L) (71 – 2035) (p = 0.773). Mean peak lipase in the NP group was 8739 (u/L) (range 513 – 39914) versus 5184.4 (u/L) (632 – 24,002) (p=0.0518) in the AP group.

Thirty patients (93.8%) received antibiotic therapy in the NP group versus 11 (34.3%) in the AP group. The most common antibiotics used amongst the patients in both groups were piperacillin/tazobactam and meropenem with a combination of one or both being used in all 30 NP patients versus 8 AP patients.

The most common long term complication in the NP group was pancreatic fluid collection (PFC) (n=23), followed by endocrine insufficiency (n=10) necessitating insulin therapy, and exocrine insufficiency (n=2) requiring pancreatic enzyme replacement therapy. Fifteen of the 23 patients with PFC underwent drainage. Five patients (15.6%) had positive fluid cultures of their PFC's: one grew alpha streptococci, the remaining four patients had multiple organisms despite being on previous antibiotic therapy. The most common isolated organisms were *Candida* species (n=3), *E. coli* (n=2), *P. aeruginosa* (n=1), *Bacteroides* (n=1), and *Stenotrophomonas* (n=1). Two patients in the NP group, both with significant comorbidities ultimately died as a result of their necrotizing pancreatitis. There were no deaths in the AP group.

Conclusions: Pediatric patients with NP had a statistically higher BMI and BMI %ile than those with AP. This finding is similar to adult studies demonstrating that obesity has a clinically relevant impact on the severity of acute pancreatitis which may be in part due to a chronically low inflammatory state.

While patients in our series with necrotizing pancreatitis tended to have higher amylase and lipase levels, there was no statistical significance between the two groups which is in line with previous adult and pediatric studies that demonstrate no significance between levels of pancreatic enzymes and severity.

227 COST ANALYSIS OF SEROLOGICAL VERSUS BIOPSY-PROVEN DIAGNOSIS OF PEDIATRIC CELIAC DISEASE.

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Introduction: Celiac disease (CD) affects approximately 1% of the population in Canada and the United States. In North America, the gold standard diagnosis requires duodenal biopsy, however, there is emerging research and European guidelines validating serological diagnosis (SD). There is also increasing pressure to ensure cost efficiency and effective resource utilization in public health care. At Stollery Children's Hospital in Edmonton, Canada, we have evaluated prospectively a SD approach for CD and, in 2016-2017, it became routine practice in our clinic. This study compared the costs of SD versus ED at our institution.

Method: Micro-costing methods (identification, valuation, and quantification) were used to determine health care resource use in patients undergoing ED or SD. SD testing included anti-tissue glutaminase antibody (aTTG) ≥ 200 IU/mL (on two occasions), Human Leukocyte Antigen (HLA) DQA5/DQ2, blood sampling, transport, and laboratory costs. ED diagnosis included gastroenterologist, anesthetist, histopathologist, OR equipment, staff and overhead. Cost of each unit of resource was obtained from the Stollery hospital, schedule of medical benefits (Alberta) and reported average ambulatory cost for endoscopy (2016 CAN\$).

Results: Between January-December 2016, 202 patients were referred for diagnosis of CD; 125 had ED and 55 SD. Estimated cost for ED was \$1240 per patient; for SD was \$85 per patient (6.8% of ED cost). Based on 55 patients not requiring endoscopy there was a saving of \$1155 per patient (\$63,525 in total). In addition, we did not need to book 8.5% additional elective upper endoscopy procedures that year (591 were performed in total).

Conclusions: A SD-based diagnostic strategy is significantly less costly than ED; further it may free scarce endoscopy resources, and spare patients from an invasive procedure. Our costing data can be used in combination with emerging evidence on the test performance of SD vs ED to determine cost-effectiveness of serological diagnosis for pediatric CD. Given the potential for cost saving and more efficient operating room utilization, SD for pediatric CD warrants further investigation in North America.

228 UNDERSTANDING THE EFFECTS OF THE GLUTEN FREE DIET AND PROCESSED GLUTEN FREE FOODS ON NUTRITIONAL STATUS IN PEDIATRIC PATIENTS DIAGNOSED WITH CELIAC DISEASE. Karine Amirikian¹, Naire Sansotta^{2,3}, Stefano Guandalini², Hilary Jericho². ¹Department of Pediatrics, The University of Chicago Medicine, Chicago, IL; ²Section of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, The University of Chicago Medicine, Chicago, IL; ³Department of Pediatrics, University of Verona, Verona, Italy

Objectives: The aim of our study was to determine the effects of the gluten free diet (GFD) on BMI in children with celiac disease (CeD) at the University of Chicago Medicine (UCMC). We hypothesized that with the rise of processed gluten free products on the market, GFD adherent patients would have increased BMI, perhaps even to an unhealthy range.

Methods: We conducted a retrospective chart review of children who were seen at the UCMC Celiac Disease Center from January 2002 to May 2016. BMI was recorded at the start of the GFD well as at any of the following available timepoint intervals since starting the GFD: 6 months, 1 year, 2 years, 3 years, and 4+ years. Adherence to the GFD was assessed by patient report and monitoring of celiac serologies. Age at diagnosis and gender were also recorded. It appears that processed gluten free products became increasingly popular after 2011. We compared the rate of BMI increase in children who were diagnosed before 2011 vs after 2011.

Results: There were 894 patients in the Celiac Disease Center database, 554 patients met diagnostic criteria for CeD, and 399 of these patients were children. There were 147 children who met inclusion criteria: BMI recorded at diagnosis and at at least one follow up timepoint. 49% of patients were diagnosed before 2011 and 51% were diagnosed after 2011. The mean age at diagnosis was also similar for both groups, 8.8 years for those diagnosed before 2011 and 8.3 years for those diagnosed after 2011. There were more females (66%) overall compared to males (34%) in our cohort. The mean BMI at diagnosis was 17.8 (standard deviation 3.9) for those diagnosed before 2011 and 17.1 (standard deviation 2.7) for those diagnosed after 2011. Based on a mixed-effects random-intercept random-slope regression model, there was no evidence for a significant difference in BMI change over time for those starting the GFD before versus after 2011 (p-value=0.36). However, both groups showed an overall increasing trend in BMI over time, which is consistent with the idea that the duodenum slowly heals and nutritional absorption improves over time. In addition, we also analyzed this trend separately in three different age groups, 0-6 years, 7-12 years, and 13-18 years. The same conclusion was reached, (p-value= 0.18, 0.31, 0.63, for each group, respectively).

Conclusion: Our research shows that there did not appear to be a statistically significant greater rise in BMI in celiac children on a strict GFD seen at UCMC after 2011 as compared to those seen prior to 2011, the year gluten free processed foods surged on the market. This may have been biased by the vigorous celiac program offered at UCMC, including nutritionists highly knowledgeable and experienced with the GFD who steer patients toward more natural gluten free options and away

from the processed alternatives. This finding may also have been biased by including only pediatric patients, whose diets are often driven by their health conscious parents. Follow up studies assessing the change in BMIs pre and post 2011 in adults and in celiac patients elsewhere are warranted to ensure unhealthy rises in BMIs have not risen in line with the 2011 surge in processed gluten free food options.

229 THE CD-GEMM STUDY: IMPACT OF MODE OF DELIVERY, GENETIC PREDISPOSITION, AND ANTIBIOTIC EXPOSURE ON MICROBIOME AND METAGENOMIC PROFILES IN INFANTS AT-RISK OF CELIAC DISEASE.

Maureen Leonard^{1,2,3}, Gloria Serena^{2,3}, Stephanie Camhi², Victoria Kenyon², Francesco Valitutti⁴, Salvatore Cucchiara⁴, Nur Hasan⁵, Poorani Subramanian⁶, Brian Fanelli⁶, Rita Colwell^{5,6}, Alessio Fasano^{1,2,3}.
¹Pediatric Gastroenterology and Nutrition, MassGeneral Hospital for Children, Boston, MA; ²Center For Celiac Research and Treatment, MassGeneral Hospital for Children, Boston, MA; ³Harvard Medical School, Boston, MA; ⁴Pediatric Gastroenterology and Liver Unit, Sapienza University of Rome, Rome, Italy; ⁵University Of Maryland, College Park, MD; ⁶CosmosID, Rockville, MD

Background: The intestinal microbiome is important to the development of the immune system and perturbations during its development have been suggested to increase the risk of future chronic inflammatory diseases such as celiac disease (CD). CD is an autoimmune enteropathy for which genetic predisposition and gluten ingestion are necessary but not sufficient for disease development. Environmental factors such as birthing delivery mode and exposure to antibiotics may alter the developing microbiome and have been implicated as risk factors in the development of CD.

Aim: To compare alpha diversity and metatranscriptome profile during the first 6 months of life in infants at-risk for CD according to birthing delivery mode, antibiotic exposure at birth, and stratified by genetic risk for CD (high vs. standard vs. no risk).

Methods: As part of a larger prospective birth cohort study, 17 infants with a first-degree relative with CD were included in a pilot analysis. DNA was extracted from stool samples collected from infants at 7-10 days, 3 months, and 4-6 months of age. Samples were analyzed using shotgun metagenomic sequencing for microbial identification using the CosmosID metagenomics platform at the species and subspecies levels and to identify antibiotic resistance genes.

Results: Infants with standard risk genes for CD demonstrated greater bacterial, fungal, protist and viral alpha diversity compared to infants with highest or no genetic risk of developing CD. The bacterial, fungal, viral, and protist alpha diversity of infants exposed to antibiotics at birth was reduced at all time points while respiratory virus diversity at 7-10 days and 3 months after birth was increased compared to infants not exposed to antibiotics at birth. Infants born vaginally had greater bacterial and protist alpha diversity at 4-6 months compared to infants born via cesarean section (c-section). Infants born by c-section had greater protist alpha diversity at 7-10 days and greater respiratory virus diversity at 3 and 4-6 months of age. Infants exposed to antibiotics at birth and those born by c-section were colonized with a lower relative abundance of *Bifidobacterium longum* and *Bacteroides fragilis* during the first 6 months of age and had a greater abundance of *Enterococcus faecalis* at birth. Three infants who were born via c-section and not exposed to antibiotics showed an increase in relative abundance of *Bacteroides Fragilis* over time compared to infants born via c-section exposed to antibiotics. All infants harbored antimicrobial resistance genes irrespective of their exposure status.

Conclusions: Genetic risk for CD appears to influence species diversity and species abundance in the metagenome. Antibiotic exposure reduced infant alpha diversity in microbiome, fungiome and protistome in the first 6 months compared to infants not exposed to antibiotics. Infants born vaginally had greater bacterial and protist alpha diversity at 4-6 months compared to infants born via c-section. Respiratory virus diversity increased in both infants exposed to antibiotics at birth and infants born via c-section. Antibiotic exposure and c-section delivery were associated to a paucity of protective, beneficial species, including *Bifidobacterium longum* and *Bacteroides fragilis*.

230 OPIOID PAIN MANAGEMENT IN DIFFERENT AGE GROUPS OF CHILDREN WITH ACUTE

PANCREATITIS. Jonathan Miller¹, Michael Dolinger¹, Samuel Bitton², Peter Nauka³, Nina Kohn⁴, Toba Weinstein².

¹General Pediatrics, Steven and Alexandra Cohen Children's Medical Center, Northwell Health, New Hyde Park, NY; ²Pediatric Gastroenterology, Steven and Alexandra Cohen Children's Medical Center, Northwell Health, New Hyde Park, NY; ³Hofstra Northwell School of Medicine, Hempstead, NY; ⁴Biostatistics unit, Feinstein Institute for Medical Research, Great Neck, NY

Objective: Abdominal pain is the most common presenting symptom in children with acute pancreatitis (AP), however pain management in AP can be challenging. Treatment of AP in children includes IV fluids, enteral nutrition and analgesia. It is reported that up to 94% of children with AP receive opioid analgesia, yet limited data exists. This study compares the difference in utilization of opioids for analgesia between younger (≤ 10 yrs) and older (> 10 yrs) children with AP.

Methods: A retrospective chart review of children with a discharge diagnosis of pancreatitis at Cohen Children's Medical Center from 2011-2017. Patients met criteria for AP based on the presence of ≥ 2 of the following: abdominal pain, serum amylase and/or lipase >3 times the upper limit of normal, and imaging findings of AP. Patients with recurrent AP or chronic pancreatitis were excluded as well as those with incomplete information regarding opioid analgesia. The age groups were compared according to the amount of morphine equivalents per kg (eq/kg) and total number of opioid doses each child received. Initial lipase levels were recorded and compared between opioid and non-opioid recipients in each age group. Data were compared by Mann-Whitney test for continuous variables and chi-square or Fisher exact test for categorical variables.

Results: 84 children were admitted with pancreatitis, 61 met inclusion criteria. There were 15 younger (10M, 5F, mean[SD] 4.87 yrs. [2.4], range 1-10) and 46 older children (25M, 21F, mean[SD] 14.87 yrs.[1.8], range 11-18). Sex distribution did not differ between groups. Etiologies of AP by age (%younger, %older) were idiopathic (53, 50), gallstone (7, 22), medication (13, 11), infection (7, 7), hyperlipidemia (0, 7), trauma (7, 2), choledochal cyst (13, 0) and post-ERCP (0, 2). 34(56%) patients received opioids. Those not receiving opioids received non-narcotic analgesia with NSAIDs and/or acetaminophen. There was no statistical difference in the amount of younger (8, 53%) vs older (26, 57%) children receiving opioids. Younger children received significantly greater morphine eq/kg (0.195 vs 0.055, $p < 0.033$) [Table 1], though there was no difference in total opioid doses received (median 3.5 vs 3.5) [Table 2]. When assessing lipase levels in patients who received opioids compared with non-opioid recipients in the same age group, older children had significantly greater initial lipase elevation (median lipase U/L 1092 vs 511, $p < 0.005$) while younger children did not (median lipase U/L 1385 vs 1033). There was no difference in the median length of stay (7.0 days vs 4.5 days) or number of NPO days (2.0 days vs 2.0 days) in the younger vs older age group regardless of opioid use.

Conclusions: In our study 56% of children with AP were managed with opioid analgesia which is less than reported in prior pediatric studies. While there was no difference in the number of children receiving opioids or the number of doses of opioids between age groups, younger children did receive significantly more morphine equivalents/kg compared to older children. Since there is a maximum morphine dose, it is plausible that some older children reached the maximum dose accounting for lower morphine equivalents received by the older children. However older children with higher lipase elevation required opioids for pain management, while those with lower elevations were effectively managed with non-opioids. This was not true in younger children. Prospective studies with larger sample sizes are needed to better characterize pain management in children with AP.

Table 1

Total Morphine Eq/kg					
Age (years)	N (% of age group)	Median	Minimum	Maximum	P value
1-10	8 (53%)	0.195	0.05	3.44	<0.033
11-18	26 (57%)	0.055	0.01	2.30	

Table 2

Total Number of Opioid Medication Doses					
Age (years)	N (% of age group)	Median	Minimum	Maximum	P value
1-10	8 (53%)	3.50	1	114.0	<0.705
11-18	26 (57%)	3.50	1	52.0	

231 CHILDHOOD ACUTE AND RECURRENT ACUTE PANCREATITIS: EXPLORATION OF CLINICAL PRESENTATIONS, ETIOLOGIES AND OUTCOMES. Rafael Guerrero-Lozano¹, Viviana Fonseca^{1,2}.

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Introduction: Knowledge on acute pancreatitis (AP) in children is partly extrapolated from adult population.

Objective: To describe epidemiology and clinical practice in childhood AP and RAP (recurrent acute pancreatitis).

Methods: Cases were identified from clinical charts with the corresponding ICD code (2010-2015) and classified as AP or RAP; relations with clinical and paraclinical parameters were analyzed.

Results: In 130 patients, aged 11.4 ± 3.8 years, 62.3% girls, abdominal pain and vomiting were the predominant symptoms (91.5 and 71.5%, respectively). RAP was diagnosed in 23.8%. Etiology was not clarified in 29.2%; most frequent causes were anatomical (29.6%), pharmacological (19.2%) and biliary (14.6%). Comorbidities, present in 31.5%, included leukemia (11.5%) and epilepsy (5.4%).

Mean initial amylasemia was 795.9 (13-4367) U/L and lipasemia 578.1 (16.7-4162). The most used image was abdominal ultrasonography (85.4%). Fasting was ordered during 3.5 ± 3.8 days. Parenteral nutrition was prescribed in 26.9% for 10.8 ± 11.3 days. No child received jejunal feeding. Fifty four patients (41.5%) required ICU. Complications included acute renal injury (8.5%) and hypotension or shock (9.2%). A statistical association was found between RAP and anatomical ($p = 0.02$) and pharmacological etiology ($p = 0.01$). Mortality was 3.1%, none attributable to AP.

Conclusion: Local information about AP is presented. Complete etiologic screening is not achieved; however, infections appear to have now less weight, whereas anatomical and drugs become important. Clinical diagnosis remains supported by enzymatic levels and ultrasound. Fasting, discussed nowadays, is maintained and tube enteral feeding not used. AP is associated with high frequency of RAP. Mortality attributable to AP was low.

232 PANCREATIC GENE EXPRESSION DURING RECOVERY AFTER PANCREATITIS REVEALS UNIQUE TRANSCRIPTOME PROFILES. *Kristy Boggs¹, Ting Wang¹, Abraham Orabi¹, Tao Sun¹, John Eisses¹, Farzad Esni², Wei Chen¹, Sohail Husain¹.* ¹*Pediatrics, U of Pittsburgh, Pittsburgh, PA;* ²*Surgery, U of Pittsburgh, Pittsburgh, PA*

From studies in animal models, it is well-known that pancreatic recovery after a single episode of injury such as an isolated bout of pancreatitis occurs rapidly. It is unclear, however, what changes are inflicted in such conditions to the molecular characteristics of the pancreas. What we know from the common chemical hyperstimulation mouse model of pancreatitis, induced with the cholecystokinin analog caerulein, is that the murine pancreas has the remarkable ability to regenerate and recover by histological appearance within one week of the injury. In this study, we sought to characterize by RNA-sequencing the transcriptional profile of the recovering pancreas up to two weeks post-injury. We were intrigued to find that one week after injury there were 319 differentially expressed genes (DEGs) compared with baseline and that after two weeks there were 53 DEGs. Intriguingly 12.5% (40) of the DEGs persisted from week one to week two, and another 13 DEGs newly emerged in the second week. Overall, the DEGs were related to trypsinogens and the protein translation and exocytosis machinery. The enriched pathways were of protein digestion and absorption, growth signaling, differentiation, and tissue remodeling. To our knowledge, this is the first characterization by deep sequencing of the transcriptome during pancreatic recovery, and it reveals on a molecular basis that there is an ongoing recovery of the pancreas even after apparent histological resolution. The findings also raise the possibility of a novel emerging transcriptome upon recovery.

Figure 1

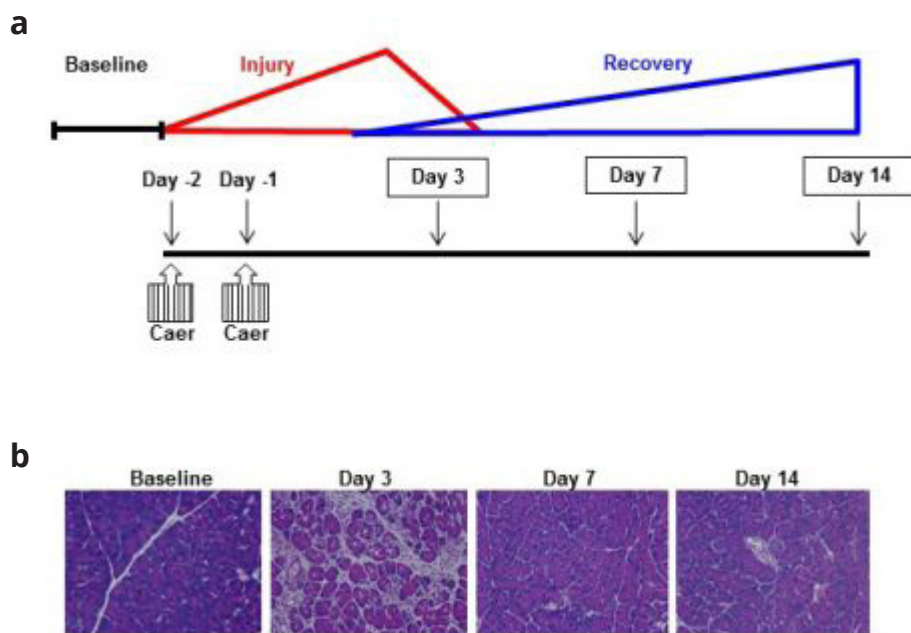
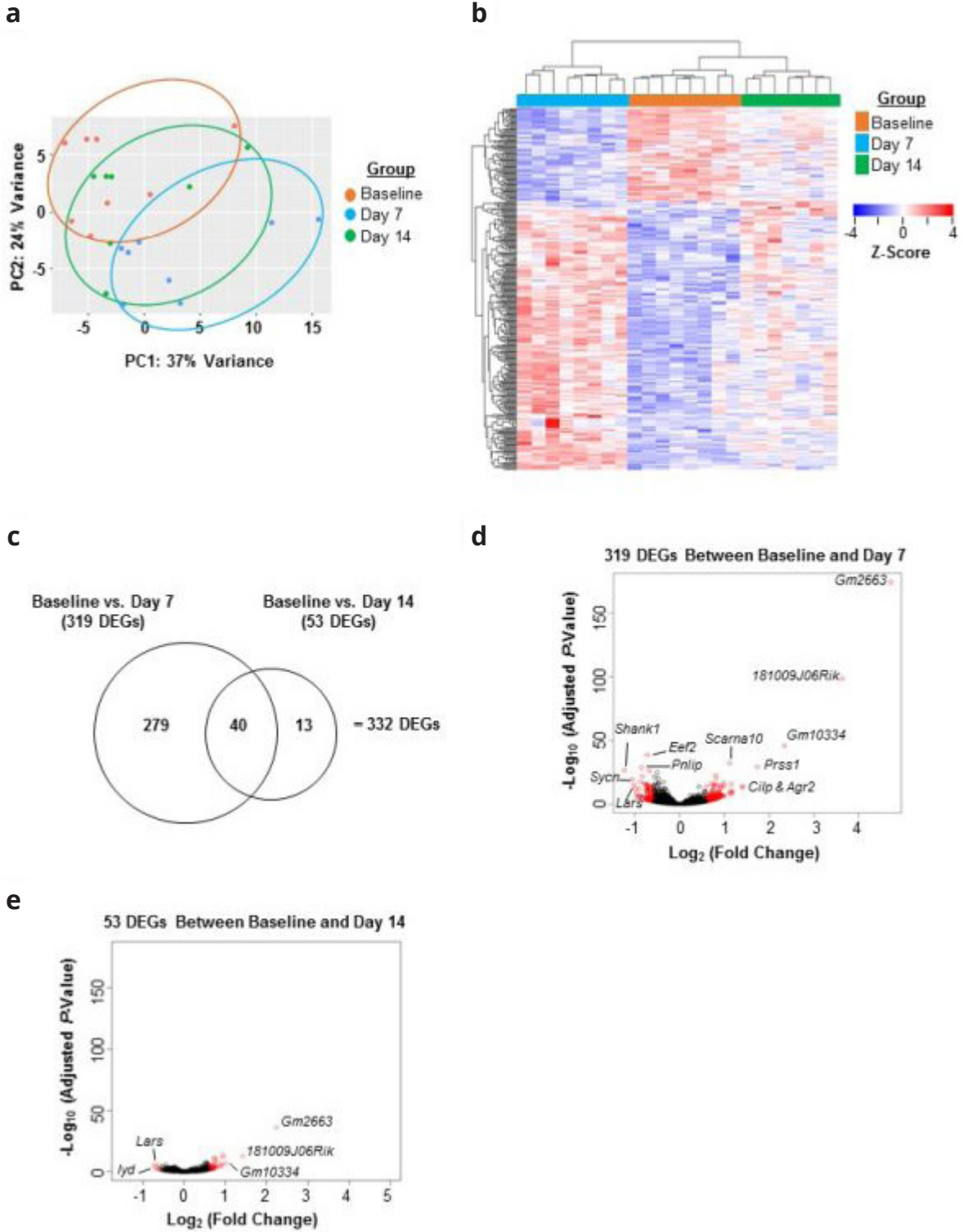


Figure 1



PLENARY SESSION

Friday, November 3

8:00am – 10:00am

233 William Balistreri Prize

NEUROSTIMULATION FOR FUNCTIONAL ABDOMINAL PAIN DISORDERS IN CHILDREN-A RANDOMIZED, DOUBLE BLIND, SHAM-CONTROLLED TRIAL. Katja Kovacic¹, Keri Hainsworth²,

Manu Sood¹, Gisela Chelimsky¹, Rachel Unteutsch¹, Melodee Nugent¹, Pippa Simpson¹, Adrian Miranda¹. ¹Department of Pediatrics, Medical College of Wisconsin, Brookfield, WI; ²Department of Anesthesiology, Medical College of Wisconsin, Milwaukee, WI

Background: There is an urgent need to develop safe and effective non-pharmacological therapies for pediatric functional abdominal pain disorders (FAPDs). A non-invasive, FDA-cleared device (NeuroStim®, Innovative Heath Solutions, IN, USA) delivers percutaneous, electrical nerve field stimulation (PENFS) to the external ear. Auricular branches of several cranial nerves (CN V, VII, IX, X) from the ear project to brainstem nuclei. Recent animal data indicates that PENFS modulates central pain pathways by reducing amygdala and lumbosacral neuronal firing, thereby attenuating visceral hyperalgesia. This study evaluated the efficacy of PENFS in adolescents with FAPDs.

Methods: In this randomized, sham-controlled trial, we enrolled 115 adolescents (11–18 years) who met Rome III criteria for one or more FAPDs. Subjects were randomized to active treatment vs. sham for 5 days each week x 4 consecutive weeks. The active device delivered 3.2V of stimulation 2 hours on/2 hours off for 5 days below sensation threshold. The sham lacked electrical charge. The primary end points were improvement in 1) worst abdominal pain and 2) composite pain score using the Pain Frequency-Severity-Duration (PFSD) scale after 3 weeks of therapy (as subjects did not return after this). The PFSD incorporates multiple aspects of pain: # of days in pain + usual and worst abdominal pain severity over past week (0-10 numeric scale). Secondary endpoints were: $\geq 30\%$ reduction in worst and usual abdominal pain, global symptom improvement based on a symptom response scale (-7 to +7; 0=no change), disability (Functional Disability Inventory) and anxiety (STAI-C). Long-term response was assessed at a follow-up visit 8-12 weeks after therapy.

Results: 104 subjects (57 treatment; 47 sham) were included. The treatment group had greater reduction in worst pain at all weeks vs. baseline ($p \leq 0.001$) with a lower score vs. sham after three weeks: Median (IQR): 5 (4-7) vs. 7 (5-9) ($p=0.005$). Effects were sustained at follow-up (Median follow-up 9.2 weeks) in the treatment group: baseline to follow-up Median (IQR): 8.0 (7-9) to 6.0 (5-8) vs sham: 7.5 (6-9) to 7.0 (5-8) ($p \leq 0.001$) (Fig. 1). PFSD composite scores also decreased significantly in the treatment group (24.5 to 8.4) compared to sham (22.8 to 15.2) ($p=0.005$) after 3 weeks and at follow-up ($p=0.018$). 60% of treatment vs. 22% in sham had $\geq 30\%$ reduction in worst pain ($p \leq 0.001$). After three weeks, 73% in treatment group compared to 35% in sham had a symptom response scale score ≥ 2 ($p \leq 0.001$). The treatment group also showed much greater improvement in functional disability compared to sham (Fig. 2). No differences between groups were found in the anxiety measures. Patient satisfaction was particularly high in the treatment group: 79% expressed satisfaction with therapy (vs. 40% in sham; $p=0.007$), 86% would repeat the trial (vs. 47% in sham; $p=0.049$) and 95% would recommend it to a friend/family (vs. 72% in sham; $p=0.003$). No serious side effects were reported.

Conclusion: PENFS is a safe and novel treatment for adolescent FAPDs with sustained efficacy for abdominal pain, global well-being and functioning.

Study was supported by a grant from the American Neurogastroenterology & Motility Society (ANMS)



Fig 1. PFSD Worst pain (scale 0-10) showing significant improvement in treatment group compared to baseline at all time points (p

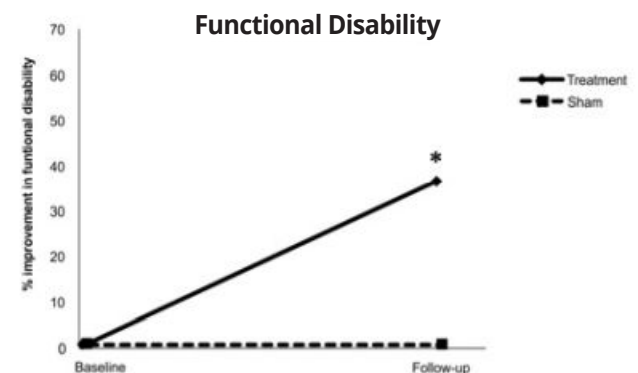


Fig 1. Functional Disability Inventory improved by 36% from baseline to follow-up in the treatment (17.0; 7.8 – 27.5 to 11.0; 6.0 – 22.3) compared to 0% change in the sham group (17.0; 11.0 – 29.0 to 17.0; 6.0 – 26.0) (* $p=0.01$). Higher score indicates greater disability.

234 Fellow Research Award

SYMPTOMS UNDERESTIMATE ENDOSCOPIC ACTIVITY IN PSC-IBD. Amanda Ricciuto, Nicholas Carman, Jennifer Fish, Eileen Crowley, Peter Church, Aleixo Muise, Thomas Walters, Binita Kamath, Anne Griffiths. *Gastroenterology, Hospital for Sick Children, Toronto, ON, Canada*

Objectives: Inflammatory bowel disease (IBD) occurring in the setting of primary sclerosing cholangitis (PSC), or “PSC-IBD,” has been found to have a distinct phenotype in adults, characterized by extensive colitis and an increased risk of colorectal cancer, but relatively mild symptoms. Given this disconnect between cancer risk, which is driven by ongoing inflammation, and paucity of clinical symptoms, we hypothesized that symptoms, as reflected by the Pediatric UC Activity Index (PUCAI), underestimate endoscopic activity in pediatric PSC-IBD. We also aimed to test the hypothesis that fecal calprotectin (FC), which has not previously been studied in PSC-IBD, performs superiorly as a monitoring tool and to determine its test characteristics for identifying mucosal healing (MH) in pediatric PSC-IBD.

Methods: In this single-center prospective study performed at the Hospital for Sick Children in Toronto, PUCAI and FC were measured in all children with PSC-IBD undergoing colonoscopy between February 2016 and March 2017. Children with colonic IBD without PSC served as controls. Colonoscopies were recorded and scored by two blinded physicians using the Mayo Endoscopic Subscore (MES), the UC Endoscopic Index of Severity (UCEIS), both applied to the rectosigmoid, as well as a modified version of the UCEIS applied to the entire colon (“extent UCEIS”). Spearman correlations were determined between variables. Endoscopic scores were compared between PSC-IBD and IBD only patients in clinical remission (PUCAI <10). ROC curves were used to compare the ability of FC and PUCAI to identify MH, defined as an extent UCEIS score of 0.

Results: 84 children (37 with PSC-IBD and 47 with IBD only) were included. 71% of PSC-IBD patients were in clinical remission vs. 42% of IBD only patients, while the proportion of patients with FC <250 µg/g and the distribution of UCEIS scores were similar between groups. 45% of PSC-IBD patients had their worst area of endoscopic disease proximal to the rectosigmoid. PUCAI-endoscopy and FC-endoscopy Spearman correlations were very good in the IBD only group (r=0.7-0.8). In the PSC-IBD group, FC-endoscopy correlations remained good (r=0.7-0.9) but were significantly poorer for PUCAI vs. endoscopy (r=0.45-0.5). PSC-IBD patients in clinical remission also had higher endoscopic activity scores than IBD only patients in clinical remission (p<0.05). FC demonstrated excellent ability to discriminate MH (sensitivity 89%, specificity 100%, AUC 0.93) with an optimal cut-point of 92 µg/g. FC was superior to PUCAI in this regard (AUC 0.56, p=0.07).

Conclusion: MH should be the target in treating PSC-IBD, particularly given the increased cancer risk and as-of-yet unclear association between ongoing colitis and PSC progression. Symptoms appear to underestimate endoscopic activity in pediatric PSC-IBD and should not be relied upon to determine if a child has reached this target. We provide the first data on FC as a colitis monitoring tool in PSC-IBD, which suggests it performs well. A value <100 µg/g strongly suggests MH. The fact that almost half of PSC-IBD patients had their most severe endoscopic disease proximal to the rectosigmoid highlights the need for an endoscopic tool that considers the entire colon in this population.

235 Young Faculty Investigator Award

ALTERED BILIARY DIFFERENTIATION OF BILIARY ATRESIA-RELEVANT HUMAN iPSC LINES. Lipeng Tian¹, Zhaohui Ye², Robert Anders³, Dylan Stewart⁴, Kathleen Schwarz⁵, Yoon Young Jang¹. ¹Oncology, Johns Hopkins Medical Institutions, Baltimore, MD; ²FDA, Silver Spring, MD; ³Pathology, JMHI, Baltimore, MD; ⁴Surgery, JHMI, Baltimore, MD; ⁵Pediatrics, JHMI, Baltimore, MD

Background: Biliary atresia (BA) is the most common cause of pediatric end-stage liver disease. Primary treatment, which involves surgical biliary drainage via hepatic portoenterostomy, is usually just palliative with most children ultimately requiring liver transplantation. Our current lack of understanding of molecular mechanisms of this disease is a major hurdle to developing effective treatment strategies. Although its etiology is not yet clear, evidence suggests that BA results from interactions between genetic susceptibility and environmental factors. GWAS have identified adducin 3 (ADD3) and glypican-1 (GPC1) as BA susceptibility genes. Animal studies have also provided functional evidence that knock-downs of these genes result in biliary defects. Development of human cellular models capable of identifying agents that can either reverse the putative biliary developmental defects or shed light on the disease-causing environmental factors could also serve as a means of exploring possible therapies. Because of their differentiation capability, human induced pluripotent stem cells (iPSCs) have advantages over other cell lines in studying defects in the early stage of biliary development.

Methods: To determine the functional significance of the BA susceptibility genes in human biliary development, we have taken a genome-editing approach to create iPSC lines with defined mutations in these GWAS BA loci. Using the CRISPR/Cas9 system, we have created isogenic iPSC lines deficient in BA-associated genes (GPC1 and ADD3 knockouts in healthy human iPSCs). We have also generated a panel of disease-specific iPSC lines from multiple BA patients (n=5) (and from their age-matched controls) based on a virus free non-integrating episomal method using 3 episomal plasmids MOS, MMK and GBX. We performed *in vitro* bile ductal differentiation with these iPSCs.

Results: *In vitro* biliary differentiation of human iPSCs deficient in GPC1 or ADD3, as well as BA patient-specific iPSC lines, demonstrated decreased formation of ductal structures and decreased expression of biliary tissue markers CK7 and CFTR at both mRNA and protein levels ($P < 0.01$), compared to their respective controls. Along with the altered biliary differentiation, increased fibrosis markers SMA and Collagen 1 ($P < 0.05$) have been detected in the BA-related iPSCs compared to their controls.

Conclusions: These BA-relevant human iPSC lines showed significant deficiency in biliary differentiation, a key disease phenotype of BA, suggesting important functional roles of these genes in human BA development. These iPSCs along with the biliary differentiation technology will provide a critical human BA model for understanding molecular basis of abnormal bile duct development in BA children, and an opportunity to identify agents that have potential therapeutic effects on BA.

236 Gerard Odell Prize

MIXED LINEAGE KINASE 3 INHIBITION ATTENUATES MURINE NONALCOHOLIC

STEATOHEPATITIS. Kyoko Tomita¹, Rohit Kohli³, Petra Hirsova¹, Qianqian Guo¹, Luz Gutierrez Sanchez⁴, Harris Gelbard², Burns Blaxall³, Samar Ibrahim⁴. ¹Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; ²Pediatrics, University of Rochester Medical Center, Rochester, NY; ³Pediatrics, University of Cincinnati, Cincinnati, OH; ⁴Pediatric Gastroenterology, Mayo Clinic, Rochester, MN; ⁵Pediatrics, Children's Hospital Los Angeles, University of Southern California, Los Angeles, CA

Background/Aims: With the increase in obesity worldwide, its associated co-morbidities including nonalcoholic steatohepatitis (NASH) have become a public health problem that still lacks effective therapy. We recently reported that Mixed Lineage Kinase 3 (MLK3)^{-/-} mice were protected against a nutrient excess diet-induced NASH. Because of the critical need to identify new therapeutic agents, we sought to examine whether the pharmacological MLK3 inhibitor URM-099 would be effective in reversing diet-induced murine NASH.

Methods: C57BL/6J mice were fed either a diet high in saturated fat, fructose, and cholesterol (FFC) or chow diet for 24 weeks. Mice were treated with either URM-099 (10 mg/kg) or vehicle, twice daily by intraperitoneal injection during the last 2 weeks of the feeding study. The mice underwent metabolic phenotyping using a comprehensive laboratory animal monitoring system (CLAMS) after 1 week of URM-099 administration. Insulin resistance was calculated by homeostatic model assessment of insulin resistance (HOMA-IR). Liver steatosis, injury, inflammation, and fibrosis were evaluated histologically and biochemically.

Results: URM-099 therapy was well tolerated by the study animals. FFC-fed mice receiving URM-099 displayed no difference in body weight, liver to body weight ratio, caloric intake, HOMA-IR and metabolic phenotype when compared to mice on the same diet receiving vehicle. All FFC-fed mice developed a similar degree of hepatic steatosis as assessed by histology, CARS microscopy and measurements of neutral triglycerides. Importantly, FFC-fed mice treated with URM-099 had significantly less macrophage-associated hepatic inflammation as assessed by Mac-2 stain (a marker of phagocytically active macrophages), and by the mRNA expression of macrophage surface markers (CD14, CD68), activation markers (TNF α , MCP1) and proinflammatory polarization markers (IL12p40). Furthermore, liver injury in URM-099-treated FFC-fed mice, when compared to vehicle-treated mice on the same diet, was significantly reduced as assessed by serum ALT levels (ALT mean; 127 vs 257 U/L, $p < 0.001$) and the number of TUNEL-positive apoptotic hepatocytes. In addition, liver fibrosis as sequelae of active hepatic inflammation was markedly reduced when examined by Sirius red stain and mRNA expression of profibrogenic markers including collagen1a1 and osteopontin.

Conclusions: URM-099 is well tolerated in mice and effective in reversing nutrient excess diet-induced NASH. Taken together, our data support the use of URM-099 in early phase clinical trial as a candidate therapeutic agent to reverse NASH.

237 Grand Watkins Prize

IMPROVEMENT IN GGT PREDICTS EVENT-FREE SURVIVAL IN PRIMARY SCLEROSING CHOLANGITIS REGARDLESS OF URSODEOXYCHOLIC ACID TREATMENT: DATA FROM THE PEDIATRIC PSC CONSORTIUM.

Mark Deneau¹, Reham Abdou², Khaled Alqoaer³, Mansi Amin⁴, Achiya Amir⁵, Marcus Auth⁶, Fateh Bazerbach⁷, Annemarie Broderick⁸, Matthew DiGuglielmo³⁰, Wael El-Matary²⁹, Mounif El-Youssef⁷, Federica Ferrari⁹, Katelyn Furuya⁷, Madeleine Gottrand¹⁰, Frederic Gottrand¹⁰, Nitika Gupta¹¹, Matjaz Homan¹², Kyle Jensen¹, Binita Kamath¹³, Kyung Mo Kim¹⁴, Kaija-Leena Kolho¹⁵, Anastasia Konidari¹⁶, Bart Koot¹⁷, Raffaele Iorio¹⁸, Cara Mack¹⁹, Mercedes Martinez²⁰, Parvathi Mohan²¹, Alexandra Papadopoulou²², Amanda Ricciuto¹³, Lawrence Saubermann²³, Pushpa Sathya²⁴, Eyal Shteyer²⁵, Vratislav Smolka²⁶, Atushi Tanaka²⁷, Pamela Valentino²⁸, Raghu Varier³¹, Veena Venkat³², Bernadette Vitola³³, Miriam Vos¹¹, Marek Woynarowski³⁴, Albert Chan²³, Jason Yap³⁵, Tamir Miloh³⁶. ¹University of Utah, Salt Lake City, UT; ²State University of New York Buffalo, Buffalo, NY; ³Prince Salman North West Armed Forces Hospital, Tabuk, Saudi Arabia; ⁴University of California San Francisco, San Francisco, CA; ⁵Tel-Aviv University, Tel

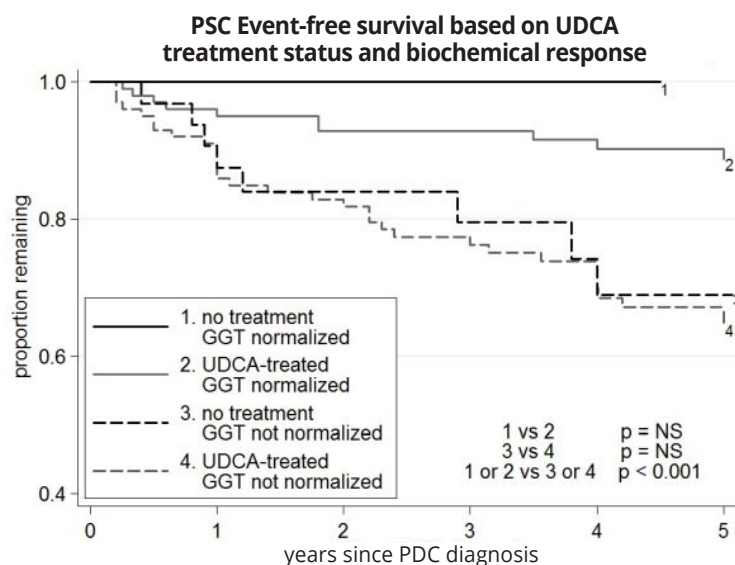
Aviv, Israel; ⁶University of Liverpool, Liverpool, United Kingdom; ⁷Mayo Clinic, Rochester, MN; ⁸University College Dublin, Dublin, Ireland; ⁹Sapienza University of Rome, Rome, Italy; ¹⁰Lille University Hospital of Lille, Lille, France; ¹¹Emory University, Atlanta, GA; ¹²University of Ljubljana, Ljubljana, Slovenia; ¹³University of Toronto, Toronto, ON, Canada; ¹⁴University of Ulsan, Seoul, Korea (the Democratic People's Republic of); ¹⁵University of Helsinki, Helsinki, Finland; ¹⁶University of Manchester, Manchester, United Kingdom; ¹⁷Academic Medical Centre, Amsterdam, Netherlands; ¹⁸University of Naples Federico II, Naples, Italy; ¹⁹University of Colorado, Aurora, CO; ²⁰Columbia University, New York, NY; ²¹Children's National Medical Center, Washington, ; ²²University of Athens, Athens, Greece; ²³University of Rochester, Rochester, NY; ²⁴Memorial University, St. John's, Canada; ²⁵Shaare Zedek Medical Center, Jerusalem, Israel; ²⁶Palacky University, Olomouc, Czech Republic; ²⁷Teikyo University, Tokyo, Japan; ²⁸Yale University, New Haven, CT; ²⁹University of Manitoba, Winnipeg, MB, Canada; ³⁰Thomas Jefferson University, Wilmington, DE; ³¹Northwest Pediatric Gastroenterology LLC, Portland, OR; ³²University of Pittsburgh Medical Center, Pittsburgh, PA; ³³Medical College of Wisconsin, Milwaukee, WI; ³⁴Children's Memorial Health Institute, Warsaw, Poland, ³⁵University of Alberta, Edmonton, AB, Canada. ³⁶Texas Children's Hospital, Houston, TX, USA.

Background: Ursodeoxycholic acid (UDCA) is commonly used to treat primary sclerosing cholangitis (PSC) in children. Randomized-controlled trials in adults with PSC demonstrate that UDCA does not improve survival with native liver. We evaluated the effect of UDCA on clinical and biochemical outcomes in children with PSC using a large, multicenter cohort.

Methods: The pediatric PSC consortium is a research collaboration between 36 international centers. We recorded liver biochemistries at diagnosis and 1 year, and UDCA treatment status. Survival analysis from PSC diagnosis to several clinical events was performed: 1) portal hypertensive complications (ascites, encephalopathy, varices), 2) biliary complications (stricture requiring dilation, stenting or drainage), 3) liver transplantation (LT), 4) cholangiocarcinoma (CCA) or 5) liver-related death. A biochemical response (BR) was defined as GGT >50 U/L at diagnosis and <50 at 1 year. Event-free survival (EFS) at 5 years was calculated in four groups: UDCA treated (T) and untreated (U) patients, with or without BR.

Results: The cohort consisted of 309 patients, 40% female, mean age 11.4 years, with mean 6.6 years of follow-up. Inflammatory bowel disease (IBD) occurred in 84%, autoimmune hepatitis (AIH) in 39%, and large duct involvement in 74% studied patients. UDCA was used in 81% at mean dose of 17 mg/kg/day. T and U groups had similar mean liver biochemistries at diagnosis [GGT 314 vs. 300 U/L; ALT 239 vs. 175 U/L (p=NS)], lower values at 1 year [GGT 99 vs. 175 (p=0.002); ALT 63 vs. 96 (p=0.008)], and greater reduction over the first year [GGT decreased by 215 vs. 125 (p=0.039) and ALT by 175 vs. 79 (p=0.037)]. BR occurred in 45% overall. Patients with and without BR had similar baseline liver biochemistries, AST to platelet ratio index, age and prevalence of IBD, AIH and large duct involvement (all p=NS). Despite biochemical improvement, T and U patients had similar rates of adverse events: portal hypertensive complications 19 vs. 18%, biliary complications 6 vs. 8%, LT 11 vs. 12%, CCA 1 vs. 0%, and death 1 vs. 0% (all p=NS). The 5-year EFS was 91% in patients with BR (90% in T vs. 100% in U, p=0.45) and 67% in patients without BR (66% in T vs. 69% in U, p=0.96), p<0.001.

Conclusions: UDCA treatment resulted in improved GGT and ALT but no reduction in rates of adverse clinical outcomes. Patients with GGT <50 at one year do markedly better than those with GGT >50, regardless of UDCA treatment. These data support GGT as a surrogate marker of hepatobiliary inflammation and fibrosis in PSC.



CONCURRENT SESSION I – NUTRITION

Friday, November 3

10:30am – 12:00pm

238 RISK FACTORS FOR HOSPITALIZATION AMONG PEDIATRIC INTESTINAL FAILURE

PATIENTS. *Tatyana Hofmekler, Janet Figureroa, Hilina Kassa, Rene Romero, Andi Shane. Emory University, Atlanta, GA*

Children with intestinal failure are dependent on parenteral nutrition received through a central venous catheter. Complications due to underlying disease, parenteral nutrition, complications associated with central venous access such as vascular catheter associated infections (VCAIs), predispose patients to hospitalizations. Hospitalizations are poor prognostic indicators and contribute to high costs. Our aim was to identify demographic, social, and medical factors that contribute to hospitalization of children who received their medical care in a multidisciplinary intestinal rehabilitation clinic (IROC), with the long-term goal of focusing resource allocation on identified modifiable risk factors. We conducted a retrospective single center cohort study of children enrolled in IROC clinic. The primary outcome was total number of hospitalizations during follow-up time. Secondary outcomes included length of stay and risk of first hospitalization. As bloodstream infections lead to hospitalizations, we also studied the relationship of VCAIs and the number of hospitalizations. Forty-seven patients had 310 hospitalizations with a median duration of 4 days (1-84) per hospitalization. Results from unadjusted negative binomial models suggest that number of VCAIs (IRR 1.22 (1.06-1.42)) and therapy for small bowel bacterial overgrowth (IRR 1.92 (1.00-3.67)) were significant individual risk factors for number of hospitalizations. Social and demographic factors such as race (IRR 1.03 (0.53-1.99)), age at referral (1.00 (0.99-1.01)), and maternal age at delivery (0.96 (0.90-1.02)) were not risk factors for predicting number of hospitalizations. Survival analysis showed that presence of a colon, an ileocecal valve and short bowel syndrome diagnosis were individually protective against the risk of first hospitalization. Twenty-one (45%) children did not have a recognized VCAI during the study period, although VCAI rate and number of hospitalizations were positively correlated (Pearson correlation coefficient=0.54) among children who had a VCAI. In our single-center cohort of children enrolled in a subspecialty clinic, social and demographic factors were not found to be risk factors for hospitalization while anatomical factors were found to be protective against hospitalization frequency. Receipt of care in a multidisciplinary clinic likely reduced the impact of traditional social and demographic risk factors associated with hospitalization and VCAI, justifying resource allocation to a multidisciplinary subspecialty care clinic environment.

Table 4: Vascular catheter associated infection count and rate for all pediatric intestinal failure patients followed in the Intestinal Rehab of Children's clinic from July 1st 2010 through February 1st 2016. (N=47)

Vascular Catheter Associated Infection count	N (percent of patients)
0 infections	21 (44.7%)
1-3 infections	21 (44.7%)
>4 infections	5 (10.6%)
Median Vascular Catheter Associated Infection rate (per 1,000 line days)	3.53 (0.0-6.94)
Total study vascular catheter line days	18,355

Note: Only those that were admitted had any CLABSI infection. Furthermore, when we compared those who were admitted < 3 days vs. > 3 days, only those with >3 days had any CLABSI infection.

239 EFFECT OF N-3 FISH OIL VERSUS N-6 SOYBEAN OIL PREDOMINANT PARENTERAL LIPID EMULSIONS ON HEPATIC NEUTRAL LIPID, FATTY ACID AND PHYTOSTEROL COMPOSITION IN NEONATAL PIGLETS.

Daniela Isaac¹, Diana Mager^{1,2}, Celeste Lavallo^{1,2}, Abeer Alzaben², Vera C. Mazurak², Jason Yap¹, Pamela R. Wizzard¹, Patrick N. Nation³, Consolato Sergi³, Paul W. Wales^{1,4,5,6}, Justine Turner^{1,2}. ¹Department of Pediatric Gastroenterology and Nutrition, University of Alberta, Edmonton, AB, Canada; ²Department of Agricultural Food and Nutritional Science, University of Alberta, Edmonton, AB, Canada; ³Department of Laboratory Medicine & Pathology, University of Alberta, Edmonton, AB, Canada; ⁴Research Institute, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada; ⁵Division of General Surgery, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada; ⁶Group for Improvement of Intestinal Function and Treatment, Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Background: Determining the most appropriate lipid emulsion in parenteral nutrition (PN) support for pediatric intestinal failure patients remains an important clinical question, with the critical aim of optimizing growth while minimizing the risk of parenteral nutrition associated liver disease (PNALD). Hepatic steatosis is a clinically relevant histopathologic finding in PNALD. This study aimed to examine hepatic neutral lipid, fatty acid (FA) and phytosterol composition in neonatal piglets receiving parenteral nutrition with n-3 fish oil (FO) containing or n-6 soybean oil (SO) predominant lipid emulsions.

Methods: Ten neonatal piglets received iso-caloric, iso-nitrogenous parenteral nutrition (PN) at 5 g/kg/day with variation only in the type of lipid emulsion provided: SO (n=5) versus FO (n=5). Five healthy neonatal ad libitum sow fed (SF) piglets comprised the reference group. Liver tissue was assessed on day 14 of PN for: 1) histology, 2) neutral lipid accumulation using Oil Red O staining, 3) hepatic FA composition including triglyceride (TG), total phospholipid (TPL), phosphatidylcholine (PC) and phosphatidylethanolamine (PE) fractions using gas chromatography, and 4) phytosterol composition using chromatography coupled with mass spectrometry. The following blood chemistries were also assessed on day 14 of PN: GGT, ALT, bile acids and total bilirubin. Descriptive data were expressed as the mean plus or minus the standard deviation. Independent t-test was used to compare blood chemistries and hepatic FA compositions between PN fed groups. ANOVA was utilized to compare phytosterol levels between FO, SO and SF groups.

Results: Total serum bile acids were 3-fold higher in SO versus FO piglets ($30 \pm 19 \mu\text{mol/L}$ vs $11 \pm 5 \mu\text{mol/L}$, $p=0.06$). Liver histology scores were not different between FO and SO groups (3.8 ± 0.8 vs 4.6 ± 0.9 , $p=0.18$). Oil Red-O staining showed a two-fold higher trend in neutral lipid staining in the SO compared to the FO group (2.0 ± 1.0 vs 0.8 ± 0.8 , $p=0.07$). Total FA in the TPL fraction was significantly lower in the FO compared to the SO group ($4852 \pm 472 \mu\text{g/g}$ vs $7333 \pm 1177 \mu\text{g/g}$, $p<0.01$). The proportion of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) was significantly higher in the FO versus SO piglets in the TG, TPL, PC and PE fractions ($p<0.05$). The FO and SF groups were markedly lower in campesterol (FO $1.3 \pm 0.2 \mu\text{g/mg}$ vs SO $8.2 \pm 1.1 \mu\text{g/mg}$ vs SF $0.9 \pm 0.6 \mu\text{g/mg}$, $p<0.0001$), stigmasterol (FO $0 \mu\text{g/mg}$ vs SO $3.7 \pm 0.7 \mu\text{g/mg}$ vs SF $0 \mu\text{g/mg}$, $p<0.0001$) and β -sitosterol (FO $0 \mu\text{g/mg}$ vs SO $14.5 \pm 1.4 \mu\text{g/mg}$ vs SF $0.05 \pm 0.1 \mu\text{g/mg}$, $p<0.0001$).

Conclusions: Compared to SO, FO lipid emulsion is associated with lower FA and phytosterol accumulation, and higher proportions of EPA and DHA in the liver of neonatal piglets. Although no significant difference was found, there was a trend to higher bile acids and neutral lipid accumulation in the SO piglets suggesting an increased risk for cholestasis. Alterations in hepatic lipid, FA and phytosterol composition in PN fed piglets given SO lipid emulsion may contribute to PNALD.

CONCURRENT SESSION I – IBD

Friday, November 3

10:30am – 12:00pm

240 PROCOLLAGEN III N-TERMINAL PROPEPTIDE (PIIINP) AS A CIRCULATING BIOMARKER FOR ACTIVE STRICTURE DEVELOPMENT IN PEDIATRIC CROHN'S DISEASE. Cortney Ballengee¹, Jarod Prince¹, James Markowitz², Neal LeLeiko³, Lee Denson⁴, Jeffrey Hyams⁵, Robert Baldassano⁶, Subra Kugathasan¹. ¹Pediatrics, Emory University, Atlanta, GA; ²Cohen Children's Medical Center of New York, New York City, NY; ³Rhode Island Hospital, Providence, RI; ⁴Cincinnati Children's Hospital, Cincinnati, OH; ⁵Connecticut Children's Medical Center, Hartford, CT; ⁶Children's Hospital of Philadelphia, Philadelphia, PA

Background: Up to 40% of Crohn's disease (CD) patients eventually require surgery due to fibrous strictures. Extracellular matrix components, including type III collagen, play a vital role in the development of intestinal fibrosis and stricture in Crohn's disease. We have shown that at diagnosis, genes involved in extracellular matrix accumulation are upregulated in pediatric patients with inflammatory (B1) disease who later develop stricturing (B2) disease. There are currently no clinically useful biomarkers to predict the risk for development of strictures in patients with inflammatory (B1) Crohn's disease.

Aim: To determine if patients who develop strictures (B2) have elevated plasma PIIINP concentration at diagnosis or within 90 days of documented stricture development as compared to patients with B1 phenotype and controls

Methods: Subjects were selected from the RISK cohort, an inception multicenter CD cohort where treatment naïve patients were enrolled at the time of diagnosis and prospectively followed for up to 60 months with baseline and yearly plasma collection. Subjects were separated into 4 groups. Group 1 included 40 children with B1 phenotype at diagnosis, group 2 included 33 children with B2 phenotype at diagnosis, group 3 included 48 children with B1 phenotype at diagnosis who developed strictures (B2) at any time during the 60 month follow up, and group 4 included 38 children with B1 phenotype at follow up who developed stricture within 90 days of plasma collection. ELISA (Biomatik EKU06786) for procollagen III N-terminal propeptide (PIIINP) was performed on plasma of the 4 groups and 56 children without IBD (controls). Mean

plasma PIIINP concentration was compared between each group and controls using ANOVA and adjusting for multiple comparisons (Tukey method).

Results: Plasma PIIINP concentration was significantly higher in the patients at diagnosis who went on to develop strictures (group 3) when compared with B1 patients who never developed stricture (2515 vs 1803 pg/mL; $p=0.01$) and controls (2515 vs 1464 pg/mL; $p<0.01$). PIIINP concentration was also significantly higher in patients who developed a stricture within 90 days of plasma collection (group 4) as compared to B1 patients (2481 vs 1803 pg/mL; $p=0.02$) and controls (2481 vs 1464 pg/mL; $p<0.01$).

Conclusion: Plasma concentration of PIIINP was significantly elevated in children with B1 Crohn's disease phenotype at diagnosis who developed strictures during 60 month follow up and in children with B1 disease within 90 days of stricture. These results are supported by the known pathogenesis of excess collagen deposition leading to tissue fibrosis. We speculate that circulating serum PIIINP may be clinically useful to predict the development of strictures in patients with Crohn's disease.

Diagnosis	Group 1 (B1) N=40	Group 2 (B2) N=33	Group 3 (B1-B2 dx) N=48	Group 4 (B1-B2 sx) N=38	Control N=56
Mean (95% CI)	1803 (1485, 2120)	2140 (1790, 2489)	2515 (2225, 2804)	2481 (2155, 2807)	1464 (1196, 1732)

F=9.50, $p<0.001$

CONCURRENT SESSION I NEUROGASTROENTEROLOGY AND MOTILITY

Friday, November 3

10:30am – 12:00pm

241 PEG 3350 VS LACTULOSE FOR TREATMENT OF FUNCTIONAL CONSTIPATION IN CHILDREN AGED 6 MONTHS TO 6 YEARS. A MULTICENTER, PROSPECTIVE, RANDOMIZED STUDY. *Dorota Jarzebicka¹, Joanna Sieczkowska-Golub¹, Jaroslaw Kierkus¹, Piotr Czubkowski¹, Piotr Socha¹, Dariusz Lebensztejn², Monika Kowalczyk-Kryston², Bartosz Korczowski³, Grzegorz Oracz¹. ¹Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, The Children's Memorial Health Institute, Warsaw, Poland; ²Department of Pediatrics, Gastroenterology and Alergology, University Hospital in Bialystok, Bialystok, Poland; ³Department of Pediatric Gastroenterology, Regional Clinical Hospital No. 2 in Rzeszow, Rzeszow, Poland*

Objectives/Study: According to ESPGHAN/NASPGHAN guidelines, polyethylene glycols (PEG) - 3350 or 4000 is recommended as a first-line treatment, but it has not been compared to lactulose in young children. The aim of the study was to compare PEG 3350 (Dicopeg Junior) with lactulose in constipation and evaluate clinical efficacy and side effects.

Methods: The study had a randomized, prospective, open-label, multicentre comparative design and was performed in three academic hospitals in Poland. Functional constipation was defined according to Rome III Criteria. Patients with organic causes of constipation were not included. The study covered 12 weeks of treatment and 4 weeks follow-up. During the first visit patients were randomized into two groups – treated with PEG 3350 (Dicopeg Junior) at maximum dose 20 g/day or lactulose (Lactulose MIP) 2 ml/kg. Patients were asked to fulfill the diary, to make the defecation training and to use the proper diet. Telephone consultation was made after 4 weeks from enrolling. In case of lack of clinical improvement in group treated by PEG 3350, dose change was advised. In case of intolerance or lack of efficacy of lactulose, treatment with Dicopeg Junior was proposed, in accordance with the dosage as in the first group and overall duration adjusted so as to complete the 12-week study. On the final visit at week 12 the effectiveness of treatment and assessment of adverse events were recorded. At week 16 state of the child, was checked during call visit. As a good treatment result was considered 3 or more bowel movements per week and stool consistency according to the Bristol scale at least 2. The results were statistically analyzed.

Results: We enrolled 102 patients (M 57, F 45) aged 3.62±1.42 years. There were 14 patients who earlier terminated study. Mean duration of constipation before enrolment was 19.3 months. Mean number of bowel movements per week was 2.14 (median 2). Fifty-one patients were randomized to the group treated with PEG 3350 and 51 patients to the group with lactulose. After 4 weeks of treatment 5 patients changed the course of treatment from lactulose (which was not effective) to PEG. In per protocol analysis at week 12 patients in the group treated with PEG 3350 had significantly more bowel movements per week compared to the lactulose group [7.9±0.6 vs. 5.7±0.5 ($p=0.008$), respectively]. Moreover, significantly

more side effects were observed in the lactulose group (15 vs. 23 respectively, $p=0.02$). The most common side effect were periodically bloating and gases or abdominal pain. At week 12 both groups presented with similar frequency of defecation with pain (5% vs. 5%), stool retention (7% vs. 10%), large volume of stools (30% vs. 31%) and hard stools (7% vs. 13%).

Conclusion: Polyethylene glycol 3350 is more effective with fewer side effects than lactulose in the treatment of constipation in infants and young children.

242 **COMPARISON OF CLINICIAN DIAGNOSES AND QPGS-ROME IV QUESTIONNAIRE DIAGNOSES FOR PEDIATRIC FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN AND ADOLESCENTS.**

Russell Zwiener¹, Olafur Palsson², Samuel Nurko³, Miguel Saps⁴, Carlo Di Lorenzo⁴, Robert Shulman⁵, Jeffrey Hyams⁶, Paul Hyman¹, Miranda van Tilburg^{2,7,8}. ¹Pediatric Gastroenterology, LSUHSC, New Orleans, LA; ²Pediatric Gastroenterology, UNC Department of Medicine, Chapel Hill, NC; ³Pediatric Gastroenterology, Harvard - Boston Children's, Boston, MA; ⁴Pediatric Gastroenterology, Nationwide Children's, Columbus, OH; ⁵Pediatric Gastroenterology, Baylor College of Medicine - Texas Children's, Houston, TX; ⁶Pediatric Gastroenterology, Connecticut Children's, Hartford, CT; ⁷Clinical research, Campbell University, Buies Creek, NC; ⁸Social Work, University of Washington, Seattle, WA

Objective: Functional gastrointestinal disorders (FGIDs) are common. Pediatric Rome IV criteria include several changes to existing disorders as well as new diagnoses, but the newly developed Questionnaire on Pediatric Gastrointestinal Symptoms for Rome IV (QPGS-RIV) has not yet been validated. The purpose of the present study was to evaluate the agreement between expert clinician driven Rome IV diagnoses with the QPGS-RIV questionnaire in children and adolescents.

Methods: Subjects were mothers of 106 new pediatric GI patients, 4 to 17 years of age (mean age 10.7 years), 57% females, seen in six tertiary pediatric gastroenterology clinics in the United States diagnosed with an FGID. Each site identified at least 17 child and adolescents with a physician diagnosis of an FGID.

Results: Functional Constipation (FC) was the most common clinician diagnosis in the sample, followed by Irritable Bowel Syndrome (IBS), Functional Abdominal Pain NOS (FAP-NOS) and Functional Dyspepsia (FD); see Table. All other FGID were diagnosed in less than 10% of the sample and not included in analyses. Eleven children (10.4%) did not meet criteria for any Rome IV diagnosis by QPGS-RIV. The QPGS-RIV showed 62.5% sensitivity in identifying corresponding clinician diagnoses. Agreement of the QPGS-RIV diagnoses with clinician diagnosis was best for FD (63.6%), and all Functional Abdominal Pain Disorders (FAPD) combined (76.05%), while lowest for FAP-NOS (10%). Almost half (48.4%) of these patients suffered from FD by QPGS-RIV. Since FAPD and FC often co-exist or are difficult to differentiate we examined overlap of these conditions. Of the clinician diagnosis of FC, 23.9% had a QPGS-RIV diagnosis of FAPD. Of physician diagnosis of FAPD, 2.8% had a QPGS-RIV diagnosis of FC.

Conclusion: This is the first study to examine the new pediatric Rome IV criteria. Sensitivity of the parent questionnaire is fair to reasonable. Overall these results suggest that the QPGS-RIV has reasonable validity in a pediatric population. Larger prospective studies are needed to further validate the Rome IV criteria and include child report as well.

Agreement of QPGS-RIV diagnoses with physician diagnoses

FGID diagnosis	Clinician diagnosis (number of cases)	Same Rome IV diagnosis by QPGS-RIV
Functional Constipation	40	19 (47.5%)
Irritable Bowel Syndrome	27	14 (51.9%)
FAP-NOS	20	2 (10%)
Functional Dyspepsia	11	7 (63.6%)
FAPD (FD, IBS, FAP-NOS, Abdominal Migraine)	71	54 (76.05%)

POSTER SESSION II

Friday, November 3

12:00pm – 2:00pm

*Poster of Distinction

ENDOSCOPY/QI/EDUCATION

248 **THE ASSESMENT OF SOCIAL, DEMOGRAPHIC AND ENDOSCOPIC FINDINGS OF INFANTS WITH CORROSIVE AGENT INGESTION.**

Günsel Kutluk¹, Özben Ceylan², Nafiyе Urgancı³, Feyzullah Cetinkaya⁴. ¹Pediatric Gastroenterology, University of Health Sciences Kanuni Sultan Süleyman Education and Research Hospital, Istanbul, Turkey; ²Pediatrics, University of Health Sciences, Süleymaniye Education and Research Hospital, Istanbul, Turkey; ³Pediatric Gastroenterology, University of Health Sciences, Hamidiye Sisli Etfal Education and Research Hospital, Istanbul, Turkey; ⁴Pediatrics, International Hospital, Istanbul, Turkey

Introduction/Aim: Accidental ingestion of caustic substances produce oropharyngeal and gastroesophageal injuries and can cause significant morbidity and mortality in pediatric population. The aim of this study was to assess the social, demographic and endoscopic findings of infants with caustic agent ingestion.

Methods: Infants (1-24 months) who were admitted to our hospital for suspected corrosive substance ingestion were evaluated retrospectively.

Results: The study included 359 infants [(227 boys (63.2 %), 132 girls (36.8 %)]. 89.5% of the patients were older than 12 months and the mean age was 18.12±5.14 months. Most of the mothers were not working (94.4 %) and had a low education status; 65.5 % of the mothers had primary training, 14.5 % were illiterate. The highest amount of accidents occurred in summer (46%). Inappropriate storage of the cleaning materials was found in 42.9% of the families. After ingestion of the caustic agent 77% of the patients had vomited or were given water, milk or yoghurt by their parents. Most of the patients (39%) had ingested bleach and grease cleaners (24%) Physical findings of the patients were as follow: 36.2 % of patients had mucosal burn, 10.6 % had hypersalivation, 3.6 % had dysphagia, 1.4 % had respiratory distress and 2 % had toxic appearance. The endoscopic findings were normal in 73.3 % of the patients. Lesions in the esophagus were detected in 20.4% of the infants, mostly slight changes (grade I and IIa esophagitis) were present. Three patients had grade IIb and only one infant had grade III esophagitis. Gastric lesions were found in 1.9 % of the patients whereas in 5.8 % of the cases stomach and esophagus were both affected. Grease cleaners and household hydrochloric acid seemed to cause more serious mucosal damages (43.4% and 68.4%). Complication developed in four patients (1.1 %); esophageal stenosis in two patients, sepsis in one patient and gastric perforation in one patient.

Conclusion: Ingestion of caustic substances can cause severe gastroesophageal injuries. Grease cleaners and household hydrochloric acid seemed to cause more serious mucosal damages. Risk ratio is higher in boys and in families with low socioeconomic and sociocultural levels. Inappropriate storage of the cleaning materials is another confounding factor. Guidance and education of the families are important preventive tools and it is necessary to restrict access to caustic agents by prohibiting their free commercialization.

249 **PEDIATRIC GASTROENTEROLOGY FELLOW'S SELF ASSESSMENT OF ENDOSCOPY SKILLS.**

Heidi Hagerott¹, Joel Friedlander². ¹Pediatric Gastroenterology, A.I. duPont Hospital for Children/Thomas Jefferson University, Wilmington, DE; ²Aerodigestive Program, Digestive Health Institute, Children's Hospital Colorado, University of Colorado School of Medicine, Aurora, CO

Objective: Endoscopy is a fundamental procedural skill learned during a pediatric gastroenterology fellowship. Lack of procedures in the pediatric population to meet the minimum requirement to achieve competency is a concern. Our goal was to determine the number of procedures completed by fellows per year of training, assess perceived competency and determine anxiety scores as a reflection of competency.

Methods: A survey link was emailed to the NASPGHAN PEDI GI Fellows listserv composed of 372 fellows. Procedural count of 8 routine procedures, a Visual Analog Scale (VAS) measuring the fellow's perceived competency for each procedure (0=not competent, 100=competent independently) and the General Anxiety Disorder-7 scale (GAD7) was evaluated. The data was collected and stored using RedCap.

Results: 167 fellows (45%) completed the survey, 28% 1st year, 41% 2nd year and 31% 3rd year. 43% participated in programs with 2 fellows per year, 27% with 1, 20% with 4 and 10% with 3.

3rd year fellows reported (# procedures/competency, SD): Diagnostic EGD 197±96 /96, EGD with non-variceal bleed 8±8/ 60, EGD with variceal bleed 7±8/53, EGD with dilation 10±8/67, EGD with foreign body removal 16±11/84, EGD with PEG placement 10±8/69, colonoscopy 103±62/81, colonoscopy with polyp removal 8±7/66.

2nd year fellows reported (#procedures/competency): Diagnostic EGD 124±76/ 90, EGD with non-variceal bleed 5±8/50, EGD with variceal bleed 4±3/47, EGD with dilation 5±9/48, EGD with foreign body removal 12±14/72, EGD with PEG placement 6±5/52, colonoscopy 65±46/72, colonoscopy with polyp removal 6±8/60.

1st year fellows reported (#procedures/competency): Diagnostic EGD 73±52/ 76, EGD with non-variceal bleed 3±2/40, EGD with variceal bleed 3±3/38, EGD with dilation 3±3/44, EGD with foreign body removal 6±5/60, EGD with PEG placement 5±5/43, colonoscopy 27±27/55, colonoscopy with polyp removal 4±4/42.

Therapeutic EGD with control of non-variceal/variceal bleeding scored the lowest on the competency scale in first year fellows and remained relatively low during the 3 years of training.

Percentage of 3rd year fellows who responded that met the training guidelines recommendations of minimum procedure count (3 months prior to completion of fellowship): 88% Diagnostic EGD, 24% EGD with non-variceal bleed/variceal bleed, 27% EGD with dilation, 70% EGD with foreign body removal, 35% EGD with PEG placement, 24% colonoscopy, 31% colonoscopy with polyp removal.

22% of fellows reported mild anxiety, 7% moderate anxiety and 3% severe anxiety. 43 % of fellows reported difficulty managing their lives.

Conclusion: Our data shows that a majority of 3rd year fellows near the end of fellowship do not reach the minimum number of procedures required to achieve recommended competency. Perceived competency scores were relatively low after 3 years of training. Anxiety may play a role in overall perceived competency emphasizing the need for cognitive skills training. Due to the lack of procedures available in the pediatric population, additional learning modalities should be implemented to achieve full competency. Survey of skills via program directors or research regarding recommended procedural goals is needed.

250 AN ACTION PLAN FOR PEDIATRIC CONSTIPATION EDUCATION.

Hilary Michel¹, Bridget Wagner², Benjamin Miller³, Arvind Srinath¹. ¹Gastroenterology, Children's Hospital of Pittsburgh, Pittsburgh, PA; ²Cook Children's Hospital, Fort Worth, TX; ³Children's Hospital of Pittsburgh, Pittsburgh, PA

Introduction: Constipation is a common and costly problem in pediatrics. Inpatient admission is sometimes required for bowel cleanout prior to starting maintenance therapy. It is the duty of pediatric residents to provide discharge instructions to these patients and families. Action plans have been used with other chronic pediatric diseases to provide discharge education and anticipatory guidance. Prior to this study, there were no standardized tools at Children's Hospital of Pittsburgh for providing this education. The goals of this study were to create a written constipation action plan which included information about constipation and its management, use that action plan to increase residents' knowledge about constipation management, and increase resident confidence in and comfort with the education they were providing to patients and families.

Hypothesis: The use of a written constipation action plan during discharge education for patients admitted for constipation cleanouts will improve resident knowledge about outpatient constipation management as well as confidence in and comfort with their ability to provide this education.

Methods: Pediatric residents at Children's Hospital of Pittsburgh were recruited to participate in a voluntary, anonymous survey via email that assessed knowledge, confidence, and comfort with educating families about outpatient constipation management. Residents were oriented to the constipation action plan at a noon conference and could access and edit the document in the "discharge instructions" section of the electronic medical record. The plan could then be personalized, printed and reviewed with patients and families upon discharge. Residents were re-surveyed approximately 6 months later.

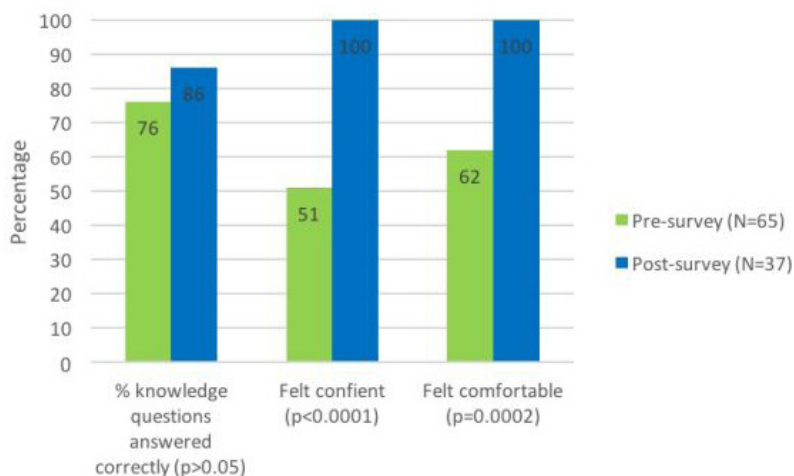
Results: 65 and 37 residents from PGY1-PGY5 took the pre- and post-surveys, respectively, with no significant difference in composition between pre- and post-survey groups. Participants answered knowledge questions accurately 76% of the time on the pre-survey vs. 86% of the time on the post-survey (did not reach statistical significance). 51% of participants reported feeling confident with the educational material they provided on the pre-survey vs. 100% on the post-survey (p<0.0001). 62% of participants reported feeling comfortable educating families on the pre-survey vs. 100% on the post-survey (p=0.0002). All participants found the action plan helpful.

Conclusions: There was a statistically significant increase in resident confidence in and comfort with providing discharge education in those who used the constipation action plan. Residents who used the action plan unanimously thought it was

helpful. Future directions could include creating similar action plans for other common pediatric diagnoses, assessing parent and patient satisfaction with the action plan, and evaluating the ability of the action plan to decrease readmissions.

Significance: Providing discharge education to patients and families is an essential resident role. An accurate, user-friendly educational tool increases resident comfort with and confidence in their ability to perform this task.

Grant support: This project was supported by the National Institutes of Health through Grant Number UL1-TR-001857.



251 CLINICAL PRESENTATION OF PEDIATRIC PATIENTS REQUIRING INTERVENTIONAL ENDOSCOPY FOR UPPER GASTROINTESTINAL BLEEDING.

Hillary Bashaw, Lee Bass. *Pediatric Gastroenterology, Ann & Robert H. Lurie Children's Hospital, Chicago, IL*

Background: Upper gastrointestinal bleeding (UGIB) in pediatrics might present with either anemia, hematemesis and/or melena. There are few studies that correlate the presentation of bleeding with endoscopic findings in pediatric patients undergoing endoscopic treatment for UGIB.

Aim: Describe the presentation of patients requiring interventional endoscopic treatment for upper gastrointestinal bleeding at a single center.

Methods: Retrospective chart review at Ann & Robert H. Lurie Children's Hospital of Chicago of all patients undergoing an interventional upper endoscopy for UGIB between October 1, 2011, and May 31, 2017. Students T test was used to compare groups. This study was approved by the institutional review board at Lurie Children's Hospital.

Results: At our institution during the timeframe in question, 71 patients underwent 103 endoscopies for treatment of UGIB. Median age of patients at the time of endoscopy was 124 months. Prior to endoscopy, patients presented with anemia alone (6 occurrences, 5.8%), hematemesis alone (48 occurrences, 47%), melena alone (33 occurrences, 31%), and a combination of both hematemesis and melena (16 occurrences, 16.2%). Sixty procedures (58%) were performed in 36 patients with underlying liver disease. Common underlying liver diseases included biliary atresia (28%), portal vein thrombosis (25%), and portal hypertension following liver transplant (15%).

Overall, 46 patients had esophageal varices (44%), 25 patients (24%) had gastric ulcers, and 24 patients (23%) had duodenal ulcers. Varices receiving treatment were classified as large and 34/46 (74%) had stigmata of bleeding. A majority of the gastric ulcers (88%) had evidence of active bleeding and, similarly, 71% of the duodenal ulcers had stigmata of bleeding. Other findings included Dieulafoy lesions, gastric varices, intestinal varices, and AVMs of the stomach. There was no significant relationship noted between the location of the bleeding lesions and the presenting symptoms. Patients who presented with either melena alone or hematemesis and melena had a significantly lower median hemoglobin at presentation than those presenting with hematemesis alone (p=0.011).

Eighty patients (77%) received a blood transfusion. The median hemoglobin of patients receiving a blood transfusion was significantly lower than those not receiving transfusion (7.2 vs 9.7 mg/dL, p<0.001). Patients receiving a blood transfusion were more likely to have underlying liver disease (OR=2.74 [1.05-7.1], p=0.039). Patients with liver disease who had varices as the cause of bleeding were significantly younger than patients with liver disease who had other lesions as the cause of bleeding (p=0.003). Furthermore, patients receiving sclerotherapy of esophageal varices were significantly younger than those undergoing band ligation (p<0.001). Treatments for non-variceal lesions included argon plasma coagulation

(n=13), epinephrine combined with hemostatic clips (n=17), epinephrine combined with bipolar cautery (n=6), as well as combinations of treatment modalities (n=17). No significant difference was noted in outcomes based on treatment method used. Three patients with bleeding duodenal ulcers had unsuccessful treatment of their bleeding lesions at the time of endoscopy. Two of those patients had angiography and one underwent a surgical repair. One patient with gastric varices was referred for TIPS.

Conclusion: The presence of melena or underlying liver disease is correlated with a more severe presentation in patients requiring an interventional endoscopy for upper gastrointestinal bleeding, as indicated by lower hemoglobin and increased need for blood transfusion. All current modalities for non-variceal upper gastrointestinal bleeding demonstrated similar efficacy in our cohort. Combining different endoscopic treatments to achieve hemostasis might be necessary. Prospective multi-center studies are needed to further characterize the presentation of patients with upper gastrointestinal bleeding in a broader population.

252 **THE INCIDENCE AND NATURAL HISTORY OF POUCHITIS IN CHILDREN WITH FAMILIAL ADENOMATOUS POLYPOSIS: SINGLE CENTER EXPERIENCE.**

Medhat Farwati¹, Luz Gutierrez Sanchez¹, Imad Absah^{1,2}. ¹Pediatric Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; ²Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN

Background: Familial adenomatous polyposis (FAP) is a hereditary cancer syndrome that is characterized by involvement of the entire gastrointestinal tract. Most FAP patients will undergo surgical colectomy and ileal pouch anal anastomosis (IPAA) due to the high risk of developing colon cancer. Patients with IPAA, frequently experience complications, like pouchitis. The current reported rate of pouchitis in children with FAP is up to 12%

Aim: assess the rate of pouchitis and the natural history of pouchitis in children with FAP.

Methods: We performed a retrospective chart review study of children (≤ 18 years) with the diagnosis of FAP who underwent colectomy and IPAA between 1992 and 2016. This study was approved by the Mayo Clinic institutional review board (IRB). Data abstraction included demographic data, age at colectomy, histological findings and any subsequent exams or interventions. The diagnosis of clinical pouchitis was considered based on the following documented symptoms: increased frequency and looser consistency of bowel movements compared to baseline, abdominal and/or pelvic cramping, rectal bleeding, urgency, and/or fecal incontinence. Pouchitis was defined as chronic if the patients had >3 episodes per year, active pouchitis symptoms lasting >4 weeks despite antibiotic therapy, or requiring chronic antibiotic use to control their symptoms.

Results: We identified 50 children (25 males) with a mean age of 13 years (range 4-18) with FAP who underwent colectomy and IPAA. 12 children (24%) were found to have clinical pouchitis. The average time between the surgery and development of clinical pouchitis was 33 months (range 6-87). Out of 12 children with pouchitis, 10 children (83%) required antibiotics, while symptoms self-resolved in 2 (17%) children. Five patients (41%) had at least one recurrence of clinical pouchitis requiring antibiotics within 10 month (range 7-12) from the initial pouchitis. Only 2 (16%) of those patients met the criteria of chronic pouchitis.

Eight of the children with clinical pouchitis underwent pouchoscopy within 8 weeks from presentation, 3 had endoscopic evidence of inflammation and 5 had normal pouchoscopy (3 of those received antibiotics prior to the pouchoscopy).

Conclusions: The incidence of pouchitis in this cohort of children with FAP is higher than what was reported in the literature. Most of those children responded to one course of antibiotics, with two patients developing chronic pouchitis. Prospective studies are needed to clarify the natural history and true rate of pouchitis in children with FAP.

*253 **ALGORITHM TO PREDICT WHICH CHILDREN WITH CHRONIC ABDOMINAL PAIN ARE UNLIKELY TO BENEFIT FROM ENDOSCOPY.**

Jacob Mark^{1,2}, Robert Kramer^{1,2}. ¹Digestive Health Institute, Children's Hospital Colorado, Denver, CO; ²Section of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, University of Colorado School of Medicine, Denver, CO

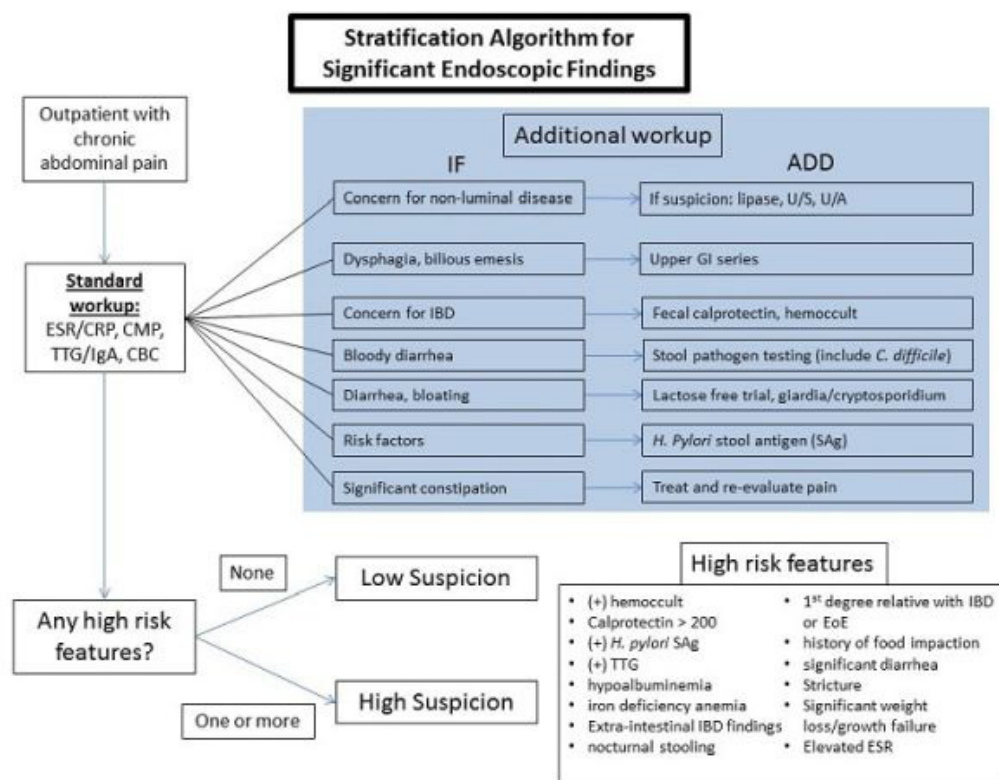
Objective: Endoscopy is often performed for children with chronic abdominal pain (CAP) because of the difficulty of excluding organic disease noninvasively. The aim of this study is to develop and test a diagnostic algorithm to improve prediction of children with CAP who are unlikely to benefit from endoscopy.

Methods: We created an algorithm using previous data and literature to evaluate diseases which may present with CAP in children and require endoscopy for diagnosis. Figure 1 depicts this algorithm, which utilizes standard and directed non-invasive evaluation and clinical features to determine patients with low suspicion (LS) or high suspicion (HS) to benefit from diagnostic endoscopy. We then applied this algorithm retrospectively to 150 patients who presented to a gastroenterology clinic for abdominal pain who underwent esophagogastroduodenoscopy (EGD) with or without colonoscopy. LS or HS

assignment was performed blind to endoscopic findings. We compared significant endoscopic findings (diagnoses which are likely to change management and/or are unable to be effectively diagnosed or treated without endoscopy) between the LS and HS groups.

Results: Of 150 patients, 98 were assigned to LS group and 52 to the HS group. In the LS group, Non-significant diagnoses (normal endoscopy, peptic irritation, or lactose intolerance) accounted for 91% of final diagnoses compared to 59% in the HS group ($p < 0.00001$). There were no cases of inflammatory bowel disease (IBD), celiac disease, or other significant findings in the LS group compared with 12%, 10%, and 7% in the HS group respectively ($p < 0.014$). There were no significant differences in rates of *Helicobacter* gastritis (3 vs 7%), eosinophilic esophagitis (2 vs 1%), nonspecific acute colitis (2 vs 1%), or eosinophilic colitis (2 vs 1%) between LS and HS groups.

Conclusions: We found 65% of patients who presented to a gastroenterology clinic for CAP and underwent endoscopy were in the LS group. 91% of patients in the LS group had endoscopic findings which could be diagnosed or managed without endoscopy. This algorithm may help risk stratify patients to decrease the number of unnecessary endoscopies in children.



256 IMPROVED LABORATORY UTILIZATION IN IBD PATIENTS RECEIVING INFLIXIMAB INFUSION THERAPY. Maura Downing¹, Erin Bracey², Anita Puma², April Taylor², Alison Marx¹, Elizabeth Maxwell¹, Andrew Grossman¹, Jonathan Flick¹. ¹Division of Gastroenterology, Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; ²Children's Hospital of Philadelphia, Philadelphia, PA

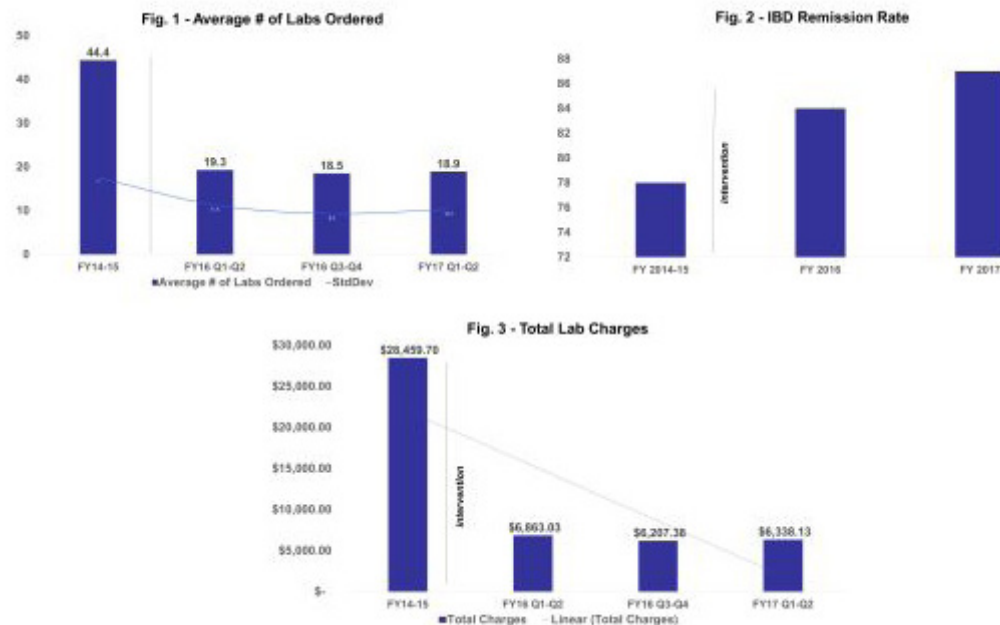
Aims: The primary aim was to reduce the frequency of lab testing in inflammatory bowel disease (IBD) patients on maintenance infliximab therapy, improving their experience and without affecting rate of remission in these patients. Patients with both Crohn's disease and ulcerative colitis were included. A secondary aim was to reduce laboratory-associated charges (and thus cost to patients, payers and the system) and thereby increase the value of care provided.

Methods: Patients on maintenance infliximab therapy receive repeated infusions at 4-8 week intervals. Typically, routine lab studies (including CBC with differential, comprehensive metabolic panel and inflammatory markers) are obtained at the time of each infusion. In contrast, lab studies for IBD patients on home adalimumab therapy are obtained approximately every 3-4 months. To understand our baseline data based on the current process, we collected and compared two sets of data: the volume of lab tests ordered (impacts cost) and sustained remission rates (quality). The data collected were analyzed and tests of change were outlined.

Test & Implement: 1) Establishment of lab monitoring guidelines based on expert opinion and dissemination of guidelines to ordering clinicians. 2) Epic-based tool to highlight date of most recent lab results at time of placing infliximab orders for upcoming infusion. 3) Monitoring of IBD remission rates through Improve Care Now database.

Results: mean # of labs ordered for this population decreased from 44.4 in FY14 and FY15 to 19.3 in FY16 Q1-Q2 ($p < 0.01$) (Fig. 1). Corresponding remission rates were 78% vs. 83% (Fig. 2). There was a 3-fold decrease in charges related to laboratory testing (Fig. 3).

Conclusions: We demonstrated that laboratory monitoring of IBD patients on maintenance infliximab therapy could be performed at a reduced frequency without adversely affecting their rates of remission. Cost savings for families and payers were also realized. As payer pressure to address costs associated with infusions mounts, our data provide evidence that quality may not be negatively affected by a reduction in lab frequency. Results also suggest that similar Epic-based tools can be used by other hospital-based specialties to reduce unnecessary lab testing as learnings from this pilot are shared.



262 IMPROVED NORMALIZATION OF PEDIATRIC CELIAC SEROLOGY WITHIN 18 MONTHS OF DIAGNOSIS. Mary Shull¹, Ivor Hill¹, Tracy Ediger¹, Sean Bingham¹, Kevin Dolan², Sandhya Ramachandran², Anne Trout¹, Brendan Boyle¹. ¹GI, Nationwide Children's Hospital, Columbus, OH; ²QIS, Nationwide Children's Hospital, Columbus, OH

Background: Literature describing practitioner adherence with guidelines for follow up care in patients diagnosed with celiac disease (CD) is limited. NASPGHAN CD guidelines recommend all newly diagnosed patients have repeat serology testing 6 months after diagnosis and every 6 months until normalization. Our Celiac Disease Center targeted serology normalization within 18 months of diagnosis as a quality initiative. Adherence with these recommendations has not been previously described.

Objectives: To review institutional adherence with national guidelines for patients newly diagnosed with celiac disease, with a goal of improving patient follow up and serology normalization. We aimed to increase the percentage of patients having normalized serology within 18 months of diagnosis from a baseline of 34% to 60% by December 2016.

Methods: Key drivers to improvement included the creation of a reliable tracking registry and the implementation of a local standard of care. The celiac QI team outlined these divisional expectations through practitioner educational sessions and reporting of practitioner adherence to national guidelines. Tissue transglutaminase antibody (TTG) was checked every 6 months until normalization. For those patients whose serology did not normalize within 18 months (defined as TTG <20), detailed chart reviews were performed looking to identify factors that could influence delayed normalization. Factors identified included poor adherence with the gluten free diet, comorbidities such as Type 1 diabetes or mental health disease, and highly positive initial TTG (over 1000). Patients with poor adherence were referred to the dietitian with celiac disease expertise for additional education.

Results: Baseline data showed the percentage of patients with documented serology normalization within 18 months of diagnosis was 34% (Q1 2009-Q4 2011). Implementation of quality improvement methods increased this percentage to 55% who had completely normalized with TTG <20 (Q1 2012-Q4 2015)-p=0.000. Exploratory analyses found that 82% of patients had TTG <40 within 18 months after diagnosis. In those 22 patients from Q1 and Q2 2015 that had continued abnormal serology, we found that 14% (3/22) had comorbid type 1 diabetes, 18% (4/22) had comorbid mental health disease, 5% (1/22) had classic presentation of celiac disease in a very young child with malabsorption, and 23% (5/22) had known or suspected ongoing gluten exposure. Of these patients, 41% (9/22) had no clear comorbidities or apparent cause of delayed normalization; 56% (5/9) of these had very high initial TTG >1000 and 33% (3/9) had initial TTG at the upper limit of detection (TTG >4965).

Conclusions: The development and implementation of processes to improve adherence with guidelines for serologic monitoring for children with celiac patient improved the delivery of care. By 18 months, 55% of patients had normal TTG levels and >80% of patients had TTG levels < 40. Detailed chart analysis of patients who did not normalize within 18 months allowed insight into common factors that may have delayed or prevented serologic normalization. Consistent follow up also encouraged multidisciplinary care, including additional specialized dietitian education as well as psychological support when indicated.

263 **A NOVEL DERIVATIVE OF EICOSAPENTAENOIC ACID MODULATES EICOSANOID SYNTHESIS AND CONTROLS POLYP BURDEN IN A MOUSE MODEL OF FAMILIAL**

ADENOMATOUS POLYPOSIS. Masako Nakanishi¹, Matthew Hanley^{1,2}, Gary Mathias³, Frank Scivolino², Mark Hull³, Daniel Rosenberg¹. ¹Center for Molecular Medicine, UConn Health, Farmington, CT; ²Thetis Pharmaceuticals, Branford, CT; ³St. James's University Hospital, University of Leeds, Leeds, United Kingdom

Background: Familial adenomatous polyposis (FAP) is a rare genetic disease characterized by the formation of numerous colorectal polyps beginning in childhood or adolescence. Without colectomy, typically in the 2nd or 3rd decade of life, FAP patients have a 100% lifetime risk of colorectal cancer (CRC). Though curative, surgery imposes a significant psychosocial burden and has serious iatrogenic consequences. The timing of colectomy depends on the rate at which colorectal polyp burden increases. There are no agents currently approved to control increases in FAP polyp burden, though several studies suggest that eicosapentaenoic acid free fatty acid (EPA-FFA) may be effective for this indication. However, EPA-FFA lacks credentials for commercialization. TP-252 is a derivative of EPA designed to deliver therapeutic levels of EPA-FFA to the colon. The present study investigates the effects of TP-252 on intestinal polyp burden and bioactive lipid profiles in the *Apc*^{Δ14/+} mouse model of FAP.

Methods: 90 *Apc*^{Δ14/+} mice were randomized at 6 weeks of age into 5 groups (n=18) and fed an experimental diet for 11 weeks. Group 1 was fed an AIN-93G diet modified to contain corn oil (Research Diets, NJ). Groups 2-5 were fed isocaloric diets containing TP-252 at 1%, 2% and 4% by weight. Group 5 was fed an isocaloric diet containing EPA-FFA at 2.5% that delivered a dose of EPA-FFA equivalent to TP-252-4%. All mice were sacrificed after 11 weeks of treatment, at which time spleens, small intestines (SIs) and colons were collected by standard techniques and polyp size and number were quantified. Lipids were isolated from colon tissue samples and used for LC-MS-MS lipidomic profiling.

Results: TP-252 was associated with dose-dependent reductions in SI polyp burden, with 1%, 2% and 4% diets reducing polyp numbers by 20%, 46% (P<0.01), and 56% (P<0.001). TP-252 was also associated with reductions in colonic tumor burden, with the largest reduction associated with TP-252-4% (34%, P<0.05). TP-252-4% was associated with a 19-fold increase (P<0.001) in mucosal EPA-FFA and a corresponding 2.4-fold (P<0.001) decrease in arachidonic acid (AA). Correspondingly, TP-252-4% was associated with increases in anti-tumorigenic metabolites of EPA (PGE3, 99-fold increase, P<0.001; 15(S)-HEPE, 49-fold increase, P<0.001) and decreases in pro-tumorigenic metabolites of AA (PGE2, 2.1-fold decrease, P<0.001; 12-HETE, 3.8-fold decrease, P<0.001). For both tumor burden and lipidomic endpoints, the effects of TP-252-4% were equivalent to EPA-FFA-2.5%.

Conclusions: The present study indicates that chronic administration of TP-252 effectively controls increases in polyp burden in the *Apc*^{Δ14/+} mouse model of FAP. TP-252 treatment was associated with a concomitant increase in EPA-FFA and decrease in AA within colonic tissue. Furthermore, TP-252 increased colonic levels of anti-tumorigenic eicosanoids derived from the cyclooxygenase and lipoxygenase pathways, and decreased levels of pro-tumorigenic eicosanoids. These lipidomic data suggest that TP-252 shifts the colonic microenvironment to an anti-tumorigenic state by modulating bioactive lipid profiles. Taken together, these data support the continued development of TP-252 as an FAP therapy.

267 SALIVARY CORTISOL AS A BIOMARKER OF STRESS IN CHILDREN UNDERGOING UPPER OR LOWER DIGESTIVE ENDOSCOPY. Eleyine Zarour², Fella Chennou², Gianpiero Teolis², Martha Dirks^{1,2}, Prévost Jantchou^{1,2}. ¹Gastroenterology, CHU Sainte-Justine, Montréal, QC, Canada; ²CHU Sainte-Justine Research Center, Montreal, QC, Canada

Background: Salivary cortisol (s-Cortisol) has been used in several pediatric studies to determine the levels of stress in children prior to various medical conditions. Although reference values for s-Cortisol in healthy children have been established, its clinical utility has never been assessed in children undergoing digestive endoscopy. In a previous study, we have shown that nearly one fourth of the children in our cohort expressed a significantly high level of pain during endoscopy.

Objectives: The primary objective of this study was to compare the level of s-Cortisol in adolescents before and after endoscopy. Secondary objectives were: 1) to investigate the correlation between s-Cortisol and the anxiety visual scale, 2) to investigate the correlation between s-Cortisol and age, sex, previous endoscopy history and the type of procedure and 3) and the change in level of s-Cortisol according to pain during endoscopy.

Methods: Between July and August 2016, all children aged 10 to 18 years old undergoing a digestive endoscopy under intravenous sedation were included in the study. s-Cortisol was obtained preoperatively (Pre-op) on the day of endoscopy after parental and children consent. Cotton-based Salivette tubes were used. A swab was chewed by the patient for sixty seconds and then placed in a sterile plastic tube. Before the procedure, children were asked to rate their level of anxiety on a visual anxiety scale (0 to 10). Endoscopic procedures were performed after administration of Fentanyl and Midazolam +/- Ketamine). Following the procedure, a second specimen was collected (Post-op). The Salivette tubes were centrifuged and frozen at -80 °C, then assayed simultaneously. A commercial ELISA based technique for s-Cortisol was used for analysis. The quality of sedation (assessed by a pain scale from 0 to 10) was evaluated by a single evaluator during the endoscopy.

Results: 53 children were prospectively recruited in the study (mean age 14 years-old, 25 males). In total, 102 samples were taken (2 per patient). The mean (sd) level of cortisol was 56.5 (32.7) nmol/L and 41.9 (34.9) nmol/L for the Pre-op and the Post-op samples respectively. Baseline s-Cortisol was lower in the group of patients (n = 35) who had an adequate sedation, than those who experienced high levels of pain (n=13) (mean s-Cortisol 54.7 +/-34.8 nmol/L and 71.0 +/- 27.7 nmol/L respectively).

The visual anxiety scale was correlated with Pre-op s-Cortisol ($R^2= 0.21$). An increase of one unit on the visual anxiety scale was associated with an increase of 5.9 nmol/L of s-Cortisol ($p=0.0007$).

The following factors were associated with a higher level of sCortisol at baseline : age between 10 and 12 years old, female gender and having a digestive endoscopy procedure for the first time. The mean difference of cortisol between Pre-op and Post-op was 14.9 nmol/L ($p = 0.01$). The mean decrease in s-Cortisol was greater in the well-sedated group as compared to the group of children with procedural pain (17.9 nmol/L vs 22.1 nmol/L respectively ($p = 0.0021$)).

Conclusion: s-Cortisol appears to be a reliable marker of stress in children undergoing an endoscopic procedure. We found a good correlation between s-Cortisol and visual anxiety scale. As general anesthesia is not available for all children, this non-invasive biomarker could be helpful to identify a subgroup of patients who would benefit from some specific measures before the endoscopy, like premedication by anxiolytics or other measures such as hypnosis or music therapy. A randomized trial will be performed to validate our findings.

268 FOCAL ADENOMATOUS TRANSFORMATION IN PEDIATRIC NON-SYNDROMIC JUVENILE POLYPS: AN UNDERRECOGNIZED ENTITY. Nadia Ibrahim¹, Brian Lee¹, Raj Shah², Anchal Sethi², Ruba abdelhadi¹, Seth Septer³, Thomas Attard¹. ¹Health Services and Outcomes Research, Children's Mercy Hospital/University of Missouri Kansas City, Kansas City, MO; ²University of Missouri Kansas City, Kansas City, MO; ³Gastroenterology, Children's Hospital Colorado, Denver, CO

Background: Juvenile polyps (JP) are hamatomatous lesions that are most frequently diagnosed in children, usually presenting as painless hematochezia, as isolated, more frequently left sided lesions that are removed endoscopically. Multiple (≥ 5 - 10), proximal (small intestinal / gastric), or any juvenile polyps with a positive family history of polyposis define patients as harboring polyposis and at heightened risk of colorectal cancer (CRC). Adenomatous transformation within JP is considered a characteristic of syndromic JP and an intermediary in the progression toward CRC, however adenomatous foci have been reported in sporadic JP and adenocarcinoma of the colon has been reported in both children and adults with JP. The significance of adenomatous transformation in non-syndromic JP is unknown; herein we report a cohort of patients with non-syndromic JP but with adenomatous transformation/foci noted on histology.

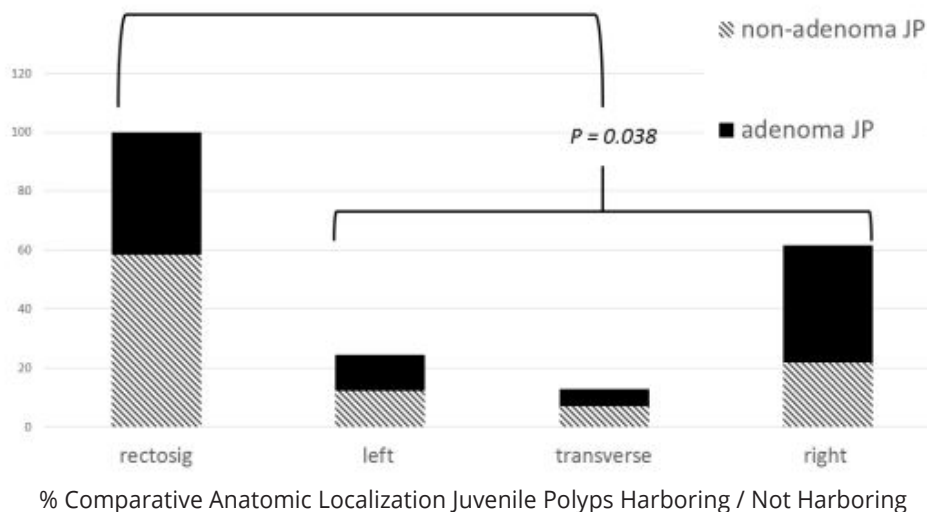
Methods: Children ages birth to 18 years, who underwent colonoscopy with polypectomy at Children's Mercy Hospital were identified through the corresponding billing codes queried from Children's Mercy Medical Information Technology

Department from 1/1/2003 to 3/1/2017; retrospective chart review was performed. Abstracted data included basic demographics, age at first colonoscopy, clinical presentation, extent of colonoscopy, endoscopic findings including number, size and location of polyps, histological findings including size, pathologic characteristics, dysplastic or adenomatous changes noted. Recurrence of polyps was also noted on repeat colonoscopy.

Children with sporadic juvenile polyps defined as polyp burden ≤ 10 , no family history of Juvenile Polyposis Syndrome and no Juvenile Polyps proximal from the colon were included. Children with incomplete medical records, other polyp histologic subtypes, other hereditary polyposes were excluded. Statistical analysis of data was performed using Stata, version 14.1®.

Results: During the Study period 214 subjects (115M, mean age 7.03years SD 3.96) underwent 361 procedures and 506 polypectomies for non-syndromic JP. Juvenile polyps harboring adenomatous foci (aJP) were reported at least once in 26 (12%) patients (age; median:IQR :4.8: 3.8, 9.3 years) There was no association with gender, age at initial presentation or racial background but aJP were significantly more likely to be proximally distributed than non-adenoma harboring polyps (Figure 1.), tended to be larger (pathologist reported volume - non-aJP / aJP; 1.62 / 2.09 cm³ NS) and were as likely solitary lesions during colonoscopy for painless hematochezia as was the observation with non adenoma harboring JP (p 0.98). Patients with aJP were significantly more likely to be rescoped than non-aJP (p 0.011) but polyp recurrence was not significantly different in the two groups (non-aJP / aJP 13.90% / 19.23% p 0.551). Upon chart review colorectal cancer was not reported in either subgroup.

Discussion: The presence of adenomatous foci in juvenile polyps is a histologic characteristic of unclear significance in pediatric as in adult patients, we cannot speculate on the natural history of the finding in pediatric juvenile polyps but note that adenocarcinoma has been reported in adults and rarely children with sporadic juvenile polyps. Our observations suggest that juvenile polyps harboring adenomatous foci are more likely to be proximally distributed reiterating the need for pancolonoscopy in suspected cases. Adenomatous transformation tends to be more prevalent in larger polyps. Re-colonoscopy may be the more cautious approach until we better understand these lesions, but we can offer no evidence that these polyps are any more likely to recur upon follow up.



EOE/GERD/AERODIGESTIVE

269 EOSINOPHILIC ESOPHAGITIS AND THE POTENTIAL FOR MALIGNANCY: A SYSTEMATIC REVIEW OF ATOPIC DISORDERS, ALLERGIC INFLAMMATION AND EOE. Amanda Muir¹, Kelly Whelan², Michael Dougherty³, Evan Dellon³, Elizabeth Jensen⁴. ¹Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA; ²Gastroenterology, University of Pennsylvania, Philadelphia, PA; ³Gastroenterology, University of North Carolina, Chapel Hill, NC; ⁴Wake Forest, Winston-Salem, NC

Introduction: Chronic inflammation is a known risk factor for the development of malignancy. However, there is controversy over whether allergic inflammation is protective or contributory to the development of malignancy in the involved organ. While it is possible that increased immune surveillance could lead to the protection from cancer, chronic injury over time may also lead to damaged cell repair mechanisms increasing malignancy risk. This is a particular question in eosinophilic

esophagitis (EoE), where the first case series was reported in 1993, and long-term prospective natural history studies have not been possible. However, some insight may be gained in the context of asthma in the lung and eczema in the skin.

Aim: To explore the association of allergic inflammation in the skin, lung, and esophagus and the development of organ-specific malignancy by performing a systematic review.

Methods: In accordance with the PRISMA guidelines, we used PubMed, Embase, and Web of Science to perform a systematic review. In conjunction with a research librarian, 3 searches were conducted: 1) eosinophilic esophagitis and esophageal cancer 2) eczema and skin cancer and 3) asthma and lung cancer. Two authors independently screened abstracts for inclusion, with any conflicts adjudicated by a third author. We eliminated case reports and review articles as well as any articles evaluating therapies, environmental exposures (including tobacco), or metastatic lesions. Data including sample sizes, effect sizes, study design, and odds ratios were abstracted into data tables. Given heterogeneity between studies, meta-analysis was not performed.

Results: After screening 1556 abstracts, 42 full articles were reviewed and 23 met inclusion criteria: 18 in the lung, 4 in the skin, and 1 in the esophagus. In asthma, most were cohort or case-control studies with 9/18 showing increased risk of lung cancer with asthma, 2/18 showing decreased risk and the remainder indicating null associations (Table 1). In the skin, 2/4 showed an increased risk of all skin cancers in eczema while the remainder had non-significant findings. Lastly, there was only one retrospective study that followed 13 EoE patients overtime. This study found that 53% of these patients also had developed Barrett’s esophagus, but none had dysplasia or malignancy.

Conclusions: Approximately half of identified studies show that asthma may be an independent risk factor for the development of lung cancer, but half did not. Findings were similar for eczema, and no cases of cancer due to EoE were identified. Case control and natural history studies in the esophagus are needed to further evaluate cancer risk in EoE.

Author	Year	Study Design	Cases	Controls	OR (95% CI)
El-Zein et al	2014	Case control	1,169	1,486	1.06 (0.54-2.09)
Wang et al	2009	Case control	212	292	4.78 (1.23-18.63)
Wu et al	1995	Case control	354	1,151	1.67 (1.1-2.5)
Gorlova et al	2006	Case control	280	242	0.92 (0.41-2.06)
Jian et al	2014	Cohort	32,759	17,859,318	Male 1.57 (1.48-1.67) Female 1.35 (1.24-1.47)
Gonzalez-Perez et al	2006	Cohort	129,860	200,000	1.35 (1.15-1.59)
Ji et al	2009	Cohort	402	140,425	2.28 (2.14-2.43)
Koshiol et al	2009	Case control	2,100	2,120	Males 0.48 (0.3-0.78) Females 1.1 (0.57-2.3)
Lim et al	2011	Case control	702	1,578	1.01 (0.66-1.56)
Alavanja et al	1992	Case control	610	1,402	2.7 (1.4-5.4)
Brenner et al	2011	Case control	886	1,765	1.4 (0.9-2.1)
Brown et al	2005	Cohort	196	9,087	3.54 (1.93-6.42)
El Zein et al	2010	Case control	756	512	0.93 (0.5-1.7)
Brownson et al	2000	Case control	676	700	1.1 (0.7-1.7)
Colak et al	2015	Cohort	5,691	94,079	0.6 (0.1-5.1)
Denholm et al	2014	Case control	12,739	14,945	Males 0.44 (0.24-0.79) Females 0.64 (0.28-1.43)
Vesterinen et al	1993	Case control	895	77,952	Males 1.32 (1.22-1.42) Females 1.66 (1.39-1.94)
Boffeta et al	2002	Case control	713	92,986	Females 1.62 (1.24-2.08) Males 1.31 (1.10-1.56)

270 THE CLINICAL FEEDING EVALUATION HAS POOR RELIABILITY IN THE ASSESSMENT OF PEDIATRIC SWALLOW FUNCTION AND CAUSES DELAYS IN THE DIAGNOSIS OF ASPIRATION.

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Background: The evaluation of pediatric swallow function has historically been a two-step process, with radiologic studies typically obtained only after a clinical feeding evaluation (CFE) raises sufficient concern. Prior studies have suggested inconsistent agreement between CFE and videofluoroscopic swallow studies (VFSS) but these studies included small numbers of patients and showed varying degrees of agreement between the tests; however, there remains reluctance on the part of providers to obtain VFSS in all cases. CFEs are also frequently utilized for follow-up assessments of swallow function to determine if thickening can be weaned. The aim of this study was to determine the reliability of CFE in making the diagnosis of aspiration compared to VFSS in children.

Methods: We retrospectively reviewed the records of all children who had evaluation for oropharyngeal dysphagia by both CFE and VFSS at Boston Children's Hospital from January 2015 to December 2015 and compared the timing of and correlation between these assessments. All clinical feeding evaluations were performed by speech language pathologists and all videofluoroscopic swallow studies were read by attending radiologists.

Results: We evaluated 127 total subjects with a mean age of 8.99±0.68 months who had both CFE and VFSS performed. Presenting symptoms for evaluation included choking (28.3%), coughing (52%), congestion (15.7%), cyanosis (18.9%), noisy breathing (19.7%), recurrent pneumonia (11.8%), poor feeding (33.9%), vomiting (23.6%), and reflux (26.8%). We found poor agreement between the two assessments of swallow function, as shown in the tables. The CFE incorrectly identified 61.3% of patients as having no oropharyngeal dysphagia when in fact aspiration or penetration was present on VFSS. The two approaches were found to be poorly concordant by McNemar's test (p=0.0004) with sensitivity 43%, specificity 63%, positive predictive value 67.3%, and negative predictive value 38.7% of CFE compared to VFSS. Follow-up CFEs compared to follow-up VFSS testing also showed poor correlation (p=0.001). Failure to detect aspiration on initial clinical feeding evaluation led to a 26.5±12.3-day delay in obtaining a confirmatory VFSS in children with aspiration who were found to have a normal CFE compared to those who had an abnormal CFE (p<0.05).

Conclusions: There is poor agreement between the clinical feeding evaluation and VFSS results. The evaluation of oropharyngeal dysphagia in young children should always include an assessment of VFSS as clinical feeding evaluations are inadequate to assess swallow function and lead to delays in making a diagnosis of aspiration.

Table 1: Comparison between Clinical Feeding Evaluation and VFSS Findings

	Aspiration	Penetration	Normal
Clinical Feeding Evaluation	40.9% (52)	0% (0)	59.1% (75)
VFSS	39.4% (50)	24.4% (31)	36.2% (46)

Data are expressed as % (n)

Table 2: Disagreement between Clinical Feeding Evaluation and VFSS Results

		VFSS Results		
		Aspiration/Penetration	Normal	Total
CFE Results	Aspiration/Penetration	27.6% (35)	13.4% (17)	40.9% (52)
	Normal	36.2% (46)	22.8% (29)	59.1% (75)
Total		63.8% (81)	36.2% (46)	100% (127)

Data are expressed as % of total (n)

271 IMPEDANCE PH MONITORING IN CHILDREN WITH GASTROESOPHAGEAL REFLUX AND RESPIRATORY SYMPTOMS.

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Gastroesophageal reflux is one of the most frequent causes of pediatric and gastroenterology consultation and when the symptoms are associated with respiratory symptoms the diagnosis becomes a challenge. In patients with unexplained respiratory symptoms, some association with gastroesophageal reflux has been sought, overdosing and initiating unnecessary medical or surgical treatment. Impedance-pH monitoring is a method that could describe acid, weakly acidic and alkaline

reflux allowing a more precise diagnosis and evaluate if respiratory symptoms are secondary to gastroesophageal reflux. The objective of the present study was to describe the findings found in impedance-pH monitoring in children with respiratory symptoms and gastroesophageal reflux.

Material/Methods. Patients with clinical suspicion of gastroesophageal reflux and respiratory symptoms sent to the department of the Gastroenterology of a third-level pediatric hospital between January 1, 2013 and May 30, 2016. These patients were submitted to impedance-pH monitoring to confirm the diagnosis. The following data were obtained from the clinical files: age, sex, respiratory symptoms (chronic cough, recurrent upper airway infections, recurrent pneumonias, life-threatening events, stridor, cyanosis), reflux index, acid reflux (PH <4), weakly acidic (pH 4-7) and non-acidic (pH > 7), and likelihood of association of symptoms, as well as the final diagnosis, regardless of whether or not they had pathological reflux. For the statistical analysis we use descriptive statistics, and the X2 test to compare the number of patients diagnosed with reflux with phmetry vs impedance.

Results. A total of 45 patients were studied, 24 were female (53.3%), with a mean age of 39.5 months, 20 patients had chronic cough, 11 upper respiratory tract infections, 14 recurrent pneumonias, 8 ALTE (Apparent life threatening events), 11 wheezing, and 1 cyanosis.

The findings of pH impedance monitoring are summarized in Table 1. Of the 45 patients, 24 patients had acidic or weakly acidic reflux. Of these, 21 only had acid reflux and 3 had weak acid reflux, a non-significant p (p 0.073) was obtained when comparing the number of patients diagnosed with GER by pHmetry vs impedance test.

The findings of the ph-impedance monitoring were described according to the symptoms (Table 2)

Conclusions. Respiratory symptoms may be secondary to gastroesophageal reflux, 53% of our population had this association. On the other hand, only 3 patients were diagnosed with GER by impedance monitoring, this reinforces the value of pHmetry alone for the diagnosis of reflux

Table 1

	Mean	SD
Episodes of reflux (phmetry)	75.9	99.7
Reflux index	12.7	16.7
Mean clearance time minutes (total)	170.5	179.7
Mean clearance time minutes (upper)	70.6	89.2
Mean clearance time minutes (recumbent)	191.7	246.9
Longest episodes	51.5	88.3
Episode longer than 5 minutes	5.7	8.2
Episodes of acidic reflux (impedance)	19.7	29.2
Episodes of weakly acidic reflux (impedance)	19.3	20.1
Episodes of non acidic reflux (impedance)	.78	2.6

Table 2

Variable	Chronic cough (DE)	Recurrent pneumonias (DE)	Recurrent upper airway infections (DE)	ALTE
Reflux index	8.08 (±2.2)	9 (3.83)	14.9 (5.7)	14.93 (5.08)
Number of acidic reflux	13 (±2.44)	15 (3.24)	38.6 (12.1)	12.3 (3.78)
Number of weakly acidic reflux	16 (±3.76)	20.7 (6.2)	25.43 (7.2)	18.6 (6.5)
Number of alkaline reflux	1 (±1.2)	1.82 (1.43)	0.57 (0.5)	0.13 (0.12)
Symptom association probability (Number of patients)	8	4	2	0

272 PREVALENCE OF ESOPHAGITIS IN CHILDREN AND ADOLESCENTS BEFORE AND AFTER THE ERA OF PRE-ENDOSCOPY PROTON PUMP INHIBITOR USE. Francis Kim¹, Yuanxin Liang², Daniel Rust², Zella Garrett³.¹Pediatrics, Tufts Floating Hospital for Children at Tufts Medical Center, Boston, MA; ²Pathology, Tufts Medical Center, Boston, MA; ³Pediatric Gastroenterology and Nutrition, Tufts Floating Hospital for Children at Tufts Medical Center, Boston, MA

Background: Definitive diagnosis of eosinophilic esophagitis (EoE) can only be made by endoscopy. However, the presence of eosinophils alone does not confirm the diagnosis, as some children have other forms of esophagitis, such as proton pump inhibitor (PPI)-responsive esophageal eosinophilia (PPI-REE) or other forms of acid-related esophagitis. In order to distinguish EoE from non-EoE esophagitis, there has been a shift in the past 7 to 8 years towards starting patients on PPI therapy for 8 weeks prior to the first endoscopy. This practice is useful in potentially saving the child an additional endoscopy if significant eosinophil counts are identified at the first endoscopy after pre-endoscopy PPI use. However, it is possible that underlying PPI-REE or other non-EoE esophagitis cases are being partially treated during the 8 week period of acid suppression, resulting in normal biopsies and potentially misleading prognosis, long-term therapeutic goals, and management decisions.

Aim: We aimed to identify the prevalence of EoE and non-EoE esophagitis before and during the era of pre-endoscopy PPI use. We hypothesized that there would be a significantly lower prevalence of non-EoE esophagitis in the setting of pre-endoscopy PPI use.

Methods: We obtained the first 15-20 consecutive endoscopic pathology reports per season for patients aged 0 to 18-years-old, who underwent endoscopy at our institution in 2007 (before the era of pre-endoscopy PPI use, N = 71) and in 2015 (during the era of pre-endoscopy PPI use, N = 85). Respective patient charts were reviewed for basic demographic information, documentation of high-dose PPI for at least 8 weeks prior to endoscopy (“pre-endoscopy PPI”), and whether the patient underwent endoscopy alone or with colonoscopy. EoE was defined as any biopsy containing ≥ 15 eos/hpf, non-EoE esophagitis was defined as any biopsy revealing inflammation without meeting EoE criteria, and normal biopsies did not contain any inflammation or eosinophils. Relative proportions were compared using chi-squared analyses, with $\alpha = 0.05$.

Results: The average ages of patients who underwent endoscopies in 2007 and 2015 were 10-years-old and 11-years-old, respectively. A higher proportion of patients with non-EoE esophagitis were male ($p < 0.05$), while a higher proportion of patients with normal biopsies were female ($p < 0.05$). There was no statistically significant increased use of pre-endoscopy PPI therapy in 2015 compared with 2007 (47.9% vs 51.8%, $p = 0.63$). There was a higher prevalence of non-EoE esophagitis in 2015 compared to 2007 (20.0% vs 4.2%, $p < 0.05$), and a lower prevalence of normal biopsies in 2015 compared to 2007 (63.5% vs 88.7%, $p < 0.05$). Of patients undergoing endoscopy alone, those with EoE or normal biopsies had significantly higher proportions on PPI therapy in 2015 compared to 2007, respectively (70.0% vs 16.7%, $p < 0.05$; or 58.3% vs 20.6%, $p < 0.05$), while there was no statistically significant difference in the proportion of patients with non-EoE esophagitis on PPI therapy when comparing years (63.6% vs 33.3%, $p = 0.35$). Of those on a pre-endoscopy PPI, there was a higher prevalence of non-EoE esophagitis in 2015 compared to 2007 (22.7% vs 2.9%, $p < 0.05$), and still 18.1% and 5.1% had evidence of EoE in 2015 and 2007, respectively ($p = 0.44$).

Conclusions: Despite a practice trend toward pre-endoscopy PPI use since 2007, we found no significant difference in PPI use when comparing endoscopies from 2007 and 2015. Contrary to our hypothesis, we observed an increase in prevalence of non-EoE esophagitis in 2015, a decrease in prevalence of normal biopsies, and no significant difference in the prevalence of EoE. In combination, these data suggest that current practice trends of pre-endoscopy PPI use may not be masking esophagitis.

273 PEDIATRIC EOSINOPHILIC ESOPHAGITIS IS NOT A RARE DISEASE IN UTAH. Jacob Robson¹, Rafael Firszt², Amber McClain¹, Krishna Mutyala¹, Raza Patel¹, Cassandra Davis², Carlos Barbagelata¹, Kathryn Peterson³, Molly OGorman¹, Stephen Guthery¹. ¹Pediatrics, Gastroenterology, University of Utah / Primary Children's Hospital, Salt Lake City, UT; ²Pediatrics, Allergy, University of Utah / Primary Children's Hospital, Salt Lake City, UT; ³Internal Medicine, Gastroenterology, University of Utah, Salt Lake City, UT

Background: Eosinophilic esophagitis (EoE) is an immune mediated inflammatory disease, which can lead to significant esophageal symptoms and is unlikely to remit without life-long medical management. EoE is currently classified as a rare disease, with prevalence consistently reported as less than 60 cases per 100,000 people. However, perception amongst pediatric gastroenterologists is that EoE is a relatively common disease. Herein, we report the annual and 5-year pediatric EoE incidence in Utah.

Methods: In Utah, pediatric endoscopists submit tissue biopsies to pathologists who report in a common, searchable pathology database. We searched this repository for all patients <18 years old (at the time of endoscopy) who had an esophageal biopsy between 2012-2016, with a pathology report containing keywords: “eos,” “eosinophil (-ic, -ia, -s),” or “EoE.” All patients with esophageal eosinophilia underwent medical record review. EoE cases required all of the following criteria, based on recent consensus guidelines: 1) symptoms of esophageal dysfunction, 2) 15 or more esophageal eosinophils in at least one high power microscopy field (HPF), 3) disease isolated to the esophagus, AND 4) exclusion of other co-morbid conditions known to cause esophageal eosinophilia. Disease incidence was calculated using Utah Census Bureau data.

Results: Esophageal biopsies were performed in 9,025 unique pediatric patients during the study window. Of 1,276 patients with 15 or more eosinophils in a HPF, 217 were excluded: 86 were not from Utah, 23 had no esophageal symptoms, 27 were found to be diagnosed with EoE prior to the study window, 59 had eosinophilic gastrointestinal disease and 22 had a co-morbid syndrome known to cause eosinophilia. We identified 1,059 incident cases of EoE in the past 5 years. The average annual EoE incidence per 100,000 child-years in Utah over the course of the study was 23 and the cumulative 5-year incidence was 112. The demographics of our EoE population were similar to previously reported population-based pediatric data: the majority were male (69%), Caucasian (91%) and diagnosed by a pediatric gastroenterologist (90%).

Conclusions: Incident cases from this study period alone show that EoE is not a rare disease in Utah. The incidence reported here is almost 2-fold higher than the previously reported highest pediatric EoE rate and has been stable over the past four years. We speculate this is due to the prevalence of known EoE risk factors in Utah, including Caucasian predominance, high atopy rates, high EoE penetrance through large families, and high levels of air pollution. Identifying EoE as a common disease is important. This will likely stimulate disease awareness, prompt early referral to pediatric gastroenterologists and spur future research. Earlier disease diagnosis and optimal medical management will be key in the prevention of long-term EoE complications.

Pediatric EoE Cases in Utah: 2012-2016

	2012	2013	2014	2015	2016
New EoE Diagnoses	165	221	228	227	218
Utah Pediatric Population	925316	932013	941985	948765	958167
Annual Incidence	17.8	23.7	24.2	23.9	22.8
Cumulative Incidence over the 5-Year Study Window	17.8	41.5	65.7	89.6	112.4

Incidence calculations based on cases per 100,000 child-years

274 **PROVIDER FOCUSED RANDOMIZED CLINICAL TRIAL TO IMPROVE DIAGNOSIS AND MANAGEMENT OF INFANT REGURGITATION AND GASTROESOPHAGEAL REFLUX DISEASE.**

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Objective: Non-adherence to clinical guidelines for infant regurgitation leads to over-diagnosis of gastroesophageal reflux disease, misdiagnosis of other conditions, over prescribing unnecessary medications and unnecessary medical testing. We hypothesized that provider focused interventions using the electronic medical record (EMR) would improve diagnosis and management of infant regurgitation and gastroesophageal reflux disease.

Methods: We conducted a prospective, randomized clinical trial among 34 primary care providers over a 20 week timeframe.

Results: Our results demonstrated that initial baseline training among both groups (N=34 providers) improved diagnoses of infant regurgitation rate from 0.53% (6/1121 infants) to 1.30% (17/1310 infants), p=0.19; and gastroesophageal reflux disease diagnoses in both groups was reduced from 5.00% (56/1121 infants) in the prior month to 3.59% (47/1310 infants) p=0.12. After the first four weeks of the clinical trial, the intervention group regurgitation diagnoses was 1.82% (12/660 infants) compared to 0.77% (5/650 infants) of controls, p=0.09; and infant gastroesophageal reflux disease was in the intervention group 3.33% (22/660 infants) compared to 3.85% (25/650 infants) of controls, p=0.71. After 20 weeks, the intervention group regurgitation diagnoses was 1.23% (49/3169 infants) compared 1.01% (32/3169 infants) of controls, p=0.02, and infant gastroesophageal reflux disease was in the intervention group 4.25% (136/3169 infants) compared to 3.28% (109/3169 infants) of controls, p=0.15.

Conclusions: Initial baseline training and intervention demonstrated some success in changing provider practice for infant regurgitation and gastroesophageal reflux disease, yet overtime providers tended to regress back to baseline performance. EMR focused interventions alone may not be sufficient to change provider clinical practice.

275 **PEDIATRIC EOSINOPHILIC ESOPHAGITIS: IN OFFICE AND UNDER THE MICROSCOPE.**

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Background: Eosinophilic esophagitis (EoE) is a chronic immune mediated state of eosinophil predominant esophageal inflammation manifesting as a myriad of symptoms such as abdominal pain, vomiting, dysphagia and feeding difficulties. EoE is considered a clinicopathological disease, with symptoms of esophageal dysfunction in the setting of ≥ 15 eosinophils/

hpf in any one of the biopsies from the mid or distal esophagus in spite of adequate acid suppression. As no single symptom, endoscopic or histological finding is pathognomonic for the disease, diagnosis and continued surveillance can be challenging. This study aimed to assess the association between clinical symptoms, eosinophilic inflammation and esophageal site involvement in children with EoE.

Methods: Retrospective data was collected for seventy two (72) children aged 17 years and under, diagnosed with EoE, who underwent treatment at University of Maryland Medical Center between January 2012 and June 2015. Study participants were identified with the ICD9 code for EoE: 530.13. Data collected during this study included clinical symptoms, histological findings at the time of diagnosis and with first follow up biopsy following treatment initiation. Patients were divided into two groups based on the eosinophilic burden: > 15 eosinophils/hpf and <15 eosinophils/hpf. Clinical symptoms of five domains: abdominal pain, vomiting, reflux, dysphagia, and poor weight gain (weight <10th percentile for age) were summed to generate Symptom Scores ranging from 0-5. Data were analyzed using Chi square test of independence and Fishers exact test.

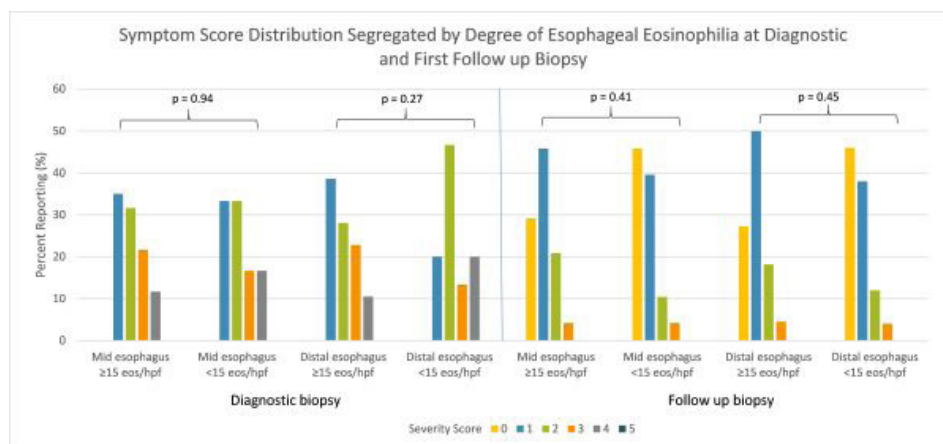
Results: Data was collected for seventy two (72) children, with demographics demonstrating a predominance of age less than 10 years (75%), male gender (61%), and atopy such as asthma (35%), eczema (36%) and allergic rhinitis (58%), which is similar to the findings reported by recent studies. No statistically significant association was found between symptom burden and the degree of eosinophilia. Symptom score remained similar across the disease location as well. In mid esophagus, the frequency of reporting a Symptom Score of 1 at diagnosis was similar in both the groups (33% for <15/hpf and 35% for ≥15/hpf), regardless of the degree of eosinophilia. Similarly, the frequency of reporting Symptom Score 4 were comparable at 12% and 17% between these groups (Fig. 1). The symptom burden decreased after instituting therapy, with no patient reporting a Symptom Score of 4 when assessed after initial treatment. About 63% subjects presented with inflammation affecting both mid and distal esophagus. In subjects with only one segment of the esophagus involved, the mid and distal areas were affected with equal frequencies (19% and 18% respectively) (Table 1).

Conclusions: With this study, we conclude that there is no association between the symptoms reported and the degree of esophageal eosinophilia. As this is true across the disease location, there seems to be a tendency for EoE to present with eosinophilia in both the mid and distal esophagus. However, when the disease presents with a patchy distribution, it is not likely for one segment to be more involved than the other. Data also corroborates the existing diagnostic criteria for EoE by supporting that both the mid and distal portions of the esophagus are equally necessary and essential in adequate assessment of disease activity. Since this study didn't find any association between clinical symptoms and biopsy findings, we suggest that true diagnosis and monitoring of disease cannot be reliant on clinical symptoms alone.

Further, we have previously reported data on patients with primarily distal esophageal involvement who responded well to the diet therapy and/or Topical steroid therapy (TST). This study also helps us to conclude that not all distal segment eosinophilia represents Gastroesophageal reflux disease (GERD), and should be carefully evaluated for EoE, in the context of clinical symptoms.

Table 1: Location of eosinophilic inflammation on diagnostic biopsy

	Eosinophilic inflammation (%) (N=72)	Missed diagnosis with single biopsy (%) (N=72)
Mid esophagus	14 (19%)	13 (18%)
Distal esophagus	13 (18%)	14 (19%)
Mid and distal esophagus	45 (63%)	0 (0%)



276 VITAMIN D RECEPTOR AS A REGULATOR OF EOSINOPHIL ACTIVATION IN EOE.

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Background: Eosinophilic esophagitis (EoE) is a chronic immune-mediated inflammatory disease characterized by increased eosinophils in the esophagus. Eosinophil recruitment to the esophagus is abnormal, and their presence and activation *in situ* is considered to mediate pathology associated with EoE. Esophageal remodeling can occur in EoE through several mechanisms including activation of transforming growth factor- β (TGF- β) and phospho-Smad2/3. Identification of which patients develop fibrosis is not known. Vitamin D receptor (VDR) signaling can inhibit TGF- β 1/Smad3 signal transduction on fibroblasts in fibrotic disease states. Although eosinophils express VDR, the effects of VDR on TGF- β regulation in eosinophils is unknown. We hypothesized that dysregulation of eosinophil VDR function promotes TGF- β release by eosinophils in EoE.

Methods: Blood collected from 21 pediatric patients evaluated for EoE from Jan-Feb 2017 was used to purify eosinophils by magnetic bead separation. Purity and basal activation of eosinophils were determined by flow cytometry based on scatter properties and expression of surface markers. Purified eosinophils were used for two different assays. First, gene expression of VDR- and TGF-associated genes (*VDR*, *RXRB*, *RXRA*, *TGFA*, and *TGFB*) was compared between patients and controls. For this, eosinophil RNA was extracted with an RNA purification kit and 50 ng of each sample was converted to cDNA. Gene expression was determined by qPCR with an ABI7500 Sybr green system using *HPRT1* as the housekeeping gene for normalization. Changes in gene expression were determined using the $2^{-\Delta\Delta Ct}$ method as a fold change over non-EoE patient eosinophils. Second, eosinophil response to 1,25(OH)₂D was determined. For this, purified eosinophils were exposed to 500 nM vitamin D and analyzed 24 hours later for changes in activation markers CD40, CD69, CD80, CD86, MHC I, and MHC II by flow cytometry. Flow cytometry data were analyzed by FlowJo software to determine changes over vehicle control.

Results: In our cohort, 24% were diagnosed with EoE (Table 1). Peripheral blood eosinophils were MHC I^{hi}, CD44^{int}, and CD69^{lo} at baseline. Eosinophils from EoE patients had reduced *VDR* expression and increase in *TGFB* expression compared to non-EoE controls. In addition, *RXRA* and *TGFA* were downregulated in eosinophils from EoE patients. While vitamin D treatment stimulated eosinophil activation *in vitro*, there were no significant differences in activation markers between EoE and non-EoE patient eosinophils.

Conclusions: Our preliminary studies show that eosinophils may have altered gene expression based on disease status and that peripheral blood eosinophils are responsive to vitamin D stimulation. Our current data are from a limited number of patients and collected as test data to validate assays. Ongoing studies in our lab will delineate the impact of VDR stimulation on TGF- β production by eosinophils. The successful completion of studies will help determine if vitamin D can benefit patients with EoE.

Demographics

	Control	EoE
Total Patients	16 (76%)	5 (24%)
Mean Age	11.3±4y	8.1±4y
Sex (%Male)	44%	100%
Race (%Non-Hispanic Caucasian)	68.88%	80%

277 INDIVIDUALIZED DIET THERAPY BASED ON FOOD CHALLENGES IN CHILDREN AND ADOLESCENTS WITH EOSINOPHILIC ESOPHAGITIS.

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Background: Dietary elimination is a common approach to pediatric patients with eosinophilic esophagitis (EoE). An empiric elimination of common food triggers has become a mainstay of dietary elimination. The six food elimination diet (SFED) restricts cow's milk, soy, egg, wheat, nuts (peanuts/tree-nuts), and fish/shellfish. It is the most common empiric elimination diet for EoE but may be either overly- or under-restrictive based on an individual patient's allergies. Optimally, food

elimination in EoE is limited to only the foods the patient definitively reacts to. In order to achieve this goal, a wider array of potential food triggers must be considered, and patients must be re-evaluated as dietary changes are made.

Methods: We followed patients with EoE at our center as they underwent food challenges based on a combination of allergy testing and empiric adjustment in their diet. Each diet change was followed by an endoscopy with biopsy to assess disease activity. Patients were classified as responding to dietary elimination if they had less than 15 eosinophils (eos) per microscopic high powered field (HPF) on esophageal biopsies and as being in remission if they had 5 or less eos/HPF. Results from patients between July 2015 and the present are detailed.

Results: A total of 228 food challenges were done in 70 patients during the study period (3.25 challenges per patient). 101 foods were tested with 54 leading to recurrence of esophagitis. Some foods tested contained multiple ingredients. 52 of 70 patients (74%) were responders to food elimination, 46 (65%) of whom were in remission. Excluding 11 patients who were also on swallowed corticosteroids, 81% responded and 72% were in remission. 26 patients (37%) reacted to a food not included in a SFED and would have failed SFED. 29 patients (41%) tolerated a food included in SFED and would have had an overly restricted diet on SFED. The most common food involved in failed trials was apple. When patients were challenged with top-six antigens, the failure rates were similar for milk (40%), wheat (42%), fish (44%), and nuts (42%), and lower for soy (13%) and egg (27%).

Conclusions: Individualized diet therapy based on a series of food eliminations and re-introductions demonstrated 54 different foods that led to active EoE, suggesting the breadth of potential food antigen triggers in EoE is underappreciated. Using sequential removal and reintroduction, we achieved a histologic response in 74% of our patients and remission in 65%. These results are comparable to previously reported success rates using SFED. Steroid users were less likely to achieve response and remission. Excluding this difficult to treat subset, response and remission rates were higher than seen traditionally with SFED (81% and 72%, respectively). In our population at least 37% of patients would have failed SFED, making individualized diet therapy superior. Additionally, SFED would have been overly restrictive in 41% of our patients. When challenged with top-six antigens, soy and egg were more likely to be tolerated than milk, wheat, fish, and nuts. We believe individualized therapy is a superior approach to empiric dietary elimination in pediatric EoE.

278 **CLINICAL ASPECTS OF DIETARY THERAPY IN CHILDREN WITH EOSINOPHILIC**

ESOPHAGITIS. *Jonathan Wong, Susan Goodine, Zhu Wang, Wael Sayej. Pediatrics, University of Connecticut, Hartford, CT*

Background: Objective evaluation of dietary elimination in the treatment of eosinophilic esophagitis (EoE) requires pre and post-elimination diet endoscopy with biopsy. The appropriate length of treatment with dietary elimination before repeating the endoscopy has never been evaluated. This study seeks to further investigate factors that may contribute to the success or failure of dietary therapy.

Design/Methods: A retrospective study of patients who had been treated for EoE at Connecticut Children's Medical Center (CCMC) was conducted. Data was obtained from a database of all children with EoE (n = 345) maintained by the Division of Digestive Diseases, Hepatology and Nutrition at CCMC. Potential confounders for this study included compliance and ancillary therapies such as medications. Endoscopy results of patients treated with dairy free diet (DFD), dairy and soy free diet (DFSFD) or six-food elimination diet (SFED) were examined. Additional variables examined included presence of atopy (asthma, eczema, allergic rhinitis), prior treatment with PPI, concomitant treatment with PPI, and pre-treatment endoscopy findings. Diagnosis of EoE was based on the presence of ≥ 15 eos/HPF and response defined as < 15 eos/HPF. The target population for this research was all patients diagnosed with eosinophilic esophagitis.

Results: Overall, we identified 300 patients who were started on dietary therapy. 154 patients were excluded due to non-compliance, lost to follow-up, or insufficient data. 146 patients (Age 9.1 ± 5.2 yrs, 77% male) met the inclusion criteria for initial treatment with DFD (n=102), DFSFD (n=10), or SFED (n=34). A subset of 16 patients were initially treated with DFD but failed and were subsequently treated with SFED as a secondary therapy (Age 8.9 ± 4.9 yrs). Response rate was found to be 58/102 (57%) for DFD. Of those, 11 underwent therapy for < 10 weeks, 22 between 10-12 weeks, and 69 were treated for > 12 weeks. Response rates were 82%, 50%, and 55% respectively. Response rate for DFSFD was found to be 5/10 (50%). Of those, 3 underwent therapy for < 10 weeks, 3 between 10-12 weeks, and 4 were treated for > 12 weeks. Response rates were 67%, 33%, and 50% respectively. Response rate for SFED was found to be 20/34 (59%). Of those, 9 underwent therapy for < 10 weeks, 10 between 10-12 weeks, and 15 were treated for > 12 weeks. Response rates were 78%, 50%, and 53% respectively. Response rate for SFED as a secondary therapy was 6/16 (38%). Of those, 7 underwent therapy for < 10 weeks, 4 between 10-12 weeks, and 5 were treated for > 12 weeks. Response rates were 57%, 50%, and 0% respectively. Overall, average age was 9.7 ± 5.3 yrs for responders and 8.6 ± 5.0 yrs for non-responders. Statistical analysis of previously mentioned variables with respect to responders vs. non-responders was largely insignificant. Concomitant treatment with PPI's was found

to be associated with better outcomes (P=0.012) and atopic disease in patients undergoing SFED as a secondary therapy was associated with failure to respond (P=0.008).

Conclusion(s): Patients with shorter intervals between endoscopy after treatment with dietary therapy led to higher response rates. Patients undergoing dietary intervention with concomitant PPI had higher response rates than those that did not. For primary therapy, treatment response was not dependent on presence of atopy, however patients who failed DFD and subsequently failed SFED were more likely to have atopic disease than those who responded.

Primary Therapy				
DFD				
	<10 weeks	10-12 weeks	>12 weeks	Total
Failure	2	11	31	44 (43%)
Response	9	11	38	58 (57%)
Response Rate	82%	50%	55%	
DFSFD				
	<10 weeks	10-12 weeks	>12 weeks	
Failure	1	2	2	5 (50%)
Response	2	1	2	5 (50%)
Response Rate	67%	33%	50%	
SFED				
	<10 weeks	10-12 weeks	>12 weeks	
Failure	2	5	7	14 (41%)
Response	7	5	8	20 (59%)
Response Rate	78%	50%	53%	
Secondary Therapy				
SFED				
	<10 weeks	10-12 weeks	>12 weeks	
Failure	3	2	5	10 (62%)
Response	4	2	0	6 (38%)
Response Rate	57%	50%	0	

279 SOCIOECONOMIC FACTORS PREDICT TREATMENT CHOICE IN EOSINOPHILIC

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Introduction: Eosinophilic Esophagitis (EoE) is a chronic immune-mediated inflammatory disorder of the esophagus. Primary treatment choices include topical corticosteroids or elimination diet. The effect of socio-economic factors on treatment choice in EoE has not been previously studied.

Methods: Subjects with EoE, previously consented to a prospective database were included in this cross-sectional study. Parents were administered a phone survey regarding their initial treatment choice (swallowed steroid/diet elimination). Socio-economic factors including parental education, household income, treatment cost, side effects, convenience and ease of treatment were addressed. Patients were stratified into diet and steroid groups for analysis. Mann-Whitney, fisher's exact, logistic regression were used for analysis with p<0.05 considered significant.

Results: 91/125 patients (mean age 6 years, 79% male, 90% Caucasian) were reached by telephone and completed the survey. 64 (70%, 95%CI 0.6-0.8) selected elimination diet, and 27 (30%, 95%CI 0.2-0.4) selected treatment with topical steroids. There were no differences in gender, age, or race between the two groups. Parents expressed concern for weight loss (9%), nutritional deficiencies (8%) and the multiple invasive procedures required for elimination diet (6%). Concerns with steroids

included effects on bone density (10%), growth (21%), behavior (14%), and excessive weight gain (6%). Adjusted for age and gender, higher income, higher education and concern for medication side effects were predictors of elimination diet selection ($p<0.05$). Factors influencing steroid treatment selection included cost, ease of maintaining therapy and concern for cross contamination ($p<0.05$).

Conclusion: Cost, convenience, ease of treatment, side effects, and cross-contamination are significant factors that affect treatment choice in children with EoE. Higher income and education level are associated with selection of elimination diet. This study identifies parent reported barriers that influence treatment choice and are thus critical to consider when discussing treatment options with parents of children with EoE.

Socioeconomic factors differ between diet elimination and swallowed steroid patients

Characteristic	Elimination Diet	Swallowed Steroid	p-value
Age [Mean +/- SD]	6.1 +/- 4.4	6.6 +/- 4.6	0.64
Gender [Male N(%)]	49 (76.6)	23 (85.2)	0.41
Maternal education (Median)	College Graduate	College Graduate	0.03
Paternal (Median)	College Graduate	Some College	0.003*
Household Income (Median)	76-100k	51-75k	0.01*
Convenience (Mean +/- SD)	0.8 +/- 2.6	6.9 +/- 3.8	$p<0.0005^*$
Ease of Treatment (Mean +/- SD)	1.4 +/- 3.1	6.5 +/- 3.9	$p<0.0005^*$
Concern for side-effects (Mean +/- SD)	6.7 +/- 3.8	2.2 +/- 3.9	$p<0.0005^*$
Cost of Rx (Mean +/- SD)	0.2 +/- 1.3	1.0 +/- 2.7	0.04*
Cross-Contamination [N(%)]	13 (20)	13 (48)	0.01*

280 DO SYMPTOMS RELIABLY IDENTIFY ESOPHAGEAL STRICTURE IN PATIENTS WITH

ESOPHAGEAL ATRESIA? Julie Khlevner¹, Charlotte Hawks², William Middlesworth³. ¹Department of Pediatrics, Columbia University Medical Center, New York, NY; ²Institute of Human Nutrition, Columbia University Medical Center, New York, NY; ³Department of Surgery, Columbia University Medical Center, New York, NY

Introduction: Esophageal atresia/tracheoesophageal fistula (EA/TEF) is a complex congenital aerodigestive anomaly with an estimated incidence of 1 in 2500-4000 live births. Patients with EA/TEF may experience many associated complications, including esophageal stricture, gastroesophageal reflux disease (GERD), Barrett esophagus, esophageal dysmotility, dysphagia and chronic lung disease, all of which can adversely affect health related quality of life. Of these complications, an anastomotic esophageal stricture, defined as a narrowing at the level of esophageal anastomosis, is the most common. Despite this, there are no widely accepted criteria that determine when anastomotic narrowing, which is almost always present, can be called a stricture. Initial treatment is dilation, with multiple described methods (bougies, trans-endoscopic balloons, fluoroscopically guided balloons). Intralesional steroid injection or mitomycin-C have been employed to treat refractory strictures. Recognition of esophageal stricture depends on clinical signs and symptoms that vary with age. Dysphagia, food impaction, vomiting and nutritional failure are among these symptoms. Respiratory symptoms like cough, congestion, recurrent respiratory infections or hoarseness can also be caused by esophageal stricture. But these signs/symptoms are non-specific, and may also be caused by esophageal dysmotility or GERD. Conversely, anastomotic stricture may be present without symptoms, especially in infants, whose oral intake is exclusively liquid. Examining symptom correlation with presence of a stricture is imperative to guide and improve patient care.

Aims: To determine whether symptoms reliably predict the presence of an esophageal stricture in infants and children with repaired EA/TEF, and whether patients with “long gap” esophageal atresia have a higher rate of stricture than those with standard gap atresia.

Methods: The study population is 79 pediatric patients followed in the EA/TEF clinic, founded at Columbia University Medical Center in 2013. Clinic patients underwent diagnostic testing either for routine surveillance or for clinical suspicion for stricture, and were identified through retrospective chart review. 59 patients (31M/28F, median age 1.9 years) who

underwent esophagram, esophagogastroduodenoscopy (EGD) or both were included in the analysis. A total of 215 diagnostic tests were performed on these 59 patients. Symptoms recorded in the medical record within one month of a diagnostic test were included in the analysis, and were correlated with presence or absence of a documented esophageal stricture. We performed a subset analysis on 12 patients with “long gap” esophageal atresia (based on the operative note) to assess whether or not long gap atresia was associated with increased risk of recurrent stricture.

Results: 59 patients underwent 215 diagnostic studies; 77/215 (36%) studies demonstrated a stricture. 26/77 (34%) were performed on infants (<1 year of age); 31% of the time, the infant was asymptomatic. 51/77 (64%) were performed on children (age 1 to 19 years); 14% of the time, the child was asymptomatic. 138/215 (64%) diagnostic studies showed no stricture. Of these, 54/138 (39%) tests were performed in infants. 89% of the time the test was performed in infants with symptoms suspicious for stricture, and 11% of the time the infant was asymptomatic. 84/138 tests (61% of negative studies) were performed in children. 85% of the time, the child had symptoms at the time of the study, and 15% of the time they did not. Feeding difficulty was the most common symptom in both infants and children. Subset analysis of the 12 patients with long gap EA/TEF showed that patients required an average of 16 dilations per patient compared to the standard gap patients, who had an average of 4 dilations per patient to achieve symptomatic relief.

Conclusions: Swallowing difficulty is common among children with EA/TEF, and does not reliably indicate the presence of esophageal stricture. In fact, the majority of patients in our study population with symptoms (both infants and children) did *not* have an esophageal stricture (89% and 85% of the time respectively). A significant number of asymptomatic infants were found to have a stricture, suggesting that surveillance testing may be important in this age group. Conversely, 70% of infants with symptoms of stricture had a negative diagnostic study suggesting that clinical symptoms are not good predictors of stricture in this age group. Children with strictures are more likely to have clinical symptoms than are infants, though symptoms do not reliably predict presence of stricture with any confidence. Finally, patients in our study population with long gap esophageal atresia are at an increased risk of stricture and require more dilations to relieve symptoms.

283 **SIZE AND PREVALENCE OF PEDIATRIC AERODIGESTIVE PROGRAMS IN 2017**

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Background: Multidisciplinary pediatric Aerodigestive programs appear to be part of an increasing movement towards providing coordinated care to complex, medically-fragile children at medical centers throughout North America and the world. Pediatric gastroenterologists are considered an essential part of these programs. As Aerodigestive programs proliferate, little is known about the number of centers, how they function, who are the key providers, and which pediatric specialty provides leadership for these programs. We hypothesized that Aerodigestive multidisciplinary programs are increasing in size, prevalence, and in the number of patients that they serve. Our survey set out to identify the number, type (key provider components), duration (i.e. time in formal existence), size, and numbers of patients served by pediatric Aerodigestive programs.

Methods: The new NASPGHAN Aerodigestive Special Interest Group leadership created an 11-question survey to characterize programs in terms of size, patient volume, and leadership. The survey was submitted to the PEDS-GI list serve, as well as re-administered to specific healthcare centers known to have an Aerodigestive program who did not respond to the initial mailing.

Results: Thirty-four programs responded; twenty-five were based in academic centers, 1 in a private practice setting and 8 represented a hybrid of private and academic settings. Programs were diffusely located (based on US Census Bureau classification): 6 (17.6%) northeast, 6 (17.6%) midwest, 7 (20.5%) southeast, 8 (23.5%) west, and 3 (8.8%) southwest. 4 (11.8%) were internationally based: 1 in Canada, 2 in Europe, and 1 in Central America. The mean (SD) time that the Aerodigestive programs were in existence was 5.3 years (SD 4.3 range 1-17 years). For each program, there was a lead primary specialty driving the program growth and development; 12 programs identified gastroenterology as the primary specialty, 15 identified otolaryngology as the primary specialty, and 4 identified pulmonary as the primary specialty. The average number of gastroenterologists seeing patients in the Aerodigestive programs was 2 (SD 1.1). The mean number of half day clinic sessions per month per center averaged was 2.8 (SD 2.9). The mean number of procedure days for combined “triple” scopes per month was 2.6 (SD 2). There was a wide range of patients seen in these programs; the mean number of total patients (new patient and follow up) seen per year in each program was 184 (SD 168, range 10-750).

Conclusion: Pediatric Aerodigestive programs are becoming increasingly prevalent across North American and the world. Our survey showed that the centers are predominantly based in academic settings. The number of patients cared for by Aerodigestive centers varies widely depending on size and age of program. Our observations suggest the need for the creation of additional subspecialty interest groups to represent the multi-disciplinary nature of Aerodigestive medicine, better definitions of key providers needed for optimal function of Aerodigestive programs, as well as critical resources needed to maintain quality and growth and key questions for research.

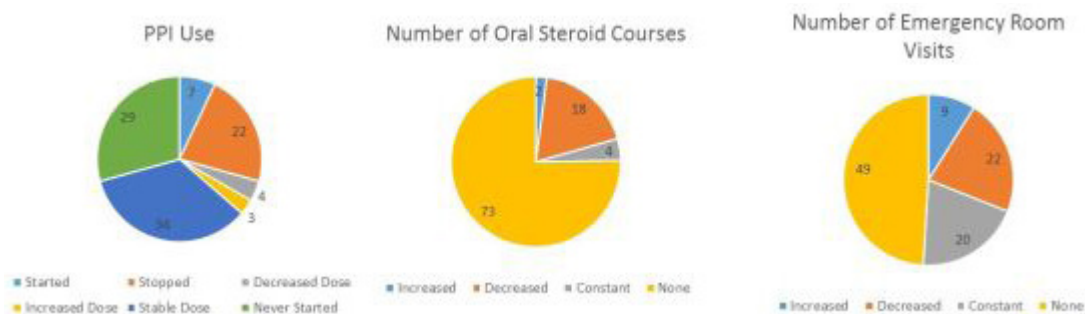
284 AN IMPROVEMENT IN QUALITY OF CARE FOR PATIENTS SEEN IN A MULTIDISCIPLINARY AERODIGESTIVE PROGRAM. Neerav Dharia¹, Kara May², Thomas Martin², Eitan Rubinstein¹, Kara Larson¹, Lisa Hester¹, Rachel Rosen¹. ¹Gastroenterology, Boston Children's Hospital, Boston, MA; ²Pulmonology, Boston Children's Hospital, Boston, MA

Background: Oropharyngeal dysphagia/aspiration is a common diagnosis in aerodigestive clinics and there is significant variability of management of these patients and there is very little that has been published on the outcomes of these patients. It was the goal of this study to determine if there is evidence for improvement in care when patients are seen by pulmonary, gastroenterology, and feeding therapists at the same visit.

Methods: We retrospectively reviewed 45 consecutive patients presenting with a history of aspiration on videofluoroscopic swallow study who were followed for at least 6 months within the aerodigestive clinic. We reviewed the patterns of PPI prescribing before and within 1 year of the visit and the frequency of oral thickening before and within one year of the visit. We also reviewed the history to determine if there were reductions in oral steroid use and ER visits, in the 6 months after the initial visit compared to the 6 months before the visit.

Results: The mean age of patients at the time of the initial visit was 13.8±12.8 months. 36% of patients aspirated thick liquids, 33% aspirated nectar thick liquids, 14% aspirated honey, and 17% aspirated purees. Eighty percent of patients received oral thickening as a result of the initial swallow study. Changes in PPI prescribing, oral steroid courses and emergency room visits are shown in the Figure. 58% of patients never started a PPI, stopped their PPI or had a dose reduction in their PPI prescriptions in the year after their initial aerodigestive visit. 18% of patients had a reduction in the number of oral steroid courses they received and 22% of patients had a reduction in their number of ER visits in the 6 months after the visit compared to the same time interval before the visit.

Conclusion: Visits to a coordinated program result in a reduction in PPI use, a reduction in oral steroid use and a reduction in ER visits. Additional studies are needed to determine if there is an associated reduction in cost or quality of life.



285 EMSY IS INCREASED IN CHILDREN WITH EOE AND ACTIVATES TSLP EXPRESSION.

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Background: Genome wide association study data show a strong association between eosinophilic esophagitis (EoE) and a novel gene locus, c11orf30-EMSY, whose role is unknown in the esophageal epithelium. Initially described as a breast cancer-associated protein that interacts with the breast cancer protein 2 (BRCA-2), recent studies have shown that EMSY is a transcriptional regulator of a variety of genes. The function of EMSY in the esophagus has yet to be defined.

Objective: To investigate the role of EMSY in normal esophageal epithelium as well as in EoE. Specifically, we measured EMSY RNA levels in children with EoE and we silenced EMSY in immortalized esophageal epithelial cells in order to determine the effects on expression of epithelial-derived mediators important in EoE pathogenesis.

Methods: RNA was isolated from esophageal biopsies of control and EoE patients with either active or inactive esophagitis. Gene expression was determined using digital multiplex gene expression analysis (Nanostring). An immortalized human esophageal epithelial cell line was then transfected with either silencing RNA (siRNA) targeting EMSY mRNA or “All Stars” negative control siRNA using a lipofectamine RNAiMAX protocol. TaqMan gene expression primers for EMSY, calpain 14 (CAPN14), interleukin (IL)-33, and thymic stromal lymphopoietin (TSLP) were utilized in real time-PCR experiments in order to assess gene expression. Western blot confirmed reduction in EMSY protein expression.

Results: In Nanostring experiments, EMSY is significantly upregulated in active EoE biopsies compared to controls and inactive EoE. Successful transfection of esophageal epithelial cells with EMSY siRNA resulted in the following changes in gene expression: 61% reduction in EMSY, 41% reduction in TSLP, 77% reduction in CCL5, and no significant change in CAPN14 or IL33. Western blot analysis confirmed a 61% reduction in EMSY protein expression.

Conclusions: EMSY is significantly increased in biopsies of children with active EoE. Inhibiting the gene expression of EMSY results in repression of the epithelial derived cytokine TSLP. This suggests that EMSY may be important in EoE pathogenesis by inducing the activation of TSLP, a crucial cytokine in EoE pathogenesis.

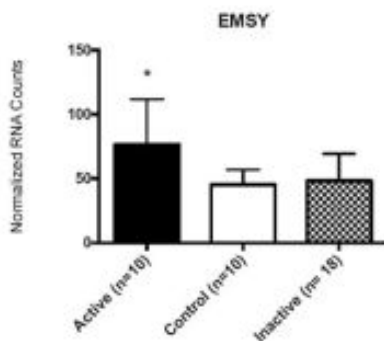


Figure 1. EMSY Expression in Active EoE, Inactive EoE and Control Patients.

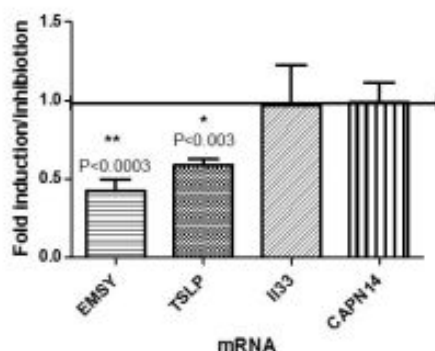


Figure 2. Changes in Gene Expression.

286 QUALITY OF LIFE IN CHILDREN WITH TYPICAL AND ATYPICAL SYMPTOMS OF GASTROESOPHAGEAL REFLUX. Lisa Mahoney, Rachel Rosen. *GI/Nutrition, Boston Children's Hospital, Boston, MA*

Introduction: Symptoms of gastroesophageal reflux can have a significant impact on quality of life (QOL) in children. Adult studies suggest that patients with typical esophageal symptoms have worse QOL scores compared to patients with atypical or extraesophageal manifestations. However, little is known about the impact of reflux symptom type on QOL in children.

Methods: We performed a prospective study of 47 children ≥ 5 years of age who were undergoing multichannel intraluminal impedance with pH (pH-MII) testing and upper endoscopy for evaluation of suspected gastroesophageal reflux. The pH-MII study was considered abnormal if there was > 73 reflux episodes or if the pH < 4 for $\geq 6\%$ of the study. Patient reported QOL scores were assessed using the validated Pediatric Gastroesophageal Symptom and Quality of Life Questionnaire (PGSQ), which provides subscales for symptom burden as well as daily, school and total impact. Higher scores indicate

more significant impact on daily life. Previously reported mean scores for healthy control patients are < 0.2. Symptoms reported during pH-MII were categorized into typical reflux symptoms (heartburn, chest pain, epigastric abdominal pain and regurgitation) and atypical reflux symptoms (cough, dysphagia, throat clearing, gagging, nausea, vomiting, spitting, hoarseness, gulping and dyspnea). Children with erosive esophagitis, eosinophilic esophagitis, prior thoracic or abdominal surgeries, esophageal motility disorders, significant developmental delays which would preclude symptom reporting, cystic fibrosis, and those who did not report symptoms during the impedance study were excluded.

Results: The mean PGSQ score was 0.96 ± 0.66 for the symptom sub-score, 1.45 ± 3.42 for the impact on everyday life sub-score, 0.56 ± 0.92 for the school sub-score and 1.03 ± 0.72 for the total score. There were no significant differences in PGSQ total and sub-scores in patients who reported typical symptoms and those who reported atypical symptoms ($p > 0.06$). When examining individual symptoms reported during pH-MII testing, patients who reported heartburn had a worse QOL with higher symptom ($p = 0.04$), school ($p = 0.04$) and total scores ($p = 0.03$) compared to patients without heartburn. Patients reporting pain had higher symptom ($p = 0.01$) and total ($p = 0.03$) scores. Reports of nausea during pH-MII was associated with higher symptom ($p = 0.008$), school ($p < 0.0001$) and total ($p = 0.03$) scores. Patients reporting vomiting had a higher total score ($p = 0.02$). There were no differences in QOL scores for any other symptoms. Twenty-eight percent of patients had an abnormal pH-MII study and 19% of patients had microscopic esophagitis present on histology. Neither reflux/acid burden on pH-MII testing nor the presence of microscopic esophagitis had any significant impact on QOL scores ($p > 0.17$).

Conclusions: There are no significant differences in QOL scores in children with typical versus atypical reflux symptoms. Specific reports of heartburn, pain, nausea and vomiting during pH-MII testing are associated with worse QOL scores. Abnormal reflux or acid burden on pH-MII and the presence of microscopic esophagitis is not associated with worse QOL scores.

287 OUTCOMES OF INFANTS WITH SEVERE MILK-SOY PROTEIN INTOLERANCE TREATED WITH MESALAMINE FOR PERSISTENT SYMPTOMS DESPITE AMINO ACID BASED FORMULA FEEDING. *Maria Rojas Gallegos, Karen Crissinger. Pediatrics, University of South Alabama, Mobile, AL*

Methods: Retrospective chart review from January 2009 to December 2012. All infants less than 12 months old treated with mesalamine were selected and a parallel group was used as a control. Statistical significance was calculated using Fisher's exact test and a two-tailed p value was obtained with significance at $p < 0.05$.

Results: A total of 580 patients with MSPI were identified. 50 patients were treated with mesalamine and 44 met inclusion criteria. On FS 59% had evidence of lymphonodular hyperplasia in the rectosigmoid colon. Biopsies revealed duodenitis (>10 eosinophils/hpf) in 82% with proctocolitis in all infants with an average of 20 eosinophils/hpf in both sites. 38 infants (86%) also underwent an esophageal pH study, 34% were positive for GE reflux. Before mesalamine was started, infants were on AAF for an average of 1½ months. Fecal occult blood test (FOB) was positive in 36%. The most common symptoms included spitting up/vomiting (100%), irritability/fussiness (93%), watery or hard stools (93%), choking/gagging (84%) and visible blood and/or mucus in the stools (81%). Other symptoms included gassiness, hiccoughs, refusal to eat/decreased appetite, back arching and congestion/coughing/wheezing. The average age of initiation of mesalamine treatment (dose 40-60 mg/kg/day) was 3½ months for an average time of 100 days (range 13 – 222 days). After treatment only 2 patients continued to have a positive FOB test. Two patients discontinued mesalamine due to 1 who developed a black tongue and 1 who had coughing that started on mesalamine and resolved on discontinuation. As compared to infants who received only AAF, those who received adjunctive mesalamine had significantly higher rates of improvement in symptoms of food refusal (82.6% vs 25%, $p=0.0001$), spitting up or vomiting (81.6% vs 38.1%, $p=0.0001$), and watery or hard stools (55.2 vs 15.8%, $p=0.0001$). Symptoms of back arching, choking/gagging and respiratory problems were somewhat improved. Other symptoms did not differ significantly between the groups. In addition, the mesalamine group was less likely to be diagnosed with failure to thrive and more likely to tolerate the introduction of cow's milk (85% vs 22%) or soy milk (42.3% vs 22%) at 15 and 14 months, respectively. Before mesalamine 84% of patients were also receiving treatment with a histamine H2 antagonist (HH2A) and 53% with a proton pump inhibitor (PPI). After initiation of mesalamine treatment, HH2A treatment decreased to 57% and PPI treatment to 25%.

Conclusions: The addition of mesalamine to treatment with AAF in infants with persistent proctocolitis led to improvement of the most common symptoms of severe MSPI and was associated with improved tolerance to introduction of cow's milk or soy milk after 12 months of age. An incidental finding was that despite nearly 100% clinical reflux symptoms in these patients, only 34% had a positive pH impedance study. Effective treatment of MSPI resulted in decreased use of HH2A and PPI medications. In conclusion, a short course of mesalamine may be beneficial adjunctive therapy for infants with refractory symptoms and persistent proctocolitis despite AAF feeding.

***288 COMPARING COMBINATION THERAPY WITH PROTON PUMP INHIBITORS AND TOPICAL STEROID VERSUS TOPICAL STEROID ALONE FOR THE TREATMENT OF EOSINOPHILIC ESOPHAGITIS.** Matthew Heisel^{1,2}, Judy-April Oparaji^{1,3}, Thomas Baker⁴, Fouad Moawad⁵, Steve Min¹. ¹Department of Pediatrics, Walter Reed National Military Medical Center, Bethesda, MD; ²Pediatric Gastroenterology Fellowship Program, National Capital Consortium, Bethesda, MD; ³Pediatric Residency, National Capital Consortium, Bethesda, MD; ⁴The Joint Pathology Center, Defense Health Agency, Silver Spring, MD; ⁵Department of Medicine, Walter Reed National Military Medical Center, Bethesda, MD

Background: Proton pump inhibitors (PPI) are used in patients with Eosinophilic Esophagitis (EoE) as a tool to fulfill diagnostic criteria, as well as for treatment. Understanding of the anti-inflammatory mechanisms behind the PPI's therapeutic effects on EoE has grown in recent years, specifically with its ability to downregulate the expression of the chemoattractant eotaxin-3 through an acid-independent pathway. Interestingly, a recent in-vitro study showed increased suppression of eotaxin-3 secretion in esophageal epithelial cells derived from patients with EoE, when they were treated with both fluticasone and omeprazole together, than when treated with either drug alone. Our aim was to compare the histologic outcomes of patients with EoE between those treated with combined PPI and topical steroid versus those treated with topical steroid alone.

Methods: We performed a retrospective cohort study using the Walter Reed National Military Medical Center (WRNMMC) EoE registry consisting of 366 subjects diagnosed with EoE at WRNMMC between 2006 and 2015. Subjects were included if they underwent an esophagogastroduodenoscopy (EGD) showing ≥ 15 eosinophils (eos)/high power field (hpf) while on PPI therapy for at least 4-8 weeks, and then underwent a repeat EGD following treatment with 8-10 weeks of either topical steroids (swallowed fluticasone or viscous budesonide) or topical steroid plus PPI. Exclusion criteria included PPI responsive esophageal eosinophilia (PPI-REE), additional gastrointestinal autoimmune disease (ie, celiac, IBD), less than 4 weeks of PPI treatment before the initial EGD, and the use of systemic steroid treatment within 4 weeks of an EGD. Ultimately, 52 adult and pediatric subjects met strict inclusion/exclusion criteria and were included in the analysis. 31 subjects with EoE received treatment with both topical steroid and PPI, while 21 received treatment with topical steroid alone. The primary outcomes were the number of subjects with positive treatment response (defined as < 15 eos/hpf following treatment) as well as the overall change in peak esophageal eosinophil counts following treatment, for each of these therapy groups.

Results: The two exposure groups were not significantly different from one another with respect to gender, ethnicity, age, comorbid atopic disease, or type of topical steroid used. The mean (\pm SD) peak esophageal eosinophils in the pre-treatment biopsies were similar in the combination therapy group (61.7 ± 55.8 eos/hpf) and the topical steroid only group (72.6 ± 64.7 eos/hpf, $p=0.52$). Mean (\pm SD) peak esophageal eosinophils in the post-treatment biopsies were also similar between both groups, with combination therapy group having mean of 46.0 ± 68.9 eos/hpf and the topical steroid group having a mean of 22.2 ± 28.1 eos/hpf ($p=0.16$). The topical steroid group had a larger proportion of subjects with a positive treatment response (57%), than the combination therapy group (45%); however, the difference was not statistically significant ($p=0.40$). There was no significant difference between the change in peak esophageal eosinophils before and after therapy (Mean (\pm SD) of **50.4 ± 70.1 eos/hpf in the topical steroid group compared to 15.8 ± 83.7 in the combination group $p=0.13$**).

Conclusion: We found no significant difference in treatment response, or histology (peak esophageal eosinophils) between subjects with EoE treated with combination PPI with topical steroid versus those treated with steroid alone. This limited retrospective cohort study is, to our knowledge, the first attempt at clinically investigating this question. Further prospective studies are needed to examine the clinical utility of PPI and topical steroids for the treatment of EoE.

FUNCTIONAL/MOTILITY

290 GROUP TREATMENT OF FECAL INCONTINENCE: A DESCRIPTION OF AN INTERDISCIPLINARY INTERVENTION. Kelsey Gonring³, Bridget Dolan^{2,3}, Theresa Kapke^{2,3}, Andrea Begotka^{3,1}, Manu Sood¹, Alan Silverman¹. ¹Pediatrics, Medical College of Wisconsin, Milwaukee, WI; ²Department of Clinical Psychology, Marquette University, Milwaukee, WI; ³Children's Hospital of Wisconsin, Milwaukee, WI

Introduction: Fecal incontinence is a widespread problem during childhood, affecting approximately 5% of children in the U.S.. We have previously shown that families of children with fecal incontinence are also likely to experience poor family functioning, including higher rates of family conflict and caregiver psychiatric symptoms. Joint NASPGHAN and ESPGHAN constipation guidelines have highlighted the importance of caregiver and patient education in ensuring treatment compliance and success of medical management. Yet, approximately 20% of patients fail medical management alone. The goal of the current study is to evaluate combined medical-behavioral group-based treatment for fecal incontinence in school-aged children and to present a description of clinical effectiveness.

Method: The current study included children, ages 5-8 years, and their caregiver(s). Poop Group is a 6-week, caregiver-assisted, protocolized evidence based group intervention combining behavioral therapy and medical management for families of children with fecal incontinence. Families were referred after failing standard medical care of fecal incontinence with constipation following NASPGHAN guidelines for clinical management. Child and at least one caregiver attended each session. The intervention consisted of sessions focusing on: (1) physiology of fecal incontinence, (2) medication management, (3) toilet sits, (4) hydration, (5) fiber, and (6) behavioral contracting. Families were followed as individual patients after the conclusion of group. Outcomes were evaluated by caregiver completed measures of stooling frequency, stool quality, soiling events, medication adherence, and dietary habits. Weekly nurse practitioner and psychologist clinic notes were also reviewed as a method of validating caregiver reports. After groups caregivers were given the opportunity to provide feedback in the form of an open-ended satisfaction questionnaire.

Results: Twenty families were enrolled into the study and 19 had complete data. 47% were reported to have improved appropriate stooling frequency ($Z=1.98$, $p = .048$), 79% had reduced soiling ($Z=-3.10$, $p = .002$), and medication adherence was improved from 47% to 95% pre- to post treatment and maintained at 1-month follow up. Caregivers reported improved condition knowledge and higher levels of peer and professional support.

Conclusion: Group treatment of fecal incontinence is an effective and efficient means of treatment. Children and caregivers alike seem to benefit from the peer support and interdisciplinary treatment approach. Treatment effects are sustained for a short duration past the conclusion of the group sessions.

291 PERCUTANEOUS ELECTRICAL NERVE FIELD STIMULATION (PENFS) INCREASES VAGAL TONE IN ADOLESCENTS WITH FUNCTIONAL ABDOMINAL PAIN DISORDERS. *Katja Kovacic¹, Adrian Miranda¹, Thomas Chelimsky², Liyun Zhang¹, Pippa Simpson¹, Gisela Chelimsky¹. ¹Department of Pediatrics, Medical College of Wisconsin, Brookfield, WI; ²Department of Neurology, Medical College of Wisconsin, Milwaukee, WI*

Background: Novel and non-invasive therapies for functional abdominal pain disorders (FAPDs) are scarce. We have recently demonstrated efficacy of a novel auricular neurostimulation device (NeuroStim®, Innovative Heath Solutions, IN, USA) in adolescents with FAPDs. This device delivers percutaneous electrical nerve field stimulation (PENFS) to branches of cranial nerves including the auricular branch of the vagus nerve (CN X). Anatomical tracing studies show that these branches project to brainstem nuclei including the nucleus tractus solitarius. Preliminary animal data from our group confirms that PENFS modulates the firing of vagal efferent fibers. The aim of this study was to determine if PENFS influences vagal (parasympathetic) tone in adolescents with FAPDs.

Methods: A total of 115 adolescents ages 11-18 were enrolled in a prospective, randomized, double blind, sham-controlled trial from an outpatient, tertiary care pediatric gastroenterology clinic. All patients met Rome III criteria for at least one FAPD based on the Rome III diagnostic questionnaire (QPGS III). Subjects were randomized to active vs sham PENFS therapy for 5 days per week x 4 consecutive weeks. The PENFS device delivers 3.2V of stimulation with alternating frequencies of stimulation (1 and 10Hz), cycling 2 hours on/2 hours off for 5 days. The sham device was identical but without electrical charge. A subset of subjects underwent heart rate variability (HRV) testing before (pre) and 8-12 weeks after the last week of therapy (post). Three minute HRV recordings were performed in supine, sitting and standing positions. HRV data was analyzed using Kubios software and the root mean square of successive differences (RMSSD) and high frequency (HF) domain were used as a surrogate of vagal tone. Low frequency (LF) domain was also analyzed.

Results: Data was obtained at two time points (pre and post) on 45 subjects (27 PENFS; 18 sham). 91% of the entire cohort were female. The mean age of the PENFS group was younger (14.2 years) than the sham (15.4 years) ($p=0.034$). Median time to follow up (post) was 9.2 weeks. The RMSSD standing (mean \pm SD) parameter showed significant improvement from pre (40.9 ± 25.9) to post (68.1 ± 47.9) time points ($p<0.00001$). In contrast, the sham group did not show any increase in standing RMSSD from pre to post treatment ($p=0.845$). Other positions (supine, sitting) did not show similar changes in the treatment group. The HF power similarly increased significantly from pre (1016.5 ± 1110.9) to post (2436.1 ± 2793.8) in the treatment group ($p=0.001$) while there was no improvement in sham ($p=0.711$). The LF power also improved in the treatment group from pre (646.9 ± 718.4) to post (1225.5 ± 1474.1) ($p=0.009$), and did not improve in the sham group ($p=0.845$). These increases were also reflected in the total power in the treatment group pre (1759.5 ± 1726.2) to post (3828.3 ± 4130.5) ($p=0.001$) but not in the sham ($p=0.913$).

Conclusions: PENFS as opposed to sham therapy, modulates several indices of HRV which correlates with increased vagal tone in adolescents with FAPDs. The improvement in the standing position only likely reflects strengthening of the baroreceptor stress response. The results indicate that the effects are sustained up to two months following neurostimulation therapy. Vagal efferent modulation through peripheral stimulation may be an important mechanism responsible for the therapeutic effects of this novel technology.

292 USE OF MULTIDIMENSIONAL CLINICAL PROFILES (MDCP) TO CHARACTERIZE PEDIATRIC PATIENTS WITH PAIN-PREDOMINANT FUNCTIONAL GASTROINTESTINAL DISORDERS (FGID).

Beate Beinvogl¹, Elizabeth Burch¹, Julie Snyder Christiana¹, Neil Schechter², Fiona Paul¹, Karen Warman¹, Yoshiko Okazaki¹, Amelia Sparrow¹, Samuel Nurko¹. ¹Gastroenterology, Boston Children's Hospital, Boston, MA; ²Anesthesiology, Perioperative and Pain Medicine, Boston Children's Hospital, Boston, MA

Children with Functional Gastrointestinal Disorders (FGID) can be severely disabled and difficult to treat. Severity is a guiding factor in clinical decision-making but current treatment guidelines do not address this. There is growing evidence that disease severity is a multidimensional concept. Multidimensional clinical profiles (MDCP) in children and adolescents were introduced in the recent Rome IV criteria with the goal to provide a comprehensive, individualized understanding of patients, incorporating the bio-psycho-social aspects of the individual's illness experience. There is no literature available evaluating the utility of applying the MDCPs in the diagnosis of FGID in Children or Adults.

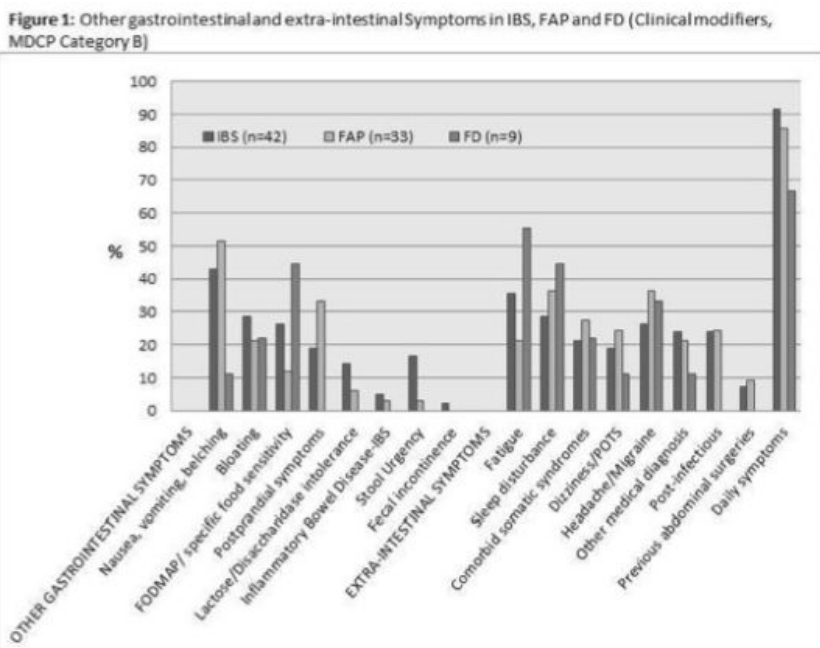
Method: A retrospective review of 84 patient charts was performed. All patients were seen in a multidisciplinary pain clinic and met ROME III criteria for Functional Abdominal Pain (FAP), Irritable Bowel Syndrome (IBS) or Functional Dyspepsia (FD). All were referred for intractable pain and/or severe disability. Patients were classified based on the MDCP profile including the Primary diagnosis per ROME III (Category A), Clinical modifiers including other gastrointestinal and extra-intestinal symptoms (Category B), Impact on daily life based the Functional Disability Index (FDI 0 = none, FDI 1-12 = mild, FDI 13-29 = moderate, FDI 30+ = severe) (Category C), Psychosocial Modifiers including Anxiety, Depression, PTSD, Abuse, Traumatic life events (Category D) and Physiologic Modifiers including objective abnormalities of wall structure or activity, motility, sensitivity or inflammation (Category E). Primary outcome are the relative frequencies of clinical, psychological and physiological modifiers and degree of disability within the selected FGIDs. These were compared across groups with an ANOVA.

Results:

Demographics: Gender distribution was 73.8% female and 26.2% male (n=84); Mean age was 15.07±2.74 years; Mean duration of symptoms prior to presentation was 25.8±30 months. Patients were seen for 2.1±2.4 follow-up visits.

Classification based on MDCP: Category A: FAP 39.3%, IBS 50% and FD 10.7%. IBS-subtypes included 37.5% IBS-Constipation, 37.5% IBS-Mixed and 25% IBS-Diarrhea. Category B: Figure 1 shows the relative frequency of gastrointestinal and extra-intestinal clinical modifiers. Category C, D and E are detailed in Figure 2.

Conclusion: Classification based on MDCP profiles confirms the complexity and multidimensional nature of IBS, FAP and FD, and the need for a multidisciplinary treatment approach. There is significant overlap of disability, clinical, physiological and psychosocial modifiers but also characteristic differences between these FGIDs. Further studies are needed to assess the applicability of MDCP classification, which may facilitate risk stratification and/or more targeted therapy in the future.



293 FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS AND TODDLERS: PRIVATE CONSULTATION VERSUS HEALTHY CHILD CONSULTATION. Carlos Velasco-Benitez¹, Eder Villamarin¹, Jose Gomez^{2,3}. ¹Pediatrics, Universidad del Valle, Cali, Colombia; ²Universidad Libre, Cali, Comoros; ³Pontificia Universidad Javeriana, Cali, Colombia

Introduction: There are few studies of prevalence in functional gastrointestinal disorders (FGDs) in infants and toddlers.

Objective: To determine the prevalence and possible associations of the FGDs in Colombian infants and toddlers from a private and the healthy child consultation from Cali and El Dovia, Colombia.

Methodology: Parents and guardians of infants and toddlers were interviewed from a private clinic in Cali, Colombia (capital city), the healthy child consultation from Cali, Colombia (capital city) and the healthy child consultation from El Dovia, Colombia with the Spanish Questionnaire for FGDs Rome III. Sociodemographic (sex, age, city), family (single child, first-born, divorced/separated parents and intrafamilial DGFs) variables were taken into account. Statistical analysis included measures of central tendency, univariate and bivariate analysis with OR and their respective 95% CI, with being statistically significant a $p < 0.05$.

Results: A total of 963 children, 51.5% of the male gender, 62.2% ($n = 599$) of the private clinic of Cali, 23.7% ($n = 228$) of the consultation of the healthy child of El Dovia and 14.1% of the healthy child consultation of Cali. The prevalence for presenting some FGDs was 26.6%: colic in 1.2% (1-4 months of age), dyschezia in 1.4% (1-5 months of age), regurgitation in 2.0% (1-12 months of age) functional diarrhea in 1.0% (1-48 months of age), functional constipation in 18.2% (1-48 months of age), rumination in 4.2% (1-24 months of age). There was a predominance in the private consultation of the FGDs (OR = 5.0 IC95% 3.0-8.7 $p = 0.0000$) and functional constipation (OR = 3.2 IC95% 1.9-5.6 $p = 0.0000$) and for functional diarrhea in the female gender (OR = 4.3 IC 95% 0.8-41.7 $p = 0.0451$).

Conclusions: One third of the infants and toddlers presented some FGDs, the main ones being functional constipation, rumination and cyclic vomiting syndrome, with predominance of FGDs and functional constipation in the private consultation and the female gender in the functional diarrhea.

294 A MUTATION IN SMOOTH MUSCLE MYOSIN MYH11 CAUSES DOMINANTLY-INHERITED VISCERAL MYOPATHY AND DYSMOTILITY WITH SEVERE ESOPHAGEAL DISEASE, HIATAL HERNIA AND GASTROPARESIS. David Piccoli^{1,3}, Melissa Gilbert^{2,4}, Nancy Spinner^{2,4}, Kristin Fiorino^{1,3}. ¹Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; ²Division of Genomics, CHOP, Philadelphia, PA; ³Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA; ⁴Pathology, University of Pennsylvania School of Medicine, Philadelphia, PA

Background: The majority of motility disorders are idiopathic although multifactorial inheritance has been proposed. The utilization of exome sequencing in patients with gastrointestinal motility defects has identified several associated genes, with the majority of these defects inherited in an autosomal recessive or mitochondrial fashion. We report a 7 member family demonstrating dominant inheritance of a spectrum of motility disorders, in whom we identified a candidate mutation in the *MYH11* gene, which encodes the protein smooth muscle myosin heavy chain 11 (*MYH11*). The MYH11 mutation segregates with the clinical findings which are present in one parent and four of the five children, including a set of monozygotic twins.

Clinical Features: The general clinical features of the family members are presented in Table 1 and include early onset GERD, esophagitis, esophageal stricture and hiatal hernia, manifested by an elevated Z-line and inflammatory esophageal disease with strictures. Symptoms of gastroesophageal reflux, vomiting, dysphagia, and abdominal pain were present in the affected members. Three had significant anemia secondary to esophageal bleeding. In all four children the Z-line was significantly elevated and the underlying gastric tissue was commonly inflamed, and inflammation remained despite medical therapies as assayed by subsequent biopsies. Despite maximal medical acid blocking therapy, three developed strictures requiring repeated dilatations, and 3 of 5 have required fundoplication, with similar plans for the remaining affected members. Gastroparesis was present in two, and in one case was severe and refractory to prokinetics and intra-pyloric botulinum toxin, ultimately requiring jejunostomy feeding and a duodenojejunostomy for draining. Three members underwent high-resolution esophageal manometry, and in each of them the amplitude and propagation of peristalsis was normal only in the skeletal muscle portion of the esophagus with minimal or no detectable muscle activity in the mid and distal esophagus. The LES pressures were low, but generally relaxed normally. In one extensively studied patient, annual gastric emptying studies demonstrated emptying of 1-7% at 30 minutes, 6-10% at 60 minutes, and 16-22% at 120 minutes. Antroduodenal motility demonstrated MMCs but the presence of low amplitude duodenal and jejunal contractions consistent with intestinal myopathy. Colonic motility study demonstrated the absence of contractions consistent with colonic myopathy, and an anorectal manometry study was essentially normal.

Genomic Results: Exome sequencing revealed the presence of a 2 base pair insertion at the end of *MYH11* in all affected family members [NM_022844.2(MYH11):c.5798_5799insCA]. This insertion occurs at the 6th to last amino acid of the SM2 isoform of *MYH11* and is predicted to result in a frameshift that produces an elongated protein product containing 90 unique amino acids additionally.

Conclusions: The presence of this mutation in every family member with significant esophageal disease, including other motility abnormalities, provides strong evidence that *MYH11* variants are a cause of smooth muscle visceral myopathy.

	MYH11 Mutation	Hiatal Hernia	Esophageal Stricture	Abnormal HREM	Gastroparesis	Fundoplication
P1	Yes	yes	unknown	ND	Unknown	Yes
P2	no	-	-	-	-	-
C1	yes	yes	yes	ND	No	Yes
C2	yes	yes	yes	Abnormal	unknown	Yes
C3	yes	yes	no	Abnormal	yes	Pending
C4	yes	yes	yes	Abnormal	presumed	Pending
C5	no	no	no	ND	ND	No

P (parent), C (child), ND (not done), HREM (high-resolution esophageal manometry)

295 PAIN-PREDOMINANT FUNCTIONAL GI DISORDERS: IDENTIFYING VULNERABILITIES AND TRIGGERS IN PEDIATRIC PATIENTS PRESENTING IN A MULTIDISCIPLINARY FUNCTIONAL ABDOMINAL PAIN PROGRAM.

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Background: The genesis of pain-predominant functional gastrointestinal disorders (p-FGIDs) is complex and not well understood. It has been described that many predisposing factors exist but the specific vulnerabilities, environmental influences, genetic factors, and triggers have not been described in a well characterized cohort of patients with p-FGIDs. Furthermore, even though well-defined triggering events such as infections have been described, it is not clear what predisposes patients to develop p-FGIDs. The aim of this study was to define predisposing factors in children with p-FGIDs.

Methods: Retrospective study of a well categorized cohort of patients evaluated in the Multidisciplinary Functional Abdominal Pain Program. Each patient completed a comprehensive intake and was classified per Rome III criteria. Only patients with functional abdominal pain or IBS were included.

Results: 202 patients were reviewed. 71% were female (mean age 13.5 years). The average Abdominal Pain Index score was 26 and Functional Disability Inventory score was 19. Eighty-three percent of patients had an identified trigger and/or vulnerability; a small subset of patients (17%) had neither. Sixty-three percent had a known trigger and 6% had more than one trigger. Identified triggers were GI infection (27%), extra-intestinal infections (11%), psychological stress event (10%), concussion (7%), onset of organic disease (7%), surgery/physical injury (5%), and vaccination/medication reaction (3%). Fifty-four percent had a vulnerability, characterized as developmental delay (13%), sensory sensitivity (24%), or early life event (39%), with 23% of patients having more than one vulnerability. Identified early life events were recurrent infections (9%), colic/reflux (7%), prematurity (7%), difficult pregnancy/delivery (5%), food allergies (3%), feeding intolerance/failure to thrive (3%), hospitalizations (3%), infant hypoxia (1%), and neglect/stress event (1%). There was no statistical significance when comparing vulnerabilities in patients with or without triggers.

Of all patients, 48% had a psychiatric diagnosis at the time of evaluation. There was a positive mental health family history in 64% of patients, and a family history of pain-predominant disorders in 52%. For patients with a psychiatric diagnosis, family histories of mental health disorders (74%) and pain-predominant disorders (57%) were more prevalent. In the subset of patients without a trigger or vulnerability (17%), 35% had a psychiatric diagnosis and 68% had either a family history of a mental health or pain-predominant disorder.

Discussion: Our findings emphasize that patients with p-FGIDs are susceptible to pain conditions due to their genetic makeup, early life experiences, environment, and psychological health. We identified a large percentage of patients with a well-defined trigger, with infections being the most prevalent followed by psychological stressors. A significant amount of patients had a genetic/environmental predisposition, as related to family history of pain and mental health disorders. A small percentage of patients had no vulnerabilities or trigger, but had a high prevalence of family mental health and pain conditions. Our data provides more insight into the pathophysiology of p-FGIDs, and may lead to earlier detection and treatment of patients at risk for the development of these disorders.

298 FAMILY HISTORY OF PAIN IS THE MOST IMPORTANT PREDICTOR OF DISABILITY IN PEDIATRIC PATIENTS DIAGNOSED WITH FUNCTIONAL GASTROINTESTINAL DISORDERS.

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Background: Pediatric patients with FGIDs can present with severe disability. While the predisposing factors that lead to the disability are not known, it has been suggested that psychiatric comorbidities or family history can be contributors.

Aim: Determine the relationship between family history of pain, family history of mental illness and patient psychiatric diagnosis as they relate to the level of disability.

Methods: This is a retrospective study of a well-characterized cohort of pediatric patients meeting Rome III criteria for FGIDs (Functional Abdominal Pain/IBS). Patient mental health history and family pain/mental health history was obtained during the intake evaluation via self/parent report. Severity of abdominal pain was assessed via scores on the Abdominal Pain Index (API); level of dysfunction was measured via scores on the Functional Disability Inventory (FDI).

Results: The charts for 202 patients were reviewed. 71% were female (mean age 13.5 years). 48 % were diagnosed with one or multiple mental health disorders, with more than half being diagnosed with anxiety disorders (53%); depressive disorders (24%) were also prevalent, in addition to neurodevelopmental disorders (11%). 26% of patients were prescribed one or more psychiatric medications; SSRI's accounted for half of all medications prescribed. The mean API score was 26. The mean FDI score was 19; 71% of patients had an abnormal FDI.

As seen in the table we found a significant difference on the FDI when comparing patients with a psychiatric diagnosis, positive family mental health history, and positive family pain history. No differences on the API were found amongst these groups. Through multivariate analysis we found that when controlling for age, gender, known triggers, early life events, family mental health history, family pain history and patient psychiatric history that family pain history was the only significant predictor of an abnormal FDI score (p = .003).

Conclusion: An abnormal FDI is associated with family pain history, family mental health history, and patient psychiatric history; however, the only predictor of abnormal functioning was family pain history. This suggests that family modeling influences disability in this population.

This information provides insight for those conducting evaluations as it speaks to the importance of obtaining a more detailed family history and may offer additional considerations when treating pediatric patients diagnosed with FGIDs.

	Family Mental Health History		Family Pain History		Patient Psychiatric Diagnosis	
	Yes	No	Yes	No	Yes	No
API	26.7 (.7)	25.0 (1.13)	26.5 (.74)	25.6 (1.00)	25.7 (.81)	26.5 (.90)
FDI	20.5(1.24)	16.0 (1.48)	21.5 (1.21)	15.6 (1.50)	21.1 (1.39)	16.8 (1.32)

299 IDENTIFICATION OF EDUCATIONAL GAPS AMONG GASTROENTEROLOGISTS RELATED TO PEDIATRIC CONSTIPATION. Justin Barnes¹, Brandon Coleman¹, Sharon Hwang¹, Aleksandra Stolic², Samuel Nurko³, Athos Bousvaros³, Greg Salinas¹. ¹CE Outcomes, LLC, Birmingham, AL; ²Independent Medical Education & External Affairs, Takeda Pharmaceuticals U.S. A., Inc., Deerfield, IL; ³Boston Children's Hospital, Boston, MA

Background: Approximately one-third of pediatric patient visits to gastroenterologists are related to pediatric constipation. In 2015, NASPGHAN and ESPGHAN developed a clinical guideline based on the available evidence, but it is unclear how frequently the recommendations in the guideline are being followed. With the intention of informing the design of future continuing medical education (CME) programs, we conducted a study of gastroenterologist, gastroenterology nurse practitioner/physician assistant, and primary care physician practice patterns related to pediatric constipation.

Methods: We developed a case-vignette survey, in collaboration with a clinical expert (AB), which featured three patient cases: Case 1, a 3-year-old female, incompletely toilet trained, with a 6-month history of abdominal pain, bloating, and large painful bowel movements; Case 2, a 6-year-old male with a one-year history of constipation despite prior treatment with PEG and senna, and signs suggestive of a potential spinal anomaly; and Case 3, a 16-year-old male patient with a 10-year history of constipation refractory to treatment despite a thorough evaluation and visits to two prior pediatric gastroenterologists. Each case was followed by a series of questions to investigate how healthcare providers diagnose, assess, and manage pediatric patients with constipation. The instrument was pilot tested with two healthcare providers in each target audience, and invitations to the finalized online survey were distributed to a random sample via email. Screening criteria required all respondents to regularly see pediatric patients with constipation.

Results: Responses to the survey were collected, including 197 from gastroenterologists (78% pediatric gastroenterologists). The gastroenterologists saw an average of 45 pediatric patients per week, 36% of whom were being treated for constipation. 63% practiced in an academic setting, 2% in VA/military/government facilities, and the remaining 35% were in private practice. Quantified practice patterns were compared to ESPGHAN/NASPGHAN guideline recommendations, and several opportunities for future CME were identified. In Case 1, stool withholding was the only applicable ROME III diagnostic criteria used by more than 80% of gastroenterologists when performing the initial evaluation. In addition, 85% of gastroenterologists performed more testing than recommended by the guideline in Case 1, while 98% did not perform all recommended tests in Case 2. In Case 3, despite clinical features suggesting depression, 28% of gastroenterologists would not refer for a psychological evaluation. Of note, gastroenterologists generally selected recommended medications for all three patients.

Conclusions: This study identified several key educational gaps: application of the ROME III criteria, matching evaluation approach to patient presentation, and referring for psychological evaluation. Future CME programs focusing on these topics will provide maximal benefit to gastroenterologists and enable optimal care to be delivered to this patient population.

303 FUNDOPLICATION IN ESOPHAGEAL ATRESIA: DOES IT MAKE A DIFFERENCE? Denise Brito¹, Gabriela Gomez¹, Justin Wheeler², Khalil El-Chammas², Ajay Kaul². ¹Pediatrics, Faculdade de Ciências Médicas, Campinas, São Paulo, Brazil; ²Gastroenterology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: Gastroesophageal reflux (GER) is common in children who have had a repair of esophageal atresia (EA) and/or tracheoesophageal fistula (TEF). In many cases, fundoplication surgery is performed to prevent complications of gastroesophageal reflux disease. Little data is available on repercussions of fundoplication on reflux characteristics in these children.

Objective: To compare GER characteristics and esophageal clearance in children with EA/TEF repair with and without fundoplication, using impedance pH-metry (MII-pH).

Methods: The database of Cincinnati Children's Hospital Medical Center was examined to identify all children with EA/TEF repair who had undergone a minimum 18 hour MII-pH study (2007-2014) for dysphagia or feeding disorders. GER characteristics, mode of feeding, esophageal biopsies and co-morbidities were compared in the two subsets.

Results: Twenty-five subjects fulfilled inclusion criteria; seven had fundoplication (2 males, mean age 5 years) and 18 did not (11 males, mean age 6.8 years). Total GER events were similar in those with fundoplication and in those without (median 57 vs 63, P=0.89). Median Reflux Index was 1.9% in the fundoplication subset and 2.6% in those without fundoplication (P=0.69). Median of Mean Bolus-Clearance Time (MBCT) was 18.4 seconds in those who had fundoplication and 12.5 seconds in those that did not (P=0.067). Esophagitis was reported in 71% of those with fundoplication and in 47% in those without (P=0.38). There were more children with genetic syndromes/comorbidities in the fundoplication subset (71% vs 39%, P=0.35) and 83% of them had an enteral device for feeding (compared to 22%, P=0.015).

Conclusion: Even though GER characteristics were similar in the two subsets, there was a trend towards more esophagitis in those that had a fundoplication. Fundoplication surgery was more commonly performed in the more medically complex cohort and this subset was significantly more likely to have an alternative mode of feeding.

306 IMPROVING CONSTIPATION CARE: A UNIQUE PEDIATRIC GASTROENTEROLOGY-PRIMARY CARE CHILDHOOD CONSTIPATION COLLABORATIVE FOR DEVELOPMENT OF A CONSTIPATION TOOL KIT TO ENHANCE DETECTION AND STANDARDIZE MANAGEMENT OF CONSTIPATION IN CHILDREN IN THE AMBULATORY PEDIATRIC DEPARTMENT OF AN INNER-CITY HOSPITAL.

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Introduction: Constipation is common in children with estimated prevalence ranging from 0.7-29.6%. It may become chronic and with associated complications. The most common type is functional i.e., absence of an underlying organic cause. Factors like low-income families, childhood obesity, exposure to stress and conflict, some dietary patterns etc., have shown association with constipation. These factors disproportionately affect some ethnic minorities in the US; many of who utilize Medicaid- supported health insurance. Moreover, there's evidence showing constipation is underreported and, hence, potentially under diagnosed in some groups like African American children. Failure to recognize constipation by parents or pediatricians in a timely manner may lead to chronic symptoms and decrease the likelihood of successful treatment. Thus, under the auspices of CaseCAN- a workforce development program funded by the Ohio Department of Medicaid, Medicaid Technical Assistance and Policy Program (MedTAPP) Healthcare Access (HCA) Initiative SFY 16 and SFY 17, we piloted a model of collaboration between the disciplines of Pediatric Gastroenterology and Primary Pediatrics with the following goals:

1. Increase awareness about importance of early detection of constipation in children using systematic screening in Primary Care.
2. Develop a comprehensive constipation tool-kit to facilitate high quality, evidence-based care.

Methods:

1. We designed a brief, easy-to-understand Bowel Habit Survey Questionnaire (BHSQ) as a screening test to parents of children presenting for well childcare.
2. We have developed a comprehensive constipation tool kit for Pediatricians.

Results: We received 843 patient surveys out of the 1362 surveys administered (62% survey return rate.). The sensitivity and specificity of the Bowel Habit Survey Questionnaire as a screening tool for constipation in well childcare was ~100% and ~80% respectively. Rate of diagnosis of constipation with BHSQ was higher as compared to routine diagnosis of constipation (11.9% observed rate vs. 5.4%, $P < 0.001$; Chi Square).

Conclusions: Active screening for constipation in primary care pediatrics yields a higher rate of constipation diagnosis as compared to routine well childcare. This strategy has the potential for early diagnosis and improved outcomes in childhood constipation. Our comprehensive constipation tool kit is ready. This includes:

1. Electronic health record (EHR) order smartest for pediatric providers; and
2. Interactive, easy-to understand constipation instructional handout for families with low literacy skills.

307 PREDICTORS OF SYMPTOM RELIEF FOR BILIARY DYSKINESIA BY CHOLECYSTECTOMY.

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Biliary Dyskinesia, also known as acalculary biliary pain, is defined as an abnormal emptying of bile from the gall bladder, in the absence of bile stone disease, leading to vague symptoms of abdominal pain and nausea with possible vomiting. Causes can include sphincter of Odi malfunction, poor coordination and/or speed of biliary duct contraction. Biliary dyskinesia was increasingly being diagnosed in the pediatric population during the time of this study. It is unknown if this correlates with increasing BMI seen in the United States. Cholecystectomy has been utilized to remedy biliary dyskinesia. Predicting outcomes based on signs and symptoms or procedures / testing has been difficult. Most surgeons use an ejection fraction (EF) $< 45\%$ as a cutoff for identifying patients for cholecystectomy. Past studies have shown that around 70% of patients with EF $< 45\%$ have abdominal pain relief with cholecystectomy, and that patients with EF $< 15\%$ have better outcomes versus those with EF of 15% to 30%.¹

The aim of this study was to evaluate post-operative symptom relief status-post cholecystectomy for biliary dyskinesia, and to compare symptom relief to pre-operative EF% and BMI in order to determine a correlation and to compare our outcomes to previous studies.

This study looked at patients ages 10 through 18 who underwent cholecystectomy from January 2005 to January 2010 for symptomatic acalculous biliary dyskinesia and had an EF <45%. Ninety-three patients fit the criteria and a retrospective review of demographics, diagnostic tests, medication use, pathology findings, and symptoms and duration were recorded. Univariate analysis was performed between patients with symptoms pre and post-surgery. Logistical regression was performed on BMI versus EF%. Student t-test was also performed.

In our cohort, overall reduction of abdominal pain, RUQ pain, nausea, fat intolerance and weight loss was seen with cholecystectomy for biliary dyskinesia. There was no correlation between EF and BMI. There was no reduction in epigastric pain or diarrhea with cholecystectomy. Patients with a BMI of <25 had better outcomes in regards to abdominal pain resolution with cholecystectomy. An EF <15% vs 15-30% doesn't predict better outcomes as previously shown by other studies.

In conclusion, cholecystectomy continues to be an effective strategy for relief of symptoms from symptomatic biliary dyskinesia, including abdominal pain and nausea with 72% and 67% resolution, respectively, but we failed to correlate pain relief with EF as described previously.¹

1. Carney, D. E., Kokoska, E. R., Grosfeld, J. L., Engum, S. A., Rouse, T. M., West, K. M., ... Rescorla, F. J. (2004). Predictors of successful outcome after cholecystectomy for biliary dyskinesia. *Journal of Pediatric Surgery*, 39(6), 813-816. DOI: 10.1016/j.jpedsurg.2004.02.017

309 **GASTROJEJUNOSTOMY TUBES IN CHILDREN WITH MOTILITY DISORDERS: OUTCOMES AND COMPLICATIONS.**

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Background: Gastrojejunostomy (GJ) tubes are utilized in children in order to support nutrition in patients who are unable to advance enteral feeds to meet caloric goals and/or minimize potential risk of aspiration. Motility disorders are often characterized as feeding intolerance and can be challenging to treat, with GJ tubes placed to reduce symptoms associated with inadequate enteral intake. Although GJ tubes have been used for several years and are generally regarded as safe, there are observed complications. The aim of this study was to describe outcomes and complications after GJ tube placement among children at risk for dysmotility.

Methods: We retrospectively reviewed the records of children who underwent dysmotility evaluation (1- hour Gastric Emptying Study (GES) or antroduodenal manometry (ADM)), had GJ tube placement, and had established follow up at Boston Children's Hospital. Patient medical records were reviewed for primary diagnosis, GJ tube indications in order to determine overall patient characteristics. We retrieved data on complications (i.e. intussusception, coiling, infection, granulation tissue, dislodgement, clogging and leakage) and outcomes which was defined as symptom improvement (advancing feeds or decreasing parenteral nutrition).

Results: There were a total of 105 patients with GJ tubes who had undergone motility evaluation. Indications for GJ tube placement were feeding intolerance (n= 66, 62%), risk for aspiration (n= 19, 18%), or both (n=10, 19%). A total of 79 (75%) patients had complications which included dislodgement (n=18, 17%), granulation tissue (n=16, 15%), leakage (n=14, 13%), clogging (n=10, 10%), coiling (n=9, 09%), infection (n=8, 08%), intussusception (n=5, 05%) and bleeding (n=2, 02%). Complications overall were not associated with abnormal ADM or GES results. We found that overall feeding improvement was observed in 80 (76%) patients, with no correlation to motility study (GES or ADM) outcomes. There were 36 (35%) patients among our cohort with a Nissen fundoplication and GJ tube. Children with a documented response to erythromycin stimulation (EES) on ADM were more likely to have feeding improvement if they also had a Nissen fundoplication (p= .051).

Conclusions: Gastrojejunostomy tubes is an option considered in patients with known abnormal motility, risk for aspiration, and continued feeding intolerance who have failed other forms of medical management. Studies evaluating dysmotility (ADM or GES) prior to GJ tube placement were not predictive of future complications, such as intussusception, or outcomes. There was a tendency towards improved feeding tolerance among children with Nissen fundoplication and response to EES in ADM studies. However, the overall results suggest a limited role of motility testing among children undergoing GJ tube placement.

310 **ALTERED ESOPHAGEAL COMPLIANCE IS SUPERIOR TO DISTENSIBILITY IN QUANTIFYING ESOPHAGEAL HISTOLOGIC REMODELING IN PEDIATRIC PATIENTS WITH EOSINOPHILIC ESOPHAGITIS.**

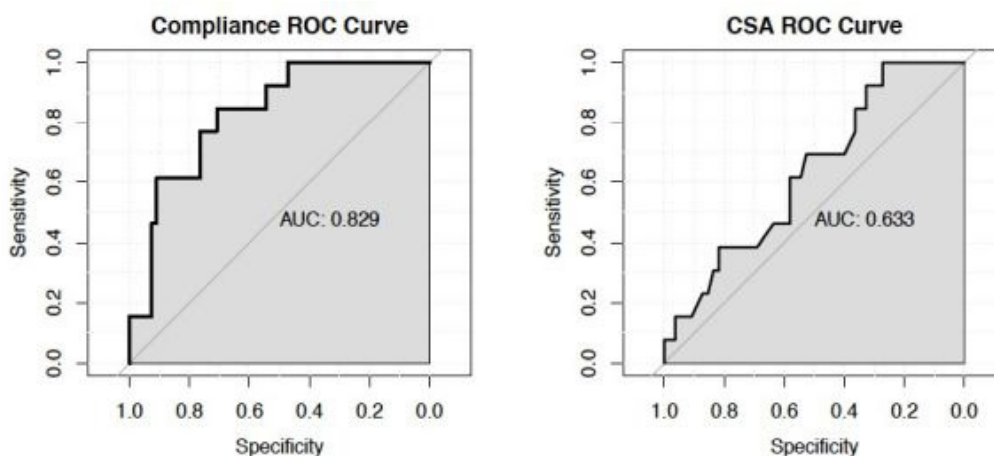
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Background: Management of eosinophilic esophagitis (EoE) relies on the number of eosinophils on esophageal mucosal biopsy and clinical symptoms resulting from esophageal dysfunction. This approach is limited given that underlying esophageal epithelial and fibrotic remodeling can occur in the absence of robust inflammation. We have used Functional Luminal Impedance (FLIP), an FDA approved device, in pediatric patients with EoE primarily to assess esophageal mechanics. Thus far, it's been reported that decreased distensibility in pediatrics is associated with active EoE and when gross remodeling parameters such as esophageal rings and symptoms of dysphagia are present. We aim, in this study, to test the utility of measuring esophageal compliance in addition to the measurement of distensibility.

Methods: In this prospective observational study, we enrolled patients age 5-18yrs who underwent upper endoscopy (EGD) with biopsies for either suspected or established diagnosis of EoE. Based on endoscopic and histologic findings, patients were placed into 2 groups -- group 1: EoE, and group 2: controls. All patients had a FLIP study at the time of the upper endoscopy. FLIP consists of a balloon catheter with 17 electrodes along its length. The balloon is inflated to sequentially higher volumes generating increasing pressure within the esophagus. We calculated esophageal distensibility and compliance for proximal, mid, distal esophageal segments, and for the entire esophagus. Distensibility was represented by the narrowest cross sectional area (CSA_{min}) with maximal balloon inflation. For each esophageal segment, esophageal biopsies were also evaluated for number of eosinophils per high power field, histologic remodeling score, and fibrosis score.

Results: We found that compliance is significantly reduced in EoE patients compared to controls. There is a strong correlation between eosinophilic density, as well as epithelial remodeling score, with decreased compliance. Having an epithelial remodeling score ≥ 2 (compared to < 2), is significantly associated with lower compliance at the proximal, mid, distal and entire esophagus; changes in distensibility had a trend with no significant findings. The area under the ROC curve for compliance as a predictor for epithelial remodeling score ≥ 2 was 0.829 (95% CI: 0.718 to 0.941), while that for distensibility was 0.633 (95% CI: 0.473 to 0.793). The sensitivity and specificity of compliance, when set at 0.66 %ml/mmHg, was also significantly higher than that of distensibility, when set at 217mm² (85% and 70% v. 69% and 53%, respectively).

Conclusion: Compliance is more sensitive and specific than distensibility in detecting epithelial remodeling changes at proximal, mid, distal and entire esophagus. Longitudinal studies are needed to evaluate the changes in esophageal compliance in response to different therapeutic approaches.



311 PREVALENCE OF CELIAC DISEASE AND HYPOTHYROIDISM IN PEDIATRIC PATIENTS PRESENTING WITH CONSTIPATION TO A TERTIARY PEDIATRIC ACADEMIC CENTER. Maireade McSweeney, Beate Beinvoogl, Jessica Kerr, Samuel Nurko. *Gastroenterology & Nutrition, Boston Children's Hospital, Boston, MA*

Background: Limited literature exists as to whether or not routine screening for celiac disease and hypothyroidism should be obtained in patients presenting to a physician's office with functional constipation. Current NASPGHAN guidelines reviewing the evaluation and treatment of functional constipation recommend against the routine screening of hypothyroidism and celiac disease in patients in the absence of alarm symptoms.

Methods: A retrospective review of billing data was conducted of 4,482 patients, >6 months age, presenting to pediatric gastroenterology clinic at Boston Children's Hospital with a new primary diagnosis of functional constipation using ICD-9 and ICD-10 codes when appropriate (564.0X, 560.32, 787.60-.61, K56.41, K56.0X, R15.0, R15.9). Clinic visits between February 1, 2013 and March 31, 2017 were reviewed. Timing of screening laboratory tests for either celiac disease (using

tissue transglutaminase IgA (TTG IgA)) or hypothyroidism (using TSH) were assessed, and billing codes were reviewed to decipher if patients were diagnosed with celiac disease (using 579.0 and K70.0 diagnosis codes) or hypothyroidism (using 244.9, E03.8, E03.9 diagnosis codes) at their initial GI clinic visit or during a subsequent visit.

Results: 4,482 patients presented with a new diagnosis of constipation. 2149 (47.9%) were male. 1,519 (33.9%) patients had a TTG IgA ordered at their first GI visit, and of those screened, 37 (0.8%) were subsequently diagnosed with celiac disease at their initial visit. An additional 80 patients (1.8%) were diagnosed with celiac disease at a subsequent visit. 1,445 patients (32.2%) patients underwent an initial TSH screen at their first GI visit, and of those screened, 11 (0.76%) were diagnosed with hypothyroidism. An additional 15 (0.3%) patients were diagnosed with hypothyroidism at a subsequent visit. 1.2 (0.4, 2.7) months and 6.3 (1.5, 16.1) months were found between patients' first visit for constipation and diagnosis of celiac disease and hypothyroidism, respectively.

Discussion: Although the prevalence of celiac disease and hypothyroidism is low among patients presenting with a primary diagnosis of functional constipation, a subset of patients will go on to develop celiac disease and hypothyroidism and will be missed if no further screening tests are performed. Further research is needed to decipher if certain clinical characteristics can help better predict which patients require additional testing, or if revisions to the national guidelines for the evaluation of secondary causes of functional constipation should be made at patients' initial gastroenterology clinic visit for constipation.

312 ASSESSING CHILDREN'S REPORT OF STOOL CONSISTENCY: THE AGREEMENT BETWEEN THE PEDIATRIC ROME III QUESTIONNAIRE AND THE BRISTOL STOOL SCALE. *Mana Vriesman^{1,2}, Carlos Velasco-Benitez³, Carmen Ramirez⁴, Marc Benninga¹, Carlo Di Lorenzo², Miguel Saps². ¹Gastroenterology and Nutrition, Emma Children's Hospital / Academic Medical Center, Amsterdam, Netherlands; ²Division of Gastroenterology, Hepatology and Nutrition, Nationwide Children's Hospital, Columbus, OH; ³Department of Pediatrics, Universidad del Valle, Cali, Colombia; ⁴Hospital Regional Maria Inmaculada, Florence, Colombia*

Background: The adequate assessment of stool consistency is highly relevant for diagnosis, patient management and the evaluation of the efficacy of treatments for functional constipation (FC) in children. The reliability of child's report of stool consistency has not been previously studied.

Aims: To assess the agreement between the Questionnaire on Pediatric Gastrointestinal Symptoms-Rome III (QPGS-RIII) and the Bristol Stool Scale (BSS) in evaluating stool consistency and the diagnosis of FC in children.

Methods: Children, aged 8-18 years, were recruited from public schools and asked to describe their stool consistency in the previous month according to the QPGS-RIII and the BSS. Stool consistency according to both instruments was categorized into 3 categories: 'hard', 'normal' or 'liquid'. The reported stool consistency using the BSS was compared to the child's report of stool consistency using the QPGS-RIII. The intra-rater agreement between the QPGS-RIII and BSS was measured by using the Cohen kappa coefficient (κ). The diagnosis of FC was based on the Rome III criteria incorporating the assessment of the consistency of the stools per the QPGS-RIII and the BSS.

Results: A total of 1835 children were included. Only slight agreement existed between the QPGS-RIII and the BSS for assessing stool consistency ($\kappa = 0.046$, $p = 0.022$). Significant more children reported hard stools on the BSS compared to the QPGS-RIII (18.0% vs. 7.1%, $p = 0.000$). The prevalence of FC was 8.6% using the QPGS-RIII and 9.3% using the BSS ($p = 0.134$).

Conclusions: Only slight agreement exists between the QPGS-RIII and the BSS in the evaluation of stool consistency in children. Better instruments are needed to assess the consistency of stools with a high degree of reliability, both in research and clinical setting.

314 HOW WE STOPPED ADMITTING CHILDREN FOR BOWEL CLEANOUTS. *Mark Deneau¹, Krishna Mutyala¹, Linda Book¹, Anna Ermarth¹, Stephen Guthery¹, Janet Harnsberger¹, Catalina Jaramillo¹, Daniel Jackson¹, Kyle Jensen¹, Marianne Kavan¹, Amber McClain¹, Molly OGorman¹, Raza Patel¹, John Pohl¹, Jacob Robson¹, David Sandweiss¹, Thomas Sutton¹, Raghu Varier², Christopher Maloney¹. ¹Pediatric Gastroenterology, University of Utah, Salt Lake City, UT; ²Northwest Pediatric Gastroenterology LLC, Portland, OR*

Background: Functional constipation can be effectively managed with home laxative and behavioral therapy in virtually all patients. We noticed a practice of admitting these children from our emergency department (ED) for inpatient bowel cleanouts (IBC) at rates in excess of all other children's hospitals in the US, as well as high rates of manual fecal disimpaction (MFD) procedures in the operating room (OR). We undertook a quality improvement initiative to eliminate these practices for otherwise healthy children with functional constipation.

Methods: We interviewed physician stakeholders throughout our community and also reviewed the electronic medical records of the last 100 inpatient bowel cleanout admissions at our hospital to identify common themes and misconceptions about pediatric constipation management. Major issues identified were beliefs that home bowel cleanouts were ineffective, lack of a definition of a “home bowel cleanout”, under-dosing of home laxatives, under-dosing and underutilization of enemas in the ED, over-use and misunderstanding of the term “fecal impaction”, reliance on abdominal radiographs to diagnose constipation or “fecal impaction” and incorrect interpretation of digital rectal exam findings. Over 18 months we implemented several changes to our hospital policies targeted at directly addressing these themes and misconceptions, including:

1. Elimination of ‘direct admissions’ (without first going through the ED) for IBC,
2. Requiring a discussion with the on-call gastroenterologist prior to any IBC,
3. Limiting the volume of and time over which nasogastric PEG3350 could be administered during IBC,
4. Establishing a standardized definition and dose of outpatient oral laxative bowel cleanouts and requiring all patients to have tried this prior to IBC,
5. Training all ED nurses in a standardized large volume normal saline enema protocol,
6. Requiring administration of least two of these large volume enemas in the ED prior to IBC, and
7. Creating a standardized triage and management algorithm for constipation in our ED that incorporated all of the above points.

We measured the proportion of all children seen in the ED for constipation (as defined by ICD-10 codes) who were admitted for an IBC, and the proportion of admissions that involved a MFD in the OR, in six month blocks before, during and after implementation of the above interventions from 2015-2016. We excluded patients with anorectal malformations, neuromuscular disorders, and violent behavioral disorders since the interventions were not targeted at these populations.

Results: There were 1,106 visits to our ED for a primary diagnosis of constipation during the study period. Prior to our interventions, 10.1% of patients were admitted from the ED for IBC, and 21.9% of admissions involved MFD in the OR. During the intervention these rates dropped to and 3.6 and 8.3%, respectively. After all interventions, only 1.2% of ED visits for constipation resulted in admission for IBC and no child with functional constipation underwent a MFD procedure in the OR.

Conclusions: A multifaceted quality improvement initiative nearly eliminated the practice of admitting otherwise healthy children with functional constipation to our hospital for IBC or MFD.

315 CONSTIPATION IN TODDLERS: THE UNTOLD STORY. Mark Fishbein^{1,2}, Kathryn Benton⁴, Maria Manuel-Rubio³, Rychlik Karen², Miguel Saps³. ¹*Pediatric Gastroenterology, Northwestern University, Chicago, IL;* ²*Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL;* ³*Pediatric Gastroenterology, Nationwide Children’s Hospital, Columbus, OH;* ⁴*Pediatric Psychology, Northwestern Medicine Cadence Health, Winfield, IL*

Chronic constipation is a common occurrence in toddlers and frequent reason for referral to physicians. Stool withholding and toileting refusal are confounding factors and often attributed to typical behavioral and developmental tendencies for this age. However, there has been little attention given to elements of sensory processing disorder that could have an influential role. Sensory processing disorder (SPD) has been linked to autism and other developmental disorders, yet research has also shown that many typically developing children exhibit features of SPD that impact functioning and adjustment. SPD has not yet been studied in chronic constipation of early childhood, particularly in the general population. Yet, skills impacted by different types of sensory processing are necessary to bowel train. These may include proprioception (body awareness), touch, and registration (awareness of input). In addition, young children with sensory issues affecting bowel training may exhibit sensory processing difficulties in other areas such as visual, auditory and oral input. When children do not receive the best input from their senses, they struggle to tolerate daily sensory experiences such as bathing, dressing, and toileting. In some cases, this may lead to maladaptive responses that become habitual and are difficult to change (e.g. stool withholding, toileting refusal).

Methods: Toddlers, age 3 to 5 years, attending pediatric GI clinic for an initial visit with a complaint of chronic constipation were eligible for participation. Inclusion criteria included children with functional constipation according to Rome IV criteria. Exclusion criteria included children with autism, severe delay or neurologic impairment. Parents were requested to complete Sensory Profile 2 (5, almost always to 1, almost never) and toileting questionnaire (1, almost always to 5, never) to enroll. The Sensory Profile 2 is a standardized tool to help evaluate a child’s sensory processing patterns in the context of everyday life.

Each form yields summary scores for different sensory systems, behavioral, and sensory pattern scores

- Sensory system scores: Auditory, Visual, Touch, Movement, Body position, Oral.
- Behavior scores: Attention, Behavioral, Social-emotional
- Sensory pattern scores: Registration, Seeking, Sensitivity, Avoiding

An age matched control group was selected randomly from the original pool of nationally recruited subjects for the SP-2. Approximately 10% of the control population included children with various conditions including children with autism spectrum disorder, attention deficit/hyperactivity disorder, learning disabilities, expressive and/or receptive language disorder, and intellectual disability. Paired t-tests were performed to determine differences in the 13 sensory areas of the Sensory Profile 2.

Results: Constipation group was paired with controls (n=61) by age (within at least 6 months) and gender. Constipation group had more oral defensiveness (23.3±11.2) than controls (17.1±6.6, p<.001) and a heightened sensitivity pattern (35.3±14.3) compared to controls (30.8±8.6, p=.04). Nearly 1/3 of study participants (n=19) had extreme oral defensiveness (highest quintile). However, constipation group had a lower visual score (11.9±5.2) than controls (14.2±3.4, p<.01) and a lower movement system score (13±6.3) than controls (15.4±5.7, p=.04). Toileting differences were observed between highest quintile and mid to lower quintile for oral system classification. (see table)

Discussion: Toddlers with constipation exhibit differences in their sensory processing skills in comparison to their peers. The most significant differences were observed for the oral system and sensitivity pattern. The underlying mechanisms for these differences is unknown. However there is preliminary evidence to suggest that children who have extreme oral sensitivity also tend to exhibit ritualistic tendencies with regard to toileting behavior including how, when, and where bowel movements can comfortably occur. This subset of children may represent a vulnerable and previously undescribed phenotype and may require a more comprehensive and tailored approach to therapy.

Oral Sensory System

	Highest quintile (n=19)	Mid to lower quintile (n=35)	p value
My child hides while having bowel movements	2.89±1.70	3.23±1.40	ns
My child asks for a diaper when he feels the need to have a bowel movement	3.17±1.92	4.32±1.25	0.01
My child refuses to sit on the potty or toilet to defecate	2.21±1.72	2.91±1.60	ns
My child always follows the same ritual when having a bowel movement	1.53±1.12	2.85±1.52	<0.001
My child seems to feel pain when having a bowel movement, even if the stool is soft	2.78±1.17	3.44±1.40	ns
My child refuses to go to the bathroom outside of the house	2.56±1.58	3.68±1.45	<0.05
My child's reaction to the odor of his/her feces is exaggerated	3.95±1.27	4.31±1.11	ns
My child refuses to wipe or be wiped after having a bowel movement	3.78±1.52	3.83±1.41	ns
My child does not seem to feel the urge to have a bowel movement	3.21±1.36	3.38±1.28	ns
My child does not realize he has soiled (feces) his clothes	4.21±1.08	4.06±1.25	ns

1, almost always to 5, never

316 OSTEOPATHIC FINDINGS AND TREATMENT IN CHILDREN WITH ABDOMINAL PAIN: A PILOT STUDY. Maryam Shambayati, Issam Halabi. *Pediatric Gastroenterology, University of Oklahoma HSC, Oklahoma City, OK*

Background: According to the 2015 Osteopathic Medical Profession Report, there are more than 96,000 osteopathic medical physicians in the United States. Doctors of Osteopathic Medicine, or DOs, have an additional treatment modality, osteopathic manipulative treatment, or OMT, that can be used as solitary or adjunct therapy for many medical conditions. While OMT has been shown to help adults with abdominal pain secondary to IBS and there are published studies correlating osteopathic findings with gastrointestinal endoscopic findings, there are no published studies on osteopathic findings and pediatric abdominal pain. The purpose of this pilot study is to identify osteopathic findings in children with abdominal pain and to see if there is improvement in abdominal pain if those osteopathic findings are treated in adjunct to the current medical standard of care.

Methods: Subjects (n=11) were established patients of University of Oklahoma Pediatric Gastroenterology clinic ages 7-18 years who had been diagnosed with functional abdominal pain prior to the study. Subjects had one visit every two weeks for a total of four visits. During each study visit, the abdominal pain index questionnaire was obtained from the parent and from subjects over age 10. Subjects then underwent a full osteopathic physical exam, documenting osteopathic findings for all spine levels and Chapman's points. Any somatic dysfunction found on exam was treated with OMT.

Results: Data was analyzed using the Shapiro-Wilk Test for Normality and the paired T-test. Parent pain level decreased significantly from visit 1 to visit 4 (p=0.014) as did spinal dysfunction from visit 1 to 3 (p=0.031) and 1 to 4 (p=0.050).

Conclusion: Osteopathic findings are present in children with abdominal pain, and the treatment of those findings with OMT does correlate with improvement of parental perception of abdominal pain level. This is the first study to examine osteopathic findings and OMT in children with functional abdominal pain in the United States.

INFLAMMATORY BOWEL DISEASE

320 WHY AND HOW ADOLESCENTS AND YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE USE CANNABIS. Edward Hoffenberg^{1,2}, Brittany Murphy², Susan Mikulich-Gilbertson³, Shannon McWilliams³, Analice Hoffenberg⁴, Christian Hopfer³. ¹Pediatrics, University of Colorado Denver, Aurora, CO; ²Digestive Health Institute, Children's Hospital Colorado, Aurora, CO; ³Psychiatry, University of Colorado Denver School of Medicine, Aurora, CO; ⁴Preventive Medicine, University of Colorado Denver School of Medicine, Aurora, CO

Introduction: Cannabis use (CU) is increasingly viewed as safe and possibly beneficial for medical treatment of many conditions including IBD. Yet there is little data on frequency and motivation for use, and perceived risks and benefits with use. Colorado has legalized medical and recreational use of cannabis.

Methods: An ongoing state-funded observational study is investigating CU among adolescents and young adults 13-23y old with IBD followed at our institution. Approximately 70% of approached eligible subjects enrolled and completed questionnaires we developed to assess frequency and motivations for CU. We also collected clinical information and quality of life measures via ImproveCareNow electronic data capture. Serum cannabinoid levels were measured in a research lab.

Results: Of 90 subjects enrolled to date, 64% Crohns, 26% UC, and IBD-U (undifferentiated) 10%; 55% were male, mean age 16 +/-2y, quiescent/mild 81%. Past CU was endorsed by 27% (n=28) and this group was about 1y older (16.9 +/-1.8y) than the never use (15.8 +/-2.0y) group. Four reported possession of a state issued medical registry card. Ever and never use groups were similar for gender, race, disease type, disease activity, and measures of QOL and anxiety. A belief of moderate or great risk of harm with regular smoking of cannabis was endorsed by 18% in the ever use group and 76% in the never use group.

Of 28 with past CU, 6 reported using more than one time a day. Past 30 days was reported by 18 subjects; median days of use was 16, range 1-30 days. All 18 had detectable serum cannabinoid levels.

Typical route of use was smoking 40%, dab 22%, ingested as edible 18%, oil 11%, and vape 7%. Most common reason for use was combination of medical plus recreational, reported by 86% (n=24). The specific benefits reported by more than half were for physical pain, anxiety, mood, and euphoria. A problem with use was reported by 38% (n=11). The most commonly reported problems were "having a craving or a strong desire or urge to use marijuana" (21%, n=6); "needing increasing amount for same effect" (18%, n=5) and "over-using" (18%, n=5).

Discussion: Almost 30% of adolescent and young adult IBD subjects have used cannabis, 20% within the past 30 days, and 10% are daily or almost daily users. Most of those with regular CU do not perceive risk of harm and report improvement in pain, anxiety, and mood. These potential benefits must be weighed against the recognized risks including motor vehicle accidents, psychosocial decline and addiction. Use of cannabis by adolescent and young adult IBD patients needs further study.

321 LACK OF MUCOSAL HEALING FROM MODIFIED SPECIFIC CARBOHYDRATE DIET IN PEDIATRIC PATIENTS WITH CROHN'S DISEASE. Ghassan Wahbeh, Teresa Wachs, Dale Lee, Matthew Giefer, David Suskind. *Seattle Children's, University of Washington, Seattle, WA*

Exclusive enteral nutrition is effective in pediatric Crohn's disease but challenging as maintenance therapy. There is interest in food-based therapies such as the specific carbohydrate diet (SCD) but paucity of data on efficacy and effect on mucosal healing; an evolving target of IBD therapy. We conducted a retrospective review of the mucosal healing effect of the SCD in pediatric CD. The endoscopic findings for children <18 with Crohn's disease treated exclusively with the SCD or modified SCD (mSCD; SCD + addition of "illegal foods") were reviewed before and after the diet. Ileocolonoscopy exams were scored according to the Simple Endoscopic Exam for Crohn's disease (SES-CD) and findings on upper endoscopy were described. Seven subjects were identified, all on mSCD. The average age at starting the SCD was 11 ± 3.4 years and median duration of SCD/mSCD therapy was 26 months. All subjects reported no active symptoms prior to repeat endoscopic evaluation on mSCD, the majority had consistently normal CRP, albumin and hematocrit assessments, and mildly elevated fecal calprotectin (FCP >50 mcg/g, median 201, range 65-312) at any point within 3 months before the repeat endoscopy. One patient showed complete ileocolonic healing but persistent UGI tract ulceration. Complete macroscopic mucosal healing of both the ileocolon and UGI tract was not seen in any patient.

322 VEDOLIZUMAB IS ASSOCIATED WITH DEEP REMISSION IN PEDIATRIC IBD PATIENTS. Bridget Dowd, Jacqueline Jossen, Marla Dubinsky. *Pediatrics, Mount Sinai Icahn School of Medicine, New York, NY*

Background: Vedolizumab (VDZ) is an $\alpha4\beta7$ integrin antibody approved for adults with inflammatory bowel disease (IBD). Differences in clinical outcomes have been described between patients who are anti-TNF exposed versus naïve. The open-label extension phase of the GEMINI studies demonstrated combined histological and mucosal healing in 20.8% of Crohn's disease (CD) patients and 32% of ulcerative colitis (UC) patients. Similar studies are lacking in children. We aimed to study the endoscopic and histologic remission rates in VDZ treated pediatric IBD patients and determine the influence of anti-TNF exposure on outcomes.

Methods: This study is part of an ongoing observational cohort of biologic treated pediatric IBD patients at a tertiary care IBD center. All patients who underwent a colonoscopy within 8 weeks of starting VDZ and had a follow up colonoscopy while on VDZ were included. Data on demographics, disease location and behavior (Paris Classification), disease activity, treatment history, and mucosal and histologic reports were collected. Comparisons were made between subjects who were anti-TNF exposed versus anti-TNF naïve with respect to mucosal healing (Mayo endoscopic score = 0 in UC or SES-CD ≤ 3 in CD), histologic remission (normal or chronic inflammation without activity), clinical remission (partial Mayo ≤1 for UC and wPCDAI <12.5 for CD), and normalization of CRP (<5 mg/L). Descriptive statistics were used.

Results: Of the 21 patient included in the analysis; 12 have CD and 9 UC (median age 19, IQR 13-23). For disease location; 67% of UC patients were E3 (extensive colitis) and 67% of CD patients had L3 (ileocolonic), 17% L1 (small bowel only) and 16% L2 (colon only).

10 subjects (47.6%) were anti-TNF naïve. Of the 11 anti-TNF exposed, 7 had only one anti-TNF, 3 had two and 1 had received three anti-TNF agents. Median duration between last anti-TNF dose and initiation of VDZ was 90 days (range 15-546). The mean duration on VDZ prior to repeat endoscopic assessment was 51 weeks (range 16-104). Endoscopic remission was found in 78% of anti-TNF naïve subjects and only 45% of anti-TNF exposed patients. Histologic remission was observed in 80% of anti-TNF naïve subjects versus 54.5% of anti-TNF exposed. Two-thirds (14/21) of patients were on corticosteroids at the time of VDZ initiation and 7/21 were still on steroids at the time of follow up endoscopy. Clinical remission was achieved in 70% of anti-TNF naïve patients (3/6 UC and 4/4 CD) compared to 45% of anti-TNF exposed (1/3 UC and 4/8 CD). There was no difference between the two groups with respect to normalization of CRP (62.5%).

Conclusion: This is the first study to report the effectiveness of vedolizumab in inducing deep remission in pediatric IBD. The proportion of patients with both endoscopic and histologic remission was higher in anti-TNF naïve patients. Larger studies are needed to help guide recommendations regarding the sequence of therapies in pediatric IBD.

324 **VITAMIN D STATUS IN INFLAMMATORY BOWEL DISEASE PATIENTS FOLLOWED AT STEAD FAMILY CHILDREN HOSPITAL, UNIVEVERSIY OF IOWA.** *Jamal Kriem. Pediatrics, University of Iowa, Iowa City, IA*

Background: Patients with inflammatory bowel disease (IBD) are at increased risk of nutritional deficiencies. This could be secondary to malnutrition, malabsorption or chronic inflammation. Vitamin D deficiency is common among patients with IBD. Vitamin D is a fat-soluble vitamin. The Calcitriol form (vitamin D3) is the active form. Vitamin D regulates bone, calcium, and phosphorus metabolism and it influences immune system function. The association between low vitamin D level and IBD disease activity has been reported.

Purpose: A quality improvement project that is run on two stages. The first one is to evaluate the rate of vitamin D deficiency in our center. The second stage is to reduce the deficiency rate by using pre-visit planning form to inform the primary GI providers about the vitamin D levels and emphasize the need to address identified deficiency.

Methods: Retrospective cohort study of the IBD patients enrolled in ImproveCare Now network who are followed at the main campus at the University of Iowa. Vitamin D levels were documented in the last three occasions and recorded, in addition to patient's demographics and documented vitamin D supplementation.

Results: A total of 126 IBD patients were included (45% females), with age range 4 to 18 years old, that were seen in our main campus in 2016-2017. Sixty seven percent of patients had Crohns disease, 26% had ulcerative colitis, and 7% had undetermined IBD. Vitamin D deficiency was defined as a level < 20 ng/ml and with insufficiency defined as a level between 20-29 ng/mL. We have a total of 347 vitamin D measurements. Fifty eight patients (46%) were found to have at least one level in the deficiency range. Fifty five patients (44%) had levels in the insufficiency range (without a deficient level). Only 9 patients had levels that were all above 30 ng/ml of the three measurements.

Discussion: Vitamin D deficiency is higher than expected in our IBD patient population when levels of vitamin D were assessed on the last three measurements over the last 1-2 years. Non-adherence to supplement recommendations could be of major importance; however, living in Iowa where sun exposure is limited in winter is likely an additional factor. We are hoping by raising awareness of pediatric GI providers about the need to assess and address low vitamin D levels through the pre-visit form will facilitate reducing the deficiency rate among our patients.

325 **SIX MONTH ORAL MEDICATION ADHERENCE EARLY IN DISEASE COURSE AS A PREDICTOR OF INFLAMMATORY BOWEL DISEASE-SPECIFIC OUTCOMES OVER TIME.** *Marisa Millenson², Jason Shapiro¹, David Barker⁴, Meaghan Mallette⁵, Heather Moniz⁵, Katey Amaral⁵, Renee Bright⁵, Sheryl Kopel⁴, Sarah Hagin⁴, Elizabeth McQuaid⁴, Ron Seifer⁴, Christopher Schmid², Samir Shah^{5,6}, Bruce Sands³, Debra Lobato⁴, Neal LeLeiko¹. ¹Pediatric Gastroenterology, Nutrition and Liver Diseases, Hasbro Children's Hospital/Warren Alpert Medical School of Brown University, Providence, RI; ²Biostatistics, Brown University, Providence, RI; ³Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, NY; ⁴Child Psychology, Hasbro Children's Hospital/Warren Alpert Medical School of Brown University, Providence, RI; ⁵Gastroenterology, Rhode Island Hospital, Providence, RI; ⁶Warren Alpert Medical School of Brown University, Providence, RI*

Background: There are a variety of medications used to control the symptoms of inflammatory bowel disease (IBD). Adherence early in disease course to two commonly prescribed medications, mercaptopurine (6-MP) and mesalamine (5-ASA), may be associated with fewer disease complications over time. We examined the relationship of adherence to 6-MP and 5-ASA during the first six months after IBD diagnosis with measures of disease complication including hospital encounters, surgical resections, and corticosteroid use in children and adolescents over a median 6.4 years of follow-up.

Subjects: 39 IBD patients (74% Crohn's disease, 26% ulcerative colitis; mean enrollment age=12.6 years; 54% female; 85% white) co-enrolled in a longitudinal inception cohort and institutional biobehavioral health registry were included for analysis (see Table 1).

Methods: Among 39 children and adolescents aged 6 to 15, we used the Medication Event Monitoring System (MEMS TrackCap) to electronically measure the fraction of medication doses actually taken compared to the expected number of doses in the first six months after diagnosis to designate patients as adherent (>80% of expected doses taken) or nonadherent (≤80% of expected doses taken). Over a median follow-up period of 6.4 years, we measured the number of hospital encounters and corticosteroid courses for each patient as well as their age at the time, if any, of first hospital encounter after diagnosis, at first resection, and at first prescription of a biologic. We estimated incidence rates of hospital encounters and corticosteroid courses and estimated cumulative hazards of first hospitalizations, resections, and biologic use in nonadherent patients as compared to adherent patients.

Results: After covariate adjustment, we found a suggested association between adherence status and time to first hospitalization, resection, and biologic use, as well as number of hospital encounters. Nonadherent patients had a hazard of hospitalization 2.3 (95% confidence interval [CI]: 0.8, 6.9; p=0.43) times that of adherent patients, a hazard of resection 3.9 (95% CI: 0.7, 20.2; p=0.26) times that of adherent patients, and a hazard of biologic use 1.3 (95% CI: 0.4, 4.0; p=0.34) times that of adherent patients. The incidence rate ratio (IRR) of hospitalization comparing nonadherent patients to adherent patients was 3.7 (95% CI: 1.4, 10.0; p=0.01). We found no association between adherence status and number of corticosteroid courses (IRR=1.1; 95% CI: 0.5, 2.3; p=0.82), nor between adherence status and number of months in which corticosteroids were taken during the first year after diagnosis (IRR=1.0; 95% CI: 0.5, 1.9; p=0.97).

Conclusions: In this pediatric cohort, adherence to 6-MP and 5-ASA early in disease course was associated with lower risk of hospital encounter, surgical resection, and escalation to biologics over time, although adherence was not associated with risk of corticosteroid use.

Table 1: Sociodemographic Characteristics of Patients Co-Enrolled in the Ocean State Crohn’s and Colitis Area Registry (OSCCAR) and the Pediatric IBD Biobehavioral Health Registry (BBH), N=39

Age at OSCCAR enrollment, mean (SD), year	12.6	(2.7)
Male (%)	18	(46%)
Diagnosis (%)		
CD	29	(74%)
UC	10	(26%)
Disease Severity at Baseline (%)		
Inactive	15	(38%)
Mild	13	(33%)
Moderate / severe	11	(28%)
Race (%)		
Caucasian	33	(85%)
African American	1	(3%)
American Indian	1	(3%)
Mixed / other	4	(10%)
Latino ethnicity	6	(15%)
Household		
Parents—living together (%)	29	(74%)
Mean maternal education (SD), year	14.3	(2.1)
Full-time employment (%)	34	(87%)
Mean annual income (SD)	\$59,468	(\$32,059)
Adherence to 5-ASA and 6-MP medications (%)		
Adherent (>80% adherence rate)	25	(64%)
Nonadherent (≤80% adherence rate)	14	(36%)

Table 2: Hazard ratios calculated from crude and adjusted^a Cox proportional hazards regressions for the outcomes of time to first hospitalization, time to first surgical resection, and time to first use of biologic medication, as well as time to the first event of any of the three outcomes. Ratios compare hazards in nonadherent patients to hazards in adherent patients.

Outcome of interest	Hazard ratio (unadjusted)	95% confidence interval (unadjusted)	p-value (unadjusted)	Hazard ratio (adjusted)	95% confidence interval (adjusted)	p-value (adjusted)
First hospitalization	2.009	(0.792, 5.097)	0.134	2.301	(0.773, 6.853)	0.432
First resection	3.908	(0.924, 16.530)	0.046	3.858	(0.737, 20.192)	0.262
First biologic use	1.870	(0.687, 5.090)	0.213	1.322	(0.442, 3.952)	0.340

a- Regression model adjusted for age at disease diagnosis and baseline disease severity

327 AGE INFLUENCES CHOICE OF INITIAL THERAPY IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE. Roxanne Cheung, Trudy Lerer, Jeffrey Hyams. *Digestive Diseases, Connecticut Childrens Medical Center, Hartford, CT*

Background: The increasing use of biologics (BIO) in children with inflammatory bowel disease (IBD) is changing clinicians' approach to treatment.

Aims: To determine whether patient age influences the timing of first BIO and immunomodulator (IM) usage in children with IBD.

Methods: Data were obtained from the Pediatric IBD Collaborative Research Group Registry (2002-2014), a prospective observational study of newly diagnosed children with IBD ≤16 years of age. Patient data were recorded at diagnosis, 30 days later, and then every 3 months. Patients were managed by physician dictate, not protocol. Disease activity was classified by physician global assessment (PGA). IBD-U was exclusionary. The primary outcome was frequency and timing of BIO and IM in older children (≥12 years) compared to younger children (<12 years). Early use was defined as ≤3 months from diagnosis, late use as >3 months. BIO use included infliximab (IFX), adalimumab (ADA), and certolizumab (CTZ). IM use included thiopurines and methotrexate (MTX).

Results: 1,442 children with Crohn's disease (CD) and 560 with ulcerative colitis (UC) had data available for review. Demographic and disease characteristics are shown in the Table 1. Table 2 shows overall BIO use in 47.3% of CD patients (<12 yrs, 47.6%; ≥12 yrs, 47%). Early BIO was used significantly more in older CD children (31.3%) than younger CD children (19.5%, p<0.001). IFX was the main agent used in early BIO (<12 yrs, 100%; ≥12 yrs, 97.4%). Patients ≥12 yrs with moderate CD (29.1%) or severe CD (47.1%) received early BIO significantly more than patients <12 yrs with moderate CD (20%, p<0.05) or severe CD (29.9%, p<0.045). IM was used in 81.1% of CD patients, (<12 yrs, 80.2%; ≥12 yrs, 81.8%). Older patients with mild CD (67.5%) received early IM significantly more than younger patients (52.6%, p=0.009). Thiopurine was the main early agent used for children with CD (<12 yrs, 89.3%; ≥12 yrs, 89.3%). BIO was used in 26.8% of UC patients (<12 yrs, 25.1%; ≥12 yrs, 28.2%). IFX was the main agent used in both age groups. IM was used in 50.4% of UC patients (<12 yrs, 51%; ≥12 yrs, 49.8%). Early IM was used significantly more in older UC children (53.2%) than younger UC children (31.2%, p <0.001). Thiopurine was the main agent used in early IM for children with UC (<12 yrs, 100%; ≥12 yrs, 98.8%). Patients ≥12 yrs with severe UC (83.8%) received early IM significantly more than patients <12 with severe UC (50%, p=0.012). Early thiopurine use was significantly more in patients ≥12 yrs with severe UC (83.8%) than patients < 12 with severe UC (55.6%, p=0.045).

Conclusions: BIO use is now seen in almost 50% of children with CD and 25% of those with UC regardless of age. Overall, there is more early BIO use in older children with CD and UC across all PGAs. For patients ≥12 yrs with moderate CD, severe CD and severe UC, early BIO use is significantly greater than patients <12 yrs. This may reflect the concern of clinicians for the impact of disease on growth in adolescents. Our data suggest that age has an impact on clinician management regardless of disease severity.

Table 1. Characteristics of Study Population at Diagnosis

	Total	<12 years	≥ 12 years
CD			
Mean age	11.9 ± 2.8	9.4 ± 2.2	13.9 ± 1.1
% male	59%	60%	58%
Mild PGA	30%	31%	29%
Moderate PGA	52%	51%	53%
Severe PGA	18%	18%	18%
Follow Up >2 years	74%	76%	73%
UC			
Mean age	11.6 ± 3.5	8.4 ± 2.8	14.2 ± 1.2
% male	51%	50%	52%
Mild PGA	33%	36%	31%
Moderate PGA	49%	52%	46%
Severe PGA	18%	12%	23%
Follow Up >2 years	68%	66%	69%

Table 2. BIO and IM Use

	< 12 years	≥ 12 years
CD		
BIO ever	47.6%	47.0%
Early BIO	19.5%	31.3%*
Late BIO	80.5%	68.7%
IM ever	80.2%	81.8%
Early IM	66.9%	72.0%
Late IM	33.1%	28.0%
UC		
BIO ever	25.1%	28.2%
Early BIO	20.6%	32.2%
Late BIO	79.4%	67.8%
IM ever	51.0%	49.8%
Early IM	31.2%	53.2%**
Late IM	68.8%	46.8%

*Early BIO use in ≥ 12 years old compared < 12 years, p < 0.001

**Early IM use in ≥ 12 years compared to < 12 years, p < 0.001

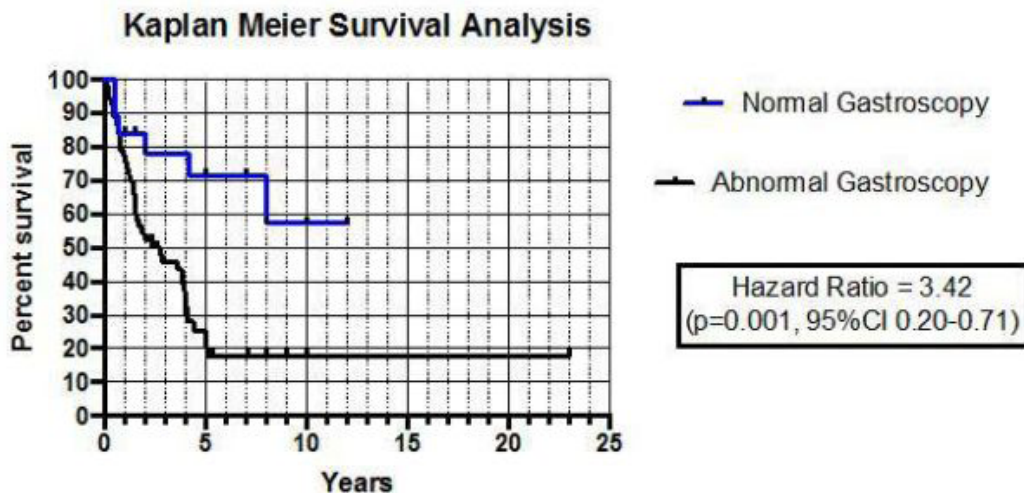
328 DIAGNOSTIC ESOPHAGOGASTRODUODENOSCOPY PREDICTS OUTCOME FOLLOWING INTESTINAL RESECTION IN PEDIATRIC CROHN'S DISEASE. Vanessa Tan¹, Kosana Kiranmai², Nicholas Croft², Sandhia Naik², Jeffrey Savarino³, Jess Kaplan³, Edward Giles¹. ¹Department of Paediatrics, Monash University, Melbourne, Victoria, Australia; ²Department of Paediatric Gastroenterology, Royal London Hospital, London, United Kingdom; ³Pediatric Gastroenterology, MassGeneral Hospital for Children, Boston, MA

Background/Objectives: Post-operative recurrence (POR) is relatively common in Pediatric Crohn's disease (CD). Previous surgical resection, internal penetrating phenotype and smoking have been identified as risk factors for early POR in adults. The aim of this study was to identify factors that influence POR following intestinal resection in children with CD.

Methods: Pediatric CD patients who underwent ileal resection and/or right hemicolectomy with primary anastomosis were identified on databases at the Royal London hospital and Massachusetts General Hospital between 2000-2013 and 2000-2014, respectively. CD patients were subdivided into recurrence and non-recurrence groups. Recurrence was defined as clinical, endoscopic, radiographic or histologic recurrence. Data analysed included patient demographics, diagnostic esophagogastroduodenoscopy (EGD) and colonoscopy findings, Montreal classification, operation details, pre-operative and post-operative pharmacotherapy, relapse and additional follow-up information.

Results: 96 children were identified, of which 57 (59%) had POR with a median time to recurrence of 1.88 years. Female gender (p=0.004) and ileocolonic disease location (p=0.022) were associated with CD recurrence. Children with abnormal histology findings at diagnostic EGD had a higher rate of POR, with a cumulative recurrence of 82.2% at 10 years, compared to those with normal diagnostic EGD findings, who had a cumulative recurrence of 42.7% at 10 years (Hazard ratio 3.42, p=0.001) (Figure 1). On multivariate analysis, abnormal diagnostic EGD was a significant predictor for POR (Odds Ratio 1.37, p= 0.012). Alteration of pharmacotherapy post-operatively was associated with a lower incidence of recurrence (p=0.0065).

Conclusion: This multicenter retrospective study showed a number of risk factors for POR in Pediatric CD. Most interestingly, this is the first study to demonstrate that an abnormal EGD at the time of diagnosis is predictive of post-operative recurrence in children with CD.



329 UNDERSTANDING THE RELATIONSHIP BETWEEN MOOD ISSUES AND HEALTH CARE UTILIZATION AND COSTS AMONG PEDIATRIC PATIENTS WITH IBD. Jessie Wong^{1,2}, Rachel Bensen³, Helen Yu³, Donna MacIsaac³, Zachary Sellers¹, Anava Wren³, Cindy Kin¹, KT Park^{3,1} ¹School of Medicine, Stanford University, Hayward, CA; ²Center for Innovation to Implementation, Palo Alto VA Health Care System, Palo Alto, CA; ³Pediatrics, Stanford University, Stanford, CA

Background/Aim: Mood disorders, consisting of anxiety and depression, are prevalent and highly comorbid among children and adolescents with inflammatory bowel disease (IBD). Emerging evidence demonstrates concomitant mood problems to be associated with increased healthcare utilization and costs in IBD. This association is virtually unexplored in pediatric IBD. We aimed to determine the differences in healthcare utilization between patients with and without a documented mood issues among pediatric patients with IBD from a large nationwide dataset.

Methods: We analyzed the Truven Health MarketScan Database from 2007 to 2015, merging inpatient, outpatient, emergency room (ER), procedure and diagnostic tests, and pharmaceutical claims datasets. ICD-9-CM (ICD-10-CM) codes 555.xx (K50.xx) and 556.xx (K51.xx) identified patients age 6-21 years with Crohn's disease (CD) or ulcerative colitis (UC) with at least 2 consecutive health plan enrollment years. Cohort stratification into [+]Mood and [-]Mood was dependent on whether the patient had at least one diagnosis of a depression or anxiety disorder and/or prescription of an antidepressant, anxiolytic, and/or antipsychotic medication present in any claim.

Results: A total of 29,074 pediatric patients with IBD met inclusion criteria (11,659 [+]Mood; 17,415 [-]Mood). The [+]Mood cohort was 54% female with a mean age of 16.6 years; the [-]Mood cohort was 43% female with a mean age of 15.9 years. The mean annual healthcare cost per patient was \$27,329 in the [+]Mood cohort and \$17,143 in the [-]Mood cohort. Differences in healthcare utilization were most notable for proportion with annual inpatient services (51.9% [+]Mood vs 35.8% [-]Mood), ER visits (78.9% [+]Mood vs 61.6% [-]Mood) and median number of outpatient clinic visits per year (14.1 [+]Mood vs 8.4 [-]Mood). Based on medians for the groups, the [+]Mood cohort underwent a median of 0.11 more radiographic tests and 0.03 more endoscopic evaluations per year than the [-]Mood cohort. Finally, a greater proportion of the [+]Mood patients were prescribed opioid pain control medications annually (67.9%) and corticosteroids (72.1%) compared to [-]Mood (50.3% and 64.0%, respectively), but interestingly had less frequent use of biologics based on a preliminary analysis.

Conclusion: We report the first quantitative, nationwide analysis of the healthcare utilization differences in pediatric patients with IBD and concomitant mood disorder. Given the reciprocal nature of mental and physical health, particularly related to IBD, and the observed difference in health service utilization reported here, our analysis raises the question of appropriateness of care in pediatric IBD management and the need for further integration of mental health services in routine care.

330 SUBSTANCE USE AND SELF-MANAGEMENT IN COLLEGE STUDENTS WITH INFLAMMATORY BOWEL DISEASES (IBD). *Jill Plevinsky^{2,3}, Steven Miller², Michele Maddux⁴, Laurie Fishman¹, Joshua Noe⁵, Stacy Kahn¹, Rachel Greenley². ¹GI/Nutrition, Boston Children's Hospital, Cambridge, MA; ²Department of Psychology, Rosalind Franklin University of Medicine and Science, Chicago, IL; ³Department of Psychiatry and Human Behavior, Brown University Alpert Medical School, Providence, RI; ⁴Developmental and Behavioral Sciences, Children's Mercy Hospital, Kansas City, MO; ⁵Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI*

Background: College students with chronic medical conditions, including IBD, are at particular risk for poor self-management. Additionally, given that youth with chronic medical conditions are at least as likely, if not more likely, to engage in substance use compared to healthy peers, college students with IBD are likely at a particular risk for engaging in problematic substance use. Yet, limited research addresses substance use and self-management in this population. Therefore, the present study aimed to explore how types of problematic substance use, disease management skills, and correlates of self-management cluster together among college students with IBD.

Methods: One hundred and three college students with IBD completed questions assessing problematic substance use over the last 30 days, including tobacco use, binge drinking, and marijuana use. Participants completed two measures of disease management skills: Transition Readiness Assessment Questionnaire (TRAQ) and Allocation of Treatment Responsibility (ATR). Participants also completed the IBD Self-Efficacy Scale for Adolescents and Young Adults (IBDSES-A), the Student Adaptation to College Questionnaire (SACQ), a measure developed for this study assessing patient-provider communication about substance use, and measures of disease activity, as well as demographic and disease-related information.

Results: Cluster analyses resulted in six distinct groups based on types of substance use. Approximately half of the sample (N=52, 51%) fell within the "Global Abstainers" cluster and denied substance use. The second largest cluster, "Exclusive Binge Drinkers," represented 19% of the total sample (N=20). The third largest cluster, "Global Users," represented 12% of the total sample (N=12). Both measures of disease management skills varied significantly between clusters with a large effect sizes ($p=0.213$, $V=0.62$; $p=0.013$, 0.67) such that those within the "Global Users" clusters demonstrated the lowest disease management skills. College adjustment also varied significantly between clusters with a medium effect size ($p<0.001$, $V=0.45$) such that the majority of those endorsing low college adjustment fell within the "Global Users" cluster. Gender and disease activity also varied significantly between clusters with medium effect sizes ($p=0.003$, $V=0.42$ and $p=0.074$, $V=0.32$, respectively). Specifically, the majority of females fell within the "Global Abstainers" cluster and all participants classified in the "Global Users" and "Smokers Engaging in Binge Drinking" clusters endorsed active disease.

Conclusions: Overall, results suggest that males as well as those with poorer disease management skills, poorer college adjustment, and greater disease activity are at the greatest risk for engaging in problematic substance use. Identifying college-bound adolescents with IBD at risk for poorer self-management prior to the transition to college may promote more optimal self-management and reduce problematic substance use during college and into adulthood as well.

331 THE NATURAL HISTORY OF ANTI-DRUG ANTIBODY FORMATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS ON BIOLOGIC MEDICATIONS. *Kristin Lambert-Jenkins², Anna Herrick¹, Judy Splawski¹, Thomas Sferra¹, Jonathan Moses¹. ¹Pediatric Gastroenterology, Rainbow Babies and Children's Hospital, Cleveland, OH; ²Case Western Reserve University School of Medicine, Cleveland, OH*

Introduction: Loss of response in pediatric inflammatory bowel disease (PIBD) patients treated with biologic medications can be due to development of anti-drug antibodies (ADA). Natural history of ADA development has not been well described in PIBD. The primary aim of this study was to describe a single center experience of the natural history of ADA.

Methods: We performed a retrospective, single-center chart review of PIBD seen at the Division of Pediatric Gastroenterology, Hepatology and Nutrition at the UH Rainbow Babies and Children's Hospital from 2010-2015. Patients were treated with infliximab or adalimumab and had one or more evaluation for anti-drug antibodies (ADA) utilizing the homogenous mobility shift assay. Demographics, laboratory data, and clinical disease activity were collected.

Results: A total of 75 subjects are included in the analysis. 81% of subjects were treated with infliximab with the remaining 19% of subjects treated with adalimumab. Eleven subjects developed ADA (10 to infliximab and 1 to adalimumab); average time to ADA formation was 13.2 ± 7.3 months. Longer duration of IBD, ileal location in Crohn's disease, and not having had immunomodulator prior to biologic were found to be associated with higher risk of antibody formation. Infliximab/adalimumab levels were not found to be associated with either remission or antibody positivity.

Conclusion: 11 of 17 patients (14%) developed ADA in our cohort within the first year of therapy. Prior immunomodulator use, duration of disease, and location in Crohn's disease may affect antibody formation. Natural history data could better inform clinical management in regards to dosing of biologics and/or the use of immunomodulators.

332 LONG TERM FOLLOW UP OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE WITH DIFFERENT AGE AT ONSET IN A LATINOAMERICAN CENTER. *Judith Cohen Sabban¹, Julieta Gallo¹, Viviana Yusti Caicedo¹, Veronica Busoni¹, Daniel Dagostino¹, Josefina Etchevers³, Gaston Elmo², Carlos Lifschitz¹, Marina Orsi¹. ¹Pediatric Gastroenterology Unit, Hospital Italiano, Buenos Aires, Argentina; ²Pediatric Surgery, Hospital Italiano, Buenos Aires, Buenos Aires, Argentina; ³Adult Gastroenterology unit, Hospital Italiano, Buenos Aires, Argentina*

Aim: Compare the clinical severity at diagnosis and after 10 years of follow up in children with inflammatory bowel disease (IBD) at different age of onset.

Materials and Methods: Retrospective study of children with IBD followed for a mean of 10 years (SD +/- 1 year), diagnosed between 1996-2007 at a reference center in Argentina. Diagnosis: clinical, biochemical, imaging, endoscopic and histological data. Exclusion criteria: syndromic, monogenic forms. Patients divided according age at diagnosis : Group I: (GI) <6 years old ; Group II (GII): > 6 years old. Variables: median age, clinical/endoscopic scores, relapses, required treatment, extraintestinal manifestations, complications at onset and after 10 years follow up.

Results: Fifty one patients were identified: GI 16; ulcerative colitis (UC) 10, Crohn's disease (CD) 6; GII 35; UC 22, CD 13. Median age at diagnosis: GI: 3 years (2-5), GII: 11 years (7-14), endoscopic diagnosis at diagnosis: GI: mild 25% -moderate 56% -severe 19%, GII: mild 34 % Median relapses: GI 1 (1-2), GII 2 (1-3), extraintestinal manifestations GI 4 (25%), GII 1 (3%) (p= 0.013).

Treatment: Steroids GI: 7 (44%), GII 20 (57%), thiopurines GI 44%, GII 60%, surgery GI 2 (13%), GII 4 (12%), biologics GI 1(6%), GII 6 (17%). Complications: GI=1 liver trasplantation, GII= 3: Portal vein thrombosis ; Burkitt lymphoma (UC);chronic myeloid leukemia (CD)

Conclusion: In this Latinoamerican cohort,early onset IBD children had a more benign long term outcome than previously described. This may be due to local environmental factors or higher CU prevalence.

Clinical score	Debut		p at debut	At 10 years of follow up		p at 10 years
PUCAI/PCDAI	GI n=16	GII n=35		GI n=16	GII n=35	
Remission						
Mild	9 (56%)	14 (40%)	0.54	16 (100%)	20 (8%)	0.05
Moderate	6 (37%)	17 (49%)		0	7 (21%)	
Severe	1 (6%)	4 (11%)				

333 **EXPERIENCE OF USTEKINUMAB EFFECTIVENESS IN PEDIATRIC CROHN'S DISEASE.**

Judy Dayan, Keith Benkov, David Dunkin, Jacqueline Jossen, Joanne Lai, Nanci Pittman, Ghonche Hashemi, Archana Ramaswami, Elizabeth Spencer, Marla Dubinsky. *Pediatrics, Mount Sinai New York, New York, NY*

Background: Ustekinumab (UST), a human monoclonal anti-body against interleukin-12 (IL-12) and IL-23 has recently been approved for adults with Crohn's Disease (CD). There is increasing off-label use in the pediatric population, and its effectiveness in this age group is not well known. We aimed to describe real world experience with UST in pediatric CD at a tertiary care inflammatory bowel disease (IBD) center.

Methods: As part of an ongoing observational cohort study of biologic treated pediatric IBD patients, we collected demographic, treatment and surgical history data, as well as data on disease behavior and disease location (Paris Classification), CRP levels and disease activity using the Harvey Bradshaw Index (HBI), at baseline, week 8 and at last follow up, for all UST treated pediatric patients. Endoscopy outcomes were recorded when available. Primary outcome was CRP remission at week 8, (HBI \leq 4 and a normal CRP). Secondary outcomes were clinical remission at week 8 (HBI \leq 4) and at last follow up, proportion of patients still on UST at last follow up, frequency of infusion and injection site reactions and serious adverse events. Endoscopic healing was defined as complete absence of ulcerations, and histologic remission was defined as the absence of active inflammatory changes.

Results: Fourteen of 20 (70%) pediatric CD patients initiating UST had 8 week outcomes. 15 patients were induced with the IV formulation of UST at a mean dose of 360mg (6mg/kg), and 5 patients received subcutaneous induction at a mean dose of 270mg (5mg/kg.) Median age at UST initiation was 17.1 (range 9.6-19.9) years and median duration of UST treatment at last follow up was 3.5 (range 1-10.7) months. 17 patients (85%) had failed \geq 1 anti-tumor necrosis factor (TNF), 45% failed \geq 2 anti-TNFs and 30% failed at least one anti-TNF as well as vedolizumab. Only 2 patients were primary anti-TNF non-responders and the remaining 18 had lost response; 25% developed anti-infliximab antibodies (ATI) and 3 stopped anti-TNF due to drug induced psoriasisiform dermatitis. Seven (35%) patients were on an immunomodulatory (IMM) agent at the start of UST. Week 8 CRP remission and clinical remission was seen in 46% and 71%, respectively. At last follow up, 93% of patients were still on drug and 85% were in clinical remission. Mucosal or histologic healing was not seen in the 4 patients who had undergone a treat to target endoscopy 6 months after UST induction and 1 patient had surgery 5 weeks after starting UST. There were no infusion/injection reactions or serious adverse events/infections as of last follow up. Two of the 3 patients with skin reactions to anti-TNF improved on UST.

Conclusions: Our results suggest that ustekinumab is efficacious and safe in the pediatric CD population refractory to other biologic therapies. Registration trials are underway in children and long term follow up, including endoscopic outcomes, are needed.

Key Words: ustekinumab, pediatrics, inflammatory bowel disease, Crohn's disease, ulcerative colitis.

334 **ACP353 AS A USEFUL SEROLOGIC MARKER FOR DIAGNOSIS OF CROHN'S DISEASE IN JAPANESE CHILDREN: A PILOT STUDY.**

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Background: Mitsuyama et al. reported antibodies to Crohn's disease (CD) peptide 353 (ACP353) as a novel serologic marker for diagnosis of CD in adults (Clin Exp Immunol 2011 and J Gastroenterol 2014). In the CD patients, ACP353 had a higher sensitivity and specificity (63% and 91%, respectively) than anti-Saccharomyces cerevisiae antibodies, ASCA (47% and 90%).

Aims: We aimed to clarify whether ACP353 is useful for diagnosis of CD in children.

Methods: In a single-center study using enzyme-linked immunosorbent assay, serum ACP353 levels were determined in 10 patients with CD, 26 with ulcerative colitis (UC), 4 with other intestinal diseases, and 11 healthy controls. All subjects were under 17 years old. We set cut-off value for positivity at 2.94 U/ml for ACP353. We compared sensitivity for diagnosis of CD in 5 early-onset CD patients (EOCD, under 10 years old) with those in 5 late-onset CD (LOCD, 10-16 years old).

Results: ACP353 levels were elevated in CD patients (median, 7.12 U/ml) than UC (0.64 U/ml; P=0.08), the other intestinal diseases (0.61 U/ml; P=0.14), and healthy controls (0.58 U/ml; P=0.01). The sensitivity and specificity for diagnosis of CD were 50% and 98%, respectively. The sensitivities for diagnosis of CD in EOCD and LOCD were 20% and 80%, respectively.

Conclusions: ACP353 may be a useful serologic marker for diagnosis of pediatric CD, particularly, LOCD. Further investigation is ongoing as a multicenter prospective study in Japan.

336 GOOD COMPLIANCE WITH FECAL CALPROTECTIN TESTING IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS. Karen Queliza, Michael Wang, Richard Kellermayer. *Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX*

Background: Fecal calprotectin (FC) is an increasingly utilized biomarker of lower gastrointestinal inflammation, particularly in the diagnosis and management of inflammatory bowel disease (IBD). Limitations, however, include patient compliance with performing the stool test. A recent study indicated 35% compliance with FC testing in adult IBD patients. This question has not been examined in pediatric IBD care.

Methods: We studied 100 consecutive patients who were diagnosed with IBD between 2014 and 2015 at Texas Children’s Hospital and enrolled into the Improve Care Now database. The number of FC orders and results after the initial diagnosis was examined.

Results: Fifty-six percent (56%) of patients were male and median age was 13.7 years (range 2.1-19.3 years) at diagnosis. Fifty-eight percent (58%) of patients were diagnosed with Crohn’s disease, 27% with ulcerative colitis, and 15% with unclassified IBD. Following initial diagnosis, FC was utilized in the management of 84% patients. Patient compliance rate with FC orders was 70.3%.

Conclusion: Our findings indicate good compliance with FC testing in pediatric IBD patients. This result should aid further prospective studies with respect to non-invasive laboratory-based assessment of pediatric IBD.

338 UTILITY OF A STANDARDIZED STEROID TAPER FOR TREATMENT AND MANAGEMENT OF INFLAMMATORY BOWEL DISEASE. KL Adams, RA Lirio, JR Lightdale. *UMASS Medical School/UMASS Memorial Children’s Medical Center, Worcester, MA*

Objectives: Intra- and inter-provider variability in dosing and duration of treatment with oral steroids for pediatric inflammatory bowel disease (IBD) remains a persistent challenge. Patients and families may misunderstand individually prescribed tapers, which can contribute to poor compliance. The aim of our study was to determine whether a standardized prednisone taper calendar for each patient being initiated on prednisone at our institution would improve patient care processes and outcomes.

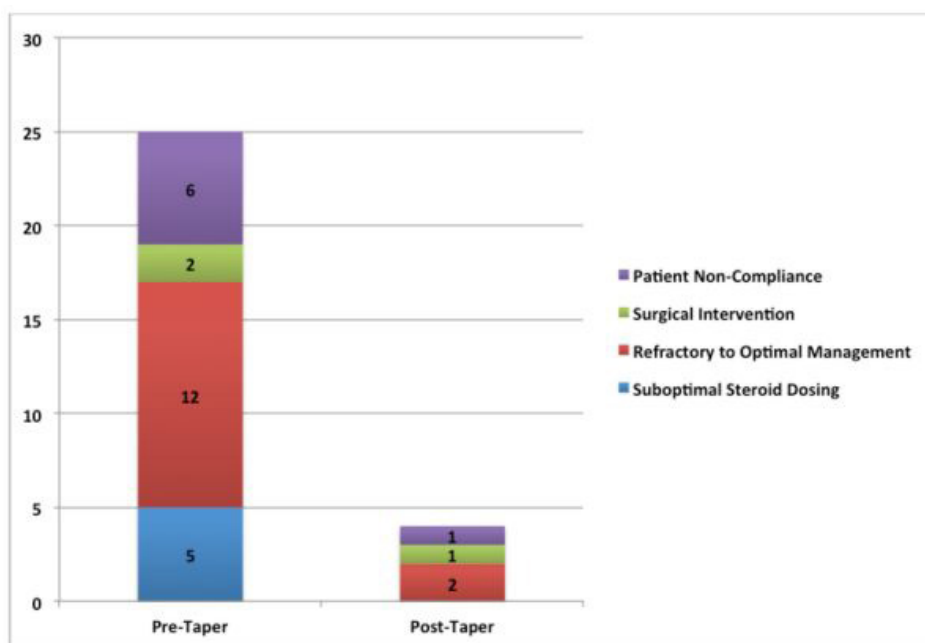
Methods: Data on hospitalized IBD patients was collected at UMass Memorial Children’s Medical Center from January 2015 through June 2017. Beginning in November 2016, a standardized steroid taper calendar was given to each patient initiated on oral steroids, and a copy was placed in the chart. (See example in Figure 1.)

Results: 32/127 (25.2%) unique IBD patients (16 male; 11 ulcerative colitis, 1 indeterminate colitis) followed by pediatric gastroenterologists (n=6) at our center during the study period were hospitalized. Hospitalizations occurred in 11 for new diagnoses, 18 for escalation of care in known diagnoses and 3 for surgical intervention. More patients were hospitalized for escalation of care prior to initiation of the standardized calendar compared with after (20 vs. 4, (p < 0.0005)). Of the 20 admissions before the implementation of the taper calendar, 5 met criteria for sub-therapeutic steroid dosing (<1mg/kg/day at onset), and 6 involved patient non-compliance. After the implementation of our taper calendar, no patients were admitted with sub-therapeutic steroid doses, and 1 patient was documented as non-compliant.

Prednisone Taper - Start dose: 60 mg								Tablet Size: 10 mg	
Name:	xxxxxx							Date:	20-Jul-2016
Week 1									
Date:	20-Jul-16	21-Jul-16	22-Jul-16	23-Jul-16	24-Jul-16	25-Jul-16	26-Jul-16		
Tablets:	3/3	3/3	3/3	3/3	3/3	3/3	3/3		
Week 2									
Date:	27-Jul-16	28-Jul-16	29-Jul-16	30-Jul-16	31-Jul-16	1-Aug-16	2-Aug-16		
Tablets:	3/2	3/2	3/2	3/2	3/2	3/2	3/2		
Week 3									
Date:	3-Aug-16	4-Aug-16	5-Aug-16	6-Aug-16	7-Aug-16	8-Aug-16	9-Aug-16		
Tablets:	2/2	2/2	2/2	2/2	2/2	2/2	2/2		
Week 4									
Date:	10-Aug-16	11-Aug-16	12-Aug-16	13-Aug-16	14-Aug-16	15-Aug-16	16-Aug-16		
Tablets:	2/2	2/2	2/2	2/2	2/2	2/2	2/2		
Week 5									
Date:	17-Aug-16	18-Aug-16	19-Aug-16	20-Aug-16	21-Aug-16	22-Aug-16	23-Aug-16		
Tablets:	2/1	2/1	2/1	2/1	2/1	2/1	2/1		
Week 6									
Date:	24-Aug-16	25-Aug-16	26-Aug-16	27-Aug-16	28-Aug-16	29-Aug-16	30-Aug-16		
Tablets:	2.5/0	2.5/0	2.5/0	2.5/0	2.5/0	2.5/0	2.5/0		
Week 7									
Date:	31-Aug-16	1-Sep-16	2-Sep-16	3-Sep-16	4-Sep-16	5-Sep-16	6-Sep-16		
Tablets:	2/0	2/0	2/0	2/0	2/0	2/0	2/0		
Week 8									
Date:	7-Sep-16	8-Sep-16	9-Sep-16	10-Sep-16	11-Sep-16	12-Sep-16	13-Sep-16		
Tablets:	1.5/0	1.5/0	1.5/0	1.5/0	1.5/0	1.5/0	1.5/0		
Week 9									
Date:	14-Sep-16	15-Sep-16	16-Sep-16	17-Sep-16	18-Sep-16	19-Sep-16	20-Sep-16		
Tablets:	1/0	1/0	1/0	1/0	1/0	1/0	1/0		
Week 10									
Date:	21-Sep-16	22-Sep-16	23-Sep-16	24-Sep-16	25-Sep-16	26-Sep-16	27-Sep-16		
Tablets:	0.5/0	0.5/0	0.5/0	0.5/0	0.5/0	0.5/0	0.5/0		
Week 11									
Date:	28-Sep-16	29-Sep-16	30-Sep-16	1-Oct-16	2-Oct-16	3-Oct-16	4-Oct-16		
Tablets:	0.5/0	0	0.5/0	0	0.5/0	0	0.5/0		
Week 12									
Date:	5-Oct-16	6-Oct-16	7-Oct-16	8-Oct-16	9-Oct-16	10-Oct-16	11-Oct-16		
Tablets:	0	0	0	0	0	0	0		

Use of the standardized steroid calendar also decreased the number of patients who remained on prednisone for >12 weeks (5 vs. 2, NS).

Conclusions: Pediatric Gastroenterologists, patients and their families, may benefit from a standardized approach to tapering steroids. Although variation in management may be difficult to completely avoid due to individual disease characteristics and severity, our medical center has found that a standardized taper decreases baseline practice variation and improves care processes. A standardized calendar may also improve patient compliance.



339 INTRAVENOUS IRON THERAPY FOR IRON DEFICIENCY ANEMIA IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Krishnapriya Marangattu Prathapan, Jyoti Mani, Bulent Ozgonenel, Ronald Thomas, Mohammad El-Baba. Pediatrics, Children's Hospital of Michigan, Detroit, MI

Background: Iron deficiency anemia (IDA) is one of the most common complications of inflammatory bowel disease (IBD) and is caused by multiple factors, including chronic intestinal blood loss from the inflamed mucosa, impaired absorption due to inflammation and poor intake from loss of appetite. The primary aim of this exploratory, pilot study was to evaluate the use of various forms of IV iron in pediatric IBD patients with IDA and to assess the clinical response with change in hemoglobin. The secondary aim was to describe the side effect profile and safety of co administering other IV IBD medications.

Methods: A retrospective chart review was done on all pediatric IBD patients at Children's Hospital of Michigan who received IV iron infusion from January 2008-January 2017. Patients who met the WHO criteria for iron deficiency anemia and received IV iron therapy were included. Patients who had blood transfusion within 1 month of IV iron infusion, had no follow-up laboratory values within 8 weeks of infusion, moderate to severe disease with acute flare-up during infusion, patients who received different forms of IV iron during a treatment course were excluded. Adverse events and co-administration of other IBD medications were noted descriptively. Mean comparisons between groups were conducted using a parametric paired samples T-test, ANCOVA and a non-parametric Wilcoxon Sum Rank and Kruskal Wallis test.

Results: Twenty-five patients (8 with ulcerative colitis, 17 with Crohn's Disease) received a total of 77 infusions. Seventeen received ferric gluconate, 8 received iron sucrose, 4 received ferumoxytol and 4 received multiple treatment courses. The mean number of doses that each patient received was 2.6 ± 2.4 . The mean doses (mg/kg/dose) of ferric gluconate, iron sucrose and ferumoxytol were 1.4 ± 0.3 , 3.4 ± 1.1 , and 8 ± 2.5 respectively. The mean pre-transfusion Hb was 8.7 ± 1.3 , mean post transfusion Hb was 10.8 ± 1.7 . The mean increase in Hb after transfusion was 2.05 ± 1.4 ($p \leq 0.001$). The mean increase in Hb with ferric gluconate, iron sucrose and ferumoxytol infusions were 1.6 ± 1 , 2.3 ± 0.7 and 3.4 ± 2.6 , respectively. There was a statistically significant difference in the increase in Hb between users of ferumoxytol and ferric gluconate ($p=0.043$), however only 4 patients received IV ferumoxytol. There was also a statistically significant increase in MCV ($p \leq 0.001$) and ferritin ($p=0.003$). Four adverse effects (5.1 %) were noted which included phlebitis, nausea, hypotension and back pain. No anaphylactic reactions were noted. Eight patients (32%) received other IV IBD medications including Infliximab ($n=7$) and Vedolizumab ($n=1$) on the day of iron infusion and tolerated them well without any adverse reactions.

Conclusion: This exploratory, pilot study demonstrated that IV iron is effective and safe in treatment of IDA in pediatric IBD patients. Higher hemoglobin increments were achieved with ferumoxytol, however it was used in a small number of patients and a higher dose was administered. The results demonstrated that it may be safe to co-administer IV iron infusion along with other IV IBD medications.

340 CONTRIBUTION OF INDIVIDUAL PEDIATRIC CROHN'S DISEASE ACTIVITY INDEX (PCDAI) SUBSCORES TO REMISSION IN PEDIATRIC PTS WITH CROHN'S DISEASE: RESULTS FROM IMAGINE 1 TRIAL. Jeffrey Hyams¹, Frank Ruemmele², Joel Rosh³, Dan Turner⁴, Marla Dubinsky⁵, Andreas Lazar⁶, Bidan Huang⁷, Joel Petersson⁷, Gabriela Alperovich⁸, Anne M. Robinson⁷. ¹Connecticut Children's Medical Center, Hartford, CT; ²Universite Sorbonne Paris-Cite, Hospital Necker-Enfants Malades, Paris, France; ³Goryeb Children's Hospital/Atlantic Health, Morristown, NJ; ⁴Shaare Zedek Medical Center, Jerusalem, Israel; ⁵Icahn School of Medicine at Mount Sinai, New York, NY; ⁶AbbVie Deutschland GmbH & Co. KG, Ludwigshafen, Germany; ⁷AbbVie Inc., North Chicago, IL; ⁸AbbVie Spain S.L.U., Madrid, Spain

Introduction: PCDAI assesses symptoms, laboratory indicators of inflammation, and physical examination results. Previous studies have shown that in patients (pts) who responded to treatment, PCDAI subscores of symptoms, albumin, and weight contributed the most to changes in total PCDAI in the short term.¹

Aims: To analyze the contribution of individual components of PCDAI to overall PCDAI at baseline (BL) and to change in overall PCDAI according to remission status at 4, 26, and 52 weeks (wks).

Methods: Pts (N=188) who received adalimumab for up to 52 wks in IMAGINE 1 were included in the analysis. Pts who prematurely discontinued or escalated to blinded weekly adalimumab were imputed as non-responders (NRI).² PCDAI, its subscores, and mean changes from BL at 4, 26, and 52 were assessed by remission (PCDAI≤10) at respective week and are presented as observed.

Results: Symptom subscores (abdominal pain, stool frequency, and general well-being) contributed the most to the overall PCDAI at BL (Table 1). Symptom subscores represented over 50% and weight and abdomen examination combined represented about 20% of the overall PCDAI change at all time points regardless of remission. ESR contributed more to the PCDAI reduction in pts with remission at 26 and 52 wks than in those without remission (Table 2).

Conclusions: Symptom-related subscores represented the majority of the change in PCDAI at BL, 4, 26, and 52 wks. Symptoms and abdomen examination subscores contributed to PCDAI decrease regardless of remission status at 4, 26, and 52 wks.

1. Kundhal et al. *JPGN* 2003;36:83–89. 2. Hyams, et al. *Gastroenterol.* 2012;143:365.

Table 1. Proportion of PCDAI subscores in overall PCDAI at BL.

	N=188
Mean PCDAI at BL, points	41.1
Proportion of PCDAI subscores in overall PCDAI at BL, %	
Abdominal pain	20.4
Stool frequency	14.3
General well-being	19.6
Hematocrit	1.8
Erythrocyte sedimentation rate	5.5
Albumin	2.4
Weight	8.2
Height	10.5
Abdomen examination	8.9
Peri-rectal	5.4
Extra-intestinal manifestations	3.2

Table 2. Contribution of PCDAI subscore changes in overall PCDAI decrease from BL by remission status at 4, 26, and 52 wks.

	Remission, Yes/No					
	4 weeks		26 weeks		52 weeks	
	Yes n=52	No n=136	Yes n=63	No n=44	Yes n=53	No n=17
Mean PCDAI decrease from BL, points	32.9	18.5	35.8	21.9	34.9	18.8
Contribution of subscore change to PCDAI reduction, %						
Abdominal pain	21.0	22.3	19.7	23.3	19.8	20.2
Stool frequency	14.6	15.3	14.2	13.5	12.3	12.8
General well-being	22.8	24.3	20.8	21.8	20.6	23.4
Hematocrit	1.0	0.3	0.6	1.0	1.1	0
Erythrocyte sedimentation rate	5.2	4.9	4.1	1.6	4.6	0
Albumin	2.6	Increased*	1.3	0	1.1	Increased**
Weight	10.2	10.9	9.1	9.3	9.5	8.0
Height	4.1	2.2	10.0	8.3	10.6	20.2
Abdomen examination	10.2	11.9	10.2	10.4	9.2	6.4
Peri-rectal	3.2	5.3	5.1	8.3	7.4	1.6
Extra-intestinal manifestations	5.0	3.2	5.1	2.6	4.6	9.6

*An increase of 0.04 points. **An increase of 0.29 points.

343 MICROBIAL CHANGES ASSOCIATED WITH PSYCHOSOCIAL STRESS IN PEDIATRIC CROHN'S DISEASE. Laura Mackner¹, Michael Bailey², Wallace Crandall³. ¹Center for Biobehavioral Health, Nationwide Children's Hospital, Columbus, OH; ²Center for Microbial Pathogenesis, Nationwide Children's Hospital, Columbus, OH; ³Division of Pediatric Gastroenterology, Hepatology and Nutrition, Nationwide Children's Hospital, Columbus, OH

Objective: Research regarding the role of psychosocial stress in IBD has been mixed, although prospective, longitudinal studies uniformly demonstrate a relationship between stress and disease activity. Studies in laboratory animals have demonstrated that exposure to psychological stressors can worsen inflammatory colitis and that some of these effects are due to alterations of the intestinal microbiota. Relationships between stress and the microbiome have not been investigated in humans in IBD. This study examined microbial profiles of adolescents with Crohn's disease to investigate whether microbial community structure is altered in patients reporting higher levels of stress.

Methods: As part of a larger study, adolescents with Crohn's disease (n=22; 36% male), ages 11-21 ($M_{age}=17.00$, $sd=2.75$), provided a stool sample and completed the Perceived Stress Scale within 24 hours. Their gastroenterologists completed the short PCDAI. The samples were processed by extracting bacterial DNA from the stool samples, amplifying the DNA using PCR, and sequencing the V3-V4 region of the 16s rRNA gene using 2x250 paired end Illumina MiSeq sequencing. The sequence data were then processed using the software program QIIME.

Results: Disease activity and perceived stress were significantly correlated, $r=.477$, $p=.039$. Girls reported higher levels of stress than boys ($M_{female}=17.07$, $sd=8.03$; $M_{male}=12.13$, $sd=6.71$), approaching statistical significance in this small sample ($p=.104$). For analyses of the microbial community structure, the sample was divided into high and low stress groups via median split. Although overall alpha and beta diversity measures did not significantly differ between high and low stress groups, there were statistically significant differences in individual bacterial taxa. At the phylum level, higher stress was associated with significantly lower relative abundances of Firmicutes ($p=.009$). There were several bacterial genera in the Firmicutes phylum whose relative abundances differed in a gender-dependent manner. The relative abundances of Anaerostipes ($p=.015$), Anaerotruncus ($p=.015$), and Blautia ($p=.009$) were significantly lower in the high stress group, but further examination revealed this was only true for girls. Similarly, relative abundances of Parabacteroides ($p=.016$) were significantly higher in those with higher stress, but only for girls when examined by gender.

Conclusions: This study provides further evidence for a relationship between psychosocial stress and disease activity, as well as a potential link with the microbiome in pediatric Crohn's disease. Adolescents with higher stress had worse disease and different microbial community structure than those with lower stress, and gender may play a role. Gender differences have not been previously reported in studies of the microbiome or stress, although they have been found in other areas of psychosocial functioning in our previous work. Prospective, longitudinal studies are needed to further investigate relationships between stress, disease and the microbiome.

347 USING LABORATORY VALUES TO PREDICT SUSTAINED CLINICAL RESPONSE TO INFLIXIMAB IN AN ETHICALLY DIVERSE POPULATION OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE.

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Background: Infliximab (IFX) has been increasingly used to induce and maintain remission in pediatric Inflammatory Bowel Disease (IBD). Current research, however, cites treatment failure rate of 10-38% owing to primary non-response and the development of IFX antibodies. There is no consensus regarding means to predict long term response to IFX. Furthermore, there is a dearth of research published in this area focused on minority populations. This study investigates whether routine laboratory tests can be used to predict sustained positive response to IFX in an ethnically diverse, urban pediatric IBD population.

Methods: A retrospective chart review was conducted for all IBD patients treated with IFX at the Children's Hospital at Montefiore (CHAM) between 2006 and 2016. Patients with clinical information of ≥ 12 months since start of IFX were included. Demographic information and laboratory values (ESR, CRP, hemoglobin and albumin) were collected at 3, 6, and 12 months after start of therapy. Change from baseline was calculated for both 3 and 6 month values. Sustained positive response was defined by continued use at 12 months, indicating that IFX was successfully maintaining clinical remission. Patients were grouped based on whether they were on or off IFX at 12 months. Independent sample median tests were used to compare groups. Receiver operating curves were constructed for lab values found to be significantly associated with remaining on IFX. A sub-analysis was done including patients with ≥ 18 months of clinical information.

Results: 70 of 97 patients treated with IFX at CHAM met inclusion criteria. Crohn's Disease (CD) was the most common IBD diagnosis (73%). 67% of the cohort was male, 33% was female. 69% of the cohort was Black or Hispanic. The mean ages at diagnosis and IFX initiation were 13.4 and 15.7 years, respectively. Among patients with CD, 57% had colonic or ileocolonic disease while 35% had ileocolonic and upper tract involvement. 49% had stricturing or penetrating disease and 39% had perianal disease. 63 of 70 patients (90%) remained on IFX at 12 months. Those remaining on IFX at 12 months had higher 3 month median hemoglobin levels compared to those off by 12 months (12.2, interquartile range (IQR) 11 – 13.3 versus 9.45, IQR 8.2 – 10.6; $P=0.032$; area under curve (AUC) 0.867), higher albumin levels (4.3, IQR 3.9 – 4.6 versus 3.5, IQR 3.3 – 4; $P=0.039$; AUC 0.829), and greater decrease in median CRP from 3 months to baseline (-0.6, IQR 0.1 – 2 versus 0.05, IQR -1.8 – 0.38; $P=0.032$; AUC 0.772). Sub-analysis included 55 patients. 41 of 55 patients (75%) remained on IFX at 18 months. Median hemoglobin was significantly higher at 6 months among patients continuing on IFX at 18 months compared to those off by 18 months (12.6, IQR 10.8 – 13.8 versus 10.7, IQR 9.8 – 11.8; $P=0.05$; AUC 0.721).

Conclusions: At 3 months, higher hemoglobin and albumin levels as well as greater decrease in CRP from baseline are associated with ongoing positive response to IFX therapy at 12 months. Higher hemoglobin levels at 6 months are associated with ongoing positive response to therapy at 18 months. Additional research in this patient population may further illuminate the significance of routine labs in predicting clinical response to IFX.

348 UTILIZING INFORMATION TECHNOLOGY TO IMPROVE INFLUENZA VACCINATION IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. *Darla Shores, Lindsay Wilson, Maria Oliva-Hemker, Pediatric Gastroenterology, Hepatology and Nutrition, Johns Hopkins Medical Institutions, Baltimore, MD*

Pediatric patients with inflammatory bowel disease are under-vaccinated against influenza, and gastroenterology nurses are ideally situated to assist in improving vaccination. The objective of this study was to evaluate the implementation of Information Technology prompts within the electronic medical record toward improving influenza vaccination during specialty clinic visits. The proportion of patients with yearly influenza vaccination was evaluated at baseline, Year 1, and Year 2 following the implementation of nursing and provider education and use of prompts to facilitate vaccine ordering and documentation. At baseline, only 10% of a random sample had documented influenza vaccination. Vaccination documentation improved to 39% (96/246) by year 1 and to 61% (175/287) by Year 2 ($p<0.001$). Vaccine counseling improved from 27% to 77% by Year 2 for unvaccinated patients ($p<0.001$). Among patients seen by gastroenterology nurses, the proportion of patients with either documented vaccination or counseling was 94% by Year 2, compared to 70% if seen by only a physician ($p<0.001$). Documentation of influenza vaccination improved with the use of customized prompts. Patients seen by a gastroenterology nurse had higher vaccination documentation and vaccine counseling than those who were seen by a physician alone.

349 CLOSING THE EMPIRICAL GAP: THE ASSOCIATION BETWEEN BIOMARKERS AND ANXIETY SYMPTOMS IN PEDIATRIC PATIENTS WITH IBD.

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Introduction: It is well-documented that pediatric patients with inflammatory bowel disease (IBD) are vulnerable to symptoms of psychosocial distress, including anxiety and depression (Reigada et al., 2011). There have been recent efforts to better understand the association between anxiety and healthcare utilization in pediatric patients with IBD, with preliminary findings suggesting that anxiety may be associated with increased hospital-based interventions (e.g., emergency room visits and surgical intervention). We have limited understanding, however, of how to explain this association and how measures of psychosocial functioning, such as anxiety, relate to disease activity in IBD. In the current study, we aim to describe the relationships between anxiety, disease-specific psychosocial functioning, and biomarkers of disease activity. In addition, we examine the association between measures of psychosocial functioning and medical management approach (e.g., medication, dietary therapy, etc.).

Methods: Participants were 77 youth with IBD seen for psychosocial evaluation as part of their outpatient GI clinic visit. All data for the current study was gathered via retrospective chart view. Psychosocial functioning measures included the MASC (self-report measure of child anxiety) and the IMPACT III (an IBD specific quality of life measure). Biomarkers of disease activity and medical management approach were recorded based on review of the medical chart.

Results: Findings suggest that steroid use is positively correlated with self-reported anxiety symptoms and negatively correlated with quality of life as measured by the IMPACT. Several correlations between IMPACT scores and biomarkers of IBD were revealed. Greater quality of life, as measured by the IMPACT, was associated with lower erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), as well as higher albumin and hematocrit levels.

Conclusions: This study offers meaningful information to the scientific community regarding the association between emotional functioning and biomarkers of IBD in pediatric patients. It is possible that IBD-specific measures of psychosocial functioning, such as the IMPACT, will have more robust associations with disease activity or medication use. Our findings have many important clinical implications and will hopefully lead to further study of the ongoing overlap between disease activity and emotional functioning in pediatric IBD.

351 RELATIONS BETWEEN PHYSICAL ACTIVITY, BODY COMPOSITION, BONE HEALTH, AND HEALTH-RELATED QUALITY OF LIFE IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE.

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Background: The presence of lean body mass (LBM) deficits in pediatric patients with IBD is well established and these deficits persist despite achievement of remission and restoration of body mass. LBM deficits are associated with both short and long-term negative health outcomes including decreased physical function, sarcopenia, metabolic dysregulation, increased risk of infection, compromised peak bone mass accrual, and development of osteopenia/osteoporosis. The lean mass deficits seen in patients with IBD are multifactorial in nature though largely explained by chronic malnutrition due to enteric nutrient losses, inadequate dietary intake, malabsorption of nutrients, and increased energy needs. In addition to malnutrition, physical activity (PA) may also play a role in the low LBM and sarcopenia noted in IBD patients. Unfortunately, PA in youth with IBD has been largely understudied. As such, the present cross-sectional pilot study aims to describe relations between PA, body composition, bone health, and health-related quality of life (HRQoL) in a sample of pediatric patients with inflammatory bowel disease.

Methods: 31 patients with inflammatory bowel disease aged 8-18 years (mean age = 14.39 years; 61% female; 52% Crohn's Disease) completed the study protocol. Assessment measures included: PA (Godin Leisure Time Exercise Questionnaire), Body Composition and Bone Density (Dual-energy X-ray Absorptiometry; DXA), and Disease Status (physician-rated disease status obtained at the time of the recruitment clinic visit). Analyses included independent samples t-test to evaluate differences between disease groups and two-tailed Pearson correlations to evaluate relations between variables of interest across groups. Data collection is ongoing.

Results: No statistically significant differences were found on any variables based on disease group though this is likely due to the relatively small sample size. Correlational analyses (N = 31) revealed that greater total weekly time spent in moderate to vigorous PA was significantly associated with participation in organized sports ($r = .62$), higher LBM ($r = .71$) and lower

fat mass ($r = -.71$). Bone health, as measured by bone mineral density z-score, was significantly associated with older age ($r = .46$), being male ($r = -.41$), higher BMI z-score ($r = .67$), lower disease activity ($r = .53$), and higher LBM ($r = .75$). Lastly, HRQoL was significantly associated with higher BMI z-score ($r = .47$) and higher LBM ($r = .67$).

Conclusions: Understanding, and ultimately promoting, health behaviors associated with the development of LBM, including PA, are key to improving growth and development outcomes in pediatric patients with IBD. The present study suggests the need for further research into physical activity as a means of promoting short and long-term health and well-being for pediatric patients with IBD through improvements in LBM.

***352 CANCER IS MORE COMMON IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE, REGARDLESS OF IMMUNOSUPPRESSION REGIMEN.** Mark Deneau, Stephen Guthery. *Pediatric Gastroenterology, University of Utah, Salt Lake City, UT*

Background: Cancer is associated with inflammatory bowel disease (IBD). Immunosuppressive medications may put patients at a higher risk, especially children. We sought to examine incidence rate of cancer in pediatric patients with and without IBD in Utah.

Methods: The Utah Population Database (UPD) contains birth certificates, medical records and genealogy data for over 6.5 million people in the Intermountain West. It is linked to the Utah Cancer Registry (UCR), a state-wide cancer surveillance and reporting network. We linked all known pediatric IBD patients in the area born from 1986-2011 to ten controls matched on birth year, multiplicity and gender, to the UPD. We compared incidence rates of cancer using the UCR in a case-control fashion.

Results: Cancer occurred in 9 of 388 (2.3%) IBD patients (6 with ulcerative colitis, 3 with Crohn's disease) at a median age of 14.9 [IQR 12.5-16.6] years during 7,478 person-years of follow-up including 3 cases of lymphoma (1 natural killer cell type, 1 precursor T-cell type and 1 Hodgkin type), 2 cases of leukemia (1 precursor T-cell type and 1 acute myeloid type), 2 cases of cholangiocarcinoma, 1 case of colonic adenocarcinoma, and 1 case of cervical carcinoma in-situ. 4 of 9 (44%) patients never received immunomodulatory or biologic medicines, 3 of 9 (33%) were exposed to immunomodulators alone, and 2 of 9 (22%) were exposed to both medication classes. The incidence rate of all cancer and of hematologic malignancy in pediatric IBD was 12.0 and 7.1 cases per 10,000 person-years, respectively. Cancer occurred in 7 of 3,880 (0.2%) non-IBD patients at a median age of 2.7[0.1-13.9] years during 74,819 person-years of follow-up including 3 cases of precursor-B cell acute lymphoblastic leukemia, 2 cases of retroperitoneal neuroblastoma, 1 case of soft tissue medulloepithelioma, and 1 case of pilocytic astrocytoma. The incidence rate of all cancer and of hematologic malignancy in non-IBD controls was 0.9 and 0.45 cases per 10,000 person-years, respectively. Cancer occurred at older ages in IBD patients vs. non-IBD patients, $p=0.013$. The incidence rate ratio (IRR) for all cancer in IBD patients compared to controls was 12.9 (95%CI 4.3-40.6, $p<0.001$). The IRR for hematologic malignancy in IBD patients compared to controls was 15.8 (95%CI 3.1-101, $p<0.001$)

Conclusions: Pediatric IBD patients in Utah had an increased risk of developing malignancy compared to non-IBD controls. This risk was increased even among patients who did not receive immunosuppressive medications. 9 cancers occurred in IBD patients (including 4 where there was no exposure to immunosuppressive medications) during the observed period when less than 1 would be expected from the background rate alone. The complex genetic, immunologic and environmental interactions that create an IBD phenotype may also lead to a propensity for cancer development, regardless of immunosuppression. We are extending the follow-up to further analyze the association between IBD and cancer.

353 IDENTIFYING THE PREVALENCE OF KNOWN PEDIATRIC INFLAMMATORY BOWEL DISEASE (IBD) GENE MUTATIONS AND ESTABLISHING PHENOTYPES IN NEW YORK BASED PEDIATRIC IBD PATIENTS. Martine Saint-Cyr¹, Steve Lipkin¹, Xiaomu Wei², Solomon Aliza¹, Robbyn Sockolow¹. ¹*Pediatric Gastroenterology, Weill Cornell Medical Center, Manhattan, NY;* ²*Weill Cornell University, Ithaca, NY*
Authors: Martine Saint-Cyr MD, Steve Lipkin MD PhD, Xiaomu Wei PhD, Aliza Solomon DO, Robbyn Sockolow MD

Background: Inflammatory bowel disease (IBD) is a heterogeneous group of conditions which comprises of Crohn's disease (CD), ulcerative colitis (UC), and inflammatory bowel disease unclassified. Epidemiological evidence has shown that there is a strong genetic component to IBD. There are >163 known IBD risk loci and >20 pediatric monogenic IBD predisposition genes. The prevalence of mutations in monogenic IBD predisposition genes in different patient groups characterized clinically and in terms of ethnic background is not well understood.

Methods: 141 patients diagnosed with IBD < 18 yrs were recruited. GEMINI database and GATK identified 23 known pediatric monogenic IBD predisposition genes for analysis. Demographic, anthropometric, laboratory and clinical information on individuals with any identified known and novel mutations were collected.

Results: A total of 102 patients met criteria for whole exome sequencing. In the initial 28 patients, 15 candidate mutations of unknown clinical significance were identified in 26/28 (93%) patients. Variants with frequency < 1% in gnomAD database were included as candidate significant variants (SV) (50%). In our patients with candidate SV and family history of IBD, 7/13 (54%) and those without a family history of IBD was 6/13 (46%) were identified. 6/13 (46%) of cohort with SV had CD and 3/6 (50%) with CD and family history of IBD. 7/13 (54%) had UC and 4/7 (57%) with UC and family history of IBD.

Conclusions: We are analyzing data on the 102 and will report more specifically on the clinical significance and characteristics of the identified mutations.

References:

Ashton JJ, Andreoletti G, Coelho T, Haggarty R, Batra A, Afzal NA, Beattie RM, Ennis S. **Identification of Variants in Genes Associated with Single-gene Inflammatory Bowel Disease by Whole-exome Sequencing.** *Inflamm Bowel Dis.* 2016 Oct;22(10):2317-27.

Bianco AM, Girardelli M, Tommasini A. **Genetics of inflammatory bowel disease from multifactorial to monogenic forms.** *World J Gastroenterol* 2015; 21(43): 12296-12310.

355 VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE: A CASE SERIES IN A SOUTH FLORIDA POPULATION. Mary Wood, Annette Medina, Desiree Sierra, Alice Huang, Lina Felipez, Alisa Muniz-Crim. *Pediatrics, Nicklaus Children's Hospital, Miami, FL*

Background: Inflammatory Bowel Disease is a complex disorder that requires a genetically susceptible host, environmental triggers and exaggerated mucosal immune response to commensal microorganisms. 20-30% of IBD cases are diagnosed prior to age 18. Very Early Onset IBD (VEOIBD) refers to a subset of patients diagnosed before age 6. VEOIBD patients have less exposure to environmental antigens, and disease pathogenesis is likely more reliant on genetic factors.

Genome Wide Association studies have identified over 180 susceptibility loci for IBD. VEOIBD is more likely to be monogenic versus adult onset IBD. Genetic screening panels focus specifically on monogenic defects to screen for VEOIBD or IBD-like illnesses and include testing for immunodeficiency. VEOIBD patients are more likely to present with only colonic involvement, even in the diagnosis of Crohn's, and are more likely to have relevant family history than adult IBD patients. VEOIBD patients presented with failure to thrive (FTT) up to 44% of the time in some studies.

Objective: To describe the genotypic and phenotypic presentation of 13 patients with VEOIBD at our institution.

Methods: A chart review of 13 patients with VEOIBD was performed. Diagnosis of VEOIBD was based on history, physical exam, radiological, endoscopic, and histopathologic findings. Eligible cases included patients with Ulcerative colitis (UC), Crohn's disease (CD), indeterminate colitis (IC) diagnosed before 6 years of age. Patient data at the time of diagnosis were collected and analyzed.

Results: Thirteen cases were reviewed. The mean age at diagnosis was 3 year 7 months. Eight patients (62%) were male. Nine patients (69%) described their ethnicity as Hispanic. Bloody stools were a frequent presenting symptom, seen in ten patients (77%). Ten patients (77%) described loose stools at presentation while two patients (15%) had severe constipation. Other concomitant diagnoses included: sclerosing cholangitis with transaminitis (one of thirteen), recurrent perirectal abscess (one of thirteen), autism with decreased oral intake and oral aversion (one of thirteen). Z-scores for BMI or weight-for-height at diagnosis ranged from -1.6 to 1.07. All thirteen patients had abnormal colonic findings on histopathologic examination. Ten patients (77%) had gastric or esophageal involvement. Nine patients (69%) had small bowel involvement. All patients with IBD sgi Diagnostic™ results (eleven of eleven) had at least one Single Nucleotide Polymorphisms (SNP) variant detected including: *ATG16L1* (six of eleven), *ECMI* (seven of eleven), *NKX2-3* (eight of eleven), and *Stat3* (six of eleven). Five patients (38%) had Early-Onset Inflammatory Bowel Disease Sequencing Panel performed: one patient had a heterozygous c.238G>A(pV801) variant of the *MVK* gene of unknown significance. Six of thirteen (46%) patients were receiving infliximab therapy at most recent follow up. One patient was on adalimumab, two were on vedolizumab, one was on 6-mercaptopurine (6-MP), one was steroid-dependent, and one patient was on mesalamine. One patient underwent a total colectomy with jejunostomy.

Conclusion: Seventy-seven percent of patients had disease involvement outside the colon which varies from prior data showing a higher prevalence of colonic only involvement in younger patients. Z-scores at diagnosis were not uniformly low, challenging the stereotype of the IBD patient as malnourished. Using the Smart Diagnostic Algorithm of the IBD9 sgi Diagnostic™ panel, all eleven patients tested were identified as having results consistent with IBD. A majority of patients identified themselves as Hispanic. To our knowledge this is the largest case series describing a predominantly Hispanic VEOIBD population in the literature. Some studies have shown Hispanics present with IBD at a younger age and have a more severe course. Further investigation is warranted to determine genetic and other predisposing factors that affect the disease onset and progression.

LIVER

361 VARIABILITY IN ACCEPTANCE OF ORGAN OFFERS BY PEDIATRIC LIVER TRANSPLANT CENTERS AND ITS IMPACT ON WAITLIST MORTALITY.

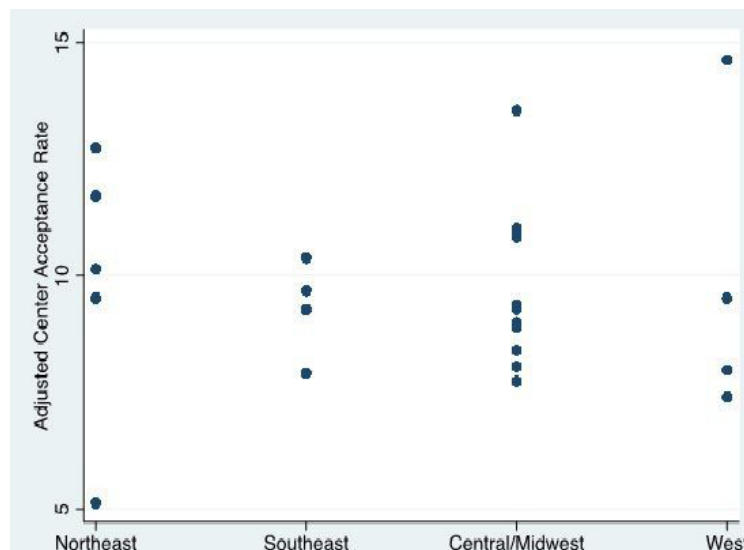
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Introduction: While the focus of variability in access to transplantation has been units of geography, the transplant center itself can greatly impact the probability that a patient will be transplanted or die on the waitlist. A major source of this variability occurs in the decision to accept or decline an organ offer. While differences in acceptance patterns and the impact on patient outcomes has been studied in adults, there are no data on center-level variation in acceptance of organ offers and its impact on children waiting for a liver transplant.

Methods: We evaluated OPTN/UNOS data on all match runs (organ offers) between 5/1/07 and 12/31/15. We restricted analyses to match runs that: 1) ≥ 1 pediatric patient was included; 2) the liver was accepted for a patient ranked in the top 40 of a match run ($>98\%$ of pediatric recipients are transplanted at this rank); and 3) the offer was for a brain-dead donor < 50 years of age. We excluded patients listed for multiple organs and patients listed at low volume centers (< 7 transplants in study period). We fit mixed-effects logistic regression models with patient-and center-level random intercepts to quantify and test for variability in acceptance rates after adjusting for recipient and donor characteristics.

Results: There were 4,088 pediatric patients analyzed among a total of 27,094 match runs. The strongest factors associated with an organ offer decline were: lower initial MELD/PELD, smaller recipient body surface area (BSA), donor Public Health Service increased risk designation, larger donor BSA, and match run rank (ranked at position 5-40). Despite adjusting for donor and recipient factors, there was significant variation in among-center acceptance rates ($p < 0.001$), with adjusted center-level acceptance rates ranging from 5.1% to 14.6% (Figure 1). Center-level acceptance rates impacted waitlist survival, with an 11% increased risk of waitlist death for every 1% decrease in a center's adjusted acceptance rate (adjusted OR=1.11, 95% CI 1.01-1.19).

Discussion: There is significant variability in pediatric transplant center behavior concerning accepting liver offers for waitlisted patients. This undue variability in practice directly impacts whether a child will be transplanted or die waiting. Consideration for public reporting of data and/or work to standardize acceptance practice is necessary to mitigate the risks of a child dying while waiting for a liver transplant.



*362 CORRELATION OF IMMUNE MARKERS WITH SHORT-TERM OUTCOMES IN BILIARY ATRESIA FOLLOWING IVIG TREATMENT.

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Biliary atresia (BA) is a progressive fibroinflammatory cholangiopathy of infancy that is associated with activation of innate and adaptive immune responses targeting bile ducts. A multi-center phase I/IIA trial of intravenous immunoglobulin (IVIg) in BA was recently completed in the Childhood Liver Disease Research Network. The aims of this study were to determine if the peripheral blood mononuclear cell (PBMC) immunophenotype was altered in response to IVIg over time and to determine if changes in specific immune markers were associated with clinical outcomes.

Methods: In 29 infants with BA, IVIg was given on days 3-5, 30 and 60 post- Kasai portoenterostomy (KPE). Flow cytometry of PBMC cell surface markers [natural killer (NK), macrophage subsets, T and B cell subsets, regulatory T cells (Treg)] and activation markers (CD38, CD69, CD86, HLA-DR) was performed. Plasma cytokine analysis was performed with Luminex bead assay. To examine correlations between changes in markers and a change in total bilirubin from baseline to Day 90, Spearman's Rank Correlation was used. Cox proportional hazard models were used to assess changes in markers from baseline to Day 60 in relation to transplant-free-survival at Day 360. Results: Of 29 BA patients, 41% had a liver transplantation (median time to transplantation= 149.5 days post-KPE). Otherwise, all patients completed the Day 360 visit and were censored at that point. Spearman correlations (ρ) of change of an immune marker from baseline to Day 90 with change in serum bilirubin level revealed that a decrease in total bilirubin was significantly correlated with 1) decreased % HLA-DR⁺CD38⁺ NK cells ($\rho=0.775$; $P=0.002$), decreased expression of NK cell activation markers CD69 ($\rho=0.742$; $P=0.004$) and HLA-DR ($\rho=0.588$; $P=0.035$); 2) increased % Tregs ($\rho=-0.653$; $P=0.011$); and 3) decreased level of IL-8 ($\rho=0.681$; $P=0.001$). Cox models of survival with the native liver at Day 360 revealed that increased % of HLA-DR⁺CD38⁺ NK cells at Day 60 (HR= 1.15; 95% CI: 1.00-1.32; $P=0.055$) and increased plasma IL-8 levels at Day 60 (HR=1.01; 95% CI: 1.00-1.01; $\rho=0.001$) were significantly associated with an increased risk of transplant or death by Day 360.

Conclusion: Favorable outcomes in BA were associated with decreased activated NK cells and IL-8 levels, and increased Tregs in the first 60 and 90 days post-KPE. It is unclear if IVIg treatment was responsible for these changes, or if they represented the natural history of BA. Future studies aimed at determining the specific role of NK and Treg cells and IL-8 in bile duct injury could result in the use of immunotherapies targeting inhibition of NK cells and IL-8 and enhancement of Tregs.

364 HEPATIC DYSFUNCTION IS LINKED TO A DISTINCT PHENOTYPE OF ACTIVITY AND DISTRIBUTION OF BOWEL DISEASE IN AN INCEPTION COHORT OF PEDIATRIC PATIENTS WITH ULCERATIVE COLITIS. James Squires¹, Sonia Davis², Margaret Collins³, Kristen Critelli¹, Yael Haberman⁴, Cary Sauer⁵, James Markowitz⁶, David Mack⁷, Brendan Boyle⁸, Anne Griffiths⁹, Neal LeLeiko¹⁰, Subra Kugathasan⁵, Thomas Walters⁹, Lee Denson⁴, Jeffrey Hyams¹¹, Alexander Miethke⁴. ¹Pediatric Hepatology, Children's Hospital of Pittsburgh, Pittsburgh, PA; ²University of North Carolina, Chapel Hill, NC; ³Pathology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ⁴Gastroenterology and hepatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ⁵Emory, Atlanta, GA; ⁶North Shore University Hospital, New York, NY; ⁷Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; ⁸Nationwide Children's Hospital, Columbus, OH; ⁹Sick Kids, Toronto, ON, Canada; ¹⁰Brown University, Providence, RI; ¹¹Connecticut Children's Medical Center, Hartford, CT

Background/Aims: Hepatobiliary complications are common in ulcerative colitis (UC). The PROTECT (Predicting Response to Standardized Pediatric Colitis Therapy) Cohort enabled us to assess the prevalence of liver function test (LFT) elevation at diagnosis and to compare differences in the clinical phenotype in children with and without evidence of liver dysfunction.

Methods: The PROTECT cohort includes 431 children (4-17 years) newly diagnosed with UC. Endoscopic mucosal changes were reported in standardized fashion and rectal biopsies were centrally reviewed. AST, ALT, GGT, bilirubin and alkaline phosphatase, were measured. Demographic data and disease phenotype were analyzed in four groups: 1) 8 subjects with a

concomitant diagnosis of autoimmune liver disease (AILD; AIH n=1, PSC n=5, and overlap syndrome n=2), 2) 29 subjects with elevated LFTs but without a diagnosis of AILD, 3) 77 subjects with documented normal LFTs, and 4) those with documented normal or incomplete LFTs at the baseline visit (n=394).

Results: In subjects with liver dysfunction (groups 1 and 2) compared to controls (groups 3 and 4), fold changes in GGT as marker for cholestasis were higher than those for hepatocellular injury (ALT, AST; Table 1). Liver injury, based on serum chemistries, was more severe in subjects with concomitant AILD. Demographics, clinical severity of colitis (PUCAI), Mayo endoscopy subscore, histologic findings, fecal calprotectin and ESR, and presence of auto-antibodies (ANCA) were analyzed. Despite most having pancolitis, subjects with liver dysfunction had lower PUCAI scores ($p \leq 0.01$), infrequent severe colitis (PUCAI > 65) and lower fecal calprotectin levels ($p = 0.05$) consistent with milder intestinal inflammation. Notably, ileal erythema ($p \leq 0.02$) and high-grade rectal mucosal eosinophilia ($p < 0.01$) were more common in those with elevated LFTs. Higher ESR in groups 1 and 2 suggested an association between systemic inflammation and hepatic dysfunction. Positive ANCA titers were present in all patients with AILD and more prevalent in group 2 subjects compared with controls. Presence of recorded values for all LFTs necessary for assignment to group 3 appeared to bias to a more severe colitis phenotype compared with group 4. Still, differences in activity and distribution of colitis, presence of ileal erythema and mucosal eosinophilia counts remained different between subjects with hepatic dysfunction and the larger control group.

Conclusions: Hepatic dysfunction was present in 8.6% of children at the time of diagnosis of UC and was associated with a distinct phenotype characterized by mild colitis and rectal eosinophilia. We speculate that systemic inflammation contributes to cholestatic liver dysfunction. Further studies will need to elucidate causality between this UC phenotype and risk factors for development of chronic liver disease. (DK 095745-01)

Serum liver biochemistries for participants enrolled with UC by liver disease categories

Characteristic	Concomitant Hepatobiliary Disease (1) (n=8)	Hepatobiliary Biomarker Elevation (2) (n=29)	Normal LFTs (3) (n=77)	Normal or missing values for LFTs (4) (n=394)	P-value for level (1+2) vs 3	P-value for level (1+2) vs 4
ALT (U/L) Median (IQR)	97.5 (54.0,129.5)	53.0 (28.0,87.0)	14.0 (11.0,19.0)	17.0 (11.0,22.0)	<0.001	<0.001
AST (U/L) Median (IQR)	87.5 (40.0,100.0)	49.5 (23.5,88.0)	20.0 (16.0,24.0)	21.0 (16.0,27.0)	<0.001	<0.001
Direct Bilirubin Median (IQR)	0.2 (0.2,0.3)	0.2 (0.1,0.3)	0.1 (0.1,0.2)	0.1 (0.1,0.2)	0.02	0.002
GGT (U/L) Median (IQR)	260.0 (178.0,474.0)	95.0 (51.5,244.5)	10.0 (8.0,12.0)	11.0 (9.0,15.0)	<0.001	<0.001
ALP (U/L) Median (IQR)	543.0 (346.0,705.0)	168.0 (108.5,288.0)	109.0 (82.0,161.0)	125.0 (91.0,169.0)	<0.001	<0.001

366 LACK OF DIET1 DISRUPTS THE LINK BETWEEN BILE ACIDS TO OBESITY AND NAFLD.

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Patients with obesity and obesity related fatty liver disease (NAFLD) have been observed to have lower serum bile acid levels. This serum bile acid level is increased as weight is lost after weight loss surgery. Bile acid production is regulated by the hepatic Farnesoid X Receptor (FXR) -Small Heterodimer Partner(SHP) signaling pathway which is in turn activated by the entero-hepatic hormone fibroblast growth factor 15/19 (FGF15/19). Recent work suggests that FGF15/19 itself is secreted from the enterocyte dependent expression of an intestinal protein called Diet1.

Hypothesis/Aim: We hypothesized that the absence of Diet1 would result in decreased FGF15/19 release from the intestine and the subsequent uncoupling of serum bile acid level from obesity.

Methods: We used Diet1 knock out (Diet1KO) mice fed a high fat high carbohydrate (HFHC) diet to investigate the role of FGF15 signaling in the setting of diet induced obesity and NAFLD. 6-8 weeks old female mice (n=4-5) of C57Bl6/J strain (wildtype, WT) and Diet1KO were fed HFHC (high fat 58% kCal; high carbohydrate: 2.31% fructose, 1.89% sucrose) diet for 16 weeks. All mice gained weight on a HFHC diet, and despite being lower in weight to begin with, the Diet1 mice had the same bodyweight as WT mice after 16 weeks on the HFHC diet. Further, we observed no difference in the liver triglyceride concentration among the wildtype and Diet1KO mice group ((463.66 ± 89.71 mg/dL (16 week WT female); 471.15 ± 102.47 mg/dL (16 week Diet1KO female)). No difference in the fasting total serum bile acid concentration was observed either ((5.41 ± 0.79 μmole/L (16 week WT female); 5.45 ± 0.41 μmole/L (16 week Diet1KO female)). Finally, as expected after 12 and 16 weeks on the HFHC diet, a negative correlation of serum bile acid level to body weight was observed among the wildtype female mice (r = -0.86, p= 0.02 (12 week WT female); r= -0.91, p=0.01 (16 week WT female)). However, no such correlation of serum bile acid level to body weight was observed among the Diet1KO mice (r = 0.57, p= 0.11 (12 week Diet1KO female); r= -0.59, p=0.10 (16 week Diet1KO female)).

Conclusion: The absence of Diet1 disrupts normal enterohepatic bile acid synthesis feedback. This signaling pathway appears to be critical in the suppression of bile acid production seen in obesity and NAFLD. These findings suggest further work maybe important to understand the role of Diet1 as a potential therapeutic target for the treatment of obesity and NAFLD.

368 LIVER ENZYMES IN HYPERCKEMIA. Jiawei Cui^{2,1}, Amit Shah¹, Elizabeth Kichula³, Henry Lin^{1,4}. ¹GI/Hepatology/Nutrition, Children's Hospital of Philadelphia, Chapel Hill, NC; ²School of Medicine, University of North Carolina, Chapel Hill, NC; ³Neurology, Children's Hospital of Philadelphia, Philadelphia, PA; ⁴Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA

Introduction: Aspartate transaminase is an enzyme present in liver and other organs including muscle, while alanine transaminase is significantly more liver-specific. Traditional clinical reasoning assumes that patients with hyperCKemia likely have an elevated AST:ALT as creatinine kinase (CK) is a specific marker of muscle damage. Subsequently, a CK is rarely ordered during the evaluation of elevated liver enzymes even though it may be of diagnostic value.

Purpose: The objective of this study is to describe the ratio of AST to ALT in patients with hyperCKemia and associated transaminitis.

Methods: A retrospective review was conducted on children with elevated CK level as well as an elevated AST or ALT who subsequently had a CK level checked between 2008-2015. Clinical records were reviewed for presenting features, diagnostic evaluation, as well as ultimate diagnosis.

Results: A total of 103 patients had hyperCKemia (>1.5 times normal). Reasons for checking CK included pauci symptoms[1] (54% [56/103]), elevated LFTs (36% [37/103]), and rhabdomyolysis (13% [13/103]). The average peak CK was 11,1150 and average AST 164, ALT 125.

Thirty-seven patients had CK levels checked because of abnormal liver enzyme values, the average AST was 218 (range 39-534) and ALT was 196 (range 42-795). Average AST:ALT ratio was 1.19 (range 0.62-1.98) with an average peak CK of 9509 (range 418-37909).

62% (23/37) presented with pauci symptoms including myalgia, cramping, fatigue, and motor delay. There was no clinical significance between the symptomatic and asymptomatic groups for CK or AST, however, there was a significantly higher ALT in symptomatic patients (p < 0.05). 59% (22/37) had neurologic physical exam findings[2]. Patients with physical exam findings had significantly higher AST (p < 0.05) and ALT (p < 0.05) than those without, but there was no clinically significant difference in CK.

Six of the 37 patients had liver biopsies, 5 of whom had them done prior to the CK being checked and 1 who received the liver biopsy for an underlying liver condition. All 6 were diagnosed with various forms of muscular dystrophy. The average liver enzymes levels prompting a liver biopsy were AST 248 (range 69-525) and ALT 317 (range 74-795).

68% (25/37) were given a definite diagnosis. Diagnoses included Becker's muscular dystrophy (32%), Limb-Girdle muscular dystrophy (24%), Duchenne's muscular dystrophy (16%), metabolic disorders (4%) and other (24%).

Conclusion: In patients with transaminitis due to a muscular etiology, there is no specific pattern for AST:ALT ratio. It is important for gastroenterologists to recognize when it is appropriate to check CK to avoid missing a critical muscular diagnosis. The majority of patients referred to neurology because of elevated liver enzyme levels are given a serious muscular diagnosis. Presenting symptoms and physical exam findings should significantly raise suspicion for a muscular disorder.

However, physicians should still consider checking CK levels in the setting of transaminitis, regardless of the presence of symptoms or PE findings, especially prior to pursuing a more invasive procedure like liver biopsy.

1. Pauci symptoms include myalgia, cramping, fatigue, motor delay, myoglobinuria, rhabdomyolysis, FTT and exercise intolerance.
2. Physical exam findings include weakness, sensory loss, hypotonia, calf pseudohypertrophy, tight heel cords, toe walking, scoliosis, and hepatosplenomegaly.

***370 EFFECT OF SEBELIPASE ALFA ON SURVIVAL TO 3 YEARS OF AGE AND LIVER FUNCTION IN INFANTS WITH RAPIDLY PROGRESSIVE LYSOSOMAL ACID LIPASE DEFICIENCY.** Simon Jones¹, Anaïs Brassier², Joanne Hughes³, Dominique Plantaz⁴, Roshni Vara⁵, Catherine Breen¹, J. Gargus⁶, Sachin Marulkar⁷, Mark Friedman⁷, Vassili Valayannopoulos^{2,8}. ¹Manchester Centre for Genomic Medicine, Central Manchester Foundation Trust, University of Manchester, Manchester, United Kingdom; ²Hôpital Necker-Enfants Malades and IMAGINE Institute, Paris, France; ³The Children's University Hospital, Dublin, Ireland; ⁴Hôpital Couple-Enfants CHU Grenoble, Grenoble, France; ⁵Evelina Children's Hospital, Evelina, United Kingdom; ⁶University of California, Irvine, Irvine, CA; ⁷Alexion Pharmaceuticals, Inc., New Haven, CT; ⁸Sanofi-Genzyme, Cambridge, MA

The objective of this ongoing phase 2/3 study is to evaluate the safety and efficacy (including survival) of enzyme replacement with sebelipase alfa (SA) in infants with rapidly progressive lysosomal acid lipase deficiency (LAL-D). Previously reported data show improved survival of patients treated with SA compared with a historical cohort whose median age at death was 3.7 months [Jones et al. *Genet Med.* 2016;18(5):452-8]. Other outcomes being assessed include changes in markers of liver injury, hematological effects, weight centiles, and functional development. Nine infants with confirmed LAL-D were enrolled. All had significant liver dysfunction at baseline. Median (range) age at treatment initiation was 3.0 (1.1–5.8) months. As of August 28, 2016, 5 patients had survived to 3 years of age or older. Assessments of the 5 patients as of August 28, 2016 showed improvements, with median percentage change (range) for serum alanine aminotransferase, –38% (–85% to +11%); aspartate aminotransferase, –59% (–64% to –34%); hemoglobin, +29% (0% to +75%); and albumin, +11% (+3% to +79%). Median weight percentile changed from 3.1% at baseline to 37.0%; gastrointestinal symptoms improved and hepatosplenomegaly was reduced. The most recent Denver II Developmental Screening Test assessments showed all 5 ongoing patients scored as normal. Over the 1 year prior to this assessment there were 2 unrelated serious adverse events (croup and malabsorption [hypoalbuminemia] in 2 different patients); none discontinued treatment because of tolerability or infusion reactions. Of 7 patients tested for anti-drug antibodies, 4 had detectable titers, 2 of whom developed neutralizing antibodies; all 4 continued treatment and no association has been made between presence of antibodies and safety and efficacy. In conclusion, SA is associated with a substantial survival benefit compared with historical controls, a favorable safety profile, and sustained improvements in disease manifestations in infants with LAL-D. Investigators report all patients have exhibited normal development.

***371 THE ILEAL BILE ACID TRANSPORT INHIBITOR A4250 REDUCED PRURITUS AND SERUM BILE ACID LEVELS IN CHILDREN WITH CHOLESTATIC LIVER DISEASE AND PRURITUS: FINAL RESULTS FROM A MULTIPLE-DOSE, OPEN-LABEL, MULTINATIONAL STUDY.**

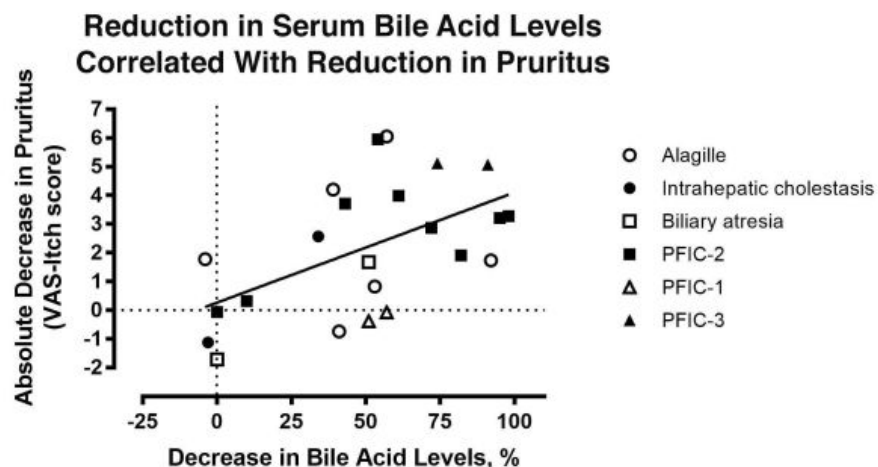
Ekkehard Sturm¹, Ulrich Baumann², Florence Lacaille⁶, Emmanuel Gonzales⁷, Henrik Arnell⁸, Bjorn Fischler⁸, Marianne Horby Jorgensen⁴, Richard Thompson³, Jan Mattsson², Mats Ekelund², Erik Lindström², Per-Göran Gillberg², Kristina Torfgard², Paresh Soni⁹. ¹Pediatric Gastroenterology and Hepatology, University Children's Hospital Tuebingen, Tubingen, Germany; ²Albireo AB, Gothenburg, Sweden; ³Institute of Liver Studies, King's College London, London, United Kingdom; ⁴Pediatric and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark; ⁵Klinik für Pädiatrische Nieren-, Leber- und Stoffwechselerkrankungen, Medizinische Hochschule Hannover, Hannover, Germany; ⁶Pediatric Gastroenterology Hepatology-Nutrition, Necker- Enfants Maladies Hospital, Paris, France; ⁷Pediatric Hepatology and Liver Transplantation, University Hospitals of Paris-Sud, Bicetre, France; ⁸Pediatric Gastroenterology, Hepatology and Nutrition, Astrid Lindgren Children's Hospital, Karolinska University Hospital, Stockholm, Sweden; ⁹Albireo Pharma, Boston, MA

Background: Ileal bile acid transporter (IBAT) inhibition is a novel therapeutic concept for cholestatic pruritus and progression of cholestatic liver disease. A4250, a potent, selective inhibitor of IBAT, is minimally absorbed by the gut and binds reversibly to IBAT to decrease enteric bile acid reuptake.

Methods: This phase 2 study in children with cholestatic liver disease and pruritus evaluated the safety and tolerability of A4250 and explored changes in serum bile acid levels (primary efficacy endpoint), pruritus, and sleep disturbance, among others. A4250 was administered orally once daily for 4 weeks at 5 doses (10–200 µg/kg).

Results: Twenty patients (8 females) aged 1 to 17 years were enrolled (4 patients were re-entered per protocol and treated at a different dose): progressive familial intrahepatic cholestasis (PFIC type 1, 2, or 3; n=13; 3 re-entries), Alagille syndrome (n=6), biliary atresia (n=3), intrahepatic cholestasis (n=2; 1 re-entry). No serious AEs were deemed treatment related, and most AEs, including some increased transaminases, were transient. Serum bile acid levels were high at baseline (26–564 $\mu\text{mol/L}$; >20x ULN in 12 out of 20 patients) and were reduced in a majority of patients (0–98% reduction (Figure). Patient-reported diary data also documented improvements in pruritus (as measured by 3 separate scales) and sleep. The greatest improvement was in the 100 $\mu\text{g/kg}$ cohort with absolute mean ($\pm\text{SEM}$) decreases of 2.9 ± 1.1 points for pruritus (visual analog scale [VAS-Itch]; 0–10) and 3.0 ± 0.9 points for sleep disturbance (patient-oriented score of atopic dermatitis-sleep; 0–10). Reductions in VAS-Itch were significantly correlated with reductions in serum bile acids ($P\leq 0.008$; Figure).

Conclusion: In this study of pediatric cholestatic diseases, A4250 was well tolerated and reduced serum bile acid levels, pruritus, and sleep disturbance in most patients. A4250 has the potential to be a significant and novel advance for the treatment of pediatric cholestatic disease.



376 ASSOCIATION OF DIETARY CARBOHYDRATES AND SUGARS WITH NONALCOHOLIC FATTY LIVER DISEASE: A SYSTEMATIC REVIEW. Kathryn Harlow^{1,2}, Elizabeth Yu^{1,2}, Shivali Joshi³, Nidhi Goyal^{1,2}, Kimberly Newton^{1,2}, Jeffrey Schwimmer^{1,2}. ¹Gastroenterology, University of California San Diego, San Diego, CA; ²Gastroenterology, Rady Children's Hospital, San Diego, CA; ³University of California San Diego, San Diego, CA

Objective: Many studies have examined the relationship between diet and nonalcoholic fatty liver disease (NAFLD). In particular, there has been much enthusiasm surrounding the role of dietary carbohydrates in the development and progression of NAFLD. However, no consensus has been reached and major gaps in our knowledge remain. Because dietary counseling is a major component in the management of NAFLD, a thorough understanding of the evidence is needed to support treatment recommendations. Therefore, we performed a systematic review of the extent literature to evaluate the relationship between dietary carbohydrate intake and NAFLD.

Methods: We conducted a search of PubMed for original research articles, available through April 2017, using key words “dietary sugar” and “NAFLD.” Studies were limited to those in human subjects and published in English. We included observational studies in both children and adults. Eligible studies reported an exposure variable of dietary carbohydrate or dietary sugar intake, as well as the outcome variable of fatty liver or a commonly used surrogate measure. Studies with small sample size ($n<15$) were excluded.

Results: We evaluated a total of 17 studies, which included 22,234 participants. Of those, 5 studies were done in children and included 2,683 participants. In these pediatric studies, fatty liver was assessed by liver histology in 6%, magnetic resonance spectroscopy in 3%, and ultrasound in 91%. Total carbohydrates were evaluated in 5 studies; of these, one study had a positive relationship with NAFLD, and four studies had no relationship with NAFLD. Total dietary sugar intake was evaluated in 2 studies and no association with NAFLD was found. Free sugar intake was examined in 5 studies, all of which showed no association with NAFLD. In a total of 12 adult studies ($n= 19,551$), fatty liver was assessed by liver histology in 3%, ALT in 81%, CT scan in 13%, ultrasound in 3%. Total carbohydrates were evaluated in 5 studies, with varying results. There was an inconsistent association with ALT and no association with US. Studies with liver histology reported a positive association between total carbohydrate intake with either steatohepatitis or presence of inflammation. Total dietary sugars were evaluated in two studies, both using US, with one study showing a positive association between total sugar intake and NAFLD and the

other with no association. Free sugar intake was evaluated in 7 studies and was positively associated with hepatic steatosis in 4 of these studies, and not associated with hepatic steatosis in 3 of these studies. Free sugar intake was positively associated with the severity of fibrosis in 3 of these studies.

Conclusion: Dietary modification is a mainstay in the treatment of NAFLD and there is an increasing focus on dietary carbohydrates. Data to date do not support a NAFLD-specific recommendation regarding dietary carbohydrate and sugar intake. Only 10% of available data are in children and there are roughly equal numbers of positive and negative studies for association with hepatic steatosis or fibrosis. To move the field ahead, adequately powered studies with standardization in the measurement of exposure and outcome variables are required.

378 **BILE ACID SYNTHESIS DISORDERS IN ARABS: A 10-YEAR PROSPECTIVE SCREENING STUDY USING SERUM TOTAL BILE ACIDS WITH CONFIRMATORY MASS SPECTROMETRY AND GENETIC ANALYSES FOR DIAGNOSIS AND FOLLOW-UP TO CHOLIC ACID THERAPY.**

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Objectives: Early diagnosis of bile acid synthesis disorders (BASD) is important because, untreated these conditions can be fatal. Our objective was to screen Saudi Arabian children with cholestasis or unexplained liver disease and to evaluate the effectiveness of cholic acid therapy in patients with confirmed BASD.

Methods: Serum total bile acids (sTBA) were measured on children with cholestasis, liver cirrhosis, and liver failure. Patients were screened for BASD by fast atom bombardment ionization-mass spectrometry (FAB-MS) analysis of urine, and molecular analysis confirmed diagnosis. Treatment response to oral cholic acid (10-15 mg/kg bw/day) was assessed from serum liver chemistries and fat-soluble vitamin levels. FAB-MS analysis of urine was used to monitor compliance and biochemical response to therapy.

Results: Between 2007 and 2016, 626 patients were evaluated; 450 with infantile cholestasis. Of 626 serum samples analyzed for sTBA level, low or normal sTBA levels (<10mmol/L) were observed in 18 of the 541 specimens collected from cholestatic cases (\approx 3%). Abnormal urinary bile acid metabolites identified by FAB-MS analysis and characteristic of BASD were observed in 12 of the 18 patients and definitively confirmed on repeat analysis in 11 patients, but not in one initially suspected as having Δ^4 -3-oxosteroid 5 β -reductase deficiency (AKR1D1) deficiency. 3 β -hydroxy- Δ^5 -C₂₇-steroid oxidoreductase deficiency (HSD3B7) deficiency was confirmed in 8 cases and AKR1D1 in 3 cases. The remaining patients had urinary bile acid profiles consistent with non-specific cholestasis. Three patients from the 85 cases of non-cholestatic liver disease that were tested were confirmed to have HSD3B7 deficiency by direct urine FAB-MS analysis alone and these included an 8-year old boy presenting with cirrhosis, and two 18-month old boys presenting with hepatomegaly and rickets. Among the 523 patients with cholestasis and elevated sTBA concentrations, urine FAB-MS analysis revealed abnormal bile acid metabolites suggestive of a BASD in 2 out of 216 urinary specimens tested. Repeat analysis confirmed one to be Zellweger Spectrum Disorder (ZSD), confirmed by genetic testing, and one suspected AKR1D1 deficiency was not confirmed. Of the 15 cases of BASD diagnosed by FAB-MS and genetic testing, 12 of the 450 tested presented with infantile cholestasis (2.7%). Overall, 11 were caused by 3 β -hydroxy- Δ^5 -C₂₇-steroid oxidoreductase deficiency, three from Δ^4 -3-oxosteroid 5 β -reductase deficiency, and one had ZSD. In all but one (ZSD), sTBA were normal or low. After tabulation of the results of sTBA levels in a 2X2 format, and using urinary FAB-MS as the reference gold-standard test for diagnosis, the use of low/normal sTBA level to initially screen for BASD among infants and children with cholestatic liver disease had an overall sensitivity of 92% and specificity of 97%. With cholic acid therapy, 10 are alive and healthy with their native liver. Liver failure developed in 3 infants despite initiation of therapy; 2 died, and one underwent liver transplantation.

Conclusion: BASD are rare but treatable causes of metabolic liver disease in Saudi Arabia. Screening for BASD should be considered in all infants with cholestasis and the finding of a normal/low serum total bile acid concentrations offers a simple tool to pinpoint potential BASD, specifically the two most common disorders, the HSD3B7 and AKR1D1 deficiencies.

380 TIGHT JUNCTION PROTEIN 2 (TJP2) GENOTYPE AND GENOTYPE IN THE ERA OF NEXT GENERATION SEQUENCING. Kishwer Kumar¹, Ali Syed Akhatur¹ Hassan¹, Mohamed Barr¹, Dieter broering¹, Husa Al Hussaini², Mohammad Shagrani¹. ¹Pediatric Transplant Hepatology, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia; ²Department of Pathology and Laboratory Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh, Riyadh, Saudi Arabia

Objectives/Study: Tight junction protein 2 (TJP2) mutation is now recognized as a distinct clinical entity. Previously individuals with this genetic mutation were misdiagnosed because of phenotypic and laboratory features which are also found in other cholestatic liver diseases

The main function of TJP2 is to prevent the back diffusion of bile salts from the canaliculi to the blood circulation at the Para cellular level. This is why children with TJP2 mutation present with normal GGT, high serum bile acid and fat malabsorption. Though it remains unknown, but these patients eventually develop progressive cholestasis with high liver enzymes and bilirubin progressing to end stage liver disease. This course also resembles that we find in progressive intrahepatic cholestasis types 1 and 2.

Previous literature documents missense mutations in TJP2 gene in patients having oligogenic inheritance with familial hypercholanemia. These patients were described as a having a benign disease treatable with early initiation of UDCA.

However we have observed a much severe course in TJP2 mutation patients which is in striking contrast to earlier literature. This makes it imperative to make an early accurate diagnosis of these patients so that timely intervention can be made to keep their health in optimum condition.

Methods/Results: We used next generation sequencing-based multi-gene panel for the first time to diagnose familial cholestasis diseases at our center.

In our retrospective cohort there were seven patients out of 98 patients turned out to have TJP2 mutations, four of whom had novel mutations. Prior to the next generation sequencing, these patients had been erroneously diagnosed as having various diagnoses. The genetic tests sent initially did not prove any genetic disorder. Based on clinical and biochemical profile five of them were labeled and being managed as progressive intrahepatic cholestasis type 2, one was diagnosed as hepatoblastoma and the 7th was diagnosed as having congenital hepatic fibrosis. Their age at presentation varied between 8 days to 7 years. All had high bile acids, high ALT, AST and bilirubin except the one who was initially diagnosed as having congenital hepatic fibrosis. All of these children required liver transplantation at different ages ((from neonatal period up to 12 years of life). All the explanted livers obtained from the affected children showed end stage biliary cirrhosis with florid ductular reaction (fig 1 &2). The liver parenchyma showed unusual features not commonly seen in association with pediatric cholestasis. One of the most striking feature is diffuse giant cell transformation of the hepatocytes with severe degree of cholestasis This feature is far more than seen in liver with progressive familial cholestasis type 2. The other feature is the abundance of cytoplasmic mallory hyaline bodies in most of the liver cells.

Conclusions: Since there is an overlap in the biochemical profile and the phenotypic presentation of TJP2 gene mutation and other cholestatic liver diseases such as PFIC1 and PFIC2, we therefore emphasize the importance of confirming the diagnosis by genetic studies wherever possible.

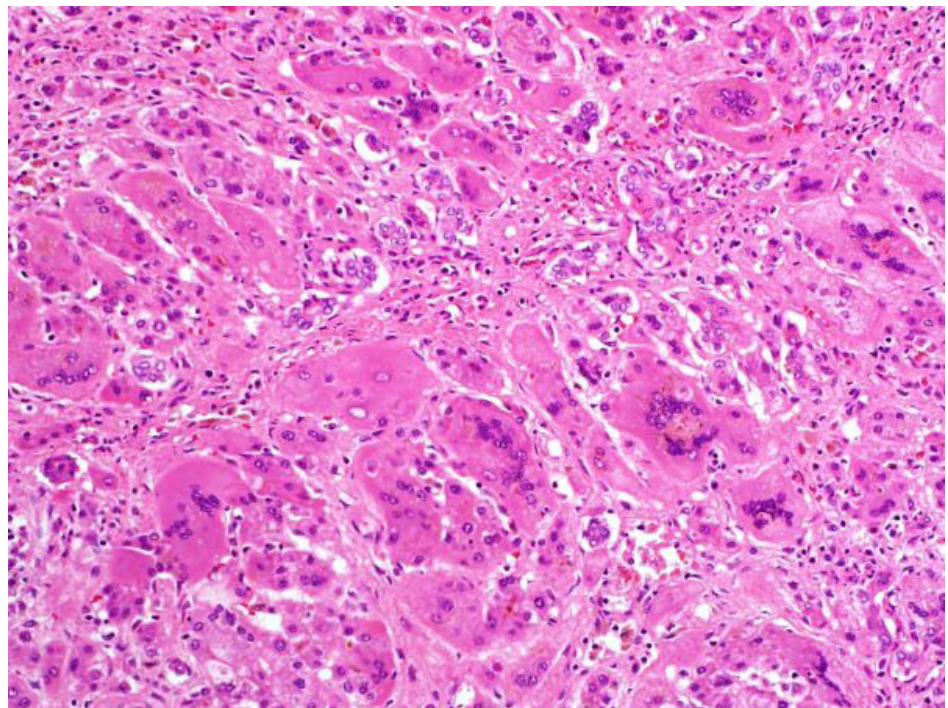


Figure 1: Light microscopy showed prominent giant cell transformation of the liver cells (HE X20)

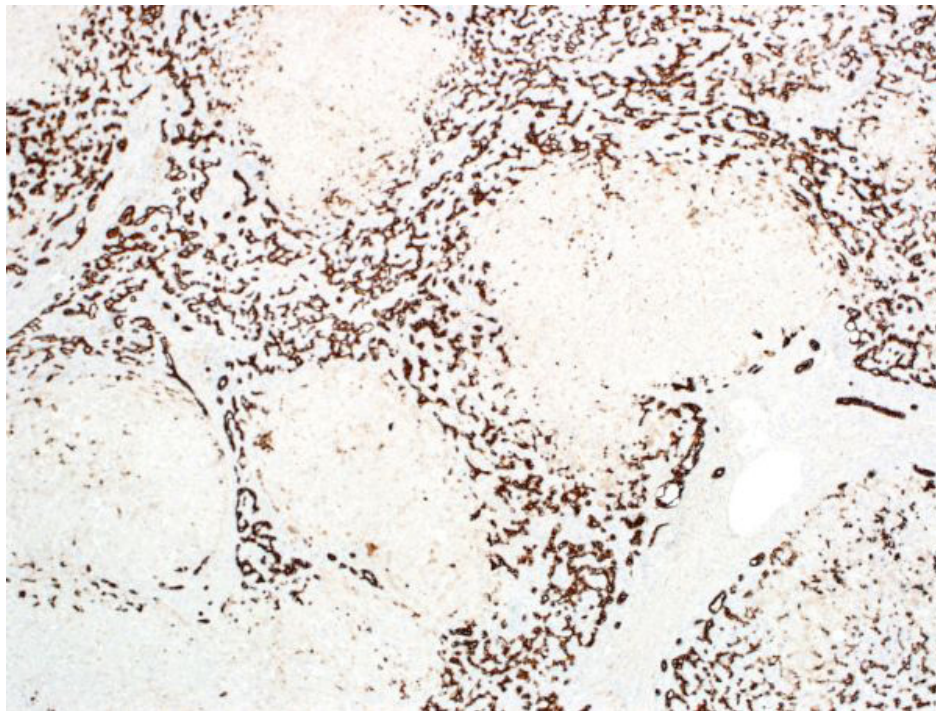


Figure 2: Cytokeratin 19 illustrated severe degree of ductular proliferation

387 **LISTING HYPONATREMIA ASSOCIATED WITH INCREASED MORTALITY RISK IN PEDIATRIC LIVER TRANSPLANT CANDIDATES: A UNOS DATABASE ANALYSIS FROM 2005-2015.**

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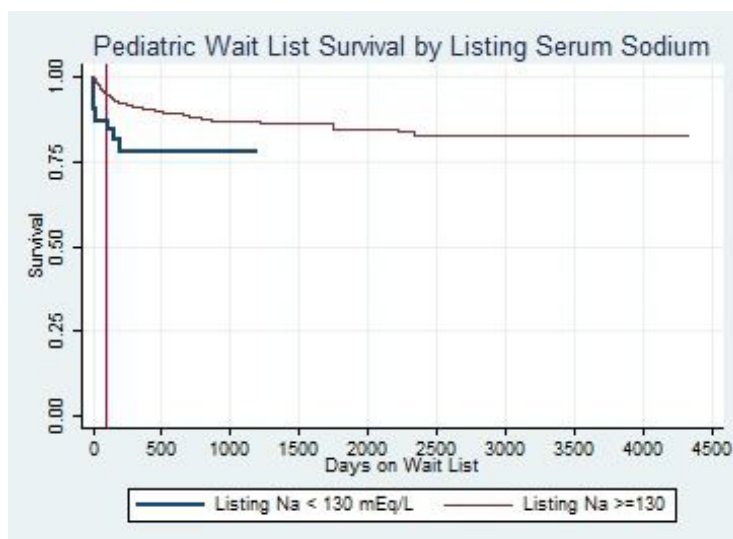
Background: Donor organ allocation to registrants on the liver transplant waiting list is based on severity of liver disease. The PELD score, a calculation from measurable medical criteria, determines priority on the list in children. Despite decreases in waiting list mortality with PELD implementation in 2002, by 2005 less than half of pediatric registrants were transplanted at their allocated PELD at many centers, with a majority requiring exception points for successful transplantation. In adults, inclusion of serum sodium (Na) into MELD calculation was found to improve its accuracy in predicting disease severity. Serum Na as an independent prognostic factor in pediatric liver disease has been demonstrated in 2 small studies, but not yet clearly elucidated on a large scale in the US pediatric transplant population. Our aim was to assess the effect of Na on PELD score at listing.

Method: Using the UNOS database we analyzed patients ≤ 18 years with chronic liver disease listed for isolated liver transplant from 2005 -2015. We excluded multi-organ, history of prior liver transplant, multiple listings & standard exceptions. Hyponatremia was defined as $\text{Na} < 130 \text{mEq/L}$. Univariable associations to death were performed using Mann-Whitney test & χ^2 . Cox proportional hazard modeling was used.

Results: 4728 patients in the cohort; at listing 49% were < 2 years, 51% white, 44% diagnosed with biliary atresia. Median MELD/PELD was 13 (range -11, 67) & 159 (3%) had hyponatremia at listing. 4246 underwent transplant/recovered, 298 (7%) didn't survive through transplantation & 184 remained on waiting list at censorship. 13% with hyponatremia died vs 6% with normal Na ($p < 0.01$). Those with $\text{Na} \geq 130 \text{mEq/L}$ at listing had lower risk of death ($p < 0.01$, HazardRatio 0.26, CI 0.17-0.41) than those with $\text{Na} < 130 \text{mEq/L}$. Kaplan-Meier survival curve demonstrated poor survival in the hyponatremic group ($p < 0.01$). Total chronologic time on wait list for those who died pre-transplant was 29 days if hyponatremic vs 165 days if not hyponatremic ($p = 0.04$).

Conclusion: Hyponatremia at listing identifies pediatric patients with an increased risk of pretransplant mortality; this has been demonstrated in prior adult studies & 2 smaller pediatric studies. This study demonstrates the significance of hyponatremia at listing as a poor prognostic factor for pre-transplant mortality for all pediatric liver transplant registrants across the United States from the UNOS database. Since half of pediatric liver transplantations do not occur at calculated

PELD, which currently does not account for Na, consideration should be given to update PELD calculations with inclusion of Na to more accurately reflect true pre-transplant mortality.



388 WILLIAMS SCORE APPLIED TO MAGNETIC RESONANCE IMAGING IN THE EVALUATION OF CHILDREN WITH CYSTIC FIBROSIS. Marilisa Baldissera¹, Matias Epifanio¹, Leonardo Pinto¹, Rita Mattiello¹, Diego Roman², Francisco Santos³, José Marostica⁴, Bruno Hochhegger², Matteo Baldisserotto². ¹Pediatric, PUCRS, Porto Alegre, Brazil; ²Radiology, PUCRS, Porto Alegre, Brazil; ³PUCRS, Porto Alegre, Brazil; ⁴Pediatric Pulmonology, Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil

Background: Cystic fibrosis liver disease (CFLD) has become more frequent with the increase in patients survival. Early diagnosis is one of the challenges involved in the follow-up of cystic fibrosis (CF) patients, because CFLD may remain clinically silent up to advanced stages.

The development of cirrhosis and portal hypertension occurs in nearly 5% of CF patients and often starts in the first decade of life. However, in 90% of patients the diagnosis of CFLD is only established at around 20 years of age. Noninvasive methods for monitoring a CFLD are extremely necessary. Magnetic resonance imaging (MRI) plays a growing role and may contribute to change diagnostic techniques in the near future. The aim of our study was to describe some abnormalities found on the MRI of CF children and to correlate these abnormalities with US findings, especially with regard to parameters of hepatic parenchyma, liver edge, and liver fibrosis described in the ultrasound scoring system proposed by Williams et al.

Methods: Prospective study including patients with confirmed diagnosis of CF. Only patients old enough to undergo MRI without sedation were included in the study. Informed consent was obtained from all parents or legal guardians. The children also gave assent. The patients underwent clinical and anthropometric assessment, US, and MRI. MRI scans were obtained without contrast. Liver was evaluated according with the score proposed by Williams et al., which was applied to assess US and MRI findings.

Results: Twenty patients aged from 8 to 20 years (mean 15.1±3.3) were included in the study. Five patients (25%) met the criteria for CFLD. Four of these patients had a score of 7, and one patient had a score of 9. When Williams criteria were used to assess MRI findings, all of the five patients had a score of 9. Of the five patients with CFLD, four had a score of 1 on the ultrasonographic assessment of fibrosis. However, these same four patients had a score of 3 when assessed by MRI. The remaining 15 patients did not exhibit changes in hepatic parenchyma, liver edge, and liver fibrosis either on US or on MRI. Hepatic parenchyma, liver edge, and liver fibrosis could be properly assessed using the US criteria developed by Williams et al by MRI scans. Other MRI findings included four patients with liver right lobe atrophy, three with regenerative nodules, and two with esophageal varices. Four patients (20%) presented with RPN. One of these patients did not show any change in the other hepatic parameters; even so, an association was observed between the presence of RPN and fibrosis on MRI assessment (p=0.032).

Conclusion: This study found that there was a good agreement between the liver assessment results obtained from US and MRI. Both US and MRI were able to evaluate hepatic parenchyma and liver edge with significant agreement. However, in four patients, MRI identified changes related to liver fibrosis (an important criterion for the evaluation of CFLD) that were not

identified by US. Since CFLD is a progressive disease, the use of a scoring system that may determine the progression and the severity of this condition is highly relevant for clinical follow-up. A scoring system for CFLD based on MRI findings has not been described yet. We observed that criteria regarding hepatic parenchyma, liver edge, and periportal fibrosis as defined by Williams et al. may also be applied to MRI findings, but additional parameters may be added to the scoring system based on these findings. MRI has a great potential yet to be explored in the evaluation of CFLD, since the advances in the quality of the management of lung complications and the increase in patient life expectancy may raise the prevalence of CFLD in the coming years and monitoring disease progression will be essential in long-term follow-up.

US and MRI hepatic findings in CFLD patients.

Hepatic parameters	US n (%)	MRI n (%)	Agreement measures*	95%CI	p
Hepatic parenchyma	5 (25.0)	5 (25.0)	K=1.00	-	<0.001
Liver edge	5 (25.0)	5 (25.0)	K=1.00	-	<0.001
Periportal fibrosis	1 (5.0)	5 (25.0)	K=0.27	-0.16 to 0.71	0.076
Total, mean ± SD	4.1±2.0	4.5±2.7	ICC=0.97	0.92 to 0.99	<0.001

CFLD: cystic fibrosis liver disease; US: ultrasonography; MRI: magnetic resonance imaging; 95% CI: 95% confidence interval.

* Kappa (K) or intraclass correlation coefficient (ICC)

Individual distribution of hepatic parameters assessed by US and MRI

Patient	Sex	Age (years)	US				MRI				RPN	RN	ARL
			Hepatic parenchyma	Liver edge	Periportal fibrosis	Total	Hepatic parenchyma	Liver edge	Periportal fibrosis	Total			
1	M	8	1	1	1	3	1	1	1	3	-	-	-
2	F	9	1	1	1	3	1	1	1	3	Present	-	-
3	F	10	1	1	1	3	1	1	1	3	-	-	-
4	M	10	1	1	1	3	1	1	1	3	-	-	-
5	M	11	1	1	1	3	1	1	1	3	-	-	-
6	F	14	1	1	1	3	1	1	1	3	-	-	-
7*	M	14	3	3	1	7	3	3	3	9	Present	Present	Present
8	M	14	1	1	1	3	1	1	1	3	-	-	-
9*	M	14	3	3	1	7	3	3	3	9	-	-	-
10	M	15	1	1	1	3	1	1	1	3	-	-	-
11*	F	15	3	3	3	9	3	3	3	9	Present	Present	Present
12	M	15	1	1	1	3	1	1	1	3	-	-	-
13	F	16	1	1	1	3	1	1	1	3	-	-	-
14	M	16	1	1	1	3	1	1	1	3	-	-	-
15*	M	18	3	3	1	7	3	3	3	9	-	Present	Present
16	M	18	1	1	1	3	1	1	1	3	-	-	-
17	M	18	1	1	1	3	1	1	1	3	-	-	-
18*	F	18	3	3	1	7	3	3	3	9	Present	-	Present
19	M	18	1	1	1	3	1	1	1	3	-	-	-
20	F	20	1	1	1	3	1	1	1	3	-	-	-

US: ultrasonography; MRI: magnetic resonance imaging; RPN: right posterior hepatic atch sign; RN: regenerative liver nodule; ARL: atrophy of the right lobe; M: male; F: female.

* Patients diagnosed with cystic fibrosis liver disease.

389 THROMBOPHILIA PROFILE IN PEDIATRIC PATIENTS WITH CIRRHOSIS AND LIVER FAILURE FROM THE PEDIATRICS HOSPITAL, AT THE WESTERN NATIONAL MEDICAL CENTER.

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Introduction: The liver plays a central role in the hemostatic system. The coagulation system in patients with cirrhosis is in a state of “rebalance” between antihemostatic and prohemostatic factors. The observation of inherited thrombophilia (protein C deficiency, protein S deficiency, antithrombin III deficiency, mutation of factor V Leiden, gene mutation of prothrombin G20210A, polymorphism of methylenetetrahydrofolate reductase (MTHFR) C677T and A1298C, and polymorphism of angiotensin converting enzyme (ACE-1) increase the risk of thrombosis of the portal vein in patients with cirrhosis. It is suggested that hypercoagulability may play a role in thrombosis of the hepatic artery after liver transplantation.

Objective: To characterize the profile of thrombophilia of pediatric patients with cirrhosis and liver failure at the Hospital of Pediatrics, Western National Medical Center.

Material and Methods: A study was conducted in pediatric patients, carriers of cirrhosis and liver failure at the Hospital of Pediatrics. Anticoagulant activity protein (protein C, protein S and antithrombin III) and factor VIII were determined by clotting assay. Mutations of thrombophilia panel, including factor V Leiden mutation, prothrombin gene mutation G20210AA,

MTHFR C677T and A1298C polymorphisms, and polymorphism of angiotensin converting enzyme ACE-1 were determined by the technique of polymerase chain reaction.

Results: There were 25 children, 13 males, 12 females. The average age was 50.76 ± 46.96 (4-189) months. The main cause of cirrhosis was biliary tract atresia (72%). Distribution based on the Child - Pugh stadium was the following: stage A 24%, stage B 48%, and stage C 28%. It was identified protein C deficiency in 14 patients (56%), protein S deficiency in 3 patients (12%), antithrombin III deficiency in 9 patients (36%). Factor VIII elevated in 92% of the population was documented. The main identified mutation was polymorphism deletion ACE-1 in 8 patients (34.7%), the MTHFR C677T polymorphism was the second cause with 21.7%, MTHFR A1298C polymorphism in 8.6%, compound heterozygote of MTHFR C677T / A1298C in 17.3%.

Conclusions: It is considered that the deficiency of anticoagulant proteins and elevation of factor VIII is acquired secondary to chronic liver disease itself. The highest frequency of submission of ACE-1 may be due to the association of ACE-1 in metabolic processes of the liver and liver fibrogenesis participation.

391 NORMAL RANGE OF MAGNETIC RESONANCE ELASTOGRAPHY MEASURED LIVER STIFFNESS IN CHILDREN WITHOUT LIVER DISEASE. Mary Catherine Huckaby^{1,2}, Kathryn Harlow^{1,2}, Jorge Angeles¹, Craig Bross¹, Nidhi Goyal^{1,2}, Kimberly Newton^{1,2}, Alexandra Schlein³, Jonathan Hooker³, Ethan Sy³, Claude Sirlin³, Jeffrey Schwimmer^{1,2}. ¹Pediatrics, University of California San Diego, San Diego, CA; ²Pediatric Gastroenterology, Hepatology and Nutrition, Rady Children's Hospital, San Diego, CA; ³Radiology, University of California San Diego, San Diego, CA

Background: Hepatic fibrosis is a key determinant of clinical outcome for children with chronic liver disease. Traditionally, fibrosis stage is determined by liver pathology. Magnetic resonance elastography (MRE) is an emerging tool for the noninvasive evaluation of liver fibrosis and is now in clinical use. In the recent MAGNET study, among children with nonalcoholic fatty liver disease, a cutoff of 2.77 kPa distinguished between children with and without liver fibrosis. However, there are no normative data available in children free of liver disease. Therefore, the study aim was to determine the normal range of MRE measured liver stiffness in children without liver disease.

Methods: Children ages 8 to 17 years without liver disease were recruited from primary care physicians and community health fairs. All participants had normal liver chemistry and no history of liver disease. History, physical examination, and laboratory evaluation were performed. Magnetic resonance exam included measurement of proton density fat fraction (PDFF) and 2-D MRE. We excluded children with hepatic steatosis as determined by PDFF ≥ 5.0 .

Results: The study included 82 children (49 boys and 33 girls) with a mean (SD) age of 12.6 (2.6) years, mean BMI of 25.3 (6.5) kg/m², and mean ALT of 16 (7) U/L. All children completed the magnetic resonance examinations. The mean liver PDFF was 2.9 (1.1) %. The distribution of MRE values was: median 2.37 kPa, range 1.67- 4.11 kPa, and 95th percentile 3.18 kPa. Furthermore, 24% of children had an MRE value exceeding the previously identified 2.77 kPa fibrosis cutoff. There was no significant difference in ALT (p=0.49) or BMI (p=0.08) between children with MRE above or below 2.77 kPa. However, children with MRE values ≥ 2.77 kPa were significantly younger than those with MRE values < 2.77 kPa (11.7(2.9) vs 13.4 (2.9) years; p = 0.03). The 95th percentile for MRE was not significantly (p = 0.21) different for children < 13 years (3.21 kPa) versus children ≥ 13 years (3.15 kPa).

Conclusion: MRE was well tolerated in children ages 8 to 17. Unexpectedly, nearly one quarter of children without evidence of liver disease had high MRE values above 2.77 kPa. Younger children were more likely to have high MRE values, although the 95th percentile for MRE was comparably high in both school aged children and adolescents. Therefore, MRE should be interpreted with caution in children. Further research is needed to understand and correct the source of potentially misleading MRE stiffness elevation in children without liver disease.

***392 IN VITRO DIFFERENTIATION OF INDUCED PLURIPOTENT STEM CELLS TO DEFINITIVE ENDODERM: PROTOCOL OPTIMIZATION BY HIGH-THROUGHPUT GENE EXPRESSION ANALYSIS.** Marie-Agnès M'Callum², Sarah Lépine², Toan Quang Pham², Claudia Raggi², Massimiliano Paganelli^{1,2}. ¹Gastroenterology, Hepatology and Nutrition, Sainte-Justine Hospital, Université de Montréal, Montreal, QC, Canada; ²Hepatology and Cell Therapy Lab, Sainte-Justine Hospital, Université de Montréal, Montreal, QC, Canada

Background: induced pluripotent stem cells (iPSCs) can be differentiated *in vitro* into most tissues of the body, and are considered among the best candidate cells for regenerative medicine. Many of the organs targeted for such an application, such as the liver, pancreas, trachea and lungs derive from the definitive endoderm (DE). Several *in vitro* differentiation protocols mimicking embryogenesis have been described to generate DE cells from iPSCs. Nevertheless, with each of such protocols the efficiency, quality and reproducibility of the obtained DE is extremely variable among iPSC populations. High

cell death experienced with many iPSC populations increases costs and hands-on time, complicating the use of DE-derived cells for disease modeling and cell therapy.

Aim: this study aimed at comparing several differentiation conditions in order to define an efficient protocol to consistently obtain high-quality DE from various iPSC population.

Methods: We used 3 previously characterized human iPSC populations having showed in earlier experiments a good (P01), intermediate (P02) and bad (P03) potential to differentiate into hepatocytes *in vitro* following published protocols. Such cells were differentiated into DE over 5 days mimicking embryogenesis. We assessed the effect of modifying several conditions over the quality of the DE obtained at day 5 with the 3 populations. The following variables were considered: activin A concentration; presence/absence of FGF, low-dose knock-out serum replacement (KOSR) or retinoic acid; presence/absence of BMP, MEK, Wnt or PI3K inhibitors; type of coating (vitronectin, laminin(LMN)-521, LMN-521/111). High-throughput real time RT-qPCR (Biomark HD, Fluidigm Inc.) was used to assess the expression of 96 genes expressed in pluripotent cells and along differentiation. The quality of DE was measured according to the level of expression of FOXA2, SOX17 and CXCR4 (TaqMan RT-qPCR, immunofluorescence and flow cytometry).

Results: The expression of pluripotency markers SSEA, OCT3, NANOG, TRA1-81 and SOX2 (mRNA by Taqman RT-qPCR and proteins by immunofluorescence and flow cytometry) was comparable to embryonic stem cells for the 3 iPSC populations, with no significant difference among them. At single-cell level (flow cytometry), 81.8%±3.2% and 85.2%±2.5% of cells were double-positive for NANOG and OCT3 and for NANOG and SOX2, respectively, with no difference among the 3 populations. Population doubling level (by BrdU incorporation) was higher for P03 (p<.05). Upon differentiation to DE using a standard protocol, the 3 populations were indistinguishable (increased mRNA and protein expression of FOXA2, CXCR4 and GATA4, and downregulation of NANOG, OCT3 and SOX2) except for SOX17 mRNA expression, which was lower in P03 (p<.05). Nevertheless, a significant cell death was noted for P01 and P02 (≥90%), while it was negligible for P03 (<10%). Upon differentiation towards hepatocytes, P01 showed higher albumin and urea secretion and Cyp3A4 activity than P03 (p<.05), with P02 performances between the two (p=ns). A total of 30 differentiation conditions were assessed in biological duplicates on the 3 iPSC populations. Whereas P03 showed almost no cell death in any tested condition, >80% cell death was recorded in all (P01) or most (P02) conditions without KOSR. The presence of 20 ng/ml FGF2 during the first 24h or coating with vitronectin or LMN-521 (instead of LMN-521/111) allowed to reduce cell death for both populations. Supplementation with 1% KOSR reduced cell death to <10%. No difference in cell morphology was noted. Overall, the expression of SOX17 and CXCR4 was significantly different among the 3 populations at day 5 (p=.035 and p=.02, respectively). Supplementation with KOSR had no significant effect on SOX17 expression (0.64±0.66 fold change, p=.313), while it increased the expression of CXCR4 (106.4±121 fold change, p=.0313). The effect of all other variables on FOXA2, SOX17 and CXCR4 expression was very different between the 3 iPSC populations. Using 24h Wnt pathway activation, 5-day high-dose of activin A without any BMP, MEK or PI3K inhibition, and 1% KOSR on LMN-521 we obtained 78.6%±0.8% of FOXA2-positive cells and 73.1%±4.9% of CXCR4/SOX17 double-positive cells, with negligible cell death. We were able to reproducibly generate highly functional hepatocyte-like cells (urea: 1.57±0.2 µg/24h/1x10⁶ cells; albumin: 274±54 ng/24h/1x10⁶ cells) from the DE obtained from each of the 3 populations.

Conclusions: KOSR allows solving the problem of cell death that complicates *in vitro* differentiation of certain iPSC populations. We established a simplified protocol allowing to obtain high-quality homogeneous DE from most iPSC population. Nevertheless, important differences in response to differentiation conditions were noted among different populations. We are now studying the determinants of such variable responses to identify how to adapt the differentiation protocol to any iPSC population.

393 DEVELOPMENT OF AN IN VITRO MODEL OF HEREDITARY TYROSINEMIA TYPE 1 USING PATIENT-DERIVED INDUCED PLURIPOTENT STEM CELLS. Toan Quang Pham², Marie-Agnès M'Callum², Paula Waters³, Ugur Halac¹, Suleen Raad², Chenicka-Lyn Mangahas², Claudia Raggi², Massimiliano Paganelli^{2,1}. ¹Gastroenterology, Hepatology and Nutrition, Sainte-Justine Hospital, Montreal, QC, Canada; ²Hepatology and Cell Therapy Lab, Sainte-Justine Hospital, Montreal, QC, Canada; ³Genetic Biochemistry Lab, Centre Hospitalier de l'Université de Sherbrooke, Montreal, QC, Canada

Background: Hereditary type 1 tyrosinemia (HT1) is a severe inborn error of liver metabolism caused by the deficiency of fumarylacetoacetate hydrolase (FAH). Without treatment, HT1 causes the accumulation of toxic compounds leading to more than 80% mortality before 2 years of age. The long-term effects of the only effective treatment available (the herbicide NTBC) are unknown. No *in vitro* model of HT1 is currently available.

Aim: To develop an *in vitro* model of HT1 using hepatocyte-like cells (iHeps) differentiated from patient-derived induced pluripotent stem cells (iPSCs).

Methods: Peripheral blood mononuclear cells from HT1 patients were reprogrammed into iPSCs, cultured in strict feeder-free and xeno-free conditions, and extensively characterized. iHeps were generated from iPSCs using our *in vitro* differentiation protocol mimicking liver development, and fully characterized for the expression of hepatocytes' markers and functions, as well as for the accumulation of toxic compounds. iHeps derived from iPSCs reprogrammed from healthy subjects served as control.

Results: Of the 10 iPSC populations reprogrammed from 2 patients carrying 2 different FAH mutations, 2 highly-pure populations were fully characterized (HT1-iPSCs). FAH mRNA expression was very low in both healthy and HT1-iPSCs, while the protein was not detectable. HT1-iPSCs' self-renewal potential was not affected by the absence of NTBC supplementation. Succinylacetone (SA), a toxic by-product of tyrosine metabolism, was undetectable in HT1-iPSCs' conditioned media (by LC/MS) even in the absence of NTBC. Hepatocytes differentiated from HT1-iPSCs (HT1-iHeps) expressed markers and performed functions typical of neonatal hepatocytes. mRNA-Seq profile of HT1-iHeps was not different from healthy iHeps. FAH and all the enzymes involved in the tyrosine degradation pathway were progressively expressed upon differentiation into iHeps (with only FAH being absent only in HT1-iHeps). SA accumulated in HT1-iHeps' conditioned media, and significantly increased upon supplementation with L-tyrosine or homogentisic acid (259 ± 28 nM with supplementation of $300 \mu\text{M}$ homogentisic acid for 24h v. 51 ± 5 nM without, $p < .05$). Apoptosis (caspase-3/7 levels quantified by live cell imaging) and cell mortality progressively increased with higher doses and longer exposures. NTBC treatment (50 - $300 \mu\text{M}$) prevented SA accumulation upon high-dose supplementation with L-tyrosine, with negligible cell death and no apoptosis. SA was undetectable in iHeps derived from healthy iPSCs. We corrected the disease-causing mutation in HT1-iPSCs through genome editing by CRISPR/Cas9d10a (double-nicking approach), and verified the correction of FAH mutation by DNA sequencing. No difference in cell proliferation and pluripotent phenotype was noted after editing. iHeps differentiated from such corrected iPSCs were indistinguishable from HT1-iHeps (mRNA-Seq) except for the absence of SA accumulation.

Conclusions/Perspectives: To our knowledge, this is the first representative human in vitro model of HT1. HT1-iHeps faithfully replicate HT1 phenotype, allowing us to study the pathophysiology of the disease and the effect of NTBC on a human model under controlled conditions, for the first time. FAH expression in HT1-iPSCs is not significant. Such cells can hence be easily expanded without the need of NTBC supplementation, providing unlimited material for disease modeling. Genome editing with a highly-specific approach allowed the correction of the disease phenotype, representing a proof of concept for other inborn errors of liver metabolism for which autologous cell therapy could be envisioned.

394 NON-ALCOHOLIC FATTY LIVER DISEASE IN CHILDREN AND ADOLESCENTS: EFFICACY OF LIFESTYLE CHANGE - A SYSTEMATIC REVIEW AND META-ANALYSIS. Melina Melere³, Cristina Ferreira³, Bernardo Horta², Matias Epifanio³, Angelo Mattos¹, Marialena Mouzaki⁴. ¹ Gastroenterologist, Federal University of Health Sciences of Porto Alegre (UFCSPA), Porto Alegre, Rio Grande do Sul, Brazil; ²Postgraduate Program in Epidemiology, Federal University of Pelotas - FAPEAM, Pelotas, Rio Grande do Sul, Brazil; ³Pediatric Gastroenterologist, Santo Antônio Hospital, Santa Casa de Misericórdia Complex of Porto Alegre / RS, Porto Alegre, Rio Grande do Sul, Brazil; ⁴Pediatric gastroenterologist, University of Toronto, Hershey, PA

Objective: To analyze the impact of lifestyle changes on body mass index (BMI), aminotransferases and steatosis in children and adolescents with nonalcoholic fatty liver disease (NAFLD).

Methods: a researcher reviewed PubMed, BIREME, Scopus, EMBASE, Medline and Web of Science databases up to April 2015, seeking studies in intervention on the lifestyle of children and / or adolescents with NAFLD. Manuscripts included were published in Portuguese, English and Spanish. The participants of intervention should be less than 18 years of age. Two reviewers performed the data extraction independently and differences were resolved by consensus. Outcome measures were BMI, serum levels of aminotransferases and the presence of hepatic steatosis.

Results: The literature search identified 71,012 articles, after excluding 46,397 duplicates and those obviously irrelevant, 89 publications remained to read in full and 55 studies were excluded at this stage. Subsequently, 18 were excluded for lack of data and three articles were found in the review of the references of previously identified articles. Therefore, 19 studies that evaluated 923 subjects (477 boys and 446 girls) aged 6-18 years were included in the review. In most studies, the intervention included aerobic exercise and diet. In nine studies, BMI showed a significant decrease after the intervention. The vast majority of studies evaluated reported a benefit from the intervention on aminotransferases levels. The effect was also significant in the presence of steatosis, reducing the risk by 61%.

Conclusion: Lifestyle change has significantly improved BMI values, aminotransferases and hepatic steatosis in children and adolescents with NAFLD.

395 PILOT STUDY OF ACOUSTIC RADIATION FORCE IMPULSE (ARFI) IMAGING FOR LIVER STIFFNESS ASSESSMENT IN CHILDREN WHO HAVE UNDERGONE FONTAN PROCEDURE.

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The Fontan procedure leads to chronically elevated right sided heart pressures. Congestive hepatopathy is a well-recognized complication of Fontan physiology. Non-invasive assessment of liver stiffness and readily available biomarkers of fibrosis may allow longitudinal assessment of hepatic injury in Fontan patients, perhaps decreasing the need for liver biopsy.

Methods: Studies performed as part of a multidisciplinary clinic for long term follow up of patients who have a had a Fontan included: transjugular liver biopsy with determination of hepatic venous pressure gradient (HPVG), catheterization data, Doppler ultrasound with ARFI determination and routine laboratory testing (CBC, PT INR and liver blood tests). Biopsies were scored by the congestive hepatic fibrosis score (J Thorac Cardiovasc Surg 2017;153:656). ARFI elastography is the average of 10 measurements in the right lobe. APRI and Fib4 were calculated by standard formulae.

Results: 10 children (5 male, mean age 14 yrs, range 11-20 yrs), 11 years post Fontan (SD 3) were evaluated. ARFI was successful in all patients (Table 1). Five of nine had significant hepatic fibrosis on liver biopsy: 4 with significant portal fibrosis (4 or 5/5) or whom 3 had significant sinusoidal fibrosis (3/3). One subject had significant sinusoidal fibrosis with minimal portal fibrosis. AST ($r=-0.71$) and FIB4 ($r=0.40$) were correlated with time since fontan. Elastography was most correlated with Fontan pressure ($r=0.32$) but not fibrosis stage.

Conclusions: ARFI is feasible in Fontan patients. Like other elastography measurements, single values did not correlate with fibrosis. FIB4 may be a useful screen for hepatic injury in Fontan. Longitudinal studies of measures of hepatic fibrosis should be performed.

TEST	MEAN	ST DEV
Fontan pressure (mmHg)	13	2
HVPG (mmHg)	1.4	1.0
APRI	0.64	0.17
FIB4	0.61	0.20
ARFI median (m/s)	1.95	0.52

396 ACCURACY AND REPEATABILITY OF MAGNETIC RESONANCE IMAGING BASED VOLUMETRIC LIVER FAT FRACTION COMPARED TO HISTOLOGY IN CHILDREN.

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease and it increases the risk of advanced liver injury as well as future risk of diabetes and cardiovascular disease. Liver biopsy is considered the best approach for confirming NAFLD, but it is invasive, expensive and has potential complications. There are relatively few studies validating magnetic resonance imaging (MRI) based measurements of liver fat in children and validation studies in comparison to liver biopsy are needed. Volumetric liver fat fraction is a chemical-shift based magnetic resonance imaging method for measuring liver fat.

Methods: Fifty children (7-19 years) scheduled for a clinically indicated liver biopsy were recruited and liver steatosis was measured using volumetric liver fat fraction (VLFF) by MRI (HepaFat Scan[®]) as well as magnetic resonance spectroscopy (MRS) within 48 hours of the biopsy. Histologic categorization of steatosis grade using the NIH NASH clinical research network (CRN) system and MRS measurements were set as reference standards. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for the diagnostic cutoff point of 5% to detect hepatic steatosis. Twenty-one children were randomly selected, repositioned and underwent a second acquisition of VLFF by MRI for inter-examination repeatability. Bland Altman plotting was constructed to test the repeatability.

Results: The VLFF ranged from 0.3%-35.4% and increased across the histologic grade of steatosis (beta coefficient=6.99, $p<0.001$). Using pathologist assigned "grade of steatosis" as the reference to define hepatic steatosis (≥ 1 vs. 0), the sensitivity,

specificity, PPV and NPV for VLFF at the 5% cutoff point were 96.7%, 88.2%, 94.1% and 93.8%, respectively. There was a strong agreement between biopsy and VLFF for diagnosis of hepatic steatosis (Cohen's Kappa coefficient = 0.86). In addition, there was excellent agreement between the two acquisitions of VLFF by MRI (limit of agreement: -1.84% to 1.73%.)

Conclusions: VLFF measured by MRI is a non-invasive, precise and accurate method for measuring hepatic steatosis with excellent PPV and NPV for hepatic steatosis in children. This study demonstrates validity of this method for detecting hepatic steatosis in children.

399 **EXPERIENCE OF 900 ACUTE HEPATITIS CASES IN CHILDREN: IDENTIFYING THE HIGH RISK GROUP FOR COMPLICATIONS IN HEPATITIS E INFECTION.** Neelam Mohan, Shivprasad Dubey, Sakshi Karkra, Deepak Goyal. *Dep. of Pediatrics Gasstroenterology and Hepatology, Medanta Hospital, Gurgaon, India*

Background: Acute viral Hepatitis E infection (HEV) is common in developing countries and is thought to be self-limiting in most of the patients except pregnant women. It can spread through feco-oral route or zoonotic route outside endemic areas. Information on occurrence of complications, outcome and high risk group for developing serious complications with HEV in children is relatively lacking.

Aim: To study the etiology of acute hepatitis cases in children and identify the incidence of acute liver failure, its outcome and the high risk group in HEV vs Hepatitis A infection (HAV).

Method: Retrospective analysis of acute hepatitis cases presenting to department of pediatric gastroenterology in a tertiary referral centre in North India, from January 2006 to December 2016, was performed. The patients were in the age group 1-18 years.

Results: Acute viral hepatitis A&E infection either in isolation or co infection constituted 58.5 %(n=339) of the viral hepatitis infection(n=579) followed by dengue 36.9%(n=209) and hepatitis B infection 1.72%(n=10). Non-viral causes of hepatitis (n=321) included enteric hepatitis, NASH, sepsis, other non-viral infections, drugs/toxins and liver trauma. Among the hepatotropic viral infection HAV constituted 296(84.8%), HEV 27(7.7%), Hepatitis A and E co-infection (A+E) 16(4.55%) and Hepatitis B 10(2.8%) cases. However, the incidence of acute liver failure (ALF) in HEV alone and with A+E was 15 (55.5%) and 4 (25%) respectively as compared to 68(22.9%) with HAV. Spontaneous recovery in ALF was seen in 50/68(43%) of HAV, 13/15(86%) of HEV and 3/4th of A+E cases. Interestingly when there was underlying chronic liver disease (CLD) (n=44), the incidence of ALF was 66.6% with HEV as compared to 12.8% with HAV.

Conclusion: HAV was 10 times more common than HEV in children. Acute liver failure was more than twice as common in HEV as compared to HAV. Spontaneous recovery of ALF in HEV was twice as compared to that in HAV. When there was underlying CLD incidence of developing ALF was seen in 2/3rd of the patients in HEV which was more than 4 times as compared to HAV with underlying CLD.

402 **CHOLANGIOCARCINOMA IN CHILDREN; LITERATURE AND SEER DATA BASE REVIEW.** Jennifer Newsome¹, Rajkumar Venkatramani², Andras Heczey², Douglas Fishman¹, Tamir Miloh¹. ¹GI, Texas Children's Hospital, Houston, TX; ²Oncology, Texas Children's Hospital, Houston, TX

Cholangiocarcinoma (CCA) is a bile duct malignancy found primarily in the adult population. The incidence of CCA in children is unknown, and the current literature consists primarily of case reports. The aim of this study was to describe the characteristics of CCA in the pediatric population (younger than 18 y).

Methods: We conducted a Surveillance, Epidemiology, and End Results Program (SEER) database analysis of pediatric patients with CCA registered between 1973-2013. In addition, we reviewed the data from previously published pediatric patients with CCA.

Results: Fifteen pediatric patients with CCA were identified from the SEER registry with incidence of 0.036/1,000,000 in patients <20 years. Two-third were male, and majority were Caucasian with mean age at diagnosis of 15.7±2.86 years. Nine tumors were intrahepatic, 3 were extrahepatic, and 3 were unspecified. A third were localized, third regional and a third with distal metastases at diagnosis. Eight patients died from malignancy. The median length of survival was 6 months with a range of 2-40 months. Surgical resection was performed in 7 patients with 57.1% survival. Liver transplant was performed in 2 patients with 100% survival. One patient was treated with radiation alone and 3 received no treatment. None of the patients without surgical treatment survived. Twenty two reported cases of CCA in children were found in the literature, of which the mean age was 13.6y, 50% male, 90% had underlying risk factor: congenital biliary malformation 32% and PSC 32% (twice more common with Crohn's than ulcerative colitis), biliary atresia 14%, and Familial intrahepatic cholestasis 9%. Most common symptoms were pain 9 (41%), jaundice 7 (32%), pruritus 5 (23%), fever 3 (14%) and abdominal distention, weight

loss and gastrointestinal bleed 2 each (9%). Median CA 19-9 was 112 IU/mL (2.5-89,000) and bilirubin was 7.2 mg/dL (0.9-31). Tumor was intrahepatic in 9 (41%), extrahepatic in 9 (41%) and perihilar in 2 (9%).

Conclusion: CCA in children is rare with poor survival and mostly associated with history of biliary disease. Surgical resection is necessary for cure.

	SEER	Literature
Patient number	15	22
Median age (years)	17 (11-19)	14 (3-18)
Male	67%	50%
Intrahepatic	60%	41%
Perihilar	20%	9%
Extrahepatic	20%	41%
localized	33%	
Regional	20%	
Distant	33%	
Treatment; Liver transplant	13%	18%
Resection	47%	36%
Radiation/chemotherapy	7%	17%
Comorbidity: PSC		32%
Choledocal cyst		32%
Cirrhosis		21%
Alive at last report	47%	41%

MICROBIOLOGY/INFECTIONS/PROBIOTICS

404 **THE ROLE OF A BUTYRATE-YIELDING SYNBIOTIC IN COLONIC PROTECTION IN MICE DURING ANTIBIOTIC AND CLOSTRIDIUM DIFFICILE EXPOSURE.** Gail Cresci^{1,3}, Jennifer Cadnum², Mark Obrenovich², Curtis Donskey². ¹Gastroenterology, Cleveland Clinic, Cleveland, OH; ²Infectious Diseases, Cleveland VA Medical Center, Cleveland, OH; ³Pathobiology, Cleveland Clinic, Cleveland, OH

Background: Antibiotics destroy both pathogenic and commensal gut microbiota creating an environment supporting *Clostridium difficile* (CD) germination and growth. While overall incidence of CD infection (CDI) is rising, amongst pediatric population, the rate of asymptomatic CD colonization is also increasing. While antibiotic treatment is the major risk factor for CD colonization, treatment of CDI also involves antibiotic therapy. Gut dysbiosis results in negative alterations in metabolic byproducts of gut microbiota. The short-chain fatty acid butyrate is important for colonic health. CD toxin induces colonic tissue damage. Both butyrate-producing bacteria and butyrate are decreased with CDI. This study investigated if a butyrate-producing synbiotic could protect colonic integrity and provide colonization resistance during antibiotic and CD exposure.

Methods: Female CF-1 mice housed individually received daily subcutaneous injections of clindamycin (1.4 mg/d) for 3 days. Three days later, mice were exposed to VA17 (4-log₁₀ CFU), an epidemic North American pulsed-field gel electrophoresis type 027 (NAP1) CD strain. Throughout the treatment period, mice were randomized to one of the following daily treatments: saline (control), *Faecalibacterium prausnitzii* (FP), resistant starch (RS), FP + RS, or FP+RS supernatant. Fresh feces were collected for bacterial culturing of gram negative, enterococci and CD at baseline, day 1 after antibioticS, and days 1, 3, and 5 after CD exposure, as well as for measurement of butyrate by flame ionization detection/mass spectrometry. Mice were euthanized 5 days after CD exposure and proximal colon (PC) was isolated for RNA preparation for gene expression via real-time PCR and protein expression via immunohistochemistry analysis.

Results: Antibiotic treatment resulted in overgrowth of enterococci and gram negative bacteria in all groups. Despite the FP+RS group exhibiting the highest fecal butyrate levels, overall there was no difference in CD colonization between treatment groups. However, via mRNA expression of PC tissue, the FP+RS group appeared to be able to mount and resolve

inflammatory cytokine responses compared to the control group. This was associated with preservation of expression of tight junction proteins and anion exchangers in the PC.

Conclusions: Taken together, these data indicate butyrate is important for colonic protection during antibiotic and CD exposure. While these responses were not associated with decreased CD colonization following a single CD exposure, future work investigating beneficial effects on repeated antibiotic and CD toxin exposure are warranted.

405 THE EPIDEMIOLOGICAL CHARACTERISTICS OF HELICOBACTER PYLORI INFECTIONS IN GASTRODUODENAL PATHOLOGIES IN CHILDHOOD. Gokhan Tumgor¹, Nilgun Uyduran², Mehmet Agin¹, Togrul Nagiyev³, Oguz Uskudar⁴, Figen Doran⁵, Fatih Koksali³. ¹Pediatric Gastroenterology, Cukurova University Medical Faculty, Adana, Turkey; ²Pediatrics, Cukurova University Medical Faculty, Adana, Turkey; ³Microbiology, Cukurova University Medical Faculty, Adana, Turkey; ⁴Gastroenterology, Cukurova University Medical Faculty, Adana, Turkey; ⁵Pathology, Cukurova University Medical Faculty, Adana, Turkey

Background: To determine the frequency of *H. pylori* infections of patients applied to Çukurova University Medicine Faculty Pediatric Gastroenterology polyclinic with dyspeptic complaints and indicate the distribution of virulence factors, the importance of intrafamilial transmission, and also resistance to macrolide and quinolon group antibiotics by identifying epidemiological characteristics of them at the genotype level.

Methods: A total of 110 patients with dyspeptic complaints referred to hospital between 13 January 2015-1 December 2016 were included in the study. Of the cases, those with *H. pylori* positivity and dyspeptic complaint and 7 parents whose upper gastrointestinal system endoscopy was conducted by adult gastroenterology department were also involved in the study. *H. pylori* was searched by means of histopathological, culture and glmM-PCR methods. In the patients whose PCR was identified as positive, the determination of *vacA*, *cagA* and *cagE* genes was performed; in addition, E-test was performed to establish the resistance of clarithromycin and levofloxacin of *H. pylori* strains isolated in culture. A2142G and A2143G point mutations held responsible for clarithromycin resistance were identified with PCR-RFLP method. The effect of *H. pylori* strains on the clinics of cases was investigated and the impact of intrafamilial *H. pylori* transmission was evaluated.

Results: *H. pylori* was established as positive in 30 (27.3%) out of 110 pediatric patients. The average age of the cases was 12.2 ± 4.39 years (ranging from 3-18). 65.5% were female, 34.5% were male. In 40% of *H. pylori* positive patient samples *vacAs1*, in 56.6% *vacAs2*, in 36.7% *cagA*, in 23.3% *cagE* were positive. In 6.6% of the cases *vacAs1+cagE* association, in 16.6% *vacAs1+cagA+cagE* association and in 16.6% *vacAs2+cagA* association were determined. No significant relationship was identified between clinical findings and *H. pylori* strains in the study.

Levofloxacin resistance was only observed in one (4.3%) of the patients that could produce *H. pylori* in the culture. In the patient involved, both genetic mutations of A2142G ve A2143G were found as positive. In 8 patients (34.7%), clarithromycin resistance was established. In all patients whose A2142G mutation was determined as positive and in 55% those whose A2143G mutation was identified as positive, clarithromycin resistance was observed.

H. pylori strains determined in the parents of pediatric patients involved in the study were established as different from *H. pylori* strains in the children.

Conclusions: *H. pylori* infection was determined as positive in approximately one third of children with dyspeptic complaints. In children applying to hospital with dyspeptic complaints, it was observed that *vacAs2* is the mostly seen genotype. Of the genetic mutations A2142G ve A2143G, even having at least one of them carries a potential for resistance to antibiotics. High resistance was identified for clarithromycin used in the standard triple treatment of *H. pylori* in children.

406 ACCURACY OF HEMATOXYLINE-EOSIN STAINING FOR DIAGNOSING OR EXCLUDING HELICOBACTER PYLORI IN CHILDREN WITH GASTRITIS. Jay Fong¹, Stanley Lau², Theresa Smith³, Xiaofei Wang³, Kanwaljit Singh⁴, JR Lightdale¹. ¹Pediatrics, Umass Medical School, Grafton, MA; ²Pediatrics, New York Hospital Cornell Medical School, New York, NY; ³Pathology, Umass Medical School, Worcester, MA; ⁴Pediatrics, Umass Medical School, Worcester, MA

Introduction: Gastritis found during esophagogastroduodenoscopy (EGD) in children may herald Helicobacter Pylori (HP), not always visualized with standard histopathology stains. The aim of our study was to examine the value of routinely performing specialized stains for HP in pediatric patients.

Methods: With institutional approval, we reviewed consecutive children undergoing EGD over 18-months. “True positive” HP was defined as presence of organisms detected with specialized staining (either Warthin Starry (WS) and/or immunohistochemical (IHC)). Sensitivity analyses were used to examine the accuracy of standard hematoxyline and eosin (H&E) staining for HP in pediatric gastric biopsies.

Of 421 children undergoing EGD during the study period, 393 (93%) had both H&E, as well as at least one type of specialized stain (WS, n=390; IHC 3; WS and IHC, 20). 212 (50%) had no evidence of gastritis. Prevalence of “true positive” HP was 2.5% (n=10). H&E had 30% sensitivity, 100% specificity, 100% positive predictive value and 98.2% negative predictive value for detecting HP. Patients with chronic active gastritis were more likely to have HP than patients with chronic inactive gastritis (7.7% vs. 1%, p = 0.047). The accuracy of H&E for diagnosing HP in pediatric gastric biopsies was 98.2%.

Conclusion: Our results suggest staining with H&E is sufficiently accurate for routine evaluation of HP during pediatric EGD. Although the uniform performance of specialized stains will likely reveal a few children with organisms not seen on standard staining, in the great majority of instances, the practice of routinely performing both types of stains is redundant.

Table 1: Characteristics of patients undergoing upper Endoscopy

Patient demographics (n=421)	
Male Gender, n (%)	199 (47.3%)
Age in yrs, mean range	12 yrs, 1-12
Symptoms (%) n (%)	165 (28%)
-Abdominal pain	247 (59%)
-Diarrhea	60 (14%)
-Dysphagia/feeding difficulty	35 (8%)
-GI Bleed	49 (12%)
-Reflux/heartburn	60 (14%)
-Vomiting	391 (66)
-Weight loss/poor growth	12 (3%)
Patients undergoing procedures for chronic disease monitoring, n (%)	88 (21%)
-Celiac disease	49 (55%)
-Eosinophilic Esophagitis	11(13%)
-Esophageal Varices	1(1%)
-Failure to Thrive	2(2%)
-Gastroesophageal Reflux Disease	8(9%)
-Inflammatory Bowel Disease	22(25%)
H&E pathology findings, n (%)	
-Normal	212 (50%)
-Minimal or post gastritis	31(7%)
-Chronic inactive gastritis	95 (23%)
-Chronic active (or NOS) gastritis	80 (19%) ¹
-H pylori visualized	3 (1%)
WS staining H Pylori findings, n (%)	
-Not performed	31 (7%)
-Negative	378 (90%)
-Equivocal	2 (1%)
-Positive	10 (2%)
Immunostaining, n (%)	
-Not performed	402 (96%)
-Negative	19 (5%)
-Positive	0 (0%)

¹Some patients had more than one comorbidity documented

²Some patients had more than one chronic disease documented

Table 2. Sensitivity and Specificity of H&S Stains n, (%)

H&E	WS Positive for HP	WS Negative for HP	Total
Positive for HP	3	0	3 (PPV=100%)
Negative for HP	7	383	390 (NPV=98.2%)
Total	10 (SENS=30%)	383 (SPEC=100%)	393

H&E = Hematoxylin and Eosin stain; WS = Warthin Starry stain; HP = Helicobacter Pylori; PPV= Positive predictive value; NPV = Negative predictive value; SENS = Sensitivity, SPEC=Specificity

408 A SINGLE CENTER EXPERIENCE OF TREATMENT FAILURE IN HELICOBACTER PYLORI AMONG INNER CITY CHILDREN. Jubin Mathews, Debra Pan. *Pediatric Gastroenterology, Children's Hospital at Montefiore, Bronx, NY*

Background: According to the updated *Helicobacter pylori* (*H. pylori*) guidelines by NASPGHAN/ESPGHAN (2016), the goal eradication rate is >90%. Previous international studies have shown eradication rates to first line therapy ranging from 80-90%. There are limited pediatric studies in the United States. One study demonstrated a lower eradication rate due to alarming resistance rates >40% to clarithromycin and metronidazole. As there is regional variation, it is increasingly important to identify the local eradication rates and resistance patterns to ultimately guide antibiotic selection.

Methods: Retrospective chart review was conducted to evaluate patients aged 1-21 years who were diagnosed with *H. pylori* via stool Antigen and/or histology from 2013-2015. These patients were treated by our pediatric gastroenterology division and had documented good compliance. Their treatment outcomes were analyzed.

Results: A total of 165 patients were diagnosed with *H. pylori*, of whom 148 completed first line therapy. Eighty-five percent of these patients (125/148) were treated with Amoxicillin/Clarithromycin/Proton pump inhibitor (PPI), 8.8% with Amoxicillin/Metronidazole/PPI, <1% Amoxicillin/Metronidazole/Bismuth, and 6.1% with non-standard first line combinations. Eighty-one of 148 patients (54.7%) were tested for *H. pylori* eradication and 67/148 (45.2%) were not tested for eradication. Of those who were tested for eradication, 58/81(71.6%) had treatment success evidenced by negative stool antigen (46/58), negative histology (10/58), or negative for both (2/58). Among those tested with stool antigen for eradication, 20 patients were not on PPI and 16 were on PPI at the time of testing. Remaining 10 patients' PPI status was not clear due to inadequate documentation. Twenty three of 81 patients (28.3%) had treatment failure as evidenced by positive stool antigen (10/23), positive history (8/23), or both (5/23). Among those with treatment failure, 18/23 used Amoxicillin/Clarithromycin/PPI, 3/23 used Amoxicillin/Metronidazole/PPI, and 2/23 used non-standard combinations.

Conclusion: This study showed an eradication rate of 71.6% and treatment failure rate of 28.3%, indicating that our study population has a poor eradication rate. We hypothesize that antibiotic resistance is the primary cause for treatment failure since all patients in this study had documented good compliance. Further studies are needed to evaluate the resistance pattern of each antibiotic.

409 DO OSMOTIC OR STIMULANT LAXATIVES USED TO TREAT CONSTIPATION ENHANCE THE RISK OF C. DIFFICILE INFECTION IN CHILDREN? Julie Khlevner, Yasmine Delgado Jimenez, Esi Lamoué-Smith. *Columbia University Medical Center, New York, NY*

Background: Constipation is a common pediatric problem. Treatment often includes the use of osmotic or stimulant laxatives or a combination thereof. The rates of both community acquired and hospital associated *C. difficile* infection have been steadily increasing. Common risk factors include: antibiotic use, long term use of proton pump inhibitors, frequent hospitalizations, and autoimmune enteric diseases. Fluctuations in stooling pattern in children compliant with a bowel regimen may prompt clinicians to test for *C. difficile* in the setting of persistent diarrhea. Recent recommendations caution against testing patients for *C. difficile* within 48 hours of laxative initiation to prevent inappropriate treatment of asymptomatic colonized patients. However, it is not known whether long term use of common medications used to treat constipation may enhance the risk of *C. difficile* associated diarrheal disease (CDAD) in children.

Objective: To address the hypothesis that single or combination use of medications commonly used to treat constipation in pediatric patients enhances the incidence of CDAD.

Methods: This was a 3-year retrospective chart review from a single center. We included all patients ages 1-18 years. We collected the following parameters: age, medical diagnoses, medications used at time of *C. difficile* diagnosis, diagnosis of CDAD. We performed chi square analysis to evaluate the impact of laxative medications on the risk of CDAD. Results: A total of 582 patients with constipation treated with laxatives were identified. 414 patients did not undergo testing for *C. difficile* as they were asymptomatic. 115 patients treated for constipation that developed diarrhea despite stopping the laxative were negative for *C. difficile*. 52 patients tested positive for CDAD, or **31%** of all patients tested for *C. difficile* infection which was determined to be statistically significant ($p < 0.0001$) based upon published *C. difficile* infection rates of 3-10% in pediatric patients. The percent of children with other complex medical conditions testing positive for CDAD and diagnosed with constipation was **20% vs 29%** in the CDAD negative cohorts (n.s.). The distribution of children using osmotic, emollient, or stimulant laxatives alone or in combination who developed CDAD was 50%, 12%, 13% and 15% respectively and significantly different from the distribution in those who did not develop CDAD ($X^2 (5) = 26.77, p < 0.0001$). 10% of patients were treated with other medications (lubiprostone, enema, etc).

Conclusions: Our results indicate a high rate of *C. difficile* infection in patients treated for constipation and in whom diarrhea develops and does not improve after discontinuing laxative therapy. Type of laxative medication used may play a role in the risk of developing CDAD. Our results also suggest that children with complex medical diagnoses who are treated for constipation may not be at a higher risk for *C. difficile* infection. Our study was limited by the retrospective nature of the analysis thus, we could not determine: the criteria used to diagnose constipation, the length of treatment duration, the effect of the transition from toxin based to PCR based assays used during the study time period, exposure to antibiotics, history of inpatient hospitalizations, PPI exposure. We suggest that prospective studies are conducted in children with complex medical diagnoses who are taking laxatives for constipation to address these questions and to include an analysis of the intestinal microbiome.

410 DOES PRE-TREATMENT WITH ANTIBIOTICS OR ANTACID MEDICATION AFFECT THE DIAGNOSTIC YIELD OF ENDOSCOPY IN DIAGNOSING SMALL BOWEL BACTERIAL OVERGROWTH (SBBO) IN CHILDREN WITH INTESTINAL FAILURE (IF): A RETROSPECTIVE REVIEW. Kathleen Gura^{1,2}, Tania Baker¹, Andrew Beaty³, Kristine Sobolewski⁴, Danielle Stamm², Christopher Duggan².
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Symptoms associated with SBBO in children with IF are a common management challenge. Empiric courses of broad spectrum antibiotic therapy are commonly used with the hopes of abating symptoms. Antacid medications are also considered to be a risk factor for SBBO. We performed a retrospective study to determine whether these factors affected the diagnostic yield of endoscopically diagnosed SBBO in children with IF.

Methods: We reviewed the medical records of infants and children followed by the Center for Advanced Intestinal Rehabilitation Program (CAIR) who had undergone upper gastrointestinal endoscopy with duodenal aspirates and quantitative cultures to evaluate symptoms of SBBO. Demographic, anatomic and medication use data were also collected.

Results: A total of 107 infants and children (47 (44%) female, mean age 4.81 years \pm 5.91) followed by CAIR who underwent an endoscopy with quantitative cultures from a duodenal aspirate from 1997- 2012 were identified. Positive duodenal aspirate cultures were found in 33 (31%) patients.

Of 54 subjects who were treated with antibiotics during the three months before endoscopy, 22 (41%) had a positive bacterial or fungal organism cultured from the duodenal aspirate, versus 11/53 (21%) among those not receiving antibiotics ($P = 0.04$). Moreover, of 54 subjects who were treated with antibiotics during the three months before endoscopy, 14 (26%) had a gram positive organism cultured from the duodenal aspirate, versus 8/53 (15%) among those not receiving antibiotics ($P = 0.25$). Of 54 subjects treated with antibiotics, 18 (33%) had a gram negative organism cultured from the duodenal aspirate, versus 6/53 (11%) among those not receiving antibiotics ($P=0.01$).

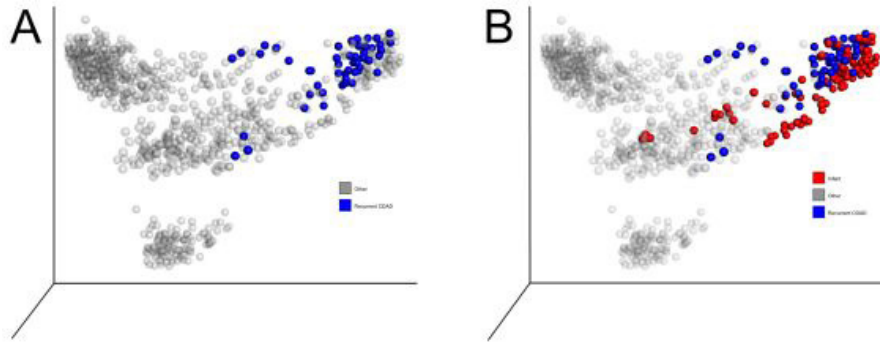
74 (69%) subjects were treated with an acid blocker during the three months before endoscopy, 27 (36%) had a positive bacterial or fungal organism cultured from the duodenal aspirate, versus 6/33 (18%) among those not receiving an acid blocker ($P = 0.1$). Among those treated with an acid blocker during the three months before endoscopy, 15 (20%) had a gram positive organism cultured from the duodenal aspirate, versus 6/33 (18%) among those not receiving an acid blocker ($P = 0.80$). In subjects who were treated with an acid blocker, 20 (27%) had a gram negative organism cultured from the duodenal aspirate, versus 5/33 (15%) among those not receiving antibiotics ($P = 0.22$).

Conclusion: In this retrospective review, exposure to antibiotics in the months preceding endoscopy did not seem to reduce the number of positive duodenal aspirate cultures when compared to non-exposed patients. However, indication bias (wherein sicker patients received antibiotics more frequently) cannot be ruled out. Exposure to antacid medications was associated with a non-significant increase in SBBO diagnosis. Prospective trials of medical management of pediatric IF are needed.

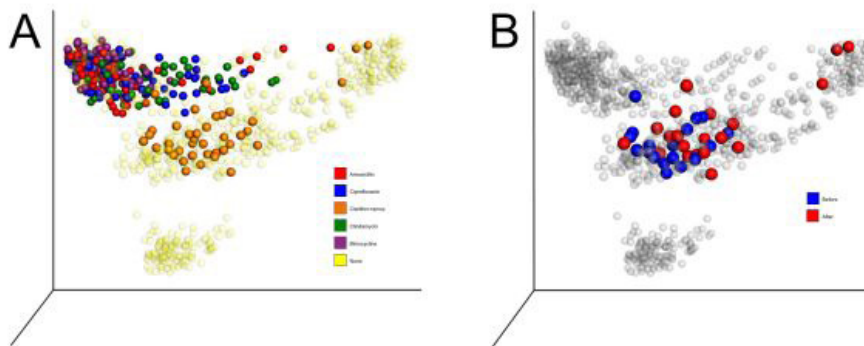
411 WHICH ANTIBIOTICS DRIVE GUT MICROBIOME COMPOSITIONS TOWARDS THOSE TYPICAL OF INDIVIDUALS WITH RECURRENT CLOSTRIDIUM DIFFICILE INFECTION?: A META-ANALYSIS AND TEMPLATE FOR ANTIBIOTIC DEVELOPMENT. Keith Hazleton^{1,2}, Catherine Lozupone³.
¹Pediatric Gastroenterology, Hepatology and Nutrition, University of Colorado Anschutz Medical Campus, Aurora, CO; ²Digestive Health Institute, Children's Hospital Colorado, Aurora, CO; ³Biomedical Informatics and Personalized Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO

The human intestine houses a community of trillions of bacteria and there is mounting evidence that they are vital in maintaining human health. The bacterial community of our intestines are susceptible to killing by antibiotics. The disruption caused by these medications has been associated with an increased susceptibility to *Clostridium difficile* associated diarrhea

(CDAD). To better define the changes to the bacterial community that lead to this increased risk of CDAD we conducted a meta-analysis of several published gut microbiome studies of patients with recurrent CDAD. Our analysis shows that the gut microbiome of adults with CDAD very closely resembles that of infants, with high levels of facultative anaerobes including Proteobacteria and relatively low levels of strict anaerobes such as the Bacteroidetes. These findings suggest that the normal anaerobic environment of the distal intestines is disrupted and allows for *C. difficile* to cause disease. Using studies of healthy individuals given antibiotics, we found that treatment with amoxicillin and clindamycin push the microbiome of the participants towards that seen in recurrent CDAD and infants, and that this effect is stronger than for minocycline. This result is consistent with clinical data showing an increased risk of CDAD with these more disruptive antibiotics. This analysis could provide a metric to assess the CDAD-causing potential of novel antibiotics.



Primary coordinates analysis plots of Unweighted UniFrac distance highlighting samples of patients with recurrent *C. difficile* associated diarrhea prior to fecal microbiota transplant (A) and a comparison between the patients in panel A with the infant gut microbiome (B).



Primary coordinates analysis plots of Unweighted UniFrac distance showing the effect of several antibiotics on the gut microbiome of either healthy volunteers or patients being treated for *Helicobacter pylori* infection (A). Both amoxicillin and clindamycin treatment moves the gut microbiome away from baseline towards the space occupied by recurrent *C. difficile* associated diarrhea and infants. In (B) the *H. pylori* patients are shown pre- and post-treatment demonstrating a clear movement towards recurrent *C. difficile* associated diarrhea and infants.

***413 SALMONELLA ENTERICA SEROVAR TYPHI MODULATES IMMUNE SYSTEM ACTIVATION IN A HUMAN BIOPSY MODEL OF INFECTION.** Kourtney Nickerson^{1,3}, Maria Rosaria Fiorentino^{1,3}, Yan Zhang², Marcelo Szein⁴, Stefania Senger^{1,3}, Alessio Fasano^{1,3}. ¹Pediatric Gastroenterology, Massachusetts General Hospital, Boston, MA; ²Institute for Genome Sciences, Baltimore, MD; ³Harvard Medical School, Harvard University, Boston, MA; ⁴Center for Vaccine Development, University of Maryland, Baltimore, MD

Introduction. Typhoid fever is a common worldwide illness, transmitted by the ingestion of food or water contaminated with the feces of an infected person, which contain the bacterium *Salmonella* Typhi. The World Health Organization estimates that 22 million cases of typhoid fever occur annually, resulting in ~200,000 deaths. In common with other enteropathogens, *S. Typhi* has developed means of breaching the mucosal epithelial barrier by usurping signaling mechanisms within host cells. At present, much remains to be uncovered concerning the host responses to *S. Typhi* infection. Current therapeutic strategies

include antibiotic treatment; however the frequency of antibiotic-resistant serovars is increasing worldwide and preventive therapeutics are only moderately protective. Additionally, in some individuals chronic *S. Typhi* colonization of the gall bladder culminates in gall bladder cancer, therefore highlighting the significant short and long-term consequences of infection. Given the adverse consequences of *S. Typhi* infection there is a critical need to understand the mechanisms of the disease process and the host immune response for the development of efficacious and cost effective vaccines.

Materials/Methods. Terminal ileum biopsies were collected from donors for direct infection. Whole biopsy (WB) infections were conducted using micro-snapwell mounting of tissue followed by addition of *S. enterica* serovar Typhi 2a to the apical surface. Related *Salmonella* serovar Typhimurium SL1344 was used as a control strain. Upon infection, changes in trans-epithelial electrical resistance (TEER), FITC-dextran flux, cytokine release, gene expression, signal transduction and cellular localization were assessed.

Results/Conclusions. Use of WB model identified specific contributions of the epithelium in response to Typhi infection as assessed by RNA-sequencing, qPCR, and cytokine secretion. Infection of WB revealed extensive transcriptional down regulation accompanied with minimal transcriptional upregulation. Moreover, the genes upregulated by Typhi were largely human-restricted and demonstrated minimal homology to *Mus musculus*. Bacterial invasion was accompanied by extensive cytoskeleton rearrangement of the mucosal epithelium in actin and tubulin-dependent manners. Importantly, infection did not cause cell death as assayed by LDH release however significant cytokine release was observed. In comparison with biopsies infected with the related serovar Typhimurium SL1344, apical cytokine release was often significant and basolateral cytokine release was impaired. Furthermore, transcriptional upregulation of cytokine genes was not observed, suggesting that release was occurring independently of cytokine store replenishment. Therefore, we looked at signaling pathways traditionally activated prior to transcriptional upregulation of cytokines and found that NFkB and MAPK (p38 and JNK) were activated in the presence of SL1344 but inhibited by Ty2. Together, our data suggests that Typhi bacteria modulate host response by targeting signal transduction resulting in an impaired immune response. For the first time, this work demonstrates how Typhi bacteria interact with human tissue to block development of an adaptive immune response.

414 EFFICACY OF LACTOBACILLUS REUTERI FOR INFANT REGURGITATION: A SYSTEMATIC REVIEW. Kristen Finn, Heidi Storm, Brian Kineman, Ryan Carvalho. *Clinical Sciences, Nestle Nutrition, Florham Park, NJ*

Background: Regurgitation is the most common functional gastrointestinal disorder (FGID) reported among infants in the U.S. While most cases self-resolve by 12 months, regurgitation causes parental anxiety and is a common reason for pediatric office visits during its peak prevalence in early infancy. Expert guidelines recommend conservative management with parental education for physiologic regurgitation. Despite these recommendations, proton pump inhibitors (PPIs) are often used, in spite of insufficient evidence supporting their efficacy in infants with uncomplicated regurgitation. Recently, concerns about long term PPI use in infancy affecting the intestinal microbiome and long term fracture risk has elevated the need for different interventions. *L. reuteri* has been studied extensively in pediatric populations and has been shown to be safe and effective in the treatment of common FGIDs like infantile colic. The purpose of this systematic review was to determine if *L. reuteri* was more effective than a placebo in reducing the symptoms of infant regurgitation.

Methods: A search of the MeSH term and keyword, *Lactobacillus reuteri*, was conducted in Medline, CINAHL, Pubmed, HealthSTAR, and Cochrane Library. The search was limited when possible to human infants (<23 months). A total of 211 abstracts were screened and 54 full text articles reviewed as of January 2017. Studies were included if they met all of the following criteria: infants \leq 12 months, test participants received *L. reuteri* drops, a placebo was used as a control, and number of regurgitations was an outcome.

Results: Four double-blind, randomized controlled trials conducted in Europe, with a total of 562 participants were included. All studies utilized the same dose of *L. reuteri* drops (1×10^8 CFU/day). All studies found a significant difference in average regurgitations per day between the *L. reuteri* and placebo groups in favor of the *L. reuteri* group (See Table 1). Although the Indrio et al. 2014 study did not detect a significant difference in mean regurgitations during the fourth week of intervention, the mean regurgitations were significantly less in the *L. reuteri* group compared to the placebo group during the twelfth week of intervention.

Conclusion: *L. reuteri* offers a safe alternative to pharmaceutical intervention and may be considered in the prevention and treatment of infant regurgitation. North American trials in infants diagnosed with uncomplicated infant regurgitation are needed.

Table 1: Average daily regurgitations at the end of study intervention

Study	Age/ Population	Feeding Mode	Duration	<i>L. reuteri</i> Group Regurgitations (mean ± SD)	Placebo Group Regurgitations (mean ± SD)	P value
Indrio 2008	3-5 Days Preterm	BF/FF	4 Weeks	2.1 ± 0.9 (n=10)	4.2 ± 1.1 (n=10)	<0.01
Indrio 2011	<4 Months GER	FF	4 Weeks	1.0 (1.0-2.0)* (n=19)	4.0 (3.0-5.0)* (n=15)	<0.001
Garofoli 2014	0-3 Days Healthy	BF	4 Weeks	9** (n=20)	18.5** (n=20)	0.02
Indrio 2014	0-7 Days Healthy	BF/FF	4 Weeks	2.7 ± 1.5 (n=238)	3.3 ± 2.3 (n=230)	0.35
			12 Weeks	2.9 ± 1.1	4.6 ± 3.2	<0.01

BF=Breastfed, FF=Formula fed, GER=Uncomplicated Gastroesophageal Reflux Diagnosis

*Median (95% confidence interval) **Means estimated from graph

416 ENGINEERING BACTEROIDES SPECIES TO SECRETE ANTI-INFLAMMATORY PROTEINS

VIA OUTER MEMBRANE VESICLES. Logan Jerger¹, Mark Mimeo², Timothy Lu². ¹Pediatric Gastroenterology, MassGeneral Hospital for Children, Boston, MA; ²Biological Engineering, Massachusetts Institute of Technology, Cambridge, MA

Background: *Bacteroides* spp. are prevalent and abundant organisms in the human microbiome. These Gram-negative, non-spore-forming bacteria release outpouchings of their outer membrane containing proteins, lipids, and polysaccharides, known as outer membrane vesicles (OMVs), to communicate with their environment. By selectively packaging materials into OMVs, the opportunity exists to facilitate purposeful communication between microbiota and host in attempts to treat disease states causing inflammation.

Objective: This study aimed to express the anti-inflammatory proteins including of Interleukin-10 (IL-10), IL-22, and superoxide dismutase in commensal organisms.

Methods: DNA primer and plasmid creation incorporated anti-inflammatory proteins (IL-10, IL-22, and superoxide dismutase), candidate OMV secretion tags, a NanoLuc reporter gene, antibiotic resistance genes for bacteria selection, and a plasmid transfer origin within an integration vector. Plasmids were assembled via Polymerase chain reaction (PCR) and exonuclease, DNA polymerase, and DNA ligase reactions. DNA material was introduced to *E. coli* via electroporation and transferred to *Bacteroides* spp. via conjugation following co-incubation. Enzyme-Linked Immunosorbent Assays (ELISAs) directed toward specific cytokines quantified protein expression of IL-10 and IL-22; superoxide dismutase assay utilizing tetrazolium salt for detection of superoxide radicals quantified superoxide dismutase activity.

Results: Bacterial supernatant from *Bacteroides thetaiotaomicron*, *B. fragilis*, and *B. vulgatus* as well as isolated OMV fractions of these bacterial species illustrate expression of both IL-10 and IL-22. Protein expression quantity varied based on anti-inflammatory protein, OMV lipoprotein, and bacterial species. Highest OMV fraction expressions of IL-10 utilized *B. fragilis* and OMV lipoprotein BVIT1 (1.6 ng mL⁻¹⁰/ug OMV). OMV fraction expression for IL-22 reached peak value with *B. fragilis* utilizing OMV lipoprotein BVIT3 (5.4 ng mL⁻²²/ug OMV). Highest superoxide dismutase activity was noted in *B. fragilis* with lipoprotein BVIT6 (1.9 U/mg OMV).

Conclusions: This study illustrates successful expression of anti-inflammatory proteins via OMVs from *Bacteroides* spp. Future directions may assess functionality of these expressed proteins both *in vitro* and *in vivo* via bioactivity assays and mouse models of colitis.

NUTRITION

418 **NEW KIDS™ TRIAGE PARENT SATISFACTION SURVEY.** Denise Kilway. *Pediatric GI, Medical College of Wisconsin, Pewaukee, WI*

Background/Significance: With the ongoing problem of childhood overweight and obesity in the United States, there is more importance placed on interventions to prevent and treat childhood obesity. There is limited literature reporting parents' knowledge and satisfaction of a Pediatric Nurse Practitioner (PNP) educational intervention in relation to childhood obesity.

Purpose: This study will evaluate parent basic knowledge of general healthy lifestyle behaviors, perception of knowledge gained after the clinic appointment, and satisfaction of information presented in a PNP educational intervention in the Nutrition, Exercise and Weight Management (NEW) Kids™ Triage Clinic. The NEW Kids™ Triage Clinic visit is the initial visit for the NEW Kids™ Program and is an outpatient clinic geared toward individualized treatment of pediatric overweight, obesity and their associated co-morbidities. This study evaluates a strategy to reduce the incidence and complications associated with childhood obesity and addresses the NAPNAP research priority of obesity.

Methods: This study has been approved by the institution's IRB. A pre-test/post-test design will be used to enroll 98 parents of children referred to the NEW Kids Triage Clinic at a single Children's hospital. The study will utilize a combination of multiple choices, open-ended and Likert scale questions to measure: 1) parental knowledge of general healthy lifestyles before a PNP educational intervention, 2) overall parental perception if new knowledge was gained following education provided by a PNP during the clinic appointment, and 3) satisfaction with communication of the education provided by the PNP.

In the pre-test, the information gathered include: parents' general knowledge regarding why their child was referred to the NEW Kids™ Triage Clinic, knowledge on healthy habits including meal consistency, sedentary activity, physical activity, and sweetened beverages. The post-test will include questions related to parents' self perception of knowledge gained regarding the aforementioned healthy habits, if they plan to change behaviors after the visit, concerns and satisfaction of the information given by the PNP. The satisfaction questions will be utilized from an established tool of PNP satisfaction. Additional data collected will be the child's BMI, BMI percentile, and BMI z-scores to determine possible correlation with parents' responses.

Findings/Implications: Results of this study showed that the pre-test results included assessment of knowledge of health lifestyles with the greatest correct answers were meal frequency (83%) and the lowest correct answers were sweetened beverages (38%). Post-test information included parents' overall ratings of satisfaction of the PNP visit were Strongly Agree (82%) and Agree (18%). The average BMI of the children was = 34.6 and Mean BMI *z-score* = 2.5

Implications for this model may include the utilization of various providers in Pediatric GI that can provide information, assessment and plan can be helpful in the education of parents on their children with obesity. This intervention could be a cost effective way to impact local, state and national obesity epidemic. Future research may include using a larger sample size and controls.

419 **EPIDEMIOLOGY AND OUTCOMES OF THE USE OF PARENTERAL NUTRITION IN HOSPITALIZED CHILDREN IN THE UNITED STATES.** Jessica Barreto¹, Desiree Sierra¹, Mary Wood¹, Balagangadhar Totapally². ¹*Pediatrics, Nicklaus Children's Hospital, Miami, FL;* ²*Critical Care Medicine, Nicklaus Children's Hospital, Miami, FL*

Background: Nutritional support is a fundamental component in the management of hospitalized children and has been associated with improved patient outcomes. The preferred mode of nutrition in patients with a functional gastrointestinal tract is the enteral route but when enteral feeding is not possible, parenteral nutrition (PN) may be considered.

Objective: To characterize the use of parenteral nutrition in pediatric hospitalizations in the United States including epidemiology, comorbidities, associated diagnoses and complications.

Methods: A retrospective analysis of the Healthcare Cost and Utilization Project Kids' Inpatient Database (KID) for the year 2012 was performed. Children aged 1 month – 17 years with a procedure code for parenteral nutrition (ICD-9-CM 99.15) were included for analysis. Chi-Square test was used to compare diagnoses in this cohort with the rest of the discharges. Sample weighting was used to produce national estimates.

Results: A total of 25,581 patients with use of PN were identified in 2012, with an overall prevalence of 134 per 10,000 discharges. Use of PN was most common in children aged 1-5 years (32.3%, OR 1.19, 95%CI 1.16-1.22). Mean age was 6.2 years (SD 5.8). Racial and gender distribution showed a higher proportion of white children (52.1%, OR 1.04, 95%CI 1.02-1.07) and males (54.1%, OR 1.14, 95%CI 1.11-1.17). The highest prevalence was seen in the western region (167/10,000)

and lowest in the southern region (102/10,000). Among patients receiving PN, 40.6% (OR 2.82, 95%CI 2.75-2.89) had a major OR procedure and 21.5% (OR 11.4%, 95%CI 11.0-11.7) were mechanically ventilated. Congenital heart disease was identified in 11.8% of patients (OR 4.4, 95%CI 4.2-4.6). Diagnoses associated with use of PN included: malabsorption and short bowel syndrome (15.5%, OR 28.4, 95%CI 27.4-92.5), obstruction and pseudo-obstruction (12.9%, OR 13.7, 95%CI 13.2-14.2), acute appendicitis (5.5%, OR 1.5, 95%CI 1.4-1.6), pancreatitis (5.1%, OR 11.3, 95%CI 10.6-11.9), Crohn's disease (3.6%, OR 10.6, 95%CI 9.8-11.3), ulcerative colitis (2.2%, OR 9.9, 95%CI 9.1-10.9), aspiration pneumonia (3.0%, OR 5.6, 95%CI 5.2-6.0), and Hirschsprung's disease (1.6%, OR 10.0, 95%CI 9.0-11.1). Common complications associated with PN were central line infections (8.2%, OR 11.5, 95%CI 11.0-12.1); liver and gallbladder dysfunction (8.2%, OR 12.9, 95%CI 12.3-13.5); thrombosis (2.2%, OR 14.6, 95%CI 13.3-15.6); potassium abnormalities (14.2%, OR 7.6, 95%CI 7.4-7.9); sodium abnormalities (12.5%, OR 8.0, 95%CI 7.7-8.3); magnesium abnormalities (4.1%, OR 12.5, 95%CI 11.7-13.3); calcium abnormalities (3.3%, OR 9.1, 95%CI 8.5-9.8); hypoglycemia (1.9%, OR 3.8, 95%CI 3.4-4.1); and hyperlipidemia (0.7%, OR 3.7, 95%CI 3.2-4.4). Median hospital charges were USD 111,193 (IQR 50,784 – 258,998) and median length of stay was 13 days (IQR 7-24). The mortality rate was 3.4% (OR 12.3, 95%CI 11.4-13.2).

Conclusions: Our analysis of the nationally representative KID database presents the prevalence of use of PN in hospitalized children and diagnoses and complications associated with its use.

420 DEVELOPMENT OF A FOOD-FREQUENCY QUESTIONNAIRE TO ASSESS FOLATE AND VITAMIN B12 STATUS IN CHILDREN WITH CHRONIC HEPATITIS B. Douglas Mogul¹, Hong Nga Brereton², Kit Carson², Kathleen Schwarz¹. ¹Pediatrics, Johns Hopkins, Baltimore, MD; ²Institute for Clinical and Translational Research, Johns Hopkins University, Baltimore, MD

Background: Epigenetic changes, including methylation of genetic material, are increasingly understood to play critical roles in health and disease pathogenesis. For example, data suggests that replication of hepatitis B virus (HBV) responds to epigenetic modifiers *in vitro* but it is unknown whether or not this occurs *in vivo*. To investigate this hypothesis in children with HBV it was necessary to develop an age-appropriate dietary methyl donor questionnaire since this type of questionnaire had previously been validated only in adults.

Methods: We developed a semi-quantitative food frequency questionnaire (FFQ) to estimate dietary intake of folate and vitamin B12 and validated this instrument against a 24-hour dietary recall, and biomarkers: red blood cell (RBC) folate, serum vitamin B12 (vit B 12) and plasma homocysteine (HC) in a cohort of 34 otherwise healthy children (11.0 +/- 3.3 years of age) chronically infected with HBV (HBV DNA level 6.55 +/- 2.74 log IU/ml). Estimates from this FFQ were then measured against methylation density from samples of viral DNA from these patients.

Results: Intake of folate /kg body weight by FFQ correlated positively with 24 hour recall ($r = 0.70030$, $p < 0.0001$) and negatively with HC ($r = -0.55996$, $p = 0.0006$). Intake of vit B12/kg body weight by FFQ also correlated positively with 24 hour recall ($r = 0.56636$, $p = 0.0004$) and serum vit B12 ($r = 0.35992$, $p = 0.0365$) and negatively with HC ($r = -0.49526$, $p = 0.0029$). No children had biomarkers in the deficient range. Neither dietary methyl donor intake (from FFQ or 24 hour recall) nor biomarkers correlated with methylation density of HBV DNA.

Conclusions: Our preliminary data do not support a role for epigenetic modification of HBV in this well-nourished North American pediatric cohort. However the positive results of this pilot study of a dietary methyl donor FFQ for children suggest that this tool could prove useful for investigating epigenetic modifiers of pediatric diseases if first validated in large-scale studies.

421 CHILDHOOD OBESITY RISK FACTORS DURING THE FIRST 1,000 DAYS IN AN URBAN WOMEN, INFANTS, AND CHILDREN (WIC) PROGRAM. Erin Elbel¹, Kayla Milne^{1,2}, Nina Quirk^{1,2}, Kelsey Nichols^{1,2}, Jennifer Woo Baidal¹. ¹Division of Pediatric GI, Hepatology, and Nutrition, Columbia University Medical Center, New York, NY; ²Institute of Human Nutrition, Columbia University Medical Center, New York, NY

Background: Racial/ethnic minority and low-income families are disproportionately burdened by childhood obesity. The “first 1,000 days” – pregnancy and infancy to age 2 years – is a critical growth period, and established childhood obesity risk factors exist during the first 1,000 days. Little research has focused on established childhood obesity risk factors during the first 1,000 days among low-income, minority populations.

Objective: To examine established childhood obesity risk factors during the first 1,000 days in low-income families in northern Manhattan, the area with the highest prevalence of childhood obesity in New York City.

Methods: We prospectively recruited pregnant women and families with infants < age 2 years in a multi-site Special Supplemental Nutrition Program for Women, Infants, and Children (WIC). Trained research staff administered validated

survey questions. Using standardized protocols, research staff measured parent and infant weight; parent height; and infant length. Outcomes were childhood obesity risk factors during pregnancy and infancy. Pregnancy risk factors were maternal pre-pregnancy overweight/obesity [body mass index (BMI) ≥ 25 kg/m²] and maternal excess gestational weight gain based on Institute of Medicine criteria. Infant risk factors were non-exclusive breastfeeding before age 6 months, early introduction of solids (before age 4 months), age-specific curtailed infant sleep, routine daily infant screen time, and high infant weight-for-length defined as sex-specific weight-for-length z-score > 2.0 per World Health Organization standards. We performed a cross-sectional analysis using descriptive statistics to determine the frequencies of established childhood obesity risk factors at baseline.

Results: Among 303 parents, 99% were female and 30% were pregnant. Mean parent age was 29 ± 6 years, 93% were Hispanic/Latino, and 74% reported annual household income under \$20,000. Among 210 participants with infants, mean infant age was 9 ± 7 months and 50% were female. For maternal risk factors during pregnancy, 58% had pre-pregnancy overweight/obesity and 84% had excess gestational weight gain. For the subset with infants, 95% reported non-exclusive breastfeeding, 45% early introduction of solids, 38% curtailed infant sleep, and 64% routine daily infant screen time. Estimated prevalence of high infant weight-for-length was 18.6% (95% CI: 13.1, 24.1), with similar prevalence between males and females.

Conclusions: In this low-income sample, childhood obesity risk factors during the first 1,000 days were common. Estimated prevalence of high infant WFL was two-fold higher than the general United States population. Future interventions to reduce childhood obesity in northern Manhattan should focus on reducing obesity risk factors during the first 1,000 days.

422 CURRENT STATUS OF NUTRITIONAL SUPPORT TEAM FOR HOSPITALIZED CHILDREN: A NATIONWIDE MULTICENTER CROSS-SECTIONAL SURVEY IN SOUTH KOREA. Eun Hye Lee¹, Seung Kim², Hye Ran Yang^{3,4}. ¹Pediatrics, Eul Ji Medical center, Seoul, Korea (the Republic of); ²Pediatrics, Severance children's hospital, Seoul, Korea (the Republic of); ³Pediatrics, Seoul National University College of Medicine, Seoul, Korea (the Republic of); ⁴Pediatrics, Seoul National University Bundang Hospital, Seongnam, Korea (the Republic of)

Background: In 2001, an independent Nutritional support team (NST) for hospitalized children was first established in South Korea. Since then, pediatric NST teams have been implemented in many hospitals and have done a lot of work to support children's nutritional improvement. The aim of this study was to investigate the current state of NST activity for hospitalized children through nationwide multicenter survey in South Korea.

Methods: Out of 344 general and tertiary hospitals in South Korea, 53 institutes having pediatric gastroenterologist and more than 10 pediatric inpatients were recruited. The questionnaire on NST activity was developed by the Nutrition Committee of Korean Society of Pediatric Gastroenterology, Hepatology and Nutrition. The questionnaires were sent to pediatric gastroenterologists in each hospital. Survey was performed by e-mail, and some incomplete answers were asked on telephone.

Results: Forty hospitals (75.5%) responded to the survey; 22 of them were tertiary hospitals, and 18 were general hospitals; 37 were university hospitals; and 7 of them had children's hospital. Twenty-two (55%) hospitals managed NST jointly without distinction of children from adults. Fourteen (35%) hospitals had pediatric NST independent of adult NST. Four hospitals (10%) answered that hospitalized children didn't receive any kind of nutrition support from NST. All required NST members including pediatrician, dietitian, nurse, and pharmacist were assigned for nutrition support of hospitalized pediatric patients in 27 (67.5%) hospitals. There were no NST consultations in 14 (35%) hospitals and less than 10 consultations every month in 10 (25%) hospitals. Monthly NST consultations were more than 100 in only 4 (10%) hospitals and between 10 and 100 in 12 (30%) hospitals. While the number of pediatric patients was 12.4% of total hospitalized patients, NST consultations for pediatric patients were 22.9% of total NST consultations. Total 90.5% of adult NST consultation fee were covered by the national health insurance, whereas only 76.0% of pediatric NST consultation fee were covered, mainly by reason of repeated consultations within a week (70.7%). From our nationwide survey, only 10 (25%) of 40 hospitals answered that their NSTs were properly managing pediatric inpatients from nutritional aspect, while the others reported that nutritional management was not appropriate in their hospitals and main barriers to NST activity were the lack of manpower and excessive work load (42.5%).

Conclusions: Although this nationwide multicenter survey was performed targeting at general and tertiary hospitals with pediatric gastroenterologists, manpower and medical resources for effective nutritional support, especially pediatric NST activity, were still insufficient for hospitalized children in South Korea. In addition, national health insurance coverage of NST consultation still needs to be modified to improve current barriers to the implementation and management of pediatric NST.

423 CELIAC DISEASE IN SOUTH JORDAN. *Eyad Altamimi. ediatrics, Jordan University of Science and Technology, Irbid, Jordan*

Introduction: Celiac Disease (CD) is an autoimmune enteropathy in genetically susceptible individuals triggered by exposure to wheat gluten (Gliadins). The objective of this study is to describe the clinical patterns of CD in children from south Jordan.

Design And Setting: Retrospective review of clinical files.

Patients And Methods: This study included children diagnosed with celiac disease between October 2009 and September 2015. Intestinal biopsies were omitted in cases with symptoms suggestive of CD with high titers of tTG and positive anti-Endomysial antibodies.

Results: Thirty five children were identified with a diagnosis of CD. Their mean (SD) age was 6.7 (3.8) years (range, 2.0-14 years). There were 17 (48.6%) female patients. The average duration between symptoms and diagnosis was (SD) 16.3 months (18.7 months). 15 (42.9%) patients presented with classical malabsorption symptoms. 6 (17.1%) patients presented with short stature. Celiac disease was diagnosed in two patients with IDDM, while IDDM developed in one of the celiac patients after one year of being diagnosed with celiac disease. Geophagia was the presenting complaint in two patients.

Two patients presented with celiac crises (severe diarrhea, severe hypokalemia and severe acidosis). The two patients with elevated liver enzymes normalized their enzymes with diet. One patient was referred by ophthalmologist after presenting with xerophthalmia due to IgA deficiency. 34(97.1%) patients had positive tTG IgA. The only patient with negative tTG IgA had IgA deficiency.

All patients treated with Gluten-free diet(GFD). Vitamins and micronutrients (Iron, Ca, ...) were supplemented according to patients' needs. Although of non-availability of tTG for objective documenting of compliance, clinical data (resolution of presenting abnormalities and growth improvement) assured acceptable compliance in 22 (62.9%) patients. On Gluten-free diet (GFD); one patient developed obesity(BMI>95th centile) and abnormal lipid profile.

CONCLUSION: CD in children may present with diverse picture. Although of the small number, the non-classical presentations are not uncommon in our rural community. GFD is the main strategy for treatment and associated with usually correction of laboratory abnormalities and improvement of growth. Although rare, GFD might have complications.

424 PRELIMINARY EXPERIENCE OF THE MODIFIED ATKINS DIET FOR CHILDREN WITH PRADER-WILLI SYNDROME. *Grace Felix¹, Eric Kossoff², Bobbie Baron³, Elizabeth Getzoff⁴, Caitlin Krekel³, Ann Scheimann¹. ¹Pediatric Gastroenterology, Johns Hopkins, Baltimore, MD; ²Pediatric Neurology, Johns Hopkins, Baltimore, MD; ³ICTR, Johns Hopkins, Baltimore, MD; ⁴Pediatric Psychology, Mt Washington Pediatric Hospital, Baltimore, MD*

Background: Prader-Willi Syndrome is a disorder of genetic imprinting characterized by the loss of the paternal copy of chromosome 15q11.2-13 with neonatal presentation of hypotonia, feeding problems and failure to thrive followed by insidious onset of weight gain accompanied by impaired satiation, varying degrees of dysfunction of the hypothalamic and pituitary axis, and behavioral features which commonly include obsessive compulsive behaviors and anxiety. Various dietary strategies have been used for weight management or weight loss for people with PWS – most commonly a hypocaloric, protein-sparing diet. Very-low energy and ketosis-inducing low carbohydrate diets are dietary strategies which have been used for appetite suppression in the general population. This is the first study of its kind to test the use of the Modified Atkins Diet (low-carbohydrate, high-fat) for children with Prader-Willi Syndrome.

Methods: IRB approval was obtained for this pilot/feasibility study. Children with Prader-Willi Syndrome between ages 6-12 who were overweight/obese (greater than 75th percentile) were included. Exclusion criteria included: diabetes, significant hyperlipidemia, hypercalciuria (defined as urine calcium/creatinine greater than 0.2), multiple food allergies or history of significant GI dysmotility. Participants and their families received diet education at the first study visit by a research dietitian. Participants went on the Modified Atkins Diet for 4 months and then returned to have anthropometry repeated including repeat labs and behavior questionnaires.

Results: To date, five children are in the study with an additional three scheduled for enrollment. Average BMI z-score was 1.87. Three participants have completed the 4-month diet trial. One participant had to leave the study early due to hypercalciuria (no clinical renal stones) that resolved off the diet. One patient lost 2.9 kg; the other two maintained their weight (gained 0.3 kg and 1.2 kg during diet period). All 3 patients saw a decrease or stabilization of their HgbA1C (average decrease of 0.23% per patient). One patient halved her insulin level from 49.3 to 24.2 mcU/mL. Regarding lipid profiles, total

cholesterol and HDL was overall stable. LDL increased by 20 to 30 mg/dL in 2 patients but decreased by 14 in one patient. Triglycerides were stable in 2 patients, and decreased by 39 ml/dL in one patient.

Conclusion: The Modified Atkins Diet is a good low-carbohydrate option for children with Prader-Willi Syndrome. In our small sample, the most impact seemed to be improving insulin resistance and HgbA1C profiles. One child of three lost weight and lipid values were stable. Completion of this prospective trial is underway.

425 **EFFECT OF PEDIATRIC NUTRITIONAL SUPPLEMENT FORMULA ON CATCH-UP GROWTH IN YOUNG CHILDREN WITH NONORGANIC GROWTH FLATERING: A PROSPECTIVE**

MULTICENTER STUDY. Hye Ran Yang^{5,6}, Jung Ok Shim², Seung Kim³, Byung-Ho Choe¹, Ji-Hyun Seo⁴. ¹Pediatrics, Kyungpook National University School of Medicine, Daegu, Korea (the Republic of); ²Pediatrics, Korea University College of Medicine, Seoul, Korea (the Republic of); ³Pediatrics, Yonsei University College of Medicine, Seoul, Korea (the Republic of); ⁴Pediatrics, Gyeongsang National University School of Medicine, Jinju, Korea (the Republic of); ⁵Pediatrics, Seoul National University Bundang Hospital, Seongnam, Gyeonggi, Korea (the Republic of); ⁶Pediatrics, Seoul National University College of Medicine, Seongnam, Gyeonggi, Korea (the Republic of)

Background: Improvement of nutritional intake by a concentrated and balanced nutritional supplement formula might have some positive effects on catch-up growth in children with growth faltering. The aim of this multicenter study is to evaluate the effect of nutritional supplementation with a pediatric nutritional formula (Pediapowder[®]) on promoting growth and improving nutritional status in children with nonorganic growth faltering.

Methods: Children aged 12 ~ 36 months whose body weight-for-age were below the 5th percentile on the Korean growth charts were enrolled prospectively for multicenter study under the consents from their parents. Children born premature or having apparent organic diseases were excluded. Children were instructed to consume 400mL of formula per day in addition to regular diet for 6 months. Pediatricians and dietitians educated the parents for nutritional intake every 2 month at each medical center. Anthropometric parameters were measured at baseline, 2, 4, and 6 months, and laboratory tests were done at baseline and 6 months in all study subjects. Good consumption group was defined as formula intake of > 60% of the recommended dose and poor consumption group as intake of < 60%.

Results: Total 63 children completed the intervention. At baseline, there were no significant differences in all variables between the 2 groups. After 6 months of follow-up, all participants had a significant improvement in the levels of hematocrit, iron, TIBC, ferritin, and prealbumin (paired t-test, all $P < 0.05$). The good consumption group significantly gained weight compared to the poor consumption group during the 6-month intervention period (independent t-test, $P = 0.023$). Height, head circumference, and mid-arm circumference had no significant differences between the 2 groups. The good consumption group revealed a significant trend for weight gaining for 6 months of formula intake compared to the poor consumption group ($P = 0.016$ on GEE analysis).

Conclusion: Nutritional supplementation with a concentrated and balanced pediatric nutritional formula along with dietary education might be an effective approach to promote catch-up growth in children with nonorganic growth faltering.

Key words: Pediatric formula, nutritional supplement, growth faltering, catch-up growth, child

426 **INFANT FEEDING PRACTICES AMONG FAMILIES IN INNER CITY, LOW SOCIOECONOMIC COMMUNITIES.** Ayelet Rosenthal, Stephanie Oliveira, Uchenna Madubuko, Hanan Tanuos, Joseph Schwab, Iona Monteiro. Rutgers New Jersey Medical School, Newark, NJ

Background: Infant nutrition in the first few months of life, whether breastfeeding, formula feeding or introduction of solid foods, is a well-studied subject in pediatrics. However, parents base their infant feeding decisions on many factors including personal experience, family practices, cultural and socioeconomic factors. Infant feeding habits have been shown to differ between immigrants and non-immigrants in the US. These differences are noticed as early as breastfeeding and continue to the type of foods introduced to the child during early life.

Aim: We characterized feeding practices among infants of immigrant mothers in comparison to infants of American-born mothers who received their care in an inner city Pediatric Continuity Clinic in Newark, New Jersey. This clinic predominantly serves low socioeconomic status (SES) families.

Methods: A survey was taken from 102 parents of infants ranging from 12-15 months of age who attended the clinic. Parents were asked about country of origin, ethnic background and time since immigration to the US. They were also questioned about breastfeeding duration and reasons for breastfeeding cessation, time of introduction of solid foods, feeding of commercially available baby food and introduction of fast foods to their infants. Statistical significance was estimated using chi-squared tests.

Results: Breastfeeding rates were higher among immigrant mothers compared to American-born mothers (88% vs. 66%, p-value 0.008). Immigrant mothers compared to American-born mothers introduce commercially available baby food less frequently (37% vs. 52%, p-value 0.029) and were less likely to feed their infants fast foods (22% vs. 50%, p-value 0.0006). Moreover, breast feeding rates decreased the longer immigrant mothers resided in the US with 53% of immigrant mothers under 5 years in the US breastfeeding for over 6 months compared to only 26% of immigrant mothers above 5 years in the US (p-value 0.034).

Formula provided by the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) did not play a significant role in changing breastfeeding habits among our low SES study population. While 94% of the study population received WIC support, only one respondent mentioned it as a reason for not breastfeeding.

Cultural perceptions played an important role in infant feeding as 64 % of immigrant mothers who switched to formula did so because they felt their milk production was insufficient whereas 93% of American-born mothers stopped breastfeeding because they perceived it to be painful (p-value 0.001).

Conclusions:

1. Infant feeding practices differ significantly between immigrant and American-born mothers.
2. The feeding practice differences diminish the longer the immigrant mothers reside in the US.
3. The differences between infant feeding practices might be due to cultural differences and perceptions among these two groups.
4. Therefore, in educating mothers about infant feeding, physicians should take into account their cultural and ethnic backgrounds.

Future Studies:

1. Explore the perception of breast feeding as painful by American-born mothers.
2. Elucidate the effect of these feeding differences on future health.

428 HIGH N-6:N-3 FATTY ACID RATIOS IN PRETERM INFANTS FROM A COASTAL SAN DIEGO POPULATION DESPITE MATERNAL N-3 DIETARY ENRICHMENT. Megha Koduri¹, Hema Ramkumar¹, Jae Kim⁴, Christian Metallo², Oswald Quehenberger³, Shira Robbins¹. ¹Department of Ophthalmology, University of California San Diego, La Jolla, CA; ²Department of Bioengineering, University of California San Diego, La Jolla, CA; ³Department of Pharmacology, University of California San Diego, La Jolla, CA; ⁴Department of Pediatrics, University of California San Diego, La Jolla, CA

Background: Studies performed in European populations revealed that concentrations of arachidonic acid (C20:4 n-6) and docosahexaenoic acid (DHA, C22:6 n-3) are positively correlated with gestational age at birth, while concentrations of total fatty acids, n-6 long chain polyunsaturated fatty acids (n-6 LCPUFAs) and monounsaturated fatty acids (MUFAs) are negatively correlated with gestational age at birth. The influence of maternal dietary fatty acids on preterm infant fatty acid status is poorly understood.

Objectives: The aim of this study was to determine the characteristics of fatty acid concentrations in preterm infants compared with full term infants in an American coastal city.

Methods: Umbilical cord blood was collected at the time of delivery from 16 preterm and 22 term infants born at University of California San Diego between 2014 and 2016. Plasma was isolated from these samples, and the fatty acid metabolite distribution of the samples was determined by high performance gas chromatography and mass spectroscopy. Mothers completed a dietary questionnaire to assess their dietary fatty acid consumption as well as use of omega-3 supplementation during pregnancy. Statistical analysis of the data was performed using the Mann Whitney U test.

Results: Compared to term infants, preterm infants were found to have significantly higher relative concentrations of total fatty acids (P = 0.021) and omega-6 fatty acids (P = 0.007). Specifically, preterm infants had higher levels (P<0.05) of pentadecylic acid (C15:0), n-9 oleic acid (C18:1), linoleic acid (C18:2 n-6), eicosadienoic acid (C20:2), dihomo-gamma-linolenic-acid (DGLA, C20:3), eurucic acid (C22:1), and docosadienoic acid (C22:2). Preterm infants significantly lower levels (P<0.05) of DHA and n-3 docosapentaenoic acid (C22:5 n-3), and lower mean concentrations of eicosapentaenoic acid (EPA, C20:5 n-3) than term infants. The n-6:n-3 fatty acid ratio was found to be higher in preterm infants (6.9) than in term infants (4.6). Most (59%) mothers enrolled in the study were found to consume omega-3 fatty acid rich diets but these diets did not significantly alter infant omega-3 levels or n-6:n-3 ratios.

Conclusions: In coastal San Diego, preterm infants have significantly higher concentrations of total fatty acids and higher n-6:n-3 ratios with significantly lower DHA concentrations compared to full-term infants. Routine maternal dietary enrichment for omega-3 including supplementation does not significantly alter infant fatty acid status. The impact of altered fatty acid profiles in preterm infants needs further evaluation as it relates to maternal diet and risk factors for prematurity and inflammatory complications of prematurity.

Fatty Acid	Preterm (pg/mL)	Term (pg/mL)	P Value
15:0	3.969 x 10 ³ ± 1.202 x 10 ³	2.795 x 10 ³ ± 8.560 x 10 ²	0.008**
16:1	1.594 x 10 ⁴ ± 4.547 x 10 ³	1.761 x 10 ⁴ ± 5.119 x 10 ³	0.378
17:0	4.837 x 10 ³ ± 1.738 x 10 ³	4.557 x 10 ³ ± 1.315 x 10 ³	0.042*
17:1	1.570 x 10 ³ ± 3.360 x 10 ²	1.409 x 10 ³ ± 2.730 x 10 ²	0.184
18:0	2.568 x 10 ⁵ ± 3.616 x 10 ⁴	2.406 x 10 ⁵ ± 4.380 x 10 ⁴	0.301
18:1	2.670 x 10 ⁵ ± 1.732 x 10 ⁴	2.328 x 10 ⁵ ± 2.581 x 10 ⁴	0.0004***
18:2	3.782 x 10 ⁵ ± 8.324 x 10 ⁴	2.930 x 10 ⁵ ± 6.100 x 10 ⁴	0.005**
18:3 n-3	3.226 x 10 ³ ± 1.523 x 10 ³	3.238 x 10 ³ ± 1.519 x 10 ³	0.984
18:3 n-6	7.996 x 10 ³ ± 3.779 x 10 ³	7.915 x 10 ³ ± 2.952 x 10 ³	0.951
20:1	7.030 x 10 ² ± 3.280 x 10 ²	5.970 x 10 ² ± 1.390 x 10 ²	0.288
20:2	4.641 x 10 ³ ± 2.363 x 10 ³	2.874 x 10 ³ ± 2.016 x 10 ³	0.048*
20:3 n-3	1.080 x 10 ⁴ ± 8.873 x 10 ³	6.362 x 10 ³ ± 4.624 x 10 ³	0.120
20:3 n-6	7.901 x 10 ⁴ ± 3.116 x 10 ⁴	5.543 x 10 ⁴ ± 2.740 x 10 ⁴	0.048*
20:3 n-9	3.490 x 10 ² ± 1.410 x 10 ²	2.760 x 10 ² ± 2.160 x 10 ²	0.309
20:4	2.650 x 10 ⁵ ± 1.330 x 10 ⁵	2.235 x 10 ⁵ ± 1.102 x 10 ⁵	0.114
20:5 n-3	9.245 x 10 ³ ± 4.792 x 10 ³	9.360 x 10 ³ ± 3.764 x 10 ³	0.113
22:0	1.291 x 10 ³ ± 3.500 x 10 ²	1.205 x 10 ³ ± 2.390 x 10 ²	0.466
22:1	1.270 x 10 ² ± 2.900 x 10 ¹	9.600 x 10 ¹ ± 2.500 x 10 ¹	0.008**
22:2	1.270 x 10 ² ± 3.600 x 10 ¹	9.300 x 10 ¹ ± 1.800 x 10 ¹	0.005**
22:4	1.043 x 10 ⁴ ± 2.603 x 10 ³	1.072 x 10 ⁴ ± 3.423 x 10 ³	0.805
22:5 n-3	1.347 x 10 ⁴ ± 8.450 x 10 ³	1.706 x 10 ⁴ ± 1.002 x 10 ⁴	0.006**
22:5 n-6	4.881 x 10 ³ ± 1.754 x 10 ³	6.377 x 10 ³ ± 3.231 x 10 ³	0.143
22:6 n-3	6.104 x 10 ⁴ ± 4.482 x 10 ⁴	8.803 x 10 ⁴ ± 5.666 x 10 ⁴	0.010*
23:0	6.200 x 10 ¹ ± 2.100 x 10 ¹	7.500 x 10 ¹ ± 2.800 x 10 ¹	0.370
24:0	6.930 x 10 ² ± 1.860 x 10 ²	6.050 x 10 ² ± 1.460 x 10 ²	0.184
24:1	1.420 x 10 ² ± 5.400 x 10 ¹	1.230 x 10 ² ± 3.900 x 10 ¹	0.313
Total FA	2.078 x 10 ⁶ ± 2.656 x 10 ⁵	1.813 x 10 ⁶ ± 2.954 x 10 ⁵	0.021*
Omega-3 FA	1.232 x 10 ⁵ ± 3.781 x 10 ⁴	1.415 x 10 ⁵ ± 4.609 x 10 ⁴	0.268
Omega-6 FA	8.552 x 10 ⁵ ± 1.840 x 10 ⁵	6.554 x 10 ⁵ ± 1.679 x 10 ⁵	0.007**

Fatty Acid Concentrations in Preterm and Term Infants (*p<0.001)

430 MULTICENTER RANDOMISED-CONTROLLED TRIAL OF THE EVALUATION OF THE TOLERANCE AND SAFETY OF EARLY ENTERAL NUTRITION IN CHILDREN AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT.

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Aim: To assess the tolerance and the safety of early (3 hours) versus delayed (8 hours) initiation of feeding after the percutaneous endoscopic gastrostomy (PEG) procedure in children. The goal is to establish an optimum post PEG feeding standard in paediatric patients.

Material/Methods: Children with clinical indications for PEG placement recruited from six medical centers in Poland were included to the study. Patients were centrally randomized to receive the first feeding bolus via a feeding tube 3 hours (group 1) or 8 hours (group 2) after the PEG placement. Preparation for the procedure, postoperative care and resumption of feeding were performed according to the study designed protocol in all patients. The primary endpoint was the number of patients who achieved full feed (total fluid and caloric requirements) within 48 hours of the first feeding bolus.

Results: A total of 97 patients were randomized; 49 patients were assigned to the group 1 and 48 to the group 2. There was no differences in the tolerance of feeding (81,6% vs 91,6%), the number of complications (25,5% vs 37,5,%) and the duration of hospitalization after PEG placement between the groups ($p>0,05$). Most complications were mild. Two patients (all in group 2) due to the PEG dislocation (6 days post PEG placement in one case and 14 days in the other) were qualified for the laparotomy. One death not related to the investigational procedure has been reported during the study (7 days post PEG placement, group 2).

Conclusions: The introduction of early feeding (3 h) after PEG placement in children appears to be well tolerated by patients. Early initiation of post PEG feeding did not have any impact on number of complications and the duration of hospitalization.

431 **INTERVENTION FOR FEEDING DIFFICULTIES IN CHILDREN WITH A COMPLEX MEDICAL HISTORY: A RANDOMIZED CLINICAL TRIAL.**

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Objective: This study aimed to compare outcomes of different multidisciplinary feeding therapy approaches in children with feeding difficulties.

Methods: Children 2-6 years with feeding difficulties and a medically complex history (MC) were recruited. Children with feeding difficulties and a non-medically complex history (NMC) were included as a comparison group. Participants attended a clinical assessment, and eligible participants were randomized to receive targeted feeding intervention incorporating either operant conditioning or systematic desensitization. Parents could elect to receive intervention in an intensive (10 sessions in a week) or weekly (10 sessions over 10 weeks) format. Both groups received immersive parent training. A review was completed three months post-intervention.

Results: In total, 98 participants were eligible to participate (MC n=43; NMC n=55). Data from 20 children from the MC group (47%) and 41 children from the NMC group (75%) were included in the final analysis. Clinically significant improvements were observed following both arms of therapy, consistent with previous research. Parents of children in the MC arm were significantly more likely to elect for intensive intervention than weekly (MC=12/20, 60%; 12/41, 29%; $p=0.02$).

Conclusions: Both therapy protocols were considered clinically effective. The difference in attrition rates between the etiological groups suggests primary differences in how service delivery should be managed. Progress for the medically complex child may be slower while medical issues are stabilized, or while the focus for parents shifts to other developmental areas. In planning services for a medically complex group, therefore, it is essential that consideration be given to medical and family needs.

432 **VITAMIN A SUPPLEMENTATION ASSOCIATED WITH IMPROVED RBC INDICES AND FETAL HEMOGLOBIN IN SUBJECTS WITH HGB SS DISEASE.**

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Background: Previous studies have shown that suboptimal Vitamin A status is prevalent in children with type SS sickle cell disease and was associated with hospitalizations, poor growth, and poor hematological status. The etiology of suboptimal Vitamin A status in SCD is unknown, but may be due to an increased requirement related to the chronic inflammatory state, low dietary intake, and/or excess loss in stool or urine. Current clinical treatment includes little nutritional care other than folic acid. Vitamin A supplementation, if effective, may prove to be a low-cost, feasible adjunct treatment of complications in this population.

Methods: As part of a larger study to investigate the optimal dose for daily oral Vitamin A in subjects with type SS sickle cell disease, hematological data were collected on 22 subjects between the ages of 9 and 20 years of age at baseline and after supplementation with either 3000IU or 6000IU of Vitamin A daily for eight weeks.

Results: One subject was lost to follow up. Of the remaining 21, 16 were on hydroxyurea at the initiation of the study. No subjects underwent any medication changes. Fetal hemoglobin overall increased from a mean 16.4 g/dL pre-supplementation to 18.8 g/dL post-supplementation ($p=0.02$). Fetal hemoglobin increased regardless of whether subjects were taking hydroxyurea; however, the effect was only significant in the hydroxyurea group. Mean erythrocyte indices showed a statistically significant improvement; mean corpuscular volume increased from 87.0 fl to 89.8 fl ($p=0.01$), while mean corpuscular hemoglobin increased from 30.7 pg to 32.0 pg ($p=0.006$). Concurrently, serum aspartate aminotransferase decreased from 53 U/L to 45 U/L ($p=0.01$). Notably, these effects were only seen in subjects taking hydroxyurea. Alkaline phosphatase decreased from 151 to 138 ($p=0.03$). Mean hemoglobin and hematocrit did not change. None of the changes were associated with a particular dose of Vitamin A.

Conclusions: Overall, these data suggest a positive, clinically meaningful response to Vitamin A supplementation, particularly in subjects established on hydroxyurea therapy. Indices of erythrocyte health are overall increased, along with a concurrent decrease in two secondary markers of hemolysis, aspartate aminotransferase and alkaline phosphatase. Furthermore, though there was no change in hemoglobin, there was a significant increase in fetal hemoglobin. Fetal hemoglobin inhibits the aggregation of hemoglobin S in erythrocytes, reducing episodes of vaso-occlusive crises. Thus, Vitamin A may be an effective, low-cost adjunct to current therapy for SCD by increasing fetal hemoglobin and improving overall erythrocyte quality.

433 CHILDHOOD OBESITY PREVENTION IN WIC: OUTCOMES OF THE MA-CORD STUDY. Jennifer Woo Baidal¹, Candace Nelson², Meghan Perkins⁴, Rachel Colchamiro², Peggy Leung-Strle², Jo-Ann Kwass², Steve Gortmaker³, Kirsten Davison³, Elsie Taveras⁴. ¹Pediatric GI/Hepatology/Nutrition, Columbia University Medical Center, New York, NY; ²Massachusetts Department of Public Health, Boston, MA; ³Harvard TH Chan School of Public Health, Boston, MA; ⁴Pediatrics, MassGeneral Hospital for Children, Boston, MA

Background: Childhood obesity prevalence remains historically high. Racial/ethnic minority and low-income children are disproportionately burdened by obesity.

Objective: To examine the extent to which an intervention delivered through the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) in two Massachusetts (MA) communities resulted in improvement in obesity-related behaviors and reduced body mass index (BMI) z-scores among 2-4 year old children.

Methods: We conducted a two-year quasi-experimental trial in two WIC programs – one in each of two MA communities selected to participate as intervention sites for MA-CORD based on size, per capita income, and prevalence of childhood overweight and obesity. MA-CORD was a multifaceted initiative to prevent obesity among low-income children through interventions in community health centers; WIC; early care and education; schools/after-school; and the community. One matched community provided usual care and served as the comparison. We assessed pre- and post-intervention behaviors using repeat, cross-sectional sampling of WIC participants and changes in BMI z-scores pre- and post-intervention in a longitudinal cohort of children. We used logistic regression models to examine changes in obesity-related behaviors and linear mixed models to examine BMI z-score change in each intervention site versus usual care over two years, adjusting for child age, sex, and race/ethnicity.

Results: For assessment of serial, cross-sectional obesity-related behaviors, 633 children were included in the pre-intervention and 732 in the post-intervention sample. WIC-enrolled children had improved prevalence of sugar-sweetened beverage elimination in both Intervention site #1 (adjusted odds ratio [AOR] 3.90 [95% CI: 2.07,7.35], p <0.001) and Intervention site #2 (3.09 [1.71, 5.56]), p<0.001) compared to usual care. Participants also had greater likelihood of improvement in sufficient sleep (i.e, at least 11 hours nightly on average) in Intervention site #1 (3.03 [1.76-5.23], p<0.001) and Intervention site #2 (AOR 2.29 [95% CI: 1.35-3.89], p<0.01) compared to those in usual care. Improvements in juice, physical activity, and TV behavioral targets were also found. For analysis of BMI z-score changes, 1,461 children were included in the longitudinal cohort. Compared to the usual care WIC program (n=626), we did not observe differences in BMI z-score among children in Intervention site #1 (n= 198) or #2 (n=637). In sensitivity analyses excluding Asian children, we observed a small decline in BMI z-score (-0.08 units/year [95% CI: -0.14 to -0.02], p=0.01) in Intervention site #2 v. usual care.

Conclusions: The WIC intervention in MA-CORD was associated with reduced prevalence of obesity risk factors in both intervention communities. A small improvement in BMI z-scores in one of two intervention communities occurred in children of non-Asian ancestry.

437 PREVALENCE AND RISK FACTORS OF VITAMIN B12 DEFICIENCY AMONG CHILDREN WITH INTESTINAL FAILURE: A CASE CONTROL STUDY. Lissette Jimenez^{1,3}, Brittany Depaula^{1,3}, Alexandra Carey^{1,3}, Sharon Collier^{1,3}, Megan McGivney³, Danielle Stamm³, Biren Modi^{2,3}, Paul Mitchell⁴, Christopher Duggan^{1,3}. ¹Division of Gastroenterology, Hepatology and Nutrition, Boston Childrens Hospital, Boston, MA; ²Department of Surgery, Boston Childrens Hospital, Boston, MA; ³Center for Advanced Intestinal Rehabilitation (CAIR), Boston Childrens Hospital, Boston, MA; ⁴Institutional Centers for Clinical and Translational Research, Boston Childrens Hospital, Boston, MA

Background: Vitamin B12 deficiency can cause bone marrow failure, neurological symptoms and psychological abnormalities. Children with intestinal failure (IF) are at risk for vitamin B12 deficiency due to surgical resection, malabsorption, bacterial overgrowth, diseases of the terminal ileum, inadequate intake, and/or concomitant use of acid blocking medications. The epidemiology of vitamin B12 deficiency in the pediatric IF population has not been well defined.

Methods: After IRB approval, we conducted a single center case-control study among IF patients followed in our multidisciplinary intestinal rehabilitation program (CAIR) between December 2004 and July 2016. Cases include patients with vitamin B12 deficiency (defined as serum B12 concentration < 190 pg/mL), and controls had normal B12 serum levels (≥ 190 pg/mL). Cases were matched with controls by primary IF diagnosis, sex, and age at B12 deficiency diagnosis. Both cases and controls were no longer receiving parenteral nutrition (PN), to avoid masking of B12 deficiency by the receipt of intravenous vitamins. We retrospectively reviewed medical records to extract primary diagnosis, operative details, complementary metabolites for B12 status within 1 month of B12 measurement (total homocysteine (tHcy) and serum methylmalonic acid (MMA)), serum citrulline levels, vitamin supplementation, and medication use. Data are expressed as mean \pm SD or number (%), and compared using a mixed model to account for pair-matching.

Results: Among 365 patients with intestinal failure, 31(8%) were identified as having vitamin B12 deficiency. The elapsed time from discontinuation of PN until B12 deficiency was 1.9 \pm 2.1 years. Cases were more likely than controls to have undergone ileal resection (30/30 (100%) vs 23/30 (77%); $P=0.01$), had shorter residual small bowel length 60.0 \pm 37.7 cm vs. 82.0 \pm 31.8 cm ($P=0.01$) and lower serum citrulline levels (25.3 \pm 8.9 vs. 37.6 \pm 16.6; $P=0.02$). Resection of the ileocecal valve was observed in 24/30 (80%) of cases vs. 7/24 (29%) controls ($P=0.001$). Residual ileal length was < 20 cm in 17 of 19 cases (89%) versus 3 of 7 controls (43%; $P=0.12$).

Conclusion: Vitamin B12 deficiency is a serious but relatively uncommon complication of intestinal failure in children. Although resection of the ileum and ileocecal valve was more common in cases, we were unable to identify an ileal length that most accurately identified those at risk of deficiency. Close monitoring of biochemical vitamin B12 parameters, starting within two years after PN discontinuation in at risk patients, is warranted to prevent potentially reversible B12 deficiency sequelae.

Table 1. Characteristics of intestinal failure patients with vitamin B12 deficiency and matched controls			
	Cases (<190mg/dL) n=31	Controls (>190mg/dL) n=31	P
Age at diagnosis (Median (IQR))	6.68yrs	6.47yrs	
Male sex	13 (42%)	13 (42%)	1.00
Underlying Diagnosis			
Necrotizing enterocolitis	13 (42%)	12 (39%)	0.31
Gastroschisis	6 (19%)	9 (29%)	0.25
Volvulus	8 (26%)	6 (19%)	0.15
Jejunal atresia	3 (10%)	4 (13%)	0.56
Ileal atresia	2 (6%)	3 (10%)	0.31
Hirschsprung disease	2 (6%)	0 (0%)	0.16
Cloacal exstrophy	2 (05%)	2 (05%)	
Residual Bowel length, mean \pm SD	60.0 \pm 37.7	82.0 \pm 31.8	0.01
Ileocecal resection	24 (80%)	7 (29%)	0.001
Past use of PN			
Elapsed time since PN (mean years \pm SD)	1.9 \pm 2.1	4.2 \pm 3.3	0.01
Medications			
PPI use	7 (23%)	10 (32%)	0.40
H2 blocker use	4 (13%)	4 (13%)	1.00
Laboratory Evaluation, mean \pm SD			
MCV (fl) (normal values 76.8- 83.3)	84.1 \pm 4.9	81.0 \pm 5.1	0.03
RDW	13.3 \pm 1.3	13.6 \pm 1.3	0.27
MMA (n=13 cases; n=1 control) (normal < 9 μ mol/L)	3.0 \pm 2.9	1.0	--
total Hcy (n=13 cases; n=1 control) (normal <10 μ mol/L)	10.6 \pm 5.0	11.6	--
Citrulline (n=16 cases; n=11 controls)	25.3 \pm 8.9	37.6 \pm 16.6	0.02

P value from a mixed model to account for the correlation between matched pairs.

*439 FIBROBLAST GROWTH FACTOR 19 SECRETION IN HEALTHY TERM AND PRETERM

INFANTS. Naureen Memon^{1,2}, Chris Lee², Aimee Herdt², Barry Weinberger³, Thomas Hegyi⁴, Mary Carayannopoulos⁴, Lauren Aleksunes⁵, Grace Guo⁵. ¹Pediatrics, Goryeb Children's Hospital, Morristown, NJ; ²MidAtlantic Neonatology Associates, Morristown, NJ; ³Pediatrics, Cohen Children's Medical Center of NY, Hyde Park, NY; ⁴Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; ⁵Rutgers University, Piscataway, NJ

Background: Fibroblast growth factor 19 (FGF19) is a hormone that is largely secreted by the terminal ileum, where its primary function is to control the hepatic biosynthesis of bile acids and to regulate glucose and lipid metabolism. Studies in animals and adult humans have shown that circulating FGF19 concentrations are low in the fasting state and increase in response to enteral feedings. However, nutritional regulation of FGF19 secretion has not been evaluated in preterm and term infants.

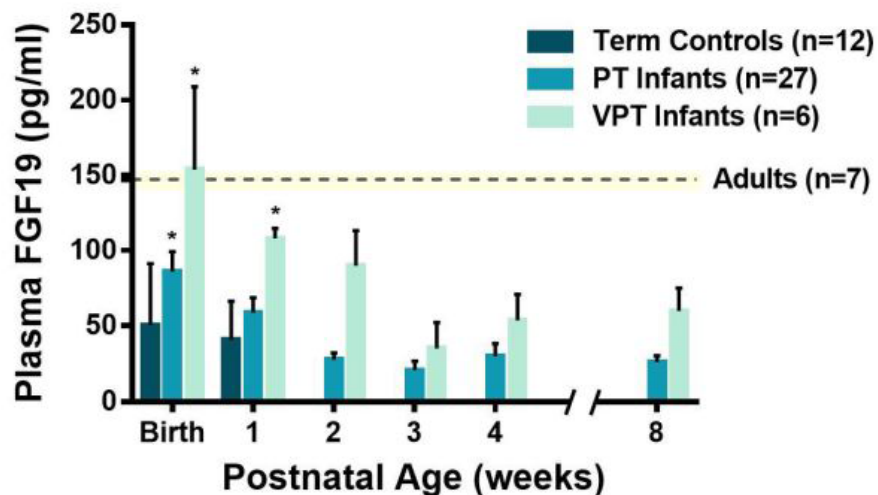
Objective: The goal of our study was to compare serum FGF19 concentrations in preterm and term infants at birth and again after full enteral feeds have been established. We hypothesized that serum FGF19 concentrations would be low at birth and increase after enteral feedings have been achieved.

Methods: Plasma FGF19 concentrations were quantified by ELISA in prospectively enrolled term (n = 12), preterm (n = 27), and very preterm (n = 6) infants. FGF19 concentrations were measured at birth and weekly thereafter until full enteral feeds had been achieved. Plasma FGF19 levels were also measured in a cohort of healthy fasting adults (n=7). Data were analyzed by Kruskal-Wallis nonparametric analysis and Dunn's multiple comparisons test. Statistical significance was set at p < 0.05.

Results: Adult reference FGF19 concentrations (mean ± SE) were 147.4 ± 13.0 pg/mL. FGF19 concentrations in term infants were low at birth (50.6 ± 11.7 pg/mL) and remained low after full enteral feedings had been established at one week of life (40.47 ± 9.1 pg/mL). Preterm and very preterm infants had statistically higher FGF19 concentrations at birth compared to term infants (85.85 ± 13.3 pg/mL, p=0.04 and 153.8 ± 55.1 pg/mL, p=0.02, respectively). As enteral feedings increased in preterm and very preterm infants, FGF19 concentrations steadily decreased to low levels that persisted out to 8 weeks postnatal age (26.2 ± 4.3 pg/mL and 59.9 ± 15.2 pg/mL, respectively).

Conclusions: In contrast to studies in animals and adults, FGF19 concentrations remain low in infants, even after establishment of full feeds; suggesting that the neonatal gut develops beyond the first few weeks of life to reach a mature level of function. Given that FGF19 prevents and protects against cholestasis, our results indicate that newborns may have increased susceptibility to liver disease. Unexpectedly, we observed that preterm infants have significantly higher FGF19 levels at birth and speculate that FGF19 may play an important role in fetal development.

FGF19 Concentrations in Infants



PANCREAS/CELIAC/MALABSORPTION

444 PANCREATIC EPITHELIAL CELL, BUT NOT IMMUNE CELL CALCINEURIN MEDIATES ACUTE PANCREATITIS. Li Wen, Tanveer Javed, Rebecca Brown, Craig Byersdorfer, Sohail Husain. Pediatrics, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA

Calcineurin (Cn) is a central Ca^{2+} responsive signaling molecule in inflammation. Among Cn sources, immune cell Cn is thought to serve as a primary inflammatory mediator. However, emerging data suggest that epithelial sources of Cn that are intrinsic to an inflamed organ contribute to organ-specific diseases. Here we show that Cn within the epithelial cells of the exocrine pancreas mediates acute inflammation in pancreatitis. We used a mouse model of post-ERCP pancreatitis (PEP) as a clinically representative model of acute pancreatitis. First, we selectively deleted pancreatic Cn sources using a novel intra-ductal delivery of adeno-associated virus (AAV) containing promoter-driven Cre recombinase into a Cn (specifically a CnB1) floxed mouse line. We found that whole pancreatic ablation of Cn (using AAV6-CMV-iCre) resulted in a 73% reduction in PEP severity, and interestingly acinar-specific deletion of Cn (using AAV6-Elastase-iCre) decreased the severity of PEP even more, by 85%. However, ductal-specific Cn deletion (using AAV6-Sox9-iCre) did not affect the severity of PEP. Second, we deleted Cn in immune cells through adoptive transfer of Cn-deficient bone marrow into Cn-sufficient mice. We found that deletion of Cn solely in the hematopoietic system did not affect PEP outcomes. The results highlight a pivotal role for pancreatic epithelial Cn, rather than for Cn in immune cell, during acute pancreatitis. The findings provide the impetus to devise translationally relevant therapies for acute pancreatitis that specifically target pancreatic Cn.

Figure 1. Confirmation of whole pancreas deletion of CnB1 deletion by infusing AAV6-CMV-iCre into the intra-pancreatic duct of a CnB1^{f/f} mouse line. From pancreas tissue, (A) PCR and (B) western blotting, along with densitometry.

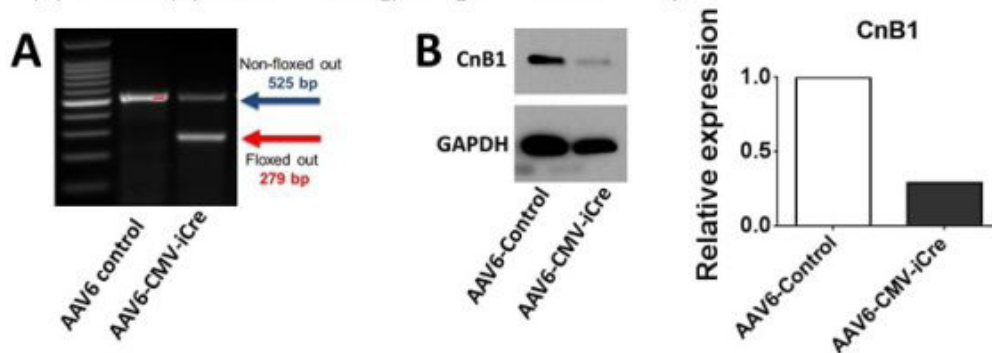
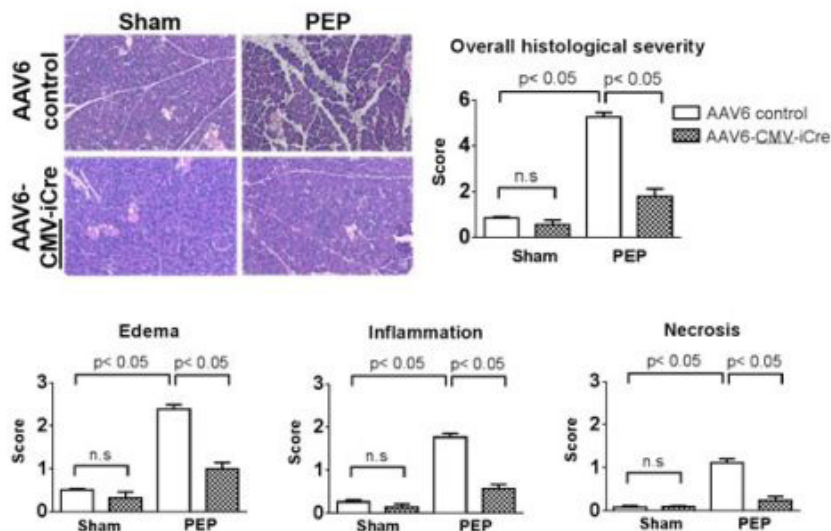


Figure 2. Whole pancreas deletion of CnB1, through intra-pancreatic ductal delivery of AAV6-CMV-iCre to a CnB1^{f/f} mouse line, protects against post-ERCP pancreatitis (PEP).



445 USE OF LIPASE AND ALANINE TRANSAMINASE TO PREDICT ACUTE GALLSTONE PANCREATITIS IN THE PEDIATRIC POPULATION. Maisam Abu-El-Haija¹, Tom Lin¹, soofia khan¹, Lin Fei¹, Tyler Thompson¹, Jaimie Nathan². ¹Pediatrics, Cincinnati Children's Medical Center, Cincinnati, OH; ²surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Objectives & Study: Gallstone Pancreatitis (GP) in children occurs at a lower incidence when compared with adult patients. Early markers for diagnosis of GP in paediatrics have not been well studied. The ability to adequately differentiate GP in children from other causes of acute pancreatitis (AP) poses significant implications including early diagnosis leading to prompt intervention when indicated. We sought to assess the laboratory findings and clinical variables for early GP diagnosis from a prospectively enrolled registry of pediatric patients presenting with their first occurrence of AP.

Methods: Children <21-years-old presenting with their first episode of confirmed AP were prospectively enrolled in an internal registry at a large, tertiary care children's hospital. A cross sectional analysis from this registry between March 2013 to October 2016 was performed. AP cases with an etiology other than a gallstone etiology were classified as non-GP (viral, systemic illness, drug induced, metabolic, trauma, or idiopathic). Fisher's exact test and Wilcoxon rank sum test were used to compare demographic and clinical variables between the two groups GP and non-GP. In order to optimize prediction of GP, a multivariable logistic regression model was derived based off significant p-values, the Receiver Operating Characteristics (ROC) curve using stepwise selection.

Results: Within the study period, there were 114 patients enrolled into the AP registry; 21 GP, 93 non-GP. A univariate comparison between GP and non-GP patients found no significant differences in gender, age distribution, initial amylase elevations X upper limit of normal (ULN), creatinine, or total bilirubin. Comparing GP to non-GP, the median (IQR 25%, 75%) was found to be statistically higher for GP patients in: lipase XULN on admission: 31 (8.37, 78.4) vs 7 (3.8, 17), weight percentile for age: 86 (9, 99.9) vs 46.8 (0, 99.7), alanine aminotransferase (ALT): 302 (168, 441) vs 26 (20, 59), aspartate aminotransferase (AST): 170 (118, 260) vs 33 (20, 58), gamma-glutamyl transferase (GGT): 411 (197, 650) vs 29 (13, 111). Two variables remained significant on multivariate analysis: logALT and logLipase. A model built using these two variables for prediction of GP identified an ROC of 0.85. At a predictive probability of 0.35, the model had a 80% sensitivity, 93% specificity, 76% positive predictive value, 95% negative predictive value.

Conclusion: From our pediatric prospective AP registry, we identified significantly higher elevations in lipase ULN, weight percentile, ALT, AST and GGT that appear to differentiate AP patients presenting with GP. We built a model for predicting GP in the pediatric population that could help clinical management of AP patients. Future studies are needed to validate the use of laboratory findings and clinical variables in the work up of gallstone etiologies in the AP patients.

446 A NOVEL ENTEROID MODEL OF CONGENITAL TUFTING ENTEROPATHY SHOWS PHENOTYPIC DEFECTS AND ALTERATIONS IN ULTRASTRUCTURE. Kevin Okamoto¹, Matt McGeough¹, Nassim Durali¹, Philip Kozan¹, Ron Marchelletta¹, Soumita Das¹, Mamata Sivagnanam^{1,2}. ¹UCSD, La Jolla, CA; ²Rady Children's Hosp, San Diego, CA

Congenital Tufting Enteropathy (CTE) is a severe diarrheal disease of infancy[nd1] resulting in intestinal failure. CTE is characterized by changes in the small intestinal epithelium. Typical findings include total or partial villous atrophy and crypt hyperplasia, but the most characteristic pathologic abnormalities are focal epithelial tufts in the small intestine. We previously identified mutations in Epithelial Cell Adhesion Molecule as the cause of CTE.

We developed an inducible *in vivo* mouse model of CTE based on EpCAM mutations found in patients (Δ4). In order to establish enteroids, intestinal crypts were isolated from inducible (ind.) *Epcam*^{Δ4/Δ4} mice pre-TAM treatment. Isolation was performed using cold chelation buffer (5mM EDTA/ HEPES buffer) and crypts were cultured in matrigel with DMEM/F12 supplemented with N-acetylcysteine, vitamin B12, and Glutamax. The resulting spheroids were incubated with required growth factors and showed progression to enteroids. Enteroids were then incubated in specialized culture media supplemented with the required growth factors: Noggin, EGF and R-spondin. Like mice, enteroids are induced by tamoxifen exposure *ex vivo*. Enteroids were evaluated using microscopy, immunohistochemistry and electron microscopy.

Immunohistochemistry confirmed decreased and mislocalized EpCAM expression in ind. *Epcam*^{Δ4/Δ4}/TAM enteroids compared to controls. Post induction, striking alterations in the structure of ind. *Epcam*^{Δ4/Δ4}/TAM enteroids vs. littermate control/TAM enteroids were observed, such as slow growth of enteroids, lack of a clear luminal compartment, and central heaping of cells and luminal contraction. Significant decrease in total diameter and luminal compartment size in ind. *Epcam*^{Δ4/Δ4}/TAM enteroids vs. littermate control/TAM enteroids was measured. Assessment of ultrastructure was performed using electron microscopy (EM). EM data demonstrated the Endoplasmic Reticulum (ER) compartment to be highly dilated in mutant EpCAM enteroids when compared to control enteroids. Furthermore, the brushborder is disorganized in mutant enteroids compared to control enteroids.

Here we establish the first enteroid model of Congenital Tufting Enteropathy demonstrating phenotypic changes. This model will allow for enhanced understanding of the pathophysiology of this disease and testing of therapeutic options.

447 FOLLOW UP CARE IN PEDIATRIC PATIENTS WITH CELIAC DISEASE: QUALITY IMPROVEMENT PROJECT. Erin Crawford, Maricruz Crespo, Thomas Sferra. *Pediatric Gastroenterology, Hepatology, and Nutrition, University Hospital-Rainbow Babies & Children's Hospital, Cleveland, OH*

Background: Celiac Disease (CD) is one of the most common causes of malabsorption. It is estimated that 1% of the population worldwide suffers from this disease. Interestingly, close to 85 percent of the population with CD are not diagnosed. CD is known to be a multisystem disease and given its variable presentation, it is imperative that patients with CD have close follow up in a multidisciplinary clinic, including physicians, nutritionists, and social workers. Unfortunately, it is known that a majority of the patients don't receive consistent follow-up medical care. Moreover, current guidelines for the care of patients with CD have different recommendations for follow-up care.

Objectives: To improve the adherence to follow-up appointments in pediatric patients with a diagnosis of celiac disease.

Methods: This work is part of a quality improvement (QI) project at our institution. We conducted a retrospective chart review of patients at UH Rainbow Babies & Children's Hospital between January 1, 2014 and September 20, 2016. Only those patients with newly diagnosed CD by biopsies were included. Demographics, laboratory test results, and dates of medical evaluation and care visit dates were collected.

Results: 220 patients with CD were identified. 62 were included in the study. The median time from initial consultation visit with a pediatric gastroenterologist to endoscopy was 25 days (interquartile range 12-39). The median time between endoscopy and first follow up after diagnosis was 18 days (interquartile range 13-28). 45 percent of the patients were seen by the dietitian at the first visit after diagnosis. After the first visit following diagnosis, 15% of the patients were lost to follow up. In 2017, only 39% of the patients had follow up appointments. 40% of the patients diagnosed during this time period had normalization of tTG.

Conclusions: As previously reported, patients with celiac disease tend not to be compliant with follow up appointments, even when tTG levels have not normalized. More studies are needed to provide a more specific recommendations and to better educate patients with celiac disease on the importance of follow up visits. The next steps in our QI project will be to (i) establish internal recommendations for follow-up care, these will be consistent throughout our practice, (ii) educate our providers, and (iii) develop and implement a protocol that specifically will address times of follow up visits with the dietitian and physician.

449 PAIN RESOLUTION WITH GOOD GLUCOSE CONTROL IN PEDIATRIC PATIENTS WITH CHRONIC PANCREATITIS AFTER TOTAL PANCREATECTOMY WITH ISLET CELL AUTOTRANSPLANTATION. Mark Kijek¹, Natalie Fillman¹, Lindsay Basto¹, Karolina Golab¹, Agata Krenc¹, Kamil Cieply¹, Evelyn Konsur¹, Julia Solomina¹, Ling-jia Wang¹, Martin Tibudan¹, Ruba Azzam², Andres Gelrud³, Jeffrey Matthews¹, Piotr Witkowski¹. ¹Department of Surgery, University of Chicago, Chicago, IL; ²Department of Pediatrics, University Of Chicago, Chicago, IL; ³Department of Medicine, University Of Chicago, Chicago, IL

Introduction: Chronic Pancreatitis (CP) is a condition leading to irreversible, functional, and morphological changes secondary to prolonged pancreatic inflammation and fibrosis often hereditary; driven by metabolic defects related to gene mutations PRSS1 and CFTR. Common consequences for children who are afflicted with this disease burden include the following: severe recurrent pain, bouts of acute pancreatitis, narcotic dependence leading to compromised quality of life, and missed school days. Total pancreatectomy (TP) remains the last option for these patients since this chronic debilitating pain is refractory to medical, endoscopic, and other surgical therapies. The main disadvantage is an extensive intra-abdominal operation leading inadvertently to postsurgical diabetes. Subsequent glucose control in these patients is especially challenging due to complete lack of beta and alpha cells resulting in the "brittle" form of diabetes. Therefore, islet autotransplantation (IAT) has been developed to prevent diabetes, or at least to improve glucose control by providing endocrine cell function after total pancreatectomy. The aim of the study was to assess the outcome of total pancreatectomy and islet autotransplantation (TP-IAT) in the pediatric population at our center.

Material/Methods: We analyzed the results in pediatric patients with chronic pancreatitis, who exhausted all medical and surgical interventions to relieve constant or frequent recurring pain, and underwent TP-IAT at The University of Chicago. Over the last 8 years we have performed 6 TP-IAT procedures in pediatric patients with a median age of 16 (11-21) and BMI of 22 (18-33). The median follow-up time was 31 months (5-50). A genetic mutation (CFTR or PRSS1) was responsible for chronic pancreatitis in 5 (83%) patients. The remaining patient suffered from autoimmune pancreatitis, gastritis, ulcerative colitis, and primary sclerosis cholangitis.

Results: Patients suffered from CP for a median of 5 years (1-19). Over that time, five (83%) patients required opioid therapy despite three (50%) of which, had multiple endoscopic/surgical procedures (cholecystectomy, MRCP, EUS, and stent placement). After TP-IAT, two patients (33%) required periodic pain therapy with opioids and/or acetaminophen. Chronic pain in one patient was due to autoimmune gastritis and follow-up stopped at 20 months. Exogenous insulin therapy was implemented for all patients for at least 6 weeks after the procedure to support islet autograft recovery and engraftment. Patients were subsequently weaned off, if possible. Three patients achieved long-term insulin independence (50%) with excellent glucose control (HbA1c<6). Remaining three patients (50%), presented long-term partial islet graft function (c-peptide positive), which allowed for stable glucose control with some insulin support. Their median HbA1c was 7 (5.5-7.4) and patients did not report any severe hypoglycemic or hyperglycemic episodes. The median islet tissue pellet volume was 8 ml (2-15 ml). Transplanted beta cell mass was significantly higher in patients currently insulin free compared to those with insulin therapy, 216 kIEQ (171-220 kIEQ) vs 93 kIEQ (76- 229 kIEQ), respectively. Islet mass per kilogram of patient body weight was also substantially higher in the same group 4,193 IEQ/kg (3,483-4,614) vs 1,069 IEQ/kg (1,005-2,897 IEQ/kg), respectively. Duration of chronic pancreatitis prior to surgery was significantly lower in insulin independent patients compared to the insulin dependent group, median 4 years (2-8) vs 12 years (1-19). Moreover, patients with a lower BMI prior to TP-IAT were insulin independent compared to patients with a higher BMI which became dependent, median 18.5 (18-20.4) vs 27.3 (23.6-33.2). Lastly, all patients reported that their quality of life has improved substantially after TP-IAT.

Conclusion: Total pancreatectomy and islet autotransplantation effectively preserved beta cell function in pediatric patients with recurrent chronic pancreatitis, driven by genetic mutations, allowing for insulin independence in 50% of patients, and stable glucose control in insulin dependent patients. The success was correlated with shorter duration of chronic pancreatitis prior to the procedure, higher islet cell transplanted mass, and lower BMI. TP-IAT provided resolution of pain related to chronic pancreatitis and significant improvement in quality of life.

450 ACCURACY OF SEROLOGIC MARKERS IN THE SCREENING OF CELIAC DISEASE IN CHILDREN WITH TYPE 1 DIABETES MELLITUS: A RETROSPECTIVE ANALYSIS FROM A TERTIARY CENTER. Mary Ayers², Sophia Patel¹, Sumana Narasimhan³, Praveen Kumar Conjeevaram Selvakumar¹ *Pediatric Gastroenterology, Cleveland Clinic, Cleveland, OH;* ²*Pediatrics, Cleveland Clinic, Cleveland, OH;* ³*Pediatric Endocrinology, Cleveland Clinic, Cleveland, OH*

Background: Celiac disease (CD) is approximately 6 times more prevalent in children with type 1 diabetes mellitus (T1DM) compared to general population. Hence, the general recommendation is to screen all children with T1DM for CD with serologic tests. IgA antibody against tissue transglutaminase (TTG IgA) is widely used for screening, however there is no evidence regarding timing or optimal screening methods. Moreover, recent studies have reported spontaneous normalization of TTG IgA without gluten free diet (GFD) in children with T1DM. Although highly sensitive and specific in the general population, the accuracy of TTG Ig A and other antibody assays is not well studied in children with T1DM.

Aim: To evaluate the accuracy of TTG IgA, anti-endomysial IgA (EMA) and anti-gliadin (AGA) IgA antibodies in the diagnosis of CD in children with T1DM.

Methods: We performed a retrospective chart review of children (aged 5-18 years) with T1DM attending Pediatric Endocrinology clinic from January 2011 to December 2016. T1DM patients with normal total IgA and at least one TTG IgA screen were included for analysis. Data on EMA, AGA and duodenal biopsies (DB) were also collected. Antibody assays were considered to be positive based on established cut-offs and intestinal biopsies were interpreted based on Modified Marsh criteria. Sensitivity (SEN), specificity (SPE), positive predictive value (PPV) and negative predictive value (NPV) were calculated for these antibodies using DB as the gold standard test.

Results: A total of 644 children were included for analysis and 52.6% of them were males. 68 children had positive TTG IgA screen indicating a prevalence of about 10.5% of which DB were available for 58 patients. DB were positive for CD in 23 children indicating an approximate prevalence of 3.6% (23/644) in this cohort. TTG IgA identified children with CD with SEN, SPE, PPV and NPV of 100%, 47.1%, 53.8%, and 100% respectively. Information on EMA and AGA were available for 125 and 331 children respectively. The prevalence of EMA and AGA positivity in these children were 21.6% (27/125) and 9.7% (32/331) respectively. SEN, SPE, PPV and NPV of EMA were 72.2%, 61.5%, 56.5%, 76.2% and SEN, SPE, PPV and NPV of AGA were 43.8%, 77.8%, 53.9%, 70.0% respectively.

Conclusion: In our large cohort of children with T1DM, TTG IgA was extremely sensitive in CD screening however it lacks SPE and PPV. Interestingly, AGA and EMA had better specificities than TTG IgA. Therefore, combination of these antibody assays, rather than TTG IgA alone, improves the accuracy of CD screening in children with T1DM, thereby avoiding unnecessary endoscopies or institution of GFD.

451 PRELIMINARY FINDINGS OF A PROSPECTIVE STUDY CHARACTERIZING THE PSYCHOSOCIAL AND COGNITIVE FUNCTIONING OF YOUTH WITH CELIAC DISEASE.

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Background: Celiac disease (CD) is a chronic autoimmune enteropathy triggered by gluten in susceptible individuals. Currently the only treatment is life-long elimination of gluten from the diet, an often burdensome endeavor. Unlike other pediatric chronic illnesses, little is known about the psychosocial and cognitive functioning of youth newly diagnosed with celiac disease or how this may change with initiation of the gluten-free diet. Current research in this area is limited and contradictory, although families and clinicians often suspect that changes exist for children with CD.

Objectives: To gain greater understanding of the psychosocial and cognitive functioning of youth newly diagnosed with CD, which is essential in order to identify factors which may impact adherence and risk for health-related consequences.

Methods: A prospective, longitudinal study was conducted to describe the psychosocial and cognitive functioning of youth with celiac disease at diagnosis and then again after one year on a gluten-free diet. Participants included 84 patients aged 2-17 years who were newly diagnosed with CD based on serology and duodenal biopsies (73% female, mean age=10.2 years). Patients were still eating a regular diet or had only started the gluten-free diet for less than 6 weeks. Caregivers and those patients 8 years or older completed a battery of standardized questionnaires, including a measure of psychosocial functioning (BASC-3, Behavior Assessment System for Children, Third Edition) and cognitive functioning (BRIEF, Behavior Rating Inventory of Executive Functioning).

Results: Of the 84 patients with celiac disease, 13.1% exhibited clinically significant depressive symptoms and 7.1% exhibited anxiety symptoms. With regard to executive functioning deficits, 19.7% exhibited clinically significant difficulties with inhibitory control (e.g., acts wild or silly, gets out of control, is unable to sit still) and emotional control (e.g., becomes upset easily, is tearful, reacts more strongly in situations than other children). In addition, 28.7% exhibit clinically significant difficulties with working memory (e.g., has difficulty following multiple step instructions, forgets things easily, has a short attention span, has difficulty concentrating, needs help from an adult to stay on task).

Conclusions: Current findings indicate a relatively low rate of depressive and anxiety symptoms among newly diagnosed youth with celiac disease. However, with regard to cognitive functioning, youth with celiac disease exhibit challenges with behavioral regulation (inhibition and emotional control) and working memory. These challenges with executive functioning (memory, inhibition, and emotional control) may impact disease management, adherence to the gluten-free diet, and health related outcomes. These findings represent the first prospective data obtained utilizing a standardized, normed measure of cognitive and psychosocial functioning. It is unclear based on these data if cognitive impact of celiac disease is transient and improves with the initiation of the gluten-free diet or if there are more lasting cognitive consequences. This study is ongoing and the same battery of questionnaires will be repeated after one year on a gluten-free diet.

452 FREQUENCY AND PRESENTATION OF PEDIATRIC NON-CELIAC GLUTEN SENSITIVITY IS SIMILAR TO ADULTS.

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Background: Non-celiac gluten sensitivity (NCGS) is a heterogenous clinical entity, estimated to affect approximately 6% of the population, in which patients experience gastrointestinal or extra-intestinal symptoms in relation to ingestion of gluten. Unlike celiac disease (CD), a sensitive and specific biomarker indicating the active state of NCGS has yet to be identified. Given this, the prevalence of NCGS is unknown. NCGS is diagnosed clinically after exclusion of CD or wheat allergy as the causative agent of symptomatology. Further complicating the picture, the clinical presentation of NCGS is variable with patients reporting both gastrointestinal and extra-intestinal manifestations. While NCGS has been studied in adults, little data exists regarding the clinical presentation of NCGS in pediatric populations.

Aim: To identify the clinical characteristics and presentation of children with NCGS presenting to our quaternary care center.

Methods: We reviewed the medical records of patients seen at our center over a 3.5 year period (July 2013-January 2017) who consented to participate in our research registry. All patients provided written informed consent indicating permission for use of their medical information. Patient/parent-completed clinical intake forms were considered in conjunction with physician-verified information, extracted directly from the patient's electronic medical record, to gain an accurate understanding of each patient's symptoms and medical history.

Results: Of the 312 pediatric patients who consented to participate in our research registry during the study period, 22 children (7%) were identified as having NCGS. After CD exclusion, a physician-confirmed diagnosis of NCGS was made due to reported complaints associated with and temporally related to the ingestion of gluten, subsequent improvement in symptoms as a result of gluten exclusion from the diet, and relapse with gluten re-introduction. In NCGS children gastrointestinal (91%) and extra-intestinal (82%) symptoms were prevalent in response to the ingestion of gluten. The most common complaints associated with gluten-ingestion were abdominal pain (64%), constipation (36%), disturbances in mood (36%), disturbances in behavior (32%), rash (32%) and bloating (32%). Neurological symptoms of ataxia, headache, and/or tremors were present in 27% of NCGS children, as were feelings of fatigue/malaise (27%). Additionally, 77% of children with NCGS reported concomitant allergic/atopic disease including hay fever, food allergy, eczema or asthma.

Conclusion: Though lack of a validated biomarker makes it difficult to estimate the population-wide prevalence of NCGS, the frequency of NCGS in children approximates that of adults presenting for evaluation at a quaternary care center. While our pediatric NCGS population is small, the myriad clinical presentation also mirrors that which has been previously reported in adults. Children were most likely to present with gastrointestinal complaints, however, rash, fatigue, and disturbances in mood or behavior were also common. To ensure an accurate diagnosis, it is of the utmost importance for children to be evaluated by a gastroenterologist and closely monitored by a dietitian to maintain a well-balanced diet to thrive without gluten.

457 **EVALUATION OF LINACLOTIDE AS RESCUE THERAPY FOR INTESTINAL DISEASE IN CF.**

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Obstructive disease of the intestine in cystic fibrosis (CF) is the end result of defective traffic of mutant CFTR into the brush border membrane that leads to loss of Cl⁻ and HCO₃⁻ secretion. Intestinal disease in CF is a major cause of morbidity that manifests as meconium ileus in CF infants and constipation and distal intestinal obstruction (DIOS) in older children and adults with CF. Although CF patients with intestinal disease have derived some benefit in weight gain and histologic improvement following the combination of Lumacaftor (corrector)-Ivacaftor (potentiator), Orkambie is cost prohibitive (estimated \$259,000/year), with significant side effects. More importantly, there is no evidence that it improves intestinal fluid secretion since CF patients continue to require daily laxative therapy for obstructive symptoms. We are investigating the mechanism of action of the synthetic GC-C agonist peptide, linaclotide (Linzess) an FDA-approved drug used for adult patients with Irritable Bowel Syndrome with Constipation (IBS-C) and Chronic Idiopathic Constipation (CIC). Our data in native intestinal tissues and human colon indicate that linaclotide activates intestinal fluid secretion by stimulating CFTR traffic into the enterocyte brush border membrane (BBM). Preliminary data indicate that linaclotide also stimulates traffic of DF508CFTR into the BBM in a CF mouse model. We propose studies to evaluate linaclotide as a rescue therapy and alternative to Orkambie for treating obstructive intestinal disease in CF given its potential for increasing CFTR fluid secretion. Another major advantage of this drug is that is FDA approved and costs \$4,500/year (57X lower) when compared to Orkambie.

459 **IS SIX MONTHS OF GLUTEN-FREE DIET ENOUGH FOR REMINERALISATION OF BONE IN CHILDREN WITH CELIAC DISEASE?**

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Introduction: Celiac disease (CD) is an immune mediated disorder, characterized by villus atrophy of small intestines after gluten ingestion. Malabsorption of many nutrients as well as calcium is the end. Spontaneous fractures occur in many patient with CD. Gluten-free diet improves malabsorption and thus after diet bone mineralization improves dramatically. Dual-energy X-ray absorptiometry (DXA) of the femoral neck and lumbar spine is considered the gold standard to confirm the diagnosis of osteoporosis.

Materials and Methods: Total 57 patients are diagnosed with CD between January 2015 and December 2016. 46 of them were included in the study (two of patient had associated diseases, six were not attending strictly to diet, three patients left study). Positive serology and duodenal biopsy was done to all patients. Bone Mineral Density (BMD) using DXA (lumbar spine and femoral neck, Horizon, Hologic) was done at the diagnosis and after 6 months of gluten-free diet. Z-score (standard deviations for age, sex, weight) were analyzed. Z score below -2 was considered as osteoporosis, between -1 and -2 as osteopenia and above -1 as normal.

Results: 46 patients (18 males, 28 females), average age at diagnosis was 8.1 years (range 1.7–17.3), z score for weight and height in girls at diagnosis was -1.2 (±1.04) and -1.49 (±1.06), boys -1.27 (±0.99) and -1.57 (±1.33) respectively. Vitamin D concentration was 17.8±9.3 in girls and 16.5±6.3 in boys, and after diet 25.2±7.2 in girls and 27.9±11.2 in boys. Before diet

normal DXA was observed in 14 patients (9 girls, 5 boys), osteopenia in 17 patients (10 girls, 7 boys), and osteoporosis in 15 children (9 females, 6 males). After 6 months of gluten-free diet osteopenia was observed in 14 patients (8 girls, 6 boys) and osteoporosis is detected in 8 patients (4 girls and 4 boys). Significant improvement in osteopenia and osteoporosis with average Z-score from -1.58 ± 1.22 to -0.94 ± 1.06 was observed.

Conclusions: Strict gluten-free diet may readily improve BMD in a short period as 6-9 months.

APGNN

462 PATIENT AND PARENT/CARER SATISFACTION SCORING: COMPARISON BETWEEN A VALIDATED PEDIATRIC SCORING QUESTIONNAIRE AND NRC/PICKER® RESPONSE IN A PEDIATRIC DAYCASE ENDOSCOPY SETTING. Jennifer Walden¹, Priya Narula², Thomas Attard¹.

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Introduction: The determinants of quality in ambulatory endoscopy includes parent and patient experience; survey instruments require validation based on the model of healthcare and societal expectations. There is a paucity of available tools to reproducibly determine the quality of the experience within a pediatric ambulatory endoscopy suite in the United States. Herein we compare our experience with a modified, validated questionnaire developed in the UK with the satisfaction scoring based on a broadly disseminated global hospitalization experience questionnaire that is broadly applied in the US.

Methods: Patients treated in our endoscopy suite were administered a modified (abbreviated) version of the survey instrument described by Griffiths E et al (JPGN 5/2015:60;1, 331-332) and Wan JWY et al (ADC 2017:102(1);A76-A77), the results were collected anonymously and were compared with the corresponding responses in the same population, over the same period (8/2016 - 3/2017) of a randomly selected, anonymized, mailed out questionnaire (NRC Picker®) described elsewhere (Co JP et al. Acad Pediatr. 2011:May-Jun;11(3):S59-67). Questionnaire items reflected the measures on the Quality of Patient Experience Domain of the UK P-GRS (paediatric endoscopy global rating scale). Responses were categorized as percent preferred response rates and statistical inferences were developed using Graphpad Instat®.

Results: Respondents to the endoscopy questionnaire included more female patients (F:M 1.4:1) with a mean age (SD) of 11.49(4.6) years; 146 patients/parents responded to the 21 item; (10 dichotomous 9 Likert Scale) endoscopy questionnaire whereas 111 patients/parents responded to the 34 relevant items in the standard NRC Picker questionnaire. Table 1. summarizes the comparison between the results obtained by the two instruments, significant differences were noted in the response to patient environment (P: 0.014) and aftercare (P: 0.0009), other domain responses correlated closely between the two instruments.

Discussion: In our patients undergoing elective day-surgery gastrointestinal procedures in a tertiary center, our modified questionnaire correlates well with the responses obtained by the more cumbersome (34 item), less contextualized standard tool. Differences in aftercare may relate to the timing of the questionnaire (NRC/Picker later). There are limitations to this analysis including relatively small sample size but further development of a specific endoscopy related experience reporting tool is encouraged.

Domains	Pediatric Endoscopy Satisfaction Score			NRC/Picker® Score			P value
	Items	Sample size	% positive	Items	Sample size	% positive	
Consent and patient information	8	147	90.1	9	110	87.2	0.4656
Patient environment	2	142	94.5	1	109	85.3	0.0143
Respect and dignity	2	140	95.5	6	111	92.3	0.4622
Comfort	3	146	89.6	8	109	71.1	0.2868
Aftercare	4	133	96.3	4	111	83.9	0.0009
Overall	2	126	91.5	6	111	88.8	0.4856

Comparison in Preferred Response Rate for GRS Domains from Modified Pediatric Endoscopy Satisfaction Score and NRC/Picker Score

463 THE UTILITY OF DISACCHARIDASE TESTING. *Lindsay Wilson, Esther Kang, Terri Reagan
Pediatric Gastroenterology, Hepatology and Nutrition, Johns Hopkins Children's Center, Baltimore, MD*

Disaccharidase testing by duodenal biopsy is often done at our institution at the time of endoscopy as an additional diagnostic aid. Some providers order it based on symptoms, others for the sake of completeness. In most cases we are looking for lactase deficiency. The patient is billed about \$95.00 for the test. Lactase deficiency can also be diagnosed by breath hydrogen test (BHT), which could potentially eliminate the need for endoscopy if symptoms respond to a lactose free diet. The cost of a BHT is approximately \$250.00

As GI nurses we are responsible for sending the disaccharidase biopsy to the lab and also conveying the results to the parents. We wanted to find out how often the test was positive and to see if there was a particular set of symptoms that would predict an increased likelihood for a positive test.

Methods: A chart review of 80 consecutive patients undergoing disaccharidase testing was performed. Ages ranged from 1 year to 21 years, 46 female, 34 male. Data was collected on symptoms including abdominal pain, diarrhea, bloating, constipation, and vomiting.

Results: There were 46 positive tests. 12 patients had both pain and diarrhea, 9 patients had pain alone, and 5 patients had pain and constipation. The remainder had vomiting and symptoms grouped under an 'other' category such as failure to thrive. Of the 34 negative tests, 14 had pain as the only symptom, 2 patients had pain and diarrhea, 3 had diarrhea alone, 4 had pain with other symptoms with the rest having constipation, vomiting and 'other' symptoms.

Conclusion: Over 50 percent of patients had a positive test. Although you were somewhat more likely to have lactase deficiency if you had both pain and diarrhea, there was not a correlation with a particular set of symptoms and a positive result. If endoscopy is necessary for other reasons disaccharidase testing in a fairly inexpensive test and can benefit the patient.

464 "TROUBLESOME" TUBES: A DESCRIPTIVE ANALYSIS OF ENTERAL TUBE COMPLICATIONS AND NURSING INTERVENTIONS IN PEDIATRIC PATIENTS. *Lori Parker-Hartigan, Fiona Paul. GI,
Boston Children's Hospital, Arlington, MA*

Aims:

1. To track and describe the number of patients seen in outpatient clinics with troublesome enteral feeding tube
2. To understand the type and frequency of enteral tube complications in this population.
3. To identify interventions to treat and prevent complications from enteral tubes

Background: Our institution, a tertiary pediatric teaching hospital in an urban setting, has multiple gastroenterology (GI) specialty clinics. These clinics average 250 patient visits per month for patients with an enteral feeding tube. A review of this population suggested a trend of increasing numbers of "troublesome" enteral tubes and complications. Complications related to enteral tubes result in an increase in demand for provider and nursing time and resource utilization. Patients and families have also voiced dissatisfaction with the impact of these complications (including infection, pain, leaking, and granulation tissue) and the need for frequent medical attention.

Methods: A quality and charge capture survey (QCC) was developed to track "troublesome" enteral tubes. "Troublesome" was defined as the tube having a problem that was a concern to the provider/nurse and/or the patient/parent or guardian. This 6 question survey asks if the tube is troublesome, how it is troublesome, and what interventions were performed. The survey is triggered when a medical provider or nurse submits a billing code pertaining to an enteral feeding tube. Since April of 2015 data has been collected (n=5,393) and analyzed using descriptive analyses, run charts, and Pareto charts.

Results: Of all patients with enteral tubes being seen in the GI outpatient program, 35% had a "troublesome" tube. 40% of these complications were related to granulation tissue. Other common complications included leaking, bleeding, and pain at the tube site. When the enteral tube was troublesome, an intervention was performed 94% of the time. The most common interventions: tube stabilization, silver nitrate, stomahesive powder and education.

Discussion: Enteral feeding tube complications are common. They consume significant nursing time and can be a source of patient/parent dissatisfaction. Nurses have a unique role in development of innovative interventions to manage complications of enteral feeding tubes including granulation tissue.

465 **PROCESS IMPROVEMENT FOR PHONE CALL MANAGEMENT IN A PEDIATRIC GASTROENTEROLOGY OFFICE: THE GOOD, THE BAD AND THE UGLY.**

Kimberly Dietrich, Julia Anderson, Renee Fages, Krista Kissinger, Carrie Romano, Angela Turner.
Gastroenterology, Cincinnati Children's Hospital, Cincinnati, OH

Issue/Background: Changes in healthcare funding are driving many changes within the healthcare setting. Complaints about the return of phone calls are common in healthcare. The registered nurses (RN) at Cincinnati Children's Hospital Gastroenterology department have consistently been the funnel for all calls but this model of care can no longer be maintained because the healthcare environment is dictating that we do more with less. Therefore, work that can be delegated to medical assistants and administrative assistants needs to be considered and embraced. Making changes in call management with the intent of having non-nursing issues managed addressed by other team members is an important initiative. Awareness of the customer needs throughout the day is a more efficient process than waiting until the RN has time to take the call. Creating a team concept so that calls can be managed by the appropriate team member is crucial.

Objective: To establish guidelines for routing of phone calls to the correct team member to handle the call. To improve customer satisfaction by the correct person handling the call and therefore delays in care will be avoided when necessary. Our smart aim was defined as decrease incoming calls and voicemail rate to the RN direct line.

Improvement Model/Methods: We utilized the improvement model known as Continuous Improvement which involves planning and designing, implementing, evaluating, assessing, and reassessing. We created guidelines and a process for routing the phone call. Using the process, the team involved in the improvement initiative made recommendations for changes and their feedback was incorporated into the model.

Findings: A process was designed and guidelines were created, We were able to make changes by establishing a team structure, a patient/family call specific line, call routing guidelines and a routing schema. We were able to decrease calls to the direct RN line from an average of 68 incoming calls to 20 incoming calls per week. We were able to decrease messages left on voicemail from 67 calls per week to 12 calls per week. We were able to increase calls to patient/family call line from 0 to 130 calls per week.

Conclusion/Implications for Practice: The bad is that phone calls will likely never go away. The ugly is that healthcare human resources will not likely increase. The good is that we can plan for this by working on improvement initiatives focusing on processes that facilitate efficiency thereby improving customer service and satisfaction.

466 **COLONOSCOPY UNIVERSAL CORD LOWER BACK ANCHORING BELT.**

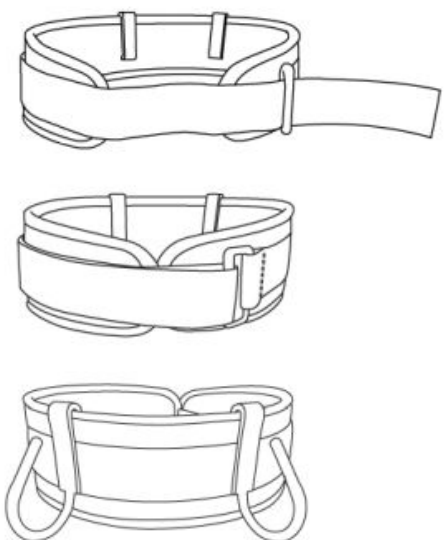
Abdul Shahein, Melissa Severyn. Pediatric Gastroenterology, Woman and Children Hospital of Buffalo, Buffalo, NY

Several endoscopists in the field of Gastroenterology have struggled with positioning the colonoscopy universal cord in a convenient position to allow comfortable access and mobility during the procedure. Physicians have utilized different techniques that can cause significant burden on their joints and muscles, for example, hanging the scope shaft over their shoulder and/or let it fall underneath their back. To our knowledge, there have been no previous safe solutions to this problem. The disclosed invention will help endoscopists performing colonoscopies by safely attaching the universal cord closer to their lower back, which can also help with focusing their muscular maneuvers on the procedure.

Materials: Our proposed technology is composed of a lower back support belt with two disposable hook attachments on the backside of the belt that allows the colonoscopy universal cord to rest on and close to the trunk of the endoscopists.

Advantages:

1. Improves ergonomics of the colonoscopy procedure,
2. Help avoid excess strain on the endoscopist's musculoskeletal system,
3. Allow endoscopists to freely maneuver the endoscopy shaft and cut down procedure time,
4. the belt is very simple to clean and inexpensive to produce,
5. **Disadvantages:** It may limit the distance that the endoscopists can be away from the Colonoscopy.



The belt from front, side and back with anchoring hooks

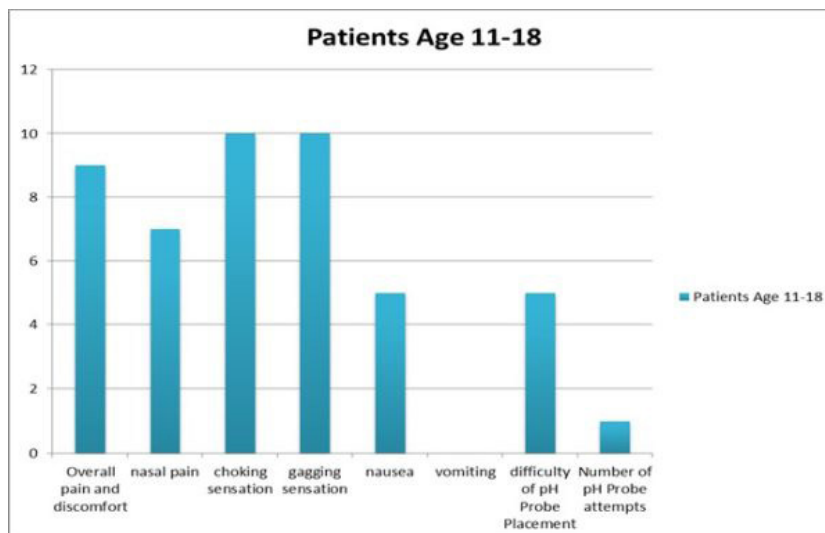
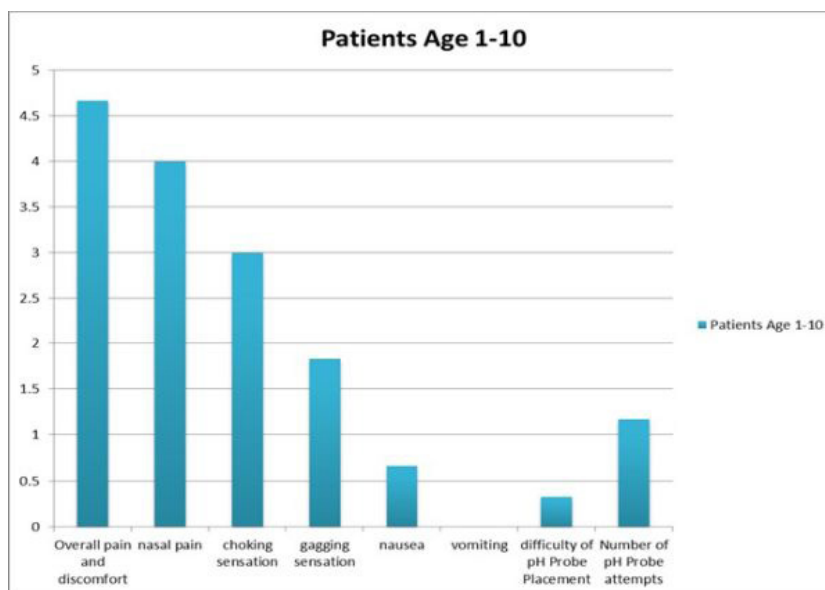
467 PDSA: LIDOCAINE & BENZOCAINE FOR ANESTHETIC USE DURING PH PROBE INSERTION IN PEDIATRIC PATIENTS. David Murchio. *Pediatric Gastroenterology, University of New Mexico Hospital, Albuquerque, NM*

Objective: The aim of the study was to evaluate the efficacy of using a 2 % Lidocaine gel with a 20% Benzocaine oral spray as a pre medication before pH Probe placement

Methods: To recruit the families of patients ages 0-10 years and 11-18 years who were scheduled to have a pH probe placed to participate in the study. Each of the two age groups were expected to have 10 participants. Each patient had a pH probe placed 5 minutes after the administration of 2% nasal lidocaine and 20% Benzocaine oral spray. The medication utilized during this process was determined based on age and dosing criteria. Participants were scored using the appropriate pain indicator scale (FLACC, Wong Baker, Numeric Pain Scale) and were scored based on overall pain and discomfort, nasal pain, choking sensation, gagging sensation, nausea, vomiting, difficulty of pH probe placement, and number of pH probe attempts.

Results: Due to the time restraints of the testing and lack of patients who participated only 6 patients between the ages of 0-10 participated and only 2 patients participated between the ages of 11-18. Overall pain for patients 1-10 years was 4.66667. Overall pain for patients between the ages of 11-18 years was 9.

Conclusion: 2% Lidocaine gel and 20% Benzocaine spray given 5 minutes before pH probe placement helped with overall pain in patients between the ages of 0-10 years. Patients between the ages of 11-18 years did not show any significant pain relief.



468 IMPORTANCE OF NURSING OBSERVATIONS IN THE INTERPRETATION OF MANOMETRY TESTING IN CHILDREN: A CASE SERIES. *Roberta Chaney¹, Charmaign Albright¹, Denise Howe¹, Peter Lu¹, Desale Jacob¹, Mhd Louai Manini^{1,2}, Karla Vaz¹, Carlo Di Lorenzo¹.* ¹*Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Nationwide Childrens Hospital, Columbus, OH;* ²*Division of Gastroenterology, Mayo Clinic, Rochester, MN*

Background: Manometry testing is important in the evaluation of children with suspected gastrointestinal motility disorders. The literature on manometry testing in children has thus far focused on interpretation of the manometric data collected. Nurses are critical to the performance of manometry testing, and are involved from before the study begins through completion. The objective of this case series is to illustrate the importance of nursing input in the performance and interpretation of manometry testing for children with suspected gastrointestinal motility disorders.

Case Presentations: We describe 3 cases involving children who underwent manometry testing where nursing input impacted interpretation of testing and affected management. The first case is that of a 9 year old male with severe constipation and fecal incontinence who underwent colonic manometry testing. The family reported that he was unable to sense the urge to defecate. The nurse was present and documented observations throughout the duration of the 6-hour study. After administration of bisacodyl during the study, the nurse noted that the patient appeared to be in pain, had facial flushing, stiffened his body, and extended his legs while denying the urge to defecate. Based on this observation, the interpreting physician recommended behavioral strategies to recognize the urge to defecate and decrease stool withholding. The second case is that of a 16 year old female with a long history of effortless, postprandial vomiting who underwent antroduodenal manometry testing. The nurse was present and documented observations throughout the study, including any coughing, sneezing, laughing, or vomiting that occurred. The nurse observed that episodes of vomiting coincided with simultaneous contractions throughout all sensors, which led the interpreting physician to diagnose the patient with rumination syndrome. The third case is that of a 12 year old male with severe constipation and a 2-year history of daytime urinary incontinence who underwent colonic manometry testing. The patient reported that he was unable to sense the urge to urinate. Extensive prior evaluation did not show an etiology of his urinary incontinence. The nurse was again present and documented observations throughout the duration of the study, and observed that the patient was experiencing discomfort. After asking him to sit on the commode, his discomfort was relieved by voiding. The nurse's observations led the interpreting physician to conclude that the patient's urinary incontinence was largely behavioral

Conclusion: Interpretation of manometry testing requires close observation of clinical symptoms throughout the study. This is particularly relevant to the pediatric population. Nursing input is critical to the performance and interpretation of manometry testing, and can have a significant impact on subsequent management recommendations. Based on the experiences we described in this case series, we recommend that manometry testing in children involve close observation by nursing staff and that interpretation include analysis of both manometric data and nursing input.

469 THE USE OF TRANSANAL IRRIGATIONS (TAI) IN PEDIATRIC PATIENTS WITH ORGANIC DEFECATORY DISORDERS. *Fiona Paul, Amelia Sparrow.* *GI, Boston Children's Hospital, Boston, MA*

Organic defecatory disorders can have a major impact on a child's ability to function and quality of life. Aim to study the use of TAI in pediatric patients with organic defecatory disorders.

Methods: Prospective longitudinal study using a convenience sample of patients referred for TAI. Participants are evaluated before and after the initiation of a TAI. Inclusion criteria: pediatric patients with organic defecatory disorders who have failed to achieve satisfactory bowel management with other therapies. Exclusion criteria: TAI contraindicated.

Participants receive a private two hour standardized TAI training session from the same NP. During training the appropriate balloon and fluid volumes are decided, and they are instructed on its use. Participants will have access to written and video education materials created by study investigators.

Participants complete the Neurogenic bowel dysfunction scale (NBD) a 10-item questionnaire, and fecal incontinence quality of life scale (FIC-QOL) a 51-item questionnaire, validated instruments which are correlated to measure impact on QOL. Participants rate overall satisfaction of their bowel management on a 0-10 Likert-like scale. Participants provide feedback on newly created educational tools. Data is collected prior to the initiation of a TAI program and at regular intervals post training. Statistical analysis performed on the survey items before and after with pair matched Wilcoxon signed rank test and chi square.

Results: Initial data from 18 patients has been reviewed. Age ranged 7-24 years (mean 18.8 ±5.6). Seven underwent the MACE procedure and failed to achieve satisfactory bowel control with antegrade colonic enemas (ACE), and 11 were candidates for the MACE procedure but elected to try TAI before. All participants completed the FIC-QOL and the NBD

Scales (0-very minimal dysfunction, ≥ 14 - severe dysfunction), and an overall satisfaction with their bowel management on a 0-10 Likert-like scale prior to starting treatment with TAI. There was a statistically significant improvement in bowel control and care (table 1), neurogenic bowel dysfunction scores, and bowel satisfaction scores.

From the 7 patients that failed MACE, all but 1 patient stopped ACE, and 3 became fully continent. Of the 11 patients referred for MACE surgery 7 became fully continent, and none required surgery.

Discussion: Preliminary data suggests the use of TAI in pediatric patients with organic defecatory disorders may prevent the need for surgery and can improve quality of life.

Variable	Pre Mean \pm SE Mean	Post Mean \pm SE Mean	P value
Accidents / wk	1.8 \pm 0.8	0.8 \pm 0.16	0.03
patients with incontinence	77%	54%	0.03
BM/day	1.2 \pm 0.2	0.85 \pm 0.15	0.04
BM in toilet	81% \pm 7	98% \pm 1	0.03
Time of bowel care	54 \pm 7	32 \pm 3	0.002

470 **A TEAM APPROACH TO CONSTIPATION MANAGEMENT: DEFECATION DISORDERS CENTER.**

Susan Peck^{1,2}, Kari Baber^{1,2}, Ritu Verma^{1,2}. ¹Division of Gastroenterology, Lustgarten Motility Center, Philadelphia, PA; ²Children's Hospital of Philadelphia, Philadelphia, PA

Functional constipation is a common problem in pediatrics. While there can be organic causes for constipation, the majority of children with functional constipation have no underlying medical disease. Functional constipation often results from stool withholding and can result in encopresis. Functional constipation and encopresis cause significant distress to children and caregivers, impact quality of life for the family and have consequences that extend beyond the family (e.g., impacting school functioning).

We created the Defecation Disorders Center (DDC) in the Lustgarten Motility Center at the Children's Hospital of Philadelphia in 2015. The goal was to create an expert care team consisting of a pediatric nurse practitioner, a pediatric psychologist and an attending gastroenterologist who would see families frequently and provide consistent medical management, emotional support and behavioral therapy to promote adherence. Patients with functional constipation diagnosed by a pediatric gastroenterologist are referred to the DDC. They are seen by medical and behavioral health providers at each visit. The first visit consists of education, review of the current care plan, and identification of targets for behavioral modification. A medical and behavioral health plan is determined. Visits are scheduled for every 2 weeks. Treatment is guided by the ESPGHAN/NASPGHAN Guidelines developed in 2014 and evidence-based practices in the field of pediatric psychology.

Twenty-eight patients have enrolled and completed at least 1 visit in the DDC program. Ten (36%) initially presented to CHOP for second opinion of constipation. For 22 patients seen by a CHOP gastroenterologist prior to enrolling in DDC, the average number of visits prior to referral was 4.5. Twenty-one (75%) had longstanding encopresis at the time of their initial DDC visit. Nineteen (68%) had a history of stool withholding and subsequent constipation. Eight (29%) had failed toilet training, continuing to defecate in a diaper or pull-up. Three (11%) were referred for NG GoLytely cleanout at the outset of treatment in the DDC. Five (18%) benefitted from EMG biofeedback and six (21%) benefitted from rectal therapy.

Families are educated about the causes of constipation and encopresis. A three pronged strategy includes medical therapy (stool softeners, lubricants, stimulants, rectal therapy), dietary management (dietary fiber, fiber supplements, adequate fluid intake) and behavioral management (structured toilet sitting, support for improved body positioning, positive reinforcement for health behaviors). Patients/families are asked to keep a record of stools, soiling accidents and toilet sitting.

This program has been successful in improving constipation management for patients who have been resistant to conventional care. Frequent visit provide families with ongoing review and reinforcement of the recommended therapies. The medical and behavioral plans are adjusted as needed, in collaboration with the family. Ongoing evaluation of the program will be occurring. Future studies will look at the role of biofeedback as well as alternative support measures.

471 **NASPGHAN Nutrition Prize**

QUALITY IMPROVEMENT IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: A SUCCESSFUL STRATEGY TO IMPROVE DISEASE-SPECIFIC KNOWLEDGE IN PATIENTS AND PARENTS.

Christine Pasquarella, Jill Frawley, Katheen Raig, Praveen Kumar Conjeevaram Selvakumar, Lori Mahajan. Pediatric Gastroenterology, Cleveland Clinic Children's, Cleveland, OH

Background: Mean age at the diagnosis of inflammatory bowel disease (IBD) is approximately 12.5 years with about 20-30% of patients diagnosed before the age of 20 years. Increasing prevalence of pediatric IBD imposes a huge burden on transitional care of adolescent patients to adult Gastroenterology practice. However, models assessing the patient medical knowledge and thereby the readiness to transition are very limited. In addition, intervention models to improve patient/parent medical knowledge have not been studied well.

Aim: To assess disease-specific knowledge in adolescents and young adults with IBD and to evaluate improvement in medical knowledge with a medical health card containing disease pertinent information.

Methods: A survey containing questions on disease characteristics, medications, surgical procedures and maintenance care was formulated and completed by patients (12-21 years of age) with established IBD and their accompanying parents during Infiximab infusions. The survey was scored by study investigators with a total score of 11. A health card containing patient's disease-related medical information was developed and provided to them following completion of the survey. The survey was repeated at a subsequent infiximab infusion to evaluate for improvement in patient/parents' knowledge following provision of health card containing their disease-related information.

Results: A total of 50 patients and 44 parents were included in the study. Mean age of the patients at the time of survey was 16.2 years, mean disease duration was 4.7 years and 50% of them were females. There was a significant improvement in patient's mean pre-and post-health card survey scores (7.6 vs. 8.8; p-value < 0.001). In contrast, there was no difference in mean pre-and post-health card survey scores of parents. On stratified analysis, we found a significant difference between pre-and post-health card survey scores pertaining to disease location for both patients (0.27 vs. 0.83; p-value < 0.001) and parents (0.50 vs. 0.69; p-value 0.019). Age of patient and disease duration did not have any correlation with change in survey scores following provision of the health card.

Conclusion: Our study showed an improvement in disease-specific knowledge among adolescents and young adults with IBD after an implementation of a health card containing disease pertinent information. Improvement in disease-specific knowledge among IBD patients can increase medication compliance, reduce hospitalization rate, and more importantly help in transitioning care to adult practice.

472 IMPROVING CARE FOR OUR IBD POPULATION THROUGH THE NURSE PRACTITIONER-LED ANNUAL VISIT. Elizabeth Yarger, Pam Morgan, Kelly Sandberg. *Gastroenterology, Dayton Children's Hospital, Dayton, OH*

The current healthcare systems are challenged to provide safe, quality care for the increasing numbers of patients with chronic illness (Watts et. al., 2009). The nurse practitioner (NP) complements the primary GI physician in developing a shared focus on specific areas, targeting self-management goals, resulting in improved care processes, health outcomes, impacting cost and patient satisfaction (Litaker et. al, 2009, Katon et. al., 2001). The increasing demand for preventative care while preserving the quality of care can be addressed by an innovative model of intraprofessional collaboration and standardization. By providing an effective, standardized annual visit, pediatric patients with inflammatory bowel disease (IBD) receive comprehensive and improved quality of delivered care.

The patient's primary physician identifies eligible patients for annual visit. Eligibility criteria includes: quiescent/mild disease, no annual visit within the past 12 months, and are not concurrent enrollment in a clinical research study. Eligible patients are also reviewed at our department-wide population management meeting, led by the NP including: reviewing growth and nutrition, laboratory results, medications, and previous screenings. The average annual visit appointment time is 45 minutes, and includes assessments by the NP, registered nurse, dietitian, social worker, psychologist, and QI coordinator.

The four domains addressed include:

1. Health Maintenance Monitoring (eye exam, skin exam, bone health, standard labs, and surveillance screening)
2. Immunosuppression Monitoring and Support. We ensure all patients being treated with immunosuppressive agents are receiving the scheduled non live vaccinations.
3. Self-Management Support and Transition-readiness Assessment. Increases successful transition of care to an adult gastroenterologist. Patients can identify disease extent, symptoms of disease flare, and navigate through the adult healthcare system.
4. Age-based psychosocial screening. Assessment of the patient's well-being identifies potential risk factors and stressors.

Since November 2016, 20% of our eligible population have gone through an annual visit (N=34). In a 100% of our sample, we found gaps in health maintenance.

Optimization of immunization is critical in preventative care in the IBD patient (Lester et. al., 2015). Among the 34 participants, 50% have received a flu vaccination within the past 12 months.

By fostering independent adolescents and young adults living with a chronic disease, they attain knowledge and self-management skills through early education and intervention (Paine et.al, 2014; Naylor et. al., 2008). We identified 48% have had prior transition readiness screening.

Research shows IBD patients are at increased risk for depression. Their physical, behavioral, and emotional health should be taken seriously (Rufo et. al., 2012). Based on our findings, 0% have had a psychosocial screening.

A standardized comprehensive approach to health maintenance, immunosuppression monitoring, self-management, transition readiness and psychosocial screening is critical in the treatment of a patient with chronic illness. The NP-led annual IBD visit is an effective way to improve the health of IBD patients with improved overall quality of delivered care.

CONCURRENT SESSION II – NUTRITION

Friday, November 3

2:30pm – 4:00pm

473 **EARLY PREDICTORS OF SEVERE ACUTE PANCREATITIS IN A PROSPECTIVE PEDIATRIC**

COHORT. David Vitale¹, Lindsey Hornung², Tom Lin¹, Tyler Thompson¹, Jaimie Nathan³, Maisam Abu-El-Haija¹

¹Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH;

²Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ³Division of Pediatric General and Thoracic Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Introduction: Acute pancreatitis (AP) is increasing in incidence in the pediatric population, but nonetheless is poorly studied. The natural course of patients who develop AP can range from a mild presentation to severe acute pancreatitis (SAP), associated with morbidity and mortality. A new pediatric classification of AP was recently published by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) Pancreas Committee, which defines mild AP, moderately SAP and SAP. Early identification of pediatric patients at higher risk for developing SAP is crucial, as it is associated with increased health system cost and mortality.

Szabo et al recently utilized retrospective data to develop a prognostic tool to predict SAP. There are no studies, however, evaluating predictors of SAP using the newly defined pediatric AP classifications and prospectively collected data. The aim of this study was to evaluate for early predictors of developing SAP during first episode of AP in a prospective pediatric cohort.

Methods: Pediatric patients presenting with first episode of AP between May 2013 and January 2017 to the Cincinnati Children's Hospital Medical Center (CCHMC) were prospectively recorded in a local database. Clinical data collected during admissions were analyzed, including laboratory values within 24 hours of AP attack, any manifestations of SAP, fluid resuscitation rates and feeds on admission. Differences in groups of mild AP and SAP were analyzed using Wilcoxon-Mann-Whitney tests and a multivariable logistic regression model was derived based on significant p-values, AIC and ROC curve using stepwise selection.

Results: There were 118 patients included in analysis, of which 22 (18.6%) developed SAP. Patients who developed SAP had significantly higher BUN (20.0 vs 10.0, $p = .007$), magnesium (2.1 vs 1.8, $p = .04$), glucose (121.5 vs 98.5, $p = .03$), sodium (141.0 vs 139.0, $p = .03$), and CRP (5.5 vs 1.0, $p = .02$) [Table 1]. Patients who developed SAP had less aggressive hydration (32% vs 44%, $p = .15$), and were less likely to have feeds started within 24 hours (18% vs 27%, $p = .52$), however these findings did not achieve statistical significance. A significant multivariable model with white blood cell count, sodium and calcium (AUROC 0.79, 95% CI: 0.67 – 0.91, Sn 72.2%, Sp 76.5%, PPV 44.8%, NPV 91.2%) was generated during stepwise selection. However, when BUN was added to the model, BUN by itself as a predictor was superior to any other combination of variables (AUROC 0.75, 95% CI 0.61 – 0.89, Sn 63.2%, Sp 81.2%, PPV 42.9%, NPV 90.8%).

Conclusion: This study is the first to evaluate a prospective pediatric cohort of patients presenting with first episode of AP using the newly published pediatric SAP classification. Within 24 hours of presenting with AP, patients who developed SAP had higher BUN, magnesium, glucose, sodium and CRP than those who developed mild AP. A logistic regression model with BUN as a significant predictor of SAP was derived from our variables. These findings are useful for early identification of pediatric patients at higher risk for progression to SAP.

TABLE 1. SAP vs mild AP: First AP Attach Characteristics

	SAP (n=22)	Mild AP (n=96)	P-value
Age (years)	13.8 (7.9, 15.9) n=22	13.5 (10.2, 15.9) n=96	0.96
Sex (male)	14 (64%)	48 (50%)	0.25
Weight percentile	59.1 (9.1, 88.9) n=22	48.3 (23.1, 86.9) n=92	0.45
Height percentile	56.5 (3.1, 83.3) n=22	49.3 (21.9, 76.2) n=90	0.83
BMI percentile	63.1 (20.1, 89.2) n=22	58.4 (23.6, 92.6) n=87	0.96
Lipase x ULN	8.6 (4.8, 17.8) n=21	8.4 (3.8, 25.3) n=90	0.90
Amylase	386.0 (131.5, 521.0) n=12	194.0 (104.0, 507.0) n=75	0.35
Albumin	3.3 (2.5, 3.8) n=19	3.7 (3.1, 4.1) n=86	0.08
WBC	13.2 (8.9, 17.9) n=18	9.9 (7.3, 14.8) n=75	0.18
Creatinine	0.6 (0.5, 0.7) n=20	0.6 (0.4, 0.6) n=85	0.43
GFR	114.6 (93.1, 129.7) n=19	111.6 (98.7, 138.0) n=73	0.77
Calcium	8.6 (8.2, 9.2) n=20	9.0 (8.5, 9.4) n=83	0.10
AST	35.0 (24.0, 130.0) n=15	40.5 (21.0, 114.5) n=80	0.54
ALT	37.0 (13.0, 266.0) n=15	29.0 (21.0, 177.0) n=79	0.85
Hematocrit	38.8 (31.8, 46.2) n=14	38.1 (33.3, 41.6) n=67	0.64
Hemoglobin	13.8 (10.8, 15.9) n=16	12.8 (11.5, 14.0) n=66	0.44
BUN	20.0 (10.0, 23.0) n=19	10.0 (8.0, 13.0) n=85	0.0007
Mg	2.1 (1.8, 2.1) n=12	1.8 (1.7, 2.0) n=31	0.04
Phosphorus	3.4 (2.6, 4.0) n=18	3.8 (3.2, 4.4) n=62	0.21
Glucose	121.5 (95.5, 148.5) n=20	98.5 (88.0, 117.0) n=86	0.03
Sodium	141.0 (138.0, 143.0) n=20	139.0 (137.0, 141.0) n=84	0.03
Total Bilirubin	0.6 (0.3, 1.6) n=15	0.5 (0.3, 1.2) n=75	0.98
CRP	5.5 (1.8, 18.1) n=5	1.0 (0.4, 2.6) n=28	0.02
Procalcitonin	0.1 n=1	0.1 (0.1, 0.1) n=2	-
ICU admission (yes)	10/21 (48%)	7/95 (7%)	<0.0001

Data presented as median (25th, 75th percentile) or frequency (%)

474 NASPGHAN Nutrition Prize

INCREASE IN BODY WEIGHT OF PATIENTS WITH CYSTIC FIBROSIS RECEIVING KALYDECO TREATMENT IS DUE TO INCREASE IN ADIPOSE TISSUE. *Marielena Mouzaki¹, Julia Avolio¹, Katherine Griffin², Felix Ratjen¹, Elizabeth Tullis², Tanja Gonska¹.* ¹*Pediatrics, Hospital for Sick Children, Toronto, ON, Canada;* ²*Medicine, University of Toronto, Toronto, ON, Canada*

Introduction: Malnutrition in cystic fibrosis (CF) is associated with a more rapid decline in lung function. Achieving appropriate nutritional status requires increased caloric intake to overcome the impact of maldigestion, malabsorption and the increased high resting energy expenditure seen in patients with CF. CF Patients on Kalydeco have demonstrated significant body weight improvements, but the mechanism is not understood.

Objective: To perform a more detailed evaluation of the change in nutritional status of CF patients receiving Kalydeco.

Methods: Prospective observational study of CF patients carrying G551D/F508del (12), G551D/2622+1G>A, G551D/E585X, G551D/neg (2), G178R/F508del who receive Kalydeco and who were recruited from the Pediatric and Adult CF centres in Toronto. We performed anthropometric measurements, air displacement plethysmography (BODPOD®), indirect calorimetry (mREE) and laboratory studies before (V1), as well as 6, 12 and 24 (V6) months after starting Kalydeco.

Results: Included CF patients (n=18) were 61% female, median age was 20 years (range: 6-58) and 12 patients were pancreatic insufficient (PI). Between V1 and V6, patients demonstrated an increase in weight (mean±SD: 54 [±29] vs. 60 [±26] kg, p=0.008); and BMI (22.2 [±7] vs. 23.3 [±7] kg/m², p=0.007), irrespective of PI status. This was due to an increase in fat mass (21 [±20] vs. 24 [±19] kg, p=0.001; %fat mass: 28% [±15] vs. 32% [±14], p=0.003) with no significant change in fat-free mass (42 [±16] vs. 44 [±12] kg, p=0.263). Serum trypsinogen (mean: 21 [±22] vs. 16 [±22] ng/mL, p=0.471) did not change. There was no change in albumin, vitamin A, E and D levels between V1 and V6. In PI patients increase in body weight correlated with an increase in mREE (r=0.7, p=0.034). However, when correcting for weight (mREE/kg body weight) the mREE of all patients decreased from V1 to V6 (mREE/kg: 32 [±12] vs. 28 [±8] kcal/kg, p=0.05). This decrease in energy expenditure by weight did not correlate with the observed increase in FEV1% predicted (mean FEV1%: 76 [±20] vs. 90 [±20], p=0.003).

Conclusion: The weight gain seen in CF patients on Kalydeco treatment is largely associated with an increase in adipose tissue, suggesting that adjustment of dietary habits in this population may be necessary. Weight gain does not appear to be secondary to improved pancreatic function but may in part be due to a decrease in energy expenditure.

The study was funded by Vertex Pharmaceutical Inc as IIS.

CONCURRENT SESSION II – LIVER

Friday, November 3

2:30pm – 4:00pm

475 **THE COMBINATION OF ENTECAVIR AND PEGINTERFERON ALFA-2A IN HBEAG-POSITIVE IMMUNE-TOLERANT (IT) CHILDREN AND ADOLESCENTS WITH CHRONIC HEPATITIS B VIRUS (HBV) INFECTION: RESULTS OF THE HBRN PEDIATRIC IT TRIAL.**

Philip Rosenthal¹, Simon Ling², Steven Belle³, Karen Murray⁴, Norberto Rodriguez-Baez⁵, Sarah Schwarzenberg⁶, Jeffrey Teckman⁷, Kathleen Schwarz⁸. ¹Pediatrics, UCSF, San Francisco, CA; ²Pediatrics, University of Toronto, Toronto, ON, Canada; ³Epidemiology, University of Pittsburgh, Pittsburgh, PA; ⁴Pediatrics, Seattle Childrens, Seattle, WA; ⁵Pediatrics, Children's Medical Center Dallas, Dallas, TX; ⁶Pediatrics, University Minnesota Amplatz Children's Hospital, Minneapolis, MN; ⁷Pediatrics, Saint Louis University, Saint Louis, MO; ⁸Pediatrics, Johns Hopkins, Baltimore, MD

Background/Aim: The immune tolerant (IT) phase of chronic HBV infection is defined by high levels of HBV DNA in serum but normal ALT values and no or only mild liver inflammation and damage. Many children with chronic HBV remain in the IT phase during much of childhood. Treatment with interferon in such children is rarely effective; loss of HBV DNA or HBeAg occurring in <10% of those treated. More encouraging results have been reported with combination antiviral therapy. The aims of this open-label, single-arm study, were to evaluate the safety and efficacy of a lead-in phase of 8 weeks of entecavir monotherapy followed by 40 weeks of its combination with peginterferon in children in the IT phase of chronic HBV infection.

Methods: Entecavir was given once daily in a dose of 0.015 mg/kg (0.5 mg maximum) for 48 weeks while peginterferon alfa-2a (180 µg/1.73m² subcutaneously) once weekly was added after 8 weeks. Endpoints included sustained loss of HBsAg and HBeAg 48 weeks after stopping therapy with a primary endpoint being the lack of detectable HBeAg with HBV DNA levels below 1,000 IU/mL. Adverse events (AE) were monitored prospectively during and after therapy.

Results: 60 children/adolescents (75% female), mean age 10.9 (min-max 3.4-17.9) years, were enrolled. Most (90%) were Asian and most had HBV genotypes B (53%) or C (37%). All were positive for HBsAg and HBeAg and had high levels of HBV DNA (median 170 million IU/mL) with normal or minimally elevated ALT levels (median 39 U/L in boys and 26 U/L in girls). Fifty-five participants completed the 48 weeks of entecavir and the 40 weeks of peginterferon therapy. At 48 weeks after treatment, two participants (3%) were HBsAg-negative, lost HBeAg, and achieved the primary endpoint of lack of HBeAg and HBV DNA levels less than 1000 IU/mL. Overall, serum ALT levels were similar to baseline and median HBV DNA levels were 174 million IU/mL. The most common of the 75 AEs reported were hematologic (n=16, 21%), infection (n=12, 16%), and hepatic (elevated bilirubin or ALT) (n=8, 11%). No serious AEs were reported. Z-scores for weight, height, & BMI tended to be lower at the end of treatment than at baseline, as did height 48 weeks after treatment.

Conclusions: The combination of entecavir and peginterferon given for up to 48 weeks rarely led to loss of HBeAg with sustained suppression of HBV DNA levels and was associated with frequent but not serious AEs. More potent and more broadly targeted regimens against HBV are needed to treat children in the IT phase of chronic HBV infection.

476 **CASPASE 1 MEDIATES EXACERBATED HEPATOCELLULAR INJURY IN A STEATOTIC LIVER UNDERGOING ISCHEMIA REPERFUSION INJURY.** *Chrissy Lopez, Vasantha Kolachala, Ming Shen, Dmitry Shayakhmetov, Nitika Gupta. Department of Pediatrics, Emory University, Atlanta, GA*

Background: Non-alcoholic fatty liver disease (NAFLD) is a common chronic liver disease affecting nearly one third of the world's population. Hepatic ischemia reperfusion injury (IRI) is a major complication in shock, hepatectomies, and liver transplantation resulting in hepatocellular death, which is particularly pronounced in patients with hepatic steatosis and is driven by sterile inflammation. Caspases are endoproteases which provide critical regulatory connections between cell death and inflammation. Caspase 1 activates the highly pro-inflammatory cytokines interleukin 1b (IL-1b) and IL-18 and is driven by inflammasomes, which are key signaling platforms that detect sterile stressors (DAMPs). The aim of this study was to investigate the role of caspase 1 in mediating cell death in steatotic livers undergoing IRI.

Methods: Time course studies were carried out in lean and steatotic mouse hepatocytes (AML12 cells) with and without hypoxia for 40 minutes and reperfusion for 0, 15, 30 minutes, 1 and 2 hours. Total RNA was extracted and subjected to real time PCR with mouse specific primers for caspase 1 and IL-18. Caspase 1 enzyme activity was determined by colorimetric

assay. Cell death was measured by propidium iodide (PI) staining. Loss of function experiments were carried out *in vitro* with the caspase 1 specific inhibitor Ac-YVAD-cmk. *In vivo* experiments were carried out in male C57BL6/wild type mice, and caspase 1 KO and IL-1 receptor KO mice. The mice were fed a high fat diet (HFD) for 12 weeks then subjected to 40 minutes of ischemia followed by 2-24 hours of reperfusion. Hepatocellular injury was assessed by PI staining, histopathologic cell death scoring, and serum ALT.

Results: *In vitro* time course analysis demonstrated a two-fold increase in mRNA levels of both caspase 1 and IL-18 in FFA-treated steatotic hepatocytes at 30 minutes when compared to lean hepatocytes. Caspase 1 enzyme activity was increased in steatotic hepatocytes as compared to lean. Use of a caspase 1 specific inhibitor demonstrated significantly reduced PI staining (3.9×10^7 without inhibitor vs 2.4×10^7 (RU) with inhibitor; $p < 0.02$) suggesting reduced cell death in steatotic hepatocytes. Mice fed a HFD demonstrated a significant increase in body weight when compared to lean mice (42 ± 1.2 vs 24.6 ± 0.6 gms; $p < 0.0001$) and had a significant increase in serum ALT after IRI (WT HFD: 1536 ± 294 vs lean: 342 ± 55 ; $p < 0.007$). Caspase 1 KO HFD and IL-1R KO HFD mice showed a significant reduction in serum ALT after IRI (435 ± 134 ; $p < 0.01$ and 331.8 ± 96.6 ; $p < 0.008$, respectively). *In vivo* time course studies demonstrated a significant increase in serum protein levels of caspase 1 and IL-1b in HFD IRI at 2 hours of reperfusion.

Conclusion: Blockade of caspase 1 by genetic deletion in a KO mouse model and by a caspase 1 specific inhibitor *in vitro* protected steatotic liver and hepatocytes from cell death. This alludes to the critical role of caspase 1 in modulating steatotic liver injury, thereby providing an important target for development of therapeutics in the growing population of NAFLD.

CONCURRENT SESSION II – AERODIGESTIVE

Friday, November 3

2:30pm – 4:00pm

477 THE OROPHARYNX RATHER THAN THE STOMACH IS THE PRIMARY DRIVER OF LUNG MICROBIOME CHANGES IN ASPIRATING CHILDREN. Claire Duvallet², Scott Snapper¹, Ann Lee¹, Eric Alm², Rachel Rosen¹. ¹Gastroenterology, Boston Children's Hospital, Boston, MA; ²Massachusetts Institute of Technology, Cambridge, MA

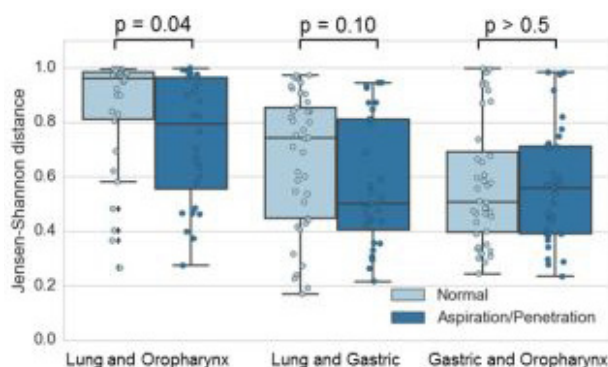
Background: We have previously shown that there is significant microbial overlap between the gastric and lung microbiota in patients with respiratory symptoms and that these populations are distinct from the oropharynx. However, it is not known if the microbial exchange between these sites differs in children with oropharyngeal dysphagia/aspiration. Clinically, these aspirating children often undergo fundoplication to prevent aspiration of microbial-laden gastric contents. These patients, however, often continue with pulmonary symptoms and pneumonias. The goal of this study is to determine the relative impact of the oropharyngeal versus gastric microbiome in shaping the lung microbiome in children with and without oropharyngeal dysphagia/aspiration.

Methods: We prospectively recruited children with and without aspiration on videofluoroscopic swallow study undergoing bronchoscopy with lavage (BAL) for the evaluation of respiratory symptoms. Patients also underwent esophagogastroduodenoscopy with biopsies and multichannel intraluminal impedance with pH (pH-MII) testing. At the time of procedures, BAL fluid, gastric fluid and posterior tongue swabs were obtained for DNA isolation and 16S sequencing. We determined differences in relative bacterial abundance and diversity between the three sites in patients who did and did not aspirate. We then performed an analysis of patients with and without significant full column reflux to determine the interaction of gastroesophageal reflux, aspiration and the lung microbiome.

Results: We recruited 111 children with (N=48) and without (N=63) oropharyngeal dysphagia/aspiration. Using the Jensen-Shannon Diversity Index to determine the degree of similarity between microbial populations in aspirating and non-aspirating patients, we found that there was significantly more similarities in microbial communities between the lung and oropharynx in aspirating patients compared to non-aspirating patients (Figure) and that the primary driver of the lung microbiome in aspirating patients was the oropharynx rather than the gastric microbiome. This is in contrast to non-aspirating patients who showed the greatest microbial overlap between the stomach and lung, rather than the oropharynx. Based on these results, we then calculated the Area Under the Curve for random forest classifiers to distinguish aspirating from non-aspirating patients; we found that the AUC for the lung microbes was 0.67 ($p = 0.007$) suggesting that the microbial communities may serve as a potential biomarker for aspiration.

Conclusions: In aspirating children, the oropharyngeal microbial communities influence the lung microbiome more than do the gastric communities. This finding may explain why many aspirating patients continue to have respiratory symptoms even after fundoplication as the primary driver of the lung microbiome was the oropharynx, not the stomach.

In aspirating patients, the lung microbiome becomes more similar to the oropharyngeal populations.



CONCURRENT SESSION II – ENDOSCOPY

Friday, November 3

2:30pm – 4:00pm

478 IMPACT OF TRAINEES ON SAFETY AND EFFICIENCY OF PEDIATRIC ENDOSCOPY. *Jacob Mark^{1,2}, Robert Kramer^{1,2}. ¹Digestive Health Institute, Children's Hospital Colorado, Denver, CO; ²Section of Pediatric Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, University of Colorado School of Medicine, Denver, CO*

Background: Gastrointestinal endoscopy training aims to prepare fellows to safely and efficiently perform procedures. Performance of the procedure by a trainee may cause concerns of higher risk of adverse events (AEs), and longer operative times (OT), resulting in increased anesthesia exposure and cost.

Objective: To determine if presence and educational level of a trainee affects rates of endoscopic AEs or OT.

Design: Prospective observational study tracking AEs in pediatric patients within 72 hours of all endoscopic procedures and retrospective analysis of OT for a random sample of these procedures at an academic tertiary free standing children's hospital from 2010-2016.

Main Outcome Measurements: AEs were categorized by severity grades: 1—no intervention; 2—outpatient evaluation; 3—hospitalization and/or repeat endoscopy; 4—surgery and/or intensive care unit admission. OT encompassing the time of scope insertion until scope removal were analyzed.

Results: 15,886 total (6,257 with trainee) including 1,627 therapeutic (733 with trainee) procedures were analyzed for AEs. 413 AEs were identified (2.60%) and 213 (1.34%) AEs \geq grade 2 requiring extra medical evaluation and cost. Fellow presence at any training level did not influence AE rates for common diagnostic and therapeutic procedures (Table 1). Median OT for 3,762 esophagogastroduodenoscopies (EGD) decreased from 17 minutes in the 1st quarter to 11 minutes in the 4th quarter of first year of fellowship but did not change after the first year. EGD without fellows were shorter (9 minutes $p < 0.0001$). Median OT of 1,291 colonoscopies with EGD decreased from 55 to 51 to 47 minutes for fellows in first half, second half of 1st year fellowship, and 2nd & 3rd year respectively ($p = 0.0004$). Colonoscopies with EGD without fellows were shorter (37 minutes $p < 0.0001$)

Conclusions: Presence of a fellow at any training level did not significantly affect rates of AEs in diagnostic or therapeutic endoscopies. Most skill acquisition for efficient EGD is accomplished in the first year of training. Efficiency of colonoscopy improves throughout and after fellowship.

TABLE 1. Adverse event rates for common diagnostic and therapeutic procedures are not significantly affected by fellow regardless of training level.

Adverse Events by Training Level					
	1st Year Months 1-6	1st Year Months 7-12	2nd & 3rd Year	No Fellow	P value
EGD					
N of procedures	1355	1176	1165	7049	
% AE grade 1	0.51	0.93	1.11	1.06	0.08
% AE grade ≥ 2	0.66	0.76	0.68	0.75	0.38
Colonoscopy with or without EGD					
N of procedures	433	372	545	1535	
% AE grade 1	2.08	1.34	1.10	1.95	0.29
% AE grade ≥ 2	1.39	2.42	1.47	1.69	0.46
EGD with Dilation					
N of procedures	60	57	85	311	
% AE grade 1	3.33	0.00	3.53	2.25	0.38
% AE grade ≥ 2	5.00	1.75	1.18	1.93	0.17
EGD with Foreign Body Removal					
N of procedures	79	76	83	112	
% AE grade 1	1.27	1.32	1.20	0.00	0.40
% AE grade ≥ 2	2.53	0.00	0.00	0.89	0.57
Colonoscopy with Polypectomy					
N of procedures	17	16	30	49	
% AE grade 1	5.88	6.25	0.00	2.04	0.43
% AE grade ≥ 2	0.00	0.00	10.00	14.29	0.18

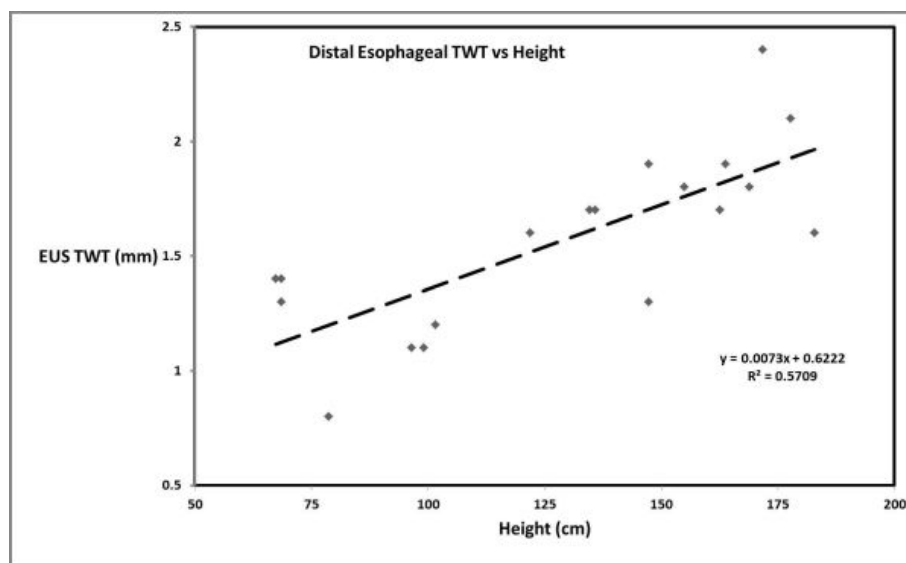
479 ESOPHAGEAL WALL THICKNESS IN CHILDREN. Simon Rabinowitz¹, Katherine Vaidy¹, Nonyelum Ebigbo³, Rachel Sklar¹, Lisa Feng¹, Evan Grossman², Steven Schwarz¹. ¹Pediatric GI, Children's Hospital at Downstate, Brooklyn, NY; ²Gastroenterology, Downstate Medical Center, Brooklyn, NY; ³Pediatrics, Richmond University Medical Center, Staten Island, NY

Introduction: Endoscopic ultrasound (EUS) has been employed to measure esophageal wall thickness (TWT) in eosinophilic esophagitis (EoE). Increases in TWT have been shown to be a marker of esophageal remodeling in EoE. In order to establish baseline values in Pediatrics, EUS measurements of TWT in children without EoE are presented.

Materials/Methods: Nineteen patients (12M; 9.0 + 6.5y; range: 0.6-20.9y) with clinical symptoms suggestive of esophageal dysfunction were part of an IRB approved research study on EoE. All 19 had upper endoscopy followed by EUS and biopsies from the mid and distal esophagus. Only those without any endoscopic or histologic features of EoE are included in the present analysis. Fifteen had clinical GERD. Four were follow up EoE patients who had been effectively treated yielding, no symptoms and no esophageal eosinophilia for >1 year. The maximum eos/hpf in this cohort was 4; most had none. A 20MHz EUS miniprobe measured TWT in the distal and mid esophagus. Subsequently, biopsies were obtained from these same two sites.

Results: TWT correlated with age, height, and BMI in both the mid and distal esophagus. The average TWT of the mid (1.57mm) and distal (1.55mm) were not statistically different (p=0.2). For both the mid and distal TWT, the values obtained in this cohort were overall less than the patients enrolled in the study with active EoE (but the difference was limited to the older, larger patients). Linear best fit approximations of predicted TWT were generated for each variable (Figure shows for height). The coefficient of determinations (R²), indicates that the height of the patient (0.57 distal, and 0.53 mid) provides a more accurate estimate of TWT than the age (0.34 distal and 0.47 mid) or BMI (0.09 distal and 0.07 mid).

Discussion: EUS permits detailed analysis and measurements of the esophageal TWT. It is imperative to have baseline values through childhood to determine if younger children with EoE are also experiencing an increase in TWT. Our data cannot be unequivocally representative of normal children, as it would not be ethical to sedate and study a completely asymptomatic cohort of children. The presented data demonstrates that among non EoE children, as they get older and larger their esophageal wall thickens. The EUS measurements in this cohort are in the range of published values obtained by various methods. In conclusion, TWT in normal children correlates best with their height. Preliminary data is presented that can be employed to estimate baseline TWT based on a child's height.



TWT measured by EUS in children without EoE

CONCURRENT SESSION II HOT TOPICS – TREAT TO TARGET

Friday, November 3

2:30am – 4:00am

480 **CD64 SUPPRESSION PREDICTS EARLY CLINICAL RESPONSE TO INFLIXIMAB INDUCTION.**

Phillip Minar, Kathryn Clarkson, Kimberly Jackson, Yi-Ting Tsai, Lee Denson. Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: Crohn's disease patients with therapeutic infliximab concentrations ($\geq 3 \mu\text{g/ml}$) and improvements in surrogate biomarkers by the end of induction have been shown to have superior rates of sustained remission. Unlike therapeutic drug monitoring, blood biomarkers provide the clinician with a more rapid evaluation and may be more cost effective than frequent drug monitoring. In a cross-sectional investigation, we found that both neutrophil CD64 index (nCD64) and soluble CD64 (sCD64) strongly correlated with endoscopic severity scores in patients with Crohn's disease and could serve as early biomarkers of treatment response. The primary aim of this investigation was to evaluate changes in CD64 during infliximab induction as a pharmacodynamic biomarker of early response in children with Crohn's disease.

Methods: Anti-TNF naïve Crohn's disease patients starting infliximab were recruited to participate in this one year prospective, single-center study. nCD64 was calculated from whole blood using flow cytometry (Trillium Diagnostics). sCD64 was determined from plasma using an ELISA (LifeSpan BioSciences). Drug concentration was determined by an ELISA (Immundiagnostik). Clinical response (CR) was defined by a weighted pediatric Crohn's disease index (wPCDAI) prior to the 4th infusion <12.5 and/or a change >17.5 points from the baseline wPCDAI. Infliximab cessation, abdominal surgery prior to the 4th infusion or patients receiving the 4th dose before 70 days were defined as treatment non-response (NR). Dose intensification was not considered treatment NR.

Results: We enrolled 54 patients with Crohn's disease, 68.5% male, 96.2% white race. Mean age was 13 (4) years old. The majority of patients (85.2%) had an inflammatory (B1) phenotype with ileocolonic (L3) location 81.5%. The median infliximab dose was 5.8 mg/kg (4-11.7) with 11% receiving >7.5 mg/kg at the first dose. Dose intensification prior to the 4th dose occurred in 20.4%. Only two patients were on an immunomodulator throughout induction. The CR rate was 64.8% at the end of induction. The baseline (pre-infliximab) nCD64, sCD64 and CRP were elevated in 81.5%, 75% and 66.7% of patients, respectively. Baseline nCD64 in CR was 1.6 (0.6-3.7) and 0.96 (0.5-4.3) in NR (p=0.0018). 72.7% of patients with a baseline elevation of nCD64 were in CR compared to a CR rate of 30% (ten patients) without a pre-infliximab nCD64 elevation (p=0.024). There was no difference in pre-infliximab sCD64 or CRP between CR and NR. We found the best early predictor for CR was a decrease (delta%) between the baseline and nCD64 at infusions 2, 3 and 4 (**Fig.1a**). Similarly, the delta% sCD64 was also associated with early CR (**Fig.1b**). There was no difference in CRP delta% between CR and nonresponders prior to the 2nd or 3rd infusion, however, CRP delta% was improved in the patients with CR compared to NR prior to the 4th infusion (p=0.034). For the forty-four patients with an elevated baseline nCD64, >40% improvement in nCD64 prior to the 3rd infusion was associated with CR rate of 91% which was superior to the 54.6% CR rate in patients who had a delta% nCD64 less than 40%, p=0.016. Patients with >40% improvement in nCD64 prior to the 3rd infliximab dose had a median infliximab concentration of 2.6 µg/ml (0.7-9.3) at the 4th infusion (41% were >3 µg/ml) compared to a median of 1.5 µg/ml (0.4-21, p=0.04) in the patients who failed to achieve a >40% improvement in nCD64 prior to the third dose (14.3% were >3 µg/ml, p<0.05).

Conclusions: nCD64 and sCD64 suppression was strongly associated with clinical response and predicted higher infliximab concentrations at the end of induction. Early utilization of longitudinal nCD64 during infliximab induction could guide infliximab dose intensifications and determine the timing of drug concentration monitoring.

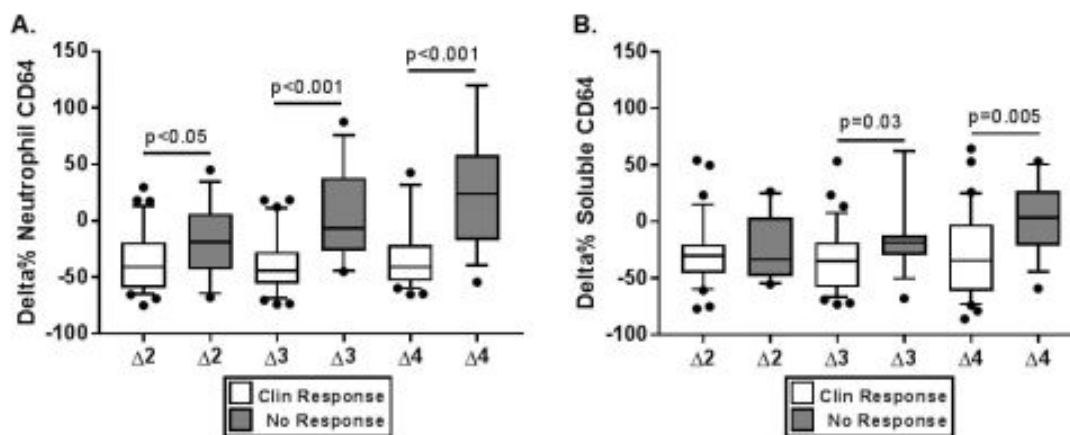


Figure 1. CD64 suppression and early clinical response. The distribution of change (delta%) in the blood biomarkers obtained prior to each of the first four infusions in clinical responders and nonresponders. Clinical response was defined by the change in weighted PCDAI from baseline and prior to the 4th infusion. A) The delta% for neutrophil CD64 index and B) the delta% for soluble CD64.

CONCURRENT SESSION III – HOT TOPICS

Saturday, November 4

8:30am – 10:00am

481 Young Faculty Clinical Investigator Award

FECAL MICROBIOTA TRANSPLANTATION IN PEDIATRIC CLOSTRIDIUM DIFFICILE

INFECTION, A MULTI-CENTER STUDY. Maribeth Nicholson¹, Erin Alexander², Mark Bartlett², Penny Becker³, Zev Davidovics³, Elizabeth Doby⁴, Michael Dole¹, Grace Felix⁵, Jonathan Gisser⁶, Suchitra Hourigan⁷, Kyle Jensen⁴, Jess Kaplan⁸, Judith Kelsen⁹, Melissa Kennedy⁹, Sahil Khanna², Jeffery Lewis¹⁰, Sonia Michail¹¹, Maria Oliva-Hemker⁵, Tiffany Patton¹⁷, Karen Queliza¹⁴, David Suskind¹², Solomon Aliza¹⁶, Steven Werlin¹³, Richard Kellermayer¹⁴, Stacy Kahn¹⁵.
¹Pediatrics, Vanderbilt University Medical Center, Nashville, TN; ²Pediatrics, Mayo Clinic, Rochester, MN; ³Pediatrics, Connecticut Children's Hospital, Hartford, CT; ⁴Pediatrics, Primary Children's Hospital at University of Utah, Salt Lake City, UT; ⁵Pediatrics, Johns Hopkins Children's Center, Baltimore, MD; ⁶Pediatrics, Nationwide Children's Hospital, Columbus, OH; ⁷Pediatrics, Inova Children's Hospital, Falls Church, VA; ⁸Pediatrics, MassGeneral Hospital for

Children, Boston, MA; ⁹Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; ¹⁰Pediatrics, Children's Center for Digestive Healthcare at Children's Healthcare of Atlanta, Atlanta, GA; ¹¹Pediatrics, University of Southern California, Los Angeles, CA; ¹²Pediatrics, Seattle Children's Hospital at University of Washington, Seattle, WA; ¹³Pediatrics, Medical College of Wisconsin, Milwaukee, WI; ¹⁴Pediatrics, Baylor College of Medicine, Houston, TX; ¹⁵Pediatrics, Boston Children's Hospital, Boston, MA; ¹⁶Weill Cornell Medicine, New York, NY; ¹⁷Pediatrics, University of Chicago, Chicago, IL

Background: *Clostridium difficile* infection (CDI) is increasingly common in children, within both hospital and community settings. Between 20 to 30% of pediatric patients will have a symptom recurrence in the days to weeks following an initial antibiotic treatment course. Multiple recurrences have been successfully treated with fecal microbiota transplantation (FMT) according to isolated cases, and small case series. The body of evidence to support FMT in pediatric patients, however, is limited.

Objective: To better understand the practices, success rates, and safety of FMT in children.

Study Design: We performed a multicenter retrospective study of patients who underwent FMT for CDI between 1/1/2006 and 1/1/2017 at pediatric centers across the United States. Demographics, baseline characteristics, FMT practices, *C. difficile* outcomes, and post-FMT complications were collected utilizing RedCap database. Successful FMT (i.e. "cure") was defined as no recurrence of CDI within 90 days after FMT.

Results: Data from 17 pediatric centers, including 322 patients who underwent FMT for CDI were included. The median age was 10 years, and 49% of patients were female. Comorbidities of patients included 101 (31.4%) with inflammatory bowel disease (IBD), 12 (3.7%) with a malignancy diagnosis, and 13 (4.3%) who had undergone a solid organ or stem cell transplantation. Of the 322 patients in the cohort, 268 had known outcome data at 3 months post-FMT, including 86 IBD patients. Of these 268 patients, 215 (80%) achieved cure. In the 53 patients who did have a recurrence, 34 (64%) underwent repeat FMT which was successful in 19 of the 34 (56%). The overall cure rate of FMT in the cohort was 87%. Of the 86 IBD patients with 3 month follow-up post FMT, 32 (37.2%) had improved activity of their IBD, 30 (34.9%) had no change, 18 (20.9%) had worsened activity of their IBD, and 6 (7%) were unknown. The cure rate among IBD patients was not different than those without IBD (Table 1). Patients who had FMT via colonoscopy had a higher success rate than the other patients in the cohort (Table 1). There were 13 adverse events in the cohort felt to be related to FMT, two of which were documented as serious, including an aspiration pneumonia (upper delivery route) and a flare of IBD requiring admission (lower delivery route). There were no FMT-related deaths in the cohort.

Conclusions: Fecal microbiota transplantation for CDI in pediatric patients appears to be efficacious and serious adverse events are rare (0.6%). Patients with IBD did not have lower rates of cure than the other patients in the cohort. Mode of delivery may affect efficacy, which awaits confirmation in future prospective controlled trials.

Table 1. Variables of Patients with and without a Successful response to FMT

	Successful FMT	Failed FMT	P value
Age (mean)	9.5	8.2	0.16 ¹
Gender			0.23 ²
Male (n=142)	110 (77.5%)	32 (22.5%)	
Female (n=126)	105 (83.3%)	21 (16.7%)	
Inflammatory Bowel Disease			0.74 ²
Yes (n= 86)	68 (79.1%)	18 (20.9%)	
No (n=182)	147 (80.8%)	35 (19.2%)	
Delivery Method			0.05 ²
Colonoscopy/Sigmoidoscopy (n=209)	175 (83.7%)	34 (16.3%)	
Upper Delivery (n=49)	34 (69.4%)	15 (30.6%)	
Enema (n=3)	2 (66.7%)	1 (33.3%)	
Capsule (n=7)	4 (57.1%)	3 (42.9%)	

¹Kruskal Wallis

²Pearson Chi² Test

CONCURRENT SESSION III – MALABSORPTION

Saturday, November 4

8:30am – 10:00am

482 PLEIOTROPIC EFFECT OF PT-GLIADIN ON PRIMARY HUMAN MACROPHAGES IS REGULATED BY EPITHELIUM RELEASED FACTORS IN CELIAC PATIENTS. *Gloria Serena, Shu Yan, Rosiane Lima, Alessio Fasano. Pediatrics, Massachusetts General Hospital, Boston, M*

Celiac disease (CD), an autoimmune enteropathy triggered by gluten, is characterized by an increased number of intraepithelial and lamina propria immune cells. Studies on murine primary macrophages and monocyte/macrophage cell lines have shown that gliadin induces the secretion of a broad spectrum of pro-inflammatory cytokines. However studies on human primary macrophages are scarce. Monocytes derived macrophages are plastic cells that can differentiate into either a pro-inflammatory subtype (M1) or an anti-inflammatory one (M2) depending on the microenvironment. Our study aims to determine which subtype of macrophages is induced by gliadin and how the cross-talk between immune cells and the epithelium contributes to this effect.

We isolated CD14⁺ monocytes from blood samples of healthy controls (HC) and CD patients and differentiated them into macrophages. At day 6 the macrophages were cultured in medium alone or with 1 mg/ml of gliadin (PTG). Alternatively the macrophages were cultured using as medium the supernatant of CaCo2 cells previously cultured with medium alone or with PTG. Real time PCR was used to measure the expression of M1 genes (IL6, IP10, TNF α) and M2 genes (TGF β and CCL22). Our data show that PTG has a pleiotropic effect on the macrophages of both groups of subjects by triggering the production of both M1 pro-inflammatory and M2 anti-inflammatory cytokines. Interestingly the macrophages cultured with the CaCo2 supernatants showed a different outcome for some of the cytokines. The production of CCL22 was significantly reduced in HC macrophages cultured with the supernatant of CaCo2 + PTG as compared to the macrophages cultured in medium + PTG (p<0.05). Conversely, in CD patients the supernatant from CaCo2 cultures + PTG triggered a significantly higher production of CCL22 as compared to the medium condition (p<0.05) and to the HC subjects as well (p<0.05). The supernatant of CaCo2 + PTG induced also an increased production of TNF α in CD patients compared to the macrophages cultured with medium and to the macrophages cultured with supernatant from non stimulated CaCo2 (p<0.05).

We did not detect differences between the two culture conditions for the other cytokines. Our experiments show that factors released by epithelial cells contribute to the effect that gliadin has on human monocytes derived macrophages and that immune cells from CD patients respond differently to these factors than cells from HC subjects. The high production of CCL22 triggered on CD patients by CaCo2 supernatant + PTG is compelling given the role that this chemokine has on recruiting Treg cells and that CD has been associated with an increased number of Treg cells. Furthermore the higher production of TNF α that we measured in the CaCo2 + PTG condition underlines that macrophages from CD patients respond differently to factors released by PTG-stimulated epithelium as compared to HC. In conclusion our data suggest that a cross talk between epithelium and immune cells represents an important component of the CD pathogenesis. Further studies are deemed to investigate the exact mechanisms and factors by which the epithelium contributes to the immune cells differentiation and function and how this may lead to the loss of tolerance in genetically predisposed individuals.

483 THE USEFULNESS OF DEAMIDATED GLIADIN PEPTIDE IN SCREENING PEDIATRIC PATIENTS FOR CELIAC DISEASE. *Michelle Gould¹, Herbert Brill^{3,4,5}, Margaret Marcon^{1,2}, Catharine Walsh^{1,2}. ¹Department of Pediatrics, University of Toronto, Toronto, ON, Canada; ²Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; ³Department of Paediatrics, McMaster University, Hamilton, ON, Canada; ⁴Department of Paediatrics, William Osler Health System, Brampton, ON, Canada; ⁵Division of Gastroenterology & Nutrition, McMaster Children's Hospital, Hamilton, ON, Canada*

Celiac disease (CD) is an autoimmune enteropathy triggered by gliadin which occurs in genetically susceptible individuals. The gold standard for the diagnosis of CD is small bowel biopsy. Screening with serologic markers is used to identify potential endoscopic candidates. The most common serologic marker used for screening is IgA anti-Tissue Transglutaminase (TTG) antibodies which have a high sensitivity and specificity for CD in IgA sufficient individuals. Antibodies to deamidated gliadin peptide (DGP) is a newer assay with studies demonstrating a diagnostic performance similar to anti-TTG. However, there is little evidence regarding the usefulness of an isolated positive anti-DGP result in pediatric patients. We sought to determine the positive predictive value of anti-DGP for biopsy proven CD in pediatric patients with negative TTG IgA testing.

Methods: A multi-center retrospective review of children referred to three centers in Ontario, Canada between January 2015 and December 2016 who had isolated anti-IgG DGP positive CD serology was completed. Data abstracted included

demographics, presenting complaint, comorbidities, family history of CD and other autoimmune conditions, BMI, hemoglobin, MVC, ferritin, IgA, anti-TTG and anti-DGP levels and duodenal histology. To be included, patients required a duodenal biopsy while on a gluten-containing diet. The diagnosis of CD was made when Marsh 3 villous atrophy was observed. The positive predictive value of isolated anti-DGP was calculated.

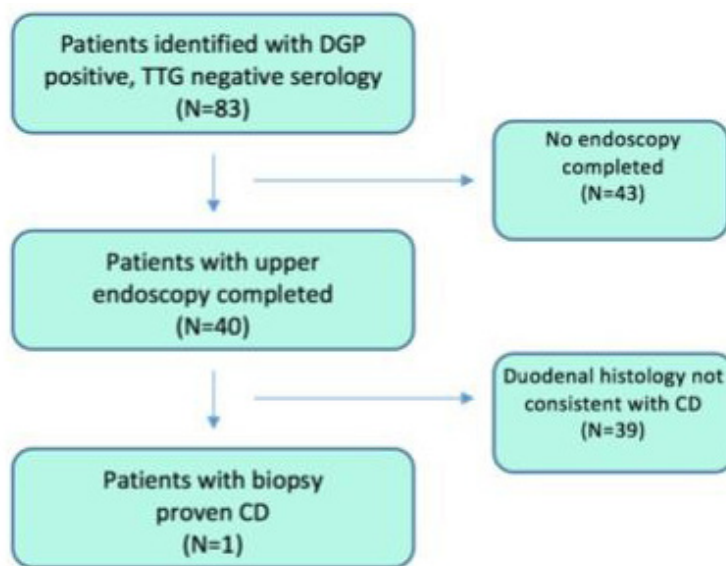
Results: A total of 83 patients were identified with anti-DGP positive, anti-TTG negative serology. Of these, 40 patients underwent endoscopy. Only 1 patient had findings consistent with CD on biopsy (Marsh 3B histology), yielding a positive predictive value of 2.5%. This patient was IgA deficient. Amongst the cohort of IgA sufficient patients (N=25), the positive predictive value of anti-DGP serology was 0%. One additional patient who was IgA sufficient had findings in keeping with Marsh 2 histology, but repeat serologic testing including TTG and DGP was negative. The most common serologic assay used was Bioplex multiple flow immunoassay (N=28) with a cutoff for a positive test of >12. The mean anti-DGP result was 89.6 (min 14.2, max >250). Five patients were found to be IgA deficient at the time of serologic testing, 25 were IgA sufficient and 10 did not have a measured IgA.

Discussion: These results suggest that in isolation, anti-DGP positive serology may not be a very specific test for CD in the pediatric population and has a poor positive predictive value for CD, especially in IgA sufficient individuals. This is the first study to systematically assess the presence of biopsy proven CD in solely anti-DGP positive pediatric patients. Our findings suggest that IgG anti-DGP testing should not be completed as part of the initial screening for CD in the pediatric population unless a compelling reason, such as IgA deficiency or age under 3 years, is present.

TABLE 1. Patient Characteristics

Variable, statistic	
Total study participants	40
Age at biopsy: median (min, max)	6.5 (1,17)
Gender: count (%)	Male: 24 (60) Female: 16 (40)
Family history of CD: count (%)	9 (22.5)
Presenting complaint leading to referral: count (%)	
	<u>Classical</u>
	Diarrhea: 1 (2.5)
	Steatorrhea: 1 (2.5)
	Failure to thrive: 5 (12.5)
	Vomiting: 2 (5)
	Constipation: 5 (12.5)
	Abdominal pain: 11 (27.5)
	Abdominal distention: 1 (2.5)
	<u>Non Gastrointestinal</u>
	Short stature: 2 (5)
	Growth failure/ poor weight gain: 4 (10)
	Iron deficiency anemia: 4 (10)
	Screening and asymptomatic: 1 (2.5)
	Screening + found to have symptoms: 3 (7.5)
Diagnosed on routine screening: count (%)	4 (10)
	<u>Reason for screening</u>
	First degree relative with CD: 3 (7.5)
	Type 1 Diabetes: 1 (2.5)
Serum IgA level: count (%)	Sufficient: 25 (62.5) Deficient: 5 (12.5) Not measured: 10 (25)

Figure 1. Summary of study patient and findings on duodenal biopsy



CONCURRENT SESSION III – MICROBIOME

Saturday, November 4

8:30am – 10:00am

- 484 LACTOBACILLUS GG MODULATES INTESTINAL GENE EXPRESSION IN A MOUSE MODEL OF INFANT GASTROINTESTINAL TRACT MICROBIOME DYSBIOSIS.** Jun Kwak², Derek Orshan², Tessa Tekieli¹, Esi Lamoussé-Smith². ¹Biological Sciences, Columbia University, New York, NY; ²Pediatrics, Columbia University Medical Center, New York, NY

Background: Antibiotics are the most commonly prescribed medication in infants and pregnant women. Antibiotic treatment of pregnant women at delivery has significant adverse effects on the initial composition and stability of the infant gastrointestinal tract microbiome (GIM) and causes GIM dysbiosis. Early life is a critical stage for GIM development and its directed priming of both GI mucosal and systemic immunity. Disruption of these intertwined processes may permanently alter mechanisms of immune homeostasis with deleterious short and long-term health outcomes. Thus, strategies that prevent GIM dysbiosis have potential clinical relevance. Probiotics are increasingly touted for their GI and systemic immune benefits. However, there are limited infant human or mouse studies evaluating defined probiotic specific effects that counteract impacts of antibiotic-driven GIM dysbiosis. We hypothesized that a single probiotic species administered directly to infant mice with GIM dysbiosis restores GIM composition and immune-related intestinal gene expression.

Methods: In our published mouse model, pregnant mice are treated with a cocktail of antibiotics for 3 days before birth of a litter to approximate the human circumstance of perinatal antibiotic administration. Notably in this model, infants are not directly treated with antibiotics. Nonetheless, the infants born to maternal antibiotic-treated (MAT) mothers exhibit profound GIM dysbiosis and susceptibility to systemic viral infection. Starting at day of life (dol) 3 and every other day thereafter, independent litters of MAT and control (CTRL) infant mice were orally fed live *Lactobacillus* GG (LGG - Culturelle®; 1e8 cfu). To distinguish tissue- and age-specific effects of treatment, ileal and colonic expression of 12 genes involved in innate and adaptive immunity were determined at dol 15 and dol 21 in MAT infant littermates relative to age matched CTRLs. 16s rRNA MiSeq and targeted qPCR analyses were performed to assess the impact of LGG treatment on the composition of the GIM.

Results: LGG treatment modulated the expression of several TLRs, MyD88, and FoxP3 in the ileum and colon of MAT infant mice. This modulation was most marked at dol 15, when the diet is transitioning from breast milk to solid chow. MAT infants demonstrated significantly decreased abundance of *Bacteroidetes spp.* and *Firmicutes spp.* in the GIM, which was only modestly corrected by LGG treatment. LGG was not consistently detected in colonic or cecal-derived stool in MAT or CTRL mice.

Conclusions: Our findings demonstrate the effect of LGG treatment *in vivo* on intestinal gene regulation of infant mice with GIM dysbiosis due to perinatal antibiotic treatment. LGG normalized expression of genes involved in innate epithelial and mucosal adaptive immunity in the intestines of treated mice. Yet, modulating gene expression *in vivo* appears to occur independent of LGG colonization in our GIM dysbiosis infant mouse model. Future aims are to use our model to: determine timing of treatment and LGG colonization in other regions of the GI tract, the effect of LGG treatment on GIM and host derived metabolites, evaluate other probiotic species, and conduct functional characterization of GI and systemic immunity modulated by probiotic treatment in MAT vs CTRL infant mice.

CONCURRENT SESSION III – GI POTPOURRI

Saturday, November 4

8:30am – 10:00am

- 485 Neurogastroenterology and Motility Prize - Clinical Science**
UTILITY OF WIRELESS CAPSULE MOTILITY IN CHILDREN WITH GASTROINTESTINAL DISORDERS. Leonel Rodriguez M.D., MS^{1,2}, Kitzia Colliard MS MA², Nicole Heinz BS.², and Samuel Nurko M.D., MPH^{1,2}. ¹Division of Gastroenterology, Hepatology and Nutrition, and ²Motility and Gastrointestinal Disorders Center, Boston Children's Hospital, Harvard Medical School, Boston, MA.

Background: Wireless capsule motility (WCM) using the SmartPill GI Monitoring System, samples and transmits intraluminal pH (to identify the location within the bowel), temperature (to identify expulsion from the body) and pressure data from a capsule at regular intervals as it travels the gastrointestinal tract. From these data gastric residency time (GRT)),

colonic transit time (CTT) and whole gut transit time (WGTT) can be assessed. We present our experience with children undergoing SmartPill testing in conjunction with Gastric Emptying Time by nuclear medicine (GET) and Sitzmark study.

Methods: Prospective study including children 8-18 yo undergoing a 4-hour standardized GET and/or a Sitzmarks study using the Metcalfe Protocol and the WCM for upper (UGI) or a lower gastrointestinal symptom (LGI) indication were included. Patients were asked to stop all medications that may affect GI motility and/or acidity 4 days prior to the study and to fast overnight the night before the study. Gastric residency time (GRT) was considered normal as per protocol previously published in healthy adults. The gastric emptying time by nuclear medicine was considered normal when retention at 4 hours was <10% as per adult normative data previously published. The WCM study was performed as per published protocol in adult patients. GRT was defined as the time interval between ingestion of capsule and the time point from which the capsule passed from the acidic antrum to the alkaline duodenum. CTT was defined as the time interval between the points of entry into the cecum and the capsule exit from the body. WGTT was defined as the time interval between capsule ingestion and its exit from the body. The capsule exit time was verified by a loss of signal and/or an abrupt drop in temperature. We compared the GET and the GRT and also the proportions of patients with normal CTT and Sitzmarks study results. We also evaluated the GET, CTT and WGTT amongst the study indications (UGI and LGI).

Results: A total of 48 children, 39 were female and median age was 16.5 years (range 8.8-17.8 years) were included. A total of 31 patients (65%) completed SmartPill testing due to a UGI and the remaining 17 patients (55%) for a LGI indication. Proportions were compared using Chi Square and medians were compared using nonparametric (Mann Whitney U) tests. A total of 23 patients (48%) completed a GET, when comparing the results both the GET and GRT were normal in 12 patients (52%) and abnormal in 13 patients (57%). Importantly, we found a discrepancy in 8 patients (35%), in 6 patients (75%) the GET was normal but the GRT was abnormal; the remainder 2 patients (25%) had an abnormal GET but a normal GRT. A total of 17 patients (35%) also completed a Sitzmarks study, both the CTT and the Sitzmarks studies were normal in 3 patients (18%) and abnormal in 6 patients (35%). A discrepancy was found in 8 patients (35%): 5 patients (63%) had a normal Sitzmarks study but an abnormal CTT whereas; the remainder 3 patients (38%) had an abnormal Sitzmarks study but a normal CTT. We found a significant difference between the median times of GET and GRT ($p=0.04$). Lastly, we found no significant difference in the GET among the 2 study indications ($p=0.21$) but we found a significantly higher CTT and WGTT in those with LGI vs. UGI indication ($p=0.004$ and 0.013 , respectively).

Conclusion: SmartPill testing can be safely performed in children with gastrointestinal symptoms. The WCM seems to be more accurate in detecting delayed gastric and colonic transit than the current gold standard studies of GET and Sitzmarks studies, respectively. Patients with UGI symptoms do not have a more prolonged GRT than does with lower LGI symptoms but patients with LGI symptoms have more prolonged CTT than those with UGI symptoms. WGTT is also significantly more prolonged in those with LGI compared to those with UGI indication, likely from the delayed CTT as the GET was no different. Larger studies are needed to further evaluate these findings.

CONCURRENT SESSION III – VIDEO ABSTRACTS

Saturday, November 4

8:30am – 10:00am

486 **ABERRANT ARTERY IDENTIFIED DURING NECROSECTOMY FOR WALLED-OFF PANCREATIC NECROSIS.** Karen Queliza, Douglas Fishman. *Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX*

Background: There are several approaches to drainage of walled-off pancreatic necrosis. Over the last several years, the paradigm has shifted away from surgical and radiological interventions to endoscopy, emphasizing the use of less invasive modalities. We present a unique case of an aberrant artery identified during endoscopic necrosectomy for walled-off pancreatic necrosis.

Case Presentation: Our patient was an 11-year-old male with EBV-positive T-cell lymphoproliferative disease, bone marrow transplant, grade 3 graft-versus-host disease, and HHV-6 encephalitis. He was initially admitted for fever, weakness, and altered mental status secondary to recurrent HHV-6 encephalitis. He later developed his first episode of acute pancreatitis, which was thought to be associated with medications or hypertriglyceridemia. His hospitalization was further complicated by Burkholderia bacteremia and pneumonia.

Evaluation for potential infectious sources led to discovery of a large peri-pancreatic fluid collection. In the absence of new symptoms and downtrending lipase, the plan was to conservatively watch the fluid collection. Two months into his

hospitalization, the patient developed increased abdominal distention requiring higher ventilator settings. At that time, a mature wall was identified around the fluid collection. We therefore proceeded with endoscopic ultrasound-guided cystogastrostomy with lumen-apposing metal stent (LAMS) placement.

Necrosectomy was planned 1-2 weeks post-stent placement, but this was postponed for an additional 2 months due to hemodynamic instability and ongoing bacteremia. Removal of some necrotic tissue and normal saline lavage ultimately revealed a large vascular structure traversing through the pancreatic collection. Subsequent CT angiography identified the vessel coursing through the collection as an arterial branch arising from the splenic artery, approximately 2.2cm from the margin of the metal stent. Interventional radiology was consulted for possible embolization. However, the procedure was deferred due to the patient's critically ill state and recurrent episodes of septic shock requiring vasopressors. Medical care was ultimately withdrawn and the patient passed away.

Discussion: A LAMS is dumbbell shape with two large flanges that allow for tissue apposition and reduced risk of migration. Risk for stent-related adverse events has been reported anywhere from 5-50%. Examples of adverse events include infection, stent occlusion, stent migration, perforation, bleeding, and buried stent syndrome.

Conclusion: Cautious debridement and prompt recognition of potential intervening structures are necessary during endoscopic necrosectomy. Interval imaging may help evaluate treatment response and minimize adverse events. Further research is needed to study pediatric patient outcomes of lumen-apposing metal stents.

487 ENDOSCOPIC AND LAPAROSCOPIC COLLABORATION FOR THE REMOVAL OF A GASTRIC TRICHOBEZOAR. Keisha Barton^{1,2}, Meredith Mason³, Sundeep Keswani^{4,2}, Richard Kellermayer^{1,2}. ¹Pediatric Gastroenterology, Hepatology, and Nutrition, Baylor College of Medicine, Houston, TX; ²Texas Children's Hospital, Houston, TX; ³Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; ⁴Pediatric Surgery, Baylor College of Medicine, Houston, TX

Introduction: Laparotomy has been the traditional and preferred method for removal of bezoars however they require surgical incision and likely a more prolonged course than other methods. Endoscopic and laparoscopic procedures alone have rarely been successful but in combination could provide significant benefit.

Case: A 12-year old female presented with sub-acute epigastric abdominal pain and bilious emesis. Her laboratory results showed elevated in her AST, ALT and GGT. There was no elevation in her conjugated bilirubin. A right upper quadrant ultrasound did not reveal gallstones but it did reveal common bile duct dilation of 5.15mm. She had continued bilious emesis and an upper gastrointestinal contrast study was performed. It revealed a moderately sized mid-gastric filling defect and dilation of the proximal duodenum. Endoscopy was planned and the surgical team was consulted. During endoscopy, a gastric trichobezoar was visualized to obstruct the pylorus. With direct endoscopic visualization, the surgical team inserted an access port (5mm trocar) into the stomach. The trichobezoar was maneuvered into the cardia for complete visualization with endoscopic retroflexion. Using graspers, the trichobezoar was completely removed. Further endoscopic advancement into the duodenum did not reveal particles of the trichobezoar to be obstructing the ampulla. This suggests there was only transient biliary obstruction. She had an uneventful post-operative course with a normal upper gastrointestinal contrast study on post-operative day 3 with subsequent advancement of her diet to clear liquids. She was tolerating a regular diet on post-operative day 6 and continues to do well. She only has two small scars from two access ports but no large incision.

488 ENDOSCOPIC ULTRASOUND (EUS) GUIDED COIL PLACEMENT FOR TREATMENT OF GASTRIC VARICES. Roberto Gugig^{1,2}. ¹UCSF, Visalia, CA; ²Stanford, Visalia, CA

Gastric varices (GVs) are seen in 18-70% of the patients with portal hypertension and are the probable source of bleeding in 10-36% of patients with acute variceal bleeding. Bleeding from GV's is often massive and often difficult to manage.

Bleeding GV's have a mortality of 10-30% and a chance of re-bleeding with glue technique is 22-37%. Emerging use of endoscopic ultrasound (EUS) not only provides a tool for confirming eradication of GV but can also serve as an innovative management strategy.

One of the endoscopic therapies for gastric varices involves direct injection of a cyanoacrylate agent (as the tissue adhesive or glue) under endoscopic guidance. This is a highly effective approach, particularly for emergency hemostasis. However, this technique may lead to efflux of glue from varix via the blood drainage route (mostly via gastro-renal shunting) into the systemic circulation and can cause pulmonary embolism. Recently, EUS-guided coiling therapy for gastric varices was developed. There are several reports showing that EUS-guided deployment of coils in the gastric varices and perforating feeding vein is more effective and safe than cyanoacrylate injection.

We report a case of a 15 year male with cryptogenic cirrhosis of liver who presented to us with recurrent bleeding GV's in spite of repeated glue injection therapy and was managed by EUS guided coil placement.

489 **ENDOSCOPIC MANAGEMENT POST-CHOLEDOCHODUODENOSTOMY FOR CHOLEDOCHAL**

CYSTS. Douglas Fishman^{1,3}, Vignesh Ramachandran³, Kevin Shah³, Frances Lee^{1,3}, Brent Keith^{5,6}, Mark Mazziotti^{2,4}.

¹Pediatric Gastroenterology, Hepatology and Nutrition, Texas Childrens Hospital, Houston, TX; ²Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; ³Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX; ⁴Pediatric Surgery, Texas Children's Hospital, Houston, TX; ⁵Gastroenterology, Hepatology and Nutrition, Children's Hospital of New Orleans, New Orleans, LA; ⁶Department of Pediatrics, LSU Health Sciences Center, New Orleans, LA

Introduction: Treatment of choledochal cysts varies based on the type (Todani classification). Of those surgically repaired a choledochojejunostomy with a Roux-en-Y or a choledochoduodenostomy are the most common.

In patients with a choledochoduodenostomy stenosis leading to obstruction with or without cholangitis has been described. We report 2 cases of biliary obstruction managed by ERCP and intraductal endoscopy.

Case 1: The first case is a 4-year-old female status post choledochoduodenostomy 15 months prior for a type I choledochal cyst. Cross-sectional imaging demonstrates a large cyst medial to the gallbladder. Clinical history is notable for intermittent epigastric pain without fever or jaundice and unremarkable physical exam. Her labs are notable for an ALT of 174 U/L GGT of 170 U/L and a total bilirubin of 0.4 mg/dL MRI demonstrated a lack of flow between the bile duct and the duodenum, consistent with an obstruction. A papillotome with a 0.021 inch wire was used to cannulate however, the cannula could not be introduced easily. A biliary dilating catheter was used beginning at 4 French extending to 7 French enabling biliary access. A radial force balloon was then introduced over a wire beginning at 4 mm up to 6 mm. Repeat cholangiogram showed some evidence of persistent cyst along with improved biliary drainage. A biliary stent was placed across the anastomosis. It was removed 2 months later and noted to have mild bile reflux gastropathy. At six-month follow-up repeat labs were normal with an ALT of 11 U/L, GGT 10 U/L and a total bilirubin of 0.5 mg/dL.

Case 2: 15-year-old male status post choledochoduodenostomy four years prior for a type IVA choledochal cyst. Clinical history is notable for recurrent cholangitis and obstruction with multiple prior ERCPs for anastomotic stricture. Two years ago had intraductal endoscopy which noted dilated dilated segments consistent with a residual cyst compounded by stenosis. The clinical history is notable for right upper quadrant pain and ultrasound with unchanged dilated ducts ALT was 2:15 and GGT was 431 and a conjugated bilirubin was elevated at 0.8 mg/dL. We balloon dilated the anastomosis to 8 mm however 8 and 9 mm endoscope could not easily pass so the 5.4 mm infant endoscope was introduced.

Using flush, suction and a 2 mm forceps, sludge and debris were removed. The patient was discharged home to complete 2 weeks of ciprofloxacin at 6 week follow-up visit and repeat labs were improved with an ALT of 30 GGT 71 and a total bilirubin of 0.5 and the patient is to be evaluated by surgery for revision.

Conclusions: In conclusion, endoscopic management of choledochoduodenostomies using ERCP and choledochoscopy is feasible. These modalities may be utilized in the setting of acute or chronic obstruction as well as acute cholangitis. Multicenter studies should be used to outline specific post-operative management and to identify at-risk patients.

490 **TECHNICAL APPROACH TO INFANT ERCP.** Quin Liu¹, Bradley Barth², Douglas Fishman³, Tom Lin⁴, David Troendle². ¹Gastroenterology, Cedars-Sinai Medical Center, Los Angeles, CA; ²UT Southwestern/Children's Health Medical Center, Dallas, TX; ³Texas Children Hospital/Baylor College of Medicine, Houston, TX; ⁴University of Cincinnati/Cincinnati Children's Medical Center, Cincinnati, OH

Endoscopic retrograde cholangiopancreatography is an advanced endoscopic procedure that can be technically challenging. Performing ERCP in infants can be even more challenging due to several factors. But the procedure is sometimes indicated in infants for both diagnostic and therapeutic purposes such as evaluating for cholestatic diseases, choledochal cyst, biliary stones, bile leaks and biliary strictures. The technical challenges to infant ERCP include the small size of the patient which usually precludes the use of the standard therapeutic duodenoscope, and therefore requires the use of the smaller pediatric duodenoscope. But the limitation to the pediatric duodenoscope are its small working and suction channel, it's metal tip that can conduct heat, limited elevator range, and the limited availability of endoscopic accessories that can fit in the smaller working channel.

This video will discuss the technical challenges to performing infant ERCP and techniques to assist with successful diagnostic and therapeutic ERCP. These will include cannulation of the bile duct, evaluation for biliary atresia, and therapy for infant choledocholithiasis.

In conclusion, infant ERCP is technically feasible and safe. But the limited tools available for infant ERCP should be considered during planning for the procedure. Development of a pediatric duodenoscope with a wider working channel and better elevator range could help alleviate some of these limitations.

491 **DUODENAL WEB REPAIR WITH ASSISTANCE OF ENDOSCOPIC VISUALIZATION.**

April Mathews¹, Reinaldo Garcia-Naveiro², Brandon Arnold¹, Avraham Schlager³. ¹Medical Education, Akron Children's Hospital, Cuyahoga Falls, OH; ²Gastroenterology, Akron Children's Hospital, Akron, OH; ³Pediatric Surgery, Akron Children's Hospital, Akron, OH

Introduction: The incidence of duodenal webs occurs approximately 1 in 10,000 to 40,000 live births, with an increased association in patients with Down's syndrome. Duodenal atresia is thought to be due to the failure of vacuolization and recanalization of the duodenal lumen at the end of the embryonic period, around the 12th week of gestation. Early diagnosis of duodenal atresia by polyhydramnios on prenatal ultrasound is possible with complete obstruction. However, delayed diagnosis is common in patients with partial obstruction, who present with vomiting, failure to thrive, or suspected reflux. The traditional surgical approach involves placement of a nasogastric (NG) tube to identify the level of obstruction, thereby directing a laparoscopic web excision. Although endoscopic visualization may increase the complexity of the procedure, it allows for more accurate localization of web and assurance of complete excision, therefore reducing possible complications.

Case Description: We describe a 1-year-old female, with a history of dysphagia, who presented with weight loss and worsening dysphagia. She was admitted for NG feeds and evaluation for gastric tube placement. Upper GI identified a partial obstruction of the duodenum, concerning for a duodenal web. She was determined to be a good candidate for a laparoscopic duodenal web excision, with endoscopic assistance. During this approach, transillumination with the endoscope is used to precisely locate the web from the serosal side of the bowel. This allows for incision at the true obstructive point. Once the web is completely traversed and excised, the endoscope is utilized to confirm a patent proximal and distal lumen.

Discussion: Duodenal webs are a relatively rare type of congenital duodenal obstruction, but can cause feeding difficulties, leading to inhibition of growth and development. These patients are at risk for significant complications if these obstructions go unrecognized. Our patient's post-operative Upper GI showed no evidence of leak or obstruction, with resolution of presenting symptoms and appropriate weight gain.

Surgical repair has advanced from open web resection and duodenoduodenostomy to more minimally invasive approaches such as triangulated laparoscopy, and more recently to the single-incision pediatric endosurgery (SIPES), endoscopic resection and endoscopic dilation. Regardless of the technique, exact location of the duodenal web remains a challenge, especially in the case of a wind-sock deformity. This is where endoscopic visualization excels over traditional nasogastric tube placement, allowing for better localization of the origin of web, while avoiding the ampulla of Vater and major duodenal papilla. Use of the endoscope for direct visualization decreases risk of misleadingly locating the web, is less challenging to navigate from a laparoscopic perspective, and is able to view the resulting patent lumen. Although SIPES and endoscopic resection are emerging surgical techniques, these have not been extensively studied, and are not widely used due to the specialized instruments required. Endoscopic visualization in correlation with laparoscopic excision is an accessible approach to improving outcomes by precise localization of a duodenal web.

492 **CONVERSION OF CHAIT CECOSTOMY TO BALLOON DEVICE UNDER ENDOSCOPIC GUIDANCE.** *Mary Boruta, Leon Reinstein. Pediatrics, Duke University School of Medicine, Durham, NC*

Antegrade continence enemas through either an appendicostomy or cecostomy can enable successful bowel management in 69% of pediatric patients with medically refractory constipation. A common form of cecostomy device is the Chait Trapdoor, which is frequently preferred due to its low profile design. However, up to 84% of pediatric patients have late complications with Chait devices including leakage, granulation tissue and unintentional dislodgement that can limit use of the device. Converting Chait Trapdoors to low profile gastrostomy balloon devices can reduce late complications in certain patients. We present using a single device enteral access dilation system under endoscopic guidance to convert a Chait Trapdoor to a balloon gastrostomy device. Through this case, we demonstrate using a guidewire to remove a Chait Trapdoor, dilate the cecostomy tract using an enteral access dilation system and insert a balloon gastrostomy device. This video highlights an endoscope assisted method of cecostomy conversion without need for fluoroscopy. Endoscopic guidance allows the proceduralist to secure the cecostomy tract, decrease injury to the colonic mucosa during stoma dilation and ensure correct sizing of the button device.

493 **HIGH-GRADE PYLORIC STRICTURE WITH GASTRIC OUTLET OBSTRUCTION (GOO) TREATED WITH SERIAL ENDOSCOPIC BALLOON DILATION.** *Racha Khalaf^{1,2}, Alyssa Woodard¹, Alexander Wilsey⁴, Emily Swan⁴, Michael Wilsey³. ¹Medical Education, Johns Hopkins All Children's Hospital, Denver, CO; ²Gastroenterology, Hepatology and Nutrition, University of Colorado, Denver, CO; ³Gastroenterology, Hepatology and Nutrition, Johns Hopkins All Children's Hospital, St Petersburg, FL; ⁴Florida State University, Tallahassee, FL*

A 17-year-old Vietnamese male presents with chronic abdominal pain, hematemesis, and a 9-kg weight loss. On admission, he was severely malnourished (z-score -5.85) and dehydrated. Laboratory evaluation revealed a metabolic alkalosis with acute renal injury.

Upper endoscopy revealed a large pyloric channel ulcer and nodular *H. pylori* gastritis. He was treated with quadruple antibiotic therapy and IV fluid hydration. He was discharged home on hospital day 5 tolerating oral antibiotics and a regular diet.

One week after discharge, he presented with progressive vomiting and inability to tolerate solid foods. UGI series showed severe narrowing at the pylorus with significant gastric outlet obstruction. Repeat endoscopy showed a high-grade pyloric stricture with over 1L of retained fluid and gastric contents. The neonatal endoscope, with an external diameter 5.9 mm, could not be advanced through the pyloric channel.

Pediatric surgery was consulted for management of his high-grade pyloric stricture. However, pyloroplasty and surgical resection was deferred by the surgery team, due to the risks involved.

We began serial endoscopic balloon dilations over a 5-month period. The diameter of the high-grade stricture was slowly increased from <6 mm to 20 mm over ten endoscopy sessions. Intra-lesional triamcinolone injections were also used in an attempt to prevent re-stricturing. Follow-up gastric biopsies and rapid urease testing for *H. pylori* were negative.

Over the course of 5 months, the patient has resumed a full, regular diet with no further vomiting. He has maintained a 10-kg weight gain.

Endoscopic therapy with serial balloon dilation is an effective therapeutic intervention for the management of high-grade pyloric strictures in pediatric patients for whom surgical therapy is not an option.

494 FORCEP-ASSISTED INTUBATION OF ICV IN PEDIATRIC COLONOSCOPY. Robert Kramer^{1,2}.

¹Pediatrics, University of Colorado, Aurora, CO; ²Pediatrics, Children's Hospital Colorado, Aurora, CO

Colonoscopy is one of the most commonly performed endoscopic procedures in pediatrics. The most common indication for colonoscopy in children is in the evaluation of inflammatory bowel disease. For this reason, intubation of the ileocecal valve to obtain biopsies of the terminal ileum is critical in performing a complete colonoscopy. ICV intubation rate has therefore emerged as one of the most important quality metrics for pediatric colonoscopy. The standard method of ICV intubation involves blind withdrawal of the colonoscope past the suspected location of the ICV orifice until a sudden change in view is identified, the scope withdrawal abruptly halted, and then the scope advanced through the valve itself. This method is limited by the poor visualization and incomplete identification of the exact location of the orifice along the ICV fold. An alternative method, using the biopsy forcep to identify, open and guide the colonoscope through the ICV is described in this video, highlighting the critical steps for success. This technique has a rapid learning curve and can help both novice and expert endoscopists decrease the time and increase the rate of successful ICV intubation in children.

495 UNSEDATED GASTRODUODENOSCOPY VIA G-TUBE STOMA FOR DIAGNOSIS OF DUODENAL WEB. Prasanna Kapavarapu¹, David Gregg⁴, Keith Oldham², Alfonso Martinez¹, Joel Friedlander³, Diana Lerner¹.

¹Pediatric Gastroenterology, Children's Hospital of Wisconsin, Wauwatosa, WI; ²Surgery, Children's Hospital of Wisconsin, Milwaukee, WI; ³Pediatric Gastroenterology, Children's Hospital of Colorado, Aurora, CO; ⁴Radiology, Children's Hospital of Wisconsin, Milwaukee, WI

We present a 10 month old female with VACTERL Association and a rare gene disorder 9p22.3 deletion. Patient underwent repair of Tracheo-esophageal fistula and esophageal atresia at 3 days of age. She had difficulty with oral feeding and a video fluoroscopic swallow study showed evidence of silent aspiration requiring parenteral nutrition. Feedings were further complicated by severe gastroesophageal reflux which eventually improved with nasojejunal feeds, however the family did not prefer this method of feeding and patient restarted slow bolus gastric feedings. Fluoroscopic study via G tube was done to evaluate for anatomic abnormalities and was normal. She underwent a Nissen fundoplication prior to discharge. At a follow-up visit, she still was not tolerating bolus feedings well and experienced frequent fussiness, discomfort and intermittent diarrhea. These symptoms improved with G tube venting. Due to recurrent hospitalizations for pneumonia she had a high sedation risk and this precluded further endoscopic evaluation of her feeding intolerance.

Gastric emptying scan showed a non-characteristic finding of accumulation of tracer in two different areas. A repeat contrast study via G tube showed contrast accumulating in two places - the stomach and then second one was what looks like a dilated duodenal bulb. On delayed images, despite contrast progressing through to the colon, the dilation persisted throughout the courses of the study concerning for obstruction at the apex of the bulb.

Due to pulmonary comorbidities and a recent pneumonia, a decision was made to attempt an unsedated gastroscopy via established 14F G tube tract. Patient was brought to the OR due to equipment and staffing support. She was given an anxiolytic doses of midazolam.

A 5.5 mm gastroscope was used to enter the stomach with mild pressure. The stomach mucosa was very friable. With further advancement, a duodenal ulcer seen which was initially mistaken to be the pylorus. The duodenal turn was challenging to

navigate but eventually could be traversed by the 5.5 mm endoscope confirming the partial nature of this obstruction. The anatomy of the small bowel was most obvious upon removal of the endoscope from the second portion of the duodenum. As the scope is withdrawn there is a narrowing, and a pseudopylorus like structure at the apex of the duodenal bulb. The first portion of the duodenum is very dilated. Removal of the endoscope from the duodenum showed the true pylorus. Our patient tolerated the procedure well and returned to the floor for further care.

This is a clear example that similarly to antral webs, duodenal webs can be partially obstructing and present with non-specific symptoms of feeding intolerance and vomiting. In partial obstruction by duodenal web it may take several months before it becomes obvious on fluoroscopy. Duodenal bulb dilatation is the key in the diagnosis of duodenal webs. The initial barium study may be normal in partially obstructing lesions or early in disease course, and an endoscopy can be diagnostic.

Unsedated gastroduodenoscopy may be considered in children who have a gastrostomy tube especially if anesthesia poses a high risk. As far as we know, this case describes the youngest patient to undergo an unsedated gastroduodenoscopy.

CONCURRENT SESSION IV – OBESITY

Saturday, November 4

10:30am – 12:00pm

496 SYSTEMIC OVEREXPOSURE TO PROTON PUMP INHIBITORS IN OBESE CHILDREN: IS LEAN BODY WEIGHT BASED DOSING THE WAY TO GO? *Valentina Shakhnovich^{1,2}, Susan Abdel-Rahman², Craig Friesen¹, Weigel Jaylene², Robin Pearce², Andrea Gaedigk², J. Steven Leeder², Gregory Kearns³. ¹Gastroenterology, Children's Mercy Kansas City, Kansas City, MO; ²Clinical Pharmacology, Toxicology and Therapeutic Innovation, Children's Mercy Kansas City, Kansas City, MO; ³Arkansas Children's Research Institute, Little Rock, AR*

Background: Childhood obesity has reached epidemic proportions, with 1 in 6 children meeting body mass index (BMI) criteria for obesity (BMI $\geq 95^{\text{th}}$ for age). Pharmacokinetic studies are severely lacking for obese children. We recently reported decreased clearance (CL/F) and increased systemic exposure (AUC_{tot}) for the proton pump inhibitor (PPI) and hepatic cytochrome P450 2C19 (CYP2C19) substrate, pantoprazole, in obese children vs. historical non-obese pediatric controls. In light of increasing concerns regarding adverse events associated with high systemic exposure to PPIs in children (e.g., osteopenia, infection, micronutrient deficiencies), we aimed to identify a pantoprazole (PAN) dosing strategy appropriate for obese children, who are six times more likely to suffer from gastroesophageal reflux disease and require PPI therapy than normal-weight peers. Given that most physiologic metabolic processes occur in lean body tissues, lean body weight (LBW) based dosing was implemented in this single-center prospective pediatric pharmacokinetic investigation.

Methods: 62 children (6-17 years of age; 39% Female), genotyped for *CYP2C19* *2, *3, *4, *17 alleles (TaqMan), received a single oral dose of liquid PAN (1.2mg/kg LBW). LBW was calculated via the Janmahasatian equation and relevant anthropometric parameters measured, including resting energy expenditure (REE) via a hand-held calorimetry device (MedGem®). Plasma PAN and PAN metabolite concentrations were measured (HPLC-UV) at 10 time-points, over 8 hours, and pharmacokinetic parameters (PK) generated via non-compartmental techniques (Kinetica v5.0). Using ANOVA, for children with at least one functional *CYP2C19* allele (n=57), select PAN PK were compared among normal-weight (BMI 10-84th for age; n=28), overweight (BMI 85-94th; n=16) and obese (BMI $\geq 95^{\text{th}}$; n=13) children, as well as among children with different *CYP2C19* activity, based on *CYP2C19* genotype. Associations between PK and anthropometric measures were explored via Spearman's correlation and regression analysis. All statistical analyses were performed using SPSS v23; $\alpha=0.05$.

Results: Using a LBW dosing strategy, systemic exposure to PAN (AUC_{tot}) was comparable in normal-weight, overweight and obese children (3.0 \pm 1.9 vs 3.3 \pm 1.6 vs 4.3 \pm 2.6 mcg*h/mL; $p \geq 0.2$). When adjusted for mg-per-kg total body weight, PAN AUC_{tot} was significantly higher in obese vs non-obese children (3.5 \pm 2.5 vs. 5.8 \pm 3.9 mcg*h/mL; $p=0.04$), with nearly 3-fold greater AUC_{tot} observed for obese *CYP2C19* intermediate metabolizers vs. normal-weight normal metabolizers (8.2 \pm 5.1 vs 2.9 \pm 1.5 mcg*h/mL; $p=0.1$). PAN apparent clearance was inversely correlated with BMI ($r^2=-0.5$; $p=0.01$) and positively correlated ($r^2=0.5$; $p=0.01$) with REE, a measure of metabolic rate that differs between obese and non-obese children (32.1 \pm 9.6 vs 25.4 \pm 7.4 kcal/kg; $p=0.03$).

Conclusions: Both *CYP2C19* genotype and obesity impact PAN disposition, such that obese *CYP2C19* intermediate metabolizers experience nearly 3-fold higher systemic exposure to PAN than normal-weight normal-metabolizers. LBW-based dosing significantly reduces systemic overexposure to PAN in obese children and may minimize their risk for adverse events associated with high-dose PPI therapy. Future pharmacokinetic-pharmacodynamic studies of PPIs in obese children are warranted. REE may be an important covariate to consider in drug metabolism.

497 **TLR4 IS RESPONSIBLE FOR METABOLIC IMPROVEMENT BUT NOT FOR WEIGHT**

REGULATION AFTER GASTRIC BYPASS. Marwa Abu El Haija¹, Yuanchao Ye², Steven McElroy³, Mohamad Mokadem². ¹Pediatric Gastroenterology, University of Iowa Hospitals and Clinics, Coralville, IA; ²Internal Medicine - Gastroenterology and Hepatology, University of Iowa Hospitals and Clinics, Iowa City, IA; ³Neonatology, University of Iowa Hospitals and Clinics, Iowa City, IA

Background: Obesity is a leading cause of morbidity and mortality in adults and children. It is linked to a state of chronic inflammation where pediatric and adult obese subjects have elevated levels of serum cytokines. Toll Like Receptor (TLR)4 is involved in innate immunity and is required for high-fat diet (HFD) induced insulin resistance and obesity-associated diabetes. TLR4 deficient mice (KO), are resistant to obesity, have decrease inflammatory markers, and improved insulin sensitivity. Animals fed HFD change their gut microbiota composition to express signs of chronic inflammation in a TLR4 dependent pathway. Roux en-Y gastric bypass (RYGB) is an effective bariatric procedure to treat obesity though not with negligible risks. The new developed gut microbiota after RYGB promotes weight loss when transferred into germ-free mice. It is not known if changes in gut microbiota after RYGB are dependent on TLR4 same as in obesity.

Hypothesis: RYGB requires TLR4 signaling to induce its metabolic effects in manner that is dependent on gut microbiota.

Methods: Diet induced obesity (DIO) was induced by 60% HFD in C57 BIK/6J mice before undergoing RYGB or sham surgery. Tissues and serum were collected at time of sacrifice (1, 3 and 10 weeks after surgery). Feces from animals were collected (during week 2 after surgery) and stored in -80 °C. Serum Cytokines were analyzed by Meso-Scale Discovery immunoassays and gene expression of TLR4 was examined in tissues using qPCR. Intestines (Jejunum) were examined for TLR 4 expression by Immunostaining and by western Blot. Feces previously collected from RYGB vs sham animals were transferred by daily gavage into lean C57Blk/6 males for 2 weeks. Food intake, body weight, and serum cytokines were measured in mice recipients of RYGB vs sham-stools. Finally, we performed gastric bypass on a group of DIO TLR4 KO mice to compare to the wild type DIO group. Food intake, body weight and glucose tolerance test were measured in wild-type and KO mice during week 3 & 4 post-surgery, sequentially.

Results: RYGB-operated mice lost more weight and body fat over time and had minimal changes in daily caloric intake compared to their sham counterparts. RYGB induced a significant decrease in feeding efficiency (gain in body weight per Kilo-joule consumed) and improvement in glucose tolerance. Serum cytokines (IFN- γ , IL-1 β , IL-4, IL-5, IL-6, KC/GRO, IL-10, and TNF- α) were not different between the two groups nor was tissue TLR4 gene expression. TLR4 expression in the jejunum of RYGB mice was significantly decreased compared to sham counterparts (by staining and by WB). Recipients of RYGB fecal material gained less body weight than sham-recipients with no significant change in food intake. TLR4 KO mice lost weight after RYGB similar to their wild-type counterparts. However they did not display similar improvement in their glucose tolerance.

Conclusion: There is no change tissue expression of TLR4 after RYGB; however, there was a significant decrease in intestine's TLR4 protein expression. Mice recipients of RYGB fecal material showed less weight gain and feeding efficiency despite consuming the same amount of food compared to sham recipients. TLR4 seems to be important for glucose but not weight regulation after RYGB.

CONCURRENT SESSION IV – EOSINOPHILIC ESOPHAGITIS

Saturday, November 4

10:30am – 12:00pm

498 **CHARACTERIZATION OF CYP2C19*17 POLYMORPHISMS AMONG CHILDREN WITH PPI RESPONSIVE ESOPHAGEAL EOSINOPHILIA AND EOSINOPHILIC ESOPHAGITIS.**

James Franciosi^{1,2}, Carolina Gutiérrez Junquera³, Sonia Fernandez Fernandez⁴, Edward Mougey⁵, Hadeel Al-Atrash^{1,2}, Andre Williams⁶, John Lima⁵. ¹Division of Gastroenterology, Hepatology and Nutrition, Nemours Children's Hospital, Orlando, FL; ²Pediatrics, University of Central Florida College of Medicine, Orlando, FL; ³Unidad de Gastroenterología Pediátrica, Hospital Universitario Puerta de Hierro-Majadahonda C, Madrid, Spain; ⁴Hospital Severo Ochoa-Leganés, Madrid, Spain; ⁵Center for Pharmacogenomics and Translational Research, Nemours Health System, Jacksonville, FL; ⁶Center for Healthcare Delivery Science, Nemours Children's Health System, Jacksonville, FL

Introduction: The mechanisms of proton pump inhibitor (PPI) medication responsive esophageal eosinophilia (PPIREE) remain poorly understood. We hypothesized that children with PPIREE and eosinophilic esophagitis (EoE) will have different PPI CYP2C19*17 pharmacogenomic profiles.

Methods: Esophageal tissues samples collected from a prospective clinical study of children using high dose PPI therapy (2mg/kg/day) to differentiate PPIREE (<15 eos/hpf) vs EoE among children who had undergone pH probe testing were selected for genotype analysis (Guitierrez-Junquera C et al., JPGN, 2016). Using existing esophageal tissue samples, formalin-fixed paraffin-embedded tissue samples were cut using a microtome and DNA was prepared using a QIAamp DNA FFPE Tissue Kit. Next, we identified *CYP2C19* alleles with particular focus on *17 without compensating loss of function alleles (*1/*17, *17/*17).

Results: Among an initial cohort of 92 children, we identified a subsample of 46 children: 32 (70%) were PPIREE and 14 (30%) were EoE. Comparing PPIREE vs EoE, basic demographics included 72% vs 57% male, mean age 10.08 (+/-3.75) vs 9.94 (+/- 4.46) years at time of initial endoscopy, 97% vs 86% Caucasian, 28% vs 21% with food allergies and 34% vs 50% with food bolus impaction. Comparing EoE to PPIREE with a logistic regression model controlling for race, sex and age, *CYP2C19**17 carriers without loss of function alleles (*1/*17, *17/*17) more likely to have EoE (OR 5.70; p value = 0.03; CI (1.22, 26.72)).

Conclusion: Children with esophageal eosinophilia who are *CYP2C19**17 carriers may need higher PPI doses to become PPIREE and maybe mischaracterized as EoE.

499 APFED Outstanding EGID Abstract Award

AGE-ASSOCIATED DECLINE IN ESOPHAGEAL AUTOPHAGY FLUX CONTRIBUTES TO FIBROSIS IN EOSINOPHILIC ESOPHAGITIS.

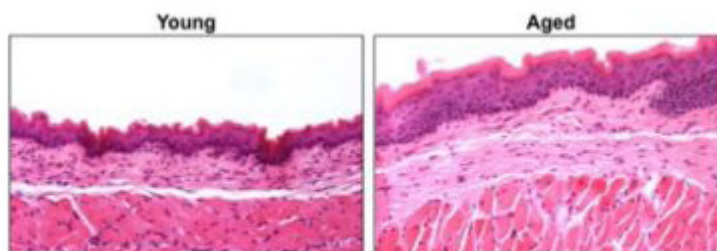
Kelly Whelan^{1,2}, Bridget Godwin^{3,5}, Benjamin Wilkins^{4,5}, Alain Benitez³, Maureen DeMarshall², Gary Falk², Amanda Muir^{3,5}, Hiroshi Nakagawa². ¹Department of Pathology and Laboratory Medicine, Temple University Lewis Katz School of Medicine, Philadelphia, PA; ²Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA; ³Division of Gastroenterology, Hepatology & Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; ⁴Department of Pathology and Laboratory Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; ⁵Department of Pediatrics, University of Pennsylvania, Philadelphia, PA

Introduction: Eosinophilic esophagitis (EoE) features esophageal eosinophilia, basal cell hyperplasia (BCH) and subepithelial fibrosis. Autophagy is activated in EoE BCH lesions to limit oxidative stress. While disease chronicity has been implicated in fibrostenotic EoE, the contribution of age-related tissue alterations to fibrotic progression remains elusive. We investigated the impact of aging upon esophageal epithelial biology and EoE disease presentation.

Methods: To determine the influence of age upon esophageal histology, we evaluated BCH and lamina propria fibrosis in biopsies from normal pediatric (<18 years) and adult (≥18 years) subjects. Expression of the basal cell marker *SOX2* was determined by qRT-PCR. Autophagy was assessed by immunoblotting and immunohistochemistry for LC3 and p62. The relationship between age and autophagy was evaluated in 3D esophageal organoids generated *ex vivo* from esophageal epithelia of young and aged mice. Autophagy flux was inhibited pharmacologically and genetically via chloroquine or *Atg7* deletion, respectively. To define the impact of age and autophagy on EoE disease presentation, we used MC903 and Ovalbumin (OVA) to induce EoE inflammation in young (<4 months) and aged (≥18 months) mice with intact or impaired *Atg7*.

Results: In normal esophageal tissue, histological evaluation failed to detect fibrosis in either children (0%; n=13) or adults (0%; n=4); however, BCH was identified in 21.4% of adults (n=15) compared to 0% of children (n=38; p<0.05). *SOX2* expression corroborated enhanced BCH in normal adults (p=0.001; n=11/group). LC3 was upregulated in BCH lesions. Accumulation of LC3 and p62 in esophageal epithelia of aged mice indicated impaired autophagy flux. Organoid formation was augmented in esophageal epithelia from aged mice as compared to their young counterparts (p<0.001; n=3) and pharmacological or genetic autophagy impairment further induced organoid formation (p<0.05; n=3). Aged mice displayed BCH and enhanced subepithelial thickness as compared to young mice (p<0.05; n=3/group) in response to MC903/OVA treatment while *Atg7* deletion facilitated enhanced fibroblast activation in young mice.

Conclusions: These studies indicate that age-associated decline in epithelial autophagy flux may facilitate fibrosis in EoE. Therapy in EoE is currently highly focused on targeting inflammatory signaling; however, our findings provide proof of concept for targeting pathways relevant to epithelial biology to limit EoE disease progression.



Young (<4 months) and aged (≥18 months) mice were treated with MC903/Ovalbumin to induce EoE inflammation. Note expansion of the subepithelium in aged mice.

CONCURRENT SESSION IV – LIVER

Saturday, November 4

10:30am – 12:00pm

500 TRENDS IN OUTCOMES BY ALLOGRAFT TYPE FOR PEDIATRIC LIVER TRANSPLANT

RECIPIENTS IN THE PELD/MELD ERA. Douglas Mogul¹, Xun Luo², Eric Chow², Allan Massie², Kathleen Schwarz¹, Andrew Cameron², John Bridges³, Dorry Segev². ¹Pediatrics, Johns Hopkins, Baltimore, MD; ²Surgery, Johns Hopkins, Baltimore, MD; ³School of Public Health, Johns Hopkins University, Baltimore, MD

Introduction: Successful pediatric transplantation is hindered by a scarcity of suitable livers. The use of technical variant donation, including split liver transplantation (SLT) and living-donor liver transplantation (LDLT), represents a potential solution. Addressing organ shortage requires further research to overcome the conflicting evidence on the outcomes of technical variant allografts.

Methods: We estimated 1-year patient and graft survival and causes of 30-day graft failure among pediatric (age <18 years) liver-only transplant recipients using the Scientific Registry of Transplant Recipients since the implementation of the PELD/MELD allocation system in March 1, 2002, until December 31, 2015. Outcomes were evaluated by allograft type with additional consideration of whether these outcomes varied in two eras (2002–2009 and 2010–2015).

Results: From 2002–2009, the 1-year patient survival for SLT was significantly worse than whole liver transplantation (WLT) (adjusted hazard ratio (aHR): 1.49; 95% confidence interval (CI): 1.11, 1.99). From 2010–2015, patient survival for SLT was equivalent to WLT (aHR: 0.86; 95% CI: 0.57, 1.31) representing a significant change between these two eras ($P = 0.03$). Patient survival was similar for LDLT and WLT in 2002–2009 (aHR: 1.22; 95% CI: 1.11, 1.99) and 2010–2015 (aHR: 0.47; 95% CI: 0.19, 1.17) and did not vary by era ($P > 0.05$). Compared with WLT, the 1-year graft survival was comparable for both SLT (aHR: 1.04; 95% CI: 0.87, 1.25) and LDLT (aHR: 0.85; 95% CI: 0.63, 1.13) and this did not vary by era. Thrombosis and primary non-function were the most commonly identified causes of graft failure, and their likelihood of causing 30-day graft failure did not change over time.

Discussion: Patient and graft survival following SLT are now equivalent to WLT. Greater use of SLT may provide an opportunity to increase organ supply for pediatric waitlist candidates and decrease pre-transplant mortality and morbidity.

501 VALIDATING THE MAYO MODEL OF PRIMARY SCLEROSING CHOLANGITIS OUTCOMES IN CHILDREN: DATA FROM THE PEDIATRIC PSC CONSORTIUM.

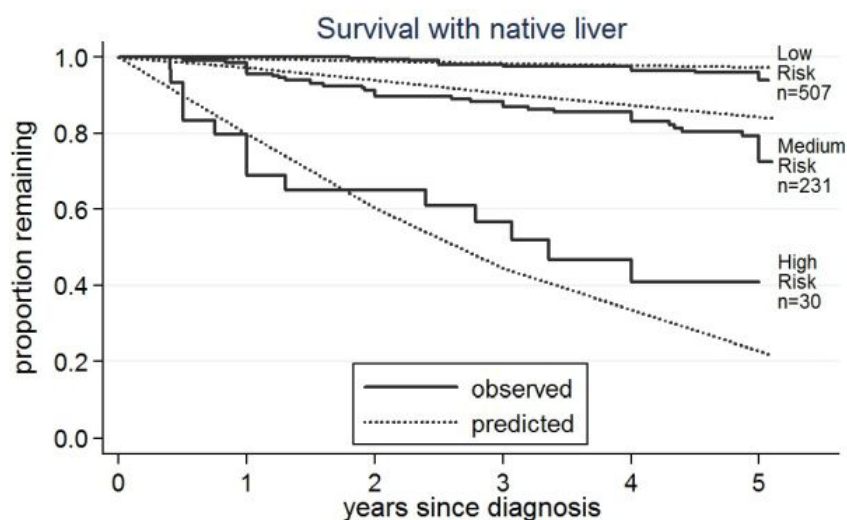
Mark Deneau¹, Reham Abdou², Khaled Alqoer³, Mansi Amin⁴, Achiya Amir⁵, Marcus Auth⁶, Fateh Bazerbachi⁷, Annemarie Broderick⁸, Albert Chan⁹, Matthew DiGuglielmo¹⁰, Wael El-Matary¹¹, Mounif El-Youssef¹², Federica Ferrari¹², Katryn Furuya⁷, Madeleine Gottrand¹³, Frederic Gottrand¹³, Nitika Gupta¹⁴, Matjaz Homan¹⁵, Binita Kamath¹⁶, Kyung Mo Kim¹⁷, Kaija-Leena Kolho¹⁸, Anastasia Konidari¹⁹, Bart Koot²⁰, Raffaele Iorio²¹, Cara Mack²², Mercedes Martinez²³, Tamir Miloh²⁴, Parvathi Mohan²⁵, Alexandra Papadopoulou²⁶, Amanda Ricciuto¹⁶, Lawrence Saubermann⁹, Pushpa Sathya²⁷, Eyal Shteyer²⁸, Vratislav Smolka²⁹, Atushi Tanaka³⁰, Pamela Valentino³¹, Raghu Varier³², Veena Venkat³³, Bernadette Vitola³⁴, Miriam Vos¹⁴, Marek Woynarowski³⁵, Jason Yap³⁶, Kyle Jensen¹. ¹Pediatric Gastroenterology, University of Utah, Salt Lake City, UT; ²State University of New York Buffalo, Buffalo, NY; ³Prince Salman NW Armed Forces Hospital, Tabuk, Saudi Arabia; ⁴University of California San Francisco, San Francisco, CA; ⁵Tel-Aviv University, Tel-Aviv, Israel; ⁶University of Liverpool, Liverpool, United Kingdom; ⁷Mayo Clinic, Rochester, MN; ⁸University College Dublin, Dublin, Ireland; ⁹University of Rochester, Rochester, NY; ¹⁰Thomas Jefferson University, Wilmington, DE; ¹¹University of Manitoba, Winnipeg, MB, Canada; ¹²Sapienza University of Rome, Rome, Italy; ¹³Lille University, Lille, France; ¹⁴Emory University, Atlanta, GA; ¹⁵University Medical Centre Ljubljana, Ljubljana, Slovenia; ¹⁶University of Toronto, Toronto, ON, Canada; ¹⁷University of Ulsan, Seoul, Korea (the Democratic People's Republic of); ¹⁸University of Helsinki, Helsinki, Finland; ¹⁹University of Manchester, Manchester, United Kingdom; ²⁰Academic Medical Centre, Amsterdam, Netherlands; ²¹University of Naples Federico II, Naples, Italy; ²²University of Colorado, Aurora, CO; ²³Columbia University, New York City, NY; ²⁴Texas Children's Hospital, Houston, TX; ²⁵Children's National Medical Center, Washington, DC; ²⁶University of Athens, Athens, Greece; ²⁷Memorial University, St. John's, Canada; ²⁸Shaare Zedek Medical Center, Jerusalem, Israel; ²⁹Palacky University, Olomouc, Czech Republic; ³⁰Teikyo University, Tokyo, Japan; ³¹Yale University, New Haven, CT; ³²Northwest Pediatric Gastroenterology LLC, Portland, OR; ³³University of Pittsburgh Medical Center, Pittsburgh, PA; ³⁴Medical College of Wisconsin, Milwaukee, WI; ³⁵Children's Memorial Health Institute, Warsaw, Poland; ³⁶University of Alberta, Edmonton, AB, Canada.

Background: No validated model to predict outcomes and risk stratify patients with pediatric primary sclerosing cholangitis (PSC) exists. Pediatricians use the Mayo Clinic revised natural history model of PSC which was created and validated with adult data. We assessed the validity of the Mayo model in a large cohort of children with PSC.

Methods: The Pediatric PSC Consortium is a research collaboration between 36 liver disease centers. For each of 781 patients we calculated predicted survival with native liver (SNL) annually using the Mayo model, which incorporates variceal hemorrhage history, patient age, total bilirubin, albumin and AST. We stratified patients into three groups based on Mayo risk score: low risk (< 0), medium risk (0-2) and high risk (>2). We compared mean predicted probability of SNL in each group using the Mayo model with observed SNL calculated using the Kaplan-Meier method.

Results: The low, medium and high risk cutoffs created three distinct populations of patients with progressively worse outcomes, logrank $p < 0.001$ between all groups. Inflammatory bowel disease was prevalent in 80 vs. 73 vs. 52%, while autoimmune hepatitis was prevalent in 29 vs. 39 vs. 52% of low, medium and high risk groups, respectively ($p < 0.001$). Large duct disease was distributed evenly among risk groups ($p = \text{NS}$). Overall, the Mayo model offered reasonable discrimination of outcomes (c-statistic of 0.77). Predicted vs. observed SNL was similar in low, medium and high risk groups at one-year (99 vs. 99, 97 vs. 98, and 80 vs. 79%, respectively), but disparate at four years (98 vs. 96, 89 vs. 79, and 33 vs. 47%, respectively).

Conclusions: The revised Mayo model of PSC closely predicts one-year survival probabilities in children. After three years the model over-estimates survival in low and medium risk groups, and under-estimates it in the highest risk groups, suggesting the need for a pediatric-specific model. Use of a Mayo risk score to triage children into general low, medium and high risk groups may be clinically helpful for pediatricians.



CONCURRENT SESSION IV – IBD NUTRITION

Saturday, November 4

10:30am – 12:00pm

502 **CREATINE TRANSPORT MEDIATES BARRIER FORMATION IN INTESTINAL EPITHELIAL**

CELLS. Caroline Hall¹, J. Lee², Louise Glover³, Sean Colgan². ¹Digestive Health Institute, Children's Hospital Colorado, Aurora, CO; ²Mucosal Inflammation Program, University of Colorado Anschutz Medical Campus, Aurora, CO; ³Merrion Fertility Clinic, National Maternity Hospital Dublin and Trinity College, Dublin, Ireland

Intestinal barrier function is integral to homeostasis in the gastrointestinal (GI) tract. The loss barrier has been implicated in a number of GI diseases, processes including inflammatory bowel disease. Sites of intestinal inflammation are characterized by significant changes in metabolic activity, where hypoxia-inducible factor (HIF) signaling predominates as an adaptive response. Our previous studies identified the creatine kinases (CK) as HIF targets and a protective role for creatine feeding in murine colitis models (PNAS 110: 19820, 2013). CK action on creatine provides an important energetic buffer in the form of phosphocreatine which can then contribute to the formation of ATP. The major creatine transporter, SLC6A8, was also identified as a HIF target gene, where hypoxia induced a nearly 10-fold increase in SLC6A8 transcript in intestinal epithelial cells (IEC, $p < 0.001$). We show here that SLC6A8 is expressed at a high level in the intact intestine, primarily on the luminal aspect of colonic IEC. Using lentiviral shRNA-mediated repression, we targeted knockdown of SLC6A8 in cultured T84

cells. This loss of transporter expression was associated with a greater than 50% decrease in the intracellular creatine pool. We demonstrated that SLC6A8 loss-of-function resulted in a nearly complete inability of cultured IEC to form barrier, as measured by transepithelial resistance and paracellular flux. This loss of barrier formation was not associated with a significant change in either cell proliferation or viability. These data suggest that a threshold level of creatine is imperative for the formation of epithelial barrier and that transport of extracellular creatine, mediated by SLC6A8, is necessary for the formation of normal epithelial barrier.

POSTER SESSION III

Saturday, November 4

12:00pm – 2:00pm

***Poster of Distinction**

ENDOSCOPY/QI/EDUCATION

503 OPTIMIZING IV FLUID USAGE IN PEDIATRIC PATIENTS WITH ACUTE PANCREATITIS.

Karen Queliza¹, Shreena Patel¹, Michael Wang¹, Ryan Himes¹, Binita Patel², Douglas Fishman¹. ¹Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX; ²Pediatric Emergency Medicine, Baylor College of Medicine, Houston, TX

Background: It is well established that early fluid resuscitation is associated with improved outcomes in patients with acute pancreatitis. The literature supports use of Lactated Ringer’s (LR) Solution compared to normal saline (NS) with respect to reducing systemic inflammatory response syndrome and inflammatory markers, as well as preventing development of pancreatitis following endoscopic retrograde cholangiopancreatography. Our institution created a hospital protocol to help guide management of acute pancreatitis beginning in the emergency department (ED).

Methods: We performed a retrospective chart review of patients who presented to Texas Children’s Hospital ED with acute pancreatitis between July 1, 2016 and December 31, 2016. To determine the efficacy of the protocol, we investigated the use of LR as initial fluid resuscitation three months before and three months after the protocol was implemented (October 1, 2016). Patient outcomes were also evaluated. To further understand the results of our chart review, we distributed an online survey of nine questions to the ED staff in May 2017, assessing their awareness of the management pathway.

Results: There were 82 ED encounters within the six-month time period (*Table 1*). Overall, 24% of patients received LR before implementation of the protocol, compared to 42% after implementation ($p=0.45$). Month-to-month data demonstrated increasing use of LR up to October with subsequent decrease as each month passed (*Figure 1*). However, the least numbers of ED visits occurred in November and December compared to prior months. When evaluating clinical outcomes of patients started on LR versus NS in the ED over the six-month period, there was no difference in length of stay between the two groups requiring admission (5.58 versus 5.34 days, $p=0.93$).

	7/1/16 – 9/30/16 (Before)	10/1/16 – 12/31/16 (After)
Number of ED Encounters	49	33
ED Use of LR for Continuous IVF (%)	24	42
Admissions (% of ED Encounters)	92	73
Average Length of Stay (Days)	5	7.7

Table 1. Comparisons between before and after implementation of the protocol.

Approximately 50% of ED physicians completed the survey. There was a slight predominance in use of NS compared with LR in the management of acute pancreatitis (54% versus 46%, respectively). When asked if they were aware that there was a protocol in place, 21% reported “Yes” and 79% reported “No.” Top answers to the question of barriers to using LR were: none (43%), no experience with LR for pancreatitis (25%), and ease of access to LR (18%).

Conclusions: Overall ED use of LR in the management of acute pancreatitis increased following implementation of the protocol. However, continued use of LR declined as time passed. Efforts need to be directed toward increasing awareness of

the pathway and identifying ways to sustain application of the guidelines to clinical practice. Additional research may include evaluation of other patient outcomes to further substantiate use of LR in the management of acute pancreatitis in children.

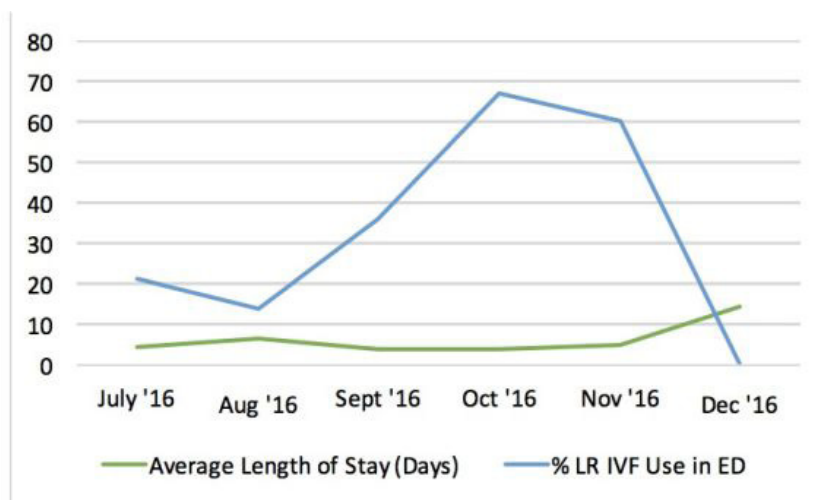


Figure 1. Percentage of LR use in ED and average length of stay over study period.

504 CLINICAL OUTCOME OF CHILDREN WITH GASTROINTESTINAL INVOLVEMENT IN GRAFT-VERSUS-HOST DISEASE AFTER BONE MARROW TRANSPLANTATION. *Nicolas Rovati¹, Gustavo Tagliaferro¹, Veronica Busoni¹, Gabriela Donato¹, Ines Ninomiya¹, Monica Makiya², Diana Altuna², Juan Santino³, Pablo Lobos⁴, Gustavo Boldrini⁵, Maria Sanchez⁵, Daniel DAgostino⁵, Marina Orsi¹.* ¹Pediatric Gastroenterology, Hospital Italiano de Buenos Aires, Capital Federal, Buenos Aires, Argentina; ²Pediatric Hemato- Oncology, Hospital Italiano de Buenos Aires, Capital Federal, Buenos Aires, Argentina; ³Patological Anatomy, Hospital Italiano de Buenos Aires, Buenos Aires, Buenos Aires, Argentina; ⁴Pediatric Surgery, Hospital Italiano de Buenos Aires, Capital Federal, Buenos Aires, Argentina; ⁵Pediatric Hepatology, Hospital Italiano Buenos Aires, Capital Federal, Buenos Aires, Argentina

Graft-versus-host disease (GVHD) is a severe complication of bone marrow transplantation (BMT), with high morbidity and mortality. The skin, gastrointestinal tract and liver are the most frequent affected organs.

Aim: Describe clinical outcome, treatment response and complications seen in the follow up of children with GVHD with gastrointestinal involvement (Gi-GVHD)

Materials and methods: Retrospective, descriptive analysis of pediatric patients with Gi-GVHD, defined according symptoms, endoscopy and histological confirmation. Steroids were the first-line treatment and in resistant cases, weekly Infliximab was added.

Results: Between 2006 and 2016, 89 pediatric patients underwent BMT. GVHD was diagnosed in 21/89 (23.6%), median age 10.3 y (1.7-19y). Cutaneous GVHD in 19/21 patients (90%), Gi-GVHD in 12/21 (57%), liver in 7/21 (33%) and ocular involvement in 2 (9.5%). Concomitant intestinal infections were ruled out. Indication for endoscopy: secretory diarrhea in 8/12, bloody diarrhea in 4/12 vomiting in 3/12, abdominal pain in 10/12. Both gastroscopy and colonoscopy were performed in 7/12, colonoscopy only in 3/12 and rectal biopsy in 2 patients. Endoscopic findings were erythema, aphthous lesions, ulcers in 7/12, and in 4/12 the mucosa had a normal appearance. An intramural duodenal hematoma complicated one patient which resolved after 2 months. 4/12 received steroids, 8/12 steroids and infliximab, unresponsive in 5/8. Mortality was 42% in those with single organ compromise, but raised to 60% in multiorgan organ involvement.

Conclusion: Despite the inherent risks, endoscopic procedures are essential to confirm Gi-GVHD diagnosis and biopsies should be performed even in those with normal appearance to start treatment and enhance recovery. Available options show low percentages of effectiveness so new alternatives are necessary to diminish morbidity and mortality.

505 IN-HOSPITAL PEDIATRIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IS ASSOCIATED WITH SHORTER HOSPITALIZATION FOR CHILDREN WITH CHOLEDOCHOLITHIASIS. *Patrick Bonasso¹, Lori Gurien¹, Jessica Staszak², Marie Saylor¹, David Troendle³, Elaine Odiase³, Lauren Lazar³, Wenly Ruan³, Bradley Barth³, Regan Williams², Melvin Dassinger¹.* ¹Surgery, University of Arkansas for Medical Sciences, Little Rock, AR; ²Surgery, University of Tennessee Health Science Center, Memphis, TN; ³Pediatrics, University of Texas Southwestern Medical Center, Children's Medical Center, Dallas, TX

Background/Purpose: Children with choledocholithiasis are frequently managed at tertiary children’s hospitals that do not have available endoscopic retrograde cholangiopancreatography (ERCP) proceduralists. Lack of equipment and experience may lead to treatment delays. We hypothesized that patients treated at hospitals without ERCP proceduralists would have a longer length of hospital stay than those treated where ERCP proceduralists are available.

Methods: Charts for patients who underwent cholecystectomy and ERCP at three tertiary children’s hospitals between July 1, 2006 and June 30, 2016 were reviewed. Trauma and complicated pancreatitis patients were excluded. Comparisons between patients requiring transfer for ERCP (Transfer) and those remaining in the admitting facility (No transfer) were made using Wilcoxon rank-sum tests for continuous variables and Fisher’s exact tests for categorical variables.

Results: One hundred and eighteen children underwent ERCP for possible choledocholithiasis during the study period: 79 (67%) in the transfer group and 39 (33%) in the no transfer group.

Median length of stay was longer in the patients requiring transfer (7 versus 5 days, $p=0.0006$). One third (34%) of the transfer patients had magnetic resonance cholangiopancreatography (MRCP) compared to only 8% of the patients that did not require transfer ($p=0.0016$).

Among patients who underwent ERCP prior to cholecystectomy, 75% required (66/88) transfer and 25% (22/88) did not. In these patients, a significant difference in median hospital LOS ($p=0.0002$), days from admission to ERCP ($p=0.0150$), and days from ERCP to surgery ($p=0.0083$) were identified (Table).

No significant differences were found in patients who underwent ERCP after cholecystectomy ($n=30$).

Conclusion: Overall median LOS was significantly shorter for patients who underwent ERCP at the admitting facility. Patients who underwent ERCP prior to cholecystectomy at hospitals without available ERCP proceduralists incurred longer LOS, increased MRCP usage, and hospital transfers, all of which affect resource utilization. Alternative strategies, such as pre-ERCP cholecystectomy with intraoperative cholangiogram may be beneficial.

Table

Comparison of hospital length of stay, time to ERCP, and cholecystectomy when ERCP performed prior to cholecystectomy.

	Transfer (N=66) 25th%; Median; 75th%	No transfer (N=22) 25th%; Median; 75th%	p-value
Hospital LOS	6;7;8	4;5;6	0.0002
Admission to ERCP	2;2;4	1;1;3	0.0150
ERCP to Surgery	1;2;4	1;1;2	0.0083

507 QUALITY INDICATORS OF UPPER AND LOWER DIGESTIVE ENDOSCOPY IN CHILDREN : A SYSTEMATIC REVIEW AND META-ANALYSIS. Astrid Bicamumpaka Shema^{1,2}, Anne-Sophie Groleau^{1,2}, Prévost Jantchou^{1,2}. ¹Gastro-enterology, CHU Sainte-Justine, Montréal, QC, Canada; ²CHU Sainte-Justine Research Center, Montreal, QC, Canada

Background : Digestive endoscopy is a useful diagnostic and therapeutic tool for children with intestinal diseases. However, unlike literature on adult population, little data exist in the pediatric literature regarding quality indicators in digestive endoscopy. Many adult quality indicators are not applicable to children. The aims of review of the literature and meta-analysis were: 1) to synthesize published data on the practice of pediatric digestive endoscopy 2) to identify potential quality indicators specific to children.

Methods: A systematic search of the literature in English and French, from 1980 to 2016, was performed via the EMBASE, Medline and PubMed databases. The data extracted were related to indications, bowel preparation, sedation, wait times, completion of the procedure, complications and outcomes (macroscopic and microscopic).

Results: Of the 301 articles identified, 23 articles were selected. The choice of sedation or general anesthesia was mainly related to the patient’s condition, the endoscopist’s preference or team’s habits. The quality of bowel preparation was

unsatisfactory in 17,3% ± 7,6% of the cases (n = 2 studies). Caecum and ileum intubation rates were respectively 88.7% ± 2.3% and 83.9% ± 0.2% (n = 3 studies). Oesogastroduodenoscopies (OGDs) were macroscopically normal in, 51.8% ± 4.3% of cases (n = 6 studies) and 47,8% ± 11,8%, microscopically normal (n = 2 studies). Regarding colonoscopies, 41,6% ± 1,7% (n = 4 studies) and 40,0% ± 10,0% (n = 2 studies) were respectively macroscopically and microscopically normal. The mean rate of complications was 3.4% ± 1.1% (n = 4 studies) for OGD and 2.5% ± 0.7% (n = 5 studies) for colonoscopies. It was also noted that 74.0% to 99.7% of endoscopies had an appropriate indication (n = 3 studies).

Conclusion: The rate of complications in pediatric digestive endoscopy is similar between studies and most of them are benign complications (eg. desaturations). The outcomes between macroscopic and microscopic analysis were high, suggesting either an inappropriate application of the current indications or a need for revision of these indicators. A success rate of colonoscopy reaching the caecum greater than 80% could be an objective to be achieved. The quality of the bowel preparation and the rate of cancellations are an other important criteria but few studies reported these outcomes. Likewise, there was few studies on wait times and the results were significantly different.

508 HANDS-ON SIMULATION AS A VALUABLE TOOL FOR ENTERAL TUBE FEEDING EDUCATION IN PEDIATRIC STUDENTS AND RESIDENTS. Rachel Herdes¹, Patricio Arias², Taylor Arnold³. ¹Pediatrics, Louisiana State University Health Sciences Center, New Orleans, LA; ²Pediatric Gastroenterology, Children's Hospital of New Orleans, New Orleans, LA; ³Mathematics, University of Richmond, Richmond, VA

Background: Medical education has traditionally involved lecture-based learning with a recent trend toward case-based learning techniques. A few studies have suggested that simulation or active participation cases are equally beneficial, if not preferred, by physicians-in-training. Evaluation of generation Y has found that this cohort values “hands-on” experiences over traditional lecture practices.

Methods: Pre and Post simulation lecture surveys were completed by pediatric medical students and residents prior to and after a 1 hour, multi-station simulation lab teaching feeding tube education. Survey questions involved 5-level Likert scale ratings to comfort level of multiple feeding tube topics. Responses were collapsed into binary categories (comfortable vs uncomfortable). Two-sample t-test was conducted, with Holm's method used to adjust p-values and using a significance level of 0.05.

Conclusions: For all survey questions, the raw portion of responses indicating comfort increased, though not all were statistically significant. Pediatric residents showed statistically significant improved comfort post-simulation in placing NG tubes (p<0.018), changing out mickey button G tubes (p<0.0001), troubleshooting G tube problems (p<0.0001), and talking to their patients about G tube care (p<0.0001). Pediatric medical students showed significant improved comfort in changing out mickey button G tubes (p<0.002), changing out bard G tubes (p<0.04), troubleshooting G tube problems (p<0.0001), talking to their patients about needing a feeding tube (p<0.022), and talking to their patients about G tube care (p<0.0001).

Discussion: Hands-on simulation lecture was successful in improving comfort level on feeding tube education for the Pediatric resident and medical student population. This teaching technique should be considered for utilization for teaching medical education to Generation Y.

509 IMPLEMENTATION OF AN ASYNCHRONOUS PILOT PEDIATRIC E-CONSULT PROGRAM. Rajitha Venkatesh. Pediatric Gastroenterology, MGH, Cambridge, MA

Electronic consultation (e-consults) have emerged as a promising approach to enhance provider communication and have demonstrated feasibility and facilitated timely specialty advice in a variety of settings. E-consults are alternatives to traditional outpatient pediatric gastroenterology visits in which a patient physically presents to the office for an in-person visit. In the literature, studies have demonstrated that e-consults provide responsive high-quality care, reduce total costs of care as well as high rates of satisfaction among both providers and patients. Nevertheless, information about e-consults in pediatrics is limited. We sought to establish an e-consult program in pediatric subspecialties and assess preliminary results. At MassGeneral Hospital for Children (MGHfC), a tertiary pediatric center, e-consults to outpatient pediatric subspecialties enable primary care providers (PCP) to submit patient-specific clinical questions to a specialist. MGHfC is part of the Partners Healthcare network, an integrated health care network and is part of several accountable care organization (ACO) contracts with a shared electronic medical record system. Structured e-consults are sent to a pediatric subspecialist who reviews the electronic data and imaging as appropriate and then provides detailed clinical recommendations to the referring doctor. The pediatric gastroenterologist is reimbursed a flat fee through the ACO. To assess the results of this pilot project, medical records were individually reviewed by a pediatric gastroenterologist. From April 2015 to April 2017 we implemented e-consult referrals by MGHfC PCPs. PCPs received recommendations within 48 hours of their referral request. The patients referred for e-consult ranged from 2 months to 18 years of age. The subspecialist referrals highest in demand were pediatric dermatology and pediatric gastroenterology. Recommendations included reassurance, indications for further testing as

well as medication and next steps. No clinical adverse events related to the e-consult were detected. Even with our initial implementation, we were able to demonstrate feasibility of a pediatric subspecialty e-consult pilot program within a large ACO. An e-consult program allows efficient, high-quality recommendations to PCPs for a variety of referral questions. This potentially results in significant cost savings by avoiding a traditional in-person visit. As a pilot study, our next steps aim to expand this to other pediatric subspecialties as well as look at provider satisfaction and cost analysis of our program.

510 TELEMEDICINE ENABLES CARE FOR GEOGRAPHICALLY DISPERSED PATIENTS.

Robert Cornfeld. Department of Pediatrics, Landstuhl Regional Medical Center, APO, MD

Background: Telemedicine is an emerging tool for patients, physicians, and medical systems, offering the ability to revolutionize the delivery of medicine. Pediatric Gastroenterology Services tend to be located in urban academic centers or Children's Hospitals, complicating access to care for children living in remote areas. Telemedicine may bridge this gap, enabling tertiary medical facility based providers to expand their care beyond their immediate footprint. Telemedicine additionally offers the ability to reduce work time missed by parents to take care of their sick child, the number one reason why parents are absent from work.

Landstuhl Regional Medical Center (LRMC) is a tertiary referral center for over 200,000 military dependents in Europe. In September 2017 a Pediatric Gastroenterology service was established at LRMC, with the mission to expand Pediatric Gastroenterology services to military dependents across Europe, many of whom live in remote medically underserved areas. Telemedicine offered an avenue for the initial evaluation and continued care for this geographically dispersed population. This study seeks to delineate the characteristics and medical conditions of Pediatric Gastroenterology patients seen via Telemedicine, determine the utility of Telemedicine, and finally determine cost savings for travel within a single medical system.

Methods: 117 consecutive Telemedicine visits by a single Pediatric Gastroenterologist at Landstuhl Regional Medical Center (LRMC) in Landstuhl, Germany were reviewed. The same physician assessed the utility of the Telemedicine visit, along with the quality of the Telemedicine connection using a standardized connectivity scale. Finally, travel cost savings and missed parental work days avoided were calculated.

Results: 70 patients with an average age of 7 years (1 month to 21 years) were seen for 117 patient visits (63 initial visits, 54 follow-up visits) via Telemedicine from September 2016 through April 2017. Patients were seen from Germany (88%), Italy (6%), Belgium (5%), Zambia (1%), and Tajikistan(1%).

Telemedicine streamlined patient care for 44% of patients. 22% of patients underwent a trial of care before an in-person visit, and 19% of initial patient visits required no further care after their initial Telemedicine evaluation. 12% of telemedicine visits directly lead to an endoscopic procedure.

The most common diagnosis from a Telemedicine visit was for Eosinophilic Esophagitis (15%); 31% of patients were diagnosed with a functional condition via Telemedicine.

The use of Telemedicine in lieu of an in-person visit saved Regional Health Command-Europe \$64,643 in travel reimbursement costs and 190.5 lost parental work days were avoided by using Telemedicine rather than in-person visits. Connectivity was primarily 'good' (66%), followed by 'fair' (27%), 'excellent' (3%) or 'poor' (3%).

Discussion: Telemedicine improves access to care for Pediatric Gastroenterology patients by streamlining in-person visits for geographically dispersed patients. Specifically, this study demonstrates how Pediatric Gastroenterologists can streamline patient care through Telemedicine by ordering additional laboratory testing before a patient is seen in person, and in coordinating for a procedure for a patient who is traveling from afar, limiting time away from home and work for families.

Although streamlining care was the primary utility of Telemedicine, the greatest benefit for Pediatric Gastroenterology patients may lie in the care of children with chronic medical conditions. Children with eosinophilic disorders are high utilizers of specialty care, and in this study they composed 18% of all Telemedicine visits. Enabling these visits to take place in from the comfort of their home diminishes missed school time for children, missed work time for parents, and overall expedites patient care. Additionally, a surprising amount of patients required no further follow-up beyond an initial consultation. Connectivity was overall satisfactory with few visits unable to be completed due to connection difficulties; with continued improvements in connectivity, the quality of connections will increase with time. Finally, there are significant savings in both the direct financial costs for travel and in decreasing parental absenteeism for their child's illness.

Future areas for research include comparing outcomes from patients seen via Telemedicine versus in-person care, and in further identifying patient populations best served and not served by this modality of care. As geographically dispersed patients become increasingly 'on-line', Telemedicine offers an avenue for Pediatric Gastroenterologists to expand their reach beyond notional boundaries.

511 MULTICENTER EVALUATION OF PROCEDURAL VOLUME IN ACADEMIC PEDIATRIC GASTROENTEROLOGY CENTERS.

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Background: Advances in endoscopic techniques and smaller endoscopic equipment has lead to an increase in the volume of diagnostic and therapeutic endoscopy performed in children. There are no readily available databases to determine the relative frequency of these procedures or to track quality metrics across institutions.

Objectives: To assess the annual volume of endoscopic procedures performed in pediatric centers and extrapolate the frequency of diagnostic procedures performed by one clinical FTE.

Methods: A Redcap survey was used to query pediatric endoscopy directors from among members of the NASPGHAN Endoscopy and Procedures Committee. Data from the 2016 calendar year for specific diagnostic and therapeutic procedures was compiled in aggregate and calculated per clinical FTE for each of the centers that participated.

Results: A total of 7 academic centers participated in the survey. There was a mean of 10.4 clinical full time equivalent (cFTE) per center surveyed (range 4.35-17.5), with a total of 15,242 endoscopic procedures performed (mean 2177.4 endoscopies per center, 212.4 endoscopies per cFTE). Of these, 1559 were interventional (10.23%) with range of 4.8 to 13.5%. Of the diagnostic procedures there was a mean of 1422.6 +/- 687.0 esophagogastroduodenoscopies (EGD), 473 +/- 224.5 colonoscopies, 59.3 +/- 53.6 flexible sigmoidoscopies, 29.7 +/- 33.0 wireless capsule endoscopies, 41.9 +/- 42.5 percutaneous liver biopsies, 79.0 +/- 83.7 pH/Impedance probe studies and 8.8 +/- 10.8 rectal biopsies. Of the therapeutic procedures there was a mean of 12.7 +/- 13.7 EGD's for control of non-variceal bleeding, 12.6 +/- 8.5 EGD's for variceal bleeding, 35.6 +/- 38.0 EGD with foreign body removals, 62.8 +/- 52.3 EGD with dilations, 30.6 +/- 31.1 ERCP's, and 31.7 +/- 36.4 percutaneous endoscopic gastrostomy placements (PEG). By provider there was a mean of 139.4 +/- 39.3 diagnostic EGD's/cFTE, 46.9 +/- 14.0 colonoscopies/cFTE and 6.2 +/- 5.6 flexible sigmoidoscopies/cFTE. Of the seven centers in the survey, three (42.9%) were utilizing a formal system to track post-procedural adverse events. In terms of motility studies, 71.4% were performing one or more types of manometry.

Conclusion: The volume and breadth of diagnostic and therapeutic procedures performed in pediatric gastroenterology centers is significant and continues to expand. Procedures for control of bleeding, however, are rare and may require ongoing training. Development of a national database for pediatric GI endoscopy would provide program directors and hospital administrators with tools necessary for clinical benchmarking and development of quality and safety programs. Accurate assessment of pediatric endoscopy volume would also increase industry partner awareness and product development for this market.

Type	Procedure	Total	Mean +/- St Dev	Range	Mean/cFTE +/- St Dev
Diagnostic	EGD	9958	1422.6 +/- 687.0	624-2365	139.4 +/- 39.3
	Enteroscopy	46	6.6 +/- 7.0	0-19	0.60 +/- 0.60
	Wireless Capsule Endoscopy	208	29.7 +/- 33.0	0-98	2.6 +/- 2.9
	Colonoscopy	3311	473.0 +/- 224.5	221-773	46.9 +/- 14.0
	Flexible Sigmoidoscopy	415	59.3 +/- 53.6	7-128	6.2 +/- 5.6
	Liver Biopsy	293	41.9 +/- 42.5	0-102	3.9 +/- 4.2
	pH/ Impedance probe	553	79 +/- 83.7	0-245	N/A
	Rectal Biopsy	53	8.8 +/- 10.8	0-24	0.61 +/- 0.90
	Esophageal Manometry	99	14.1 +/- 19.9	0-57	N/A
	Antro-duodenal Manometry	18	2.6 +/- 4.2	0-10	N/A
	Colonic Manometry	78	11.1 +/- 20.7	0-53	N/A
	Anorectal Manometry	241	34.4 +/- 33.1	0-72	N/A
	TOTAL DIAGNOSTIC ENDOSCOPY	13269	1896.2 +/- 886.8	845- 3063	186.3 +/- 50.3
Interventional	EGD/ Nonvariceal Bleeding	89	12.7 +/- 13.7	1-38	1.1 +/- 1.2
	EGD/ Variceal Bleeding	88	12.6 +/- 8.5	4-29	1.2 +/- 0.6
	EGD/ Foreign Body	249	35.6 +/- 38.0	8-106	3.1 +/- 3.0
	EGD/ Dilation	440	62.9 +/- 52.3	7-137	5.8 +/- 3.8
	ERCP	214	30.6 +/- 31.1	0-85	N/A
	Endoscopic Ultrasound	66	9.4 +/- 20.2	0-55	N/A
	EGD/ PEG	222	31.7 +/- 36.4	0-101	31.7 +/- 36.4
	EGD/ GJ placement	102	14.6 +/- 18.6	0-48	1.4 +/- 2.0
	Colon/Polypectomy	127	18.1 +/- 12.1	6-43	1.9 +/- 1.1
	Colon/ Bleeding control	13	1.9 +/- 2.0	0-5	0.16 +/- 0.13
	Colon/ Dilation	15	2.1 +/- 2.4	0-7	0.20 +/- 0.18
TOTAL INTERVENTIONAL ENDOSCOPY	1559	222.7 +/- 157.6	52-426	19.8 +/- 9.4	
TOTAL ENDOSCOPY	15242	2177.4 +/- 1068.3	929-3722	212.4 +/- 61.5	

513 THE UTILITY OF UPPER ENDOSCOPY IN ADOLESCENTS WITH OBESITY PRIOR TO VERTICAL SLEEVE GASTRECTOMY. *Ruben Colman¹, Jennifer Woo Baidal², Jeffrey Zitsman³, Ali Mencin².*
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Background: The prevalence of adolescents who qualify for bariatric surgery is rapidly increasing in the United States. Esophagogastroduodenoscopy (EGD) often is performed to evaluate for mucosal and anatomical abnormalities prior to vertical sleeve gastrectomy (SG). However, no study has evaluated how pre-bariatric EGD in adolescents impacts clinical management or outcome.

Objective: To test the hypothesis that pre-bariatric EGD among adolescent bariatric surgery patients is associated with infrequent changes in pre-operative management or post-operative outcome.

Methods: We performed a retrospective cohort study of adolescents undergoing evaluation for bariatric surgery candidacy between 10/1/2014 to 9/30/2016 at a single pediatric tertiary care center. Through review of the electronic medical record, we obtained demographic and anthropometric data in addition to EGD findings, biopsy pathology, gastrointestinal symptoms and surgical outcomes. An EGD was considered abnormal if either abnormal gross findings or abnormal pathology was reported. Patients were followed until a 6-week post-op visit. The primary aim was to determine if an abnormal endoscopy in a pre-bariatric EGD resulted in 1) any medical or surgical interventions or 2) cancellation of the bariatric procedure. A secondary aim was to examine demographic and clinical predictors of an abnormal EGD. For bivariate statistics, chi-square and Fisher exact tests were used for categorical variables. After assessing for normality, t-tests or the Mann-Whitney U test were used for continuous variables. Odds ratios were calculated with logistic regression analyses.

Results: Of 134 patients presenting for evaluation, 94 (70%) underwent pre-operative EGD and were eligible for inclusion. Median age was 16 years, 73% were female, 30% non-Hispanic white, 13% non-Hispanic black, 48% Hispanic and 9% other. Fifty-one (54%) had a normal EGD and 43 (46%) had EGD abnormalities including 4 with a possible hiatal hernia (none visualized during SG), 3 with a donut-shaped appearance due to a prior gastric band (without further intervention) and 36 with mild mucosal abnormalities. Among those with EGD abnormalities, 22% received an intervention while none had modification of their bariatric surgery. The most common post-EGD interventions were PPI administration (n=10) and H. pylori eradication (n=11). In models examining predictors of EGD abnormalities, baseline GI symptoms [odds ratio (OR) 4.9 (95% CI: 1.6,15.0); p<0.001] were the only predictor of EGD abnormalities. No demographic or clinical factors predicted likelihood of a post-EGD intervention. An abnormal EGD did not correlate with any post-operative complications.

Conclusion: In this cohort of adolescents undergoing evaluation for SG, 46% had an abnormal EGD, of which 22% received a medical intervention. Symptoms were the only predictor of EGD abnormalities. Abnormal EGD findings did not result in modification of any bariatric surgery performed.

514 THE AFFECTS OF MINIMIZING PHLEBOTOMY BLOOD VOLUME ON ANEMIA IN PEDIATRIC HOME PARENTERAL NUTRITION PATIENTS. *Ruth Go¹, Joshua Wathen², Rebecca Estanque¹, Kristine French¹, Jenifer Pelster¹, Khiet Ngo¹.*
¹Pediatrics, Loma Linda Children's Hospital, Loma Linda, CA; ²Loma Linda University School of Medicine, Loma Linda, CA

Background: Anemia is a common morbidity in many pediatric patients who require home parenteral nutrition (HPN). One of several factors that likely increases the risk for anemia in this patient population is frequent phlebotomy as part of routine monitoring. At Loma Linda University Children's Hospital (LLUCH) the majority of pediatric patients on HPN have monthly labs drawn as part of the standard monitoring protocol. In June of 2016 LLUCH began using micro-tubes for routine blood sampling. Traditional phlebotomy tube on average require 15mL of blood to be withdrawn. In contrast, micro-tubes require less than 2mL for the same tests. The purpose of this study is to understand the effect of phlebotomy blood volume minimization strategy in reducing anemia in pediatric patients requiring HPN.

Methods: This is an IRB-approved retrospective study. Since June 2016 the HPN program at LLUCH began using micro tubes for routine laboratory monitoring. Standard clinical data (age, gender, weight) and laboratory data (CBC, ALT, bilirubin, albumin) were collected prior to June 2016 and after September 2016. The primary outcome of this study was to compare the change in hemoglobin concentrations before and after the use of micro-tubes. The secondary outcome was to estimate the prevalence of anemia for age before and after use of micro-tubes for phlebotomy. Statistical analysis performed: standard descriptive analysis, t-tests, and bivariate analysis. P-value of <0.05 was considered statistically significant. The sensitivity and specificity of red cell mean corpuscle volume (MCV) and red cell distribution width (RDW) in detecting anemia for ages was calculated.

Results: 38 subjects with a mean age of 6.1 years (SD +/- 4.2 years) were included in the analysis. All patients had been on HPN for at least 3 months. The prevalence of anemia for age prior to micro-tube implementation was 22%, and 14% after

micro-tube use. For the primary outcome, the mean difference in the hemoglobin of subjects before and after implementation was +0.62g/dL (CI = 0.21 to 1.02; p=0.004). The prevalence of anemia for age prior to micro-tube implementation was 22%, and 14% after micro-tube use. A secondary bivariate analysis found no correlation between anemia for age and the following factors: age, gender, weight, ALT, and albumin level. The sensitivity of MCV and RDW for detecting anemia was 75% (CI=34.9 to 96.8%) and 91.6% (CI=61.5 to 99.8) respectively. The specificity of MCV and RDW for anemia was 48.3% (CI=29.5% to 67.5%) and 61.5% (CI=40.6% to 79.8%) respectively.

Conclusions: 1) Strategies such as micro-tubes to reduce the volume of routine blood draws in pediatric patients requiring chronic HPN may reduce the prevalence of anemia and improve their hemoglobin levels. 2) Age, weight, liver enzyme levels were not found to be independent risk factors for the presence of anemia for age. 3) RDW may be a more sensitively marker for anemia, and thus should be followed closely in conjunction with CBC and MCV 4) Limitations: single center study may limit the applicability of findings to other centers, and the short duration of monitoring after institution of micro-tubes may underestimate the mean change in hemoglobin concentration.

521 UTILIZING PATIENT ENGAGEMENT TO DEVELOP INTEGRATED MENTAL HEALTH CARE FOR PEDIATRIC GASTROENTEROLOGY: PHASE I OF THE DECADES STUDY.

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Background: Depression and anxiety are common in children with gastrointestinal (GI) disorders and can negatively impact children's physical health, adherence, and quality of life. Despite this, few empirical studies exist that describe the identification and management of mental health concerns in the pediatric GI subspecialty clinic.

Objectives: To determine patient and parent attitudes toward depression, anxiety, and mental health screening during GI visits, and to determine patient and parent preferences for communication of results and referral to mental health providers after a positive screen.

Methods: Patient engagement methods were utilized to assess patient and parent preferences. Families participated in individual interviews and group activity sessions to provide feedback on the process for providing mental health screening and consultation in the pediatric GI clinic.

Results: Overall, patients and their parents found integrated mental health care to be acceptable in the subspecialty setting. Patients' primary concerns were for the privacy and confidentiality of their screening results. Both patients and their parents emphasized the importance of mental health services not interfering with the GI visit and collaboration between the GI physician, psychologist, and primary care provider.

Conclusions: Patients and their families are open to integrated mental health care in the pediatric subspecialty clinic. The next phase of the DECADES Study will translate patient and parent preferences into an integrated mental health care system and test its efficacy in the pediatric GI office.

523 ANEMIA PREVALENCE, SCREENING, AND TREATMENT IN PATIENTS WITH PEDIATRIC INFLAMMATORY BOWEL DISEASE IN THE UNITED STATES.

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Background: Anemia is a complication of inflammatory bowel disease (IBD) in 40-80% of pediatric and adolescent patients. It is associated with low quality of life scores and poor developmental outcomes. Standards for monitoring and treatment of children with IBD and anemia are inferred from adult guidelines. We have a limited knowledge about adherence to guidelines in children. This study examines anemia prevalence, screening, and treatment using data obtained from a commercial database encompassing the years 2010 to 2014.

Aims: We aimed to examine the prevalence and subtype of anemia, prevalence of annual screening for anemia, and prevalence of treatment in patients with, and we identified associated demographic and clinical factors.

Methods: This is a retrospective study of children with IBD whose commercial claims were captured in the MarketScan database, 2010-2014. Patients aged 1-21 with at least two inpatient or outpatient encounters for IBD with available lab and pharmacy data were included. Anemia was defined by pediatric WHO criteria. Anemia screening was determined using the proportion of the population with a hemoglobin or hematocrit result available. Anemia treatment was determined using the proportion of the population treated with iron. We gathered demographic and clinical factors and determined associations with anemia and screening using logistic regression models.

Results: The eligible population included 2,449 children and adolescents including 64% with Crohn's disease (48% female) and 36% with ulcerative colitis (54% female). Mean age was 17. During the 2-year median follow-up period, 83% of individuals were screened for anemia. The prevalence of anemia among those screened was 47%. Factors associated with screening included ≥ 5 outpatient visits and age 11-17 vs. 18-21, being treated with biologic or immunomodulatory medications. Factors associated with anemia included female sex, history of inpatient admission, ≥ 5 outpatient visits for IBD, elevated CRP, and age 11-17 vs. 18-21. Users of biologics or immunomodulators were less likely to have anemia. 12% of the patient population was prescribed iron during the study period (4% intravenous, 8% oral).

Conclusions: This was the largest cohort of pediatric and adolescent patients examined for anemia. 15% of patients were not screened for anemia and only 12% of patients with anemia were treated. The limited adherence to annual anemia screening and treatment in this cohort points to opportunities for quality improvement. The low levels of treatment may reflect missing inpatient data or lack of prescriptions for oral iron, though the low prevalence of outpatient iron infusions in this frequently anemic cohort points to an opportunity for improvement. Potential target populations for quality improvement include patients aged 18-21 who are transitioning to adult care.

524 NOURISHMENT THROUGH KNOWLEDGE - ENTERAL FEEDING CURRICULUM TO IMPROVE PEDIATRIC RESIDENT PROFICIENCY. Tamir Diamond¹, Miriam Schechter¹, Inna Novak². ¹Pediatrics, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY; ²Pediatric Gastroenterology Hepatology & Nutrition, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, NY

Background: Many pediatric patients with complex medical conditions rely on enteral feeding devices for nourishment. Today, the majority of these patients are cared for in the community. Pediatricians in a variety of settings must be equipped with sufficient knowledge and confidence to provide optimal care for this patient population.

Enteral nutrition education is lacking in most post-graduate medical programs. There have been no studies to date to evaluate pediatric residents' level of knowledge in regards to enteral feeding devices, practices, and complications or residents' confidence in caring for this population. Objective of this study was to evaluate if a short curriculum during residency training can improve both knowledge and perception of preparedness.

Methods: A two-phase design, educational study of pediatric residents at a quaternary pediatric medical center was performed. Three new didactic interventions were introduced: a) hands-on teaching session about various enteral devices, b) handouts distributed to trainees during inpatient rotation, and c) interactive online educational games. Participants exposed to at least 1 intervention were considered part of study group. Residents were evaluated pre- and post- intervention by a multiple-choice knowledge quiz (MCQ) and Likert scale survey to evaluate perception of preparedness. Primary analysis focused on difference in pre- and post-intervention quiz scores and survey responses of study vs. control groups using unpaired T-test. Quiz scores were further analyzed in two subcategories: identification of devices and clinical management. Secondary analysis, using Chi-square test, focused on preparedness scale scores. Intervention and control groups were compared to pre-intervention group regarding perception of knowledge and preparedness. Statistical significance was defined as $P < 0.05$.

Results: Forty-five out of 83 residents completed the pre-intervention assessment and 23 completed curriculum and post-intervention assessment (unpaired intervention group). The pre-intervention survey showed that residents did not feel prepared to counsel or manage patients with enteral feeding devices, responses ranging from 2.1-2.5/ 5. Pre-intervention survey also showed that the residents would be interested in this new curriculum (4.4/5). The unpaired intervention group had statistically significant ($P < 0.0019$) improvement on each scale item on survey and showed significant improvement compared to pre-intervention group in total quiz score, devices identification and clinical management scores ($P < 0.0038$). Paired intervention and control groups showed similar trend but were not statistically significant.

Residents in the intervention group performed better than control group in total quiz scores 76.7 vs. 69.1 ($P = 0.1$), identification scores 85.2 vs. 78.3 ($P = 0.394$) and clinical management scores 73.2 vs. 65.3 ($P = 0.111$). Results showed a positive trend but did not reach statistical significance due to small number of participants in the post-intervention group ($N = 35$).

Conclusions: Results indicate that a short curriculum that integrates practical, theoretical and online modalities improves residents' knowledge and comfort level in caring for patients with enteral feeding devices.

525 UTILITY OF VIDEO CAPSULE ENDOSCOPY IN PEDIATRIC PATIENTS: A SINGLE CENTER EXPERIENCE. Temara Hajjat¹, Brenna Weber², Franziska Mohr¹, Wael Sayej¹. ¹Gastroenterology, Connecticut Children's Medical Center, Hartford, CT; ²Trinity Collage, Hartford, CT

Background/Objectives: Since the emergence of the Video Capsule Endoscopy (VCE), it has been widely used as a reliable and non-invasive endoscopic technique for evaluation of the small intestinal mucosa. However, studies on the clinical application of VCE in the pediatric population are sparse. VCE are usually swallowed, but in some patients who are unable to swallow the capsule, they are endoscopically placed into the duodenum under sedation or general anesthesia. These and other patient factors might affect small bowel transit time (SBTT). SBTT of endoscopically placed vs. swallowed capsules has not been previously reported in the literature in the pediatric population. We report a single center's clinical experience with the use of VCE.

Methods: Retrospective chart review of 95 VCE for pediatric patients ages between 1-21 years old who underwent VCE from April 2010 to May 2017. The indications for VCE were suspected Crohn's disease, polyps, gastrointestinal bleeding, chronic anemia, and arteriovenous malformations (AVM). All patients had normal upper endoscopy and colonoscopy results prior to VCE placement. Demographics, indications, placement techniques, pre-VCE imaging results, laboratory results, SBTT (time from the first duodenal image to the first cecal image), and complications were collected.

Results: We reviewed 95 Video Capsule Endoscopies (VCE). Four VCE readings were excluded (due to short bowel syndrome and a retained capsule). A total of 27/91 (29%) were endoscopically placed in the duodenum, and 65/91 (71%) were swallowed. An incomplete study (n=15) was reported in 30% (n=8/27) of the endoscopically placed capsules vs. 11% (n=7/64) of the swallowed capsules; (P=0.0281). Of those who had a complete VCE study (76/91; 83%), the average small bowel transit time in endoscopically placed VCE (n=22/76, 29%) was 0.93- 7.92 hours (3.8 ± 2.3 hours) and for swallowed VCE (n=54/76, 71%) was 0.97- 7.62 hours (3.6 ± 1.7 hours); (P=0.7108). There was no difference in age, gender or BMI in the endoscopically placed vs. swallowed VCE. The most common indication for VEC was gastrointestinal hemorrhage (n=34/91; 37%) followed by suspected Crohn's disease (n=33/91, 36%), and chronic anemia (n=11/91, 12%). Abnormal findings were identified in 36/91 (39%) of VCE studies. The most common abnormal finding was small intestinal lesions consistent with Crohn's disease (n=18/36, 50%).

Discussion: Our experience, which includes one of the largest single-center studies of Video Capsule Endoscopy described in the pediatric population, had a 39% yield in abnormal findings. There is no significant difference in transit time in swallowed vs. endoscopically placed capsules. Incomplete VCE studies were more likely to occur in endoscopically placed capsules.

526 **NON-SYNDROMIC JUVENILE POLYP SIZE: VOLUMETRIC ANALYSIS AND RETROSPECTIVE COMPARISON OF INTRAOPERATIVE ESTIMATE AND PATHOLOGY-HISTOLOGY SIZE DETERMINATION.**

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Background: Juvenile polyps (JP) are the most frequent lesions presenting with painless hematochezia in children. They can be associated with abdominal pain and anemia but are very rarely associated with progression or risk of colon cancer unless syndromic, defined by polyp burden, proximal (extracolonic) distribution or family history of polyposis syndrome. JP are usually isolated hamartomatous lesions occasionally harboring foci of adenomatous transformation and tend to localize to the distal colon. The relationship between polyp size and clinical presentation and indeed the reliability of endoscopist polyp size estimates in pediatric patients is unknown. Accurate estimates of the size of lesions including polyps noted during endoscopy is a necessary skill toward accurate assessment and therefore management and is a cornerstone of clinical research including chemopreventive trials in syndromic disorders. Herein we studied polyp volume, determined by lesion size and shape, compared endoscopist estimates of size/volume with pathologist measurement and polyp volume relationship with polyp burden, localization and clinical presentation in non-syndromic JP patients.

Methods: Children from birth to 18 years, who underwent colonoscopy with polypectomy at Children's Mercy Hospital were identified through the corresponding billing codes queried from Children's Mercy Medical Information Technology Department from 1/1/2003 to 3/1/2017; retrospective chart review was performed. Abstracted data included basic demographics, age at first colonoscopy, clinical presentation, extent of colonoscopy, endoscopic findings including number, size and location of polyps, histological findings including size and pathologic characteristics. Recurrence of polyps on repeat colonoscopy was noted.

Polyp volume was mathematically deduced from a formula assuming a spherical or ellipsoid shape; $\frac{4}{3}\pi abc$ where a,b and c are the reported axes dimensions either reported by the endoscopist or documented in the pathology report. Piecemeal removed lesion volume were recorded as the sum of individual recovered fragments, paired estimated and measured polyp dimensions were compared.

Children with sporadic JP defined as polyp burden ≤ 10 , no family history of Juvenile Polyposis Syndrome and no Juvenile Polyps proximal from the colon were included. Children with incomplete medical records, other polyp histologic subtypes, hereditary polyposis were excluded. Statistical analysis of data was performed using Stata, version 14.1®.

Results: During the study period 214 non-syndromic patients (115M:mean [SD] age 7.03 [3.96] years) underwent 361 colonoscopy procedures and 506 polypectomies, There were no observed significant relationships between gender, race and age at first colonoscopy with cumulative juvenile polyp burden. The most frequent presenting complaints included painless hematochezia (61%), hematochezia with pain (11.7%) and abdominal pain (10%); clinical presentation was not related to polyp burden. Polyp recurrence on repeat colonoscopy was significantly related to polyp burden (1 polyp: 1.5% / 2-4 polyps 19.2% / ≥ 5 polyps 87%: $p < 0.001$). Polyp distribution and size was significantly different amongst individuals harboring one or more polyps with isolated polyps favoring a distal distribution and larger size (Table 1). Paired values for polyp size were available in 122 polyps and showed a good correlation between the two with increasing polyp size (Spearman correlation 0.7452, p -value < 0.001), with a tendency towards overestimation of size by the endoscopist.

Discussion: JP are predominantly isolated lesions with a low risk of recurrence. Older age does not relate to increased polyp burden arguing against a cumulative burden effect over time; however in our cohort, recurrence of polyps was related to initial polyp burden even in the subgroup of patients traditionally thought of as not harboring a syndromic pattern of disease (2 - 4 polyps). Isolated larger distal lesions are the most common phenotype of non-syndromic JP. Accurate estimation of polyp size, especially with larger lesions is a critical assumption in polyp research including in children and we have demonstrated good correlation between visual estimate by endoscopist and actual pathology report.

Location (n=399)	1 Polyp		2-4 Polyps		≥ 5 Polyps		Pearson p-value
	Freq	Col %	Freq	Col %	Freq	Col %	
RectoSig	97	73.5%	63	52.1%	64	43.84%	<.001
Left Colon	15	11.4%	18	14.9%	17	11.64%	
Transverse	6	4.6%	11	9.1%	11	7.53%	
Right Colon	14	10.6%	29	24.0%	54	36.99%	
	Median	IQR	Median	IQR	Median	IQR	Kruskal-Wallis
Volume, per pathologist (n=327)	3.02	1.21, 9.65	1.06	0.27, 3.77	1.20	0.27, 5.63	0.0043
Volume, per endoscopist (n=160)	4.19	4.19, 14.14	1.77	0.11, 4.19	0.70	0.11, 16.76	0.0037

528 APPROACH TO THE MANAGEMENT OF PEDIATRIC NAFLD BY PEDIATRIC

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Background: There are 5 to 8 million children in the United States with nonalcoholic fatty liver disease (NAFLD). NAFLD can progress to end-stage liver disease and is associated with comorbidities such as type 2 diabetes and cardiovascular disease. The management of NAFLD is difficult and not standardized. NASPGHAN recently published clinical practice guidelines for the diagnosis and treatment of NAFLD in children. However, no information is available on how NAFLD is currently managed in actual practice. Therefore the study aims were: (1) to understand how pediatric gastroenterologists in the United States approach the management of NAFLD, and (2) to identify barriers to care for children with NAFLD.

Methods: We identified pediatric gastroenterologists in clinical practice across the United States. The study team conducted one-on-one, open-ended interviews to elicit how each individual pediatric gastroenterologist approaches the management of NAFLD in children. Data were collected on years in practice, type of practice, and practice location. Data were recorded based upon the responses given to include details regarding: nutrition counseling, physical activity recommendation, medications to treat NAFLD, comorbidities, and barriers to care.

Results: A total of 486 pediatric gastroenterologists were interviewed. The response rate was 72%. The mean (SD) time in practice of respondents was 12.3 (10.6) years. There were 45 of the 50 U.S. states represented. The distribution by practice type was 76% academic, 13% private practice, and 11% community practice. There were 8.4% of respondents who reported that they do not see patients with NAFLD. The mean (SD) number of children with NAFLD seen per week was 3 (3.5) with a mean of 37 minutes spent during the initial visit. Most respondents reported screening for one or more comorbidities with the top 3 being diabetes (77%), dyslipidemia (69%), and hypertension (53%). There were 18 different dietary recommendations reported and the most common was avoidance of sugar sweetened beverages (48%). There were 14 different exercise recommendations reported with walking being the most common (37%). Nearly half of respondents use medication in the management of NAFLD. After an initial visit, the mean follow-up interval was 3.4 months. We identified 25 distinct barriers to care. The most common barriers included access to diet and exercise resources (22.5%), motivation (21.7%), adherence (19.2%), family economics (14.7%), “families don’t get it” (11.6%), and access to registered dietitians (11.2%).

Conclusions: The majority of U.S. pediatric gastroenterologists encounter children with NAFLD on a regular basis. Screening for comorbidities is commonly done, but not with a uniform approach. The preponderance of varied recommendations regarding diet and exercise highlights the need for prospective clinical trials to provide the evidence base for specific interventions. Regarding the barriers to care, the message delivered by pediatric gastroenterologists was that NAFLD is a complex disease, which requires a multidimensional approach with adequate resources in the home, community, and clinical setting.

529 COLON CLEANSING IN CHILDREN: RESEARCH PROTOCOL VS. CLINICAL PRACTICE.

Yoram Elitsur, Yaslam Balfaqih, Deborah Preston. Pediatrics, Marshall University, Huntington, WV

Colonoscopy procedure is a common diagnostic procedures in children. Colon cleansing procedure is a limiting factor in achieving adequate colon condition for a successful colonoscopy. During the last years different pediatric protocols were reported which were different in the length of preparation (1- 4 days) and/or in various PEG 3550 doses (1- 4g/Kg/d). In most of the cited studies, the different protocols were performed under prospective research conditions, but the authors rarely provided evidence to show that their protocol is successful under normal clinical conditions. We hypothesize that the success rate of a cleansing protocol performed under research condition would have similar results under routine clinical practice. In 2013, we reported a comparison between 2 and 4 days colon cleansing protocols that showed adequate preparation at rate of 73.6% for 2 days protocol (Elitsur R. et al. World J Gastrointestinal Endosc 2013; 5: 165-168). Since that publication, we have incorporated the same protocol into our routine clinical practice.

Aim: To compare the success rate of a specific colonic cleansing protocol when used under research protocol vs. under routine clinical practice.

Materials: In all patients the cleansing protocol was similar to that published earlier which included 2 days PEG 3550 2g/Kg + Dulcolax 5mg/d. Patients reported the number and consistency of the stool on day 1 and 2 of the protocol. Adequate colon preparation was assessed according to Vanner SJ et al, and Barclay et al. as previously described and grading of ≥ 4.0 was considered adequate preparation.

Results: A total of 81 colon cleansing protocols performed under routine clinical practice were retrospectively reviewed. The demographic and colon preparation grades are described in Table 1. The most common clinical diagnoses for the procedures were gastrointestinal bleeding or IBD. Male to Female ratio was 1.53:1.0. The terminal ileum (TI) was intubation in most cases. Incomplete TI intubation was noted in 7 procedures from the clinical practice group of whom 2 pts had inadequate preparation, 2 pts had no TI (post-surgery), 2 pts has anatomical stenosis, and 1 pt we failed intubation. In 2 pts from the research protocol group TI was not intubated due to ICV stenosis.

Conclusion: The rate of colon preparation in the clinical practice was as good as the rate found during research protocol. We suggest that physicians should examine their colon cleansing research protocol in their clinical practice to assure adequate results for clinicians who practice in real life conditions. Without such studies, published research protocols will be buried in the medical literature without use.

	Clinical practice	Research protocol	p value
No pts.	81	38	
Age (year)	13.9 + 4.1	9.9 + 4.7	NS
M/F ratio	1.3:1.0	0.8:1.0	NS
# stools/day	6.5 + 4.2	7.9 + 4.1	NS
Stool consistency grade	5.1 + 1.2	5.5 + 0.9	NS
Colon cleansing grade	3.9 + 0.8	4.0 + 1.0	NS
Colon cleansing >4.0	60 (74%)	28 (73.6%)	NS

530 QUALITY INDICATORS FOR PEDIATRIC ESOPHAGOGASTRODUODENOSCOPY. *Karen Queliza¹, Erin McHugh², Cynthia Tsai¹, Anthony Olive¹, Douglas Fishman¹. ¹Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX; ²UT Medical School of Houston, Houston, TX*

Background: There is great interest in the identification and use of quality measures for pediatric endoscopy. Most quality improvement research in the field of gastroenterology is based on data obtained from adult patients, conferring a significant knowledge gap with respect to endoscopy metrics in the pediatric setting. We analyzed candidate quality indicators for esophagogastroduodenoscopy (EGD) at a high-volume tertiary care children’s hospital.

Methods: We performed a retrospective chart review of 100 consecutive pediatric patients who underwent EGD at Texas Children’s Hospital in 2016. Quality measures were investigated for the pre-procedure, intra-procedure, and post-procedure time periods. They included but were not limited to the following: completion of documentation, suitability of procedure indication, diagnostic process for evaluation of eosinophilic esophagitis (EoE) and celiac disease (CD), immediate adverse events, and communication of biopsy results with the family.

Results: Fifty-six percent of patients were male, 66% had at least one comorbid condition, median ASA classification was 2, and median age was 11 years (range 11 months to 20 years). One-hundred percent of cases included indications appropriate for EGD. Twenty-six percent of consent forms were incomplete, most commonly missing date or time of signatures. Fifty-nine percent of ASA classifications documented by endoscopists were congruent with anesthesiology. Of the ASA scores that were discordant, 85% were graded with a lower risk score by the endoscopist. Proton pump inhibitor (PPI) was indicated prior to EGD in 11% of cases performed to exclude PPI-responsive esophageal eosinophilia. Only 36% of these patients actually received PPI for the appropriate minimum duration of 8 weeks. Of those undergoing EGD for suspicion of EoE or surveillance of known EoE, 89% correctly had biopsies taken at multiple levels in the esophagus. With respect to evaluation for CD, 67% had at least 6 duodenal biopsies; however, there was insufficient data to determine whether biopsies were obtained from the post-bulbar region and/or bulb. In the post-procedure period, there was one adverse event involving hypotension (likely sedation-related), which was responsive to intravenous fluids. Forty-eight percent of EGDs resulted in a therapeutic intervention, and it took an average of 16 days from time of endoscopy for the family to be updated with biopsy results.

Discussion: We propose several candidate quality indicators for EGD in the pediatric setting. Areas of improvement related to EGD care include: incomplete consent documentation, underestimation of patient-specific sedation risk, suboptimal biopsy number in the evaluation of CD, and delayed communication with family regarding biopsy results. Establishment of pediatric quality indicators is essential for the development of guidelines tailored to this unique population.

EOE/GERD/AERODIGESTIVE

531 PRESENTING SYMPTOMS AND TIMING OF SYMPTOMS RELATIVE TO MEALS ARE POOR PREDICTORS OF PEDIATRIC ASPIRATION RISK. *Daniel Duncan, Kara Larson, Lisa Hester, Maireade McSweeney, Rachel Rosen. Gastroenterology, Boston Children’s Hospital, Boston, MA*

Background: Infants and children are typically referred for swallow evaluation if they have signs or symptoms suspicious for aspiration but little is known about the actual correlation between presenting symptoms and the risk of finding aspiration on clinical feeding evaluation (CFE) or videofluoroscopic swallow study (VFSS). The aim of this study was to describe the presentations of aspiration and determine if any presenting symptoms and the timing of those symptoms relative to meals could predict aspiration risk in the pediatric population.

Methods: We reviewed the records of all children under the age of 2 years who had both a CFE and a VFSS for the evaluation of oropharyngeal dysphagia at Boston Children’s Hospital from January 2015 to December 2015. We compared the presenting symptoms, timing of those symptoms relative to meals, and the correlation between these characteristics and the results of their CFE and VFSS. Data are presented as mean ± standard error.

Results: We evaluated 299 total subjects with a mean age of 9.05±0.41 months who had both CFE and VFSS performed. The symptoms and signs present at the time of testing included: 11.7% with recurrent pneumonia, 30% with reflux, 26.3% with vomiting, 59.3% with coughing, 22.7% with congestion, 1% with eye watering, 27% with noisy breathing, 11% with respiratory distress, 6.7% with slow feeding, 23.5% with poor feeding, 3.7% with an oxygen requirement, 16% with cyanosis, and 34.3% with choking/gagging. With regards to meals, 51.5% (n=154) of subjects had symptoms during meals, 9.4% (n=28) had symptoms after meals, and 21.4% (n=64) had symptoms both during and after meals. In this cohort, 38.1% (n=114) of the VFSS showed aspiration, 30.8% (n=92) showed penetration, and 27.4% (n=82) were normal. No single symptom predicted risk of aspiration (p≥0.05); even timing of symptoms relative to meals did not predict aspiration risk. The sensitivity and specificity of the CFE compared to the VFSS were 43% and 63%, respectively.

Conclusions: Presenting symptoms are varied in patients with aspiration and these symptoms cannot be relied upon to determine which patients have oropharyngeal dysphagia.

Table: Poor correlation between presenting symptoms and VFSS results compared to CFE results

	VFSS Result			CFE Result		
	Normal	Abnormal	p-value	Normal	Abnormal	p-value
Reflux	32.6% (29)	67.4% (60)	0.785	52.9% (18)	47.1% (16)	0.421
Vomiting	35.4% (28)	64.6% (51)	0.395	53.3% (16)	46.7% (14)	0.527
Coughing	31.1% (55)	68.9% (122)	1.000	48.5% (32)	51.5% (34)	0.018
Congestion	33.8% (23)	66.2% (45)	0.655	65% (13)	35% (7)	0.627
Eye Watering	33.3% (1)	66.7% (2)	1.000	50% (1)	50% (1)	1.000
Noisy Breathing	22.2% (18)	77.8% (63)	0.049	40% (10)	60% (15)	0.041
Respiratory Distress	27.3% (9)	72.7% (24)	0.694	70% (7)	30% (3)	0.525
Choking	30.1% (31)	69.9% (72)	0.895	41.7% (15)	58.3% (21)	0.016
Slow Feeding	30% (3)	70% (7)	1.000	66.7% (4)	33.3% (2)	0.689
Poor Feeding	31.4% (11)	68.6% (24)	1.000	66.7% (14)	33.3% (7)	0.288
Cyanosis	25% (12)	75% (36)	0.396	54.2% (13)	45.8% (11)	0.648
Oxygen Requirement	18.2% (2)	81.8% (9)	0.512	33.3% (1)	66.7% (2)	0.567
Recurrent Pneumonia	22.9% (8)	77.1% (27)	0.333	53.3% (8)	46.7 (7)	0.781
Symptoms During Meals	29.2% (45)	70.8% (109)	0.139	49.3% (33)	50.7% (34)	0.010
Symptoms After Meals	25% (7)	75% (21)	0.205	88.9% (8)	11.1% (1)	1.000
Symptoms During and After Meals	32.8% (21)	67.2% (43)	0.763	60% (18)	40% (12)	1.000

Data are expressed as % (n)

535 HISTOLOGICAL ASSESSMENT OF EOSINOPHIL PEROXIDASE ENHANCES DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS AND PROTON PUMP INHIBITOR-RESPONSIVE ESOPHAGEAL EOSINOPHILIA. *Nathalie Nguyen^{1,3}, Anna Baumgaerten³, Benjamin Wright^{2,4}, James Lee², Glenn Furuta^{1,3}, Joanne Masterson^{1,3}. ¹Pediatric Gastroenterology, Hepatology & Nutrition, Children’s Hospital of Colorado, Aurora, CO; ²Mayo Clinic Arizona, Scottsdale, AZ; ³University of Colorado, Aurora, CO; ⁴Phoenix Children’s Hospital, Phoenix, AZ*

Background: Distinguishing between eosinophilic esophagitis (EoE), gastroesophageal reflux (GERD), and PPI-responsive esophageal eosinophilia (PPI-REE) is difficult because symptoms overlap and no distinguishing histological features exist.

Recent evidence in adults suggests that PPI-REE may represent a subset of patients with EoE. Current EoE diagnostic guidelines recommend enumeration of eosinophils, but this may underestimate the extent of eosinophil involvement. We previously developed a histological scoring system using eosinophil peroxidase (EPX) that differentiates adults with EoE from GERD. The aim of this study is to validate the utility of the EPX scoring system in children with EoE, PPI-REE, and GERD. We hypothesized that children with EoE and PPI-REE would have similar tissue deposition of EPX, whereas children with GERD would have lower of EPX staining.

Methods: We performed EPX analysis of formalin fixed, paraffin embedded esophageal tissues from children with active EoE (defined by consensus recommendations) (Liacouras CA et al. 2011), inactive EoE (followed through treatment with diet or topical corticosteroids and <15 eos/HPF), PPI-REE prior to PPI (≥ 15 eos/HPF prior to PPI), PPI-REE after PPI (8 weeks of high-dose PPI and subsequent EGD with <15 eos/HPF), GERD (symptoms of GERD defined by a gastroenterologist) or control (underwent EGD for symptoms necessitating endoscopy with 0 eos/HPF). Immunohistochemical staining was performed using a monoclonal antibody specific for the eosinophil granule protein, EPX, (kind gift from James J. Lee, PhD) that identified degranulation products and intact eosinophils. We applied an EPX histological scoring algorithm (Protheroe C et al. 2009) which includes 5 diagnostic markers: 1) Maximum eosinophils in a single focus 2) Average number of eosinophils in five 40X HPFs 3) Level of degranulation 4) Extent of eosinophil infiltration or degranulation in maximally affected biopsy and 5) Extent of all biopsies with eosinophil infiltration or degranulation. We performed statistical analysis using GraphPad Prism.

Results: One hundred seventeen esophageal biopsies from EoE (N=25), PPI-REE (N=8), GERD (N=22) and control (N=29) subjects were assessed. Paired post-treatment samples were available for EoE and PPI-REE subjects. EPX score was significantly greater in active EoE compared to inactive EoE (41.4 ± 1.6 vs 5.3 ± 2.1 , $p < 0.0001$) and active EoE compared to GERD (41.4 ± 1.6 vs 3.8 ± 1.7 , $p < 0.0001$). Treatment of EoE with diet or steroids and PPI-REE with PPI led to significant decrease in total EPX score (42.1 ± 2.5 vs 4.1 ± 2.0 , $p < 0.0001$). No significant differences were found when comparing EPX score for active EoE and PPI-REE prior to PPI, but EPX scores were significantly elevated in both these groups compared to GERD ($p < 0.0001$). No significant differences were found between active EoE and PPI-REE prior to PPI when evaluating individual diagnostic markers of the score, including extent of degranulation.

Conclusion: Tissue staining for EPX assesses both eosinophilic infiltration and degranulation. Degranulation patterns suggest that patients with PPI-REE are similar to EoE. Quantification of EPX by our novel EPX scoring system can be used to differentiate children with EoE relative to GERD and enhance current diagnostic approaches.

536 **CATEGORIZATION AND CLINICAL OUTCOMES IN CHILDREN WITH PERSISTENT GERD SYMPTOMS ON PPI THERAPY.** Thomas Ciecieroga², Neelesh Tipnis¹. ¹Pediatrics, University of Mississippi Medical Center, Jackson, MS; ²Pediatrics, Weil Cornell Medical School, New York, NY

Background: Proton Pump Inhibitors (PPIs) are highly effective in the treatment of typical GERD symptoms. However, up to 25% of children will have persistent symptoms in spite of adequate PPI therapy. In these patients, additional testing such as endoscopy and pH-impedance testing can help better categorize and assign treatment options. Rome IV recognizes conditions where symptoms are not related to excessive esophageal acid exposure: reflux hypersensitivity and functional symptoms.

Aims: In children with persistent GERD symptoms in spite of PPI therapy, we: 1. Categorize patients based on endoscopic, histologic and ph-impedance testing; and 2. Evaluate clinical outcomes following testing.

Methods: Children with persistent typical GERD symptoms evaluated by endoscopy and pH-impedance testing were retrospectively identified. Children over age 4 with typical GERD symptoms (epigastric abdominal pain, heartburn, regurgitation/water brash, chest pain, dysphagia/poor eating) were included. Children under age 4 or with predominately extra-esophageal symptoms were excluded. Duration of PPI therapy, presence of macroscopic esophagitis (mucosal breaks), microscopic esophagitis, excess esophageal acid exposure (% time pH <4 greater than 5.4%), symptom correlation (SAP $>95\%$ or SI $> 50\%$) were used to categorize children as Eosinophilic Esophagitis (EoE), Erosive Esophagitis (EE), Non-Erosive Reflux Disease (NERD), Reflux Hypersensitivity (RH), and Functional Symptoms (FS). Follow-up duration and clinical outcome was recorded.

Results: 87 children (47 M, 40 F, mean age 10.8 ± 3.4 y) evaluated by endoscopy and ph-impedance testing were found to have persistent typical GERD symptoms on PPI therapy. Symptoms were: epigastric pain (90%), regurgitation/water brash (85%), heartburn (57%), chest pain (24%), dysphagia/poor eating (33%). Macroscopic esophagitis was present in 29 (34%), microscopic esophagitis in 41 (47%), abnormal acid exposure in 30 (35%) and positive symptom correlation in 21 (24%). Children were categorized as EoE in 19 (22%), EE in 11 (13%), NERD in 16 (18%), RH in 8 (9%) and FS in 33 (38%). Follow-up was available 54 (62%) of children. Lost to follow-up were 11/16 (68%) NERD, 2/8 (25%) RH, 20/33 (64%) FS and no EoE or EE patients. Children with EoE and EE all had improvement or resolution of clinical symptoms by the

last treatment date. In children with NERD, 4/16 were offered treatment other than acid suppression of which 3/4 (75%) improved. In children with FS, 7/13 were offered treat other than acid suppression of which 2/7 (29%) improved. In children with RH, 2/2 were offered treatment other than acid suppression of which none improved.

Discussion: In this study, nearly half of the children with persistent typical GERD symptoms on PPI therapy had conditions not associated with excess acid exposure (reflux hypersensitivity or functional symptoms). Many children were either not offered therapy beyond acid suppression or lost to follow-up after testing, suggesting that clinicians are not adept at treating neurogastroenterologic conditions, or that a lack of consensus on treatment prevents recommendations beyond acid suppression therapy in this group.

537 IN CHILDREN WITH RECURRENT LARYNGITIS, IS THE CURRENT INDICATION OF PROTON PUMP INHIBITORS A CONVINIENT THERAPEUTIC MODALITY? *Nicolas Rovati, Leandro Fanjul Regueira, Emilia Cohen Sabban, Carlos Lifschitz, Marina Orsi. Pediatric Gastroenterology, Hospital Italiano de Buenos Aires, Capital Federal, Buenos Aires, Argentina*

Proton pump inhibitors (PPI) indication in children with recurrent laryngitis (RL) assuming gastroesophageal reflux (GER) as the causative mechanism, is a very common practice worldwide. Although in 2009 guidelines it have been remarked that RL is the extradigestive manifestation with lower correlation.

Aim: Analyze Rhinofibrolaryngoscopy (RFL) findings with gastroesophageal reflux data evaluated with 24hr Multichannel Intraluminal Impedancimetry –pH (IIM-pH) and describe characteristics.

Material/Methods: Retrospective review of IIM-pH tracings of children with LR (more 2/3 episodes) sent to be evaluated because of GERD suspicion between 2010-2017 with a positive pathological RFL (Remes-Troche classification). The data collection with IIM-pH included total number of acid episodes, non-acid, bolus clearance time (BCT), ascent to proximal channels, symptomatic correlation (SAP/SI). The population was divided into two groups: GI: both pathological studies (RFL/IIM-pH), GII: pathological RFL and normal IIM- pH. T test was used as statistical method.

Results: 29 patients (12 girls) were evaluated; mean age: 6.89 years (range 2-17). GI: 11 males (37.9%) G II: 18 males (62.1%).

Conclusion: In children with laryngeal involvement, evidence of pathologic reflux was poor. In the few positive cases, longer BCT and more acid episodes with ascent to proximal channels was observed. These findings reinforce previous publications regarding the convenience to restrict PPI use to patients with proven GERD.

Results

	G1: 11 RFL+ IIM/pH+	GII: 18 RFL+ IIM/pH normal	p
Total Episodes	53.73±21.25	43.78±18.84	0.159
Acid Reflux	40.18±19.54	26.76±15.6	0.051
Non acid Reflux	14.55±6.09	16.78±9.99	0.511
BCT	130.18±120.95	55.39±38.84	0.05
Acid Ascent to Proximal channels	25.0±20.40	12.11±9.6	0.029
Non acid Ascent to Proximal channels	6.18±4.56	9.16±6.45	0.134

538 REFERRAL, EVALUATION, AND MANAGEMENT PATTERNS AT THE ALABAMA AERODIGESTIVE CENTER. *Alexandra Kraus², Rachel Kassel¹, Crawford Beth⁴, Ashley Chapman³, Leslie Boehm³, Smith Nicholas⁵, Kulbersh Brian⁵, Hector Gutierrez¹, Wiatrak Brian⁵, Reed Dimmitt¹, William Harris¹. ¹Pediatrics, University of Alabama Birmingham, Birmingham, AL; ²School of Medicine, University of Alabama at Birmingham, Birmingham, AL; ³Alabama Aerodigestive Program, Children's of Alabama, Birmingham, AL; ⁴Speech and Language Pathology, Children's of Alabama, Birmingham, AL; ⁵Pediatric ENT Associates, Children's of Alabama, Birmingham, AL*

Background: The Alabama Aerodigestive Program was founded in 2012 to meet the multidisciplinary needs of children with complex, chronic airway and digestive concerns. Currently available literature describing referral diagnoses and diagnostic evaluation of Aerodigestive patients is limited.

Objective: To report the evaluation and management of referrals to a single-center Aerodigestive Program.

Methods: Retrospective chart review of the first 200 patients referred to The Alabama Aerodigestive Program from 2012-2014.

Results: Mean age at referral was 41 months. The most common indications for referral were gastroesophageal reflux (77%), chronic cough (67%), and dysphagia (56%). Most patients (83%) were evaluated by all four disciplines: otolaryngology (ENT), pulmonology, gastroenterology, and speech pathology. Approximately 2/3 of patients underwent an endoscopic airway evaluation by flexible bronchoscopy (flex bronchoscopy, 64%), and about 3/4 with direct laryngoscopy and bronchoscopy (DLB, 70%). About half had an esophagogastroduodenoscopy (EGD, 58%). Endoscopic airway examination frequently revealed bronchitis (43%), tracheomalacia (41%), laryngomalacia (34%), and bronchomalacia (33%). A laryngeal cleft was identified in 12% of evaluations. EGD and pH/impedance studies were typically normal (66% and 70% respectively), but 16% of EGD biopsies found eosinophilic esophagitis (EoE). Reflux was only found in 11% of patients. Swallow dysfunction was common, present in 58% of patients undergoing video fluoroscopic swallowing evaluation. Nearly half (49%) of polysomnograms indicated obstructive sleep apnea (OSA).

Conclusions: Children referred to The Alabama Aerodigestive Program represent a broad spectrum of medically complex children. Most have airway abnormalities and/or swallow dysfunction. Findings of laryngeal cleft and EoE are increased in this population.

539 THE IMPACT OF UPDATED CONSENSUS RECOMMENDATION FOR EOSINOPHILIC ESOPHAGITIS ON HOSPITALIZATION AMONG PEDIATRIC AND ADOLESCENT POPULATION IN THE US. Ransome Eke¹, Duncan Vos¹, Sharat Kamath², Andrey Leonov¹. ¹Western Michigan University Homer Stryker School of Medicine, Kalamazoo, MI; ²Kalamazoo College, Kalamazoo, MI

Background: Accurate and early recognition and guideline based management of eosinophilic esophagitis (EoE) is vital for optimal care for patients with this condition. We evaluated the impact of the updated consensus recommendation on hospitalization of pediatric and adolescent population with EoE in the US.

Methods: A population based cross sectional study was conducted using the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) data from years 2008 through 2013. Children and adolescent EoE cases with ICD-9 hospital discharge code 530.13 were identified. We examined trends in hospital admissions before and after publications of updated consensus recommendations for the management of EoE. Descriptive statistics was conducted considering the demographic distribution and hospital locations. Data analyses were performed using SAS version 9.4 (SAS Institute, Cary, N.C.)

Results: Of the 7,945 EoE related hospital admissions among pediatric and adolescent patients from 2008 through 2013, 84% of the admissions were after the updated consensus recommendation and 16% were before the updated consensus recommendation. EoE hospital admissions increased from 218 in 2008 to 2065 in 2013 (p-value = 0.015). Most of hospital admissions (88%) occurred in urban teaching hospitals while 2% were in rural hospitals. Overall, children ages less than 11 years comprised 56% of the admissions, 68% were males and 74% were Caucasians. Medicaid insurance coverage decreased from 44% in 2008 to 37% in 2013.

Conclusion: The hospital admission rates for eosinophilic esophagitis among children and adolescents' patients following updated consensus recommendation for the management of this condition have increased significantly over the past six years in the US. This largely may be due to an increasing rate of recognition of this condition.

541 CHANGES IN HEALTH-CARE UTILIZATION FOLLOWING PARTICIPATION IN INTENSIVE INTERDISCIPLINARY BEHAVIORAL TREATMENT FOR REMOVAL AND PREVENTION OF PEDIATRIC GASTROSTOMY TUBES. Robert Dempster¹, Wendelin Burdo-Hartman², Elizabeth Halpin³. ¹Pediatric Psychology, Nationwide Children's Hospital, Columbus, OH; ²Complex Care, Nationwide Children's Hospital, Columbus, OH; ³Clinical Therapies, Nationwide Children's Hospital, Columbus, OH

Purpose Difficulties with feeding that lead to use of gastrostomy tubes (G tubes) are stressful for families and patients and lead to a decreased quality of life. Intensive Interdisciplinary Behavioral Treatment (IIBT) has demonstrated effectiveness in improving feeding and decreasing G tube dependence, but no studies have shown how health care spending is impacted following treatment. This study explores health care utilization changes following IIBT among children with or at risk for G tube placement.

Methods All patients participated in a 6-8 week IIBT program between July 2013 and September 2015 with the goal of decreasing G tube dependence or increasing oral intake to prevent G tube placement. Hospital charge data during the 12

months before IIBT and the 12 months following discharge from IIBT were compared. 1 participant was excluded from analyses because they moved halfway through the year post treatment, leaving a total of 9 participants.

Results Patients had significantly more hospital charges in the year before IIBT (M=\$35,506) than the year after (M=\$10,991; $t(8)=2.59$, $p=.03$). Every patient had fewer charges in the year following IIBT and chargers were 37% or less than the year before IIBT for all but one patient.

Conclusions IIBT decreases dependence on G tubes, which increases patient and family quality of life and decreases health care utilization. Patients leaving IIBT have decreases in utilization across domains, even outside of appointments focused on feeding. Implications and directions for future research are discussed.

543 **EOSINOPHIL PEROXIDASE IS A MARKER OF DISEASE ACTIVITY IN EOSINOPHILIC**

GASTRITIS. Shauna Schroeder¹, Benjamin Wright^{2,1}, Steve Taylor¹, Nora Odisho¹, Kelly Shim^{1,2}, Cindy Bauer^{1,2}, Daphne DeMello¹, James Lee². ¹Phoenix Childrens Hospital, Phoenix, AZ; ²Mayo Clinic, Scottsdale, AZ

Background: Eosinophilic gastritis (EG) is characterized by eosinophilic infiltration of the gastric mucosa. In contrast to eosinophilic esophagitis (EoE), there are no consensus guidelines defining diagnostic criteria for EG. Eosinophil peroxidase (EPX) is an abundant cytoplasmic protein stored in the secondary granules of eosinophils. Previous studies have shown that EPX is eosinophil-specific and its release in the esophageal mucosa correlates with symptoms of EoE.

Aim: To evaluate tissue EPX as a marker of disease activity in subjects with EG.

Methods: We performed a retrospective analysis of diagnostic biopsies from pediatric EG cases and non-EG controls undergoing upper endoscopy for gastrointestinal symptoms. EG subjects had >30 eos/hpf in at least 5 hpf and other causes of gastrointestinal eosinophilia were excluded. Non-EG controls had normal endoscopic findings and no histopathologic diagnosis or gastrointestinal eosinophilia. Gastric and duodenal biopsies were assessed for eosinophilic infiltration and degranulation by hematoxylin-eosin stains and immunohistochemistry using a mouse monoclonal anti-EPX antibody. EPX stains were assessed using a unique histopathologic scoring algorithm. Slides were digitized and the proportion of tissue area staining positive for EPX relative to normal tissue (%EPX) was quantified electronically.

Results: A total of 5 EG cases (mean age 14.6 yrs, 80% female, 80% atopic, mean gastric eos/hpf 85) and 5 non-EG controls (mean age 10.6 yrs, 80% female, 0% atopic, mean gastric eos/hpf 4) were analyzed. EG subjects commonly presented with clinical symptoms of abdominal pain and nausea and were more likely to have peripheral eosinophilia (median absolute eosinophil count 1008 vs. 110 cells/ μ L, $p = 0.02$). Gross endoscopic findings in EG subjects included gastropathy with hyperplastic folds (80%), antral nodularity (80%) and ulcers (60%). Median EPX scores for gastric biopsies were significantly elevated in subjects with EG vs. controls (gastric body 31 vs. 2, $p = 0.008$, gastric antrum 32.5 vs. 3, $p = 0.02$). %EPX was also markedly elevated in EG cases (gastric body 6.2 vs. 0.2%, $p = 0.008$, gastric antrum 9.4 vs. 0.3%, $p = 0.02$) (Figure 1). Peak eosinophil counts in the gastric and duodenal mucosa correlated strongly with both the EPX score and %EPX levels ($r = 0.93$, $p < 0.0001$ and $r = 0.85$, $p < 0.0001$) (Figure 2).

Conclusions: Subjects with EG demonstrate marked deposition of EPX. In cases where extensive cytolitic degranulation occurs, eosinophil counts alone may underestimate the extent of disease activity. We have developed a novel scoring algorithm and an automated assessment (%EPX) of eosinophilic infiltration and degranulation in EG that may enhance both diagnostic accuracy and efficiency. Future studies are planned to validate these EPX assessments as diagnostic markers of EG.

Figure 1: Subjects with EG demonstrate marked deposition of EPX. Serial sections of a gastric biopsy from an EG subject stained with hematoxylin-eosin (A) and anti-eosinophil peroxidase antibody (B) demonstrating the ease of identifying eosinophils as well as focal areas of degranulation (each x100).

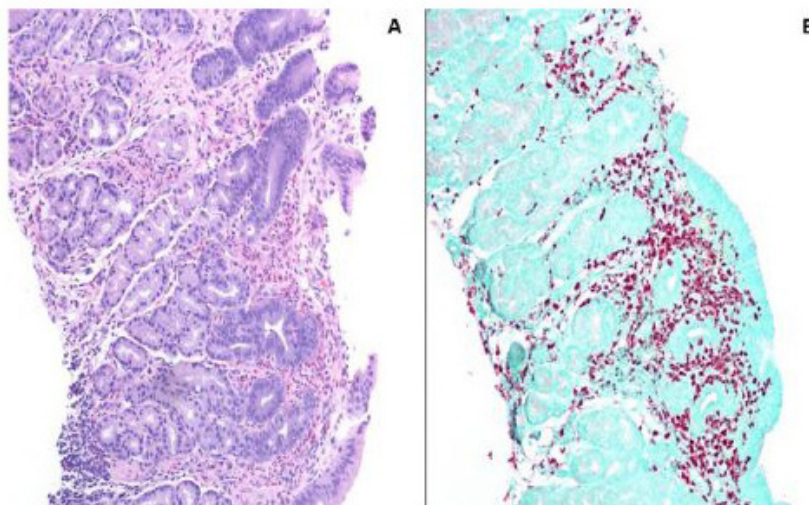
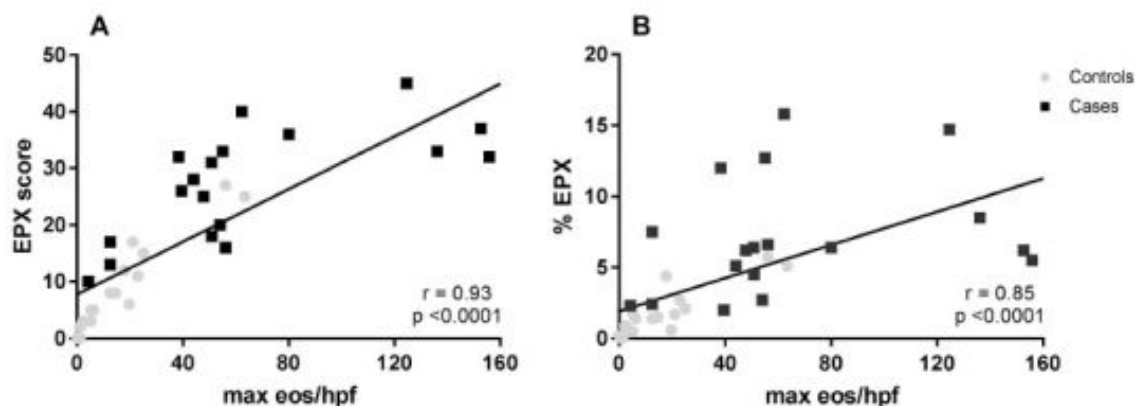


Figure 2: EPX scores and %EPX correlate strongly with tissue eosinophilia. Linear regression plots of EPX score (A) and %EPX (B) (y-axis) and max eos/hpf (x-axis). Spearman's rho values reported for each.



544 EOSINOPHILIC ESOPHAGITIS (EOE) ENDOSCOPIC REFERENCE SCORES (EREFS) IN A PEDIATRIC COHORT. *Simon Rabinowitz¹, Katherine Vaidy¹, Nonyelum Ebigo³, Lisa Feng¹, Rachel Sklar¹, Evan Grossman², Rebecca Winderman¹, Steven Schwarz¹. ¹Pediatric GI, Children's Hospital at Downstate, Brooklyn, NY; ²Gastroenterology, Downstate Medical Center, Brooklyn, NY; ³Pediatrics, Richmond University Medical Center, Staten Island, NY*

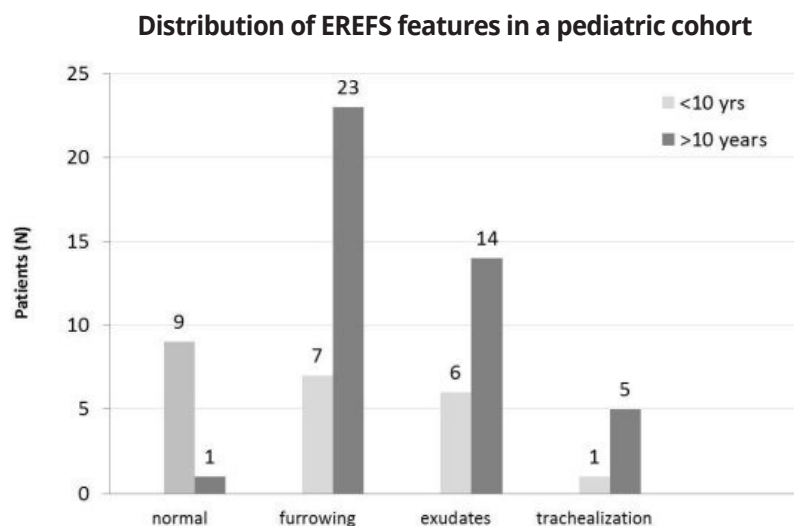
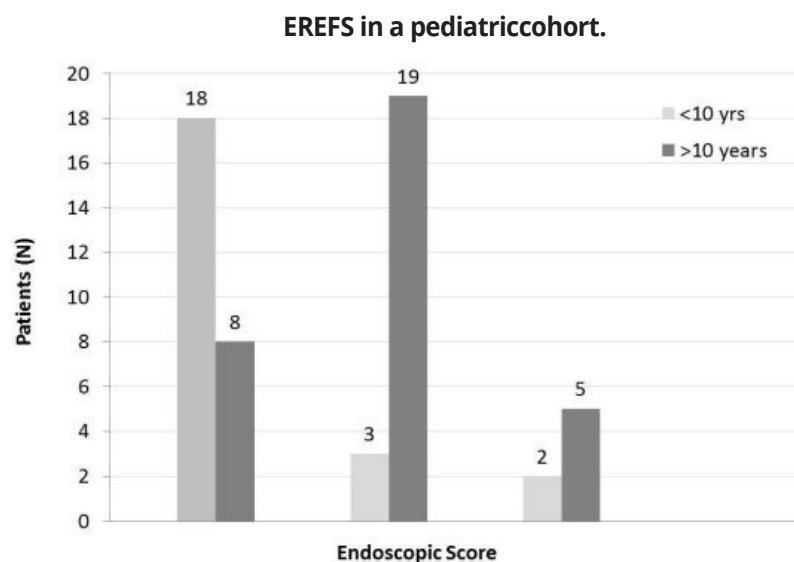
Introduction: While all patients with eosinophilic esophagitis (EoE) have an increase in esophageal eosinophilia along with esophageal dysfunction, the clinical features commonly encountered in children are not equivalent to those seen in adult EoE patients. An EoE Endoscopic Reference Score (EREFS) has been developed and validated to assist in the care and investigations of adults with EoE. This abstract describes application of the EREFS to a group of pediatric patients.

Methods: Seventy one patients enrolled in an IRB approved investigation of EoE had 116 upper endoscopies with biopsies (egd). The profile of the investigations included: 83M, 32F, mean age of 10.6 ± 5.6 years; and a range 0.3-21 years. Some EoE patients had multiple (2-8) investigations. The distribution of the studies was 37 GERD (≤ 7 eos/hpf); 55 with active EoE, EoE-A (≥ 15 eos/hpf after acid suppression and esophageal symptoms) and 24 with EoE in remission, EoE-R (EoE-A who had resolved symptoms and eos with therapy). All studies were scored for the 5 EREFS fields (edema, rings, exudates, furrows, and stricture) at the time of the egd or for earlier investigations, based on documented descriptions and a review of the endoscopic photographs.

Results: The mean EREFS was $0.1 \pm .23$ for GERD; 0.5 ± 1.1 for EoE-R and 1.9 ± 1.4 for EoE-A (ANOVA followed by post hoc analysis demonstrates $p < 0.05$). The highest score for a GERD was 1, which was only seen in two patients who both had edema. Among EoE-A patients the scores were distributed as follows: 0- 1: 47 %; 2-3: 40 %; and 4-5: 13%. For EoE-A patients >10 y the distribution was: 0- 1: 25 %; 2-3: 59 %; and 4-5: 16%. In this cohort the most prevalent finding was furrowing (55%), followed by exudates (36%), edema (35%), and rings (11%); none had stricture. Among patients >10 y the prevalence for the same findings were 72%; 44%; 41%; 16%; and 0. Ten EoE-A (18%) had scores of 0, but only one (3%) of these was >10 y.

Discussion: In this cohort:

1. The absence of specific endoscopic features of EoE was noted in 91% of GERD and in this group only edema was seen;
2. almost half of EoE-A had EREFS scores of 0-1 but scores of ≥ 2 were highly predictive of EoE-A;
3. furrowing, exudates, and edema were the most prevalent EREFS features seen in EoE-A;
4. effective therapy resulted in a significant decrease in EREFS score.



545 CASE-CONTROL STUDY OF BMI IN PEDIATRIC PATIENTS WITH ESOPHAGEAL EOSINOPHILIA. Tara Sarin, William Bennett, Emily Hon. Pediatrics, Indiana University, Indianapolis, IN

Introduction: Eosinophilic esophagitis (EoE) is a chronic food antigen-mediated disease characterized by esophageal dysfunction and significant esophageal eosinophilia. Because EoE causes feeding difficulties, vomiting, dysphagia, and strictures, it may lead to decreased oral intake and lower body mass index (BMI) in these patients. However, there are limited data on BMI in EoE, especially in children.

Aim: To assess whether esophageal eosinophilia is associated with a lower BMI in pediatric patients.

Methods: A retrospective chart review of patients diagnosed with esophageal eosinophilia at Riley Hospital for Children at IU Health was conducted using a pre-existing IRB-approved database. We included patients diagnosed with EoE and PPI-responsive esophageal eosinophilia (PPIREE) over a two-year period from January 1, 2013 to December 31, 2014. At time of their diagnosis, these patients were 2-18 years old and demonstrated symptoms of esophageal dysfunction with histological findings of ≥ 15 eosinophils/HPF. Patients were excluded if they had a diagnosis of other GI disease associated with esophageal eosinophilia such as a celiac disease, Inflammatory bowel disease, infectious esophagitis, gastroesophageal reflux disease, collagen vascular disease, drug associated esophagitis, hyper eosinophilic syndrome, and eosinophilic gastroenteritis. The following demographic data were collected: age at diagnosis, gender, race, ethnicity, and insurance status. BMI was calculated from weight and height at diagnostic endoscopy. Age-matched control patients without a diagnosis of esophageal eosinophilia at a ratio of 10:1 were obtained from the local general pediatric clinics in the Eskenazi Health and Riley Hospital for Children at IU Health using the Child Health Improvement through Computer Automation (CHICA) system.

Statistics: We calculated mean and median BMI for both esophageal eosinophilia patients and controls and constructed histograms for each distribution. We used student's t-test as a univariate comparison of mean BMI. Logistic regression was performed using BMI < 10th percentile as an outcome, and age, gender, race, and insurance status as independent variables.

Results: Patients with esophageal eosinophilia had lower mean and median BMI than age-matched control patients (60.6 and 67 vs 70.1 and 78.8, p = 0.0014). Multivariate analysis revealed that patients with esophageal eosinophilia were not more likely to be underweight (e.g. BMI<10th percentile) than age-matched control patients.

Conclusion: Children with esophageal eosinophilia have lower BMI than age-matched control patients, but did not have increased risk of being underweight when controlled for demographic factors. Thus, we believe that age, race, and socioeconomic status of esophageal eosinophilia patients play a more prominent role in why they have a lower BMI. Larger prospective studies are needed to further characterize the esophageal eosinophilia population as well as to study the complex relationship among BMI, esophageal eosinophilia and demographic factors.

548 ESOPHAGEAL BRUSHING REFLECTS DISEASE ACTIVITY MORE THAN EOSINOPHIL COUNTS IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS. Yamen Smadi¹, Chirajyoti Deb², Jeffery Bornstein¹, Karoly Horvath¹, Devendra Mehta¹. ¹Pediatrics, Arnold Palmer Hospital For Children, University of Florida at Orlando Health, Orlando, FL; ²Gastrointestinal Translational Laboratory, Arnold Palmer Hospital for Children, Orlando, FL

Background: Eosinophilic Esophagitis (EoE) is patchy and the evaluation of small-size biopsies might not accurately reflect eosinophilic involvement due to degranulation. Eosinophil-derived neurotoxin (EDN) measured in esophageal brushing is a sensitive marker to detect inflammation in EoE. Hypothesis: Measurement of EDN in esophageal brushing offers more objective method to assess the disease activity than eosinophil (eos) count in esophageal biopsies.

Methods: We conducted a prospective case-control study in children and young adults (<21 years) scheduled for routine esophagogastroduodenoscopy (EGD). We measured EDN by ELISA in esophageal brushing samples obtained through the endoscopy under direct visualization or through a nasogastric tube (NGT) prior to endoscopy. We compared EDN values to endoscopy findings and eosinophil count in esophageal biopsies. **RESULTS:** Ninety-four patients (mean age 10 years) underwent 127 endoscopies. Endoscopy scores for EoE correlated with eos count in 111 (87%) cases and there were discrepancies between the two methods in 16 cases (13%) [14 cases with positive endoscopy findings for EoE and insufficient eos count and 2 cases with negative endoscopy findings and positive eos count]. In these 16 cases of discrepancy, EDN reflected endoscopy findings in 14 (87.5%) cases. Overall, EDN reflects endoscopy findings in 95% of the cases versus eos count in esophageal biopsies which reflects endoscopy findings in only 87% of the cases (p < 0.01) (Table-1).

Conclusion: Esophageal brushing collects mucosal samples from a larger epithelial surface, and measurement of EDN in esophageal brushing is not affected by degranulation. Thus, this method provides a more reliable assessment of the disease activity than eosinophil count in esophageal biopsies.

Table-1. Correlation between EDN in esophageal brushing, endoscopy findings, and eos count in esophageal biopsies from patients with EoE

Correlation	Number of cases (%)
Complete correlation	107 (84%)
Positive endoscopy/Negative eos count/Positive EDN	14 (11%)
Negative endoscopy/Positive eos count/Positive EDN	4 (3%)
Negative endoscopy/Negative eos count/Positive EDN	2 (1.50%)
Total	127 (100%)

Eosinophil-derived neurotoxin (EDN), eosinophil (eos), eosinophilic esophagitis (EOE)

FUNCTIONAL/MOTILITY

*549 SMOOTH MUSCLE MYOSIN DYSREGULATION CAUSES MULTIPLE VISCERAL PATHOLOGIES

IN A MOUSE MODEL. Benjamin Wilkins¹, Melissa Gilbert¹, Sarah Sivilich², Manimegali Muthumani³, Reynold Panettieri³, Robert Moreland², Nancy Spinner¹, Michael Pack³. ¹Pathology and Laboratory Medicine, Children's Hospital of Philadelphia, Philadelphia, PA; ²Physiology and Pharmacology, Drexel University College of Medicine, Philadelphia, PA; ³Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA

Smooth muscle dysfunction due to contractile protein mutations are infrequently identified as the primary cause of human disease. Based on our prior work in the zebrafish model we speculate that mutations/polymorphisms that alter the regulation of smooth muscle contraction may play a role in gastrointestinal motility disorders. We previously reported a missense mutation in the zebrafish smooth muscle myosin heavy chain gene (*myh11*) that causes non-regulated tonic smooth muscle contraction in the intestine of homozygous larvae. Homozygotes develop invasive expansion of the posterior intestine that is lethal by 10 days post-fertilization. Heterozygous larvae develop normally but develop the homozygous cell invasion phenotype when exposed to redox stress. Transient rescue of the homozygous phenotype revealed markedly reduced intestinal transit in all larvae examined thus confirming altered smooth muscle function. To translate these findings to a mammalian model, we generated the identical missense mutation (*meltdown; mlt*) in the endogenous mouse *Myh11* gene and report here smooth muscle-related phenotypes in neonatal and adult mice. Homozygous *Myh11^{mlt/mlt}* pups have >90% perinatal lethality due to esophageal atresia without tracheoesophageal fistula. Mutant pups also have multiple large duodenal diverticuli at birth. Heterozygous *Myh11^{mlt/+}* mice develop normally with no overt defects in esophageal or intestinal morphology or motility. Adult females however, had pronounced reproductive phenotypes (reduced fertility and retained fetus) attributed to uterine smooth muscle dysfunction. Preliminary studies also suggest that Apc deficient intestinal polyps arising in heterozygous *Myh11^{mlt/+}* mice have a higher incidence of high grade dysplasia, thus suggesting that the cell invasion phenotype seen in zebrafish may be evolutionarily conserved. To better understand heterozygous smooth muscle physiology we measured force generation in bladder strips before and after exposure to contractile agonists. This showed that heterozygous smooth muscle was hypercontractile. Pharmacological studies are ongoing to test whether intestinal transit is altered by redox stress as in the zebrafish model. Taken together, these data suggest that genetic variants that alter the regulation of smooth muscle contraction contribute to human disease.

550 CHARACTERIZATION OF THE MAIN FUNCTIONAL GASTROINTESTINAL DISORDERS IN LATIN AMERICAN SCHOOLCHILDREN AND ADOLESCENTS.

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Introduction: In children, the major functional gastrointestinal disorders (FGDs) are functional constipation (FC), irritable bowel syndrome (IBS), and functional abdominal pain (FAP) along with FAP syndrome (FAPS).

Objective: To determine the characteristics of FGDs in children between 8 and 18 years of age from Colombia, Panama, Ecuador, El Salvador, Nicaragua and Mexico.

Methodology: A descriptive observational study was carried out in 1378 schoolchildren (n = 892) and adolescents (n = 486) of 11.6 ± 2.3 years old, 52.4% girls and 64.2% public school, in whom were determined by the Questionnaire for Gastrointestinal Symptoms of the Rome Criteria III (QPGS- RIII) Spanish version: FC (n=716, 11.9%), IBS (n=275, 4.6%), FAP (n=114, 1.9%), FAPS (n=41, 0.7%), abdominal migraine (AM, n=89, 1.5%), functional dyspepsia (FD, n=54, 0.9%), aerophagia (AE, n=43, 0.7%), adolescent rumination syndrome (ARS, n=21, 0.4%), cyclic vomiting syndrome (CVS, n=18, 0.3%) and non-retentive fecal incontinence (NRFI, n=7, 0.1%). Statistical analysis included measures of central tendency.

Results: In children with FC, 36.0% had ≤2 bowel movements per week, and presented 2 to 6 of these symptoms: pain on defecation (63.6%), retentive maneuvers (47.4%), large stools (33.4%), hard stools %, palpable fecalomas (17.5%) and fecal incontinence (11.6%). 26.2% of children with IBS had abdominal pain (AP) ≥ 1 year of evolution, 44.7% had concomitant supra and infra umbilical AP, with predominance of supra-umbilical AP (76.7%), with changes in consistency and frequency of faeces in ≥49.0% and improvement in AP after stool in 55.3%. In children with FAP and FAPS, AP was supra-umbilical in ≥63.4%, with AP ≥1 year of evolution in ≥21.9%, with symptoms associated with FAPS such as headache (48.8%), insomnia (41.5%) and extremities or back pain (36.5%). The main symptoms of children with AM were digestive upset (78.7%),

headache (74.2%) and lack of appetite (55.1%). 37.0% of children with FD had AP \geq 1 year of evolution. The most frequent symptoms in children with AE were borborygmos (67.5%), flatulence (65.2%) and abdominal distension (58.2%), and with CVS, nausea (88.9%). In 90.5% of children with ARS, symptoms occurred within the first hour after eating.

Conclusions: Depending on the DGFs that are identified, a specific characterization of the same.

552 **CORRELATION OF FUNCTIONAL DYSPEPSIA SUBTYPES AND SYMPTOMS WITH MUCOSAL MAST CELLS AND EOSINOPHILS.** Meenal Singh¹, Vivek Singh², Jennifer Schurman³, Craig Friesen

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Background: Antral mast cells and duodenal eosinophils have been implicated in the pathogenesis of functional dyspepsia (FD) in adults with less empirical data in children and adolescents. Mast cells have been reported to be increased in the postprandial distress syndrome (PDS) subtype and to be associated with psychosocial dysfunction in children and adolescents. The current study describes eosinophil and mast cell densities in the antrum and duodenum of children and adolescents with functional dyspepsia and assesses cell density correlations and relationships to symptoms and FD subtypes, PDS and epigastric pain syndrome (EPS).

Methods: Biopsies and symptoms from 116 children/adolescents (76% F; ages 8-17 years, mean 12.97 years) with FD were assessed. Peak and mean eosinophil and mast cell densities, respectively, were determined by a single investigator (MS) blinded to the clinical history.

Results: The sample consisted of 92 patients fulfilling PDS criteria and 24 fulfilling EPS criteria. Nineteen fulfilled criteria for both. Mean and peak densities were highly correlated ($r > .9$) for both cell types in both locations so peak densities were used for further analysis. Eosinophil densities were higher in the duodenum (27.4 ± 13.1 vs. 14.5 ± 10.9 , $p < .001$) as were mast cell densities (22.6 ± 8.2 vs. 18.2 ± 6.9 , $p < .001$) as compared to the antrum. Using suggested cut-off values, in the antrum, eosinophil density was >10 /hpf in 56% and mast cell density was >15 /hpf in 67%. In the duodenum, eosinophil density was >20 in 60% and mast cell density was >20 in 61%. Antral eosinophil density was correlated with duodenal eosinophil density ($r = .355$, $p < .001$). Antral mast cell density was correlated with both duodenal eosinophil density ($r = .187$, $p = .045$) and mast cell density ($r = .492$, $p < .001$). Cell densities did not differ between patients with and without EPS or between those with and without PDS. There was a trend with a moderate effect size for increased duodenal mast cells in PDS alone as compared to PDS/EPS overlap (23.8 ± 8.2 vs. 20.1 ± 8.0 , $p = .078$; Cohen's $d = 0.460$) Patients reporting headaches had increased antral eosinophil density (15.5 ± 12.5 vs. 11.6 ± 6.6 , $p = .034$) and patients reporting increased pain with eating had a trend towards increased antral eosinophil density with a moderate effect size (15.5 ± 11.8 vs. 11.1 ± 6.8 , $p = .068$; Cohen's $d = 0.457$).

Conclusion: PDS is common in children/adolescents with FD; most meeting criteria for EPS exhibit overlap with PDS. Even though criteria are not well established, the current study provides evidence that a significant proportion of FD patients have elevated mucosal eosinophils and mast cells with densities correlating across the two cell types and the two mucosal sites. Cell densities have some association with symptoms and FD subtype. FD subtype associations deserve further study in a larger cohort.

554 **TRENDS IN THE EVALUATION AND MANAGEMENT OF CONSTIPATION IN THE EMERGENCY DEPARTMENT (ED): DATA FROM A NATIONAL SAMPLE.** Michael Foreman, Sneha Raju, Lara Johnson

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Purpose: Constipation is a common pediatric complaint and cause of abdominal pain in the pediatric age group. We sought to characterize the epidemiology of ED visits for constipation and to examine resource utilization for the diagnosis and management of constipation in the ED setting.

Methods: We utilized data from the 2005-2012 National Hospital Ambulatory Medical Care Survey (NHAMCS), a nationally-representative, four-stage probability sample of ED visits. We generated descriptive statistics regarding patient characteristics and resource utilization. For all analyses, we considered separately the population of patients presenting with a chief complaint of constipation as well as those patients with physician diagnosis of constipation at the time of ED disposition. We utilized chi-squared tests for bivariate analyses. All analyses were completed using SAS 9.3 and SUDAAN 10.0.

Results: During the study period there were an estimated 202,000 ED visits each year presenting with a chief complaint of constipation ($n = 432$, 0.65% of ED visits). For those patients presenting to the ED with abdominal pain ($n = 4,263$), 8.8% ($n = 391$) received a diagnosis of constipation. At the time of disposition from the ED, 1.2% ($n = 799$) of pediatric visits had a diagnosis of constipation providing a national estimate of 366,000 patients per year. Patients with a diagnosis of constipation

had an average age of 6.1 years (SD 5.5) and were more likely to have received imaging than other ED patients (55.9% vs 32.4%, $p < 0.001$) and more likely to have received a computed tomography scan (10.4% vs 5.8%, $p = 0.005$). However, among patients who presented with a complaint of constipation, imaging and computed tomography use were not increased and the average age was 3.5 years (SD 5.0). Procedures occurred less frequently for those with a diagnosis of constipation and laboratory studies were obtained less often. Miralax (polyethylene glycol) was the most commonly used medication; enema preparations were used less frequently, and one quarter received no medications at all.

Conclusions: Constipation is a common complaint in the emergency department in the pediatric age group. Patients diagnosed with constipation were older and had more imaging utilization compared to those with patient-reported complaints of constipation. Future studies should explore the role of imaging in diagnosing constipation. In addition, opportunities may exist for patient education in order to potentially avoid ED visits for constipation.

556 INTENSIVE INTERDISCIPLINARY TREATMENT OF CHILDHOOD AND ADOLESCENT ENCOPRESIS. Navneetha Unnikrishnan¹, Meghan Gibson³, Priyadarshini Hirway², Heather Chapman⁴, Diane Dermarderosian⁴, Michael Herzlinger¹, Albert Ross¹, Linda Shalon¹, Jason Shapiro¹, Jared Silverstein¹, Carolina Cerezo¹. ¹Pediatric Gastroenterology, Hasbro Children's Hospital, Providence, RI; ²Biostatistics, Hasbro Children's Hospital, Providence, RI; ³Pediatrics, Hasbro Children's Hospital, Providence, RI; ⁴Pediatric Partial Hospital Program, Hasbro Children's Hospital, Providence, RI

Background: Encopresis or fecal incontinence is a common and distressing condition associated with negative psychosocial outcomes for children and their families. Prior reviews suggest the prevalence of encopresis in school-age children to range from 0.3-8%. Given disease complexity and comorbidities, fecal incontinence should be conceptualized within a biopsychosocial paradigm and treatment should involve collaborative practice models that incorporate behavioral, educational, and cognitive methods beyond medical management. The Hasbro Partial Hospital Program (PHP) is a unique day treatment program for children with concurrent medical and psychiatric diagnoses. Children benefit from highly intensive, family-centered, and interdisciplinary care provided by a diverse healthcare team that includes physicians, nurses, therapists, teachers, nutritionists, and social workers.

Objectives: The objective of this study is to characterize the children admitted to PHP for refractory encopresis and to determine their short and long-term outcomes after program completion.

Methods: This study is a retrospective chart review of children admitted to the Hasbro Partial Hospital Program over a six year period.

Results: Among the 24 enrolled patients, it is notable that 79% (19) of them were male and 74% (17) were between ages 4-6 years at onset. In addition, 26% (6) had ongoing encopresis for over 3 years before presentation to PHP; 4% (1) of patient had it for over 10 years. Notably 95% (23) patients had a psychiatric co-morbidity and 46% (11) patients had associated ADHD. We also found that most patients had at least one psychological stressor; 46% (11) had divorced or separated parents, 50% (12) had trauma or abuse within their household, and 54% (13) reported experiencing bullying in school. Following the interdisciplinary intervention, 75% of patients did not have encopresis at discharge. At first follow-up, only 35% (7) of patients had persistent encopresis. First follow-up occurred at less than 1 month for 37.5% (9) patients, between 1-3 months for 25% (6) patients, and ≥ 12 months for 12.5% (3). The remaining patients did not have any documented follow up.

Baseline Characteristics		n (%)
Sex	Female	5 (21%)
	Male	19 (79%)
Language spoken	English	22 (92%)
	Spanish	2 (8%)
Insurance	Public	21 (87%)
	Private	3 (13%)
Referred by	PCP	1 (4%)
	Behavioral/psychiatrist	16 (67%)
	Other*	10 (42%)
Onset age of encopresis	< 4 years**	1 (4%)
	4-6	17 (71%)
	6-10	2 (8%)
	10-15***	2 (8%)
	16-20***	1 (4%)
Duration of encopresis	< 1 year**	9 (38%)
	1-2	9 (38%)
	3-10	3 (13%)
	11-15	1 (4%)
	16-20***	2 (8%)
Use of purgatives	Yes	14 (58%)
	No	10 (42%)
	ND***	0 (0%)
Psychiatric comorbidity	Yes	23 (95%)
	No	1 (4%)
Psychological stressor	Yes	23 (95%)
	No	1 (4%)
Encopresis at discharge	Yes	2 (8%)
	No	18 (75%)
	ND***	4 (17%)
Time to first follow up	< 1 month	9 (38%)
	1-3 months	6 (25%)
	3-6 months	1 (4%)
	> 6 months	8 (33%)
Encopresis at first follow up	< 1 month	1 (12%)
	1-3 months	4 (50%)
	3-6 months	0 (0%)
	> 6 months	3 (38%)

Table 1. Descriptive characteristics (n=24).
 * Onset of encopresis at <4 years – Patients were included if they never completed toilet training.
 ** Many years was included as we found the duration to be reported in that way in some of the charts during our review.
 *** ND – not documented

Conclusion: Children and adolescents with refractory encopresis are more likely to be males and present between the ages of 4 and 6 years. A significant number of these patients also had at least 1 psychological stressor or psychiatric co-morbidity. Pediatric patients with encopresis admitted to an intensive interdisciplinary program appear to benefit at least in the short term. Early identification of patients with risk factors may be important in improving care by providing early referral to a more comprehensive treatment program.

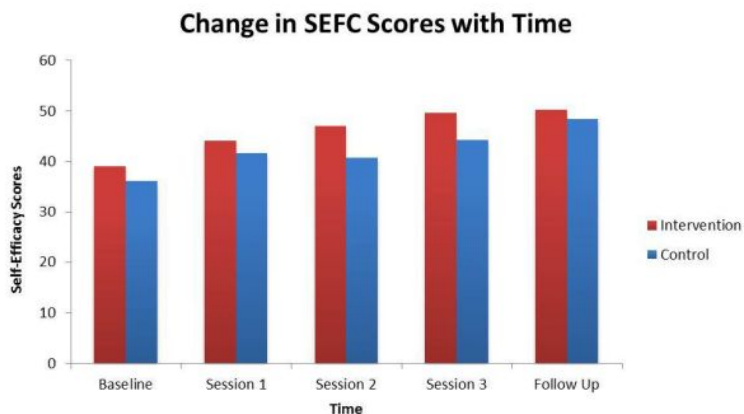
557 A PILOT RANDOMIZED CLINICAL TRIAL TO ASSESS THE EFFECT OF IMPROVING SELF-EFFICACY ON OUTCOMES IN CHILDREN WITH FUNCTIONAL CONSTIPATION. *Neha Santucci¹, Mackenzie Schindler¹, Erin Reuther^{1,2}, Miranda van Tilburg^{3,4,5}, Adam Mansfield¹, Lauren Rein¹, Paul Hyman¹. ¹Pediatric Gastroenterology, LSUHSC, New Orleans, LA; ²Pediatric Clinical Psychology, LSUHSC, New Orleans, LA; ³Clinical Research, Campbell University College of Pharmacy and Sciences, Buies Creek, NC; ⁴Medicine, University of North Carolina, Chapel Hill, NC; ⁵School of Social Work, University of Washington, Seattle, WA*

Background: Functional constipation (FC) causes constipation in >95% of children but only 50% children enjoy treatment success with current guidelines of education, disimpaction, and maintenance of soft-stools. We assessed self-efficacy (SE), the belief that one can achieve a goal, for defecation and our previous research showed that SE for FC is associated with treatment success. In this study, we designed a randomized controlled trial to assess the effect of guided mastery, a therapeutic method of raising a person’s perception to accomplish a task, on SE and treatment outcomes.

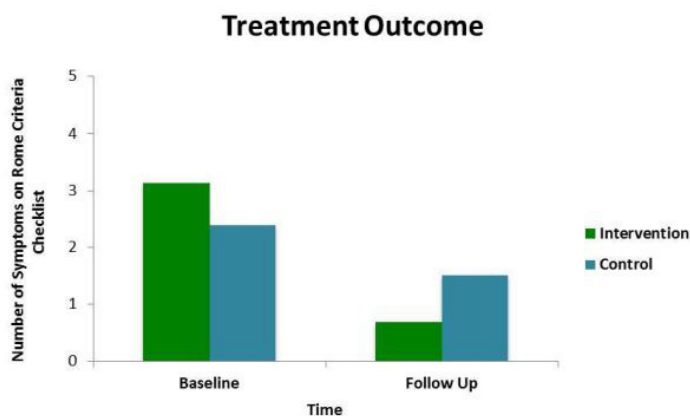
Methods: Sixteen subjects ages 7-16y, who met Rome 4 criteria for FC, received treatment as usual at their baseline gastroenterology visit. A psychologist then randomized them in a 1:1 ratio to the intervention or control group and delivered therapy once a week for 3 weeks. The treatment group received guided mastery through a stepwise protocol, while controls received information on dietary changes. Subjects completed a previously validated SE for FC questionnaire at each visit and on completion. Primary outcome included symptoms on the Rome 4 criteria checklist.

Results: Mean age was 10.62 ± 3.48y, 38% were males, 43% were Caucasian, 38% AA and 19% had fecal incontinence. Of 8 controls and 8 treatment participants, 2 in each group were non-completers. SE scores improved with time in each group (p<0.001); from 36.13 to 48.5 (max 56) in controls and 39.13 to 50.33 for intervention group. Eighty-three% of intervention subjects had treatment success compared to 50% in the control group. The main effect of treatment group and interactions were not significant, but these effects may be present with increased sample size.

Conclusion: Pilot data suggest that guided mastery may be beneficial in enhancing treatment success in FC. However, a larger sample size is required to detect significant effects. Thus, we hypothesize that children can be motivated to accomplish progressively more difficult tasks needed for defecation to resolve FC.



Change in Self-Efficacy Scores



Treatment Outcome

559 CHARACTERIZATION OF CHILDREN IDENTIFIED WITH MINOR DISORDERS OF ESOPHAGEAL PERISTALSIS ACCORDING TO THE CHICAGO CLASSIFICATION VERSION 3. *Peter Osgood, Eric Chiou; Pediatric Gastroenterology, Hepatology, and Nutrition, Texas Children’s Hospital/Baylor College of Medicine, Houston, TX*

Introduction: The Chicago Classification (CC) v3.0 was updated in 2014 with the goal of applying standardized high-resolution manometry (HRM) metrics to categorize esophageal motility disorders in adults. Although the subtyping of achalasia based on HRM findings has gained relative acceptance, the clinical significance of minor disorders of peristalsis based on CC v3.0 criteria, such as ineffective esophageal motility or fragmented peristalsis, has been less clear. Furthermore, the application of these parameters to measure esophageal physiology in children has not been well studied. We sought to apply the CC v3.0 to a pediatric cohort, and to compare the clinical and manometric characteristics of patients with normal findings versus minor peristaltic abnormalities.

Methods: Pediatric patients who underwent clinically-indicated HRM at Texas Children's Hospital from December 2007 to May 2017 were identified and retrospectively reviewed. Esophageal manometry had been performed as per a standard protocol. Patients with a history of previous esophageal surgery, esophageal stricture, or incomplete HRM study were excluded. All studies were classified per the CC v3.0 criteria. Those with major manometric abnormalities such as achalasia, absent peristalsis and distal esophageal spasm were excluded. The medical chart was reviewed to assess clinical characteristics, endoscopic findings, radiographic features of patients with minor disorders of peristalsis versus those with normal findings.

Results: A total of 125 HRM studies from 116 patients were reviewed. 47 patients were found to have normal esophagogastric junction (EGJ) relaxation and did not meet any exclusion criteria. Of these, 14 were classified as having a minor disorder of peristalsis, including 14 (100%) with ineffective esophageal motility (IEM) and 0 (0%) with fragmented peristalsis. There were 33 patients with normal HRM findings (one of whom had a repeat study 7.2 years after her first). The two groups showed similar age (median 14.9-15 years) but the normal group displayed a higher proportion of males (51.5 vs 28.6%) as well as a higher median BMI percentile-for-age (67th vs 35th percentile). Clinical indications for manometry were similar between the groups though those with minor peristalsis disorders had more nausea and forceful emesis (64 vs 45.5% in normal patients) and less rumination (28.6 vs 48.5%). Prior investigations yielded a higher rate of abnormal upper endoscopy in those with minor peristalsis disorders (62.5 vs 52%). On high resolution esophageal manometry, those with disordered peristalsis appropriately displayed lower median DCI (278.2 vs 1186.1 mmHg.s.cm) and a higher percentage of both large (9.6 vs 0%) and small breaks (25 vs 10%).

Conclusions: Identification of minor disorders of esophageal motility in children based on the CC v3.0 criteria was uncommon. Although there were some differences when compared to children with normal findings, such as lower BMI percentile and higher proportion with abnormal radiographic studies, the rates of spontaneous improvement in symptoms was similar for both groups. Further studies are needed to further characterize the clinical significance of classifying minor esophageal motility disorders in children.

560 UNMET NEEDS IN PEDIATRIC FUNCTIONAL CONSTIPATION. *Manu Sood¹, Peter Lichtlen², Claudia Perez³. ¹Division of Pediatric Gastroenterology, Hepatology and Nutrition, Medical College of Wisconsin, Milwaukee, WI; ²Sucampo AG, Zug, Switzerland; ³Takeda Development Center Americas, Inc, Deerfield, IL*

Background: Pediatric functional constipation (PFC) exerts a significant burden on the healthcare system, as well as on patients and their caregivers. Despite the current treatment options available, several gaps exist along the treatment landscape, namely, limited data on drug therapies, lack of guidance for disease management, and poorly defined disease state.

Methods: A comprehensive literature review was performed using targeted PubMed searches (2010-2016) to retrieve articles on current available treatments, clinical trial outcomes, and healthcare professionals' (HCPs) education/clinical practice. Search returns were analyzed to identify gaps and unmet medical/educational needs in PFC.

Results: Key findings and the number of publications retrieved per topic are summarized below (**Table**). Overall, few studies exist for drug therapy in PFC and there is a dearth of published literature on PFC treatment and management. Oral laxatives are the most commonly prescribed treatments for fecal disimpaction and maintenance therapy, but do not provide sustainable symptomatic relief. Dietary fibers, probiotics, and nonpharmacologic interventions are commonly used in clinical setting. While some therapies have shown promise in PFC, data from randomized controlled trials of sufficient duration are lacking and no pharmaceutical treatment has been studied following rigorous evidence-based criteria. Further, the limited knowledge and awareness among pediatricians of PFC causes and comorbidities, pathophysiology, and treatment strategies are barriers to diagnosis and disease management.

Conclusions: While several treatments are available, complete and sustainable symptomatic relief remains a key unmet medical need. Improved education, clinical research, and awareness of multimodal treatment strategies can facilitate better diagnosis and management of PFC.

Literature Review in PFC: Key Findings and Unmet Needs

	Current Treatments	Clinical Research	Education/Clinical Practice
Key Findings (# of articles)	<p>Pharmacologic: 63 Oral laxatives most commonly prescribed, but 40% of patients have frequent relapses or may not respond Growing use of probiotics/fiber</p> <p>Nonpharmacologic: 106 Short-term improvements with enemas and surgery Sacral nerve modulation benefits sustained; data limited</p>	<p>Randomized controlled trials: 61 Laxatives more efficacious than placebo short-term Limited data on prescription drug therapies Prucalopride safe and tolerated; efficacy similar to that of placebo</p> <p>Long-term outcomes: 64 Limited data; few studies with pharmacological therapies reporting quality of life improvements</p>	<p>Education: 20 Currently limited or no public health attention to PFC in pediatric residency programs Limited knowledge/understanding of idiopathic PFC pathophysiology, secondary causes, comorbidities, and treatment/management</p> <p>Clinical practice: 20 Inconsistent use of Rome criteria and treatment guidelines for diagnosis and treatment of PFC Bowel diaries used more frequently than rectal exams, X-rays, and labs for diagnosis</p>
Unmet Needs	<p>Complete, sustainable relief in a subset of patients More options for maintenance therapy</p>	<p>Well-designed trials and adequate clinical research Long-term (≥6 mo) and real-world data</p>	<p>Improved education and awareness among clinicians Implementation of multimodal treatment approaches</p>

561 NAUSEA NEGATIVELY IMPACTS QUALITY OF LIFE AND IS ASSOCIATED WITH AUTONOMIC DYSREGULATION IN ADOLESCENTS WITH FUNCTIONAL ABDOMINAL PAIN DISORDERS.

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Background: Prior data indicates that the presence of nausea in functional gastrointestinal (GI) disorders is associated with a higher GI, somatic and psychiatric symptom burden. The reason for this is unclear. Comorbid symptoms of autonomic nervous system imbalance are common in adolescents with chronic nausea. Autonomic imbalance and homeostatic dysregulation may be a plausible explanation for these refractory symptoms. To date, the symptom pattern, autonomic balance and quality of life has not been reported in adolescents with nausea.

Methods: A total of 115 adolescents ages 11-18 were prospectively enrolled in an outpatient, tertiary care pediatric gastroenterology clinic. All patients met Rome III criteria for at least one pain-related functional GI disorder based on the Rome III diagnostic questionnaire (QPGS III). Subjects underwent standard medical workup and formal autonomic testing as clinically indicated (Tilt table, Valsalva maneuver, Deep breathing and Quantitative Sudomotor Axon Reflex Testing). Subjects completed detailed symptom questionnaires on the characteristics of nausea and co-morbidities and the following validated instruments: 1) Nausea Profile assessing several dimensions of nausea, 2) PROMIS (Patient-Reported Outcomes Measurement Information System) pediatric global health measure (PGH-7) and 3) FDI (Functional Disability Inventory) assessing physical functioning (children and parents).

Results: Mean age was 15.5 (13.5-17.2) years. 90% (n=104) were female. 71% (n=82) had at least twice weekly nausea (+N) while the remaining 29% had no nausea (-N). In the +N group, mean nausea severity was 5.7 (0-10 scale) and 73% suffered from daily nausea. Most complained of morning (42%) or constant (25%) nausea while a smaller number had nausea post-prandially (16%), at random (12%) or at night (5%). Comorbid symptoms in the +N vs. -N groups were as follows: dizziness (80% vs. 41%; p<0.001), concentrating difficulties (67% vs. 27%; p<0.001), chronic fatigue (56% vs. 20%; p=0.008) and sleep problems (72% vs. 48%; p=0.19). There was no difference in the prevalence of migraine headaches: 75% in +N vs 69% in -N group met migraine criteria per the International Classification of Headache Disorders (p=0.64). 42% (n=48) of the entire cohort underwent autonomic testing; 92% (n=44) of these were abnormal. 95% (n=37 out of 39) in the +N group had abnormal autonomic test vs 78% (n=7 out of 9) in the -N group. The most common abnormality was postural tachycardia syndrome (48%) followed by autonomic neuropathy (34%). Results of Nausea Profile, PROMIS and FDI measures are shown in Table 1.

	Nausea (n=79)	No Nausea (n=33)	p-value
Nausea Profile	76.06 ± 34.85 (44.7 ± 20.5%)	48.36 ± 35.14 (28.5 ± 20.7%)	<0.001
PROMIS T-Score	37.33 ± 5.37	40.81 ± 6.46	0.004
Functional Disability Inventory (Child)	21.36 ± 11.75	15.76 ± 13.29	0.029
Functional Disability Inventory (Parent)	19.66 ± 12.82 (n=53)	13.75 ± 11.81 (n=24)	0.059

Conclusion: A large proportion of patients with functional abdominal pain disorders suffer from chronic nausea. Nausea is associated with a higher co-morbid symptom burden, worse quality of life, functional disability and autonomic instability. Few patients have meal-related nausea and functional dyspepsia may thus not be a major cause. The observed autonomic nervous system imbalance may suggest central homeostatic dysregulation. Autonomic imbalance may be a contributing factor to disease burden in adolescents with functional GI disorders and concurrent nausea and a possible therapeutic target.

562 UPPER GASTROINTESTINAL DYSMOTILITY IS COMMON IN PATIENTS WITH

BRONCHIECTASIS. Rachel Rosen, Margot Lurie, Eitan Rubinstein, Kara Larson, Ann Lee, Lisa Hester, Samuel Nurko. *Gastroenterology, Boston Children's Hospital, Boston, MA*

Background: Bronchiectasis is a concerning finding on high resolution chest CT (HRCT) but its cause is not known. While gastroenterologists are frequently consulted by pulmonologists to evaluate for reflux in these patients, aerodigestive gastroenterologists are more frequently concerned about the role of upper gastrointestinal dysmotility in these patients. We hypothesize that esophageal dysmotility and oropharyngeal dysphagia/aspiration may play a causative role in bronchiectasis.

Methods: We identified all of the patients seen in our aerodigestive center between 2013-2016 who underwent HRCT because of persistent pulmonary symptoms. Charts were reviewed to determine the results of high resolution esophageal manometry, nuclear medicine esophograms, upper GI barium imaging, and video fluoroscopic swallow studies. We then categorized patients based on adequacy of swallow function, esophageal dysmotility, and gastric dysmotility to determine possible predictors of bronchiectasis.

Results: 102 patients underwent HRCT of which 35 patients (34%) had evidence of bronchiectasis seen on HRCT. 22 patients (22%) had evidence of esophageal dysmotility on high resolution esophageal manometry, nuclear medicine esophagram or barium imaging. 13 (13%) patients had a primary motility disorder (esophageal atresia, achalasia) and 9 (9%) patients had a secondary motility disorder (stasis related to fundoplication, vascular ring, esophageal structuring). 52 (52%) patients had evidence of aspiration or penetration on video fluoroscopic swallow study. As shown in the table, oropharyngeal dysphagia/aspiration, esophageal dysmotility, and the combination of both oropharyngeal dysphagia and esophageal dysmotility are more common in patients with bronchiectasis.

Conclusion: Oropharyngeal and esophageal dysmotility are common in patients with bronchiectasis. Additional longitudinal studies are needed to determine if improving this dysmotility improves long term lung function.

Relationship between Dysmotility and Bronchiectasis

	No Bronchiectasis	Bronchiectasis
% Patients with Oropharyngeal Dysphagia	48%	57%
% Patients with Esophageal Dysmotility	19%	26%
% Patients with Oropharyngeal and Esophageal Dysmotility	10%	20%
% Patients with Abnormal Gastric Emptying	40%	45%

563 SERUM-DERIVED BOVINE IMMUNOGLOBULIN (SBI) FOR CHILDREN WITH DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME (D-IBS).

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Background: In a double-blind, randomized single center trial of adults, SBI reduced stool number and improved abdominal pain in d-IBS. (D Wilson et al. Clin Med Insights Gastroenterol 2013; 6: 49-60).

Aim: To determine if SBI improved symptoms in children with d-IBS.

Methods: In a randomized, double-blind, placebo-controlled, weighted pilot study evaluating SBI on symptoms in children 8-18 y, newly diagnosed patients with d-IBS were recruited according to ROME III criteria. We assessed baseline symptoms for 1 wk (stool number, abdominal pain, and stool type using Bristol stool scale), and we assigned patients to 5 g BID SBI or placebo at a ratio of 2:1 for 3 wk. Patients and parents completed Pediatric Quality of Life Inventory for Gastrointestinal Symptoms (PedsQOL) and the Pediatric Functional Disability Index (FDI) at the start and end of treatment. We obtained laboratory assessments at start and end of treatment to evaluate safety.

Results: We randomized 20 patients; 15 completed the study (age 13.5+ 3.6 y X+ SD y, 6 male, 12 white, 1 black, 2 Hispanic). Nine patients received SBI, 6 placebo. Both groups reported reduction in stools/wk (P=0.01), abdominal pain (P=0.002), and improved stool form (P=0.02) after 3 wk. There was a trend for fewer stools in the SBI group (13.6±5.4/wk. X+SD) compared to placebo (15.5±13.6/wk) (P=0.7). Patient FDI scores improved in the SBI group (P=0.01), but not placebo (P=0.23). Parent FDI scores improved in both groups. PedsQOL scores improved with SBI (P=0.01), but not placebo (P=0.14). Parent-assessed PedsQOL scores improved in SBI (P=0.004) and placebo (P=0.06). In IBS-related subscales of the PedsQOL questionnaire, there was significant improvement of the scores from baseline to end of treatment in the SBI group in pain and discomfort (P=0.008), discomfort when eating (P=0.01), constipation (P=0.03), diarrhea (P=0.009), worry about stomach aches (P=0.03), and communication (P=0.03), the improvement of these scores in the placebo group was not significant. No serious adverse events occurred. One patient on SBI discontinued due to emesis. Serum chemistries and hemograms were normal at baseline and end of study in all patients.

Conclusion: In this single center pilot study we demonstrated that 10 g SBI/day was safe in children with d-IBS, with improvement in d-IBS symptoms. Comforts provided to patients, including detailed explanation, reassurance, close monitoring, and ready access to researchers may have contributed to a placebo response, a bias that may lead to a systematic error in estimating the treatment effect. Unlike the European Medicines Agency guidelines that recommend treatment of 4 wks or longer to establish short-term efficacy in conditions like d-IBS which fluctuates in severity, this short 3-wk study may have biased the outcome. Larger studies, with longer treatment duration seem warranted based on these initial positive results.

564 ANTRODUODENAL MANOMETRY AS A PREDICTIVE TOOL IN OVERALL FEEDING OUTCOMES IN PATIENTS WITH UNEXPLAINED UPPER GASTROINTESTINAL SYMPTOMS.

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Introduction: Antroduodenal manometry (ADM) is increasingly being used for the evaluation and treatment guidance of unexplained upper gastrointestinal symptoms. However, information regarding the utility of ADM and clinical outcomes is limited. Therefore, we evaluated the usefulness of ADM as a predictor of overall feeding outcomes in patients with unexplained upper gastrointestinal symptoms.

Methods: Retrospective medical record review of 212 patients that underwent ADM for the evaluation of unexplained upper gastrointestinal symptoms refractory to conventional medical therapy. Patients were classified as having obstructive symptoms (abdominal distension and/or vomiting), or functional symptoms (abdominal pain and/or nausea). ADM tracings were previously analyzed by two expert physicians and reported as normal or abnormal. Recommended treatment was documented and classified as medical or surgical. Treatment response was described as complete resolution of symptoms, good with no change in therapy, partial with change in therapy or unresponsive. Successful overall outcome was described as the ability to advance enteral feeds and, if present, decrease in parenteral nutrition.

Results: Of the 212 reviewed medical records, 88 had outcome information available and were included for analysis (mean age 9.6 years, 53% male). Obstructive symptoms were present in 56 (64%) and functional symptoms in 32 (36%) of the patients. ADM was normal in 21 (24%) and abnormal in 67 (76%). The most common ADM abnormality was antral postprandial hypomotility (39%). The proportion of patients with obstructive symptoms having an abnormal ADM was significantly higher than those with functional symptoms (48/67 or 72% vs. 19/67 or 28%; $p=0.005$). Medical treatment was recommended in 67 patients (76%), surgical treatment in 5 (6%), and preexisting treatment was not changed in 16 (18%).

The most common recommended medical therapy were prokinetics (65%). Based on treatment guided by ADM results, 36 (41%) patients reported partial response to treatment that required change in therapy, 31 (35%) reported good response with no change in therapy, 19 (22%) were unresponsive and, 2 (2%) had complete resolution of symptoms. No difference was observed on treatment response whether the ADM was normal or abnormal ($p=0.85$). Information about feeding outcomes was available in 82 patients. Overall, 61 (69%) were able to advance enteral feeds and decrease parenteral nutrition and 21 (24%) were not able to advance enteral feeds. No difference was observed on feeding outcomes whether treatment was medical or surgical ($p=0.29$). The proportion of patients able to successfully advance enteral feeds was significantly higher in those with an abnormal ADM compared to those with a normal study (47/61 or 77% vs. 14/61 or 23%; $p=0.002$) and in those that had a good/partial response to treatment ($p<0.05$).

Conclusion: ADM is a useful tool for predicting feeding outcomes in patients with unexplained upper gastrointestinal symptoms. A significant proportion of patients presenting with obstructive symptoms with an abnormal study were able to successfully advance enteral feeds based on treatment guided from the ADM results. Our results highlight the value of ADM performance in patients presenting with obstructive and not functional symptoms.

565 USE OF CITALOPRAM FOR PEDIATRIC PATIENTS WITH CHRONIC ABDOMINAL PAIN REFERRED TO THE MULTIDISCIPLINARY ABDOMINAL PAIN CLINIC- A SINGLE CENTER INITIAL EXPERIENCE.

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Introduction: Selective serotonin reuptake inhibitors (SSRIs) have been found to increase central serotonin synaptic concentrations which are effective at decreasing visceral pain, decreasing gastric motility in patients with irritable bowel syndrome (IBS) with diarrhea, and increasing gastric motility in patients that have IBS with constipation (3). Earlier studies in adult patients with IBS found that citalopram decreased abdominal pain independent of mood and gastrointestinal (GI) symptoms (1). A recent study in pediatric patients with functional abdominal pain (FAP) showed that citalopram decreased their pain scores without altering their depression, anxiety, or somatization (multiple body complaints) after eight weeks of treatment (2). The aim of our study was to describe our experience with citalopram and its effect in reducing abdominal pain when used in the treatment of chronic abdominal pain (CAP) in pediatric patients in our facility.

Methods: Charts of patients seen in the Pediatric Multidisciplinary Chronic Abdominal Pain Clinic (PMCAPC), between January 2015 to February 2017 were retrospectively reviewed. Age, gender, race, history of dysautonomia, psychiatric co-morbidities, citalopram dose and CAP response to citalopram therapy were evaluated. Patients referred to the PMCAPC have seen at least one prior gastroenterologist, have failed multiple therapies and are often seeking second or third opinions for treatment of CAP. Patients seen in the PMCAPC, were evaluated by a pediatric neurogastroenterologist, pediatric pain management specialist and a pediatric psychologist. Information about improvement in abdominal pain was gathered by follow up visit documentation or phone. CAP was defined to include patients with IBS as well as functional abdominal pain by ROME III criteria. Psychiatric co morbidities were only included if the psychologist included this in the diagnosis list. Improvement was defined as the patient’s perception of improvement in abdominal pain while on citalopram.

Results: A total of 58 patients’ charts were reviewed. 18 of those were prescribed citalopram. Patients ages ranged from 11 to 18 years old, with 83.3% being female. A total of 13 (72.2%) were Caucasian, 3 were Hispanic, 1 was African American and 1 was of unknown race. 1 out of the 18 patients had documented psychiatric co-morbidities and 2 of them had history of dysautonomia. In the 18 patients that were prescribed citalopram, 11 (61.1%) reported improvement in abdominal pain (Figure 1), 0 of these 11 patients had diagnosed psychiatric co-morbidities and 1 had to wean off after 2 months due to side effects. 4 of 18 patients (22.2%) patients reported no improvement in abdominal pain; In fact, 1 of those 4 patients reported resolution in abdominal pain after discontinuing citalopram. Two (11.1%) patient responses were unknown. 1 patient of the 18 prescribed citalopram never started the medicine due to self-resolution in abdominal pain.

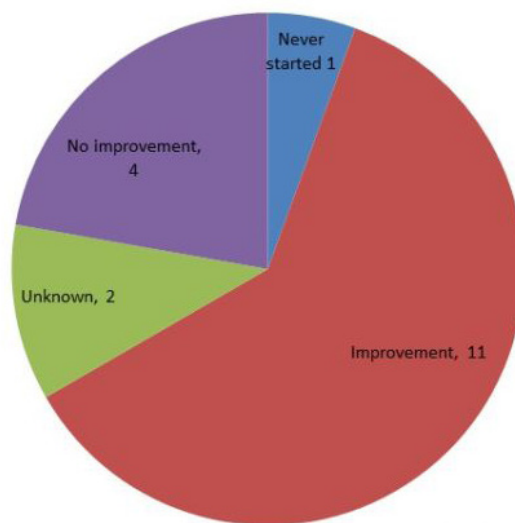


Table 1 :Citalopram use in pediatric chronic abdominal pain

Conclusion: Citalopram helped improve the abdominal pain for most of the pediatric patients that were prescribed therapy. The patients who reported improvement did not have diagnosed psychiatric co morbidities. There is limited data on the use and effectiveness of citalopram in treatment of pediatric patients with CAP. Studies with longer treatment duration in larger samples of patients are needed to further assess the efficacy of citalopram at treating pediatric CAP. Studies are also needed to determine if other SSRIs have a similar effect on abdominal pain.

References: Creed. (2006). How do SSRIs help patients with irritable bowel syndrome? *Gut*, 55, 1065–1067. doi: 10.1136/gut.2005.086348

Roohafza, H., Pourmoghaddas, Z., Saneiant, H., & Gholamrezael, A. (2014). Citalopram for pediatric functional abdominal pain: A randomized, placebo-controlled trial. *Neurogastroenterology & Motility*, 26, 1642-1650. doi: 10.1111/nmo.12444

Trinkley, K.E. & Nahata, M.C. (2014). Medication management of irritable bowel syndrome. *Digestion*, 89, 253-267. doi: 10.1159/000362405

566 **SEEING IS BELIEVING: THERE IS SO MUCH MORE TO THE ENTERIC NERVOUS SYSTEM THAN “PRESENT” OR “ABSENT”.**

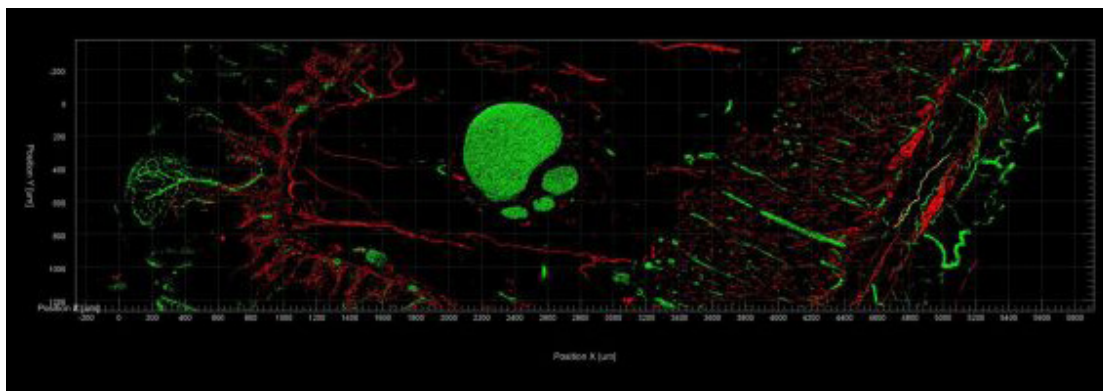
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Hypothesis: Intestinal motility disorders are common and debilitating, but remain difficult to diagnose. We hypothesize that many of these disorders occur because of defects in the structure and function of the enteric nervous system (ENS). Because the ENS is not well seen with routinely employed pathology methods, even major problems with ENS structure can be missed. Improved methods are needed and information about what is “normal” is essential if we hope to understand human intestinal motility disorders.

Methods: We established robust methods for visualizing the enteric nervous system in human bowel without tissue sectioning permitting three-dimensional visualization of important structures. We are testing a large panel of antibodies and generating confocal images from many normal and diseased bowel specimens. Our plan is to make these images freely available. As the work proceeds we will welcome collaboration since we need a really large database of images to understand the range of “normal” and to define how the ENS changes in the context of disease.

Results: We are generating remarkably beautiful images of the enteric nervous system that highlight the intricate anatomy missed by routine pathology methods. The image uploaded shows enteric glia in a full thickness 300 micron wide human bowel specimen. Although a limited number of similar images have been published, developing a large image repository will help bring this type of three dimensional evaluation of ENS structure closer to clinical practice.

Conclusions: We know from decades of work in animal models that the ENS is complex and remarkably dense. Nerve fibers from about 20 different neuron types are closely associated with every muscle fiber, with epithelial cells, and with many cells of the immune system. The ENS changes in response to injury and bowel inflammation. Most of the important structures within the ENS are not seen with routine pathology. We are now generating data needed to bring three dimensional imaging of the human ENS closer to clinical practice.



568 INITIAL EXPERIENCE WITH CO-MANAGEMENT OF PEDIATRIC PATIENTS WITH FUNCTIONAL ABDOMINAL PAIN BETWEEN PEDIATRIC GASTROENTEROLOGY AND A PEDIATRIC PAIN CLINIC WITHIN AN URBAN SAFETY NET HOSPITAL. Salvatore D'Amico, Vi Lier Goh, Claudio Morera, Laura Goldstein, Paula Gardiner, Caitlin Neri. Boston Medical Center Department of Pediatrics, Boston University School of Medicine, Boston, MA

Background: Functional abdominal pain (FAP) is the most common type of abdominal pain in children, and serves as a common source of referrals to pediatric gastroenterologists. Since functional abdominal pain is multifactorial in its origin, an ideal a solution should take an interdisciplinary approach taking into account biological and psychosocial contributors. As a safety net hospital, Boston Medical Center (BMC)'s Department of Pediatrics primarily serves an urban population of low-income patients and their families. Significant bodies of research have found substantial levels of pain relief among patients who actively participate in interdisciplinary pain treatment programs. For struggling families, socioeconomic factors can be a barrier to seeking this type of holistic care. BMC's interdisciplinary pediatric Pain Clinic aims to effectively treat chronic pain in children and introduce families to adjunctive services such as acupuncture, mind/body techniques, massage, aromatherapy, physical therapy, and therapeutic karate as such services would be otherwise unaffordable or unavailable. All of this is done in collaboration with the referring gastroenterologist in the same institution.

Methods: The Interdisciplinary Pain Clinic at BMC launched in February 2015 and utilized a team model to address pediatric chronic pain through a consult and follow-up model. The core team began with: a pediatrician, a pediatric psychologist with training in meditation, biofeedback, and hypnosis, a pediatric social worker, and a pediatric acupuncturist. In June 2016, we began enrolling patients into a study aimed to assess the feasibility of expanding services including physical therapy, massage, aromatherapy, nutrition, and therapeutic karate. Children are referred to the pain clinic through primary care or specialty providers. Upon initial consultation, a trained research assistant obtains consent and assent from pain clinic patients and their families in order to gather data on pain, coping skills, medical and family history, psychosocial stressors, and related clinical/demographic information. Following the initial clinic visit, the team collaboratively creates an individualized program, with input from the referring clinicians, and tailored medical, and non-pharmacologic interventions. The patient is then walked through the program outline and scheduled for follow-up visits with the adjunctive services as recommended. Participants are again assessed at three-month follow-up for clinical characteristics related to their pain and quality of life as well as documentation of services received. A subset of patients referred to the clinic for abdominal pain were analyzed for demographic and clinical characteristics to document the initial experience with this novel model for children from low income families with functional abdominal pain. This study was approved by the institutional review board of Boston University School of Medicine.

Results: Among 59 participants, 33 were referred for abdominal pain of more than six months duration in 51% of patients. Demographics are as follows: 52% White, 24% African-American, 24% other, with an average age of 13 years and 76% of patients insured by Medicaid. Seventy percent of participants treated for abdominal pain were referred to the Pain Clinic by a pediatric gastroenterologist from the same institution. Additional health concerns among these patients included irregular sleep (60%), self-reported co-occurring anxiety, depression, or trauma (27%), and self-reported ADHD or other behavioral problems (27%). Most common diagnoses made by the pediatric gastroenterologist were Functional Abdominal Pain (91%), Constipation (55%), and Dyspepsia (12%). Three-month follow-up data are available in nine out of 33 patients. Early results show a 100% utilization of integrative medicine services and mind/body strategies, reduction in emergency department visits and school absences, and improvement in pain scores, school functioning, and overall quality of life.

Discussion: Functional abdominal pain is among the most troublesome complaints of children with chronic pain. Though families commonly turn to specialized physicians, FAP patients have found the greatest symptom relief from utilizing an interdisciplinary approach. In this single center experience, pediatric gastroenterologists readily refer patients to an interdisciplinary pain clinic, and patients from low income backgrounds do participate in such a model. A successful co-management model for FAP is described here for low income children and families within an urban safety net hospital.

570 ACUTE GASTROENTERITIS AND THE RISK OF DEVELOPING FUNCTIONAL GASTROINTESTINAL DISORDERS. Shivani Gupta, Miguel Saps. Pediatrics, Nationwide Children's Hospital, Columbus, OH

Background: The pathogenesis of functional GI disorders (FGID) is unknown but likely multifactorial. Previous studies have shown that there is an increase in the prevalence of a FGID after acute gastroenteritis (AGE) in children (post-infectious FGID). These studies have not accounted for the possibility of some patients having a FGID at baseline.

Objective: The aim of the study is to determine the prevalence and incidence of a FGID following an episode of AGE.

Methods: A prospective study is being conducted on patients ages 4-17 years who present to the Emergency Department (ED) or Urgent Care (UC). The families completed the following standardized questionnaires: Rome III Diagnostic Questionnaire

for the Pediatric Functional GI Disorders (QPGS-III), Children's Somatization Inventory, Coping Strategies Inventory, Child Depression Score, State-trait Anxiety Inventory Children, and Pain Beliefs Questionnaire. Patients are contacted two weeks after the initial ED/UC visit to assess progress of their AGE symptoms. Subsequent follow up telephone calls are made 3 months after the initial ED/UC visit to administer the QPGS-III. Predictors of new onset FGIDs will be assessed at the end of the study

Results: This is an ongoing study. Thus far 19 patients have been recruited. We present data of our initial results. Of the 19, 7 (37%) had a positive QPGS-III for one or more FGID at baseline. At 2 weeks, 17 of 19 (89%) were still having significant symptoms of abdominal pain. At 3 months, we were able to collect data on 14 of the original 19. 7 (50%) of them had a FGID. 4 of these 7 patients had a diagnosis of a FGID at the initial encounter and 3 other patients had new onset of FGID following the AGE.

Conclusions: Our preliminary findings suggest that not all patients who have a FGID following an AGE should be considered a postinfectious-FGID. Thus, prevalence data on the prevalence of postinfectious-FGIDs may overestimate the magnitude of the problem. Preliminary data suggests that there is a need for prospective studies investigating the incidence of FGID after acute gastroenteritis.

*573 INCREASED RISKS OF IRRITABLE BOWEL SYNDROME IN CHILDREN WITH URINARY TRACT INFECTION DURING THEIR FIRST YEAR OF LIFE: A NATIONWIDE POPULATION-BASED COHORT STUDY

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Objectives: Early life events play an important role in the development of functional gastrointestinal disorders. An earlier case-control study from a US medical center shows that urinary tract infection (UTI) in infancy is a risk factor for chronic abdominal pain in childhood. However, it remains unclear whether UTI in infancy is a risk factor of irritable bowel syndrome (IBS) in Asian pediatric population. Hence, we conducted a population-based cohort study to investigate the subsequent risk of IBS in children with UTI during their first year of life.

Methods: From the National Health Insurance Research Database of Taiwan, we identified 31788 infants who had UTI between 2000 and 2011 as an UTI cohort. We identified another comparison cohort comprising 127152 infants without UTI, matched by age, gender, level of urbanization, and parental occupation. By the end of 2012, incidences of IBS in both cohorts, the UTI to non-UTI cohort hazard ratios (HRs), and confidence intervals (CIs) were measured.

Results: The incidence of IBS during the study period was 1.52-fold higher in the UTI cohort (95% CI: 1.38–14.67) than in the non-UTI cohort (2.05 vs. 1.32 per 10000 person-years). The HR of IBS was slightly greater for boys (1.53; 95% CI: 1.34–1.73) than for girls (1.50; 95% CI: 1.29–1.73). The HRs for IBS in children with UTI were greater for those with more UTI-related medical visits/per year (> 5 visits, HR: 61.3; 95% CI: 51.7–72.5), with longer hospitalization days (> 7 days, HR: 1.73; 95% CI: 1.35–2.22), and with vesicoureteral reflux (HR: 1.72; 95% CI: 1.34–2.20) (P < 0.0001, the trend test).

Conclusions: UTI during the first year of life increased the subsequent risk of IBS in childhood. This risk increased with more frequent and more severe UTI.

Table 1. The risk of irritable bowel syndrome in children with urinary tract infection (UTI) compared to children without UTI stratified by demographics in Cox proportional hazard regression

	Non- UTI			UTI			Adjusted HR [†] (95% CI)
	Event	Person-years	IR	Event	Person-years	IR	
All	1531	1161371	1.32	593	289021	2.05	1.52(1.38, 1.67)**
Sex							
Girl	653	512015	1.28	245	127574	1.92	1.50(1.29, 1.73)**
Boy	878	649356	1.35	348	161446	2.16	1.53(1.34, 1.73)**
Urbanization							
1 (highest)	481	336658	1.43	163	84092	1.94	1.32(1.11, 1.58)*
2	482	365234	1.32	183	90955	2.01	1.50(1.26, 1.77)**
3	269	225050	1.20	139	55598	2.50	2.01(1.64, 2.48)**
4 (lowest)	299	234429	1.28	108	58376	1.85	1.41(1.13, 1.76)*

IR, incidence rate, per 1,000 person-years

Adjusted HR[†], adjusted for age, sex, and urbanization

*p<0.01, **p<0.001

The risk of IBS in children with UTI compared to children without UTI stratified by demographics in Cox proportional hazard regression

Table 2. The risk of irritable bowel syndrome stratified by urinary tract infection, (UTI) related medical visits and hospitalization, and vesicoureteral reflux (VUR) in Cox proportional hazard regression

	Event	Person-years	IR	Adjusted HR [†] (95% CI)
UTI related medical visits, per year				
0	1531	1161371	1.32	1.00(Reference)
1-3	370	284788	1.30	0.97(0.87, 1.09)
4-5	70	2669	26.2	17.3(13.6, 22.0)*
> 5	153	1564	97.9	61.3(51.7, 72.5)*
p for trend<0.001				
UTI related hospitalization days				
0	312	152166	2.05	1.53(1.36, 1.73)*
≤7	145	813578	1.78	1.30(1.09, 1.54)*
>7	67	27217	2.46	1.73(1.35, 2.22)*
UTI association with VUR				
No VUR	527	261291	2.02	1.49(1.35, 1.65)*
VUR	66	27730	2.38	1.72(1.34, 2.20)*

IR, incidence rate, per 1,000 person-years
Adjusted HR[†], adjusted for age, sex, and urbanization
* p<0.001

The risk of IBS stratified by UTI related medical visits and hospitalization, and vesicoureteral reflux (VUR) in Cox proportional hazard regression

574 **TEMPORARY GASTRIC STIMULATOR PLACEMENT PRIOR TO PERMANENT STIMULATOR PLACEMENT FOR THE TREATMENT OF REFRACTORY GASTROPARESIS IN CHILDREN.**

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Gastroparesis is a chronic gastric motility disorder characterized by delayed gastric emptying of solid meals. Gastroparesis and associated symptoms are uncommon (4.6 per 10,000) with a 5:1 female to male ratio. In severe and chronic cases, patients may suffer dehydration, poor nutritional status, and poor glycemic control (in diabetics). The causes are numerous and include diabetic, post viral, post surgical, medication induced, neurologic, auto immune, and idiopathic. Idiopathic causes comprise up to half of all cases. Predominant symptoms are nausea, vomiting, early satiety, post prandial fullness/bloating, abdominal pain, and rarely weight loss. Typical treatments include pro-kinetic agents. Macrolide antibiotics, and metoclopramide are the mainstay of medical treatment, urecholine, domperidone and cisapride are less common alternatives. Gastric electrical stimulation (GES) entails the use of a set of pacing wires attached to the stomach and an electrical device that provides a low-frequency, high-energy stimulation to the stomach. In adults GES is an established treatment for gastroparesis, nausea, and vomiting refractory to standard medical treatment. The placement of the permanent gastric electric stimulator is it expensive and invasive. If the placement of a permanent stimulator is ineffective, removal requires a second operation. Our study was designed to determine if children with gastroparesis and related symptoms refractory to medical management would have beneficial effect from temporary GES as a test prior to placement of permanent GES.

Twenty-two children with gastroparesis, refractory to medical management were selected for treatment with GES. Seventeen females and 5 males, ranging from 3 years to 17 years of age were selected. Initial assessment and diagnosis of the patients with gastroparesis was established clinically. All were assessed by parental and patient questionnaire for nausea, post-prandial fullness, early satiety, and bloating. All children but one had an initial gastric emptying study.

Temporary gastric stimulator wires were placed endoscopically, either nasally or via gastrostomy and attached to the Enterra Therapy System gastric electrical stimulator (Medtronic, Minneapolis, MN). If symptoms improved significantly and the patient remained symptom free, a permanent gastric electric stimulator was placed surgically 2-3 wks later. Symptom

assessment was recorded before, and 1 week following the procedure. Statistical analysis was of the patient and parental response were performed using a paired Student's t-test. Eighteen of the patients had a positive response to the initial use of the temporary external GES. All 18 patients then progressed to placement of a permanent internal gastric stimulator. All the patients had a significant decrease in the frequency and severity of vomiting, nausea, bloating, early satiety, and postprandial fullness. Each of these 18 families elected to progress to permanent GES placement.

Gastric electrical stimulation is a valid treatment for pediatric patients with gastroparesis refractory to medical treatment. Temporary external gastric electric stimulation is a cost-effective, beneficial screening tool to determine which pediatric patients will respond to permanent gastric electric stimulation placement. The decision for permanent placement is easily assessed prior to placement, as the temporary pacing device is readily removed without significant difficulty for the patient or expense to the family. No significant adverse effects were observed in the study. We recommend additional and continued study in children to determine the long-term effects of permanent stimulator treatment.

575 SHOULD WE SCREEN CHILDREN WITH CONSTIPATION FOR CELIAC DISEASE, HYPOTHYROIDISM, HYPERCALCEMIA, AND LEAD TOXICITY? Vikram Raghu¹, Andrew Nowalk^{1,2}, Arvind Srinath^{1,2}. ¹Department of Pediatrics, Children's Hospital of Pittsburgh, Pittsburgh, PA; ²University of Pittsburgh School of Medicine, Pittsburgh, PA

Background: Constipation remains one of the most common complaints in the pediatric setting. The most recent NASPGHAN guidelines regarding the management of functional constipation cite only expert consensus to recommend against screening for celiac disease, hypothyroidism, hypercalcemia, and lead toxicity. Thus there exists a need for large scale studies to determine the prevalence of organic disease in this population.

Objective: The current study aimed to identify whether these diseases are more prevalent among children with constipation and whether any clinical data increased the likelihood of a positive result.

Methods: A retrospective cohort of patients aged 1 – 18 years presenting to the gastroenterology clinic at Children's Hospital of Pittsburgh from January 2013 through June 2015 were included if they were given a diagnosis code of constipation, encopresis, or irritable bowel syndrome and screened for any of celiac disease, hypothyroidism, hypercalcemia, or lead toxicity. Prevalence was determined based on chart review of patients with abnormal biochemical results. Odds ratios of demographics and diagnosis codes were calculated.

Results: From 10,892 encounters, 1831 unique patients with constipation had at least one screening blood test sent. Table 1 shows the prevalence of celiac disease, hypothyroidism, hypercalcemia, and lead toxicity in the study population and the literature-reported population prevalence of each. A higher prevalence of celiac disease, hypothyroidism, and hypercalcemia was seen in children with constipation. Significantly increased odds of an abnormal test result were seen in children under 5 years of age with regards to elevated lead level and children 12 years and older with regards to elevated calcium level. All 5 patients with hypothyroidism were Caucasian females under age 12.

Conclusions: Increased prevalence of celiac disease, hypothyroidism, and hypercalcemia but not lead toxicity is seen in children diagnosed with constipation. Certain demographics seem to be associated with a greater odds of a positive result. Our future studies will evaluate clinical characteristics of these children that may help us predict a positive test result.

Table 1. Prevalence of elevated lead level, hypercalcemia, hypothyroidism and celiac disease in children with constipation compared to literature-reported population prevalence.

	Frequency	Sample prevalence (95% CI)	Population prevalence
Lead > 5 µg/dL (n=441)	6	1.36% (1.23% - 1.49%)	3.33% ¹
Hypercalcemia (n=1361)	11	0.84% (0.79% - 0.88%)	0.34% ²
Hypothyroidism (n=1244)	5	0.40% (0.38% - 0.42%)	0.30% ³
Celiac Disease (n=1622)	20	1.23% (1.17% - 1.29%)	0.76% ⁴

¹Wheeler et al. www.cdc.gov., ²McNeily et al. Archives of Disease in Childhood 2016., ³Hollowell et al. J Clin Endocrinol Metabol 2002., ⁴Choung et al. Mayo Clin Proc 2000.

INFLAMMATORY BOWEL DISEASE

577 SINGLE CENTER EXPERIENCE OF LONG TERM VEDOLIZUMAB EFFICACY IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE. Namita Singh¹, Marla Dubinsky², Avantika Singh³, Morgan Check¹, Shervin Rabizadeh¹. ¹Pediatric, Cedars Sinai Medical Center, Los Angeles, CA; ²Susan and Leonard Feinstein IBD Clinical Center, New York, NY; ³Pediatric Gastroenterology, Hepatology and Nutrition, Oklahoma University Health Sciences Center, Oklahoma City, OK

Background: Off-label use of vedolizumab in the pediatric inflammatory bowel disease (IBD) remains limited following its approval for adult patients with Crohn's disease (CD) and ulcerative colitis (UC). We aimed to describe the long-term experience of vedolizumab in pediatric IBD patients at a single tertiary IBD center and to examine predictors of remission.

Methods: A prospective database identified vedolizumab-treated pediatric CD and UC patients (age < 18 years) who had at least 1 year of follow-up after vedolizumab initiation. Data on demographics, surgical history, disease behavior, location, disease activity and previous treatments were collected. Disease activity at weeks 14 and 54 was assessed using the weighted pediatric Crohn's disease activity index (wPCDAI) or pediatric UC activity index (PUCAI). Descriptive statistics and univariate analyses were performed to examine associations of clinical characteristics with therapeutic efficacy.

Results: For the 24 CD and 10 UC eligible patients, the median age at vedolizumab initiation was 15.5 (range 11.3-17.9) years and median disease duration was 3.3 (range 2-15.2) years. Standard vedolizumab dose was 6mg/kg/dose, with maximum of 300mg/dose, and infused at 0, 2, 6 weeks then every 8 weeks. Five patients had prior bowel surgery; 3 patients were switched from natalizumab. In patients with prior anti-TNF use, median time from last anti-TNF was 5.2 (range 0.2-84) months. At week 14, UC patients were more likely to be in remission than CD patients (80% vs. 38%, p=0.02). At 54 weeks, 62% were still receiving vedolizumab- 8/10 (80%) with UC, all of whom were in remission, and 13/24 (54%) with CD, 77% of whom were in remission.

UC patients were more likely to be in clinical remission at week 54 than CD patients (80% vs. 42%, p=0.04). Week 14 remission was associated with week 54 remission (p<0.01). Of 5 anti-TNF naïve patients, 100% (3/3) of UC patients and 50% (1/2) of CD patients were in remission at week 54. Shorter time from last anti-TNF to vedolizumab initiation was associated with higher rates of progressing to surgery (median 9.5 months in no surgery group vs. 1 month in surgery group, p=0.04). One (10%) UC patient and 6 (25%) CD patients underwent surgery prior to week 54. Four patients dose-escalated vedolizumab to infusions every 4 weeks, and 2 of these patients remained on vedolizumab at week 54. Neither time from last anti-TNF nor concomitant immunomodulator use was associated with week 54 clinical remission. There were no serious infections or infusion reactions.

Conclusion: Our study demonstrates that vedolizumab is safe in pediatric IBD patients, with efficacy similar to that reported in the adult studies. The efficacy of vedolizumab is higher in pediatric UC patients at both weeks 14 and 54. Further controlled pediatric trials are warranted to validate our real-world experience.

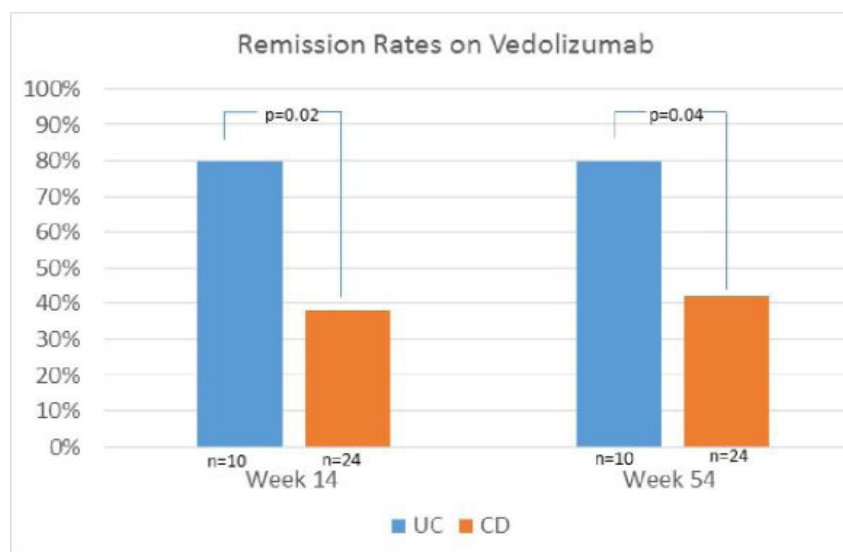
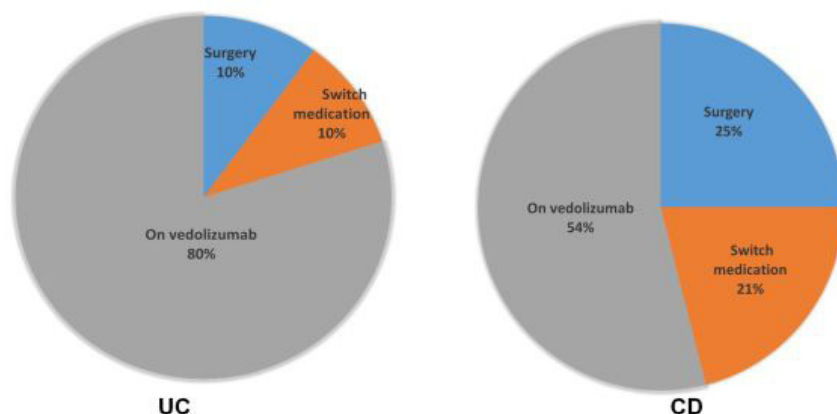


Figure 2: Week 54 Follow-up UC vs. Crohn's disease patients



578 ORAL IRON AFFECTS THE FECAL MICROBIOME IN CHILDREN WITH IBD. *Natasha Mendez, James Markowitz. Pediatric Gastroenterology, Cohen Children's Medical Center, Lake Success, NY*

Objective: Children with inflammatory bowel disease (IBD) often require oral iron replacement therapy (IRT) for iron deficiency. Reports of GI intolerance with IRT are common, as iron potentially alters the bacterial milieu within the GI tract (Jaeggi, T. *Gut*. 2015). As changes in the intestinal microbiome have been implicated in the etiology and progression of both Crohn's disease (CD) and ulcerative colitis (UC), we performed a pilot study to investigate the effect of enteral iron on the gut microbiome in children with CD and UC.

Methods: Children <18 yrs of age with an established diagnosis of UC or CD who were in remission or had mild disease activity (PUCAI < 34, PCDAI < 27.5) and were on chronic stable doses of maintenance medications were recruited after their primary GI MD identified iron deficiency requiring IRT. Each subject provided a fecal sample just prior to starting and after 3-5 weeks of IRT. The change in the relative abundance of specific fecal bacterial communities previously identified as associated with more severe or complicated disease in the RISK (Kugathasan, S. *Lancet*. 2017) and PROTECT (Schirmer, M. et al. Abstract. Presented at DDW, May 6, 2017, Chicago, IL.) cohorts were assessed using 16s rRNA technology (Illumina 16S Metagenomics, version 1.0.1.0)

Results: 8 subjects (5 CD, 3 UC) provided paired fecal samples (Table 1). In 2/5 CD subjects, IRT increased the relative abundance of *Ruminococcus*, a genus linked to the development of stricturing (B2) disease in the RISK cohort, more than five-fold. *Rothia*, a genus negatively associated with increased B2 in RISK, was not identified in any specimens. In the RISK cohort, increased *Collinsella* and decreased *Veillonella* increased risk of fistulizing (B3) CD. By contrast, IRT induced a decrease in the relative abundance of *Collinsella* in 3/5 subjects and an increase in *Veillonella*, changes potentially consistent with a lessened risk of B3 disease.

In UC, PROTECT data demonstrated an association between severe disease and decreases in *Lachnospiraceae*, *Blautia*, *Clostridiales*, *Bifidobacterium*, *Ruminococcus*, and *Roseburia*. In the 3 UC subjects receiving IRT, the relative abundance of *Lachnospiraceae* decreased by 60 and 99% in 2 subjects, *Blautia* decreased in 1 patient by 98%, *Clostridiales* decreased in 2/3 by 45% and 98%, *Bifidobacterium* decreased in 2/3 by 60% and 100%, *Ruminococcus* decreased in 1 patient by 93%, and *Roseburia* decreased in 2/3 by 4% and 100%. Increased relative abundance of *Veillonella* and *Campylobacter* were associated with severe UC activity in PROTECT. IRT was associated with a decrease in *Veillonella* by 98% and 100% in 2/3 subjects. *Campylobacter* abundance was not affected.

Conclusions: IRT affects the fecal microbiome differently in different patients, and in some cases appears to further worsen the dysbiosis that is seen in CD and UC. In CD subjects, the changes identified in this preliminary investigation appear to shift the microbiome to one more characteristic of children at risk for B2, but less at risk for B3 complications. In UC, the changes shift the fecal microbiome towards one more characteristic of patients with severe UC activity. These preliminary observations deserve further investigation, and raise the question as to whether intravenous iron replacement might be a preferable route of IRT in children with IBD.

Table 1. Relative abundance of Selected Fecal Genera

	Individual Subject's Change from Pre-IRT (%)				
	CD 1	CD 2	CD 3	CD 4	CD 5
Crohn's Disease Subjects					
Increased risk for B2 (RISK):					
<i>Ruminococcus</i>	-91	-21	+650	-40	+520
<i>Rothia</i>	ND*	ND	ND	ND	ND
Increased risk for B3 (RISK):					
<i>Collinsella</i>	-33	-71	-12	ND	ND
<i>Veillonella</i>	+259	+77	+238	+81	+3738

	UC 1	UC 2	UC 3
Ulcerative Colitis Subjects			
Decreased genera in severe UC (PROTECT)			
<i>Lachnospiraceae</i>	+90	-100	-59
<i>Clostridiales</i>	+537	-98	-45
<i>Bifidobacterium</i>	-60	-100	+125
<i>Ruminococcus</i>	+98	-93	+594
<i>Roseburia</i>	-4	-100	+5
Increased genera in severe UC (PROTECT)			
<i>Veillonella</i>	-99	-100	No change
<i>Campylobacter</i>	No change	No change	No change

*ND = not detected

579 MEDICATIONS AND SERUM BIOMARKERS ARE ASSOCIATED WITH ANTHROPOMETRIC MEASUREMENTS IN PEDIATRIC CROHN'S DISEASE. *Neera Gupta¹, Robert Lustig⁴, Cewin Chao⁴, Eric Vittinghoff², Howard Andrews³, Cheng-Shiun Leu³. ¹Pediatrics, Weill Cornell Medicine, New York, NY; ²Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA; ³Epidemiology and Biostatistics, Columbia University Medical Center, New York, NY; ⁴Pediatrics, University of California San Francisco, San Francisco, CA*

Background: Statural growth impairment (> in males) & low bone age (BA) (> in females) are common in pediatric Crohn's disease (CD). Determination of BA allows clinically meaningful interpretation of growth. Anthropometric measurements are markers of both nutritional status and disease status. Our aims were to 1) explore the distribution of anthropometric

parameters based on chronological age (CA) (CA-z-scores) & BA (BA-z-scores); 2) compare CA versus BA for the interpretation of anthropometric measurements; & 3) examine the association between medications & serum inflammatory & hormonal biomarkers with anthropometric measurements in CD.

Methods: 82 CD patients (< CA 21 yrs; 57% male) were enrolled in a cross-sectional study. 49 patients (\leq CA 15 in females, 17 yrs in males) qualified for BA analyses. Descriptive statistics, paired t-test & linear regression were applied.

Results: Mean CA=15.3 \pm 3.5 (SD; range=4.8—20.7) years. Mean subscapular skinfold, triceps skinfold & mid-upper arm circumference CA-z-scores=0.59 \pm 0.83 (-1.56—2.31), 1.02 \pm 0.74 (-0.88—2.79), & -0.64 \pm 1.39 (-5.03—2.88). Mean subscapular skinfold, triceps skinfold, & mid-upper arm circumference BA-z-scores=0.64 \pm 0.87 (-1.17—2.27), 1.10 \pm 0.72 (-1.17—2.47) & -0.54 \pm 1.30 (-2.86—2.50). Triceps skinfold, subscapular skinfold & mid-upper arm circumference BA-z-scores were 0.05 (95%CI= 0.003, 0.11; p=.039), 0.10 (95%CI= 0.04, 0.16; p=.002) & 0.35 (95%CI= 0.14, 0.55; p=.001) units higher than CA-z-scores. Tables show associations between medication & serum inflammatory & hormonal biomarkers with anthropometric CA-z- and BA-z-scores. Height CA-z-scores were 0.65 (95%CI= 0.04, 1.25; p=.038) units higher in females (not males) treated with infliximab. Hemoglobin was positively associated ($B=0.23$; 95%CI= 0.04, 0.42; p=0.018), while platelets ($B= -0.004$, 95%CI= -0.01, -0.001; p= .005), ESR ($B= -0.03$, 95%CI= -0.05, -0.01; p=.003) & CRP ($B= -0.04$; 95%CI= -0.08, -0.002; p=.039) were negatively associated with height CA-z-scores in males (not females). Albumin ($B=0.80$; 95%CI= 0.22, 1.36; p=.008) & IGF-1 BA-z-scores ($B=0.26$; 95%CI= 0.03, 0.48; p=.025) were positively associated, while ESR ($B= -0.02$; 95%CI= -0.05, -0.003; p=.029) & CRP ($B= -0.06$, 95%CI= -0.11, -0.01; p=.030) were negatively associated with height BA-z-scores.

Conclusions: Mean anthropometric parameter BA-z-scores were greater than mean anthropometric parameter CA-z-scores. Azathioprine was negatively associated, while methotrexate, adalimumab & infliximab were positively associated, with specific anthropometric parameters, suggesting a possible negative effect of azathioprine on nutritional status & disease status versus poor efficacy of the medication. Infliximab was positively associated with height CA-z-scores in females only, suggesting a possible sex difference in response to infliximab therapy from the standpoint of statural growth. Serum inflammatory biomarkers were associated with height CA-z-scores in males only, supporting our previously published findings that inflammation has a more detrimental effect on statural growth in males. Prospective multicenter longitudinal cohort studies are required to further examine these findings & determine implications for treatment of CD.

Table

**Association between Medications/Serum Biomarkers and Anthropometric Parameters
(Z-Scores Based on Chronological Age)
(N=82; Multiple Regression)**

	Mid-Upper Arm Circumference	Subscapular Skinfold	Weight	Body Mass Index
	CA-z-scores	CA-z-scores	CA-z-scores	CA-z-scores
Adalimumab		1.02 (0.18, 1.86) .018		1.17 (0.13, 2.21) .029
Azathioprine	-0.64 (-1.26, -0.02) .045	-0.47 (-0.83, -0.10) .014	-0.73 (-1.17, -0.29) .002	-0.58 (-1.03, -0.12) .013
Methotrexate		0.81 (0.10, 1.53) .027		
ESR			-0.03 (-0.05, -0.01) .010	-0.03 (-0.05, -0.004) .024

Regression Coefficient
(95% Confidence Interval)
P-Value

Table

**Association between Serum Biomarkers and Anthropometric Parameters
(Z-Scores Based on Bone Age)
(N=49; Simple Regression)**

	Mid-Upper Arm Circumference	Subscapular Skinfold	Triceps Skinfold	Weight	Body Mass Index
	BA-z-scores	BA-z-scores	BA-z-scores	BA-z-scores	BA-z-scores
WBC	-0.19 (-0.36, -0.02) .029	-0.12 (-0.24, -0.01) .040		-0.16 (-0.28, -0.04) .008	
ESR				-0.03 (-0.04, -0.01) .003	-0.02 (-0.03, -0.001) .037
CRP			-0.03 (-0.07, 0.000) .049	-0.06 (-0.10, -0.02) .008	
Albumin				0.73 (0.28, 1.18) .002	
IGF-1 BA-z-scores				0.20 (0.01, 0.38) .039	

Regression Coefficient
(95% Confidence Interval)
P-Value

580 COMBINATION INFLIXIMAB AND PREDNISONE DURING INDUCTION LEADS TO HEIGHTENED DRUG CLEARANCE. Kathryn Clarkson, Kimberly Jackson, Yi-Ting Tsai, Lee Denson, Phillip Minar. Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: Proactive therapeutic drug monitoring enables clinicians to tailor infliximab dosing regimens based on the individual's pharmacokinetics and has been shown to improve infliximab durability. In a retrospective analysis, Papamichael et al. found higher infliximab concentrations prior to infusions 2, 3, and 4 were associated with short-term mucosal healing in patients with ulcerative colitis.¹ For Crohn's disease, however, there is a paucity of data correlating infliximab concentrations during the induction phase and early clinical response (CR). In this study, our aim was to establish infliximab concentrations goals during early treatment for end of induction CR.

Methods: Anti-TNF naïve Crohn's disease patients starting infliximab were recruited to participate in this one year prospective, single-center study. Infliximab concentration was determined by an ELISA (Immundiagnostik). Non-protocol (clinical) infliximab concentrations were also determined for a subset of patients with a drug-tolerant assay (Esoterix). CR was defined by a weighted pediatric Crohn's disease index (wPCDAI) prior to the 4th infusion <12.5 and/or a change >17.5 points from the baseline wPCDAI. Infliximab cessation, those who had abdominal surgery prior to the 4th infusion or patients receiving the 4th dose before 70 days were considered treatment non-responders. Dose intensification was not considered treatment nonresponse.

Results: We enrolled 54 patients with Crohn's disease, 68.5% male with a mean age of 13 (4) years old. The median starting infliximab dose was 5.8 mg/kg (4-11.7) with 11% receiving >7.5 mg/kg at their first dose. Dose intensification prior to the 4th dose occurred in 20.4%. Only two patients were on an immunomodulator throughout induction. The CR rate was 64.8% at the end of induction. Infliximab concentrations prior to the 2nd, 3rd and 4th infusions for CR and non-responders are shown in **Figure 1a**. A receiver operating characteristic (ROC) analysis identified that an infliximab concentration prior to the 2nd dose of >22.5 µg/ml (area under the ROC curve =0.81, 95% CI 0.67-0.95, p=0.001) would predict CR with a sensitivity of 84.6% and specificity of 73%. In patients with an infliximab concentration >3 µg/ml at the end of induction, the median (range) infliximab concentration prior to the 2nd and 3rd infusion was 38 µg/ml (21-45) and 25 µg/ml (16-40) compared to 22 µg/ml (8-45) and 10 µg/ml (0.5-45) µg/ml in those with a drug level <3 µg/ml prior to the 4th dose (p<0.001 for both time points).

An infliximab level of ≥ 16 $\mu\text{g/ml}$ prior to the 3rd infusion, was 81.8% sensitive, and 84.6% specific (area under the ROC curve =0.81, 95% CI=0.82-0.99, $p<0.001$) for an end of induction infliximab concentration >3 $\mu\text{g/ml}$. Thirty-one (57.4%) patients were receiving prednisone at the start of infliximab. We found patients on prednisone (>0.5 mg/kg or 40 mg/day) during induction had a more rapid drug clearance documented by lower infliximab concentrations at infusion 2, 3, and 4 (**Figure 1b**). We found no difference in disease severity between prednisone-exposed and prednisone-unexposed as both demonstrated a comparable baseline wPCDAI, CRP, albumin, fecal calprotectin, infliximab dose (at all 3 infusions) or dosing interval (data not shown). The CR rate in prednisone-unexposed patients was 72.7% compared to 59.4% in the prednisone exposed ($p=0.39$). The median fecal calprotectin prior to the 4th infusion for prednisone-unexposed patients was 228 $\mu\text{g/g}$ (20-2161, $n=11$) compared to 1002 $\mu\text{g/g}$ (70-2161, $n=16$) in prednisone-exposed ($p=0.08$). Forty patients had proactive infliximab drug monitoring (Esoterix). The Spearman correlation was $r=0.92$ ($p<0.001$) between the two assays. 6/40 patients had antibodies to infliximab prior to the 4th infusion. All six with anti-drug antibodies had an infliximab concentration <20 $\mu\text{g/ml}$ prior to the 2nd infusion.

Conclusion: We found an association between higher infliximab concentrations prior to the 2nd and 3rd infusion and therapeutic (>3 $\mu\text{g/ml}$) infliximab concentrations prior to the 4th dose. We also discovered a novel association between prednisone exposure during induction and increased infliximab clearance.

1. Papamichael K, et al. Infliximab Concentration Thresholds During Induction Therapy Are Associated With Short-term Mucosal Healing in Patients With Ulcerative Colitis. *Clin Gastroenterol Hepatol* 2016;14:543-9.

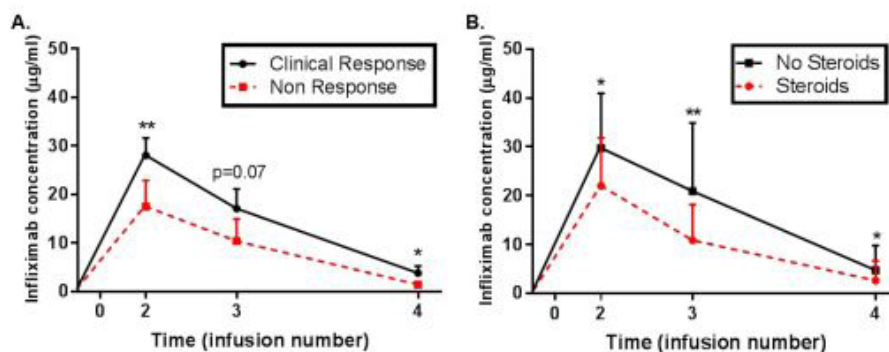


Figure 1. Infliximab pharmacokinetics during induction between A) clinical responders and non-responders and B) prednisone exposed and prednisone-unexposed. Infliximab concentration was determined by drug-intolerant ELISA prior to 2nd, 3rd and 4th infliximab infusion. Clinical response was determined prior to the 4th infusion using the weighted PCDAI. The mean (95% confidence interval) infliximab concentration were compared by the Student's t-test at each infusion. *, $p<0.05$; **, $p<0.01$.

581 PREVALENCE OF JOINT HYPERMOBILITY IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE CASE-CONTROL STUDY. Praveen Kumar Conjeevaram Selvakumar¹, Brian Maksimak¹, Sara Lappe², Hanan Nashed², Natalie Bhesania¹, Jessica Barry¹, Andrew Zefi³, Naim Alkhouri¹. ¹Pediatric Gastroenterology, Cleveland Clinic, Cleveland, OH; ²General Pediatrics, Cleveland Clinic, Cleveland, OH; ³Pediatric Rheumatology, Cleveland Clinic, Cleveland, OH

Background: Joint hypermobility (JH) could be an isolated benign variant in general population or a clinical manifestation of connective tissue diseases such as Marfan syndrome or Ehler-Danlos syndrome. The prevalence of benign JH in healthy children is reported to be highly variable (3-30%) depending on age, sex and ethnicity. Multiple adult studies have shown an increased prevalence of JH in patients with functional gastrointestinal diseases but the association between JH and organic diseases such as inflammatory bowel disease (IBD) is not well studied. Moreover, the prevalence of JH in children with inflammatory bowel disease (IBD) has not been studied.

Objective: This study aims to determine the prevalence of JH in children with IBD in comparison to that of healthy controls.

Methods: We performed a prospective case-control study involving children (aged 6-18 years) with IBD from a tertiary Pediatric Gastroenterology clinic and healthy children (aged 6-18 years) from a General Pediatrics clinic during well child visits. JH in children was assessed by using the Beighton scoring system and children with a score ≥ 4 are considered to have JH. We excluded children with history of connective tissue diseases, fractures involving those joints assessed for JH and arthritis. For comparison among groups, t test or analysis of variance was used for continuous variables and Pearson's chi-square test or Fisher's exact test was used for categorical variables.

Results: A total of 41 IBD (34 Crohn's disease (CD), 5 Ulcerative Colitis (UC) and 2 Indeterminate Colitis) patients and 27 healthy controls were included in the study. 50% of them were males and mean age at the diagnosis of IBD was 9.9 ± 3.7

years. JH was detected in 18 children with IBD (44%) and 3 healthy controls (11%). There was a significant difference in the prevalence of JH in children with IBD compared to healthy controls (44% vs. 11%; p-value 0.004). Likewise, children with IBD also had higher mean Beighton scores compared to healthy controls (2.9 vs. 1.1; p-value 0.011). The odds ratio of JH in children with IBD compared to healthy controls was 6.26. On a sub-group analysis, there was no significant difference in JH between children with CD and UC. Among children with CD, we did not find any difference in JH between those with inflammatory, stricturing and fistulizing phenotypes. Similarly, among children with IBD, there was no association of JH with age at diagnosis or treatment such as biologics, immunomodulators or both.

Conclusions: Our study showed that JH is approximately 4-times more common among children with IBD compared to healthy controls which might indicate a possible role of connective tissue defects with resultant intestinal permeability in the pathophysiology of IBD.

582 PERINATAL FACTORS AND RISK OF INFLAMMATORY BOWEL DISEASE IN THE OFFSPRING: A SYSTEMATIC REVIEW AND META-ANALYSIS. Fanny Gentilcore², Marie-Ève Chartier^{1,2}, Marie-Claude Rousseau³, Sylvie Girard^{2,4}, Shu-Qin Wei², Andrea Benedetti^{5,6}, Anne-Monique Nuyt^{2,7}, Prévost Jantchou^{1,2}. ¹Gastroenterology, CHU Sainte-Justine, Montréal, QC, Canada; ²CHU Sainte-Justine Research Center, Montreal, QC, Canada;

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Background: It has been hypothesized that exposure to environmental factors during critical windows of immune maturation may interfere with the immune system development and influence the subsequent risk for inflammatory bowel disease (IBD).

Objectives: To summarize the available data of the literature and perform a meta-analysis regarding the association between perinatal factors and the subsequent risk for Crohn’s disease (CD) or ulcerative colitis (UC) in the offspring.

Methods: We systematically searched the following electronic databases: Embase, PubMed, Medline, EBM Reviews to identify observational studies on the association between perinatal factors and IBD in the offspring up to April 2017. A meta-analysis was performed using RevMan 5 to obtain a combined effect measure and the 95% CI with random effects models. Pooled adjusted odds ratios (OR) with 95% confident intervals were calculated by combining the inverse of their variance for each factor.

Results: Twelve studies (5 cohort studies and 7 case-control studies) were identified out of 1852 studies reviewed. Maternal diabetes during pregnancy was associated with an increase risk for CD [OR(95% CI): 1.67 (1.18-2.36)] but not UC. Maternal age >35 years was associated with an increase risk for CD [1.65 (1.02-2.66)] but a decrease risk for UC [0.92 (0.86-0.98)]. The following perinatal factors were not associated with the risk for IBD: maternal infection, pre-eclampsia, birth weight, preterm, and low APGAR score. (See Table 1.)

Conclusion: This meta-analysis suggests an opposite association between advanced maternal age and risk for CD or UC. In addition, diabetes during pregnancy appears to be associated with an increase risk for CD in the offspring.

Table 1: Odds Ratio, 95% confident intervals number of studies per factors and I² statistics

Factors	Inflammatory Bowel Diseases	Crohn’s Disease	Ulcerative Colitis
Infections during pregnancy	N=3, I ² =86% 1.52 (0.58-3.99)	N=3, I ² =72% 1.46 (0.44- 4.86)	N=3, I ² =52% 1.65 (0.89- 2.71)
Preeclampsia	N= 4, I ² =0% OR: 0.95 (0.69-1.31)	N= 2, I ² =91% 2.30 (0.20-27.02)	N=2, I ² =0% 1.02 (0.50-2.10)
Diabetes	N=2, I ² =0% 1.00 (0.41-2.47)	N=2, I ² = 0% 1.67 (1.18-2.36)	N=2, I ² =0% 0.98 (0.66-1.45)
Maternal age >35 years	N=5, I ² =12% 1.08 (0.87-1.33)	N=4, I ² =82% 1.65 (1.02-2.66)	N=2, I ² =0% OR: 0.92 (0.86-0.98)
Preterm birth	N=8, I ² =48% 0.98 (0.80-1.20)	N=7, I ² =0% 0.93 (0.78-1.09)	N=5, I ² =0% 0.83 (0.63-1.11)
Birth Weight < 2500 g	N=4, I ² =0% 1.07 (0.87-1.31)	N/A	N/A
APGAR score < 8	N= 2, I ² =0% 1.12 (0.75-1.66)	N=2, I ² =0% 1.11 (0.74-1.66)	

*N= Number of studies for each factor analyzed, I²= test for heterogeneity.

583 **A SINGLE CENTER EVALUATION OF TRANSITION IN INFLAMMATORY BOWEL DISEASE.**

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Introduction: Up to one quarter of patients with inflammatory bowel disease (IBD) present before 18 years of age and require transition of care from pediatric to adult gastroenterology (GI). This transition can be a stressful process to patients, caregivers, and medical providers. A structured transition plan is important to patient care though evidence for specific best practices is lacking. The North American Society for Pediatric Gastroenterology Hepatology and Nutrition recommendations for transition include seeing adolescent patients without caregivers present prior to transition. This study aims to capture a recently transitioned population, including patients who have not transitioned successfully. This is a population that may be missed by surveys given to patients with established adult GI care. By surveying these patients, we aim to identify level of self-knowledge of disease in recently transitioned patients and establish risk factors that could leave to decreased disease control and . This study also provides insights from both patients and caregivers, populations which may have discordant experiences during transition.

Methods: We identified 98 patients with IBD currently between the ages of 18-24 who had been seen in a multi-provider, regional, pediatric GI outpatient clinic. Patients who had not yet transitioned to an adult GI provider were excluded (n=23). Patients and caregivers were contacted three times by telephone using the last available phone numbers in the electronic health record. Verbal consent was obtained and the survey administered at that time or another mutually agreeable time. The 10 minute phone survey assessed disease knowledge, current clinical control, and opinions on transition using a 5-point Likert scale. For analysis, Likert scale responses were collapsed into two groups: disagree comprised strongly disagree to disagree and agree comprised neutral to strongly agree. Results are reported as frequencies for categorical variables and medians with interquartile range (IQR) for continuous variables. Proportions were compared using Fisher exact and chi-squares tests.

Results: Of the 75 total contacted patient-caregiver pairs, 13 paired surveys were obtained. In addition, there were 10 from only parents and 3 from only patients for a total response rate of 39 (26%). Of the 26 unique patients with a survey from patient or parent, 15 (58%) were male, and 17 (73%) had Crohn's Disease. The median age of patients was 21 years (IQR 18-23 years). 23(88%) patients had successfully established care at an adult GI clinic; three patients had not established care with an adult GI provider, all of whom had public insurance. Among 16 patients, 100% knew their diagnosis and named medications though no patients were able to state the doses. Five (31%) were able to name a side effect of their medications, however, only two (22%) of those on a biologic agent noted infectious or oncologic side effects. Four (25%) knew whether their disease is large or small bowel. Twelve (75%) patients always had a caregiver present at pediatric GI appointments; 50% of patients and 30% of parents thought seeing a provider alone would have been helpful. Only half of patients attend adult GI appointments without a caregiver present. To the statement "I found the transition process stressful", 2 (12%) patients and 12 (52%) parents agreed. Seven (43%) patients and 14 (60%) parents agreed that the patient's GI disease makes it harder to live his or her life. There was no difference in the perceived stress of the transition when patients were compared by insurance type (31% public versus 68% private, p=0.5), IBD type (75% Crohn's versus 25% Ulcerative Colitis, p=0.2) or whether or not patients previously had IBD-related surgery (37% surgery versus 66% no surgery, p=0.6). Similarly, there was no difference in the perceived difficulty in life caused by disease when patients were compared by insurance type (p=0.2), IBD type (p=0.6) or whether or not patients previously had IBD-related surgery (p=0.7).

Conclusion: This study identified several areas in care transitions that should be addressed. Patient had gaps in knowledge including medication dosing and side effects as well as location of disease. In addition, it appears that the recommendation for seeing patients alone in pediatric GI clinic was preferred by patients but not caregivers who seem to have more anxiety related to transition than the patients themselves. Finally, although there were no differences reported in ease of transition, the three patients who had not transitioned successfully had public insurance which could indicate limitations in availability of adult providers. Limitations to this analysis included small sample size resulting in low power to detect differences between groups and a low response rate limiting generalizability. Larger studies are needed to better identify factors predicting difficult transitions to better target interventions.

584 **LACK OF SEASONALITY OF PEDIATRIC INFLAMMATORY BOWEL DISEASE: RESULTS OF A SINGLE CENTER REPORT.**

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Background: Due to the multifactorial etiology of Inflammatory Bowel Disease (IBD), several researchers have questioned the relationship between seasonality and both the onset of symptoms and the diagnosis of IBD. Limited studies have been

performed with conflicting results regarding adult seasonal variation in onset of symptoms in IBD. Scant seasonality literature exists on the pediatric population of patients with IBD especially in the Southern United States. The aims of this study were to determine if any seasonal pattern exists regarding the onset and diagnosis of IBD in the pediatric population and to analyze the relationship between the diagnosis of IBD and age, sex, month of birth, and body mass index (BMI).

Methods: A chart review of 134 children was conducted on patients between 1 and 21 years of age diagnosed with IBD established between January 2012 and December 2016. Month and year of symptom onset, month and year of diagnosis, age, sex, race, birth month, and BMI were all evaluated via chart review.

Results: More cases (n=31) had summer onset of symptoms, though the relationship failed to reach statistical significance. Additionally, no relationship was found between season and diagnosis of IBD in this population. However, a statistically significant relationship was found between age, sex, and race of subjects and the diagnosis of IBD. Specifically, more children diagnosed with IBD were pre-teens and teens than would be expected if age were equally distributed in the study population. Also, there were more males and fewer females than expected with the IBD diagnosis. Likewise, more Caucasians and fewer African Americans were present in the study population than were expected based on the demographics of the local population. Finally, more children with IBD in our population are underweight and fewer are normal and overweight/obese than would be expected of children living in Louisiana.

Conclusions: Our work adds to the literature on pediatric cases of IBD. Our findings concerning the association between IBD diagnosis and age, sex, race, and BMI support the literature. However, while an earlier study in Detroit demonstrated a higher incidence of fall onset of IBD symptoms in their Pediatric Detroit Clinic, more cases in our Baton Rouge clinic had summer onset of symptoms. Given speculation that environmental factors may be influential in the development of IBD, further exploration is needed to determine if seasonal environmental factors may be responsible for these nonsignificant but intriguing findings and whether geographical differences are related to environmental dissimilarities.

585 **DUODENAL PATHOLOGY AND ASSOCIATED DISEASE OUTCOMES IN PEDIATRIC CROHN'S DISEASE.** Rebecca Casini¹, Vivekanand Singh², Veronica Williams³, Ashley Sherman⁴, Valentina Shakhnovich^{1,3}.

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Introduction: It is well established that patients with Crohn's disease (CD) may exhibit histopathologic lesions in both the upper and lower gastrointestinal tract. Once thought to be uncommon, upper tract manifestations, such as duodenitis, are reported in 26% of adults with CD. Recent data from our group, suggest that nearly 50% of children with CD have duodenal pathology at diagnosis. As a major site for absorption, pathology in the duodenum may affect the absorption and drug disposition of per-orally administered (PO) medications, the therapeutic response to PO medications, and disease outcomes in children treated with PO medications.

Objective: The aim of this prospective, observational, on-going investigation is to determine whether drug disposition and disease outcomes differ among pediatric CD patients based on the presence or absence of duodenal disease.

Methods: Clinical data from newly diagnosed, treatment-naïve children with CD, who were enrolled in a research biorepository at The Children's Mercy Hospital (CMH) between September 2014 and December 2016, were reviewed to assess choice of medical therapy, drug levels (when available), and clinical outcomes in the first year after diagnosis. Clinical outcomes of interest included growth parameters and laboratory studies at 3, 6, 9, and 12 months post-diagnosis. Of the 26 eligible patients, 24 were followed at CMH for at least one year post-diagnosis and qualified for this investigation. Based on review of their gross endoscopic report, biopsy report, and independent review of biopsies by a single experienced pediatric pathologist, these 24 participants were divided into 2 groups: those with duodenal pathology (DP) and those without duodenal pathology (NDP). Clinical outcomes were compared between the two groups via descriptive statistics, independent student t-test ($\alpha=0.05$), and Wilcoxon Rank Sum test ($\alpha=0.01$), using SPSSv23.

Results: 14 DP and 10 NDP patients were identified. Of these, 37% percent (n=9) were started on azathioprine (AZA) for maintenance of remission (5 DP, 4 NDP). Genetic testing for TPMT activity was obtained for all 9 patients, 8 of whom had thiopurine metabolite levels available during the 1st year of the disease. Mean AZA doses were 2.6±0.2 mg/kg in the DP vs. 2.4±0.3 mg/kg in the NDP group (p=0.21). 6-TGN metabolite levels averaged 223.6±78.1 pmol/RBC in the DP vs. 278.7±15.0 pmol/RBC in the NDP group (p=0.29). No statistically significant differences were found in height, weight, body mass index (BMI), BMI z-score, complete blood count (CBC), albumin, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) between the two groups at baseline, 3, 6, 9, and 12 months post-diagnosis.

Conclusions: Duodenal pathology is not uncommon (>50%) at diagnosis in pediatric patients with Crohn's disease. Contrary to our hypothesis, in this small, prospective cohort, duodenal pathology did not appear to influence disease outcomes, growth parameters or plasma concentrations of the PO medication azathioprine during the 1st year of disease course.

586 CLINICAL CHARACTERISTICS OF VERY EARLY ONSET-INFLAMMATORY BOWEL DISEASE (VEO-IBD) IN A SINGLE CENTER COHORT.

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Introduction: Very-Early onset IBD (VEO-IBD) is defined as disease onset before 6 years of age. It has an estimated prevalence of 14/100,000 children in US and accounts for 4-15% of all pediatric patients with IBD. This distinct group is known to have phenotypically severe disease. Multiple studies have shown association with monogenic defects (such as IL-10 receptor deficiency, NADPH mutations, XIAP gene mutation) though the exact incidence of these associations is still unknown. This descriptive study is the first formal analysis of the VEO-IBD patient cohort from our institute. We hope the results will improve our understanding of disease history and lay the foundation for prospective studies.

Results: We did retrospective chart analysis of 51 patients that met the diagnostic criteria for VEO-IBD between 1991-2013. 39.2% were female vs 60.8% males. The mean age of diagnosis was 3.8 years (SD1.4) with 7.8% less than 2 years at the time of diagnosis. The most common presenting symptoms were hematochezia (54.9%), diarrhea (35.3%), abdominal pain (29.4%) and failure to thrive (17.6%). Based on physician assessment at time of diagnosis, Crohns disease was present in 41%, UC in 45% and 13% were classified as Indeterminate IBD. Perianal disease was found in 28.5% patients. Diagnosis was later changed from UC to CD in 7.8% (4/51) patients. Abnormal laboratory markers at presentation were; elevated ESR (43.1%), anemia (41.2%), hypoalbuminemia (29.4%) and elevated CRP (27.5%). Most patients presented with mild degree of malnutrition with mean Z score for weight and BMI of -0.18 (SD 1.1) and -0.15 (SD 1.1) respectively. Medical management was the mainstay of treatment. In our experience a large subset of patients was treated with 5-aminosalicylates/5-ASA (78.4%) and anti-TNF therapy (60.8%). As our data spans almost two decades, we also found an abundant use of flagyl (31.4%), mercaptopurine (29.4%) and methotrexate (31.4%) all of which were used either sequentially or in combination at some point. It was interesting to also note that of the 40 patients on 5-ASA, 35% were on monotherapy with this drug. 5 patients needed major surgical interventions (colectomy, ileostomy, colostomy, stricuroplasty) and 2 underwent minor surgery (fistulotomy). Positive family history of IBD was reported in 24.5% of patients. Interestingly comorbid GI conditions included autoimmune hepatitis (AIH) in 1 patient, primary sclerosing cholangitis (PSC) in 1 patient and AIH/PSC overlap in 1. The mean duration of follow-up was 9 years. Over this time frame there was clinical improvement in 37.7% of the patients which was defined as improvement in all 4 laboratory markers (hemoglobin, albumin, CRP, ESR). Finally, since 2015 we have sent whole exome sequence testing on six patients to The Hospital for Sick Children (Toronto) or Children's Hospital of Philadelphia and all have been reported negative for monogenic diseases. We did not find clinical evidence of immunodeficiency diseases in our cohort.

Conclusion: Some of our data is consistent with other studies on VEO-IBD reporting higher incidence in males, high frequency of perianal disease, strong family history and predominance of colonic symptoms. Diagnosis of UC was more common than CD at presentation, though some patients were later found to have Crohns disease. Our patients were mainly managed medically and clinical improvement was seen in more than 1/3rd. Only few patients underwent surgery. We suspect that VEO-IBD is a disease spectrum ranging from monogenetic aggressive disease non-responsive to conventional therapies, to milder phenotypic forms similar to polygenic IBD. Prospective studies comparing these patients with pediatric IBD controls are needed to determine if the natural history of VEO-IBD is similar to pediatric IBD. Lastly, we did not find any monogenic defects in our cohort which could be due to the small sample size. However, this raises the question about the true incidence of these genetic abnormalities and therefore the clinical implications as well as cost effectiveness of testing all patients with VEO-IBD.

***588 SEROLOGIC AND GENETIC MARKERS ASSOCIATED WITH GROWTH STATUS IN CHILDREN WITH CROHN'S DISEASE.**

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Francisco, CA; ⁷Children's Hospital of Philadelphia, Philadelphia, PA; ⁸Northwell Health, Lake Success, NY; ⁹Connecticut Children's Medical Center, Hartford, CT; ¹⁰Mount Sinai Hospital, New York, NY; ¹¹Medical College of Wisconsin, Milwaukee, WI; ¹²Nationwide Children's Hospital, Columbus, OH; ¹³Boston Children's Hospital, Boston, MA; ¹⁴Cedars-Sinai, Los Angeles, CA; ¹⁵Goryeb Children's Hospital, Morristown, NJ

Background: Crohn's disease is associated with growth impairment and malnutrition in children. Several factors contribute to poor growth, including insufficient caloric intake, chronic inflammation, malabsorption, and suppression of growth-promoting hormones. Currently there is not a clinical strategy to predict which patients are at risk for growth impairment and/or malnutrition.

Methods: We conducted a retrospective cohort study to determine the growth status of children with Crohn's disease enrolled in the RISK Stratification Project, which was supported by the Pediatric Research Organization for Kids with Intestinal Inflammatory Diseases (PROKIIDS). From 2008-2012, 28 centers in the United States and Canada gathered serologic, genomic, microbial, and histologic data on patients with newly diagnosed Crohn's disease. Children who had stricturing or penetrating disease at diagnosis or who developed it within 90 days of enrollment were excluded.

Our study used data from the RISK Project, including demographic data and serum laboratory results for hemoglobin, platelets, eosinophil count, sedimentation rate, C-reactive protein, and albumin. The disease location was characterized as upper intestinal tract, ileal, or colonic. The following serologic markers associated with inflammatory bowel disease were evaluated: ASCA IgA, ASCA IgG, ANCA, I2, OmpC, CBirFla, GM-CSF, IGF-1, IL-6, and TNF α . Biopsies taken from the ileum underwent RNA sequencing to conduct expression analysis of genes associated with inflammatory bowel disease.

Regression analysis was performed to determine any association between an outcome of growth failure and effector clinical and genetic variables. Growth impairment was defined as a height z-score <-2 and malnutrition was defined as a weight z-score <-2. A BMI z-score <-2 identified patients with poor growth and/or malnutrition. Only variables which had less than 20% of the data missing were analyzed. A p-value of 0.05 was considered significant for the clinical variables, and a p-value of 5E-8 was used for the gene expression analysis. If the SNPs were located in exons, the surrounding genes were reported.

Results: The RISK Project included 913 children under the age of 18 years with Crohn's disease who had an inflammatory phenotype at the time of diagnosis. Our study evaluated a subgroup of 772 children who had all the serologic and genetic data obtained. The statistically significant clinical variables associated with growth impairment were the presence of hypoalbuminemia (p=0.0052) and anti-GM-CSF antibodies (p=0.0110). Immunochip data of 121,487 SNPs associated with inflammatory bowel disease were analyzed, but no statistical significance was observed for growth impairment or malnutrition. Genes with p-values <5E-5 were evaluated for clinical significance. For growth impairment, the genes with p-values <5E-5 were the following: OR5D14, OR5L1, OR4C6, OR5D13, KCNH8, EFHB, TAP2, LINC00574, LOC102724511, PAPOLG, VAV3, HLA-DOB, and TAP2.

Children with malnutrition were more likely to be female (p=0.0401) and have hypoalbuminemia (p=0.0081) and thrombocytosis (p=0.0162). Genes with p-values <5E-5 are the following: RMI2, LOC101927131, GLP2R, C8orf87, LINC00535, SKAP2, AGBL1-AS1, ANXA6, and LOC105371083.

Patients who had a BMI z-score <-2 were also more likely to have hypoalbuminemia (p=0.0061) and thrombocytosis (p=0.0011). Genes with p-values <5E-5 are the following: CCR7, SMARCE1, TAGAP, and LOC101929122.

Discussion: Children with newly diagnosed Crohn's disease who have growth impairment and malnutrition are likely to have hypoalbuminemia and thrombocytosis. Anti-GM-CSF antibodies were associated with growth impairment. No specific genetic sequences, on their own, were significant for an association with growth impairment or malnutrition. However, genes closest to significance for growth impairment act as olfactory receptors and transport proteins. The genes which are likely to contribute to malnutrition assist with DNA repair and intestinal growth. Interestingly, genes with the highest likelihood of an association with a low BMI are involved with activation of B and T cell lymphocytes in the regulation of inflammation. Thus, these findings assist in identifying children with Crohn's disease who have growth impairment and malnutrition.

592 LYMPHANGIOGENESIS AND EXPRESSION OF LYMPHANGIOGENIC GROWTH FACTORS IN ACUTE AND CHRONIC COLITIS. Senthilkumar Sankararaman¹, Liya Liu², Aling Shen², Youqin Chen², Thomas Sferra¹. ¹Pediatrics (Pediatric Gastroenterology Division), UH Rainbow Babies & Children's Hospital/Case Western Reserve University School of Medicine, Cleveland, OH; ²Pediatrics (Pediatric Gastroenterology Division), Case Western Reserve University School of Medicine, Cleveland, OH

Background: Lymphangiogenesis, the formation of new lymphatic vessels, is present in many disease states including inflammatory bowel disease (IBD). However the exact role of lymphangiogenesis, whether beneficial or detrimental,

remains unclear. The key lymphangiogenic growth factors include the vascular endothelial growth factors (VEGF C and D), their receptors (VEGFR2 and VEGFR3), and their co-receptors (neuropilins, NRP 1 and 2). The differential role of lymphangiogenesis in acute and chronic colitis has not been explored.

Objectives: To evaluate lymphangiogenesis and the differential expression of lymphangiogenic growth factors in acute and chronic colonic inflammation.

Methods: For mice experiments, 3% DSS was used to establish experimental acute and chronic colonic inflammation in 6-8 weeks old BALB/c mice. We investigated three groups of mice: controls (n=3), acute colitis (n=10), and chronic colitis (n=8). Immunohistochemistry for LYVE-1 (lymphatic marker) and CD-31 (blood vessel marker) was carried out to examine the relationship between lymphatic vessel density (LVD) and blood vessel density (BVD), respectively. The expression of VEGF C and D, VEGFR 2 and 3 and NRP 1 and 2 were assessed by both immunohistochemical and western blot analyses. Downstream signaling pathways such as p-AKT, p-JNK, and p-ERK were evaluated by western blot analyses. For human studies, similar methodology using colon biopsy samples from archived specimens were utilized in the evaluation of lymphangiogenesis in children with ulcerative colitis and in children without colonic inflammation (control group).

Results: LVD and BVD were significantly greater in the DSS induced acute and chronic colitis compared to the normal mice. The expression levels of VEGF-C, VEGF-D, VEGFR-2, VEGFR3, NRP-1, and NRP-2 were greater in the colitis group of both mice and humans. The levels of p-AKT and p-JNK but not p-ERK were significantly increased in the DSS group as compared to the normal mice.

Conclusions: Lymphangiogenesis is induced in both acute and chronic inflammation of the colon. The expression of VEGF-C, VEGF-D, VEGFR-2, VEGFR3, NRP-1, and NRP-2 is significantly increased in colonic inflammation contributing to lymphangiogenesis. The underlying downstream signaling for lymphangiogenesis may be through p-AKT and p-JNK pathways. This is the first study to demonstrate an increased expression of NRPs in acute and chronic inflammation of the colon. Further exploration of these factors may increase our understanding of the pathogenesis of intestinal inflammation and serve as a potential therapeutic target in IBD.

594 **HIGH RECURRENCE RATE AFTER FECAL MICROBIOTA TRANSPLANT FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE.**

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Introduction: Recurrent *Clostridium difficile* infection (RCDI) increases morbidity and mortality in patients with inflammatory bowel disease (IBD). Studies have shown a more severe disease course and higher rates of colectomy in IBD patients with RCDI. Fecal microbiota transplant (FMT) is known to be very effective for RCDI in non-IBD patients with cure rates up to 91%. The same success rates of FMT have not been reported in IBD patients with RCDI, and the data in pediatrics is limited. We aimed to determine the effectiveness of FMT for RCDI in established pediatric IBD patients.

Methods: We performed a retrospective chart review of pediatric IBD patients with IBD and RCDI (defined as ≥ 3 episodes) who underwent FMT via colonoscopy at a tertiary care IBD center. The primary outcome was rate of RCDI within 60 days post-FMT. The secondary outcomes were time to recurrence, recurrence rate by 180 days, and rate of colectomy. Descriptive statistics and univariate analysis were conducted.

Results: Of the 8 eligible patients, 7 had ulcerative colitis (UC), and 1 had Crohn's Disease (CD). Median (interquartile range [IQR]) age was 13 years (11-14), and 5/8 (63%) were male. The median [IQR] disease duration of IBD at the time of FMT was 833 days [430-1458]. Patients were on a range of IBD medications at the time of FMT: anti-TNF (N=3), anti-integrin (N=3), concomitant immunomodulators (N=3), steroids (N=4), aminosalicylates (N=2), proton pump inhibitors (N=4), and probiotics (N=1). The median [IQR] follow-up time was 305 days [177-563]. Two patients (25%) had RCDI by 60 days post-FMT and another 3 patients had RCDI between 60 and 180 days. The median [IQR] time to recurrence was 101 days [40-139]. Of the 5 patients who developed RCDI after FMT, one underwent a second FMT that was curative, and 2/5 were managed with vancomycin with resolution of RCDI episode. The final two went to colectomy after FMT, one at 46 days post-FMT and the other at 229 days post-FMT. The remaining 3/8 (37%) patients, including the one CD patient, did not have a recurrence at last follow-up. There was no association between RCDI and use of proton pump inhibitors, antibiotics, immunomodulators and biologics, hospitalizations, or endoscopic disease severity scores at time of FMT. One patient developed abdominal pain and fever shortly after FMT, which required a 2 day admission with a negative work-up and resolution of symptoms. There were no other reported adverse events following FMT.

Conclusion: The rate of RCDI (63%) following FMT is markedly higher in our pediatric IBD population than reported in adult and pediatric studies of RCDI in non-IBD patients, suggesting there is decreased effectiveness of FMT in the treatment of RCDI in IBD. Larger studies are needed to determine the efficacy and safety outcomes of FMT for RCDI in pediatric patients with IBD and to identify predictors of recurrence.

596 USTEKINUMAB THERAPY IN SEVERE PEDIATRIC INFLAMMATORY BOWEL DISEASE.

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Background: Ustekinumab (UST), a humanized monoclonal antibody against interleukins 12 and 23, has recently been approved for use in adults with Crohn disease. There are limited data on UST in the pediatric population, but it may prove to be a viable therapeutic option in children with inflammatory bowel disease (IBD) refractory to biologic therapy.

Aims: To evaluate the efficacy and safety of UST in refractory pediatric IBD measured by clinical response and adverse events.

Methods: Children between the ages of 6 and 21 with severe IBD refractory to biologic therapy and initiating UST at Children's Hospital of Philadelphia since April 2015 were included. Indications for initiation of UST therapy were determined by the primary gastroenterologist. Subjects were followed prospectively via medical record review and structured telephone interviews, and clinical activity indices and outcomes were recorded at 8-week intervals. Dosing was the standard adult regimen of induction with a 6 mg/kg intravenous infusion followed by maintenance therapy with 90 mg subcutaneous injections every 8 weeks. Outcome measures included disease activity, measured by Pediatric Crohn Disease Activity Index (PCDAI), albumin, C-reactive protein (CRP), and steroid exposure.

Results: Thirteen subjects, 11 with Crohn disease and 2 with indeterminate colitis on maintenance therapy with UST were included. Seven patients completed at least 16 weeks of therapy, and 3 patients completed at least 56 weeks. The mean age at UST initiation was 15.4 (range 11-18) years. The mean PCDAI (\pm SD) at initiation of therapy was 29.2 (\pm 15.3). Clinical response (decrease in PCDAI of \geq 12.5) was seen in 6/9 (66.7%) subjects at 8 weeks and 5/7 (71.4%) at 16 weeks. Clinical remission (PCDAI \leq 10) was seen in 3/9 (33.3%) subjects at 8 weeks and 3/7 (42.9%) at 16 weeks. At baseline and week 8, serum CRP was 2.7 and 3.1 ug/mL, respectively, and serum albumin remained 4.0 g/dL at baseline and week 8. Prior to induction, 6/13 patients were treated with systemic corticosteroids, versus 5/13 at week 8. Adverse events included one report of isolated hives following initial UST injection, and one patient was hospitalized with pseudomonas aeruginosa colitis. Two patients had persistence of severe inflammatory colitis and underwent diverting ileostomy while remaining on UST. Two additional patients underwent colectomy due to intractable symptoms and had UST discontinued after 14 and 23 weeks of therapy.

Conclusions: This is one of the first prospective cohort experiences of UST therapy in pediatric IBD. Although this study is limited by its small sample size, it appears that some patients experienced clinical improvement with UST in the first 8 to 16 weeks of therapy, with 72% achieving clinical response. Remission, however, was only achieved in 33%. Overall, this therapy was well tolerated by pediatric patients with severe IBD. Larger prospective studies are required and are underway at our center, in order to provide additional data regarding efficacy and safety of UST in pediatric IBD.

***597 SIGNIFICANT DYSBIOSIS OF ORAL MICROBIOME IS SEEN IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE (IBD) WITHOUT UPPER TRACT INVOLVEMENT AND IT IS AS PREDICTIVE AS STOOL MICROBIOME IN CLASSIFYING IBD.**

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Introduction: The gut and oral microbial dysbiosis has been shown to be associated with Inflammatory Bowel Disease (IBD). However, it is not known to what extent gut and oral microbial disease markers converge in terms of their composition in subjects with IBD. In this prospective study, we aim to examine the concordance and divergence of the microbiome at different body sites in pediatric subjects with IBD and to assess its diagnostic and predictive potential.

Methods: We performed a prospective cohort study of 26 treatment naïve IBD subjects (17CD and 9UC), 16 established IBD patients (11CD and 7UC), and 17 non-related, healthy controls assessing the fecal and oral microbiome via repeated samplings. Associations between clinical characteristics such as disease activity indices and the microbiome were tested using generalized estimating equations. 16s rRNA sequencing of hypervariable regions was performed on extracted stool (n=115)

as well as oral samples (n=662); tongue (n=174), buccal surface (n=168), plaque (n=161), and saliva (n=159) from CD and UC patients and healthy controls. Data processing and analysis was performed using Mothur software referencing the SILVA database and R software.

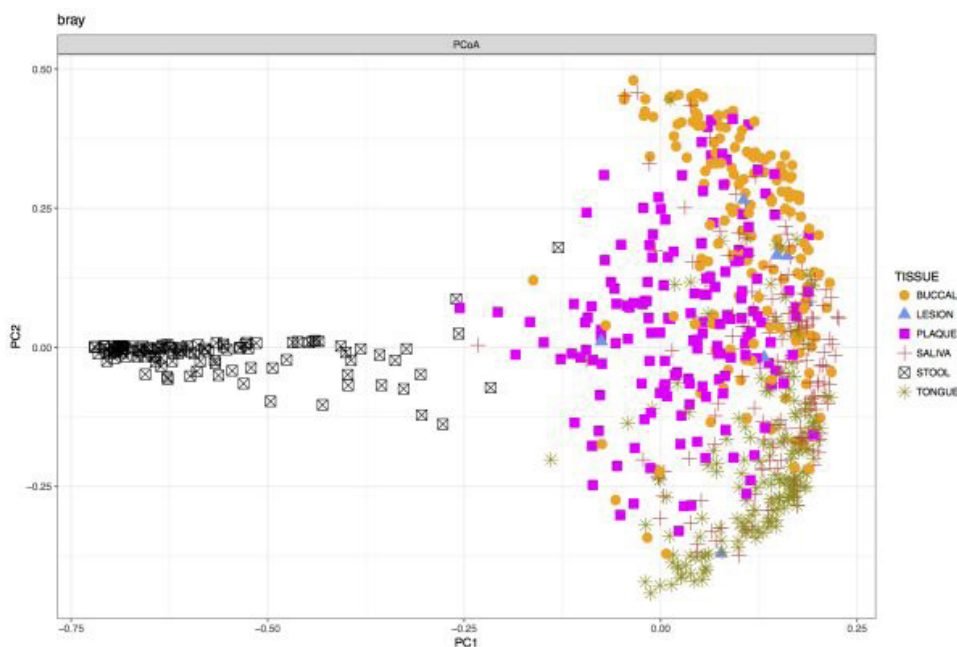
Results: A total of 42 IBD subjects were included in this pilot study, along with 17 healthy controls. A total of 777 samples were analysed. None of the IBD subjects had demonstrable oral lesions associated with IBD. After rigorous QC, filtering 1% out, a total of 755 OTU (operative taxonomic units) were included in the analysis. Lower cut off was used to include many OTUs as possible so that less common and novel microbiome can be examined. A principal coordinates analysis of the bray distance for all samples (fig 1), including individual locations within the mouth (plaque, buccal, tongue, and saliva). Dysbiosis measured by alpha and Beta diversity were as prevalent in oral microme compared to stool in IBD subjects. A Random Forest classifier between IBD cases and controls showed a mean area under the curve (AUC) of 0.7244 for saliva samples as compared to 0.6713 for stool (table 1). However, the predictive value of all oral sites are comparative to that of stool. We found differences in the composition of specific microbial genera such as *Carnobacteriaceae* (p=0.0171), *Bacillales* (p=0.0464), *Gemella* (p=0.0572) between cases and controls in salivary microbiome.

Conclusions: Oral samples and stool samples separate out on principal coordinate analysis (PCoA) indicating there are regional variations exist even in oral cavity from different locations. Oral samples cluster primarily by location on PCoA. Abundance of certain bacterial genera differentiates cases from controls as previously reported in adult IBD and pediatric cancer studies. Saliva, the least invasive and easy to obtain biospecimen, may serve as the most accurate source in predicting IBD and subtypes such as CD and UC. The remaining oral collection sites are equally as predictive as stool. Further studies will be of interest to use oral microbiome as screening tool for suspected IBD and as a monitoring tool for treatment responses.

Random Forest classifier between IBD, CD, and UC vs. Controls

Tissue	IBD_AUC_MEAN	IBD_AUC_SD	CD_AUC_MEAN	CD_AUC_SD	UC_AUC_MEAN	UC_AUC_SD
STOOL	0.6713	0.112	0.6246	0.1187	0.7356	0.1442
TONGUE	0.6537	0.1164	0.6413	0.1085	0.7292	0.1384
SALIVA	0.7244	0.1151	0.6906	0.1293	0.7371	0.1319
PLAQUE	0.676	0.1174	0.7015	0.1274	0.6461	0.1437
BUCCAL	0.6944	0.1084	0.6646	0.1146	0.6735	0.1342

AUC = Area Under the Curve; SD = Standard Deviation; CD = Crohn’s Disease;
UC = Ulcerative Colitis; IBD = Inflammatory Bowel Disease



A principal coordinates analysis of the bray distance for all samples.

599 COMPARISON OF HEPATITIS B BOOSTER VERSUS HEPATITIS B IMMUNIZATION SERIES ADMINISTRATION AND THE EFFECTS ON HEPATITIS B TITER STATUS IN PREVIOUSLY IMMUNIZED INFLAMMATORY BOWEL DISEASE PATIENTS UNDERGOING BIOLOGIC

THERAPY. Suruchi Batra¹, Mark Tufano², Bernadette Diez², Lynn Duffy². ¹Pediatrics, INOVA Fairfax Hospital, Falls Church, VA; ²Gastroenterology, Pediatric Subspecialists of Virginia, Fairfax, VA

Background: Use of biologic therapy for autoimmune disease has been shown to increase risk of opportunistic infections. Patients are routinely screened for opportunistic infections prior to initiation of biologic therapy as treatment for Inflammatory Bowel Disease (IBD), including Hepatitis B infection. Previous studies have demonstrated that immunity conferred by vaccination will wane 15 years after completion of the Hepatitis B Vaccination series in the previously vaccinated IBD patients. IBD patients found to be nonimmune to Hepatitis B are routinely advised to undergo repeat Hepatitis B vaccination with a single vaccine.

Aim/Hypothesis: To assess the titer response to a three part Hepatitis B series versus single booster immunization in IBD patients undergoing biologic therapy previously found to be non-immune to Hepatitis B. We hypothesize that a three part Hepatitis B series will result in higher Hepatitis B titers post-immunization.

Methods: Study was approved by the IRB at INOVA Fairfax Hospital. A prospective randomized un-blinded trial was conducted at an outpatient gastroenterology clinic. Enrolled subjects are randomized to receive a single vaccine or three part vaccine series; Hepatitis B titers are checked two weeks after vaccine administration.

Inclusion Criteria: Subjects with a diagnosis of IBD, between the ages of 5 and 23 years, currently being treated with or will be treated with biologic therapy, including Adalimumab (Humira), Infliximab (Remicade), Certolizumab (Cimzia), and Vedolizumab (Entyvio), and found to have a Hepatitis B Surface Antibody less than 10 and Hepatitis Surface Antigen negative.

Exclusion Criteria: Subjects found to have Hepatitis B Surface Antibody level greater than 10, Hepatitis Surface Antigen positive, or with history of severe allergic reaction to vaccine administration.

Results: 11/12 subjects developed immunity following immunization, regardless of number of vaccines administered. 1/12 was nonresponsive.

Conclusions: Preliminary data indicates that a single Hepatitis B vaccine is sufficient to provide immunity in IBD patients whose Hepatitis B immunity has waned since initial vaccine administration. Further research is needed to confirm these findings.

600 FUNCTIONAL ANALYSIS IMPLICATING SAMD9 MUTATIONS IN INTESTINAL INFLAMMATION IN PATIENTS WITH MIRAGE SYNDROME. Takashi Ishige^{1,2}, Neil Warner¹, Eileen Crowley¹, Aleixo Muise¹.

¹Cell Biology, The hospital for Sick Children, Toronto, ON, Canada; ²Department of Pediatrics, Gunma University, Maebashi, Japan

Background/Objectives: MIRAGE syndrome is caused by heterozygous mutations in the *SAMD9* gene. The syndrome is characterized by enteropathy and is often fatal within first 2 years of life. However, pathogenesis of enteropathy in the syndrome is unknown.

Case/Study Methods: We present a case of MIRAGE syndrome (gestational age 35 weeks, birth weight 1330g) who developed restriction of growth, adrenal hypoplasia, genital anomaly, and enteropathy at the time of birth. Sigmoidoscopy showed longitudinal ulcers in rectum. Apoptotic cells were observed at the mucosal biopsy specimen from the site of ulcer. To investigate the involvement of SAMD9 mutation in colitis, we transfected HEK293 cells with wild type (WT) or mutated (R1293W) SAMD9, and the difference in TNF-alpha responsiveness for apoptosis pathways were assessed using western blotting.

Results: R1293W transfected cells showed increased protein expression of cleaved Poly ADP-ribose polymerase (PARP) when compared with WT and control, which represents increased apoptosis in R1293W mutation. X-Linked inhibitor of apoptosis (XIAP) were decreased in R1293W mutations which may also explain the apoptosis observed in the patient intestinal mucosal biopsy.

Conclusion: Suppression of XIAP might contribute to increased apoptosis and intestinal inflammation observed in MIRAGE syndrome patients.

601 IDENTIFYING INFLAMMATORY CUES THAT DRIVE DIFFERENTIATION OF COLITOGENIC GRANZYME A-EXPRESSING T HELPER CELLS. Tanbeena Imam¹, Matthew Olson², Mark Kaplan². ¹*Pediatric Gastroenterology, Indiana University School of Medicine, Indianapolis, IN;* ²*Indiana University School of Medicine, Indianapolis, IN*

Background: Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the intestinal tract mediated by a dysregulated immune response. CD4⁺ T cells (Th) have been shown to be involved in the development of IBD. Granzyme A (GrA) is a serine protease associated with cytotoxicity in CD8⁺ T cells and NK cells. Surprisingly, we also observed an influx of GrA⁺ CD4 T cells into the intestines in murine models of inflammatory bowel disease (IBD). Intestinal GrA⁺ Th cells lack expression of other cytotoxic-associated genes (i.e. granzyme B, perforin) and do not significantly co-express other Th cell lineage-associated cytokines, suggesting that they may represent a novel subset of Th cells. Moreover, we have shown increased *GZMA* expression in biopsies from patients with Crohn's disease and ulcerative colitis. As a whole, these data suggest that GrA⁺ Th cells may represent novel mediators of intestinal inflammation. However the inflammatory signals that drive their differentiation are unclear. In our preliminary studies, we showed that IL-4 in combination with IL-6 was a potent inducer of GrA⁺ Th cell differentiation in vitro. Despite the expression of GrA of these cells, their colitogenic potential is currently undefined.

Objective/Purpose: Our study aims to determine the colitogenic potential of in vitro derived GrA⁺ Th cells and the requirement of GrA expression by these cells for induction of disease in a T cell transfer murine model of IBD.

Design/Methods: Naive CD4⁺ T cells were isolated from spleens of both wildtype and GrA KO mice using magnetic separation. Cells were then cultured with plate-bound anti-CD3, soluble anti-CD28, and IL-4 with and without IL-6. After 3 days in culture, the cells were removed from the coated plates and expanded in media containing the same cytokine culture conditions. After 2 days in the expanded culture, cells were harvested and transferred into RAG-1 deficient mice. The recipient mice were weighed initially, then weekly thereafter. They were monitored for development of disease between 8-12 weeks. They were then sacrificed at 14 weeks after transfer, and analyzed for presence of inflammation and immune function.

Results: We found that mice that received cells cultured with IL-4 and IL-6 exhibited enhanced weight loss and intestinal inflammation as compared to mice that received control cells or cells cultured with IL-4. Importantly, all aspects of disease required GrA expression by these cells.

Conclusions: Our study shows that IL-4 and IL-6 are capable of inducing Th cells that cause granzyme A-dependent intestinal inflammation and weight loss in a murine model of IBD. Future studies will identify how GrA influences inflammation during IBD.

602 ENDOSCOPIC SCORING TO ASSIST IN THE MANAGEMENT OF PEDIATRIC INFLAMMATORY BOWEL DISEASE. Rebecca Casini, Timothy Blaufuss, Mamta Reddy. *Children's Mercy Hospital, Kansas City, MO*

Introduction: Endoscopic evaluation is mainstay, standard-of-care practice for patients with inflammatory bowel disease (IBD). Visual and biopsy driven assessment helps guide decision making, specifically therapeutic management. While some gastroenterologists routinely include validated scores of disease activity there is no such standard practice at our institution. In an effort to standardize endoscopic evaluation, we proposed scoring of IBD patients using MAYO score for ulcerative colitis and Simple Endoscopic Score for Crohn's disease (SES-CD).

Objective: The aim of this quality improvement study was to educate practitioners on endoscopic scoring and to increase utilization of MAYO and SES-CD scores as standard of practice.

Methods: Baseline data was collected over 5 weeks to ascertain what percentage of known IBD patients (age 6-18 years) had MAYO or SES-CD scores documented in their endoscopic report. Our intervention to improve physician scoring included four PDSA (Plan-Do-Study-Act) cycles, lasting 1 month each. Specifically, in order, interventions included: 1) introduction to MAYO and SES-CD scoring via email and informational handout; 2) printed verbal MAYO and SES-CD scoring rubrics posted at every work station; 3) visual aids with pictures of how to use scores posted at each work station; 4) a brightly colored paper scoring sheet provided at every work station. Patients' endoscopic reports were reviewed after each intervention.

Results: At baseline, 8% of IBD patients at CMH had documented MAYO or SES-CD scores. After PDSA cycle 1, the scoring rate increased to 43%. After cycle 2, scoring dropped to 0%. After PDSA cycle 3, scoring improved to 22%. After the final PDSA cycle, 56% of IBD patients had either a MAYO or SES-CD documented in their endoscopic report.

Conclusions: After four successive PDSA cycles, compliance with documented MAYO and SES-CD score improved seven fold to 56%. Variability in scoring was provider dependent. Overall, more providers are now aware of MAYO and SES-CD scoring and are including these measures as standard of care. Further investigation is needed to assess the clinic utility of MAYO and SES-CD scores at our institution.

603 ROLE OF RESIDENT MACROPHAGES IN SMALL INTESTINAL HOMEOSTASIS. Tina Morhardt¹, Atsushi Hayashi², Takanori Ochi², Nobuhiko Kamada². ¹Pediatrics, Division of Gastroenterology, University of Michigan, Ann Arbor, MI; ²Internal Medicine, Division of Gastroenterology, University of Michigan, Ann Arbor, MI

The gastrointestinal (GI) tract is exposed to numerous immune stimuli, including commensal microbial and dietary antigens. Hence, the GI tract develops regulatory immunity to these resident antigens to maintain homeostasis. Once the regulatory immunity is disrupted, excessive immunity against resident antigens is induced and thereby causes disease, such as inflammatory bowel disease. Resident macrophages in the intestine are known to play a central role in regulatory immunity against commensal bacteria via production of a robust amount of an anti-inflammatory cytokine IL-10. Notably, stimulations from commensal bacteria and their metabolites require IL-10 production by resident macrophages in the colon. However, the regulation of resident macrophages in the small intestine (SI), where the abundance of commensal bacteria is considerably lower than colon, remains largely unknown. We have previously reported that the replenishment of resident macrophages and their IL-10 production in the small intestine are independent of commensal bacteria. Rather, dietary factors contribute to the functional regulation of macrophages in the SI. In this study, we further elucidate the role of IL-10-producing SI resident macrophages in regulation of homeostasis in SI. We found that IL-10 production was induced in the recovery phase of indomethacin-induced small intestinal injury. IL-10-deficient mice failed to recover from SI injury, indicating that IL-10 is crucial for the host recovery from small intestinal injury. SI injury recovery is independent of T-cell effect, as seen when RAG1 knockout mice are treated with indomethacin. Next, we demonstrated that intestinal MHC-II⁺CD64⁺CD11c⁺ resident macrophages are major producers of IL-10 during acute phase of small intestinal injury. They remain major producers through recovery phase. Consistent with this notion, depletion of intestinal MHC-II⁺CD64⁺CD11c⁺ macrophages in the SI utilizing CCR2-diphtheria toxin receptor (DTR)-depleter mice resulted in an impaired recovery from small intestinal injury as we have seen in IL-10 deficient mice. This IL-10-dependent effect was also recapitulated by using intestinal macrophage depleted CCR2-DTR mice and adoptively transferring intestinal macrophages isolated from WT or IL-10 knockout mice. Those mice receiving WT mice had homeostasis restored and were able to recover from indomethacin injury. Overall, intestinal macrophages producing IL-10 appear to hold an important role in restoring homeostasis after small intestinal injury. This cell population and their functional regulation by dietary factors could provide a potential target for conditions such as small intestinal Crohn's, autoimmune enteropathy or food-related allergy disorders.

604 ORAL VANCOMYCIN AS AN ADJUVANT TREATMENT IN IBD. Travis Ayers^{1,2}, Elaine Puppa^{1,2}, Howard Kader^{1,2}, Jaylyn Waddell², Nidhi Rawal^{1,2}. ¹Pediatric GI and Nutrition, University of Maryland, MD, MD; ²University of Maryland School of Medicine, Baltimore, MD

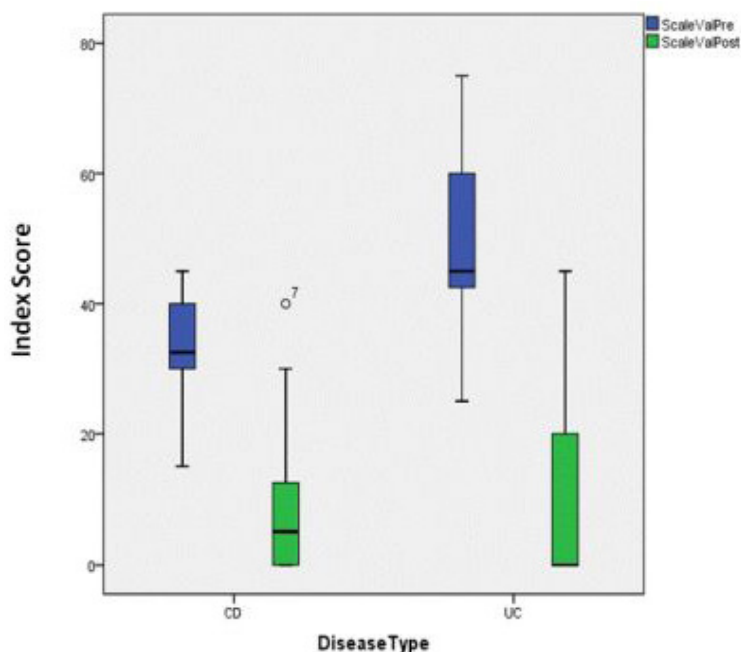
Introduction: Oral vancomycin (POV) has been shown to benefit patients with active Inflammatory Bowel Disease (IBD) and concurrent primary sclerosing cholangitis (PSC). In addition to improving PSC, initial studies showed reduction in IBD symptoms, due to a direct immunomodulatory effect on regulatory T-cells and the tumor necrosis factor-alpha pathway. Recent literature has shown beneficial effects of POV in combination with other oral antibiotics in moderate to severe IBD. Most of these papers were case reports. To date no evidence exists to suggest significant systemic absorption of POV, or increased risk of Vancomycin resistant enterococcus (VRE). This study attempts to expand on the current literature to determine efficacy of POV in treating active IBD in children.

Methods: A retrospective study was designed with a prospective arm. Patients were identified using the institution's IBD registry, ICD-9 and ICD-10 codes for IBD, and practitioners' recall of their patients on POV. Patients between ages 2-21 years were included who met the criteria for active IBD at the time of the initiation of POV. Patients with *C difficile* infection and PSC were excluded. Pre and post treatment analysis of disease activity was conducted with data to obtain Physician Global Assessment (PGA), pediatric ulcerative colitis activity index (PUCAI), and an abbreviated pediatric Crohn's disease activity index (PCDAI). Findings were then analyzed using Wilcoxon Signed Ranks test, to determine if pre and post POV intervention rankings of symptom severity significantly differed. Mann Whitney U tests were conducted to assess presence or absence of specific symptoms, such as abdominal pain, diarrhea, blood in stool and anemia, as they were the most common presenting symptoms, before and after POV initiation.

Results: Nineteen patients were enrolled into the study: 12 with Crohn's disease (CD) and 7 with ulcerative colitis (UC), (10 females and 9 males). POV improved the PGA score in 16 of 19 patients (p-value <0.001), and no patients worsened. The mean PGA score pretreatment was 3 +/-0.471, with post treatment mean of 1.58 +/- 0.769. All symptoms, including abdominal pain (p-value <0.001), diarrhea (p-value 0.002), anemia (p-value 0.002), and blood in stool (p-value <0.001) showed significant improvement. PUCAI and PCDAI scores also improved with mean score reduction of 23 in CD and 38 in UC patients indicating a reduction in symptoms after initiation of POV (p-value<0.0001). No significant differences in scores were noted between UC and CD, as both the disease groups demonstrated improvement.

Discussion: This study demonstrates that POV can be an effective adjuvant treatment for IBD. Its effectiveness is likely due to a combination of its anti-TNF- α activity, as well as its influence on the gut microbiome. The findings were found to

be statistically significant, with nearly all patients showing improvement their symptoms, PCDAI scores, PUCAI scores as well as PGA scores. Patient's original treatment regimen could have also contributed to some of this improvement. Further controlled studies of POV in IBD are warranted to determine the most efficacious use of POV in pediatric IBD.



PCDAI and PUCAI scores before and after POV therapy
 CD: Crohn's disease
 UC: Ulcerative colitis

606 PNEUMOCOCCAL POLYSACCHARIDE VACCINATION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS. Tsega Temtem^{2,1}, John Whitworth^{2,1}, Bindiya Bagga³. ¹LeBonheur Children's Hospital, Memphis, TN; ²Pediatric Gastroenterology, University of Tennessee Health Science Center, Memphis, TN; ³Pediatric Infectious Disease, University of Tennessee Health Science Center, Memphis, TN

Background: According to current recommendations, in addition to pneumococcal conjugate vaccine series (PCV13), all children with inflammatory bowel disease (IBD) age ≥ 2 years with planned or current immunosuppression should receive pneumococcal polysaccharide (PPSV23) vaccine. The primary aim was to determine the PPSV23 immunization rates in our pediatric IBD patients. The secondary aim was to determine the incidence of invasive pneumococcal disease in these patients.

Methods: The IBD database at Le Bonheur Children's Hospital was retrospectively reviewed to identify all cases diagnosed from 2003 - 2015. 106/190 IBD patients on immunosuppressive drugs, whose immunization records could be obtained from the state database, were included in the study. Medical records were reviewed to determine infections seen in these patients from the time of diagnosis to date. Results: IBD patients in our study ranged from age 2-18 years. Only 4 of 106 (3.7%) patients had received PPSV23 vaccine. Only 1 patient (0.9%) had probable pneumococcal disease, but no patients with invasive pneumococcal disease. Clostridium difficile (11 patients) and viral infections were more commonly encountered.

Conclusions: Majority of our pediatric IBD patients did not receive PPSV23 vaccine. Fortunately, we did not see a high rate of invasive pneumococcal disease in our patients suggesting that they may be protected by the primary PCV13 vaccine series. Non-pneumococcal infections were more common in this population.

610 CYTOMEGALOVIRUS COLITIS COMPLICATING PEDIATRIC INFLAMMATORY BOWEL DISEASE. Wael El-Matary¹, Camelia Sefanovici², Paul Van Caesele³, Jeff McCurdy⁴, Vini Deora¹. ¹Pediatrics, University of Manitoba, Winnipeg, MB, Canada; ²Pathology, University of Manitoba, Winnipeg, MB, Canada; ³Medical Microbiology, University of Manitoba, Winnipeg, MB, Canada; ⁴Gastroenterology, University of Ottawa, Winnipeg, MB, Canada

Background: Cytomegalovirus (CMV) colitis [JM1] may occur in patients with inflammatory bowel disease (IBD) leading to symptoms that mimic a relapse. The role of CMV colitis in children with IBD is under-reported [JM2]. It has been

recommended to perform a sigmoidoscopy with biopsies to screen for CMV reactivation in children with severe, steroid-resistant colitis. The aim of this study was to determine the frequency of CMV reactivation and its management in children with acute severe colitis.

Method: We retrospectively assessed the prevalence of colonic CMV in pediatric patients with ulcerative colitis (UC), Crohn's colitis (CC) and IBD-Unclassified (IBD-U) from a single academic center. Consecutive patients 17 years old or younger, presenting with acute severe colitis who underwent an endoscopic evaluation for CMV between December 2011 and April 2017 were included. Patients required at least one sigmoid biopsy, typically from the most inflamed colonic areas, evaluated by qualitative polymerase chain reaction (PCR) and immunohistochemistry. Management decisions for patients with positive biopsies for CMV were documented.

Results: Ninety one sigmoid biopsies were collected from 65 patients with IBD: 47 (72.7%) with UC, 14 (20%) with CC, and 4 (7.3%) with IBD-U. The median age was 12 years [interquartile range (IQR) 8-14 years] and 55% were female. All patients had severe disease endoscopically. Eight biopsy samples were obtained from colectomy specimens from patients with UC. Fifty-four (83%) patients had pre-existing IBD, while the rest were newly diagnosed. Medication exposure included corticosteroids for 46(70%) patients, and immunosuppressive and/or biologic agents for 36 (55%) patients. Twenty-seven of 65 patients (41.5%), were steroid-resistant; 16 with UC, and 11 with CC. The median number of sigmoid biopsies for CMV PCR per patient was one biopsy (IQR 1 – 2). Four of 47 patients (8.5%) with UC, 2 with steroid resistant disease, had positive sigmoid biopsies for CMV by PCR. All 4 patients had negative staining for CMV by immunohistochemistry. None of those with CC or IBD-U had positive biopsies for CMV by PCR. Patients with positive testing for CMV responded to escalated medical therapy, without a need for anti-viral therapy, and none required colectomy over a median duration of follow up of 1.1 year (IQR 1 – 1.6).

Conclusion: CMV colitis may not be common in children with IBD. Further studies are required to determine the underlying sero-prevalence of CMV in pediatric IBD populations and to determine the role of reactivation. Answers to these questions are needed to determine if the current recommendations suggesting a routine sigmoidoscopy to exclude CMV infection in steroid-resistant acute severe colitis is justified.

611 MICRONUTRIENT DEFICIENCIES IN CHILDREN NEWLY DIAGNOSED WITH INFLAMMATORY BOWEL DISEASE. Vini Deora¹, Nicole Aylward¹, AbdulRazaq Sokoro², Wael El-Matary¹. ¹Pediatrics, University of Manitoba, Winnipeg, MB, Canada; ²Clinical Biochemistry, University of Manitoba, Winnipeg, MB, Canada

Background: Inflammatory bowel disease (IBD) has been commonly linked with malnutrition. Children with untreated micronutrient deficiencies may have a complicated disease course. Screening and assessing children with IBD for under-nutrition is an essential component of routine clinical care.

Objectives: To examine micronutrient deficiencies in children with IBD at diagnosis.

Methods: Children (< 17 years) newly diagnosed with IBD had their serum vitamins and minerals measured at diagnosis. Clinical disease activity indices and inflammatory markers (C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)) were also measured. Micronutrient deficiencies in children with Crohn's disease were compared to those with ulcerative colitis (UC)

Results: 142 children, [median age = 14 years, IQR = 12 – 15; 81 girls (57.04%); 69 with CD, 66 with UC and 7 with IBD unclassified (IBD-U)] with confirmed IBD were included. At diagnosis, vitamin D and serum iron were deficient in 104 (73.23%) and 74 (52.11%) children respectively. Serum zinc and copper were also insufficient in 24.6% and 17.6% respectively. Vitamin D deficiency was significantly more common children with CD (81.5%) vs those with UC (72.7%) (P= 0.04). Copper and zinc were also significantly lower in those with CD (33.3% and 34.8% respectively) vs UC (4.5% and 16.6%, P= 0.019 and 0.023 respectively). The mean serum level of vitamin D was significantly lower in children with CD (67.4±20.8 nmol/L) compared to those with UC (80.1±22.6 nmol/L) (P=0.03). Zinc mean level was also significantly lower in children with CD (9.6±0.6 umol/L) compared to those with UC (13.6±2.1umol/L) (P=0.04).

Conclusions: Micronutrient deficiencies are common in children newly diagnosed with IBD especially in those with Crohn's disease.

***613 EFFECT OF AN ANTI-TNF THERAPEUTIC DRUG MONITORING QUALITY IMPROVEMENT PROGRAM ON INFLAMMATORY BOWEL DISEASE PATIENT OUTCOMES AT A LARGE ACADEMIC PEDIATRIC GASTROENTEROLOGY PRACTICE.** Aditi Mulgund¹, Laura Baumann², Deepika Choma¹, Puneet Sharma³, Weizhe Su^{4,5}, Lin Fei⁵, Lee Denson², Phillip Minar², Dana Dykes², Michael Rosen². ¹Department of Internal Medicine, University of Cincinnati Medical Center, Cincinnati, OH; ²Division of Gastroenterology,

Introduction: The anti-TNF drugs are highly effective in the treatment of IBD but maintaining durability of response is a challenge. Proactive therapeutic drug monitoring (TDM) has been shown to increase sustained remission and anti-TNF durability and decrease anti-drug antibody (ADA) development in adults with IBD. Reports of the feasibility and effect of incorporating anti-TNF TDM into practice-wide quality improvement initiatives are lacking. The aim of this study was to determine whether a TDM quality improvement program improved anti-TNF clinical outcomes in IBD patients at a tertiary care pediatric medical center.

Methods: In October 2014, we instituted TDM guidelines for the use of infliximab (IFX) and adalimumab (ADL) to treat patients with IBD at our pediatric medical center. The primary recommendation was to monitor drug levels after induction and annually, and adjust dose/frequency to achieve a level > 5 µg/ml. We made the guideline available online, educated providers, and incorporated recommendations into order sets and pre-visit planning. We performed a retrospective propensity score-matched observational cohort study comparing outcomes of patients initiating treatment with IFX or ADL after the institution of TDM guidelines (PostTDM, Oct 2014-Sep 2015) to those treated prior to TDM guidelines (PreTDM, Oct 2011-2013). PostTDM patients had 1-2 years of follow-up data. The primary outcome was sustained clinical remission defined as physician global assessment (PGA) of inactive at all time points between 22 and 52 weeks after anti-TNF initiation, on the same anti-TNF, without surgery, and off corticosteroids at 52 weeks (SCR22-52). Secondary outcomes were 52-week clinical remission (CR52), time to anti-TNF cessation, and time to high titer ADA (IFX >1000 ng/ml; ADA >300 ng/ml).

Results: We identified 105 PreTDM and 81 PostTDM patients and matched 81 pairs for this analysis. Baseline characteristics were similar between the two groups. SCR22-52 was achieved in 42% of PreTDM and 57% of PostTDM patients (absolute risk reduction [ARR] 15%, 95%CI 0.2-29.4%, P=0.08). CR52 was achieved in 57% of PreTDM and 68% of PostTDM (ARR 11%, 95%CI 0- 25%], p=.16). The percent of patients remaining on the same anti-TNF drug was 83% and 85% at 1 year, and 68% and 78% at 2 years in the PreTDM and PostTDM groups, respectively (HR 1.30, 95%0.66, 2.55], p=.4568). The percent without high titer ADA was 74% and 84% at 1 year, and 63% and 68% at 2 years in the PreTDM and PostTDM groups, respectively (HR 3.0, 95% 1.3-7.3, P=.01) (Fig. 1). 64% of providers were adherent to guidelines. When comparing the adherent subgroup to matched controls, effect sizes were larger than those for the overall group for SCR22-52 (ARR 17%, 95%CI 0-35%, P=.09) and time to high titer ADA (HR 3.9, 95%CI .8-18.4, P=.08). Process control chart analysis demonstrated that the practice mean monthly remission rate rose from 80% to 87% after initiating TDM guidelines (Fig. 2).

Discussion: Institution of a TDM quality improvement program at a tertiary care pediatric medical center GI practice improved key clinical outcomes in IBD patients treated with anti-TNF drugs. Implementation of measures to improve provider guideline adherence may strengthen the effect of the program on patient outcomes.

Figure 1: Kaplan-Meier curve showing time to high titer ADA between PreTDM and PostTDM groups

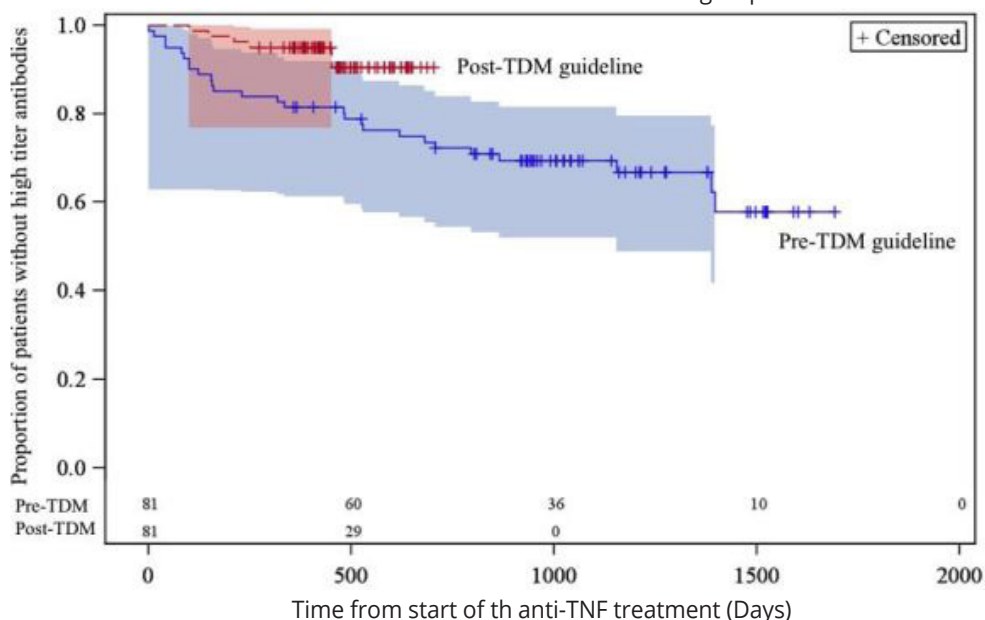
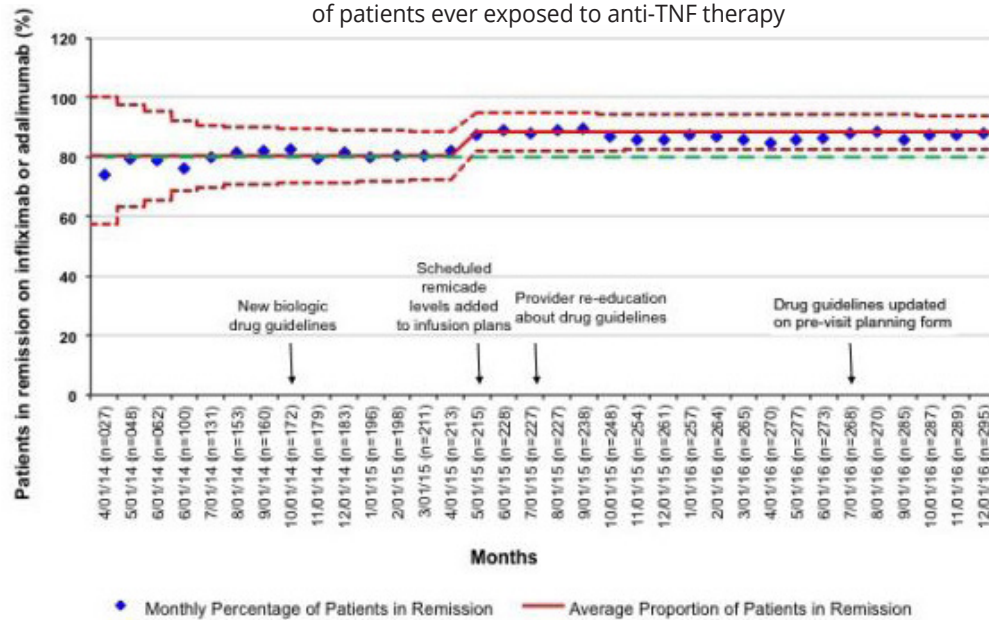


Figure 2: Process control chart demonstrating practice mean monthly remission rates of patients ever exposed to anti-TNF therapy



615 CHARACTERIZATION OF INFANTILE IBD. Alissa Galgano¹, Noor Dawany³, Máire Conrad^{1,6}, Kathleen Sullivan², Marcella Devoto^{1,5,4,6,7}, Judith Kelsen^{1,4}. ¹Gastroenterology, Hepatology, and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; ²Immunology and Allergy, Children's Hospital of Philadelphia, Philadelphia, PA; ³Biomedical Health Informatics, Children's Hospital of Philadelphia, Philadelphia, PA; ⁴Biostatistics and Epidemiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; ⁵Human Genetics, Children's Hospital of Philadelphia, Philadelphia, PA; ⁶Pediatrics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; ⁷Molecular Medicine, University Sapienza, Rome, Italy

Background: Very early onset IBD (VEO-IBD), IBD diagnosed in children 5 years or age and younger, is frequently a different disease process than older onset IBD. The severe phenotype and young age suggest a more pronounced genetic susceptibility and dysregulated immune response. Monogenic defects are detected even more frequently in children who present in the first 2 years of life. We set out to characterize the clinical features of children who present with VEO-IBD in the first 2 years of life and correlate the phenotypic findings with the genomic data.

Methods: Children diagnosed with IBD at 25 months and younger and their parents were recruited. Blood samples were obtained from the patients as well as their parents to perform Whole Exome Sequencing (WES). Interviews and medical chart review were performed to obtain demographic data including: gender, age of diagnosis, birth history including mode of delivery and breast feeding, infectious history, milk protein allergies and antibiotic exposure. Presenting symptoms and disease phenotype were recorded and included: location of disease, laboratory evaluation at diagnosis, medication exposure, extraintestinal manifestations of disease, and family history of disease.

Results: 65 patients were recruited. 69.2% were male and 30.8% were female. 49.2% of patients were diagnosed with Crohn's Disease (CD), 4.6% were diagnosed with Ulcerative Colitis (UC) and the remaining 46.2% were diagnosed with Indeterminate Colitis (IBDU). 16.9% of patients were found to have monogenic defects. 2 of the patients with monogenic defects were children of consanguineous parents. 56.4% of the patients were delivered vaginally while 43.6% were delivered via C-section. 74.4% of patients were initially exclusively breastfed, 45.8% of whom continued until at least 6 months of life. 88.1% of patients were exposed to antibiotics prior to the onset of their symptoms. 86.7% of these children received 2 or more courses of antibiotics. Milk protein allergy was diagnosed in 69.8% of patients while only 25.9% had subsequent confirmed milk protein allergy. Presenting symptoms included prolonged hematochezia in 77.2% and 73.7% of patients presented with diarrhea. Fever was present at onset of symptoms in 28.1% of patients and 47.4% presented with failure to thrive (FTT). Significant laboratory evaluation at diagnosis included anemia in 49.1% of patients. Positive family history is present in 29.2% of the patients. 1.8% of patients have a father with CD, 5.4% of patients have a mother with CD, 3.7% of patients have a mother with UC, and 3.7% of patients have siblings with IBDU. 20.4% of patients have second degree relatives with IBD.

Conclusions: The phenotype of infantile IBD is heterogeneous and can present with a broad spectrum of symptoms, most notably diarrhea with hematochezia and FTT. Misdiagnosis occurred in 45% of this population, specifically milk protein

allergy. There was a high rate of antibiotic exposure in this cohort, perhaps indicative of microbiome impact on disease. Monogenic defects were identified in 16.9% of this cohort, resulting in radical change in their therapy. Genetic analysis in the form of WES can be used to develop personalized treatment as patients with monogenetic defects do not respond to most conventional therapies.

LIVER

618 **NEUROCOGNITIVE STATUS IN ALAGILLE SYNDROME: RESULTS OF A MULTI-CENTER PROSPECTIVE OBSERVATIONAL STUDY.**

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Background: The neurocognitive status of children with Alagille syndrome (ALGS), an autosomal dominant cholestatic disease with extrahepatic involvement, has not been well characterized. The objective of this study was to determine the impact of ALGS on neurodevelopment, and compare to children with chronic intrahepatic cholestasis (CIC; \pm defined PFIC mutation) and alpha-1 antitrypsin deficiency (A1AT).

Methods: Children with native livers with ALGS, CIC, and A1AT from a multi-center longitudinal observational study (LOGIC) within the NIH-supported Childhood Liver Disease Research Network completed WPPSI-III (Wechsler Preschool & Primary Scale of Intelligence) or WISC-IV (Wechsler Intelligence Scale for Children) testing to ascertain FSIQ (Full-scale IQ). Physical exam and lab data were collected \pm 6 months of testing. We compared test scores separately by disease group to the normal distribution using K-S tests and across diseases using chi-square and Kruskal-Wallis tests and explored the impact of clinical and laboratory variables on IQ. Logistic regression was performed.

Results: 37.1% of eligible LOGIC subjects completed testing (ALGS n=66, CIC n= 43, A1AT n= 98) with a mean age of 8.2 years (range 2.7-16.9). The distribution of FSIQ scores (\geq 100, 85-99, <85) was significantly different between ALGS and A1AT (p=0.011, Table) and mean FSIQ score in ALGS was significantly lower than A1AT (94 vs 101, p=0.006). Notably, frequency of FSIQ<85 (<1 SD below average) was 30.3% in ALGS, 18.6% in CIC and 12.2% in A1AT. CIC and ALGS were not significantly different. FSIQ distribution in ALGS was also significantly lower than normal (p=0.008), while A1AT and CIC were not. After adjusting for test type and age, factors significantly associated with FSIQ < 85 in separate individual models, included ALGS diagnosis, Hispanic ethnicity, severe pruritus, xanthomas, low weight and height z-scores, total bilirubin, GGT, AST, and alkaline phosphatase. In an exploratory sub-analysis among ALGS, cardiac disease severity (n=11 severe vs n=56 mild or none) was not a significant predictor of below average FSIQ (OR 1.55, 95% CI: 0.35- 6.82, p=0.57).

Conclusions: Patients with ALGS appear to be at increased risk of lower IQ compared to children with other cholestatic liver diseases and norms. Nutritional impairment and liver disease severity (but not cardiac disease) factors appear to be related to these deficits, potentially identifying targets for early intervention.

Distribution of FSIQ Scores across diseases

FSIQ	CIC	A1AT	ALGS
≥100 (≥50 percentile)	19 (44.2%)	56 (57.1%)	26 (39.4%)
85-99 (15.8-50 percentile)	16 (37.2%)	30 (30.6%)	20 (30.3%)
	8 (18.6%)	12 (12.2%)	20 (30.3%)

620 LIVER STIFFNESS MEASUREMENT BY TRANSIENT ELASTOGRAPHY PREDICTS HEPATIC VENOUS CONGESTIONS AND LIVER DYSFUNCTION BUT NOT LIVER FIBROSIS IN CHILDREN AFTER FONTAN PROCEDURE.

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Background: The Fontan procedure results in hepatic venous congestion, with consequent liver fibrosis and dysfunction (Fontan-associated liver disease, FALD). Classical biochemical markers are bad predictors of fibrosis and hepatic dysfunction, and no intervention other than early heart transplant has been identified to alter the progression of FALD. Transient elastography (TE) has been used to assess liver fibrosis in children and adults after the Fontan procedure. Nevertheless, the ability of liver stiffness measurement (LSM) to predict liver fibrosis in patients with FALD is poor, resulting in a lack of non-invasive markers to monitor fibrosis progression.

Aims: 1) assessing LSM as a predictor of liver fibrosis and dysfunction in children and adolescents with FALD; 2) assessing whether TE can guide interventions to lower hepatic venous congestion.

Methods: We enrolled patients <18 years who underwent a Fontan procedure and had at least one LSM. Medical charts were retrospectively reviewed for demographic, hemodynamic, biochemical and imaging data. LSM was performed by TE (FibroScan), with adapted probes. Since no conversion scale is available to estimate the grade of fibrosis from LSM in patients with FALD, we used all scales validated for other liver diseases (individually and combined). METAVIR was used to grade fibrosis on transjugular biopsies. Statistical analysis was carried out with IBM SPSS v.24.

Results: Thirty-one children were enrolled (21 boys/10 girls who had the Fontan procedure at 4.4±0.9 years). Peripheral oxygen saturation was 94.6%±3.3%. The majority of patients (74.2%) had a clinically-evident hepatomegaly, while splenomegaly was less frequent (25.8%). Only 2 children suffered from exudative enteropathy. ALT and GGT plasma levels were slightly elevated in most patients (32.2±12.3 and 53.6±38.7 IU/L, respectively), and factor V level was at the lower limit of the normal (0.64±0.16), with normal total bilirubin in 80.6% (12.4±7 µmol/L) and albumin in all but 2 children (40.7±6.2). Lymphocyte count was low in 15/27 patients (1.55±0.88x10⁹/L), with normal hemoglobin level and platelet count. Lymphopenia was not correlated to the presence of splenomegaly. TE was performed 6.6±4.3 years post-Fontan. Mean LSM was 17.1±7.4 KPa, with a calculated grade of fibrosis of 3.4±0.12/4. A trend towards an increase of LSM over time was noted (15.2±8.3, 17.8±6.2 and 20.5±6 KPa <5, 5-10 and >10 years post-Fontan, respectively; *p*=ns). The presence of hepatomegaly did not influence LSM, whereas a non-significant trend was noted for splenomegaly (19.5±2.1 v. 16.3±1.6, *p*=ns). Liver biopsy was performed in 14 children (8.1±4.3 years post-Fontan). Portal fibrosis ≥F2 was evident in 13/14 patients, sinusoidal fibrosis in 100%. Cirrhosis was present in 3 (13.1±1.6 years post-Fontan). The grade of fibrosis based on LSM was significantly higher than the one measured at biopsy (3.78±0.08 v. 2.61±0.22, *p*<0.001). At univariate regression analysis, biopsy-based grade of fibrosis was directly correlated to time since Fontan (*r*=0.787, *p*=0.001) and factor V level (*r*=-0.592, *p*=0.043). No significant correlation was found with LSM or fibrosis score estimated from LSM (any conversion scale). The scale developed for patients with chronic hepatitis B allowed the best correlation of LSM with liver biopsy (*r*=0.410). LSM-based fibrosis score was correlated to INR (*r*=0.441, *p*=0.035), factor V level (*r*=-0.552, *p*=0.008), lymphocytes count (*r*=-0.526, *p*=0.006), and time since Fontan (*r*=0.405, *p*=0.024). Stepwise regression analysis allowed to build a model to predict LSM with satisfactory accuracy (*r*²=0.990, *p*<0.001) using ALT level and lymphocytes count at TE and average factor V level over the year before TE. We started using high LSM as an indication to perform cardiac catheterization. Pulmonary stenoses were found and dilated in 4 out of 5 patients examined so far. Three of them had TE repeated after the procedure, with a significant reduction of LSM in all (-9.6±1.8 KPa, *p*=0.012).

Conclusions: Fibrosis increases over time after the Fontan procedure. TE overestimates fibrosis as compared to liver biopsy. Currently available scales to estimate fibrosis from LSM do not take into account hepatic venous congestion and are inadequate for FALD. METAVIR grading system does not take into account sinusoidal fibrosis, and could underestimate liver damage in such patients. Low lymphocyte count has been previously attributed to subclinical congestive enteropathy. In our cohort, both lymphocyte count (an indirect marker of splanchnic venous congestion) and factor V levels (a marker of hepatocellular dysfunction) significantly determine LSM. Therefore, LSM might be used as a marker of liver dysfunction and venous congestion, to guide invasive testing and vascular interventions. Such an approach lead to a significant reduction of LSM in patients treated so far. Whether this will have an impact on the progression of FALD is yet to be determined.

621 LIPOPROTEIN SUBFRACTIONS SHOW INCREASED RISK IN PEDIATRIC NON-ALCOHOLIC STEATOHEPATITIS. Juna Konomi¹, Ran Jin¹, Albert Hernandez¹, Jennifer Frediani¹, Hayley Braun¹, Rebecca Cleeton¹, Maria Cordero¹, Shelley Caltharp^{2,1}, Miriam Vos^{1,2}. ¹Pediatrics, Emory University, Decatur, GA; ²Children's Healthcare of Atlanta, Atlanta, GA

Background: In patients with non-alcoholic steatohepatitis (NASH), CVD remains one of the leading causes of death and it is believed that NASH may contribute towards a more atherogenic profile than steatosis alone (NAFL). Less is known regarding the characteristics of dyslipidemia in children with NAFLD. This study sought to evaluate lipoprotein particles numbers and their subfractions and to examine differences between NAFL and NASH in children.

Methods: This was a prospective, cross-sectional study and ninety patients that were undergoing a liver biopsy for suspected NAFLD at Children's Healthcare of Atlanta consented to participate. Liver biopsies were scored using the NASH CRN pathology criteria. Fasting blood was obtained on the morning of the biopsy. Lipid profiles were measured using NMR and included lipoproteins particle number and size, cholesterol, triglycerides, apolipoproteins and a novel inflammatory marker, GlycA (performed by Labcorp). Participants with indeterminate, borderline and/or NASH were categorized as "NASH" and non-NASH as "NAFL".

Results: The mean age of the cohort was 14.8 ± 2.8 years, and 54 subjects (60%) were classified as having NAFL and 36 (40%) as NASH. No statistically significant differences were observed between NASH and NAFL in total, LDL-, or HDL-cholesterol or in total triglycerides and apolipoproteins A1 and B ($p > 0.05$). When focusing on subfractions of lipoproteins, the NASH group had higher concentrations of total triglyceride-rich lipoproteins ($124.9 \text{ nmol/L} \pm 9.99$ vs. $104.4 \text{ nmol/L} \pm 8.78$) and small HDL particles ($13.6 \text{ } \mu\text{mol/L} \pm 0.46$ vs. $12.3 \text{ } \mu\text{mol/L} \pm 0.43$), and decreased concentrations of large HDL particles ($0.98 \text{ } \mu\text{mol/L} \pm 0.26$ vs. $1.4 \text{ } \mu\text{mol/L} \pm 0.23$) ($p < 0.05$). GlycA concentrations were significantly higher in NASH vs. NAFL ($p = 0.027$).

Conclusion: The findings show differences between NASH and NAFL in lipoprotein spectrum and subfractions. Large HDL particles are believed to display anti-atherogenic effects while reduced HDL particle size is linked with cardiovascular disease. Additionally, glycA has been linked with systemic inflammation, increased CVD risk and possibly increased mortality risk. This study demonstrates statistically significant differences in NASH, when compared to NAFL in these subfractions, suggesting increased CVD risk in children with NASH.

622 GENETIC PROFILING OF CHILDREN WITH CHOLESTASTIC LIVER DISEASE :EXPERIENCE OF A LARGE PEDIATRIC LIVER TRANSPLANT CENTRE. Mohammad Shagrani^{2,1}, Dieter broering^{2,1}, Fowzan Alkuraya^{3,1}. ¹College of Medicine, Al Faisal University, Riyadh, Riyadh, Saudi Arabia; ²Organ Transplant Centre, King Faisal Specialist Hospital & Research Center, Riyadh, Riyadh, Saudi Arabia; ³Genetics, King Faisal Specialist Hospital & Research Center, Riyadh, Riyadh, Saudi Arabia

Introduction: Advanced cholestatic liver disease is a leading referral to pediatric liver transplant centers. In our country (S.A.) genetic familial and metabolic liver diseases are the leading indication for liver transplantation . This is reflecting the urgency for the need of our own gene panel for diagnosis and prevention specially with our current high volume pediatric liver transplantation service where in the year of 2016 we performed 55 Pediatric liver transplantation in our centre.

Methods: Recent advances in the molecular classification of this group of disorders promise a highly personalized management although the genetic heterogeneity also poses a diagnostic challenge. Using a next-generation sequencing-based multi-gene panel for the first time, we performed retrospective analysis of 98 pediatric patients who presented with advanced cholestatic liver disease.

Result: A likely causal mutation was identified in the majority (66%) which higher than any published data so far We did manage to reverse diagnosis in 50 % of cases present as primary diagnosis as Wilson disease to be MDR 3 disease (PFIC3)Progressive familial intrahepatic cholestasis which will change the whole management,we diagnose 7 children

with TJP2(Tight junction protein 2) rarely been reported to cause cholestatic liver disease and we showed that it has clear oligogenic presentation. In our cohort it showed that PFIC3 and PFIC2 are more prevalence than PFIC1. In addition to refining the clinical diagnosis, the panel results provided molecular explanation for a number of important clinical observations including risk of recurrence post-transplantation, which highlights the promise of applying our assay prospectively to personalize the management of these patients.

Conclusion: In summary, we describe the successful use of a next generation sequencing-based multi-gene panel to molecularly characterize a large cohort of pediatric patients with advanced cholestatic liver disease. Our results highlight the important contribution of genetic causes in this cohort and the promise of this approach when applied prospectively to personalize the diagnosis and management of these patients. We are totally believe that this new genetic panel in KFSHRC will change the future of pediatric liver diseases in all aspects and will open a new era of translation and personalized medicine research.

623 WILSONIAN FULMINANT HEPATIC FAILURE IN CHILDREN AND ADOLESCENTS: A SYSTEMATIC REVIEW OF 274 CASES. Shannon Vandriel¹, Mohammed Ayoub^{2,3}, Simon Ling⁴, V. Ng⁴, Eve Roberts^{4,5}, Binita Kamath¹. ¹Division of Gastroenterology, Hepatology, and Nutrition, Department of Paediatrics, The Hospital for Sick Children, Toronto, ON, Canada; ²Department of Paediatrics, University of Toronto, Toronto, ON, Canada; ³Department of Pediatrics, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; ⁴Division of Gastroenterology, Hepatology, and Nutrition, Department of Paediatrics, University of Toronto, Toronto, ON, Canada; ⁵Dalhousie University, Halifax, NS, Canada

Background: Wilsonian Fulminant Hepatic Failure (WFHF) is a serious condition, typically requiring liver transplantation (LT). As a result of its relative rarity, WFHF has been difficult to study in depth. Data in pediatric populations (<18 years of age) are scarce and limited to case reports and small case series. The aims of this systematic review were to examine the clinical and biochemical characteristics, treatment and outcomes of children and adolescents with WFHF.

Methods: Database searches were conducted in PubMed, Web of Science, and Google Scholar. The search was restricted to papers published in English, between January-1984 and March 01st, 2017. Papers were excluded if pediatric data were not extractable. Wilson disease (WD) was defined as per AASLD guidelines. Due to the heterogeneity of the definition of acute liver failure (ALF) in the literature, subjects were included if they were defined as having ALF by the paper's authors. The following data points were extracted from articles: study design, initial clinical and biochemical characteristics, genetic mutations, treatment and clinical outcome. If not reported, the following ratios were calculated: alkaline phosphatase (ALP) to total bilirubin (TBIL) < 2 and aspartate aminotransferase (AST) to alanine aminotransferase (ALT) > 4.

Results: A total of 56 (case reports (30), case-series (23) and cohort studies (3)) manuscripts involving 274 participants met the study inclusion criteria. The majority of studies were conducted in Asia (21) followed by 19 in North America, 15 in Europe, and 1 in Australia. Studies ranged in size from 1-61 subjects with a median age of 12.9 years at presentation (range 4.0–17.6 years). Females represented 74% (202/274) of all patients. Kayser–Fleischer rings were seen in 80% (153/191) and Coombs negative hemolytic anemia was reported in 98% (61/62). ALP/TBIL and AST/ALT ratios were evaluated in 60 (22%) and 63 (23%) of participants, respectively and were found to be < 2 and > 4 in less than 55% of subjects. 47% (128/274) of reported subjects underwent LT. Of these 58% (74/128) underwent deceased-donor LT, and 20% (25/128) received a live-donor LT. Graft type was not reported in the remaining subjects. 24% (65/274) of reported cases achieved spontaneous liver recovery with the assistance of extracorporeal liver support systems. Plasmapheresis was the most commonly used extracorporeal system and D-penicillamine was the most commonly used chelating agent in subjects who survived with their native liver. *ATP7B* mutations were only reported in 21 participants, thus limiting assessment of genotype-phenotype relationships.

Conclusion: This is the first systematic review examining WFHF in a substantial cohort of children and adolescents. The female preponderance of WFHF is clearly demonstrated in this analysis. Of note, only half of reported subjects required LT with the remaining responding to medical therapy. This finding may be driven by biased reporting of cases describing the use of liver support systems. It may also reflect subtle variations in WFHF disease definition. Prospective studies are required to explore the true frequency and necessity of LT in WFHF.

***624 THE USE OF TRANSIENT ELASTOGRAPHY IN MEASURING LIVER STIFFNESS IN PAEDIATRIC PATIENTS WITH CYSTIC FIBROSIS ASSOCIATED LIVER DISEASE.** Mora Puertolas^{1,2}, Tamara Pereira², Peter Lewindon^{3,4}, Charlton Noble³, Louise Ramm², Julie Wixey², Fariha Baloush³, Grant Ramm^{2,4}. ¹Pediatrics, Jackson Memorial Hospital, Miami Beach, FL; ²QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia; ³Royal Children's Hospital, Brisbane, Queensland, Australia; ⁴The University of Queensland, Brisbane, Queensland, Australia

Background: Liver disease develops in about 20% of patients with Cystic Fibrosis in adolescence but it is difficult to detect by conventional diagnostic tools such as ultrasound and liver function tests. Liver biopsy remains the benchmark for detecting fibrosis, however, it is invasive and only samples a small portion of the liver. Transient elastography is a non-invasive modality for measuring liver stiffness in adults but its utility in paediatric liver disease needs to be assessed. It may also be useful in determining fibrosis in Cystic Fibrosis associated liver disease (CFLD).

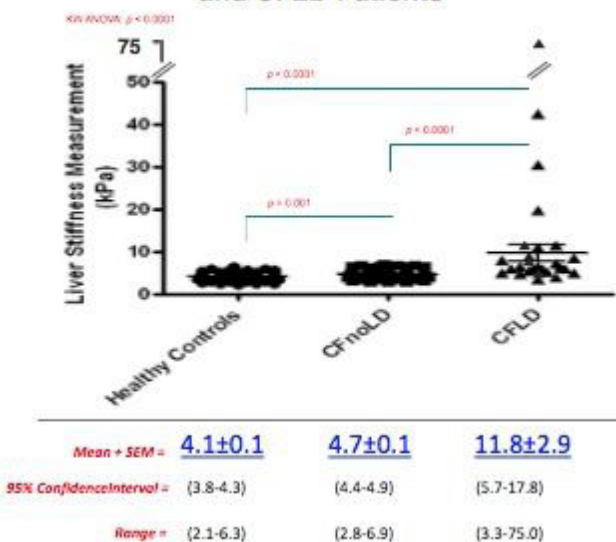
Aims: To establish the normal range of liver stiffness in healthy control paediatric subjects and to determine the usefulness of liver stiffness measurements (LSM) in detecting liver disease in patients with Cystic Fibrosis.

Method: LSM (Fibroscan™) was performed in 26 patients with CFLD, 69 patients with Cystic Fibrosis but no liver disease (CFnoLD) and 69 aged-matched healthy control subjects. Ten valid LSM were performed and the median value, expressed in kilopascals (kPa), was taken as representation of liver stiffness. Fibrosis was determined using the Scheuer scoring method in 12 CFLD patients following liver biopsy and 5 patients with abnormal ultrasound findings, variceal bleeding or portal hypertension were deemed to have stage 3-4 fibrosis.

Results: LSM were reliably performed in 72% of this paediatric cohort, which is comparable to adult populations. LSM was difficult to perform reliably in younger children (30%, 60% and 75% reliability in children 0-1, 1-4 and >4 years, respectively). There was no statistically significant effect of age on LSM ($r=0.07$, $p=0.57$). LSM was higher in CFLD patients (11.8kPa) than CFnoLD patients (4.7kPa) and control subjects (4.1kPa), KW ANOVA $P<0.0001$. There was a significant difference in LSM in control subjects vs CFnoLD patients ($p=0.001$). It was possible to distinguish CFLD from CFnoLD patients using Receiver Operating Characteristics (ROC) curve analysis; an area under the curve (AUC) of 0.81, $p = 0.0001$ gave a cut-off of LSM 5.7kPa with 70% sensitivity, 84% specificity and likelihood ratio 4.4. There was a positive correlation between Scheuer fibrosis stage and LSM in CFLD patients (Spearman rank, $r=0.77$; $p=0.0005$). CFLD patients with severe fibrosis (Scheuer F3-4) has a significantly higher LSM compared to those with early fibrosis (Scheuer F0-2) (Mann Whitney U, $p=0.002$).

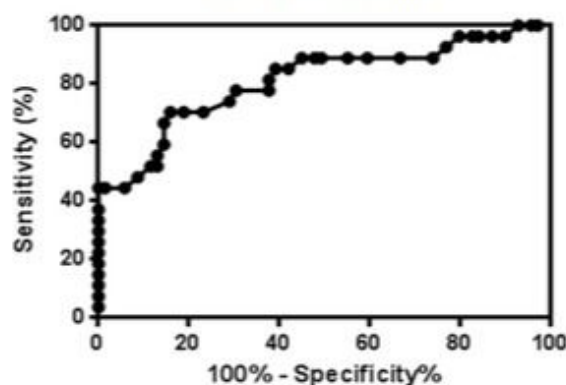
Conclusion: In this study we have shown the potential utility of transient elastography in the detection of liver disease in patients with CF and have established a normal range of LSM in a non-liver disease cohort of Control children. LSM can discriminate early from severe fibrosis in CFLD and is a useful non-invasive tool to monitor liver disease.

Figure 1: LSM in Healthy Controls, CFnoLD and CFLD Patients



LSM was higher in CFLD patients (11.8kPa) than CFnoLD patients (4.7kPa) and control participants (4.1kPa), KW ANOVA $P<0.0001$. There was a significant difference in LSM in control participants vs CFnoLD patients ($p=0.001$).

Figure 2: Receiver Operating Characteristic (ROC) Curve Analysis to Distinguish Between CFLD vs CFnoLD Patients



It was possible to distinguish CFLD from CFnoLD patients using ROC curve analysis; an area under the curve (AUC) of 0.81 ($p=0.0001$), gave a cut-off of LSM 5.7kPa with 70% sensitivity, 84% specificity and likelihood ratio 4.4.

627 DYSREGULATION OF BILE ACID SYNTHESIS IN PRETERM INFANTS. Naureen Memon^{1,2}, Chris Lee², Barry Weinberger³, Thomas Hegyi⁴, Aimee Herdt², Mary Carayannopoulos⁴, Lauren Aleksunes⁵, Grace Guo⁵. ¹Pediatrics, Goryeb Children's Hospital, Morristown, NJ; ²MidAtlantic Neonatology Associates, Morristown, NJ; ³Cohen Children's Medical Center of NY, Hyde Park, NY; ⁴Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; ⁵Rutgers University, Piscataway, NJ

Introduction: Bile acids (BA) are critical for lipid absorption. Newborns, especially preterm infants have lipid malabsorption due to decreased intraluminal BA concentrations. Decreased intraluminal BAs is, in part, due to decreased hepatic BA synthesis rates. CYP7A1 is the rate limiting enzyme in the classical pathway of BA synthesis and its expression has been shown to be developmentally regulated in numerous animal models. CYP7A1 activity has not been evaluated in preterm or term infants.

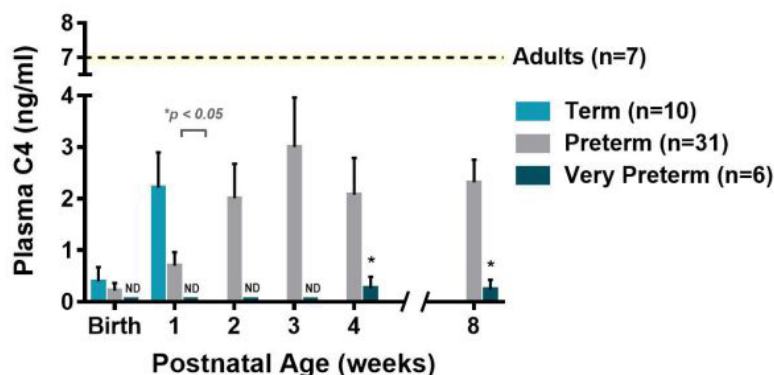
Objective: To measure CYP7A1 activity in term (≥ 35 weeks gestation), preterm (28-34 weeks gestation), and very preterm (< 28 weeks gestation) infants starting at birth and weekly until discharge. We hypothesized that CYP7A1 activity would be low in all infants at birth and that CYP7A1 activity would increase with increasing gestational and postnatal age.

Methods: Plasma levels of 7 α -hydroxy-4-cholesten-3-one (C4, a validated biomarker for CYP7A1 activity) were quantified weekly in term (n = 10), preterm (n = 31), and very preterm (n = 6) infants using HPLC-MS/MS. Plasma C4 levels were also measured in 7 healthy adult volunteers. Data were analyzed by Kruskal-Wallis nonparametric analysis and Dunn's multiple comparisons test, with statistical significance set at $p < 0.05$.

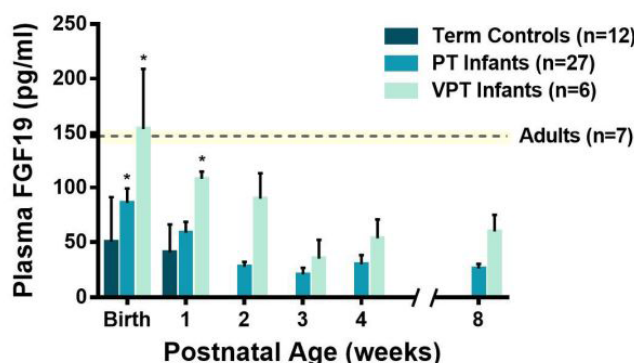
Results: Adult reference C4 concentrations (mean \pm SE) were 7.0 ± 1.4 ng/mL. C4 is minimally detectable at birth in all infants. Term infants have significantly higher C4 concentrations at one week of life (2.213 ± 0.68 ng/mL). In contrast, C4 concentrations remained low in preterm infants until 2 weeks of age (2.013 ± 0.66 ng/mL) and continued to remain very low or undetectable in very preterm infants out to 8 weeks postnatal age (0.20 ± 0.20 ng/mL).

Conclusions: CYP7A1 activity appears to be developmentally regulated in human neonates, and postnatal upregulation of the enzyme is significantly delayed in very preterm infants. Newborns with low CYP7A1 activity may have increased susceptibility to lipid malabsorption and to liver disease. Further studies are needed to determine the association between known repressors of CYP7A1 activity (e.g. phytosterol levels, cytokines, etc.) and C4 levels.

Plasma C4 Concentrations in Infants



FGF19 Concentrations in Infants



628 SEVERE HEPATOPULMONARY SYNDROME IN CHILDREN HAS A DREADED OUTCOME: CHALLENGES FACED AND STRATEGIES ADOPTED TO IMPROVE SURVIVAL >95%.

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Background: Hepatopulmonary syndrome(HPS) is a dreaded complication of end-stage-liver disease(ESLD).Pre-operative $pO_2 < 50\text{mmHg}$ and $>20\%$ shunting on Technetium^{99m}Tc-albumin-aggregated(MAA)scan are considered as strong mortality predictors, making the decision of liver transplantation(LT) difficult¹.Data on outcomes of HPS in pediatric-LT is limited.

Aim: To study spectrum of HPS in pediatric-ESLD &evaluate the complications and role of newer strategies to improve outcome /survival Post LT.

Materials/Methods: Retrospective-analysis of pediatric-LT patients between 2010-2016. HPS was identified pre-operatively by positive contrast-enhanced echocardiogram(CE-ECHO) &elevated alveolar-arterial oxygen gradient($\geq 15\text{ mm Hg}$). In CE-ECHO,appearance of few left-atrial bubbles was labelled as 'some' pulmonary-arteriovenous malformation;dense opacification was labelled 'significant'. Post-operative course of HPS patients was studied.

Results: 22 of 159 children who underwent-LT had HPS. 12 had significant,10 had some pulmonary-arteriovenous shunting. By oxygenation criteria, 11 had 'mild'($pO_2 > 80\text{ mmHg}$),5-had 'moderate-to-severe'($50\text{ mm Hg} > pO_2 < 80\text{ mmHg}$) and 6 had 'very severe'HPS($pO_2 < 50\text{mmHg}$)².Patients with 'very-severe'HPS underwent MAAScan;shunt fraction ranged from30-73%, this dint correlate with severity of hypoxemia or predict post-operative course.4/6 in 'very severe'HPS-group had $pO_2 < 45\text{mmHg}$ which seemed to predict higher morbidity and mortality. Of the4, 1 died on 7th post-operative day due to massive intracranial hemorrhage(ICH). Remaining 3patients had prolonged refractory hypoxemia requiring inhaled nitric oxide(iNO) for > 2 weeks(Range:19-42days, mean:27.3days). Their mean-duration of post-operative ventilation was 31 days, mean-ICU-stay-33days and mean-hospital-stay-47days. This was comparatively much-higher than the remaining HPS-patients(mean:duration of ventilation-3.85days, ICU stay-8.2days, hospital stay-23days). Incidence of vascular thrombosis was high.4/22 of HPS-patients developed hepatic-artery thrombosis; as against 6/137non-HPS patients. Portal-vein thrombosis occurred in 1patient. Other complications were ICH (n=2; both had pre-op $pO_2 < 45\text{ mmHg}$),seizures(n=5),ARDS (n=2)and hypertension(n=4). Overall mortality in HPS-group was 1/22(4.54%).

Conclusion: LT is the only definitive cure for HPS. LT in severe HPS is challenging, with high risk of vascular thrombosis, prolonged ventilation and ICH. In our experience meticulous care and use of iNO post-LT improved oxygenation in very severeHPS, with good survival of $>95\%$. $pO_2 < 45\text{ mmHg}$, rather than MAAScan predicted a difficult post-operative course.

629 COMPLICATIONS ASSOCIATED WITH THE RATIO OF GRAFT / HOST SIZE TO PEDIATRIC LIVING DONOR LIVER TRANSPLANTATION. TEN YEARS OF EXPERIENCE IN A TRANSPLANT CENTER.

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Introduction: pediatric living donor (LD) liver transplantation is a proven practice with excellent long-term results.

Objective: to evaluate predictive factors of post-transplant complications with LD according to the relationship between graft size (G) and recipient weight (W).

Materials/Methods: descriptive, retrospective, cross-sectional study. Of a total of 159 pediatric transplants, 67 transplanted children with LD were analyzed between 2006 and 2016 in a single center in Latin America. The relationship between the recipient's weight at the transplant and the left lateral segment volume II-III of donor measured with abdominal Angio Computed Tomography was calculated. 14 patients were excluded because they required an in situ hyper-reduction technique.

Results: of the 53 transplants analyzed, 11.3% (6) presented a G/W ratio $< 1\%$ (group A), 75.4% (40) between $\geq 1\%$ and $\leq 4\%$ (group B) and 13.2% (7) $> 4.0\%$ (group C). Mean age was 22.7 months. Mean weight at transplant: group A 12.7kgs (DS 1.3), group B 10.4kgs (DS 1.9), group C 7.5kgs (DS 0.9) ($p < 0.0001$). Patient survival at one year was 88.70% and at five years 83%, being 100% for group A. Vascular and biliary complications were more frequent in group C compared to B and A (28.57% vs 10% vs 16%) and (42.86% vs.25% vs.0%), respectively.

Conclusion: a G/W ratio greater than 4% presented more complications after LD liver transplantation. Therefore, lower transplant weight would be a prognostic factor of major impact regardless the relationship between the graft and the host size.

630 INHIBITION OF CREB BINDING PROTEIN-BETA-CATENIN INTERACTION SUPPRESSES CD133 EXPRESSION AND ACTIVATES PP2A-PHOSPHATASE AND TENSIN HOMOLOGUE SIGNALING IN TUMOR INITIATING LIVER CANCER CELLS. *Nirmala Mavila^{1,2}, Yuanyuan Tang¹.*
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WNT-beta-catenin signaling is an evolutionally conserved signaling pathway that regulates cellular homeostasis during development and tissue regeneration. Cytosolic beta-catenin stability and its nuclear translocation is regulated by multi-protein degradation complex consists of Glycogen Synthase Kinase 3beta, Axin, Adenomatous polyposis coli (APC) and Casein kinase 1 (CK1). Nuclear beta-catenin function is regulated by transcriptional co-factors such as CREB binding protein (CBP) and p300. Here we investigated the downstream effect of CBP-beta-catenin signaling on cancer stem cell antigen, CD133 in human hepatoblastoma cells and in a CD133 positive clonally expanded tumor initiating cells (TICs) developed from premalignant methionine adenosyltransferase1-alpha knockout (*Mat1a*^{-/-}) murine livers. Therapeutic disruption of CBP-beta-catenin interaction by a small molecule CBP inhibitor ICG001 reduced CD133 expression ~70-80% in human hepatoblastoma cells and in *CD133*+ *Mat1a*^{-/-} TICs respectively. In vitro CBP gene silencing decreased CD133 expression by 50%. Levels of phospho-Ser473 AKT and phosphoSer552 beta-catenin levels were down-regulated by ICG001. ICG001 treatment decreased phosphorylation of tumor suppressor, Phosphatase and Tensin homologue (PTEN) on Ser/Tyr 388/382/380 by 75% where as the levels of anti-apoptotic protein Survivin was reduced by 50%. Co-treatment with Okadaic acid, a PP2A inhibitor partially restored the PTEN de-phosphorylation induced by ICG001. ICG001 increased PP2A activity by 40% in TICs. In summary, our results demonstrate that CBP-beta-catenin complex promotes stemness, cell survival and suppresses PP2A activity in TICs. PP2A could be a novel therapeutic target in TICs to prevent tumor initiation and cancer recurrence in addition to overcoming drug resistance.

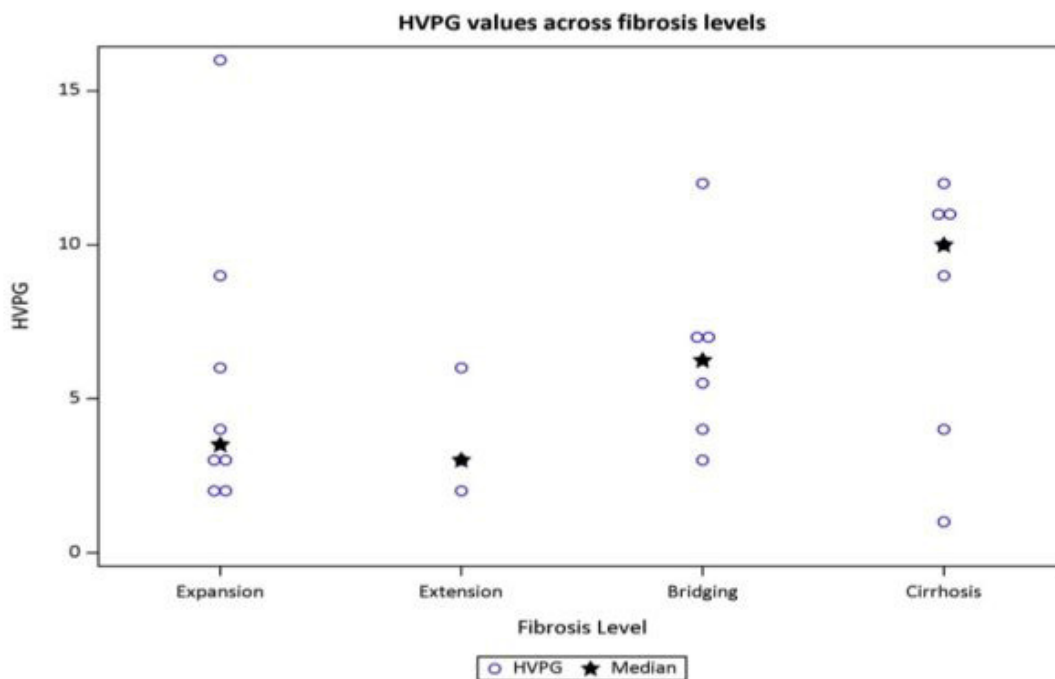
631 HEPATIC VENOUS PRESSURE GRADIENT MEASUREMENTS IN CHILDREN: SAFETY AND CORRELATION WITH HEPATIC HISTOLOGY. *Noelle Ebel¹, Kristen Carlin², Michele Shaffer^{1,2}, Giri Shivaram³, Matthew Hawkins⁴, Erin Lane¹, Kara Cooper², Will Lindquester⁴, Karen Murray^{1,2}.*
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Background: In adults with cirrhosis, an association between elevated measurements of hepatic venous pressure gradient (HVPG) and both the degree of liver fibrosis on histology and poorer clinical outcomes including variceal bleeding are well described. Similar studies have not been undertaken in children.

Methods: We retrospectively analyzed the records of children aged 5 months to 18 years who underwent simultaneous HVPG measurements and transjugular liver biopsy at Seattle Children's Hospital or Emory University Hospital between 2006-2015. Median HVPG measurements were recorded by underlying liver disease category and Spearman's correlation was used to assess the association of hepatic histology findings and HVPG measurements. Wilcoxon rank sums test was used to compare HVPG levels among subjects with and without a history of bleeding events. Safety outcomes for HVPG measurements were assessed.

Results: 44 children were identified with acute hepatitis (n=15), chronic liver disease (n=12), non-cirrhotic portal hypertension (n=7), acute liver failure (n=3) and other non-hepatic causes of ascites and splenomegaly (n=7) with a mean age of 9.7 years (median 11, IQR 12). Children with acute liver failure had the highest median HVPG measurement (10mmHg, IQR 8) followed by children with chronic liver disease (7mmHg, IQR 7), non-cirrhotic portal hypertension (4mmHg, IQR 10), other (4mmHg, IQR 10) and acute hepatitis (3mmHg, IQR 6). HVPG measurements did not correlate with histologic findings, specifically the degree of fibrosis ($\rho = 0.20$, $p = 0.20$) or portal inflammation ($\rho = 0.28$, $p = 0.22$) even when subjects with acute liver failure, non-cirrhotic portal hypertension, and other were excluded from the analysis ($\rho = 0.17$, $p = 0.39$). No difference in HVPG was found between subjects with a history of bleeding and those without ($p = 0.96$). Vascular thrombosis following HVPG measurement occurred in one subject.

Conclusions: HVPG measurements are elevated (>5mmHg) in children with ALF and chronic liver disease. HVPG measurements, however, did not correlate significantly with the degree of hepatic fibrosis on biopsy. HVPG, therefore, may be a better assessment of the global contribution of hepatic fibrosis on portal hypertension than histology, given the limitations of sample variability on needle biopsy. Alternatively, intra-hepatic shunting may limit the HVPG in children with advanced liver disease. Our study shows that HVPG measurement is safe and feasible in children, including in those with acute liver failure or chronically advanced liver disease, and is a potentially important step in determining the impact of disease on the risk of complications from portal hypertension.



633 SIMULTANEOUS VERSUS SEQUENTIAL LIVER-KIDNEY TRANSPLANTATION IN THE PEDIATRIC POPULATION: A REVIEW OF THE UNOS DATABASE. Patrick Nguyen¹, Kathleen Hosek², Abbas Rana¹, John Goss¹, Tamir Miloh². ¹Division of Abdominal Transplantation, Baylor College of Medicine, Houston, TX; ²Texas Children's Hospital, Houston, TX

Introduction: Liver or kidney transplant recipients may require transplantation of the other organ. The aim of the study was to compare simultaneous and sequential liver-kidney transplantation (LKT) in children.

Methods: All LKT between 1986-2016 in UNOS database were included if the patient received first transplant before 18 years of age. Patients with other multiorgan transplants (e.g., pancreas) were excluded from the study. Patients were divided into: "liver-after-kidney" (LAK), "kidney-after-liver" (KAL), and simultaneous (SLK). Organ and patient survivals were compared as an independent events. Subgroup analyses of patients with polycystic kidney disease (PKD) and primary hyperoxaluria (PH1) were performed.

Results: SLK 294, KAL 313, and LAK 137 met inclusion criteria. Graft and patient survival are shown in Table 1. On average, SLK recipients were older (9.1 yrs) compared to KAL (7.4 yrs) and LAK (6.9 yrs). Recipient weight and gender were similar across all strata (SLK 28.7 kg/50% female, LAK 25.5 kg/51%, KAL 27.5 kg/44%). MTBT were 12.3 y for KAL and 5.3 y for LAK. The 10-yr kidney graft survival for SLK (78.4%) was significantly higher than KAL (71.3%) and LAK (42.7%). Major indications for kidney transplant: KAL (CNI toxicity 39%), LAK (PKD 43%), SLK (oxalosis 31%, PKD 25%). Major indication for liver transplant: KAL (36% biliary malformations), LAK (34% congenital hepatic fibrosis [CHF]), SLK (31% oxalosis).

In the PKD subgroup, SLK 77, LAK 61, and KAL 15 met inclusion criteria. Graft and patient survival are shown in Table 2. SLK recipients were older

Table 1

	LAK	KAL	SLK	p
Kidney graft survival 1m	92.7%	94.5%	93.1%	P<0.01
1y	84.5%	92.1%	91.6%	
5y	59.4%	83.0%	87.1%	
10y	42.7%	71.3%	78.4%	
Liver graft survival 1m	93.9%	89.5%	93.7%	P<0.01
1y	89.7%	82.1%	89.2%	
5y	85.3%	76.2%	86.9%	
10y	83.2%	67.6%	84.1%	
Patient survival 1m	99.3%	100%	92.8%	p<0.01
1y	94.1%	98.4%	86.2%	
5y	87.3%	96.1%	82.4%	
10y	76.2%	91.7%	77.3%	

(9.0 yrs) than KAL (5.9 yrs) and LAK (5.6 yrs). The 10-year SLK kidney graft survival (89.3%) was significantly higher than LAK kidney graft survival.

In the PH1 subgroup, SLK 95, LAK 33, and KAL 22 met inclusion criteria. Graft and patient survival are shown in Table 2. No significant differences in patient demographics were observed between the strata. The 10-year SLK (69.4%) and KAL (76.8%) kidney graft survival were significantly higher than LAK kidney graft survival (23.6%). No significant difference in the 10-year patient or liver survival rates were observed between the strata.

Conclusion: Simultaneous LKT conferred superior long-term kidney graft survival compared to sequential (LAK or KAL). SLK also confers superior long-term liver graft survival compared to KAL. Though KAL had superior patient survival, this may be linked to CNI toxicity as an indication for transplant. These results suggest that SLK may be considered for multi-organ diseases, such as polycystic kidney and oxalosis.

Table 2

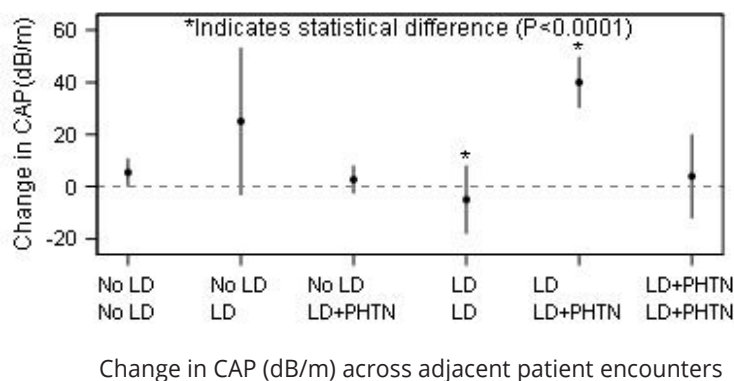
	LAK-PKD	KAL-PKD	SLK-PKD	p	LAK-PH1	KAL-PH1	SLK-PH1	p
Kidney graft survival 1m	100%	90.9%	87.2%	P<0.01	96.7%	100%	93.4%	P<0.01
1y	90.7%	86.4%	86.0%		95.1%	93.3%	93.4%	
5y	38.9%	86.4%	80.1%		75.3%	93.3%	91.4%	
10y	23.6%	76.8%	69.4%		51.2%	93.3%	89.3%	
Liver graft survival 1m	93.5%	90.9%	91.2%	p=0.73	94.9%	93.3%	98.6%	P<0.05
1y	83.3%	86.4%	86.3%		94.9%	80.0%	94.4%	
5y	81.6%	79.1%	85.0%		92.5%	72.7%	94.4%	
10y	81.6^	79.1%	85.0%		92.5%	72.7%	92.3%	
Patient survival 1m	100%	100%	90.5%	p=0.31	100%	100%	90.5%	p=0.86
1y	93.9%	95.2%	80.7%		98.4%	100%	92.0%	
5y	84.8%	90.5%	75.8%		95.0%	100%	92.0%	
10y	62.0%	90.5%	68.8%		85.5%	100%	90.1%	

635 TRANSIENT ELASTOGRAPHY AND CONTROLLED ATTENUATION PARAMETER ASSESSMENT OF LIVER DISEASE IN CHILDREN AND YOUNG ADULTS WITH CYSTIC FIBROSIS: A 3 YEAR LONGITUDINAL STUDY. Prita Mohanty¹, Paul Mitchell², Shanna Wiggins¹, Denis Nguyen¹, Sarah Harney¹, Maureen Jonas¹, Christine Lee¹. ¹Pediatric Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; ²Institutional Centers for Clinical and Translational Research, Boston Children's Hospital, Boston, MA

Background: Liver disease is the third leading cause of death in cystic fibrosis (CF) patients. Hepatic steatosis is a common, early sign of CF-related liver disease (CFLD). Controlled attenuation parameter (CAP), obtained during transient elastography (TE), can detect and quantify steatosis.

Objective: To evaluate if serial LSM and CAP can be used to identify and follow progression of CFLD. Methods: This was a longitudinal cohort study of CF patients seen for routine outpatient care at Boston Children's Hospital. CAP and LSM were obtained at enrollment (January–October 2013) and annually up to 3 years. CFLD was defined per published criteria as: No CFLD, CFLD without portal hypertension (PHTN) and CFLD with PHTN. CFLD without PHTN criteria: recent ALT>1.3xULN, on ursodiol, or abnormal liver echogenicity on imaging. CFLD with PHTN criteria: splenomegaly, esophageal varices on endoscopy, platelet count<100,000/mm³ or signs of PHTN on ultrasound. Change in CAP and LSM was compared between adjacent patient encounters of consistent or worsening disease using a generalized estimating equation.

Results: A total of 249 patients [53% male; mean age 14±7y; 7(3%)<2y and 74(30%) 18-25y] underwent baseline LSM; 127(51%) also had CAP. At enrollment, 158(64%) had no CFLD, 73(29%) CFLD without PHTN, and 18(7%) CFLD with PHTN. A total of 387 paired encounters were documented, 43(11%) reflecting a change in disease status. The median time between adjacent measurements was 12 months (IQR 10–15). Subjects with CFLD without PHTN at one encounter followed by CFLD with PHTN at the next encounter saw a greater change in CAP than those whose status remained unchanged (40.0±4.9



vs. -5.0 ± 6.6 dB/m, $P < 0.0001$). Similarly, subjects without CFLD at one encounter followed by CFLD without PHTN at the next saw greater change in CAP, although the difference was not statistically significant (25.1 ± 14.4 vs 5.5 ± 2.6 dB/m; $P = 0.19$). There were no significant differences across adjacent encounters for LSM.

Conclusion: In this 3 year study, CAP is able to detect changes in CFLD when there is no detectable change in liver fibrosis.

636 IMPROVING OUTCOMES FOR AT RISK YOUTH AFTER LIVER TRANSPLANTATION: NOVEL INTERVENTIONS IN CHILDREN'S HEALTHCARE (NICH). Rachel Bensen¹, Claudia Lopez², Bianca Agustin¹, Michael Harris³, Diana Naranjo¹, David Wagner³. ¹Pediatrics, Stanford University School of Medicine, Palo Alto, CA; ²School of Medicine, Oregon Health & Science University, Portland, OR; ³Pediatrics, Oregon Health & Science University, Portland, OR

Background: Consistent adherence to medications is essential after liver transplantation in order to prevent graft rejection, avoid excessive immunosuppression with its risk of infection or post-transplant lymphoproliferative disorders, and minimize medication adverse effects (e.g. nephrotoxicity). A small subset of youth who undergo liver transplantation live in families with concurrent psychosocial complexity (e.g. language/culture barriers, housing instability, transportation difficulties, behavioral health concerns) leading to suboptimal adherence despite standard medical and behavioral interventions. Novel Interventions in Children's Healthcare (NICH) was developed to improve health and reduce costs in high-risk children with medical and psychosocial complexity. NICH is an intensive, year-long behavioral family- and systems-based intervention that includes 24/7 patient access and service delivery in the patient's home, community, and the health system. The NICH model was applied across two health systems. This abstract reviews outcomes of youth referred to NICH who had: (1) undergone liver transplantation, (2) experienced transplant complications thought to be related to suboptimal adherence, and (3) were unresponsive to standard medical and behavioral interventions.

Methods: Chart reviews collected health outcomes from the year prior to enrollment and during the period of NICH participation. Outcome data included episodes of biopsy proven rejection and variation in outpatient immunosuppressive medication levels at least 3 and 6 months after transplant, respectively. Specifically, the standard deviation (SD) of tacrolimus levels was examined, as a lower SD of tacrolimus levels is suggestive of more consistent medication administration.

Results: Six youth age 2 to 19 years were identified. Four were female. Participants underwent liver transplantation between age 6 months and 18 years for a variety of conditions (metabolic disorders, autoimmune hepatitis, end stage liver disease associated with viral hepatitis, biliary atresia, Caroli's disease). One participant underwent combined liver and kidney transplantation. Participants showed a reduction in mean tacrolimus SD during NICH (SD = 3.2) compared to the year prior (SD = 4.4), with 83% of individuals demonstrating a lower SD. In the year prior to NICH program enrollment, a total of 4 episodes of rejection were noted compared with 3 episodes in the year after. One patient experienced graft failure prior to enrollment and received a second transplant during participation, with barriers to adherence considered adequately improved by the clinical team to allow for listing.

Conclusions: Despite high social complexity in these medically fragile patients, youth in NICH demonstrated improvement in adherence to transplant medications. Although youth continued to experience episodes of rejection while in NICH, these episodes tended to occur early in program involvement, before interventions were expected to have substantial impact, and were associated with stressors present prior to program initiation. NICH represents a promising interdisciplinary intervention for children with complex psychosocial challenges post-liver transplant experiencing complications associated with suboptimal adherence.

640 USE OF A COMPREHENSIVE 66 GENE PANEL TO DIAGNOSE THE CAUSES OF CHOLESTASIS IN >700 INDIVIDUALS. Saul Karpen^{1,2}, Binitha Kamath³, John Alexander^{4,5}, Iliia Ichetovkin⁶, Philip Rosenthal⁷, William Soliman⁸, Richard Thompson⁹, James Heubi¹⁰. ¹Department of Pediatrics, Emory University School of Medicine, Atlanta, GA; ²Children's Healthcare of Atlanta, Atlanta, GA; ³Department of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; ⁴Department of Human Genetics, Emory University School of Medicine, Atlanta, GA; ⁵EGL Genetics, Tucker, GA; ⁶Diagnostic Laboratory Services, Retrophin, Inc, San Diego, CA; ⁷Department of Pediatrics, University of California, San Francisco School of Medicine, San Francisco, CA; ⁸Hepatology & Gastroenterology, Retrophin, Inc, San Diego, CA; ⁹Institute of Liver Studies, King's College Hospital, Denmark Hill, London, United Kingdom; ¹⁰Division of Pediatric Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Background: Cholestasis occurs due to a wide variety of etiologies, often genetic in origin. Particularly in newborns, the broad overlap in clinical presentations renders utilization and prioritizing of diagnostic investigations challenging. In this setting, a timely, comprehensive assessment with a multi-gene panel by a CAP/CLIA-accredited laboratory could prove

useful to patients and clinicians. We summarize initial findings from a testing program designed to discover genetic causes of cholestasis.

Methods: The neonatal/adult cholestasis sequencing panel (EGL Genetics) containing 66 genes relevant to cholestasis was employed. Eligible patients were cholestatic, had a history of cholestasis without an identified cause (e.g., sepsis or TPN-associated), or had unexplained liver disease. In-solution hybridization with a custom capture library was used to sequence the genes of interest. Variants were classified as benign, likely benign, variant of unknown significance (VOUS), likely pathogenic (LP), or pathogenic (P) according to a clinical interpretation algorithm that incorporated many components, including variant modeling, database comparisons, and population frequency. Cases were reported as positive if there was: 1) one P or LP variant in a gene for autosomal dominant disease; or 2) two P or LP variants in a gene for autosomal recessive disease. Cases were reported as likely positive if one P or LP variant and one suspicious VOUS were found in an autosomal recessive disease gene.

Results: Over 1000 kits were distributed to clinicians in North and South America. As of Feb. 2017, 716 were submitted for testing. Median time from receipt of samples in the lab to return of reports to clinicians was 18 days. 59 cases were scored as positive (8.2%) and an additional 25 were scored as likely positive (3.5%). Diagnoses included Alagille syndrome, various PFICs, and bile acid synthesis defects (*JAG1*, *ABCB11*, *HSD3B7*, *ABCB4*) as well as a variety of other diseases such as Niemann-Pick C (*NPC1*). An additional 91 cases had 1 P or LP variant identified (12.7%). VOUSs were identified as the sole findings in 371 (52%) of cases.

Summary/Conclusions: These findings support the utility of comprehensive and rapid multi-gene testing in diagnosing cholestasis, which has the potential to influence the clinical algorithm, including the role of liver biopsy. These findings also highlight the evolving understanding of gene variants in contributing to the pathogenesis of cholestasis. Taken together, timely implementation of a broad-based gene panel has the potential to influence clinical decision-making and initiation of effective therapies in patients with cholestasis.

643 PREDICTORS OF POST-OPERATIVE RED BLOOD CELL TRANSFUSIONS IN PEDIATRIC LIVER TRANSPLANT PATIENTS. *Sharmistha Rudra¹, Meera Gupta², Kim Olthoff², Henry Lin¹. ¹Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA; ²Surgery, University of Pennsylvania, Philadelphia, PA*

Background: Patients with end-stage liver disease are at risk for bleeding from synthetic dysfunction and manifestations of portal hypertension. While pediatric liver transplant surgical techniques have improved, the operative procedure remains complex. In this study, we sought to determine variables associated with need for post-operative red blood cell transfusions.

Methods: We conducted a retrospective cohort study of pediatric liver transplants performed at the Children's Hospital of Philadelphia from 2004-2016. Patients were compared based on post-operative transfusion status (Transfusion, No Transfusion). Key variables included: primary diagnosis, allograft and donor type, intraoperative blood products, pre-operative, post-operative day(POD)0 and POD7 labs, and early allograft dysfunction (EAD). EAD was defined as peak AST >1500 or ALT>1500 within the first week; total bilirubin>10 or INR >=1.6 on POD7.

Multivariable logistic regression was performed using backwards elimination to determine variables associated with post-operative transfusion. Variables with p-value<0.05 were considered statistically significant.

Results: Of the 184 patients, 118(64%) received transfusions within POD7. Mean nadir hemoglobin(Hgb) of the Transfusion group was 7.2 g/dl versus 8.5 g/dl in the No Transfusion group. There was no difference in graft type, donor/recipient ABO incompatibility, or EAD between the two groups.

Primary diagnosis of oncologic etiology(OR 19.72;p=0.02), age(OR 1.4;p=<0.01), and POD0 INR(OR 2.20;p=0.02) were associated with transfusion. Both POD0 Hgb(OR 0.64;p=0.02) and recipient weight (OR 0.91;p=<0.01) were protective against transfusion.

Conclusions: Transplant recipient age, weight, and underlying disease play a significant role in post-operative transfusion requirement. While surgical expertise is important, patient selection and special attention in management are essential to the success of pediatric liver transplantation.

644 MMP7 AND RELEVANT CHEMOKINES IN NASH. *Shelly Choudhury¹, Susan Baker¹, Wensheng Liu², Techung Lee², Robert Baker¹, Rafal Kozielski³, Reham Abdou¹, Lixin Zhu². ¹Pediatric Gastroenterology, University at Buffalo, Buffalo, NY; ²University at Buffalo, Buffalo, NY; ³Pathology, Women and Children's Hospital, Buffalo, Buffalo, NY*

Background: Matrix metalloproteinases (MMPs) are the degrading enzymes of the extracellular matrix proteins, and are involved in tissue remodeling and repair. They may serve as disease markers and intervention targets for Nonalcoholic

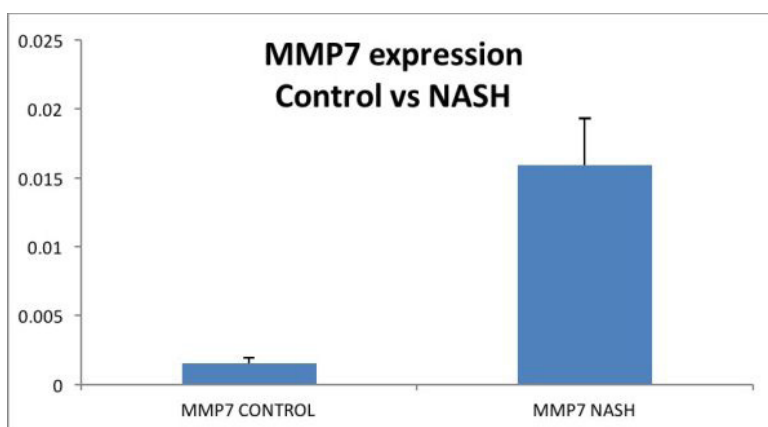
Steatohepatitis (NASH). Here we examined the expression of MMP 7, also known as matrilysin, and relevant cytokines CXCL9, CXCL10 in NASH patients and relate them to histological signs of liver injury. MMP 7 is postulated to cleave and inactivate these chemokines- CXCL9 and 10.

Methods: Messenger RNA expression of MMPs and related genes were examined with our microarray dataset. Hepatic mRNA levels of MMP-7, CXCL9, CXCL10 were confirmed by quantitative real-time reverse-transcriptase polymerase chain reaction (qRT-PCR) with a different study cohort: 24 patients (10 females and 14 males) with biopsy proven NASH and 12 non-diseased controls.

Results: Microarray data showed a trend of increased expression of MMP7 in NAFLD vs controls (fold change of 7.22, $p=0.15$); 21.55 fold of increase of CXCL9 (p value of <0.05); 3.23 fold increase of CXCL10 ($p>0.05$). With qRT-PCR, the quantity of MMP7 mRNA in liver tissue was significantly higher in patients with NASH compared to controls with a fold change of 10.36 ($p<0.05$). CXCL9 and CXCL10 exhibited a trend of increased expression in patients (with fold change of 8.83 and 3.41, respectively) but the differences were not significant. MMP7 positively correlated with stages of inflammation, fibrosis (both p values < 0.05).

Conclusion:

Significant Increase of MMP7 gene expression was found in Nonalcoholic fatty liver disease (NAFLD). It positively and significantly correlated with stage of inflammation and fibrosis. Increased MMP7 expression could be a consequence of elevated pro-inflammatory chemokines. Our results suggest that MMP7 could serve as a marker for disease severity.



645 OCCULT HEPATITIS B VIRUS INFECTION IN CHILDREN BORN TO HEPATITIS B VIRUS MOTHERS AFTER PASSIVE-ACTIVE IMMUNOPROPHYLAXIS IN JAPAN. Shogo Ito¹, Koichi Ito¹, Takeshi Endo¹, Tokio Sugiura¹, Yasuhito Tanaka², Shinji Saitoh¹. ¹Department of Pediatrics and Neonatology, Nagoya City University, Nagoya, Japan; ²Department of Virology and Liver Unit, Nagoya City University, Nagoya, Japan

Introduction: Occult hepatitis B virus infection (OBI) is characterized by the persistence of hepatitis B virus (HBV) genomes in the liver tissue (and in some cases also in the serum) of hepatitis B surface antigen (HBsAg)-negative individuals. This particular form of HBV infection appears to have a fairly frequent occurrence, not only in individuals with circulating antibodies to HBsAg (anti-HBs) and/ or hepatitis B core antigen (anti-HBc), but also in subjects negative for all HBV serum markers. In recent years, OBI has been found in infants born to HBsAg-positive mothers despite immunization. It is estimated that OBI has been established at a certain frequency in Japan, but detailed data have not been investigated so far and are unknown especially in children. The aim of this study was therefore to evaluate the prevalence of OBI in children born to HBV carrier mothers after passive-active immunoprophylaxis in Japan.

Patient: In Nagoya City University Hospital 67 infants born to HBV carrier mother followed from January, 2004 to April, 2015. All infants received immunoprophylaxis with hepatitis B immunoglobulin (200 IU) intramuscularly and hepatitis B vaccines (5ug/dose) subcutaneously. Twenty six of 67 infants with anti-HBc positive persistently were enrolled in this study.

Methods: HBV-DNA sequences spanning the entire S gene was quantified by real-time polymerase chain reaction (PCR) primers according to the previously described protocol. The detection limit of the assay was 100 copies/ml. The S and Core gene of the HBV genome was amplified by nested PCR using specific primers. Only subjects who tested negative for HBsAg but positive for HBV DNA by real-time quantitative PCR or nested PCR were considered positive for occult HBV infection. Nested PCR positive defined as both S and Core gene of HBV were positive.

Result: All 67 infants born to HBV carrier mother were HBsAg-negative at 12 months of age.

Eleven of 26 (42%) infants were S gene positive and 21 of 26 (81%) were Core gene positive by nested PCR. The prevalence of OBI defined as both positive S and Core gene was 9 of 26 (35%) in infants with anti-HBc positive. No infant had detectable HBV DNA by real-time PCR.

The association of OBI with selected factors was investigated. There was no significant difference in sex, age, anti-HBs titer, anti-HBc inhibition rate and maternal hepatitis B envelope antigen positive.

Conclusion: The prevalence of OBI was 35% in infants with anti-HBc positive in Japan. It was shown that there are a certain number of OBIs even in the prevention treatment implementation group in Japan.

647 **BASELINE LIVER ECHOTEXTURE IN CHILDREN WITH CYSTIC FIBROSIS PREDICTS CHANGES OVER TIME IN NON-INVASIVE BIOMARKERS OF FIBROSIS AND PORTAL HYPERTENSION.**

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Background: Cirrhotic CF liver disease (CFLD) is the third leading cause of death in CF and affects only 5-7% of patients. Identification of children with progressive CFLD at an early stage would enable targeted study of preventative therapies.

Methods: We studied all 251 eligible children enrolled in an ongoing multicenter study of abdominal ultrasonography (US) to predict development of cirrhosis (PUSH study, NCT01144507). Children age 3-12 years with pancreatic insufficient CF and heterogeneous liver pattern on baseline US (HTG, n=63) were matched 1:2 with children with CF and normal US (NL, n=125). We also included children with nodular (NOD, n=24) and bright homogeneous (HMG, n=39) liver patterns at baseline. We standardized US spleen size by age to yield a spleen size age-adjusted z-score (SSAZ). Blood work was taken annually and US biennially for up to 6 years. We used longitudinal mixed effects models to assess relationships between baseline US pattern and rate of change in biomarkers of liver disease severity, including GGT, ALP, AST, ALT, albumin, platelet count, AST to platelet ratio index (APRI) and fibrosis index based on 4 factors (FIB4).

Results: Median follow-up was 3.8 y (range 0 to 6.1 y), including a mean of 4 (range 1 – 7) annual blood draws per child. Baseline US pattern was associated with different baseline values of biomarkers including GGT, AST, ALT, ALP, platelet count, SSAZ, APRI and FIB4 (Ling SC et al, AASLD 2016). Compared to NL, baseline HTG predicted more rapid fall in platelet count and rise in FIB4 and SSAZ, and NOD grade predicted more rapid rise in APRI, FIB4 and SSAZ (Table). Change in AST, ALT, GGT, ALP, albumin did not differ between US groups. Rates of change in biomarkers in HTG were intermediate between NL and NOD. HMG did not differ from NL in rate of biomarker change.

Conclusion: Baseline US grade predicts rate of change of certain biomarkers of severity of liver disease. Rates of biomarker changes in HTG are intermediate between those of NL and NOD. Our findings are supportive that US patterns correlate with the severity of liver disease. Our future studies will explore associations between baseline US grades, biomarker changes and final US grade at 6-year follow-up.

Estimated slope of change in biomarkers per year, with 95% confidence intervals

Biomarkers	Baseline US grade			
	NL (n=63)	HTG (n=125)	NOD (n=24)	HMG (n=39)
Platelet count (x10 ⁹ /L per year)	-5.0(-8.4, -1.1)	-12.1(-17.3, -7.0) *	-14.4(-23.4, -5.5)	-12.0(-19.2, -4.8)
APRI (units per year)	-0.01(-0.02, 0.01)	0.02(-0.00, 0.04)	0.04(0.00, 0.01) *	0.01(-0.02, 0.04)
FIB4 (units per year)	0.01(0.01, 0.02)	0.03(0.02, 0.04)*	0.06(0.04, 0.08) **	0.03(0.01, 0.05)
SSAZ (units per year)	0.3(0.2, 0.4)	0.5(0.4, 0.6) **	0.7(0.5, 0.8) **	0.4(0.2, 0.5)

Comparison with NL *p<0.001

648 UNIQUE PATTERN OF INTRAHEPATIC T-CELL CLONALITY IN BILIARY ATRESIA: A PILOT STUDY. Sina Ogholikhan, Kathleen Schwarz, Robert Anders. *Pediatric Gastroenterology, The Johns Hopkins University, Baltimore, MD*

Background/Aims: Biliary atresia (BA) is a rare disease of unclear etiology, in which obstruction of the biliary tree causes severe cholestasis leading to cirrhosis and ultimate death if left untreated. A widely-accepted theory regarding the etiology of BA is bile duct injury due to virus-induced autoreactive T-cell-mediated inflammation or other immune mediated responses. The hallmark of T cell activity is clonal expansion of T lymphocytes expressing similar T-cell receptor (TCR) variable regions of the β -chain. We hypothesized that BA liver tissues would show clonal expansion of 1 or several TCRs when compared to a control group.

Methods: The CDR3 region of the β -chain of the TCR was characterized using next generation sequencing (NGS) of 7 BA liver samples (age 51 days +/- 14 days) and 9 intestinal control samples (age 38 +/- 16 days). Intestinal tissue was used given the lack of liver samples from age-matched patients. Following sequencing, clonality scores, various VDJ recombinations, total and productive templates, CDR3 length were measured using the immunoSEQ Analyzer.

Results: NGS revealed 1 common TCR rearrangement in 3 BA samples not found in controls. However, in general there was a highly diverse TCR population among BA liver controls. For all samples, the clonality scores ranged from 0.0004 to 0.0062 using a Shannons entropy score, with numbers close to 0 being highly diverse and numbers close to 1 being highly clonal. The top 10 TCR VDJ recombinations comprised 1.47% - 12.9% of the total population of TCR for the BA tissues and 1.05% - 10.3% for the control sample. This shows a highly diverse T-cell receptor repertoire among all of our samples.

Conclusion: Using next generation sequencing, a specific rearrangement was found among 3 of the 7 BA samples. However predominant TCR clonality was not found in any sample. Further studies are required any possible antigenic triggers responsible for the unique T-cell rearrangements observed in the BA samples.

Sample Name	Total Templates	Total Productive Templates	Productive Rearrangements	Productive Clonality	Max Productive Frequency
BA-1553996	4,298	3,049	2,903	0.0032	0.295179%
BA-1429579	575	413	399	0.0023	0.726392%
BA-132030	1,078	749	690	0.0062	0.801068%
BA-1477888	1,235	870	850	0.002	0.574713%
BA-1418804	1,045	658	653	0.0004	0.303951%
BA-1453785	170	93	91	0.0018	2.150538%
BA-153205	2,428	1,745	1,714	0.0009	0.114613%

Sample Name	Total Templates	Total Productive Templates	Productive Rearrangements	Productive Clonality	Max Productive
Control-1130953	2,046	1,385	1,336	0.0024	0.288809%
Control-1129479	203	135	131	0.0031	2.222222%
Control-1129557	648	432	418	0.002	0.462963%
Control-1026008	1,435	1,036	1,025	0.0007	0.289575%
Control-1146919	2,290	1,728	1,716	0.0005	0.231481%
Control-1354622	4,389	3,125	3,031	0.0017	0.128%
Control-107976	507	328	325	0.0006	0.609756%
Control-11372	559	352	341	0.0022	0.852273%
Control-1113604	614	390	388	0.0006	0.769231%

649 SOME CONSIDERATIONS ABOUT FIBROSCAN IN EXTRAHEPATIC CHOLESTATIC LIVER

DISEASE. Sowon Park, Seung Kim, Hong Koh. Department of Pediatric Gastroenterology, Hepatology, and Nutrition, Yonsei University College of Medicine, Seoul, Seodaemun-gu, Korea (the Republic of)

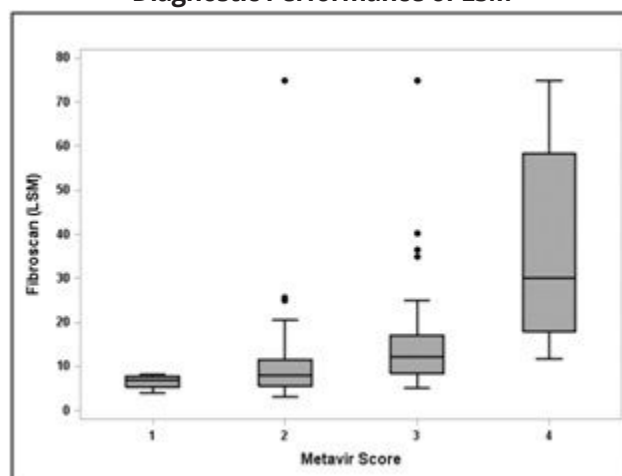
Background/Aim: Although liver FibroScan is one of the non-invasive methods which can be done easily to detect the severity of liver fibrosis, its reliability in extrahepatic cholestatic liver disease has been questioned recently. We analyzed the relationship between FibroScan and liver histology in cholestatic liver disease to validate the diagnostic performance of FibroScan.

Materials/Methods: Retrospective cohort study was done in 135 patients with biliary atresia, the most common extrahepatic cholestatic liver disease in children, at Severance Children’s Hospital from January 2007 to December 2016. Medical records were reviewed, including clinical and demographic data such as biochemical parameters indicating hepatic injuries, liver histopathology, and liver stiffness measurement. Liver stiffness measurement values in FibroScan were evaluated to see their correlations with liver fibrosis.

Results: The patients were categorized into four groups according to the Metavir score. Mean age and biochemical parameters such as total and direct bilirubin, AST, ALT, Platelet, and Prothrombin time in international normalized ratio showed statistically significant difference among the four fibrosis scoring groups. Liver stiffness measurement values were analyzed to validate the diagnostic performance of FibroScan. Liver stiffness measurement appeared to have good diagnostic performance in the extent of liver fibrosis, and especially detecting cirrhosis (Area Under Receiver Operating Characteristic of liver stiffness measurement is 0.81 (F 0~1 vs 2~4), 0.74 (F 0~2 vs 3~4) and 0.86 (F 0~3 vs 4) correspondingly). By using Youden’s index, we have calculated cut point values of FibroScan (cut point is 8.40 kilopascal (F ≥ 2), 12.20 kilopascal (F ≥ 3), and 17.90 kilopascal (F=4) respectively)

Conclusion: Liver FibroScan can be considered again as a reliable non-invasive method to find the extent of liver fibrosis in cholestatic liver disease, especially in detecting liver cirrhosis. Higher cut point values should be considered for the proper assessment for the liver fibrosis.

Diagnostic Performance of LSM



Diagnostic Performance of LSM

	F ≥ 2	F ≥ 3	F = 4
Sensitivity	61.83	65.52	83.33
Specificity	100.00	83.12	88.89
PPV	100.00	74.51	53.57
NPV	7.41	76.19	97.20
Accuracy	62.96	75.56	88.15
Cut point	8.40	12.20	17.90
AUROC	0.81 (0.77-0.85)	0.74 (0.67-0.82)	0.86 (0.77-0.95)

PPV: Positive Predictive Value
 NPV: Negative Predictive Value
 AUROC: Area Under Receiver Operating Curve

650 EFFECT OF SHORTENED OBSERVATION PERIOD AFTER PERCUTANEOUS LIVER BIOPSY

IN THE PEDIATRIC POPULATION. Svetlana Kozlovich, Claudia Phen, Anthony Sochet, Sara Karjoo, Daniel McClenathan, Ernest Amankwah, Sharon Crabtree, Sharon Gazarian, Michael Wilsey. Pediatrics, Johns Hopkins All Children’s Hospital, Pinellas Park, FL

Introduction: The observation period following percutaneous liver biopsy in the pediatric population varies greatly. Current guidelines are based upon expert opinion, rather than higher levels of evidence. However, studies in adults and limited studies

in children suggest that a shorter post-liver biopsy observation period may be safe with a minimal risk of side effects and complications. We investigated whether this observation was substantiated by our institution's experience.

Methods: After obtaining IRB approval, data was collected through a retrospective chart review of all pediatric patients undergoing outpatient percutaneous liver biopsy at Johns Hopkins All Children's Hospital from January 2009 to February 2017. The primary outcome measured was maximum pain score after liver biopsy. The secondary outcomes were complication rates of hemorrhage. These were measured by changes in vital signs, specifically heart rate and blood pressure, hemoglobin value changes, and the need for a transfusion. Additionally, we investigated the rate of readmission within the subsequent 7 days after discharge. Data was obtained via a search query through the Cerner EMR, for patients with an admission after the liver biopsy procedure. Data was examined using statistical methods in SAS. Further data analysis will take place utilizing the paired t-tests to analyze the data, with the statistical significance set for $P < 0.05$.

Results: 115 patients, with a total of 118 encounters for liver biopsy were identified at our institution. Males (69, 58.5%) were predominant compared to females (49, 41.5%). The mean age was 9.2 years. Patients were divided into two groups based on length of stay (LOS). Length of stay varied; less than or equal to 8 hours in 12 cases, and greater than 8 hours in 98 cases. Our primary outcome did not demonstrate any statistically significant difference between the two groups, with a mean of 3.83 in the less than 8 hour LOS group, and 2.64 in the greater than 8 hour LOS group. There were also no statistically significant differences in the secondary outcomes between groups, with mean systolic blood pressure of 103 to 105 mmHg and mean diastolic blood pressure of 57 to 59 mmHg post procedure. There were two patients in the greater than 8 hour LOS group who received transfusions within 24 hours of the liver biopsy. Two patients were readmitted within 7 days of discharge, and both patients had an initial admission of greater than 8 hours.

Discussion: Our preliminary results show that a shortened observation after percutaneous liver biopsy in the pediatric population has a low risk of complications. Further analysis will be performed for the patient encounters that required transfusions and resulted in readmission within 7 days. However, the overall findings suggest that shortened observation periods do not affect a patient's risk. Additionally, a shorter observation period after percutaneous liver biopsy in this patient population could improve cost-effectiveness and patient satisfaction. Further studies with larger sample sizes are needed to develop evidence-based guidelines to further guide clinical practice.

<u>Observation Period</u>	<u>Variable</u>	<u>N</u>	<u>Mean</u>	<u>Std Dev</u>	<u>Median</u>
<=8hrs	Age (Days)	12	4300.42	2429.89	4123.00
	Age (Years)	12	11.25	6.54	10.50
	Length Of Stay (Hours)	12	7.17	1.11	7.00
	Max Pain Score	12	3.83	2.69	4.00
	SBP Post Avg (mmHg)	12	103.92	11.10	101.00
	DBP Post Avg (mmHg)	12	57.67	8.06	58.00
>8hrs	Age (Days)	98	3651.54	2338.47	3768.00
	Age (Years)	98	9.53	6.44	10.00
	Length Of Stay (Hours)	98	23.15	5.04	24.00
	Max Pain Score	98	2.64	2.95	2.00
	SBP Post Avg (mmHg)	98	105.92	10.81	104.50
	DBP Post Avg (mmHg)	98	59.89	7.52	61.00

<u>Variable</u>	<u>N</u>	<u>N Miss</u>	<u>Mean</u>	<u>Median</u>
Age (Days)	118	0	3546.14	3737.00
Age (Years)	118	0	9.2457627	10.0000000
Length Of Stay (Hours)	118	0	23.2542373	23.0000000
Max Pain Score (1-10)	118	0	2.8389831	2.0000000
SBP Post Avg (mmHg)	118	0	105.2881356	103.0000000
SBP Pre Avg (mmHg)	68	50	105.8970588	106.0000000
DBP Post Avg (mmHg)	118	0	59.5677966	60.0000000
DBP Pre Avg (mmHg)	53	65	67.7547170	70.0000000
Avg Pre HR (beats/min)	32	86	91.8437500	89.0000000
Avg Post HR (beats/min)	87	31	91.2068966	82.0000000

652 **QUALITY OF LIFE IN YOUNG ADULTS WHO RECEIVED A LIVER TRANSPLANT IN**

CHILDHOOD. Zainab Mabizari², Ryan Himes¹, Saira Khadert², John Goss², Tamir Miloh¹. ¹GI, Texas Children's Hospital, Houston, TX; ²Baylor College of Medicine, Houston, TX

Intro: Through the improvement of surgical techniques and immunosuppressant therapies, patient survival after liver transplantation (LT) has markedly improved, especially in young children. Determining quality of life (QOL) as patients mature to adulthood is an important marker of success. The purpose of this study was to assess QOL in patients who received LT before 18y who have transitioned into young adulthood (18-30 y).

Methods: After IRB approval, the Hospital LT database was searched for LT performed between 1988-2016. 172 patients met inclusion; 110 were contacted by phone (excluded; 28 >30 y, 25 deceased, 9 without contact information) to participate in a QOL questionnaire based on education level, employment, socioeconomic status, adherence, mental and physical well-being. Responses were compared to national reported (NR) and adult LT rates (AR).

Results: 34 patients responded. 85% completed high-school (NR 83%), 24% were pursuing higher education, and 21% completed college. 53% were employed either part or full-time (NR 60%, AR 24%), 6% were actively seeking employment (NR 5%, AR 73%), and 33% receive social security and disability benefits (NR 2%, AR 56%). 12% were uninsured (NR 11%), 53% were privately insured, 21% received Medicaid benefits. 71% were living with parents (NR 32%), 18% were married, and 12% have children or are expecting. 91% reported being followed-up with their physician at least annually, 65% reported never missing immunosuppressant (IS) doses, 21% miss IS once a week, and 15% miss IS more than once a week. Patients endorsed feelings of sadness, anger, worry, and chronic pain at a rate of 12%, 12%, 29%, and 15% (NR 11%), respectively, with 79% reporting being physically active at least an hour a week. On average, patients rated their QOL at 8.6/10, with 21% reporting achieving life goals slower than expected and 9% reporting not achieving life goals (independence from parents, having a family, employment, and health status).

Conclusion: In conclusion, pediatric LT recipients had outcomes in educational attainment that were on par with the general population, however were more likely to live with their parents, receive disability benefits, and report higher levels of chronic pain. Pediatric recipients were more likely to be employed, than their adult LT recipient counterparts. Though they are lagging in certain measures we used to assess QOL in this study compared to the general population, pediatric LT recipients are outperforming their adult counterparts.

654 **EPIDEMIOLOGY AND NATURAL HISTORY OF CHILDREN WITH HEPATITIS C VIRUS INFECTION OVER A 30-YEAR PERIOD: A NATIONWIDE SURVEY IN JAPAN.**

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Background: Although the epidemiology of hepatitis C virus (HCV) infection among children may be rapidly changing, few reports have characterized large nationwide cohorts of children with HCV infection.

Aims: To clarify the epidemiology and natural history of HCV infection in Japanese children who were born over the last three decades.

Methods: Sixty-five pediatric centers retrospectively and prospectively recruited consecutive, otherwise healthy HCV-infected children between 2012 and 2016. Baseline and follow-up clinical information were obtained from patient records. Patient characteristics, clinical diagnosis at last visit, treatment, type of exposure, HCV genotype, and histopathologic features of liver biopsy specimens were determined. Features of the patients were compared among 3 groups defined by birth year: 1986 to 1995, 1996 to 2005, and 2006 to 2015. Patient inclusion criteria were age between 0 and 16 years at initial diagnosis, birth between 1986 and 2015, HCV RNA positivity in at least 1 serum sample, follow-up for at least 1 year after the infection was diagnosed at the observatory center, and absence of coinfection with human immunodeficiency virus or hepatitis B virus. Histopathology of the liver was evaluated using initial liver biopsy specimens obtained from children with chronic hepatitis C before they had received any interferon treatment with/without ribavirin.

Results: Entry criteria were met by 348 children. Age at initial diagnosis of infection has decreased significantly in recent years. No cases with cirrhosis or hepatocellular carcinoma were noted. Proportions of spontaneous clearance and of interferon treatment with/without ribavirin were 9% and 54%, respectively. Maternal transmission has increased significantly, representing over 99% of cases in the last decade. No transfusion-related cases have been seen after 1994. HCV genotype 2

has increased to become the most prevalent among Japanese children. Histopathologic examination of liver specimens showed no or mild fibrosis in most children with chronic hepatitis C; none showed cirrhosis.

Conclusions: We clarified the epidemiologic features and natural history of Japanese children with HCV infection over the last three decades. To our knowledge, this is the largest nationwide cohort study from Asia. None of these Japanese children developed cirrhosis or hepatocellular carcinoma. Maternal transmission increased to account for 99 % of cases during the last decade. Genotype 2 now is most prevalent in these children, although genotype 1 remains most common in adults. Histopathologically, most children with chronic hepatitis C showed no or mild fibrosis.

655 **INCREASED BILE ACID SECRETION WITHIN THE STOOL IN WILD TYPE RATS WITH 4 WEEKS OF EXERCISE.**

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Background: Preliminary data from our lab shows that rats selectively bred over several generations for high aerobic capacity have an upregulation of hepatic genes controlling bile acid (BA) and cholesterol synthesis. These rats also had an increase in fecal BA content. Rats selectively bred for low aerobic capacity, the opposite affect was found and a decrease in fecal BA content. We have also found that voluntary wheel running (VWR) in Sprague Dawley rats upregulates the same genes associated with BA and cholesterol synthesis. The biggest induction of these genes was found when VWR was combined with withdrawing the food during the dark cycle when rats normally run.

Objectives: Here we wanted to determine if overnight food withdrawal or VWR was the primary stimulus for an upregulation of hepatic BA and cholesterol synthesis genes and if these stimuli increased the excretion of fecal BA content. High aerobic capacity and VWR are known to protect against fatty liver and thus, we hypothesized that increased fecal excretion of BA associated with these features may play a protective role.

Methods: Sprague-Dawley rats were assigned to a sedentary, fed group (SED n=8), a dark phase food restricted group (DFR n=7) (food pulled from 5pm to 8 am), or a VWR plus DFR group (VWR-DFR n=7) for 4 weeks. Rats were fasted for 13 hours prior to sacrifice during the dark cycle. Stool samples were obtained for 24 hour period prior to the sacrifice. Rat livers were frozen and processed for rtPCR analysis of the following genes: cytochrome P450 family 7 (*CYP7A1*), HMG-CoA reductase (*HMGCR*), and ATP-citrate lyase (*ACLY*). Total BA content was measured in fecal samples.

Results: The VWR-DFR group had a significant increase in fecal BA content above SED (p=0.02). The DFR group also showed a trend for greater fecal BA content above SED (p=0.09). Interestingly, both VWR-DFR and DFR displayed a downregulation of hepatic *CYP7A1*, *HMGCR*, and *ACLY*.

Conclusion: These outcomes provide further evidence that exercise increases fecal BA secretion. This was especially present in VWR-DFR group. There was an upward trend in the SED-DFR group, suggesting that cyclic periods of energy deficit could also be increasing fecal BA secretion. Surprisingly, we saw a marked down regulation of cholesterol and BA synthesis genes. These effects are likely due to prolonged fasting prior to sacrifice as our previous VWR results were measured in a fed condition.

Daily exercise increased fecal BA secretion compared to SED, with similar but non-significant results being evoked by nightly food withdrawal. Further studies are needed to determine if increased fecal BA excretion plays a role in the known effects of exercise and aerobic capacity to protect against fatty liver. The use of exercise capacity (VO_{2max}) and fecal bile acid measures could be potentially used to better understand the development and treatment of fatty liver in humans.

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657 **LIVER INJURY IN CHILDREN UNDERGOING TREATMENT FOR CANCER: ANALYSIS OF A LARGE SINGLE-CENTER COHORT.**

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Introduction: Drug-induced liver injury (DILI) is associated with substantial morbidity and mortality in both adults and children. DILI is a common cause of acute liver failure (ALF) in children, and the most common cause of ALF in adults. Cancer remains the leading cause of childhood death related to disease and, as a result, new pediatric cancer therapies

continue to emerge. While conventional cancer treatments and new targeted agents can exhibit hepatotoxicity, there is limited data regarding the incidence of liver injury, and its associations and risk factors among children with cancer. Our goal of this study was to determine the frequency and presenting clinical features of liver injury among pediatric cancer patients treated at the University of Michigan.

Methods: We retrospectively reviewed the University of Michigan Pediatric Hematology Oncology (PHO) REDCap database from January 1st, 2004 to July 31st, 2016. Inclusion criteria were patients age ≤ 25 years plus any one of the following: ALT or AST $> 5 \times$ ULN or alkaline phosphatase (AP) $> 2 \times$ ULN on two consecutive lab draws within two months, or total bilirubin ≥ 2.5 mg/dl plus any elevation of AST, ALT or AP on any single lab draw. Liver injury cases after liver or bone marrow transplantation were excluded. Electronic medical record data mining software (DataDirect) was utilized to identify cases. For each case, pattern of liver injury (hepatocellular, cholestatic or mixed) was assessed and patients at higher risk of liver transplantation or death were identified based on Hy's Law (ALT $> 3 \times$ ULN plus total bilirubin $> 2 \times$ ULN). Data regarding demographics, cancer diagnosis and clinical presentation at the time of liver injury were extracted. Continuous variables were analyzed using two-sample t-tests and categorical variables using Chi-square tests. Adjustment for multiple comparisons was made by Tukey-Kramer method. Significance was defined as $p < 0.05$. SAS Software v9.4 (SAS Institute Inc. Cary, NC) was used for statistical analysis.

Results: There were 1916 patients in the PHO REDCap database. 307 (17%) of the enrolled patients had at least one episode of liver injury. There was no difference in frequency of liver injury between males and females (53% vs 47%; $p = 0.73$). The majority of the cases occurred in young children (< 1 year = 5%, 1-10 years = 51%, 11-18 years = 39%, 19-25 years = 5%). There was a significantly high rate of liver injury in patients with leukemia compared to solid tumors (56% vs 44%; $p = < 0.001$). Among the leukemia group, more patients with lymphoid leukemia vs myeloid leukemia had liver injury (45% vs 21%; $p = 0.0001$). Whereas among the solid tumor group, there was a higher rate of liver injury in patients with sarcoma (19%) vs. neuroblastoma (7%; $p = 0.018$), brain tumors (4%; $p < 0.0001$), other tumors (8%; $p = 0.002$). The most common liver injury pattern was hepatocellular (74%), followed by cholestatic (14%) and mixed (12%). 31 cases of liver injury met Hy's law criteria, including 14 solid tumors and 17 leukemia cases.

Conclusions: This study confirms that liver injury is frequent among children receiving treatment for cancer and can cause serious morbidity and mortality. Our data suggests that liver injury is equally prevalent among males and females and more common in children ages 1-11 years. In addition, children treated for leukemia have a higher risk for liver injury compared to the solid tumor patients. Our future study aim is to characterize the etiology of liver injury (DILI vs other), and in the cases of DILI describe implicated agents, severity of injury, risk factors, and morbidity and mortality with the ultimate goal to improve the safety and outcomes of cancer treatment.

659 **LACK OF ASSOCIATION BETWEEN MBOAT7 VARIANTS AND SERUM CYTOKERATIN 18 FRAGMENTS IN OBESE CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE.**

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Background/Aims: There are substantial genetic components contributing to the susceptibility of non-alcoholic NAFLD disease (NAFLD). It has recently been reported that the rs641738 C>T variant in the membrane-bound O-acyltransferase domain-containing protein 7 (*MBOAT7*) gene increased severity of NAFLD in adults of European descent. We aimed to test the hypothesis that *MBOAT7* rs641738 variant would increase serum cytokeratin 18 (CK18) fragments, a biomarker of hepatocellular injury and apoptosis, in obese children with NAFLD.

Methods: A total of 831 obese children aged 7-15 years were recruited. NAFLD was determined by ultrasonography. Because *PNPLA3* rs738409 and *TM6SF2* rs58542926 variants are known to confer susceptibility to NAFLD, we assessed the independent influence of *MBOAT7* rs641738 on serum levels of CK18 fragments after conditioning on the effect of *PNPLA3* rs738409 and *TM6SF2* rs58542926 polymorphisms.

Results: 22.7% of recruited obese children had NAFLD. *PNPLA3* rs738409 variants increase the odds ratio of NAFLD by 1.91 (95% C.I.: 1.24 - 2.94, $P = 0.003$) in subjects with CG alleles and 3.23 (95% C.I.: 1.83 - 5.70, $P < 0.001$) for GG alleles, as compared to CC alleles. *TM6SF2* rs58542926 variant was an independent risk factor of developing NAFLD with an estimated odds ratio = 2.75 (95% C.I.: 1.65 - 4.56, $P < 0.001$). However, *MBOAT7* rs641738 variants, heterozygous or homozygous, were not associated with NAFLD, insulin resistance, lipid levels, and liver enzymes. The multivariate linear regression model revealed that after adjusting for body mass index, total cholesterol and *PNPLA3* rs738409, neither *TM6SF2* rs58542926 nor *MBOAT7* rs641738 was significantly associated with serum levels of CK18 fragments.

Conclusions: The variant *MBOAT7* rs641738 genotype is not associated NAFLD and serum CK18 fragments independent of the effect of *PNPLA3* rs738409 and *TM6SF2* rs58542926 polymorphisms in our population of obese Taiwanese children.

660 UTILITY OF TRANSIENT ELASTOGRAPHY TO MEASURE LIVER STIFFNESS AS A MARKER FOR FONTAN-ASSOCIATED LIVER FIBROSIS. Yuki Cho^{1,2}, Eiji Ehara³, Yuki Kawasaki³, Suzuki Tsugutoshi³, Daisuke Tokuhara¹, Haruo Shintaku¹, Yosuke Murakami³. ¹Department of Pediatrics, Osaka City University Graduate School of Medicine, Osaka, Osaka, Japan; ²Department of Pediatrics, Kashiwara Municipal Hospital, Kashiwara, Osaka, Japan; ³Department of Pediatric Cardiology, Osaka City General Hospital, Osaka, Osaka, Japan

Background: Patients who have undergone Fontan procedures are prone to developing liver cirrhosis. Noninvasive and reliable monitoring methods are needed, because available routine laboratory tests are noninformative when screening for liver fibrosis.

Objective: To assess the usefulness of transient elastography (TE)-based measurements of liver stiffness (LSM) in assessing Fontan-associated liver fibrosis.

Methods: LSM was measured by using TE in patients who had undergone Fontan operations and their controls; the resulting data were compared between groups. In addition, LSM data were analyzed for their correlation with time since surgery, laboratory findings, and histologic evaluation of fibrosis.

Results: In total, LSM was evaluated by using TE in 48 patients who had undergone Fontan procedures (median age, 11.6 years; range, 4.2–32 years) and their controls. LSM was significantly higher in patients who had undergone Fontan surgery (16.1 ± 9.2 kPa) than in controls (4.0 ± 1.0 kPa, $P < 0.001$). Within the Fontan group, LSM lacked significant correlation with AST, ALT, hyaluronic acid, and type 4 collagen levels but was correlated with time since surgery ($\rho = 0.635$), AST-to-platelet ratio index ($\rho = 0.411$), and platelet count ($\rho = -0.683$). In addition, 4 patients (16.3 ± 2.9 y) showing high LSM (32.1 ± 13.6 kPa) underwent liver biopsy. All 4 patients demonstrated portal and sinusoidal fibrosis associated with sinusoidal dilatation, and 3 of the 4 patients had pseudolobules.

Conclusions: Liver stiffness reflects hepatic fibrosis in patients after Fontan operation. Because liver stiffness continues to increase with time after surgery, these patients should be monitored regularly by using TE.

***661 BIOPSY-RELATED ADVERSE EVENTS DURING IWITH (NCT01638559), A MULTI-CENTER IMMUNOSUPPRESSION WITHDRAWAL TRIAL.** Yumirle Turmelle⁶, Emily Perito¹, John Bucuvalas², Mercedes Martinez⁵, Katharine Spain³, Sandy Feng⁴, Investigators iWITH⁷. ¹Pediatrics, University of California San Francisco, San Francisco, CA; ²Pediatrics, Cincinnati Children's Medical Center, Cincinnati, OH; ³Rho Inc, Chapel Hill, NC; ⁴Surgery, University of California San Francisco, San Francisco, CA; ⁵Pediatrics, Columbia University, New York, NY; ⁶Pediatrics, Washington University, St. Louis, MO; ⁷NIH, Bethesda, MD

Background: Awareness that subclinical inflammation and fibrosis are common in apparently healthy grafts with normal liver tests emphasizes the importance of liver histology to guide immunosuppression (IS) decision-making for pediatric liver transplant (LT) recipients. However, concern for biopsy-related complications has likely discouraged use in standard clinical practice. We used the rigor of a clinical trial of IS withdrawal (iWITH) to provide the first report of biopsy-related complication prevalence and severity in a multi-center cohort of pediatric LT recipients.

Methods: 157 pediatric LT recipients on calcineurin-inhibitor monotherapy with persistent ALT/GGT < 50 IU/L underwent screening biopsy. 88 eligible participants initiated IS withdrawal. The protocol mandated 1) an end of study biopsy for all subjects 2) an additional biopsy for those who successfully stopped IS 1 year after the last IS dose; and 3) for cause biopsies for ALT or GGT > 100 IU/L or at investigator discretion. The protocol required the use of a 16 gauge biopsy needle and collection of ≥ 4 cms of tissue. We identified all adverse events (AEs) possibly or definitely related to biopsies per site investigators who also graded severity (mild/moderate/severe according to CTCAE Version 4.0) and assessed seriousness.

Results: Biopsy-related complications occurred in 20 of 293 biopsies (6.8%; 95% confidence interval 3.9-9.7%) (Table). Complication frequency was similar for protocol (17/230; 7%) compared to for cause (3/63; 5%) biopsies. There were 24 AEs recorded for the 20 biopsies; assigned CTCAE grades were mild (n=12), moderate (n=7) and severe (n=5). Of the 5 severe AEs, 4 were serious, requiring hospitalization to treat procedural pain, cellulitis, cholangitis, and bile leak. All 4 serious AEs resolved, over 3, 4, 7, and 18 days. The most common biopsy-related AE (n=9; 38%) was procedural or abdominal pain. All 20 non-serious AEs resolved, 8 on the same day, 9 within 1-2 days, 2 within 3 days, and 1 after 7 days. There was no biopsy-related hemorrhage that required transfusion or intervention.

Conclusions: While biopsy-related AEs were infrequent (6.8%), serious and/or severe AEs were rare (1.7%). The vast majority of AEs resolved quickly and without sequelae. The rigorous context of a clinical trial ensures complete capture of all possible biopsy-related complications. Our high quality data should inform risk-benefit decisions about surveillance biopsies to optimize immunosuppression management for pediatric LT recipients to maximize graft longevity and patient well-being.

Table: iWITH Biopsy-related Adverse Events Reported- dichotomized by Severe and all other CTCAE grades

Adverse Events	N	Relationship to Biopsy	CTCAE Grade	Serious	Interval (days)	
					Biopsy \leftrightarrow AE start	AE start \leftrightarrow resolution
Procedural pain	1	Definite	Severe	Yes	0	3
Cellulitis, biopsy site	1				7	7
Cholangitis	1				0	18*
Bile Leak	1				1	4
Procedural (n=6) or Abdominal (n=2) pain	8	Definite 4 Possible 4	Mild 4 Moderate 4	No	0 - 2	0 - 7
Viral illness	3	Definite 1 Possible 2	Mild		0 - 2	2 - 3
Biopsy site skin disorder	3	Possible	Mild		0 - 1	2 - 3
Nausea/vomiting	2	Possible	Mild		0 - 1	0
Fever post-procedure	1	Possible	Moderate		0	1
Sedation	1	Definite	Moderate		0	0
Hypotension	1	Definite	Severe		0	0
Non-hepatic tissue	1	Definite	Moderate		0	0

*Patient diagnosed with and treated for biliary stricture.

MICROBIOLOGY/INFECTIONS/PROBIOTICS

662 MICROBIOME OF TRACHEAL SAMPLES FROM MECHANICALLY-VENTILATED PATIENTS DIAGNOSED WITH GASTRIC AND SALIVARY MICROASPIRATIONS.

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Background: Mechanical ventilation (MV) is the most common intervention for intensive care unit (ICU) patients. Patients undergoing MV are primary targets for microaspiration. The MV involves insertion of an endotracheal tube (ETT). ETT insertion forces the glottis open, creating a passage for microaspiration of oropharyngeal and gastric fluids into the lung. Microaspiration causes lung injury and further respiratory problems. Pepsin A and α -amylase are the primary biomarkers for microaspiration of gastric and oral contents, respectively. They play key a role in the pathophysiology of lung injuries. It is not known how microaspiration may alter bacterial communities in the lung leading to bacterial dysbiosis and a succession of pathogens that culminates into lung injuries of MV patients. We investigated the bacterial profile changes in tracheal samples of MV patients with and without microaspirations.

Methodology: Stored samples from an ongoing IRB approved prospective study were analyzed. A total of 28 samples were selected. Control samples of ten subjects were previously tested negative for pepsin A and α -amylase and 18 samples were positive for both biomarkers (at the baseline and peak). The purified genomic DNA was used to amplify V3-V4 region of bacterial 16S rRNA gene covering both the conserved and variable regions. The analysis of metagenomic sequence data was performed using the Quantitative Insights Into Microbial Ecology (QIIME) software, version 1.9. (1R01NR014508; clinicaltrials.gov NCT02284178)

Results: Firmicutes, proteobacteria, and actinobacteria were the main phyla detected in the tested samples. The control samples showed mainly the abundance of *Streptococcus*, *Prevotella*, and *Haemophilus* genera. Subjects with microaspiration showed differences in the abundance of some bacterial species between baseline point (absence of both biomarkers) and peak (presence of biomarkers). Interestingly, one sample showed an increase of abundance of mycoplasma at the peak point of microaspiration which is a clear indication of the potential role of the microaspiration in favoring the growth of certain pneumonia causing pathogens in the lungs of MV patients.

Conclusion: Our data confirmed the low diversity of the tracheal bacterial microbiota. Bacterial profile changes were observed between baseline and peak points in MV patients. This study provides preliminary data for the potential role of bacterial dysbiosis in MV patients. In future, we will expand our study to include more subjects and matching controls. Correlation between microbial profile changes and clinical data will allow for better understanding of microbial involvement in lung injuries of MV patients.

***663 EFFECT OF PROBIOTICS AND DIETARY CHANGES ON ADIPOSITY IN CHILDREN.**

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Background: Recent studies have shown that the gut microbiome can affect adiposity and inflammation in animal models. In these studies, changing the gut microbiome has been associated with decreased fat mass and inflammation as well as improved metabolism. Probiotics may be a safe method of altering the gut microbiome in humans, and changes in diet may work synergistically with probiotics to alter the gut microbiome. Our goal was to examine the effect of probiotics in the context of a diet high in fruits and vegetables (high F/V diet) on altering the gut microbiome, decreasing fat mass, and improve inflammatory markers in overweight/obese (OW/OB) children.

Objective: To present the results of the intervention on changes in adiposity in OW/OB children.

Methods: Children between the ages of 7-16 years old were recruited to participate in the *Gut Microbiome, Adiposity and Probiotics Study (GMAP)*, a randomized double-blind placebo-controlled trial. Thirty-nine parent-child dyads with an overweight or obese child (BMI≥85th percentile) were recruited and randomized into the “probiotic (VSL#3) + high F/V diet” intervention or “placebo + high F/V diet” intervention lasting 12 weeks. Probiotic/placebo pill compliance was self-reported and new pills were supplied on a weekly basis during the intervention. Adiposity was measured with pre and post intervention DEXA scans, four (n=3 in placebo group and n=1 in probiotic group) of the children in the intervention did not have a post-intervention DEXA scan. Chi-square analysis and two sample t-tests were used to determine differences between groups.

Results: The sample included 56% males, mean age 12.5 years (SE 5.6), mean child BMI percentile 96.5 (SE 0.54). Reported adherence to pill consumption was similar in both groups, 78.95 % in probiotic group and 71.65% in placebo group (p= 0.31). There was no statistical difference between groups with regards to fat mass (p=0.23) and BMI Percentile (p=0.88) (Table 1). Analyses among those with >75% pill consumption also revealed no significant differences between groups with regards to fat mass (p=0.51) and BMI Percentile (p=0.42) (Table 2).

Conclusion: Probiotics did not affect changes in adiposity or BMI percentile among children on a high F/V diet. This may be related to multiple factors including small sample size, variability of dietary changes and duration of intervention. Given the rising trend of pediatric obesity, new and innovative treatment strategies are necessary. Although this intervention did not demonstrate changes in adiposity or BMI percentile, there were greater effects among participants with >75% pill adherence. Additional randomized clinical trials are necessary to further examine the effect of probiotics on adiposity and BMI percentile in a larger sample and with additional efforts to improve compliance.

	Probiotic (N=19)	Placebo (N=20)	p-value
Baseline %Fat Mass	39.76	39.38	0.85
Post %Fat Mass	39.36	38.26	0.59
Relative Difference %Fat Mass	-0.39	-1.12	0.23
Baseline BMI-Percentile	96.87	96.15	0.52
Post BMI-Percentile	95.73	94.91	0.63
Relative Difference BMI-Percentile	-1.14	-1.25	0.88

	Probiotic (N=12)	Placebo (N=9)	p-value
Baseline %Fat Mass	39.48	40.08	0.83
Post %Fat Mass	38.60	38.66	0.98
Relative Difference %Fat Mass	-0.88	-1.42	0.51
Baseline BMI-Percentile	96.80	97.27	0.75
Post BMI-Percentile	95.13	96.52	0.58
Relative Difference BMI-Percentile	-1.68	-0.74	0.42

665 CHANGES IN T CELL IMMUNOPHENOTYPES REFLECT IMMUNE MEMORY AFTER INTESTINAL TRANSPLANTATION. Marjorie-Anne Guerra¹, Maura Rossetti², Robert Venick^{1,3}, Elizabeth Marcus¹, Sue McDiarmid^{1,3}, Elaine Cheng³, Douglas Farmer³, Elaine Reed², Laura Wozniak¹. ¹Pediatric Gastroenterology, UCLA, Los Angeles, CA; ²Immunogenetics Center, UCLA, Los Angeles, CA; ³Transplant Surgery, UCLA, Los Angeles, CA

Introduction: Immunophenotyping of peripheral blood mononuclear cells (PBMCs) has been shown to be a useful, non-invasive method of predicting acute cellular rejection (ACR) following intestinal transplantation (ITx). Aims: To characterize (1) changes in naïve and central/effector memory T cells over time after ITx and (2) differences in the peripheral blood T cell immunophenotype during episodes of ACR and viral enteritis.

Methods: An IRB-approved, longitudinal study of ITx recipients was performed. Blood was collected during serial routine visits at least 6 months apart and episodes of graft dysfunction (high fecal outputs, nausea/vomiting, and/or gastrointestinal bleeding). Samples from routine visits were classified as early post-ITx (<5 yrs) and late post-ITx (>5 yrs). Samples during graft dysfunction were classified as ACR based on histopathology and as infectious enteritis based on infectious stool studies or respiratory viral panel. PBMC immunophenotyping was performed with multi-color monoclonal antibody panels. Cell fluorescence was acquired on an LSR Fortessa. Analysis was performed with Flowjo V10. Statistical analysis included mixed model analysis using R software.

Results: 28 ITx recipients who received 34 grafts were included. 22 patients were pediatric patients (<21 years). 79% had liver-intestinal grafts. 61 samples were analyzed (range of 1-5 samples per patient): 33 were collected on routine visits and 28 during episodes of graft dysfunction. There were multiple statistically significant differences in T cell subsets in the early (n=15) vs late (n=18) groups (Table 1). Naïve T cells were higher in the early post-ITx group and T central memory cells were higher in the late post-ITx group. There were no significant differences in Th17 effector cells, T regulatory cells, or markers of exhaustion (PD1+, KLRG1+, CD57+) of CD4+ and CD8+ T cells in normal (n=33) vs graft dysfunction (n=28). Th17 effector cells were significantly lower in ACR (n=3) compared to baseline (n=33); Difference -2.3 (95% confidence interval: -3.7, -0.9).

Conclusion: Over time, there is a shift in the T cell immunophenotype from naïve to central memory cells. Th17 effector cells are lower the peripheral blood in ACR compared to baseline, which may be due to infiltration of the intestinal graft during ACR. Additional studies are needed with larger cohorts to identify T cell differences between ACR and viral enteritis. Further elucidating T cell immunophenotypes over time will lead to a better understanding of immune memory and its clinical implications in ITx.

Table 1. Differences in T cell subsets in Late versus Early Post-ITx groups

	Difference (95% CI)	p-value
% of <u>Tregs</u>		
Naïve	-17.6 (-33.4, -1.9)	0.028
Central memory	6.3 (-1.1, 13.8)	0.096
Effector memory	9.0 (-3.5, 21.5)	0.156
% of CD4+ cells		
Naïve	-17.0 (-26.7, -7.2)	<0.001
Central memory	14.4 (6.8, 22.0)	<0.001
Effector memory	0.1 (-6.9, 7.0)	0.987
% of CD8+ cells		
Naïve	-1.7 (-19.0, 15.7)	0.851
Central memory	1.6 (0.1, 3.2)	0.034
Effector memory	0.5 (-3.1, 4.1)	0.768

666 EBV VCA IGM AND CYTOMEGALOVIRUS IGM DUAL POSITIVITY IS A FALSE POSITIVE FINDING RELATED TO AGE AND HEPATIC INVOLVEMENT OF PRIMARY EPSTEIN-BARR VIRUS INFECTION IN CHILDREN. Min Ji Sohn¹, Jin Soo Moon², Jae Sung Ko², Hye Ran Yang^{1,2}. ¹Pediatrics, Seoul National University Bundang Hospital, Seongnam, Korea (the Republic of); ²Seoul National University College of Medicine, Seoul, Korea (the Republic of)

Background: Primary EBV infection is common in childhood, and dual positivity of serum Epstein-Barr virus (EBV) IgM and Cytomegalovirus (CMV) IgM antibodies occurs in some cases of primary EBV infection in children. The aim of this study was to evaluate the cause of EBV and CMV IgM dual positivity whether it is a false positive finding or a true coinfection of EBV and CMV.

Methods: A total of 494 pediatric patients aged 18 years or less diagnosed with primary EBV infection manifesting as infectious mononucleosis, in Seoul National University Bundang Hospital from March 2004 through February 2016, were recruited. The diagnosis of primary EBV infection was based on a positive EBV viral capsid antigen (VCA) IgM antibody, and serum CMV IgM antibody and liver enzymes was checked at the same time in 149 subjects. When serum CMV IgM is positive, additional tests to confirm the diagnosis of CMV infection were evaluated.

Results: Of 149 children with primary EBV infection children, 40 (26.8%) revealed serum CMV IgM dual positivity along with serum EBV VCA IgM positivity. True CMV infection was confirmed only in one child of 40 (2.5%) who was positive for serum CMV Ag and urine CMV PCR and negative for serum CMV IgG antibody. In the other 39 children, serum CMV Ag and urine CMV PCR or cultures were all negative at the time of serum CMV IgM and EBV VCA IgM dual positivity. Dual positivity were higher in infants and lower in adolescents in children with primary EBV infection ($p = 0.013$). Laboratory markers of hepatic involvement (liver enzymes) were significantly elevated in children with dual positivity than those with negative CMV IgM ($p = 0.026$), correlating with serum EBV and CMV IgM titers.

Conclusions: Serum EBV VCA IgM and CMV IgM dual positivity is more prevalent in children with primary EBV infection than reported before. Our results indicate that this dual positivity is a false positive finding, possibly due to antigenic cross-reactivity, rather than coinfection with CMV.

Key Words: Epstein-Barr virus, cytomegalovirus, IgM, false positivity, age, liver, child

669 ASSOCIATION OF HEPATITIS C WITH DRUG PRACTICES PREVALENT IN ADOLESCENTS OF A DRUG REHABILITATION CENTER, OHIO. Neil Fernandes¹, Bonisha Sthapit¹, Philip Fragassi¹, Swagata Banik², Neelab Abdullah², Nazha Abughali¹. ¹Pediatrics, Metrohealth Medical Center, Parma, OH; ²Public Health & Prevention Sciences, Baldwin Wallace University, Berea, OH

Introduction: Hepatitis C virus (HCV) infection is a “silent epidemic” as many infected people are asymptomatic and go undiagnosed. In Ohio alone, the incidence has increased by 400% in the last 5 years projecting a health cost of 50 million in the next decade. There is a strong association of hepatitis C infection with IV drug usage which is emerging amongst adolescents. Limited, but available data internationally suggest that the hepatitis C infection rate increased in the high-risk population at juvenile detention centers. With the FDA recently approving two direct-acting antiviral drugs for pediatric use, we need standardized guidelines for routine screening of HCV in adolescents. The primary goal of this study is to determine the sero-prevalence of HCV infection in the adolescent population at a drug rehabilitation center and their associated drug using behavior.

Materials/Methods: In this prospective cohort study, adolescents admitted to a drug rehabilitation center (July '16-June '17) in Northeast Ohio were enrolled. All participants completed screening questionnaires that included drug using behavior-related questions. Those who consented underwent point of care testing for HCV.

Results: Out of 100 admitted adolescents, 85 adolescents agreed to be tested. Majority were males (60%, 51/85) and Caucasians (78%, 66/85). 5% (4/85) of the participants tested positive for HCV. The commonly used substances were marijuana (96%, 82/85), opioids (26%, 22/85) and stimulants (25%, 21/85). Heroin use was reported by 15% (13/85) adolescents and was the only drug associated with HCV sero-positivity. (100%, 4/4 vs. 11%, 9/72. $p=0.0004$).

Conclusion: Our study showed a high rate of HCV infection in adolescents using drugs, with a strong association with Heroin. With the recent approval of new drugs by the FDA, we recommend routine screening for hepatitis C be included in this high risk population.

672 **CALCIUM-SENSING RECEPTOR INHIBITION OF CYCLIC NUCLEOTIDE-INDUCED ANION SECRETION IN INTESTINES IMPLICATES DOWN REGULATION OF MULTIPLE ION TRANSPORT MECHANISMS.**

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Introduction: Treatment of infectious diarrheas remains a challenge globally, particularly in infants, young children, and immune compromised patients. Although currently recommended rehydration therapy can replace the loss of fluid, it does not stop ongoing intestinal secretion - the primary pathophysiology of secretory diarrheas. Therefore, for decades there has been a continuous search for ways to effectively stop intestinal secretion. Extracellular calcium-sensing receptor (CaSR) is a unique Class C G protein-coupled receptor that uses nutrients (e.g., calcium, polyamines and aromatic amino acids) as its ligands. Recently, we have shown that activating intestinal epithelial CaSR reverses Cl⁻ and fluid secretion, induced by cyclic nucleotides (cAMP, cGMP) and enterotoxins (cholera toxin, STa), making CaSR an attractive target. However, how CaSR inhibits this secretion is not well understood. Transepithelial secretion of Cl⁻ involves two steps: 1) Cl⁻ entry from basolateral membrane mediated by Na⁺/K⁺/2Cl⁻ cotransporter, Na⁺,K⁺-ATPase and K⁺ channel and 2) Cl⁻ exit from apical membrane mediated by CFTR Cl⁻ conductance. In a previous study, we have shown using perfused colonic crypts that activating CaSR down regulates Na⁺/K⁺/2Cl⁻ cotransporter activity. The aim of this study was to determine if CaSR inhibition of Cl⁻ secretion also implicates down regulation of other transporters, namely, the apical Cl⁻ channel, basolateral K⁺ channel, and basolateral Na⁺,K⁺-ATPase.

Methods: Taking advantage of the electrogenic property of these transporters, we assessed CaSR effects on the apical Cl⁻ channel, basolateral K⁺ channel and Na⁺,K⁺-ATPase in Ussing chamber using electrophysiological techniques. Intact and apical or basolateral membrane-bypassed rat distal colon mucosa and cultured human intestinal epithelia (Caco-2 monolayers) were prepared, mounted onto Ussing chambers, and forskolin-induced Cl⁻ secretory current responses to CaSR agonist R568 were measured under defined conditions with and without the presence of transport inhibitors.

Results: Exposure of colonic epithelia to forskolin elicited a significant amount of short-circuit current (I_{sc}^{FSK}), in the presence, but not absence, of Cl⁻ in solutions. Subsequent additions of R568, NPPB, glibenclamide, barium, or ouabain reversed I_{sc}^{FSK} . This indicates that CaSR may inhibit transepithelial Cl⁻ transport, either apically via inhibition of the Cl⁻ channel, basolaterally via inhibition of the K⁺ channel and Na⁺,K⁺-ATPase, or both. Indeed, in basolaterally nystatin-perforated colonic epithelia, forskolin stimulated the NPPB/glibenclamide-sensitive Cl⁻ current (a measure of CFTR activity); subsequent addition of R568 reversed it. Similar inhibition of the apical Cl⁻ current by R568 was also observed in basolaterally depolarized epithelia. Likewise, in apically permeabilized epithelia, forskolin stimulated the barium-sensitive K⁺ current (a measure of K⁺ channel activity); the addition of R568 also reversed it, suggesting that CaSR also inhibits basolateral K⁺ conductance. Finally, the ouabain-sensitive Na⁺,K⁺-dependent current across apically bypassed epithelia was measured. Forskolin stimulated this current and R568 reversed it, indicating that down regulation of Na⁺,K⁺-ATPase activity by CaSR may also occur.

Conclusion: CaSR abrogation of cyclic nucleotide-induced Cl⁻ secretion in intestines implicates the inhibition of multiple ion transport mechanisms. Besides inhibiting the basolateral Na⁺/K⁺/2Cl⁻ cotransporter, CaSR also inhibits the basolateral K⁺ channel, basolateral Na⁺,K⁺-ATPase, and apical CFTR Cl⁻ conductance. This pleiotropic ability of CaSR to simultaneously shutdown both entry and exit pathways of Cl⁻ secretion suggests that targeting this unusual nutrient receptor may represent an effective way to stop secretory diarrheas.

673 **THE ASSOCIATION BETWEEN ABNORMAL PLACENTAL PATHOLOGY (CHORIOAMNIONITIS) AND NECROTIZING ENTEROCOLITIS IN PRETERM INFANTS.**

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Background: Necrotizing enterocolitis (NEC) is the most common gastrointestinal complication of prematurity. Its pathogenesis is multifactorial. It is hypothesized that NEC is preceded by ischemic or toxic event that causes damage to the immature gastrointestinal mucosa and loss of mucosal integrity.

Objective: The present study examined the association between abnormal placental pathology (chorioamnionitis) and development of NEC.

Study Design: A retrospective cohort study of preterm infants (birth weight <1500 grams) admitted to neonatal intensive care unit (NICU) at Brookdale Hospital, New York, from January 2014 to April 2017. Placentas of those infants were reviewed by a single blinded pathologist to look for evidence of chorioamnionitis. Retrospective follow up of each patient was continued until discharge from the NICU to determine if the patient developed NEC (defined according to Bell's criteria; with stage II

and stage III were considered as diagnosis of NEC). Patients who died or were transferred to another center within 4 weeks of life were excluded from the study.

Statistical analysis was done using SSPS program. Differences in clinical characteristics and incidence of NEC between chorioamnionitis group and control group (normal placenta) were tested for significance by Fisher's exact test and/or chi-squared (χ^2) analysis, where applicable. A p-value <0.05 was regarded as significant.

Results: Among total of 1,363 infants admitted during the 3 years 4 months study period, 97 had birth weight <1500 g. Twelve patients were excluded from the study (9 died within 1-4 weeks of age, and 3 had incomplete clinical data or missing pathology report). The remaining 85 infants were included for analysis: mean (\pm SD) gestational age at birth was 28.4(\pm 3) weeks, with 44 (52%) male and 41 (48%) female.

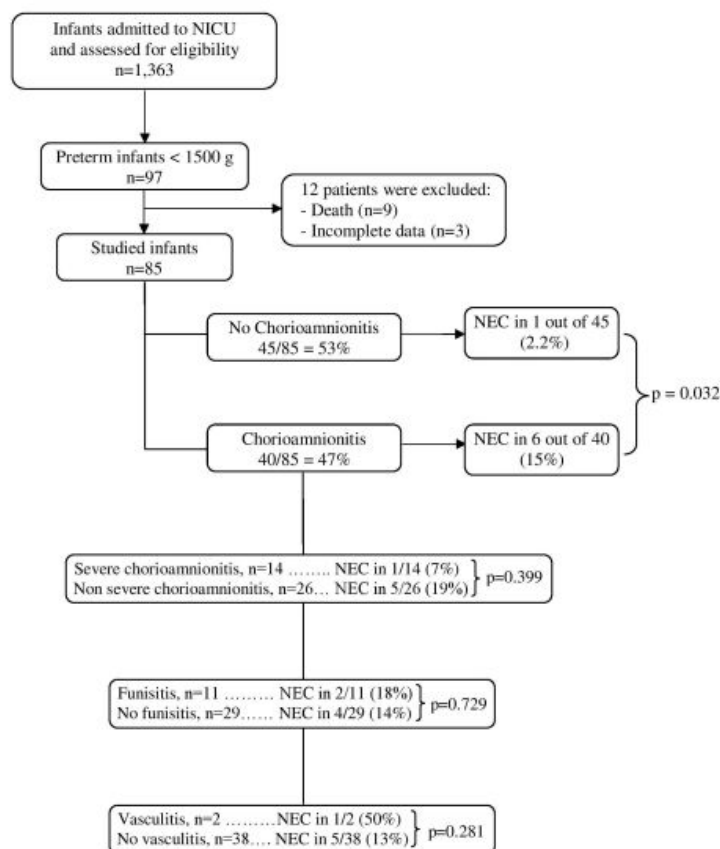
Out of the 85 preterm infants included in the study, chorioamnionitis on placental pathology was present in 40 infants (47%) with the other 45 infants (53%) had no chorioamnionitis (Figure 1). Comparison in demographic and clinical characteristics between chorioamnionitis and non-chorioamnionitis groups revealed no significant difference in birth weight, gender, race, antenatal steroids, delivery room resuscitation, PDA, or early onset sepsis ($p>0.05$).

Higher incidence of NEC was found in infants with chorioamnionitis (6/40 = 15%) compared to 1/45 (2.2%) in non-chorioamnionitis group, $p=0.032$. Therefore, chorioamnionitis was significantly associated with development of NEC.

There was no significant relationship between specific pathologic findings (such as severity of chorioamnionitis, presence of funisitis, or vasculitis) and NEC, among the 40 infants in chorioamnionitis group. NEC developed in 1 patient out of 14 with severe chorioamnionitis (7%), compared to 5 patients out of 26 with non-severe chorioamnionitis (19%), $p=0.399$. In addition, NEC developed in 2 out of 11 patients with funisitis (18%) compared to 4 out of 29 with no funisitis (14%), $p=0.729$; and in 1 out of 2 patients with vasculitis (50%) compared to 5 out of 38 with no vasculitis (13%), $p=0.281$.

Conclusion: Our study suggests that preterm infants born <1500 g with chorioamnionitis on placental pathology have increased risk of NEC; therefore, any preterm infant with chorioamnionitis should be monitored closely for development of NEC.

Flowchart for association of abnormal placental pathology and necrotizing enterocolitis (NEC) in preterm infants < 1500 grams, admitted to NICU from Jan 2014 to Apr 2017



675 REFINING A MODEL FOR HIGH-THROUGHPUT SCREENING OF INTESTINAL PERMEABILITY: TNF α IMPACT ON CaCo2 PERMEABILITY IS DEPENDENT ON CULTURE

TIME. Thomas Wallach¹, Zev Gartner². ¹*Pediatric Gastroenterology, University of California San Francisco, San Francisco, CA*; ²*Pharmaceutical Chemistry, University of California San Francisco, San Francisco, CA*

Background: Environmental enteric dysfunction (EED), a condition potentially driving the majority of stunting in the developing world, is hypothesized to be driven by chronic exposure to enteric infection. Increases in intestinal permeability has been implicated in the pathophysiology of EED, presumably as a consequence of chronic infection. We seek an in vitro model of intestinal permeability suitable for high throughput screening that will allow rapid identification of substances that modify intestinal permeability. Towards such a model, we explored the effects of TNF α on intestinal epithelial monolayer permeability. TNF α is an inflammatory mediator that is released as a response to a wide spectrum of intestinal infections. In our preliminary studies, exposure of CaCo2 gut epithelial monolayers to TNF α alters monolayer permeability, presumably through activation of NF- κ B and Caspase-8 dependent apoptotic pathways. Thus, changes in gut epithelial permeability upon TNF α exposure may represent a model for chronic exposure to enteric infections.

Methods: Caco2 cells were obtained from the central cell culture facility at UCSF. Passage numbers 24-30 were used to create monolayers on 0.4 μ m transwells, allowing for measurement of transepithelial electrical resistance (TEER) and for assessment of transmembrane flux of fluorescent dyes. Monolayers were evaluated for TEER at early (2 weeks) and late culture times (4 weeks). Further assessment with confocal microscopy will identify changes to cell structure, including mislocalization of ZO1, e-cadherin and other tight junction complexes. Cholera toxin, an agent that acts on the epithelium specifically through the activation of an adenylate cyclase, was also evaluated in the model as a positive control.

Results: Cholera Toxin reproducibly generated decreases in TEER at both 2 week and 4 week time points. However, the consequences of TNF α exposure to CaCo2 monolayer permeability was strongly associated with culture time. Use of traditional pharmaceutical guidelines for CaCo2 permeability studies (4-week culture time) showed only a modest decrease in TEER upon 48 hr exposure to TNF α . However, 2-week culture times showed significant impact on CaCo2 monolayer permeability after 48 hr exposure to TNF α , suggesting key parameters for further development of a high-throughput screen.

Conclusions: Our results demonstrate that total culture time is key parameter affecting measurements of epithelial permeability after TNF α exposure. Future studies will utilize this model for further development of the high throughput screen.

NUTRITION

***677 QUALITY IMPROVEMENT INITIATIVE TO DEVELOP A NEW ALGORITHM FOR MANAGEMENT OF FEVER IN CHILDREN WITH INTESTINAL FAILURE AND A CENTRAL**

LINE. Jennifer Damman, Danielle Barnes, Colleen Nespor, John Kerner, Rachel Bensen. *Pediatric Gastroenterology, Lucile Packard Children's Hospital, Stanford, Palo Alto, CA*

Purpose: Patients with intestinal failure (IF) are at increased risk of bacteremia and sepsis, particularly those with indwelling central venous catheters (CVC). There is a particularly increased risk of infection with gram negative (GN) organisms due to abnormal gut anatomy and small bowel bacterial overgrowth. Standard of care for pediatric IF patients with CVC and fever at our large quaternary children's hospital has been a 48-hour hospitalization and broad spectrum gram positive and GN antibiotic coverage with vancomycin and ceftazidime. Exposure to broad spectrum antibiotics can cause adverse effects such as diarrhea, hypoglycemia with interruption of parenteral nutrition, and development of antibiotic resistance. Selection of antibiotics is crucial to promptly treat impending sepsis, reduce infectious complications, and shorten the length of hospitalization. The purpose of this quality improvement initiative is to develop an algorithm for rapid detection and treatment of sepsis with targeted antibiotic therapy in IF patients with central line and fever. The goal is to provide an approach that is standardized, evidence-based, and optimized to the specific organisms in our patient population in order to improve outcomes and reduce costs.

Methods: We retrospectively reviewed the data in IF patients with CVC and fever from January 2014 – March 2016. Data included antibiotics used and blood culture results, including organism and sensitivity. Inclusion criteria was all IF patients with indwelling CVC who were <18 years of age with fever >38.0°C in previous 24 hours. Exclusion criteria was any recent positive blood culture that had not been fully treated. Physicians from the pediatric divisions of GI, critical care, emergency department, and infectious disease created an algorithm based on this clinical data that is available from any web browser via the CurbSideUp.org program. Based on our data, we implemented a change to our antibiotic algorithm in June 2016, which replaced ceftazidime with ceftriaxone. In June of 2017 we then reviewed our outcomes after this implementation. Though not

yet implemented, we also created an algorithm for observation without antibiotics in a small subset of IF patients with CVC and fever who are otherwise well appearing with normal vital signs, laboratory studies, and an alternate source of infection.

Results: A total of 180 cases were identified with hospitalization for fever in an IF patient with a CVC. Ninety-two (51%) had a positive blood culture. Of these positive cultures, 52 grew gram positive organisms, 35 grew GN organisms, and 8 grew yeast. Of the 35 GN isolates (see figure 1), 19 were SPACE organisms (*Serratia*, *Pseudomonas*, *Acinetobacter*, *Citrobacter*, and *Enterobacter*). Of the 19 SPACE organisms, 7 were *inadequately* covered by ceftazidime, but would have been covered by the broader antibiotic cefepime. The remaining 10 SPACE organisms were sensitive to all cephalosporins. Of the 16 non-SPACE organisms, 14 were sensitive to all cephalosporins. We found that ceftazidime provided no benefit over the narrower antibiotic ceftriaxone in patients who grew non-SPACE organisms, and of those patients who grew SPACE organisms, many that were inadequately covered by ceftazidime would be more appropriately covered with cefepime. Therefore, we concluded that for IF patients with no history of high-risk isolates in last 3 months, empiric coverage for GN organisms could be narrowed to ceftriaxone, with the ease of single daily dosing, and for those who had a history of high-risk isolates in previous 3 months, empiric coverage should be broadened to cefepime. We implemented this change in June 2017. Data one year later revealed 38 cases of a positive blood culture, and 31 out of 38 were empirically narrowed to ceftriaxone. There were no patients who grew an organism that was resistant to ceftriaxone but that would have been covered by ceftazidime. We also found that none of the patients who had a positive blood culture would have met criteria for observation without antibiotics based on our algorithm.

Conclusions: Our experience demonstrates continued high risk of bacteremia in children with IF and CVCs. A quality improvement approach can be used to standardize and optimize treatment for these high risk patients. Future plans include tracking use of CurbSideUp in the ED, targeted education to increase its use, as well as implementation of observation without antibiotics in a small subset of well appearing patients with CVC and fever who are otherwise well appearing with normal vital signs, laboratory studies, and an alternate source of infection.

678 EFFECT OF PARENT AND CHILD EXECUTIVE FUNCTION ON CHILD CALORIC CONSUMPTION DURING A SNACKING PARADIGM. Lourdes Herrera¹, Jessie Bowers¹, Kerri Boutelle^{1,2}, David Strong³, Kyung Rhee¹. ¹*Pediatrics, University of California San Diego, San Diego, CA*; ²*Psychiatry, University of California San Diego, San Diego, CA*; ³*Department of Family Medicine & Public Health Institute, University of California San Diego, San Diego, CA*

Background: Executive functioning (EF) refers to self-regulatory cognitive processes (e.g., inhibitory control, working memory, and cognitive flexibility) involved in monitoring and controlling thoughts and goal directed behaviors. Poor EF is associated with greater consumption of snack foods among children and adults. The impact of parent EF on child consumption of snack foods has not been examined. This relationship is critical as early child eating behaviors are influenced by parent behaviors, and can persist into adulthood with long-term implications for weight status.

Objective: To examine the effect of parent and child EF on child caloric intake of high energy density snack foods measured by the Eating in the Absence of Hunger (EAH) paradigm.

Methods: Children between the age of 4-6 years old were recruited to participate in the *CHild Inhibitory Control (CHIC) Play Study* (n=89). Baseline child EF was assessed using the Behavior Rating Inventory of Executive Function (BRIEF). Parent impulsivity was assessed using the UPPS Impulsive Behavior scale. Primary outcomes of interest were percent of adjusted daily caloric requirement consumed by the child during the EAH paradigm (%EAH) and percent of calories consumed from sweet and salty snack foods (%EAHSweet, %EAHSalty). Only baseline data was used for analysis. Pearson correlations and general linear models were conducted using SAS v9.4

Results: The sample included 54% males, mean age 61 months (SE 9.1), 24% white, 43% Hispanic, mean child BMI percentile 56.4 (S.E. 33.2). Parent median annual income was \$60,000; 54% had a college degree. Several aspects of child executive functioning were highly correlated with %EAH and %EAHSweet, but not %EAHSalty (Table 1). Lack of parent premeditation was also associated with %EAH and %EAHSweet (Table 1). In the multivariable analysis controlling for covariates, child Global Executive Functioning continued to be associated with child %EAH (B=-0.12, p=.02) and %EAHSweet (B=-0.14, p<0.01), but not %EAHSalty.

Conclusion: Both parent and child EF are associated with the percent of daily caloric requirement consumed by the child during the EAH paradigm. However, child EF is more strongly associated with caloric intake than parent EF, and is particularly driven by the consumption of sweet high energy density snack foods. Efforts to improve child EF may help to decrease excessive caloric intake from sweets and decrease the risk for childhood obesity.

Table 1: Correlation between child/parent Executive Functioning and percent of daily caloric requirement consumed during the EAH paradigm (%EAH) and percent of calories consumed from sweet snack foods (%EAHSweet) and salty snack foods (%EAHSalty)

	%EAH		%EAHSweet		%EAHSalty	
	r	p-value	r	p-value	r	p-value
Child Executive Functions	-0.24	0.06	-0.27	0.03	-0.07	0.59
Inhibitory control	-0.26	0.03	-0.26	0.04	-0.13	0.30
Ability to Shift	-0.18	0.15	-0.18	0.16	-0.09	0.47
Emotional control	-0.27	0.03	-0.28	0.03	-0.10	0.41
Working memory	-0.27	0.03	-0.30	0.02	-0.09	0.51
Plan/organize	-0.31	0.01	-0.33	0.001	-0.12	0.35
Global Executive Functioning score						
Parent Impulsivity Lack of premeditation	-0.29	0.01	-0.35	<0.01	-0.14	0.24

679 THE BREAST MILK SODIUM TO POTASSIUM RATIO IS PREDICTIVE MARKER OF BREASTMILK STATUS FOR PRETERM MOTHERS. Masahiko Murase², Youko Satou¹, Misato Hatuno².
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Background: Milk sodium concentration is a marker of tight junction closure between mammary epithelial cells. The breast milk sodium to potassium ratio (Na:K) dramatically declines in parallel with whole transcriptome changes in mammary gene expression as lactation progresses through colostrum, transitional, and mature milk production stages. Thus, milk Na:K is an objective biomarker of mammary gland progress toward mammary gland maturation. The trends of Na:K was shown for the mothers of term infants, but not for the mothers of preterm infants. Previous reports categorize lactation stage for milk collected as “colostrum” if Na:K \geq 2.0, as “transitional” if Na:K \geq 0.6 and $<$ 2.0 and as “mature” if Na:K $<$ 0.6.

The aims of this analysis was to characterize Na:K trends in mothers of preterm infants, and whether Na:K is a predictive marker of breastfeeding status. If Na:K is a predictive marker, we aimed to further analyze maternal, infant, and milk expression variables predicted by Na:K.

Methods: A prospective cohort was recruited from Showa University Hospital, Tokyo, Japan. This study enrolled mothers who delivered at $<$ 35 weeks gestation. We analyzed breast milk content using human milk analyzer (HMA, Miris, Sweden). Single regression test was used between human milk content and Na:K. The Wilcoxon rank-sum test was used for two-way comparisons. Three-way comparisons were performed by the Kruskal-Wallis test for non-normal data. A p-value $<$.05 was significant. This study was approved by the Showa University Hospital Institutional Review Board.

Results: Thirty eight mother-infant dyads were enrolled this study. Median gestational age and birth weight (25th, 75th) were 33.4 (31.0, 34.1) weeks and 1666 (1127, 1953) gm, respectively. We collected 35 milk samples each on postpartum days 3 and 7, and 28 samples on day 14. Median Na:K (25th, 75th) was 1.2 (0.9, 1.6), 0.8 (0.6, 1.0), and 0.9 (0.7, 1.2) at day 3, 7, and 14 postpartum, respectively. Significant differences were observed among study groups for Na:K ($p <$ 0.01). Na:K on day 3 was significantly higher than Na:K on day 7 ($p <$ 0.01) and day 14 ($p <$ 0.01). On postpartum day 3, 14 % samples were colostrum and 86 % samples were transitional; on postpartum day 7, 9% samples were colostrum, 77% samples were transitional and 14% samples were mature; On postpartum day 14, and all samples were transitional. Milk content and Na:K were not correlated on day 3,7, and 14 postpartum. Exclusively breastfeeding mothers on day 28 had significantly lower Na:K on day 14 than non-exclusively breastfeeding mothers on day 28 ($p =$ 0.047). However, maternal, infant, and milk expression variables did not predict Na:K.

Discussion: The mammary gland was significantly matured from day 3 to 7, but did not mature from day 7 to 14. Mothers of preterm infants have difficulty establishing and sustaining lactation compared to mothers of term infants. This could be related to difficulty of mammary gland maturation. Since breast milk content is not correlated with Na:K, milk production was not correlated with mammary gland maturation. Na:K on day 14 was predictive of breastfeeding status on day 28. This work was supported by Morinaga Foundation for Health & Nutrition.

680 ELECTRIC BIOIMPEDANCE REVEALS VARIATIONS IN BODY COMPOSITION IN CHILDREN AND ADOLESCENTS WITH CYSTIC FIBROSIS DURING HOSPITAL ADMISSION. Matias Epifanio^{1,2}, Aline dos Santos Sampaio², Vera Bosa³, Paulo Marostica³, Luiza Preto², Sabrina Fernandes⁴, Caroline a Abud Drummond Costa², Rita Mattiello². ¹Pediatric Gastroenterologist, Hospital Santo Antonio, Porto Alegre, Rio Grande do Sul, Brazil; ²Pontificia Universidade Católica do Rio Grande do Sul, Porto Alegre, RS, Brazil; ³Universidade Federal do Rio Grande do Sul, Porto Alegre, Brasil, Porto Alegre, RS, Brazil; ⁴Centro Metodista IPA, Porto Alegre, Brazil

Introduction: Structural abnormalities in the Cystic fibrosis transmembrane conductance regulator protein causes clinical symptoms in several organs and organ systems in patients with cystic fibrosis (CF), which mainly include respiratory and gastrointestinal changes. As a consequence of these changes, patients with CF usually display nutrient malabsorption, low-caloric intake, and increased energy expenditures. This results in a significant nutritional impairment. Respiratory exacerbations frequently occur in these patients, and many require hospital admission, which risks nutritional deterioration. Several treatment strategies have been offered to improve pulmonary and nutritional status. With respect to nutritional therapy during hospitalization, there is a consensus that patients should receive a hypercaloric diet with adequate replacement of pancreatic enzymes. Energy supplements should also be used to facilitate weight gain. Intervention studies suggest that the accumulation of lean mass is associated with the preservation of lung function in CF patients. Meanwhile, the loss of lean mass has been associated with increased severity of the disease, decreased lung function, respiratory muscle weakness, and increased systemic inflammation.

Therefore, aggressive nutritional support aims to achieve normal growth patterns and should lead to the maintenance of lung function. However, there is a paucity of evidence evaluating the effectiveness of the nutritional therapy recommended to inpatients. The few studies that evaluated weight gain included a limited number of participants a large age group, and it did not assess weight gain with an emphasis on body mass change as the main outcome. Therefore, the objective of this study is to evaluate the variations in body weight and composition by means of electric bioimpedance in children and adolescents diagnosed with cystic fibrosis. These patients received a high-calorie diet during hospitalization for pulmonary exacerbation.

Materials/Methods: This was a longitudinal study involving children and adolescents with cystic fibrosis, who were being followed up by the Multidisciplinary Cystic Fibrosis Team at São Lucas Hospital of PUCRS in Porto Alegre, Brazil. We included patients with a confirmed diagnosis of CF, who underwent hospital admission because of pulmonary exacerbation. The nutritional evaluation of the patients occurred at two timepoints: once during the first 24 hours of hospitalization and again 24 hours before discharge. In each case, weight and height were measured after an electrical bioimpedance analysis. The caloric intake was evaluated by describing the foods consumed using a food registry for 3 consecutive days from day 7 of hospitalization. Pulmonary function tests were performed at the time of the initial hospitalization by individuals trained according with the American Thoracic Society standards. The spirometry parameters were evaluated also.

Results: The sample consisted of 23 patients. Of these 10/23 (43.4%) were male. The mean age was 11.9 ± 3.8 years, and 9/23 (39.0%) had undergone gastrostomy. The mean length of hospital stay was 12.9 ± 3.9 days. The patients had in average moderate pulmonary compromise according to the ATS ERS classification. The results of dietary intake showed that food consumption was categorized as a hypercaloric diet.

Tables shows variations in the anthropometric parameters and body composition variables. These findings showed that there was a significant change in the means of the following variables in the patients: weight, BMI (z-score), percentage of lean mass, and percentage of fat mass.

Discussion: We found that during the hospital stay, a hypercaloric diet correlated with a significant increase in weight, BMI, and the percentage of fat mass. Meanwhile, this diet correlated with a decrease in the percentage of lean mass. It is possible that the significant gain in BMI weight and z-scores in the patients resulted from a greater caloric intake and the restriction in physical activity during hospitalization.

The observed decrease in lean mass and the increase in fat mass illustrate the importance of reviewing nutritional interventions in patients during hospitalization. The increase in fat mass and the loss of lean mass in patients with adequate nutritional status could cause harm to the health of these individuals. The loss of lean mass may have been associated with the extended time restricted to bed-rest. This emphasizes the importance of maintaining physical activity, even during hospitalization. The results of the present study show the importance of evaluating body composition and tailoring nutritional interventions to CF patients over the course of treatment.

Conclusions: In conclusion, a hypercaloric and hyperlipidic diet during hospitalization resulted in significant weight gain, a decrease in lean mass, and an increase in the percentage of fat mass in CF patients.

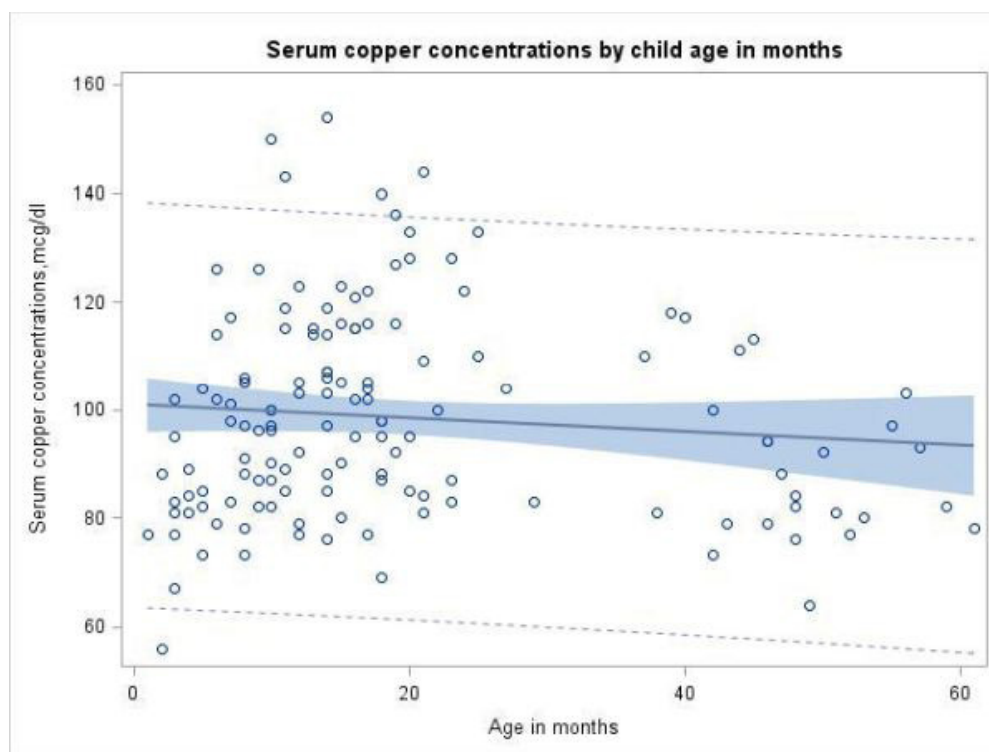
681 RISK FACTORS FOR COPPER DEFICIENCY IN PEDIATRIC INTESTINAL FAILURE PATIENTS RECEIVING PARENTERAL NUTRITION: A LONGITUDINAL ANALYSIS. Megan McGivney², Danielle Stamm², Enju Liu^{1,3}, Andrea Hale³, Kathleen Gura^{2,4}, Christopher Duggan^{1,2}. ¹Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA; ²Center for Advanced Intestinal Rehabilitation, Boston Children's Hospital, Boston, MA; ³Institutional Centers for Clinical and Translational Research, Boston Children's Hospital, Boston, MA; ⁴Pharmacy, Boston Children's Hospital, Boston, MA

Background: Copper deficiency is associated with neutropenia, anemia and osseous abnormalities, but there are limited data on its prevalence in children with intestinal failure (IF). We sought to prospectively determine the frequency of copper deficiency in this population and identify associated risk factors.

Methods: Following IRB approval, clinical, nutritional and laboratory data were prospectively collected every 2 months for 1 year or until parenteral nutrition (PN) discontinuation. All patients had IF and were PN dependent for ≥ 30 consecutive days. Copper deficiency was defined as a serum copper < 85 mcg/dl. Generalized estimating equations (GEE) for a binary outcome with the log link function and exchangeable working correlation structure were used to identify risk factors of copper deficiency.

Results: Twenty one patients (14 female, 7 male) were enrolled at mean (SD) age 14.4 (14.9) months. Mean (SD) PN duration was 366 (421) days. Over the course of the study, 15/21 subjects had low copper levels, for an overall prevalence of 71.4%. Mean (SD) IV copper intake among deficient patients was 20.3 (14.8) mcg/kg/d versus 21 (16.9) in non-deficient patients ($p = 0.93$). Univariate analysis identified age in months as positively associated with copper deficiency RR 1.02 (1.00 - 1.03) ($p = 0.03$) but not sex, birth weight, duration of PN or C-reactive protein level. Multivariate analysis identified only IF diagnosis of necrotizing enterocolitis as protective for the development of copper deficiency (RR 0.27 (0.08, 0.88) ($p=0.03$)), taking into consideration age, ethnicity and other IF diagnoses.

Conclusions: Copper deficiency is very common in children with IF, affecting more than 70% of our cohort. The risk for copper deficiency may increase with age and may be lower in children with a primary diagnosis of necrotizing enterocolitis. Because of the high prevalence and limited risk factors for copper deficiency, biochemical monitoring of copper status is indicated in all children with IF.



682 EVALUATION OF THE EFFECT OF PALM OLEIN FREE FORMULA ON INTESTINAL FLORA AND GASTROINTESTINAL TOLERANCE IN INFANTS. Merih Cetinkaya¹, Seda Yilmaz Semerci^{1,2}, Osman Ugurel², Dilek Turgut Balik². ¹Neonatology, Kanuni Sultan Suleyman Training and Research Center, Istanbul, Turkey; ²Bioengineering, Yildiz Technical University, Faculty of Chemical and Metallurgical Engineering, Istanbul, Turkey

Introduction: Palm olein oil has been used in some infant formulas to match the fatty acid profile of the human milk. Although some detrimental effects associated with palm olein oil usage in infant formulas including decreased intestinal fat, palmitic and calcium absorption were reported, there is very limited data about the effects of palm oil free (POF) formula on microbiota and development. The aim of this study was to evaluate the effect of POF formula use on intestinal microbiota, growth, gastrointestinal tolerance and calcium-phosphorus metabolism and compare it with both palm olein containing (POC) formula and mother milk.

Material/Methods: This prospective study was performed on healthy term infants who were either breastfed or formula fed. The infants randomized into three groups: group 1 breastfed (BF) infants (n=30), group 2 (n=30) infants fed with POF formula, and group 3 (n=30) infants fed with POC formulas. The maternal and neonatal demographics, follow-up weight, length, head circumference and laboratory data of infants were all recorded. Serum calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), parathyroid hormone (PTH) and blood urea nitrogen (BUN) were evaluated at the 5th and 42th day of life. Stool samples were also collected at enrollment and postnatal week 6. All stool samples were assessed with real time q-PCR for quantification of total bacteria and intestinal bacterial population, such as *Bifidobacterium*, *Lactobacillus*, *Bacteroides*, *Firmicutes* to determine impact of feeding on infant intestinal flora.

Also caregivers completed a diary for the description of stool frequency, stool consistency, colic attacks, diaper dermatitis, feeding intolerance and regurgitation throughout the study.

Results: A total of 90 infants were enrolled to the study. There were no significant differences between three groups in terms of demographic features. Final body weight and height values were statistically significantly higher in POF and POC formula infants compared with BF infants ($p<0.05$). Stool frequency, stool consistency, colic attacks, diaper dermatitis, feeding intolerance and regurgitation were statistically significantly better in BF infants than formula groups ($p<0.05$). Although initial biochemical analyses were similar in 3 groups, both Ca and P levels were significantly higher in the POF infants after formula usage ($p<0.05$). The quantity of DNA copies of *Bifidobacterium*, *Lactobacillus*, *Bacteroides*, and *Firmicutes* were not found to be statistically significantly different between the first and final samples of POF and POC formula infants (all $p>0.05$). DNA copy of *Lactobacillus* was found to be statistically significantly different between the first and final samples of BF infants ($p=0.031$).

Conclusion: POF formula usage was associated with higher Ca and P levels, decreased feeding intolerance, regurgitation and colic. Both POF and POC formulas did not have an impact on intestinal bacterial colonization such as mother milk. However, more studies including larger number of infants and long duration of follow-up are required to evaluate the role of POF on neonatal intestinal flora.

683 **THE ROLE OF AUTOPHAGY IN INTESTINAL BARRIER DYSFUNCTION IN A MOUSE MODEL OF SEVERE MALNUTRITION.** Nathan Swain^{1,2}, Marjon Feenstra², Lijun Chi², Ling Zhang², Robert Bandsma^{1,2}.

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Background: Severe malnutrition remains pervasive in developing countries and is the largest risk factor for death in children under 5 years-of-age. Enteric dysfunction is known to be associated with severe malnutrition, but its pathophysiology is poorly understood. Studies indicate malnutrition can lead to a loss of intestinal barrier integrity, and increased intestinal permeability. We generated evidence suggesting that dysregulated autophagy, a cellular recycling mechanism, contributes to the pathophysiology of severe malnutrition. The role of autophagy in intestinal integrity has not been studied in malnutrition.

Objectives: (1) To characterize an intestinal phenotype in a novel murine model of severe malnutrition. (2) To determine if modulating autophagy affects intestinal barrier integrity in malnutrition.

Methods: Severe malnutrition was induced in male weanling C57Bl6 mice through a protein deficient diet (1% protein) and compared to mice fed a control diet (18% protein). Autophagy was stimulated using daily intraperitoneal injections of rapamycin. After two weeks, mice were sacrificed and intestinal tissue was collected and histological, protein and RNA analysis were completed for the three groups.

Results: Malnourished mice showed a significant weight loss over time (18%: 18.8±0.59g vs 1%: 8.76±0.14g, $P<0.001$) accompanied by a significant decrease in villous height in the small intestine (jejunum; 18%: 429.13±16.25 vs 1%: 283.97±7.07µm, ileum; 18%: 310.55±19.06 vs 1%: 196.66±8.37µm $P<0.001$) A significant decrease in crypt depth (18%: 135.30±5.95 vs 1%: 81.77±9.39 µm, $P<0.001$), along with a significant loss of goblet cell density (18%: 7.33±0.52 vs 1%: 4.80±0.19 Goblet cell/crypt, $P<0.001$) were observed in the colon of malnourished mice. Additionally, malnourished mice had increased intestinal permeability assessed via FITC-dextran uptake. Induction of autophagy with rapamycin (RAP) treatment restored the increase in intestinal permeability (18%: 5.76± 1.15 vs 1%: 10.86±1.99 vs RAP: 4.72±0.91 µg/ml FITC in serum, $P<0.05$). The malnourished mice had an increase in pore-forming tight junction Claudin 2 protein expression, and rapamycin treatment restored these to control levels.

Significance: This study will help characterize intestinal pathology associated with severe malnutrition, and potentially identify new targets for intervention.

Conclusions: Our model of malnutrition mimics many of the phenotypic changes in intestinal biology as seen in limited human data, and modulating autophagy through rapamycin treatment has a mitigating effect on the intestinal dysfunction observed.

684 CHANGES IN DIETARY INTAKE WITH IVACAFTOR TREATMENT IN ITALIAN AND NORTH AMERICAN SUBJECTS WITH CYSTIC FIBROSIS. Nina Sainath¹, Joan Schall¹, Megan Oberle¹, Carolyn Mcanlis¹, Olivia Hess², Chiara Bertolaso³, Virginia Stallings^{1,4}. ¹Gastroenterology, Children's Hospital of Philadelphia, Philadelphia, PA; ²University of Pennsylvania, Philadelphia, PA; ³Universita La Sapienza-Policlinico, Rome, Italy; ⁴Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

Background: Treatment with ivacaftor for CFTR gating mutations results in improved weight, pulmonary function, growth status, and quality of life, and also in reduced resting energy expenditure and gut inflammation. The potential impact of ivacaftor treatment on dietary intake patterns has not previously been explored.

Aim: To assess dietary intake in subjects with CF and at least one gating mutation before and after 3 months of ivacaftor treatment. To compare the dietary response to ivacaftor in Italian (IT) subjects compared to North American (NA) subjects.

Methods: Subjects (≥5 yrs old) with one or more CFTR gating mutations were recruited from the USA, Canada and Italy. Weight and FEV1 % predicted were assessed. Dietary intake was determined by analysis of three day weighed food records. Calorie and macronutrient content were averaged over the three days. Dietary intake for NA subjects was analyzed using Nutrition Data System for Research software version 2012 and using the MetaDieta software for IT subjects. Dietary data was missing for one NA subject.

Results: Twenty-three participants, n=15 IT subjects (18.2±9.0 years, 73% female, 100% Caucasian, 73% pancreatic insufficient) and n=8 NA subjects (15.6±19.0 years, 37% female, 75% Caucasian, 75% pancreatic insufficient) completed the study. At baseline, there were no significant differences in macronutrient content between IT and NA subjects. After ivacaftor, there was a significant increase in fat intake (+11 g/d, p=0.05) in the combined sample, and IT subjects had a significant increase in both energy (+338 kcal/d) and fat intake (+16 g/d). No other significant changes in macronutrient intake were noted. Weight gain was positively correlated with energy intake (r=0.42, p=0.05) and fat intake (r=0.59, p=0.004) overall, and the association was stronger in the IT group for fat intake (r=0.72, p=0.002).

Conclusion: Treatment with ivacaftor resulted in increased dietary fat intake, possibly related to the recommendation that ivacaftor be taken with high fat food twice daily. The significant increases in energy and fat intake in the IT group may have contributed to greater improvement in weight and pulmonary outcomes. Further investigation is needed to determine why dietary changes were more evident in Italian subjects with ivacaftor treatment.

	Kcal/d	Kcal, %EER	Fat, g/d	Fat, %kcal	Protein, g/d	Protein, %kcal	CHO, g/d	CHO, %kcal	Weight, kg	FEV1, % predicted
Italian Baseline	2162	90	85	35	82	15	281	49	51	83
Italian Change	338*	13*	16***	2	7	11	44	-1	3***	12***
North American Baseline	1913	97	81	37	66	14	234	49	32	91
North American Change	-66	-5	-1	2	-5	-1	-8	-1	2**	4

*Change significant by student's paired t test within group p<0.001

686 PROVIDERS' PERSPECTIVES OF MANAGEMENT OF PEDIATRIC OBESITY-POTENTIAL BARRIERS AND HOW A CDSS COULD HELP? Saumya Joshi, Quratulain Merchant, Hristos Milonas, Jiliu Xu. Pediatrics, SUNY Downstate, Brooklyn, NY

Background: Almost one-third of children and adolescents in the United States are either overweight or obese. Literature has identified that pediatric obesity guidelines rarely translate to clinical practice, owing to implementation barriers. Computerized Clinical Decision Systems (CDSS) have increasingly been recognized as tools that involve physicians, other health-care professionals, and families in the management of chronic diseases. There is currently no available CDSS specifically designed for management of pediatric obesity.

Objective: The objective of this study was to achieve an in-depth understanding of providers' perspective of the potential barriers to management of pediatric obesity and features they would consider desirable in a CDSS designed for the same.

Methods: Qualitative open-ended interviews were obtained using a convenience sample (n=20) of care providers including pediatricians (9), pediatric residents (9) and pediatric nutritionists (2) at SUNY Downstate and Kings County Hospital. A standard questionnaire was deployed by three different interviewers and coded for emerging themes.

Results: Providers identified five potential barriers; 1) Limited time during the office visit, 2) Parental lack of understanding or denial of pediatric obesity, 3) User unfriendly electronic medical record (EMR) interface, 4) Loss to follow-up and 5) Lack of motivational interviewing and counseling. Providers also gave suggestions on how a CDSS can help overcome these barriers; 1) Flagging with Triage for BMI>85% and parent to be provided with an age-specific core questionnaire about diet and activity while in the waiting room, 2) Review of patient and parent perspective at each visit, and making it a mandatory field, 3) One-Screen Seamless Interface providing checkboxes for all patient parameters, including vitals, growth chart, nursing note, diet history, exercise history, labs, provider note to ensure minimum number of clicks and seamless and quick documentation, 4) Follow-up and referral appointments tracker with the ability to send text or email reminders and an ideal follow-up time of 1-3 months, and 5) Print out of a mutually agreeable simple yet specific plan, which the parent or patient identifies with. This can be in form of a sticker with title “Our Goals” to stress on shared responsibility.

Conclusion: Pediatric obesity care providers have identified the barriers to its management and the features desired in a CDSS to help overcome them. We are designing a CDSS based on the preferences and perspectives found from providers dealing with pediatric obesity, which can be further incorporated as part of the EMR.

689 CURRENT STATUS OF NUTRITIONAL SUPPORT FOR HOSPITALIZED CHILDREN: A NATIONWIDE MULTICENTER SURVEY IN SOUTH KOREA. Seung Kim¹, Eun Hye Lee³, Hye Ran Yang².
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Background: The prevalence of hospital malnutrition in children ranges between 15% and 30%. Although the consequences of hospital malnutrition are enormous, it is often unrecognized and not treated. The aim of this study was to identify the current status of in-hospital nutrition support for children in Korea by carrying out a nationwide survey.

Methods: Out of 344 general and tertiary hospitals in South Korea, a total 53 institutes having pediatric gastroenterologist and more than 10 pediatric inpatients were selected. The questionnaire was developed by the nutrition committee of Korean Society of Pediatric Gastroenterology, Hepatology and Nutrition. The questionnaires were sent to pediatric gastroenterologists in each hospital. Survey was performed by e-mails, and some incomplete answers were asked on telephone.

Results: Forty hospitals (75.5%) responded to the survey; 23 of them were tertiary hospitals, and 17 of them were general hospitals. Only in 21 hospitals (52.5%), all required personnel including pediatrician, nutritionist, pharmacist, and nurse were assigned to nutrition support of hospitalized pediatric patients. Routine nutritional screening was performed only in 21 (52.5%) hospitals at admission, which was lower than those in adult patients (62.5%). Nutrition screening tools varied among hospitals, and 33 of 40 (82.5%) hospitals were using their own screening tools. The most frequently used nutritional assessment parameters were weight, height, hemoglobin, and serum albumin levels. In our nationwide survey, the most frequently reported main barriers of nutritional support in hospital were the lack of manpower and excessive work load; and the second barrier was insufficient knowledge and experiences.

Conclusions: Although this nationwide multicenter survey was performed targeting at general and tertiary hospitals with pediatric gastroenterologists, manpower and medical resources for nutritional support were still insufficient for hospitalized children and standardized nutritional screening stools were not still routinely used in Korea. For appropriate nutritional management of hospitalized pediatric patients, more attention to the hospital malnutrition and additional national policies for nutritional support in hospital are needed.

691 VARIATIONS IN ENTERAL NUTRITIONAL PRACTICES AND GROWTH OUTCOMES FOR VERY LOW BIRTH WEIGHT INFANTS IN TWO TERTIARY NEONATAL INTENSIVE CARE UNITS. Tanyaporn Kaenkumchorn¹, Jacqueline Razzaghy², Myla Ebeling², Paula Meier¹, Kousiki Patra¹, Aloka Patel¹, Sarah Taylor². ¹Pediatrics, Rush Children’s Hospital, Chicago, IL; ²Pediatrics, Medical University of South Carolina, Charleston, SC

Background: Previous studies have focused on early parenteral and enteral nutritional practices, but little attention has been given to enteral nutrition in convalescing very low birth weight (VLBW) infants in the neonatal intensive care unit (NICU) prior to discharge and its potential impact on long-term growth. As VLBW infants near NICU discharge, Rush University Children’s Hospital (RUSH) transitions to unfortified mother’s milk (MM) on average at 34 weeks corrected age (CA) while Medical University of South Carolina (MUSC) maintains increased nutritional density until 42 weeks CA. Feeding unfortified MM protects MM integrity and avoids fortification cost and potential errors.

Objective: To describe differences in enteral nutritional practices employed at two high human milk feeding NICUs in convalescing VLBW infants during the period from starting oral feedings to NICU discharge, and to compare growth outcomes prior to discharge and at follow up visits.

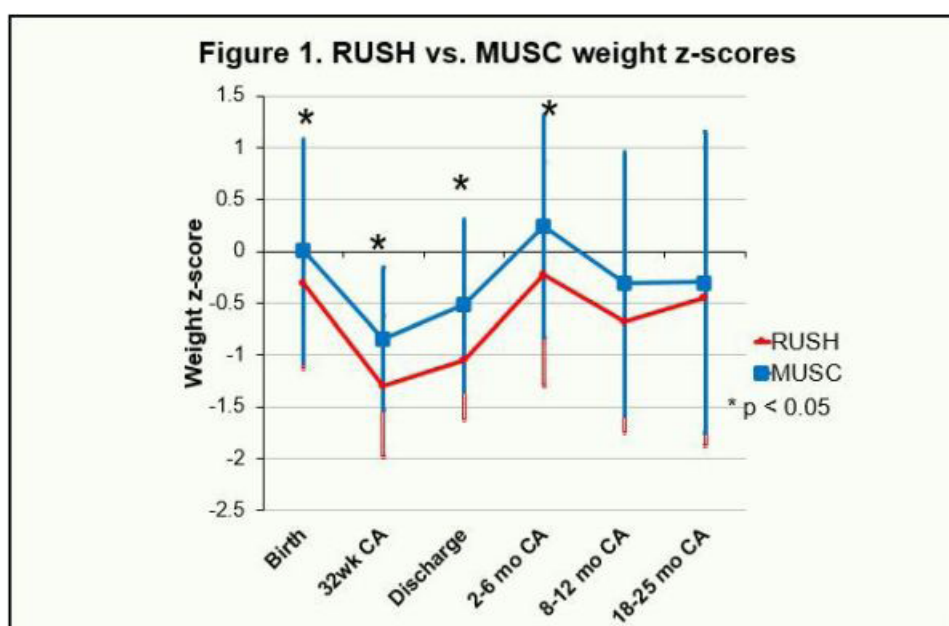
Design/Methods: In a secondary analysis of prospectively collected data, research databases at two tertiary NICUs were queried for growth, nutrition, and demographic data for appropriate for gestational age VLBW infants from 32 weeks to 42 weeks CA as well as after discharge. Daily mean enteral volume, energy, and protein intake normalized to weight (kg) were calculated for the last 14 days of hospitalization. Intake was based on assumed energy/protein content of MM for all subjects. Z-scores were calculated using the appropriate comparison chart for age (Fenton or WHO). Outcomes were compared by t-test and linear regression. Analysis was completed via SAS version 4.9.

Results: RUSH infants had significantly lower z-scores for weight at birth and 32 weeks. Although their intake volume was significantly higher than MUSC, there were no differences in energy or protein intake, likely due to more nutritionally dense feedings at MUSC. Z-scores for weight at 2-6 months were significantly associated with z-scores for weight at 32 weeks, being born at MUSC, and total volume of intake in the 2 weeks prior to discharge. Weight z-scores at 8-12 months CA and 18-25 months CA were significantly associated with z-score at 32 weeks.

Conclusions: When comparing nutritional intake in convalescing infants at RUSH and MUSC, there was a significant difference in volume intake but not in energy or protein intake, likely due to more nutritionally dense feedings at MUSC. Weight z-scores at 2-6 months CA, 8-12 months CA, and 18-25 months CA were significantly associated with weight z-score at 32 weeks. This may indicate that early nutritional practices have a more profound effect on long-term outcomes. Our data suggests that the most critical time period for MM fortification to support growth and neurodevelopment is early in the post-natal course. The convalescing infant taking MM may be able to increase volume to receive adequate nutrition in this stage of VLBW infant development.

Funding: NIH NR010009, RR021891, RR01070
Significant predictors of long-term growth (weight z-scores)

	2-6 month	8-12 month	18-25 month
Volume (10 mL/kg/day)	0.2	NS	NS
Energy (kcal/kg/day)	NS	NS	NS
Protein (g/kg/day)	NS	NS	NS
32 week weight z-score	0.65	0.59	0.35
MUSC site	0.61	NS	NS



692 NUTRITIONAL COST OF NECROTIZING ENTEROCOLITIS AMONG PRETERM INFANTS IN THE NEONATAL INTENSIVE CARE UNIT. *Thu Pham¹, Mridula Sunkara¹, Lea Mallett^{1,2}, Sugianawaty Mulia¹, Ben Barnard¹, Michelle Law¹, Joseph Cantey^{1,2}.* ¹*Pediatrics, Baylor Scott & White Healthcare, Temple, TX;* ²*Pediatrics, Texas A&M Health Science Center, Temple, TX*

Background: Necrotizing enterocolitis (NEC) is a major cause of morbidity and mortality among preterm infants. Bowel rest is a mainstay of NEC therapy. The nutritional status of infants with NEC may be compromised by the inflammation associated with NEC as well as the subsequent discontinuation of enteral feeding and administration of total parenteral nutrition. However, data regarding growth and nutrition losses among infants with NEC are limited.

Objective: To quantify differences in growth, energy intake, and macronutrient intake between infants with and without NEC.

Design/Methods: Retrospective case-control study of infants <36 weeks admitted to the Baylor Scott & White neonatal intensive care unit from January 2014 through November 2016. Cases included all infants with NEC without intestinal perforation (i.e., modified Bell criteria stages I-III). Infants with major congenital anomalies or death before NEC resolution were excluded. For each case, 3 controls were matched on gestational age, birth year, and birth weight. NEC course was defined as the day enteral feeding was held (day 1) through either the day that TPN was discontinued following reestablishment of sufficient enteral feeding or a maximum of 21 days. Kilocalories (kcal), protein, carbohydrate, and fat intake per kg body weight were recorded for each day of the NEC course and the equivalent days of life for controls. The percentage of goal for protein and kcal received, and Δz -score for weight, length and head circumference from birth to 36 weeks post-menstrual age were calculated. Average anthropometric and nutrient intake data were analyzed using t-tests and Wilcoxon Rank Sum tests. Mixed and fixed effects models were fitted to analyze daily nutrient intake.

Results: 23 cases and 69 controls were included in the study. Mean gestational age was 27.4 (± 2.2) weeks, and median birth weight was 959 g (IQR 750-1223). ΔZ -score from birth to 36 weeks for length and head circumference were not different between groups, but ΔZ -score for weight was decreased in cases compared to controls (-1.29 ± 0.54 vs. -0.92 ± 0.61 , $P=0.0139$). Average daily intake of energy and fat and percentage of energy goal met were all decreased in cases compared to controls. Protein and percentage of protein goal met were not different, but carbohydrate intake was higher in cases compared to controls (Table 1). When modeling daily nutrient intake, NEC status was a significant predictor of energy, carbohydrate, and fat intake. The day of NEC course had a significant effect on all nutritional variables.

Conclusions: Infants with NEC had increased risk for growth failure at 36 weeks corrected age compared to controls, and this was accompanied by decreased average daily energy and fat intake and decreased percentage of energy intake goal during the NEC course.

Table 1

Variable	NEC	Control	P-value
Energy (kcal/kg)	86.7 \pm 10.3	108.5 \pm 15.1	< 0.0001
Carbohydrate (g/kg)	13 \pm 1.7	11.5 \pm 1.3	< 0.0001
Fat (g/kg)	2.9 \pm 0.7	5.5 \pm 1.2	< 0.0001
Protein (g/kg)	3.6 (3.4-3.7)	3.8 (3.4-4)	0.0883
Energy goal met (%)	88.3 (80.3-92.5)	94.6 (87.5-99.9)	0.0005
Protein goal met (%)	101.7 (95.6-104.7)	96.8 (85.7-104.9)	0.1368

Values are presented as mean \pm SD for normally distributed data and median (IQR) for non-normal data.

694 SYSTEMATIC REVIEW OF HYPERSENSITIVITY TO PARENTERAL NUTRITION. *Vikram Christian¹, Cassandra Walia², Matthew Tallar¹, Praveen Goday¹.* ¹*Pediatrics, Medical College of Wisconsin, Milwaukee, WI;* ²*Clinical Nutrition, Children's Hospital of Wisconsin, Milwaukee, WI*

Background: The purpose of this review was to critically analyze available data on hypersensitivity to components of PN.

Methods: A systematic review of the literature was conducted and a workgroup was established to critically analyze each relevant article. The findings were summarized and a conclusion was generated.

Results: Twenty-five articles were analyzed. The vast majority were case reports (19), there were four case series, and two other pertinent studies. Sixteen hypersensitivities occurred in children (age range: 4 days – 17 years) while 15 were reported in adults (range: 30 – 55 years). Six of these patients had a personal history of allergy.

Hypersensitivity to PN occurred on day of starting PN in 21 patients and after that time in 10 patients (range: 0-21 days). The components identified as allergens (either suspected or confirmed) were multivitamin preparation (13 patients), intravenous fat emulsion (Intralipid [5 patients], Smoflipid [1 patient]), and amino acid mixture (4 patients). Allergy was narrowed down to a couple of components in 4 patients while the allergen could not be determined in 4 patients.

Allergic rash was the most common manifestation and was seen in 13 patients. Severe reactions (bronchospasm, hypotension, tachycardia) were seen in 13 patients. All except one severe reaction occurred within the first hour of exposure to PN. Other non-life-threatening manifestations were seen in 5 patients.

Conclusion: Hypersensitivity to PN is a rare event and can occur in patients of all ages and irrespective of atopic history. The majority of hypersensitivity reactions occurred at first exposure to PN, although reactions did occur even days after initiation of PN. Severe reactions were more likely to occur immediately after initiation of PN. The most frequently implicated allergenic agent was the multivitamin component.

695 CHALLENGES OF INFANT FEEDING: THE PROBLEM OF FREQUENT FORMULA CHANGES.

Ylma Velazquez, Yanerys Colon, Liza Gonzalez, Carlos Camacho. Pediatrics, Hospital Episcopal San Lucas, Coto Laurel,

Background: The AAP recommends exclusive breastfeeding for the first 6 months, which concurs with the recommendations by other professional organizations (ACOG, AAFP), the WHO, and the Institute of Medicine. Nevertheless, a 1990 published study in Puerto Rico revealed a breastfeeding rate of only 38%, being most infants in Puerto Rico exposed to cow's milk protein formulas early in life. This is the most frequent cause of early development of Cow's milk protein allergy, often within one week after introduction of cow's milk based formula. As a consequence, it has been described in other studies about infant feeding that infants that are exposed to cow's milk protein formula early in life, also undergo multiple changes in formulas during the first 6 months of life due to symptoms or behavior patterns perceived by parents to be related to formula intolerance. In spite of low breastfeeding/ high cow's milk base formula use in Puerto Rico, there are no published studies describing the patterns of formula changes.

Objective: This study aimed to describe the clinical characteristics and patterns of formula introduction and change in infants not exclusively breastfed in southern Puerto Rico.

Methods: A detailed 18 questions questionnaire was administered to parents of infants from birth to 18 months old at HESL and outpatient's clinics regarding feeding practices and formula changes patterns.

Results: Of the formula fed infants 68% underwent changes in their formula, most of them, (40%), were done during the first month of life to nonstandard formulas. 79% of the time the changes were ordered by the pediatrician and the most common reason was regurgitation (39%). Association between type of birth, mother's age and education and formula changes practices were analyzed but no significance was found.

Conclusion: Nonstandard formulas have been used excessively by both, the mother and the pediatrician. Most common reason for switching a formula was concern regarding common infantile symptoms or behavior patterns perceived by parents to be related to the formula.

696 MULTIVARIATE MODEL TO ESTIMATE ABDOMINAL WALL THICKNESS IN CHILDREN UNDERGOING PLACEMENT OR REPLACEMENT OF GASTROSTOMY DEVICES.

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Purpose: Abdominal wall thickness is a key measurement when replacing gastrostomy buttons. This measurement varies, depending on nutritional status, body habitus, and complex comorbidities. We have developed a model to estimate abdominal wall thickness using a compendium of body measurements.

Methods: Ultrasound was used to measure abdominal wall thickness from epidermis to peritoneum at the initial gastrostomy site in children ages 22 days to 22 years old. Other body measurements (height, weight, xiphisternum-to-pubis and waist circumference) were obtained. Multiple linear regression was used to develop the best fitting model.

Results: 71 subjects were enrolled in the study, 46 were male (64.8%) and the median age was 20 months (interquartile range, IQR: 3-108). The median height was 75cm (IQR: 61-129.5), median weight was 9.86kg (IQR 5.02-24.9), median BMI was 14.8 (IQR 13.5-17), median length from xiphisternum-to-pubis was 16 cm (IQR 11.5-20), and median waist circumference

was 45cm (IQR 38-56). The most common underlying comorbidity was neuromuscular (n=34, 47.9%), and the most common indication for GT placement was failure to thrive (n=56, 78.9%). The univariate and the best fitting multivariate regression models are shown in Table 1. The final regression equation is the following:

- Estimated abdominal wall thickness for female = $0.463 + 0.04(\text{weight in kg}) + 0.061(\text{BMI}) - 0.056$ (xiphisternum to pubis in cm).
- Estimated abdominal wall thickness for male = $0.463 - 0.11 + 0.04(\text{weight in kg}) + 0.061(\text{BMI}) - 0.056$ (xiphisternum to pubis in cm).

Thus, for a female who weighs 5.85kg with BMI of 13 and xiphisternum to pubis length of 16cm, the estimated abdominal thickness would be: $0.463 + 0.04(5.85) + 0.061(13) - 0.056(16) = 0.594\text{cm}$

Conclusion: Our model to estimate abdominal wall thickness utilizes simple measurements that can be easily obtained by those who may not have access to ultrasound. This model can be useful for determining the length of gastrostomy button at initial placement and with subsequent changes. We continue to collect more data to refine and further validate the model.

	Univariate Model	P value	Final Multivariate Model	P value	R ²
Intercept			0.463	0.024	0.89
Male	-0.248	0.108	-0.110	0.047	
Age (months)	0.005	<0.001			
Height (cm)	0.011	<0.001			
Weight (kg)	0.031	<0.001	0.040	<0.001	
BMI	0.138	<0.001	0.061	<0.001	
Xiphisternum to pubis (cm)	0.070	<0.001	-0.056	<0.001	
Waist circumference (cm)	0.035	<0.001			

697 EFFECT OF STANDARDIZED FEEDING PROTOCOL ON NUTRIENT SUPPLY AND POSTNATAL GROWTH OF PRETERM INFANTS: A PROSPECTIVE STUDY. Zahra Khan^{1,2}, Nicholas Morris¹, nadja haiden³, Sandra Holasek⁴, Berndt Urlesberger¹. ¹Division of Neonatology, Children Hospital, Medical University Graz, Graz, Austria; ²Food Science and Human Nutrition, University of Veterinary and Animal Sciences Lahore, Lahore, Punjab, Pakistan; ³Division of Neonatology, Medical University of Vienna, Vienna, Austria; ⁴Institute of Pathophysiology and Immunology, Medical University of Graz, Graz, Austria

Background: Preterm birth is a medical emergency and It is becoming evident that adequate nutrition starting in the first hours of life is of major importance for short and even more so for long-term health outcomes of the premature newborn. The aim was to analyze postnatal nutrient supply and growth patterns of preterm infants in response to a standardized feeding protocol during stay at neonatal intensive care unit (NICU).

Methods: A prospective cohort study was conducted at NICU, Children Hospital Graz. Infants were divided in two groups: <28 weeks (Extremely preterm infants, EPI); ≥28 weeks (very preterm infants, VPI).

Results: EPI compared to VPI stayed longer on parenteral nutrition and needed more time to reach full enteral nutrition, required more days on ventilation and had a higher corrected age at discharge. Moreover, fortification of enteral feeds was initiated later in EPI group (p< 0.001). As a consequence, cumulative supply of protein, fat and energy was significantly lower in EPI. However, both groups exceeded the European Society of Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommended glucose intake in week 5. At discharge, we found significant differences in all growth parameters (weight Z scores: EPI=-1.19 vs VPI= -0.71, length Z scores: EPI=-1.62 vs VPI=-0.84; HC Z scores: EPI=-1.19 vs VPI=-0.46).

Conclusion: Provision of aggressive parenteral nutrition during first 3 weeks of life and earlier fortification should be ensured. The use of mother milk fortifier resulted in glucose intake above the ESPGHAN recommendations in later weeks – this needs to be evaluated in future studies.

PANCREAS/CELIAC/MALABSORPTION

699 UTILIZATION OF ULTRASOUND IN DIFFERENT AGE GROUPS OF CHILDREN WITH ACUTE PANCREATITIS. Michael Dolinger², Jonathan Miller², Samuel Bitton¹, Peter Nauka³, Nina Kohn⁴, Toba Weinstein¹.
¹Pediatric Gastroenterology, Steven and Alexandra Cohen Children's Medical Center, Northwell Health, New Hyde Park, NY; ²General Pediatrics, Steven and Alexandra Cohen Children's Medical Center, Northwell Health, New Hyde Park, NY; ³Hofstra Northwell School of Medicine, Hempstead, NY; ⁴Biostatistics unit, Feinstein Institute for Medical Research, Great Neck, NY

Objective: Acute pancreatitis (AP) in children has been increasing in incidence over the past 2 decades. Along with abdominal pain and pancreatic enzyme abnormalities, there are characteristic imaging findings in AP. While there are multiple adult studies on imaging and findings, there are limited pediatric studies. Ultrasound (US) is utilized frequently in assessing children for AP. However, there are no studies comparing the US findings in younger vs older children with AP. We evaluated the utilization of US and compared findings in younger (≤ 10 years) vs older children (> 10 years) with AP.

Methods: A Retrospective chart review of children with a discharge diagnosis code of pancreatitis at Cohen Children's Medical Center from 2011-2017. Patients met criteria for AP based on the presence of ≥ 2 of the following: abdominal pain, serum amylase and/or lipase > 3 times the upper limit of normal, and imaging findings of AP. Those with incomplete charts, recurrent AP or chronic pancreatitis were excluded. The use and findings of US in younger vs older children were compared using the Mann-Whitney test for continuous variables and chi-square test or Fisher exact test for categorical variables.

Results: 84 children were admitted with pancreatitis, 64 met inclusion criteria. There were 17 younger (11M, 6F, mean [SD] 5.2 yrs. [2.5] range 1-10) and 47 older children (26M, 21F, mean [SD] 14.9 yrs. [1.8] range 11-18). Etiologies of AP by age (%younger, %older) were idiopathic (52.9, 48.9), gallstones (5.9, 21.3), medication (17.6, 12.8), infection (5.9, 6.4), hyperlipidemia (0, 6.4), trauma (5.9, 2.1), choledochal cyst (11.8, 0) and post-ERCP (0, 2.1). There were no differences in etiology between age groups. 16(94.1%) younger and 43(91.5%) older children had US on initial presentation. Pancreatic parenchymal changes, including enlargement and edema, consistent with AP were reported statistically significantly more frequently in younger (4, 25%) vs older (2, 5%) children ($p < 0.041$). There was no difference in biliary tree findings in younger (3, 19%) vs older (13, 30%) children. These findings included gallstones (1 vs 10), biliary sludge (1 vs 3), dilation along the biliary ducts (1 vs 0) or choledochal cyst (1 vs 0) with 1 younger patient having both dilation and sludge. 7(44%) younger and 18(42%) older children had a normal US. 2 children (1 younger, 1 older) with normal initial US developed parenchymal changes on repeat US on hospital days 4 and 3 respectively. The pancreas was not visualized in 2(13%) younger and 8(19%) older children. 2 older children had other US findings (IVC thrombus, duodenitis). No patients had reported pancreatic necrosis, acute fluid collection or pseudocyst on initial US.

Conclusions: Over 92% of our patients had an US as part of their initial assessment for AP which is higher than prior pediatric studies. Although we found no difference in the utilization of US between age groups (94% younger vs 91% older), there was a statistically significant difference in rates of parenchymal changes on US in younger children. In our study, visualization of the pancreas occurred in $> 84\%$ (87% younger, 81% older) of patients, which is higher than previously reported in pediatric studies. These findings support increased utilization of sonography in young children.

700 PREVALENCE OF NEUROLOGICAL SYMPTOMS IN CHILDREN WITH GLUTEN RELATED DISORDERS. Kajal Sangal⁴, Stephanie Camhi², Rosiane Lima², Victoria Kenyon², Alessio Fasano^{1,2,3}, Maureen Leonard^{1,2,3}. ¹Pediatric Gastroenterology and Nutrition, MassGeneral Hospital for Children, Boston, MA; ²Center For Celiac Research and Treatment, MassGeneral Hospital for Children, Boston, MA; ³Pediatrics, Harvard Medical School, Boston, MA; ⁴Boston University School of Medicine, Boston, MA

Background: The prevalence of gluten-related disorders (GRD) including celiac disease (CD) and non-celiac gluten sensitivity (NCGS) is increasing. Patients with GRD may present with gastrointestinal and extraintestinal symptoms alone or in combination, however the number of patients presenting with extraintestinal symptoms is growing. Neurologic symptoms such as ataxia, dizziness, epilepsy, "foggy brain," headaches, and neuropathy have been described in patients with GRD. However, there is little data evaluating the frequency of neurologic symptoms at presentation of GRD in the pediatric population.

Aim: To investigate the prevalence of neurologic symptoms at the time of initial presentation in children with a GRD who were evaluated at our quaternary care center.

Methods: We reviewed the medical records of patients seen at our center over a 3 year period (July 2013-May 2016). All patients provided written informed consent to participate in our research registry, indicating permission for use of their medical information. Data was extracted from the electronic medical record (EMR). Patient/parent-completed intake forms were considered in conjunction with physician-verified information from the EMR to gain an accurate understanding of each patient's symptoms and medical history. For this study, neurologic symptoms were defined as ataxia, dizziness/lightheadedness, epilepsy, memory loss/brain fog, headaches, and neuropathy.

Results: One-hundred and eighty one children were enrolled during this period and 57 patients were excluded due to incomplete data. Of the 124 children included (56%female,n=70)(mean age=10±4), 62% (n=77) were diagnosed with CD, 11% (n=14) were diagnosed with NCGS, and 27% (n=33) were deemed not to have a GRD. In children diagnosed with CD, 25% (n=19) reported a neurologic complaint at the time of presentation. CD patients reported memory loss/brain fog (13%,n=10), headache (12%,n=9), dizziness/lightheadedness (8%,n=6), neuropathy (3%,n=2), ataxia (1%,n=1), and epilepsy (1%,n=1). In children diagnosed with NCGS, 29% (n=4) reported a neurologic complaint at presentation. Patients with NCGS reported headaches (21%,n=3), memory loss/brain fog (14%,n=2), dizziness/lightheadedness (14%,n=2), neuropathy (7%,n=1), and epilepsy (7%,n=1). In children determined not to have a GRD, 21% (n=7) reported a neurologic complaint at presentation. These patients reported headaches (15%,n=5), memory loss/brain fog (9%,n=3), dizziness/lightheadedness (6%,n=2), epilepsy (3%,n=1), and ataxia (3%,n=1). **Conclusions:** Neurological symptoms were reported at presentation in 25% of pediatric patients with a GRD and 21% of pediatric patients without a GRD. The most common neurologic symptoms reported in patients with GRD included memory loss/foggy brain, headaches, and dizziness/lightheadedness. Neurological symptoms were common in pediatric patients presenting to our quaternary care center and further research evaluating the frequency of these symptoms and their response to a gluten free diet is needed.

701 BUN LEVELS: A MARKER FOR SEVERITY IN PEDIATRIC ACUTE PANCREATITIS?

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Background: Acute pancreatitis (AP) is a reversible process characterized by pancreatic inflammation, edema, and varying degrees of necrosis, apoptosis and hemorrhage. The incidence of AP can be as high as 13 per 100,000 per year in children. Pathophysiology points to aberrant generation of calcium signals followed by activation of zymogens which causes a cascade of cytokine production leading to pancreatic and ultimately systemic inflammation. The mainstay of management is bowel and pancreatic rest with fluid support. Most of the guidelines related to the details of management of AP are extrapolated from the adult literature, with limited data regarding management of AP in children.

In the adult population, Blood Urea Nitrogen (BUN) along with other criteria have emerged as important early markers that can be related to the severity of AP. Current data suggests that BUN is an important objective lab marker that can be trended early in the disease course to help identify the most severe cases. No published studies assessing the association of BUN and severity of AP currently exist in the pediatric population to the best of the authors' knowledge, prompting this study.

Methods: A retrospective chart review of patients who were diagnosed with AP was performed. Permission was granted by the local Institutional Review Board (IRB). Patients aged 0-18.9 years diagnosed with AP based on ICD-9 or ICD-10 codes in either the ED or inpatient hospital ward between 12/31/2011-12/31/2016 were included. Patients were considered who were admitted up to 12/31/2016, but must have been discharged by 1/31/17. Data was analyzed using SPSS statistics software.

Results: A total of 337 charts were reviewed. Of those, 308 met the age criteria and 199 patients met the criteria for AP. Of those 199, 121 met the criteria for AP on presentation. Of those, 93 were hospitalized only for pancreatitis and its sequelae. The BUN values and length of stay (LOS) of this cohort is presented in Figure 1. Using a linear regression model to examine the correlation between BUN and LOS, a higher BUN on admission was significantly correlated with a longer LOS [$R^2 = 0.08, p = 0.008$] One of the patients in this subset met the criteria for severe pancreatitis and was transferred to the PICU. Out of those 93, 72 had serial measurements of BUN sufficient to trend values. These values are presented in Figure 2, examining BUN levels at different points in the first 3 days. A general linear model repeated measure was used to check for statistical changes in BUN levels within 48 hours of admission. There was a significant decrease in BUN level over time ($p < 0.001$), as well as between admission (average 12.88, SD 7.36), at 24 hours (average 8.46, SD 6.76, $p < 0.001$) and at 48 hours (average 6.26, SD 5.53, $p < 0.001$).

Conclusion/Future Directions: There appears to be a statistically significant association between BUN at presentation and LOS. This suggests that higher levels of BUN may be associated with severity of the pancreatitis, but unfortunately, we do not have sufficient data at this time to identify precise BUN levels that may separate mild, moderate and severe AP. Additionally, it would appear that there is a statistically significant downward trend in BUN over the course of the hospitalization as the

patient improves. This likely represents resolution of the initial intravascular volume depletion and systemic edematous condition. As a stand alone marker, it is hard to determine how useful BUN may be in monitoring disease progression.

However, these data suggest that BUN may be a worthwhile laboratory value along with other biochemical markers and clinical findings to trend in pediatric AP to monitor overall improvement. BUN may ultimately be part of a severity criteria and resolution standard, analogous to the adult Ranson criteria. We are currently in the process of obtaining prospective data on first time AP patients, which includes BUN levels, and will allow for further investigation.

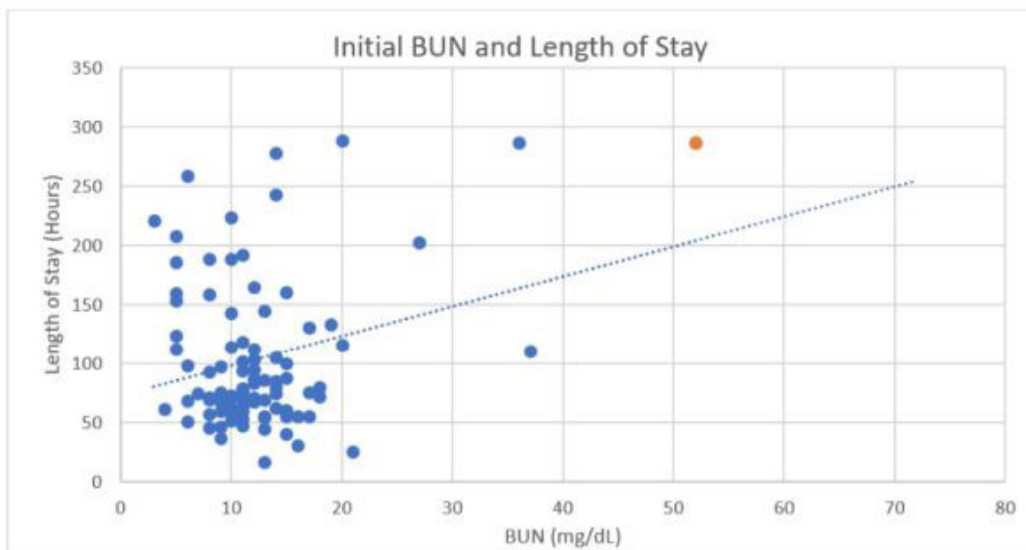


Figure 1. Initial BUN in mg/dL compared to length of stay in hours, for both mild to moderate pancreatitis (blue series) and severe pancreatitis (orange series).

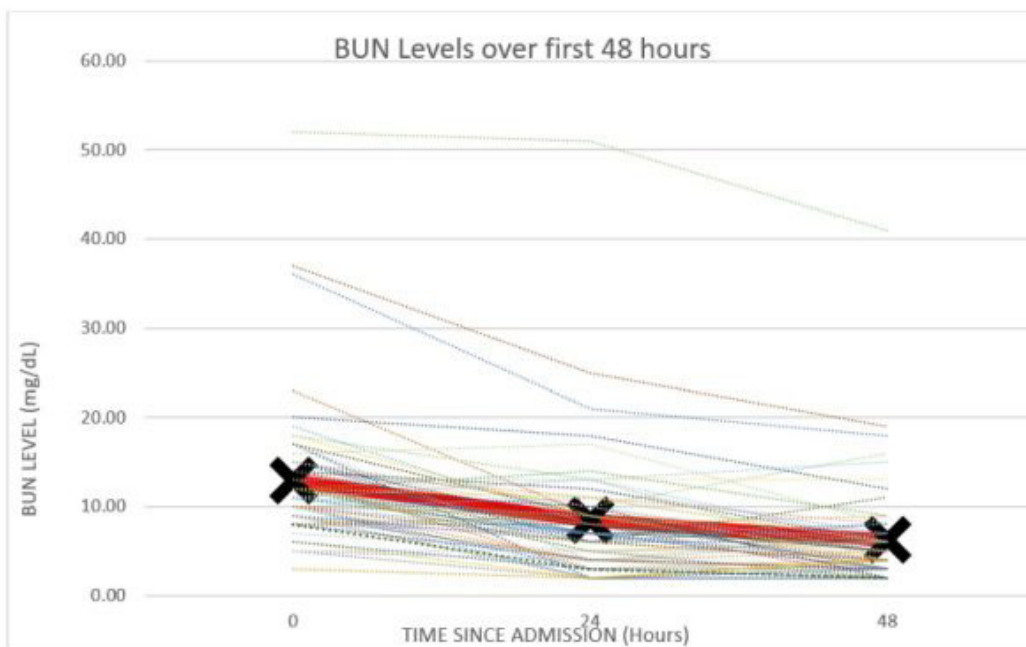


Figure 2: BUN trends in all AP patients. The heavy red line represents the average for all patients.

704 PRSS1 MUTATIONS AND AGE OF ONSET PREDICT RAPID PROGRESSION FROM ACUTE RECURRENT TO CHRONIC PANCREATITIS IN CHILDHOOD. Quin Liu¹, Maisam Abu-El-Haija²,

Sohail Husain³, Bridget Zimmerman⁴, Bradley Barth⁵, Melena Bellin⁶, Douglas Fishman⁷, Steven Freedman⁸, Cheryl Gariepy⁹, Matthew Giefer¹⁰, Tanja Gonska¹¹, Melvin Heyman¹², Ryan Himes⁷, Tom Lin², Mark Lowe¹³, Asim Maqbool¹⁴, Maria Mascarenhas¹⁴, Veronique Morinville¹⁵, Emily Perito¹², David Piccoli¹⁴, Joseph Palermo², Sue Rhee¹², John Pohl¹⁶, Sarah Schwarzenberg⁶, Uzma Shah¹⁷, David Troendle⁵, Steven Werlin¹⁸, Michael Wilschanski¹⁹, Chee Ooi²⁰, Jaimie Nathan², Brian McFerron²¹, YUHUA ZHENG²², Aliye Uc⁴. ¹Gastroenterology, Cedars-Sinai Medical Center, Los Angeles, CA; ²University of Cincinnati/Cincinnati Children's Medical Center, Cincinnati, OH; ³University of Pittsburgh/Children's Hospital of Pittsburgh, Pittsburgh, PA; ⁴University of Iowa/University of Iowa Children's Hospital, Iowa City, IA; ⁵University of Texas Southwestern/Children's Medical Center, Dallas, TX; ⁶University of Minnesota/University of Minnesota Medical Center, Minneapolis, MN; ⁷Baylor College of Medicine/Texas Children's Hospital, Houston, TX; ⁸Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, MA; ⁹The Ohio State University/Nationwide Children's Hospital, Columbus, OH; ¹⁰University of Washington/Seattle Children's Hospital, Seattle, WA; ¹¹University of Toronto/The Hospital for Sick Children, Toronto, ON, Canada; ¹²University of California San Francisco/UCSF Benioff Children's Hospital, San Francisco, CA; ¹³Washington University/St. Louis Children's Hospital, St. Louis, MO; ¹⁴University of Pennsylvania/Children's Hospital of Philadelphia, Philadelphia, PA; ¹⁵McGill University/Montreal Children's Hospital, Montreal, QC, Canada; ¹⁶University of Utah/Primary Children's Hospital, Salt Lake City, UT; ¹⁷Harvard Medical School/Massachusetts General Hospital, Boston, MA; ¹⁸Medical College of Wisconsin/Children's Hospital of Wisconsin, Milwaukee, WI; ¹⁹Hadassah University Medical Center, Jerusalem, Israel; ²⁰University of South Wales/Sydney Children's Hospital Randwick, Bondi Junction, New South Wales, Australia; ²¹Indiana University/Riley Children's Hospital, Indianapolis, IN; ²²University of Southern California/Children's Hospital Los Angeles, Los Angeles, CA

Introduction: Acute recurrent pancreatitis (ARP) and chronic pancreatitis (CP) are thought to be a disease continuum, and progression to CP occurs at a young age in children. The risk factors that determine the rapid progression from ARP to CP are poorly understood.

Objective: To determine the rate of progression from ARP to CP and to examine the risk factors in childhood utilizing the well-phenotyped INSPPIRE (INternational Study group of Pediatric Pancreatitis: In search for a cure) cohort.

Methods: Demographic and clinical information from children with ARP and CP ≤19 years of age at the time of enrollment were entered into the REDCap™ database at sixteen pediatric centers. Kaplan-Meier curves were constructed for time to progression from ARP to CP (August 2012-April 2017). A log-rank test was used to determine significance of an association for multiple risk variables.

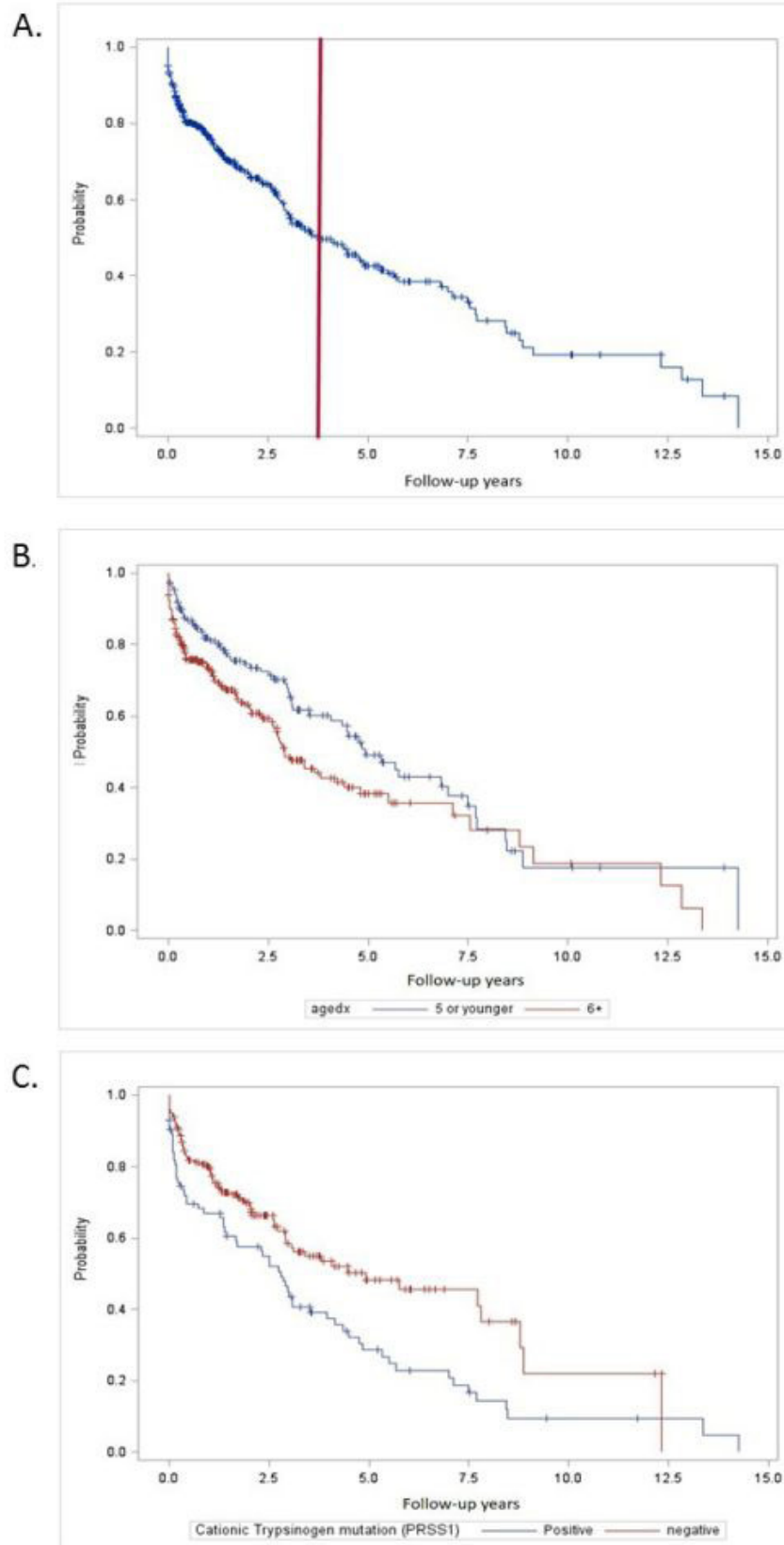
Results: 251 patients had ARP without progression to CP, and 191 patients had CP. Among patients with CP, the median time to progression from initial ARP was 3.79 years (IQR: 1.11 – 8.46) years (Figure 1). Factors associated with faster progression from ARP to CP were first episode of pancreatitis ≥ 6 years of age (median of 2.91 years versus 4.92 years; p= 0.034) and pathogenic PRSS1 variants (median of 2.52 years versus 4.48 years; p=0.001). Ethnicity, gender, CFTR and SPINK1 mutations, family history of chronic pancreatitis, obstructive or toxic/metabolic risk factors were not associated with faster progression from ARP to CP (Table 1).

Discussion: Children with ARP rapidly progress to CP and the progression is even faster if the first episode of pancreatitis occurred ≥6 years of age and/or PRSS1 mutations are present. The risk factors associated with fast progression to CP in childhood need to be further investigated.

Factors associated with faster progression from ARP to CP

Factors	Median time (IQR) yrs to CP WITH Factor	Median time (IQR) yrs to CP WITHOUT Factor	p-value
PRSS1 Mutation	2.52 years (0.25 – 5.50)	4.48 years (1.25 – 8.87)	0.001
1st attack ≥6 years of age	2.91 (0.86 - 8.79)	4.92 (1.91 - 8.46)	0.034
CFTR Mutation	3.10 (1.25-8.79)	3.10 (0.44-7.69)	0.633
SPINK1 Mutation	2.92 (1.10-8.79)	3.10 (0.94-8.42)	0.732
Female Sex	3.79 (1.01-8.87)	4.06 (1.11-8.42)	0.960
Hispanic Ethnicity	3.94 (0.59-8.57)	4.06 (1.11-8.79)	0.863
Obstructive Factors	4.75 (1.02-12.33)	3.51 (0.94-8.42)	0.413
Family History of CP	3.08 (0.59-7.10)	4.80 (1.28-8.87)	0.104

Kaplan-Meier curve of time from AP (first episode) to CP progression in **(A)** all patients, **(B)** per age at first episode of pancreatitis (red: ≥ 6 yrs; blue: ≤ 5 yrs) **(C)** per PRSS1 genetic variants (red: negative; blue: positive)



705 MICROBIOTA-DERIVED MOLECULES AMELIORATE PRO-INFLAMMATORY CYTOKINES PROFILE IN GUT ORGANOID-DERIVED MONOLAYERS FROM HEALTHY AND CELIAC PATIENTS AFTER GLIADIN EXPOSURE. Rachel Freire¹, Laura Ingano¹, Weishy Zhu¹, Anna Saponi¹, Dennis Kasper², Alessio Fasano¹, Stefania Senger¹. ¹Pediatrics, Massachusetts General Hospital/Harvard Medical School, Boston, MA; ²Microbiology and Immunobiology, Harvard Medical School, Boston, MA

Background: Celiac disease (CeD) is a systemic immune-mediated disorder triggered by the intake of gliadin and its indigestible peptides in genetically predisposed subjects. CeD has been also related to altered barrier function, increased cytokines release and, more recently, intestinal dysbiosis. A proof of concept study from our group revealed that genetically predisposed infants presented a decrease in the microbiota richness and altered levels of microbiota-derived products, such as lactate and butyrate, that preceded the onset of CeD (Sellitto et al., 2012). Given the lack of a CeD animal model, most of our understanding on the effect of gliadin on epithelial cells derives from study on suboptimal models, whole biopsies or immortalized tumoral cell lines.

Aim: To study the immune response and barrier function of human duodenum organoids-derived monolayers to gliadin peptides (PT-gliadin) and evaluate the protective role of bacterial-derived molecules lactate, butyrate and *B. fragilis* polysaccharide A (PSA), to PT-gliadin exposure.

Methods: We developed a model of human gut organoids-derived monolayers from duodenal biopsies of normal healthy control (HC) and celiac patients (CeD), according to published protocols (VanDussen KL et al., 2015). The mature epithelial monolayers from HC and CeD were pretreated with the bacterial-derived molecules lactate, butyrate or PSA. After the treatment the monolayers were challenged for 4h with PT-gliadin. TEER and Dextran-FITC passage was used to measure intestinal permeability. Cytokine concentration was measured in apical and basolateral sides by multiplex cytokines detection kit (MSD).

Results: We generate organoids and monolayers from HC (N=6) and CeD patients (N=6), representing subjects with different genetic makeup, susceptibility and/or CeD history. Both CeD and HC derived monolayers developed polarized cells, with readable TEER. Although the cells developed with different kinetics, they reached a final comparable TEER and similar paracellular permeability as measured by FITC-dextran passage. PT-gliadin promoted release of pro-inflammatory cytokines in both HC and CeD subjects. We observed different trend of cytokines profile between the two experimental groups. Pretreatment with bacterial-derived molecules, were able to modulate the cytokines secretion. Specifically Butyrate appeared to be very effective in modulating IL15.

Conclusion: Gliadin peptides stimulate cytokines release in patients derived gut monolayers. The microbiota-derived molecules here studied (lactate, butyrate and PSA) are promising factors to reduce the inflammatory profile of intestinal epithelia. Our study validate the patient derived organoid model system to further research in the field of celiac treatment.

706 UTILITY OF TOMOGRAPHIC CLASSIFICATIONS IN PREDICTING UNFAVORABLE OUTCOMES IN CHILDREN WITH ACUTE PANCREATITIS. Rafael Guerrero-Lozano¹, Yojhan Izquierdo², Viviana Fonseca¹, Luz Angela Moreno^{2,3}, Rubén Montoya^{2,3}. ¹Pediatrics, Universidad Nacional de Colombia, Bogotá, IT, Colombia; ²Radiology, Universidad Nacional de Colombia, Bogotá, Colombia; ³Hospital de la Misericordia, Bogotá, Colombia

Introduction: Incidence of acute pancreatitis (AP) in children, albeit low (3.6-13.2/100,000) has increased over the last two decades. Information regarding use of radiologic diagnostic scales in children is scarce.

Objective: To determine the utility of the Revised Classification of Atlanta (RCA) and the tomographic severity index (CTSI) in predicting unfavorable outcomes in children with AP.

Methods: A retrospective and concordance cohort study was performed, including 30 computed tomography (CT) scans of 30 patients aged 0-18 years, with AP.

Two pediatric radiologists independently interpreted CT using RCA and CTSI. Kappa coefficient was determined for each scale and associations between severe acute pancreatitis (SAP), the need for care in a specialized unit (Ne-UCEP) and CT systems were estimated (Chi-square, Fisher or U-Mann Whitney tests). A ROC curve was used for the best-performing CTSI in predicting Ne-UCEP.

Results: CTSI score was 5.1 ± 2.8 for SAP and 3.8 ± 2.7 for mild AP ($p = 0.230$). CTSI for Ne-UCEP was 5.6 ± 2.4 and 2.2 ± 2.2 for non-Ne-UCEP ($p = 0.001$). Only parenchymal necrosis $>30\%$ had a significant association with SAP ($p = 0.021$). CTSI ≥ 3 has a sensitivity of 89% and specificity of 72% to predict Ne-UCEP. None of RCA categories was associated with PAS or Ne-UCEP.

Conclusions: A CTSI ≥ 3 predicts the need for admission in a specialized care unit with good performance and acceptable interobserver variability. Pancreatic necrosis $>30\%$ seems to be the only parameter related to SAP; however, new studies are needed to validate these results.

707 MUCOSAL IGA AND MICROBIOTA ANALYSIS IN PATIENTS WITH CELIAC DISEASE. Ricardo Medina-Centeno^{1,3}, Michele Alkalay^{1,3}, Julie Mirpuri^{2,4}, Rinarani Sanghavi^{1,3}. ¹Pediatric Gastroenterology, Hepatology and Nutrition, University of Texas, Southwestern Medical Center, Dallas, TX; ²Neonatal-Perinatal Medicine, University of Texas, Southwestern Medical Center, Dallas, TX; ³Children's Health Medical Center, Dallas, TX; ⁴Children's Health Medical Center, Dallas, TX

Background: Celiac disease (CD) is an immune mediated inflammatory disease due to gluten sensitivity that affects the small bowel. The prevalence of celiac disease in children is estimated to be 3-13 per 1000, primarily affecting Caucasians. It is known certain groups have a higher risk of developing Celiac disease, including patients with serum IgA deficiency. CD is mainly diagnosed with biopsy, but the screening methods used include a measurement of total serum IgA and anti IgA tissue transglutaminase. IgA is an important mucosal antibody that is involved in control of Proteobacteria in the intestine. IgA contributes to barrier function and these antibodies are involved in immunological homeostasis. It has been suggested that mucosal IgA response may promote the progression of celiac disease.

While CD is mainly diagnosed with biopsy, the screening methods used include a measurement of total serum IgA and anti-IgA tissue transglutaminase. Mucosal IgA is not measured and is assumed to be normal if the serum IgA is normal.

Rationale/Hypothesis: In previous studies analyzing the microbiota of children with active CD, it has been shown that there is a unique microbiota marked by an increase in pro-inflammatory bacteria including Clostridium and Enterobacteriaceae (Proteobacteria) and a decrease in anti-inflammatory bacteria such as Bifidobacterium. To this date, there have been no studies looking at the relationship between serum and mucosal IgA of patients that are not deficient in serum IgA. At the same time, studies in children with CD have been done to analyze the microbiota of treated, untreated and active celiac disease, but there are no studies evaluating the differences between patients with and without serum IgA deficiency. We hypothesize that patients with CD that are not IgA deficient by serum testing, have a lower mucosal IgA and that alters their microbiota.

Methods: Patients were recruited to participate in a case-control study. Stool samples and relevant clinical data were collected during a clinic visit. The samples were analyzed for the presence of mucosal IgA utilizing enzyme-linked immunoabsorbent assay (ELISA). Microbiota analysis was done on those samples via quantitative reverse transcription polymerase chain reaction (qRT-PCR) for specific major bacterial phyla.

Results: Our data showed that patients that have CD and no serum IgA deficiency have a decreased mucosal IgA compared to controls, despite having normal serum IgA with a 56% difference, p value 0.003. In addition, untreated CD patients with decreased mucosal IgA have a higher abundance of Proteobacteria that decreases once the gluten free diet is started, p value 0.04.

Conclusions: These findings suggest that CD patients with normal serum IgA still have a decreased mucosal IgA. At the same time, untreated CD patients, compared to treated CD, have a higher load of Proteobacteria that seems to be suppressed with introduction of a gluten free diet. This study implies that mucosal IgA may play an important role in regulating the intestinal microbiota and susceptibility to CD.

710 NOVEL MUTATIONS AND GENETICS OF EPCAM IN CONGENITAL TUFTING ENTEROPATHY.

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Background: Congenital tufting enteropathy (CTE) is a rare diarrheal disorder that is caused by mutations in the EPCAM gene. These mutations are predicted to cause intestinal epithelial cell dysplasia leading to malabsorption and high morbidity and mortality. The objective of this study is to describe 12 novel EPCAM mutations and review current genetic understanding of the disease.

Methods: A literature search from 2008-2017 identified all published mutations in the EpCAM gene in association with CTE. A review of 13 studies yielded 31 distinct EPCAM mutations in a total of 72 affected patients. Review of each study examined: 1) patient mutation, 2) gender, 3) ethnicity, and 4) amount of parenteral nutrition, which served as a marker of disease severity. Chi-squared testing was performed to assess for any difference in severity of disease (Partial parenteral nutrition (PN) vs. Total parenteral Nutrition (TPN) vs. Transplant vs. Death) in the most common mutations: c.498insC and c.556-14A>G.

Patients with novel mutations were recruited from UCSD and UCLA. Informed consent of the subjects was obtained according to the Institutional Review Board guidelines. Patient and parents were recruited, blood samples were collected, and genomic DNA was extracted and analyzed.

Results: A review of 13 CTE manuscripts yielded 31 distinct EpCAM mutations or compound heterozygous mutations in a total of 72 patients. These included 15 splicing defects, 6 missense, 23 frameshift, and 14 premature truncation mutations. 14 mutations were a combination of ≥ 2 categories. TPN data was available for 52 patients: 3 had weaned off PN, 18 had partial PN (1/7-6/7 days), 7 had full TPN (7/7 days), 10 underwent transplant, and 14 were deceased. Chi-squared testing was performed to assess for significant deviation from disease outcome for the 2 most common mutations. There was no significant difference between the four disease outcomes for mutation c.498insC ($p=0.051$) or c.556-14A>G ($p=0.59$). Genetic sequencing of 15 patients in 2 separate centers yielded 12 unique novel mutations (Fig 1). One patient had a mutation of unknown pathogenicity. There were 7 compound heterozygous and 5 homozygous mutations. Of the homozygous mutations there were: 2 in-frame deletions, 2 frameshifts, and 1 splicing defect. Of the compound heterozygous mutations there were: 4 missense, 6 splicing defect, 1 inframe deletion, 2 frameshifts, and 1 unknown. Disease outcomes included: 2 patients weaned off TPN (1 due to limited access), 4 partial PN, 8 full TPN, and 1 unknown. No patients underwent transplant or died. Protein modeling of pathogenic mutations was performed revealing insights into alterations in the protein structure.

Conclusions: Review of current mutations has implications on clinical understanding and decision-making on patients with CTE. Genetic screening analysis identified 12 novel mutations in EPCAM leading to CTE. These findings add to the goal of clarifying the pathophysiology of CTE and genotype-phenotype connection.

Patient	Coding TNA	Protein	Type of Mutation	Topology	Ethnicity	Gender	Treatment	Transplant
1	c.1130>A; c.47_67del21	p.C38Y; p.Ala18_Gln24del	missense; inframe deletion	compound heterozygous	Caucasian	M	Full TPN	No
2	c.1A>C; c.38_62dup25	p.Met11Leu; frameshift	missense; frameshift	compound heterozygous	Palestinian	F	Off TPN due to limited access*	No
3	c.2870>C; c.945+118T>C	p.Gln89His; unknown consequence	missense; unknown	compound heterozygous	English	M	Full TPN	No
4	c.3070>A; c.492-5T>C	P.Gly103Arg; splicing defect	missense; splicing defect	compound heterozygous	English-Italian	M	Partial TPN	No
5	c.491+1G>A; c.556-14A>G	p.Trp143_Thr164del (del exon 4) p.Tyr196_Asp219del*	splicing defect; splicing defect	compound heterozygous	Bangladeshi	M (2)	Full TPN (2)	No
6	c.492-10>A; c.491+10>A	p.Trp143_Thr164del (del exon 4) p.Trp143_Thr164del (del exon 4)	splicing defect; splicing defect	compound heterozygous	Hispanic	M	Full TPN	No
7	c.589_511delTCA	p.I179del	inframe deletion	homozygous	Pakistani	unknown	unknown	unknown
8	c.555+1G>C	p.Ala163Metfs*23 (del exon 3)	splicing defect	homozygous	Turkish	F	Weaned off	No
9	c.579delT	p.Arg193Metfs*17	frameshift	homozygous	Israeli	M (1), F (1)	Full TPN (2)	No
10	c.589C>T	p.Gln197	frameshift	homozygous	Irqi	M	Full TPN	No
11	c.589delT; c.491+10>A	p.Phe180Leufs*30; del exon 4	frameshift; splicing defect	compound heterozygous	unknown	M (2)	Partial TPN (2)	No
12	Exon1-4F	p.Gln34_Tyr142del	inframe deletion	homozygous	Hispanic	F	Partial TPN	No

711 HIGH SMAD7 CORRELATES WITH CLINICAL INFLAMMATORY PHENOTYPE IN PAKISTANI AND ZAMBIAN CHILDREN WITH ENVIRONMENTAL ENTEROPATHY. Sana Syed^{2,1}, Vincenzo Dinallo³, Najeeha Iqbal², Laura Di Iorio³, Davide Di Fusco³, Shan Guleria¹, Beatrice Amadi⁴, Shahida Qureshi², Kamran Sadiq², Kumail Ahmed², Aneeta Hotwani², S. Asad Ali², Paul Kelly^{5,4}, Giovanni Monteleone³. ¹Pediatrics, University of Virginia, Charlottesville, VA; ²Pediatrics, Aga Khan University, Karachi, Pakistan; ³Systems Medicine, University of Rome 'Tor Vergata', Rome, Italy; ⁴Tropical Gastroenterology and Nutrition group, University of Zambia School of Medicine, Lusaka, Zambia; ⁵Blizard Institute, Barts and The London School of Medicine, Queen Mary University of London, London, United Kingdom.

Enteropathies such as celiac disease (CD) and Crohn's disease are associated with enteric inflammation characterized by impaired TGF- β signaling, decreased expression of phosphorylated (p)-SMAD2,3 and increased expression of SMAD7 (an inhibitor of SMAD3 phosphorylation). These findings are associated with increased inflammatory cytokines. Environmental enteropathy (EE) is an acquired inflammatory disease of the small intestine (SI), which is associated with linear growth disruption, cognitive deficits, and oral vaccine failure in children <5 y in resource-poor countries. We aimed to characterize EE inflammatory pathways by determining SMAD7 and p-SMAD2,3 levels (using Western blotting) in EE duodenal biopsies (N=19 children, 7 from Pakistan and 12 from Zambia) and comparing these with healthy controls (Ctl) and CD patients from Italy. Comparing groups using Mann-Whitney tests, densitometric analysis of immunoblots showed that EE SI

biopsies expressed higher levels of both SMAD7 (mean±SD, Ctl=0.47±0.20, EE=1.13±0.25, p-value<0.05) and p-SMAD2,3 (mean±SD, Ctl=0.38±0.14, EE=0.60±0.10, p-value<0.05). Qualitative immunohistochemistry showed that SMAD7 in the epithelial compartment has a nuclear localization while in mononuclear cells in the lamina propria (LP) SMAD7 localization is both nuclear **and** cytoplasmic. In contrast, p-SMAD3 is expressed only in epithelial cells and not in the LP. This suggests that normal TGF-β signaling is active in the epithelium given that SMAD7 is upregulated by TGF-β. High SMAD7 expression in the cytoplasm and nuclei of LP mononuclear cells and a lack of p-SMAD3 expression in the LP therefore suggests defective TGF-β signaling in the LP. These results support a SMAD7-mediated inflammatory pathway in EE. In contrast to prior studies on CD, p-SMAD2,3 levels were elevated in EE. These data indicate that EE relies on a different inflammatory pathway than CD. Further research in EE is needed to illustrate the relationship between SMAD proteins, TGF-β signaling, and inflammatory cytokine production, all of which may be potential therapeutic targets.

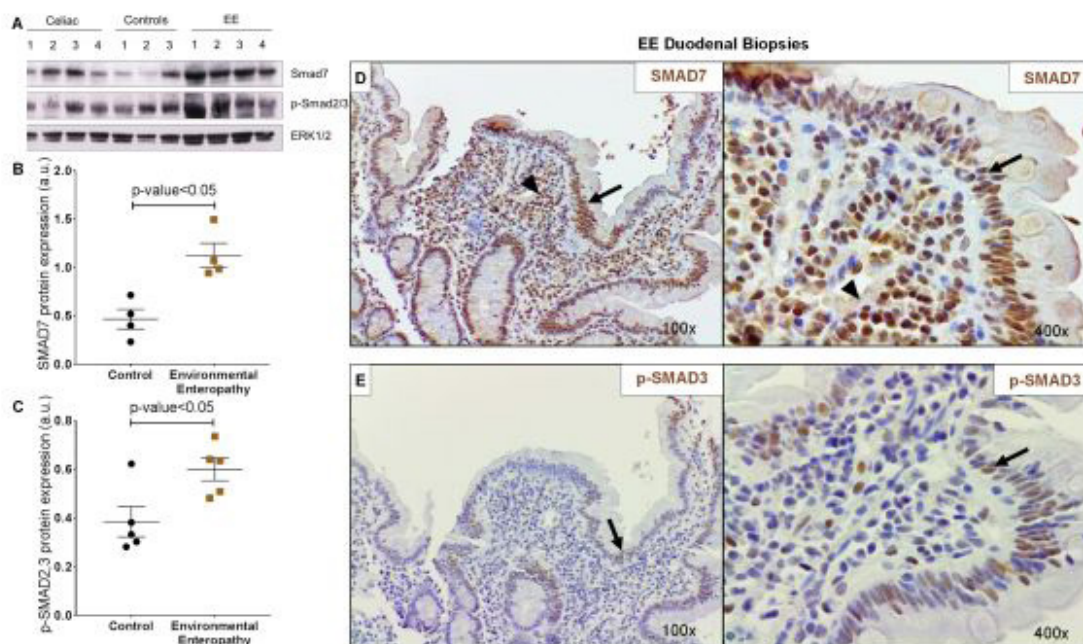


Fig. 1 SMAD protein expression data.

- A. Representative Western blot example investigating SMAD7; p-SMAD2,3 expression (using ERK1/2 as a normalizing protein) from controls (Ctl), celiac disease (CD), and environmental enteropathy (EE) patients.
- B. SMAD7 densitometry levels (arbitrary units, a.u., for all) in control and EE samples (mean±SD, Ctl=0.47±0.20, EE=1.13±0.25, p-value<0.05).
- C. p-SMAD2,3 densitometry levels in control and EE samples (mean±SD, Ctl =0.38±0.14, EE=0.60±0.10, p-value<0.05).
- D. Representative immuno-histochemical (IHC) photomicrographs at 100x and 400x from an EE duodenal biopsy showing SMAD7 staining in both the epithelium (arrows) and lamina propria (arrowheads).
- E. Representative IHC photomicrographs at 100x and 400x from an EE duodenal biopsy showing p-SMAD3 staining in only the epithelium (arrows).

713 MOST ASPARAGINASE USERS ARE PROTECTED AGAINST PANCREATITIS BECAUSE THEY HAVE THE CAPACITY TO UPREGULATE PANCREATIC ASPARAGINE SYNTHETASE.

Nayyar Ahmad, Fateema Rose, Tanveer Javed, Li Wen, Amitava Mukherjee, Sohail Husain. Pediatrics, U of Pittsburgh, Pittsburgh, PA

Drug-induced pancreatitis is a major iatrogenic etiology of pancreatitis in children. Asparaginase is a cornerstone therapy for leukemia, but an unacceptably high number of patients (6-10%) taking the cancer drug develop the complication of pancreatitis. Furthermore, discontinuation of asparaginase due to pancreatitis leads to a suboptimal duration of asparaginase treatment, and this shortfall tends to jeopardize event-free survival from leukemia. Thus there is a major need to decipher the mechanisms underlying asparaginase-associated pancreatitis. Asparaginase functions primarily to deplete asparagine. We hypothesized that most asparaginase users (90-96%) don't develop pancreatitis because they have the ability to upregulate in the pancreas the counter-regulatory enzyme which replenishes asparagine, called asparagine synthetase (ASNS). To pursue this hypothesis, we characterized the importance of ASNS in maintaining pancreatic homeostasis. In mouse, we demonstrate,

compared to other organs, that ASNS is predominantly expressed in the pancreas. Asparaginase exposure in mouse (266-6) and rat (AR42J) pancreatic acinar cell lines led to a time- and dose-dependent increase in ASNS expression. ASNS was also upregulated in primary mouse and human acinar cells in response to asparaginase exposure. The induction of ASNS was unique to asparaginase as a trigger for pancreatic injury, since other pancreatitis stimuli failed to induce ASNS expression. Further, shRNA knockdown of ASNS led to pancreatic acinar cell injury and compounded the injury seen with asparaginase exposure. Asparaginase exposure activated the NF- κ B inflammatory signaling pathway. These findings suggest that ASNS maintains acinar cell homeostasis at baseline and that its upregulation is required to mitigate asparaginase-induced pancreatic cell injury seen during pancreatitis. The study suggests that patients who succumb to pancreatitis may have intrinsic defects in mounting an adequate upregulation of pancreatic ASNS. Further, therapies that selectively augment pancreatic ASNS could be used to rescue the problem of asparaginase-associated pancreatitis.

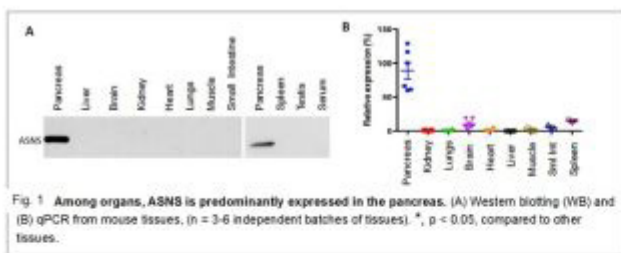


Fig. 1 Among organs, ASNS is predominantly expressed in the pancreas. (A) Western blotting (WB) and (B) qPCR from mouse tissues. (n = 3-6 independent batches of tissues). *, p < 0.05, compared to other tissues.

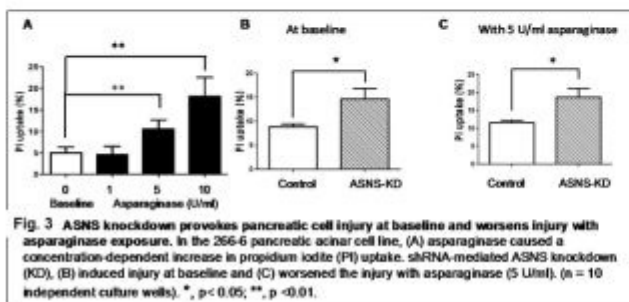


Fig. 3 ASNS knockdown provokes pancreatic cell injury at baseline and worsens injury with asparaginase exposure. In the 266-6 pancreatic acinar cell line, (A) asparaginase caused a concentration-dependent increase in propidium iodide (PI) uptake. shRNA-mediated ASNS knockdown (KD), (B) induced injury at baseline and (C) worsened the injury with asparaginase (5 U/ml). (n = 10 independent culture wells). *, p < 0.05; **, p < 0.01.

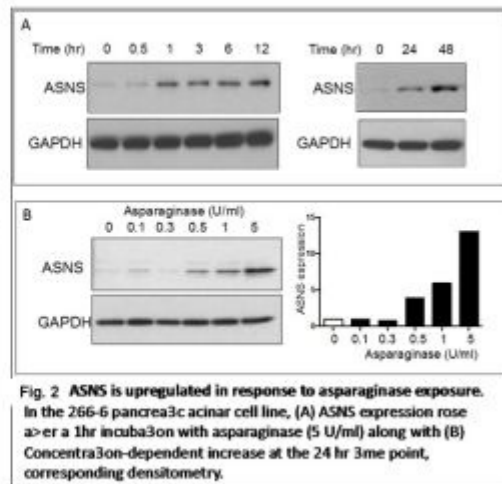


Fig. 2 ASNS is upregulated in response to asparaginase exposure. In the 266-6 pancreatic acinar cell line, (A) ASNS expression rose over a 1 hr incubation with asparaginase (5 U/ml) along with (B) Concentration-dependent increase at the 24 hr time point, corresponding densitometry.

717 AWARENESS OF ACUTE RECURRENT PANCREATITIS (ARP) AND CHRONIC PANCREATITIS (CP) SHOULD BE FURTHER ADDRESSED IN PRIMARY CARE PHYSICIANS - A SINGLE PEDIATRIC CENTER EXPERIENCE WITH DIAGNOSIS TIMING OF ACUTE RECURRENT PANCREATITIS (ARP) AND CHRONIC PANCREATITIS (CP). Yuhua Zheng. Gastroenterology, Children's Hospital Los Angeles, Los Angeles, CA

Introduction: Acute recurrent pancreatitis (ARP) and chronic pancreatitis (CP) have been diagnosed in children at increasing rates during the past decade. As pediatric ARP and CP are still relatively rare conditions, the awareness of the diagnosis remains under addressed in general pediatrician.

Aim: The aim of the study was to review a single center experience with ARP and CP diagnosis. The timing of gastrointestinal symptoms prior to first diagnosis of pancreatitis was reviewed. Chronic change of pancreas showed on image at the first episode of pancreatitis was also reviewed.

Method: Retrospective chart review of clinical symptoms, hospitalization courses, clinical visits and imaging were conducted for all patients seen in our center over past 15 year, who were identified by hospital medical record through ICD code search.

Background: Acute pancreatitis (AP) is defined as requiring 2 of the following: 1) Abdominal pain compatible with AP, 2) Serum amylase and/or lipase values =3 times upper limits of normal, 3) Imaging findings of AP, such as gland enlargement, acute inflammatory changes, fluid collections. ARP is defined as: At least 2 episodes of acute pancreatitis with complete resolution of pain and a >1 month pain-free interval between episodes. Chronic Pancreatitis is defined as: Children with at least: 1) one irreversible structural change in the pancreas with or without abdominal pain and one of the two conditions below: 2) exocrine pancreatic insufficiency 3) diabetes.

Results: 31 patients were identified carrying the diagnosis of ARP or CP. 29 patients initially presented to our center for an acute pancreatitis episode. 2 were from regular referral to gastroenterology department clinic for chronic abdominal pain. Age ranged from 4 to 20 years of age. 11 were male and 21 were Female. Among those, 17 (55%) patients had CP and 14

(45%) had ARP. 11 out of 31 patients (35%) complained somewhat gastrointestinal symptoms (abdominal discomfort, failure to thrive, poor weight gain et al) prior to their first diagnosed pancreatitis epi. The symptoms prior to their first diagnosis ranged from 3 months to 4 years, with the longest interval (4 years) in a patient with autism who had significant development delay and was nonverbal. Among the 17 patients with CP, 6 (35%) showed chronic change on image studies at their very first episode of pancreatitis prior to any gastroenterology involvement.

Discussion: Pediatric ARP and CP are still relatively rare conditions, the awareness of the diagnosis is under addressed, which may negatively impact the early detection of the diagnosis of ARP or CP. Awareness should be further addressed among pediatricians especially primary care physicians.

Conclusion: ARP and CP are still relatively rare conditions, screening for pancreatitis in patients with chronic gastrointestinal symptoms is important. Awareness should be further addressed among pediatricians especially primary care physicians.

718 EPIDEMIOLOGICAL COMPARISON OF ACUTE AND CHRONIC PANCREATITIS IN CHILDREN AND ADULTS. Zachary Sellers¹, Donna MacIsaac², Helen Yu¹, Ke-You Zhang³, Rachel Bensen¹, Jessie Wong⁴, Aditi Gupta¹, Cindy Kin², KT Park¹. ¹*Pediatric Gastroenterology, Hepatology, and Nutrition, Stanford University, Palo Alto, CA;* ²*Surgery, Stanford University, Palo Alto, CA;* ³*Pediatrics, Stanford University, Palo Alto, CA;* ⁴*VA Palo Alto Healthcare System, Palo Alto, CA*

Background: Acute pancreatitis (AP) has been reported to affect approximately 3.6-13.2/100,000 children annually in the United States with increasing incidence. This data has largely been derived from single tertiary care academic centers. Some have questioned whether this incidence is an over estimate due to referral bias, or under estimate due to missing information from community hospitals and clinic visits. The prevalence for chronic pancreatitis (CP) has been reported to be about 0.5/100,000 people, however, data for CP in children is severely lacking. Despite the relatively small numbers compared to other pediatric gastrointestinal diseases, AP and CP cause significant morbidity and mortality, as nearly one-quarter of children develop a severe complication and the mortality rate is approximately 4-10%.

Aims: Using a nationwide insurance claims database, we set out to calculate the incidence of AP, incidence and prevalence of CP, and to estimate the health care cost burden associated with AP and CP in children, and compare it to adults.

Methods: We performed a longitudinal retrospective cohort analysis of AP and CP patients in the Truven MarketScan Commercial Claims and Encounters database, consisting of insurance claims from outpatient and inpatient visits and pharmaceutical prescriptions, from 2007-2014. Patients were included if they were in the database for at least 6 months prior to diagnosis and for an additional 12 months following diagnosis. AP and CP patients were identified by their respective ICD-9 codes. The pediatrics cohort was defined as <19 years and adults as ≥19 years old.

Results: There were a total of 22,148,050 unique pediatric and 56,945,160 unique adult patients from all 50 U.S. states in the database, ranging in age from 0 to 64 years old. Of these, 10,751 pediatric and 315,677 adult patients had AP or CP. The incidence of pediatric AP was steady from 2007-2014 with a mean of 7.1/100,000 people (6.4-7.9/100,000 people). This compared to a mean incidence of 61.6/100,000 people (59.3-64.6/100,000) for adults. The mean incidence and mean prevalence for pediatric CP was 1.4/100,000 and 5.7/100,000 people, respectively. In adults, mean incidence and mean prevalence of CP was 17.8/100,000 and 75/100,000/people, respectively. The mean AP incidence, mean CP incidence, and mean CP prevalence all increased with advancing age. There were no geographical differences in AP/CP incidences or CP prevalence.

Summary: To our knowledge, this study represents the most comprehensive large-scale study of pediatric pancreatitis to date. The incidence of AP in pediatrics in our study is similar to what has previously been reported, however, our study shows steady rates in recent years. This may be due to established awareness of pediatric pancreatitis (compared to prior years), or due to a plateau in obesity rates. We show a larger incidence and prevalence of pediatric CP than has been previously reported, which may be reflecting prior years of increasing pancreatitis rates. Ongoing work with this database is characterizing these cohorts, including determining health care utilization costs. This work is important in drawing attention to the burden of pediatric acute and chronic pancreatitis on patients, families, and the health care system. This knowledge will help to appropriately allocate the necessary health care resources to improve the care for children with acute and chronic pancreatitis.

719 VARIATION IN PROVIDER ORDERING PRACTICES OF DXA SCANS IN PEDIATRIC PATIENTS WITH CELIAC DISEASE. Jennifer Webster, Ritu Verma. *Pediatric Gastroenterology, The Children's Hospital of Philadelphia, Philadelphia, PA*

Background: Celiac disease (CD) is an immune-mediated genetic disorder that occurs as a result of exposure to gluten. Research has shown that CD increases the likelihood of low bone mineral density (BMD) in children based on results of dual

x-ray absorptiometry (DXA). There are currently no published guidelines for DXA scanning to screen and monitor BMD in pediatric patients with CD. We aimed at characterizing current pediatric gastroenterologist practice in ordering DXA scans for patients with CD.

Methods: A REDCap survey was distributed via the NASPGHAN listserv. The primary outcome measure was the ordering of a DXA scan in a newly diagnosed patient with CD. The covariates included clinical information affecting the ordering of DXA scans in this population, external influences, and physician factors.

Results: Overall, 231 physicians (11%) responded to the survey covering 35 states and 3 countries. Approximately 60% of physicians never order a DXA in newly diagnosed CD. Of those, 90% did not feel a screening DXA was necessary. The least influential clinical factor in ordering a DXA at diagnosis was tTG (70% rating ≤ 2 on a scale of 1-5) and the most influential was history of fractures (75% rating ≥ 4 on a scale of 1-5). There were no consistent management plans for case scenarios provided. Physicians working in the Northeast were most likely to order a screening DXA ($p=0.03$). Physicians working in a hospital setting were also more likely to order a screening DXA, although, not statistically significant ($p=0.10$).

Conclusion: In conclusion, there is an extreme variety in physician ordering practices for DXA scans as well as management decisions with abnormal DXA scans in pediatric patients with CD. There should be more research to develop evidence based guidelines to guide physicians on appropriate use of DXA scans in this population.

Physician Factors in ordering a DXA on newly diagnosed patients with celiac disease

	Ordered a DXA scan	Did not order a DXA scan	
Region			p=0.032
Midwest	6 (17%)	29 (35%)	
Northeast	23 (48%)	25 (52%)	
South	15 (42%)	21 (58%)	
West	15 (40%)	22 (60%)	
Type of practice			p=0.108
Hospital based	54 (35%)	101 (65%)	
Non-hospital based	12 (52%)	11 (48%)	
Years practiced			
0-5 years	20 (33%)	41 (67%)	p=0.350
6-10 years	10 (31%)	22 (69%)	
11-20 years	12 (40%)	18 (60%)	
21-30 years	15 (38%)	25 (62%)	
>30 years	9 (60%)	6 (40%)	

P-values calculated with chi-square analysis

APGNN

720 DOES THE EVIDENCE SUPPORT PREMEDICATING PEDIATRIC CROHN'S DISEASE PATIENTS WITH ANTIHISTAMINES DURING INFLIXIMAB INFUSIONS? Kerri Fournier, Joan Shea. Nursing, Boston Children's Hospital, Boston, MA

Statement of the Problem: Infliximab is a chimeric monoclonal antibody designed to target and neutralize tumor necrosis factor. It is used to help manage and treat Crohn's disease, ulcerative colitis and several rheumatological conditions such as arthritis and uveitis. Administration of infliximab is associated with risk of infusion-related reactions. Reactions can include but are not limited to headache, dizziness, flushing, chest pain, tachycardia, dyspnea, and pruritus. To prevent infusion-related reactions, pre-treatment combinations of acetaminophen, intravenous steroid and an antihistamine are given. There is a high degree of practice variation, regarding pre-treatment for infliximab infusions at our institution and there is no clinical standard

nationally. This project reviews the evidence for pretreatment with an antihistamine, versus no pretreatment, in patients with Crohn's disease receiving infliximab.

Clinical Question: In pediatric patients with Crohn's disease (P), does premedicating with an antihistamine (*diphenhydramine, cetirizine hydrochloride, loratadine*) (I), versus no premedication (C), decrease reactions to infliximab (O) during the infusion (T)?

Search for the Evidence: An electronic literature search was performed using PubMed. Keywords included infliximab, Remicade, reactions, infusion reactions, pre-medication, antihistamines, Crohn's disease, and pediatrics. Eligibility criteria included adult and pediatric patients with Crohn's disease, premedication was discussed, written in English and published within the last 10 years. Seven articles met criteria for review. One additional article, considered the hallmark study in establishing maintenance infliximab infusions as the standard clinical care for Crohn's disease was also included, though it was published outside of the circumscribed date range. Three of the studies are Level I studies (systematic reviews/randomized control trial) and five of the articles are Level IV (chart reviews/surveys). There were no randomized controlled trials with infusion reaction as a primary outcome.

Critical Appraisal of the Evidence: Three of the studies concluded that antihistamines significantly increase the risk of infusion reactions and seven of the studies found that there was no benefit to giving prophylactic antihistamine. Two of the studies suggest that acetaminophen alone may decrease the risk of infusion-related reactions. All the studies agreed that more research is needed as premedication protocols have not been subjected to controlled validation and their efficacy is uncertain.

Implications:

- The efficacy of premedicating with an antihistamine is unproven.
- No randomized control trials have been performed looking at premedicating patients to prevent infusion reactions to infliximab.
- Current efforts are underway to conduct a retrospective chart review of patients who received infliximab at BCH to examine reaction history and premedication practices to further define the local problem.
- Further research regarding the efficacy of using antihistamines prior to infliximab should be considered, possibly through a randomized control trial.

721 UTILIZATION OF A CLINICAL DECISION SUPPORT TOOL FOR PATIENTS NEWLY DIAGNOSED WITH CROHN'S DISEASE. *Barbara Drobnic, Melanie Oates, Jennifer Dotson, Ross Maltz, Brendan Boyle, Amy Donegan, Jennifer Smith, Marci Johnson, Rose Schroedl, Laura Mackner, Wallace Crandall, Amy Peasley. Gastroenterology, Nationwide Childrens Hospital, Johnstown, OH*

Background: At Nationwide Children's Hospital an average of 100 patients per year are diagnosed with inflammatory bowel disease (IBD) with approximately 65 % of the patients having Crohn's disease. Our center identified a care delivery gap in that we did not have a formal clinical decision support tool regarding treatment option to use with parents and patient at the time of diagnosis. The IBD team developed a Crohn's disease care pathway that reviews treatment options based on disease severity at the time of diagnosis. Additionally, the care pathway outlines the general timeline for follow up office visits and teachings for the next 12 months.

Method: The IBD team developed a medical decision support tool outlining treatment options for patients newly diagnosed with Crohn's disease. Treatment options are divided into three categories based upon the severity of their disease including mild, moderate/severe disease or severe/high risk disease. Treatment options are divided into induction therapy and maintenance therapy and listed in order of preference as determined after extensive review of the literature and expert agreement, establishing a shared, institutional approach to care. The treatment options are divided into induction therapy and maintenance therapy. The GI attending physician determines which severity category is most appropriate for the patient and the care pathway is given to the family at discharge for further review to help with their decision making. The care pathway also reviews what to expect with regards to follow up office visits for the first year after diagnosis. The IBD nurse coordinators review this information with the family during their first teaching visit and it introduces our center's multi-disciplinary approach to care. The information includes: initial assessment: the team reviews the findings of the testing that has been completed. Month 1: Teaching Day 1: meet the team, IBD education and first office follow up with the provider. Month 2-3: Teaching Day 2, meet with the IBD social worker, IBD psychologist and follow up with the provider. Month 5-7: follow up office visit, plan for ongoing follow up every 8-16 weeks. Month 12: Annual IBD visit with IBD Nurse Practitioner, social worker, dietitian and psychologist for ongoing education and follow-up on any concerns.

Results: From January 1 to May 31 2017 51 Teaching Day 1 appointments were completed. Of the 51 teachings, 40 were Crohn's. Informal feedback from providers, IBD nurse coordinators, patients and families found the care pathway to be a helpful decision making tool and guide for what to expect in the upcoming 12 months. Providing a visual tool that the parent and patient could refer back to helped them understand their treatment options. The healthcare providers found the tool helpful to ensure information was reviewed with the patient.

Conclusion: Utilization of a Crohn's disease care pathway as a tool to support clinical decision making has provided an effective and structured method to review treatment options based on disease severity at diagnosis. Outlining a general timeline for follow up office visits creates expectations for follow-up visits and emphasizes our multi-disciplinary approach to IBD care.

722 PRELIMINARY STUDY OF ATYPICAL ULCERATIVE COLITIS AND INFLAMMATORY BOWEL DISEASE UNCLASSIFIED IN KOREAN PEDIATRIC ONSET IBD. *Sunghye Lee, Kyung Mo Kim, Seak Hee Oh. Pediatrics, Asan Medical Center, Seoul, Korea (the Republic of)*

Introduction: The prevalence of atypical ulcerative colitis (UC) and inflammatory bowel disease unclassified (IBDU) in pediatric-onset IBD (PIBD) has been increased in Korea. The revised Porto criteria was proposed to standardize the PIBD subtypes and provide a clear definition of atypical UC and IBDU which used to be subjective. This study aims to evaluate a change of diagnosis from originally diagnosed UC to atypical UC and IBDU respectively in Korea by using the revised Porto criteria.

Material/Methods: We retrospectively reviewed the medical record of 135 UC who had been diagnosed before the age of 18 by PIBD experts according to the accepted diagnostic criteria at the time of diagnosis from 2005 to 2013. Each data was categorized by its baseline and follow-up disease characteristics based on endoscopic and histologic findings.

Results: Among total of 135 patients, 48 UC patient data were eligible to evaluate the change of diagnosis based on the Porto criteria. While 20/48 (41.7%) of UC children maintained their original diagnosis, 28/48 (58.3%) of UC patients were reclassified to atypical UC and none of the patients changed to Crohn's disease (CD).

Conclusions: The Porto criteria suggested that the prevalence of atypical UC could be greater than that of CD among those who had been previously diagnosed as pediatric UC in Korea. Given the notion of atypical UC and IBDU as a true intermediate phenotype of PIBD, clinicians should consider multiple variables of the criteria and undergo complete endoscopic and histologic work-up at the time of diagnosis with repeated investigation for every PIBD patient.

723 MRI IMAGING: A PERSONALIZED APPROACH TO UNDERSTANDING FATTY LIVER DISEASE. *Paige Shyken², Joy Ito², Jie Deng², Saeed Mohammad^{1,2}, Mark Fishbein^{1,2}. ¹Pediatric Gastroenterology, Northwestern University, Hinsdale, IL; ²Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL*

MRI is the best non-invasive means to measure hepatic fat content in NAFLD. In this investigation, post-processing (colorizing) of a standard fatty liver sequence was used to highlight fatty change and provide a novel teaching tool for clinical practice. Personalized images of children with NAFLD were reviewed and discussed with their parents. Parental comprehension, recall, and health literacy were then assessed with questionnaires.

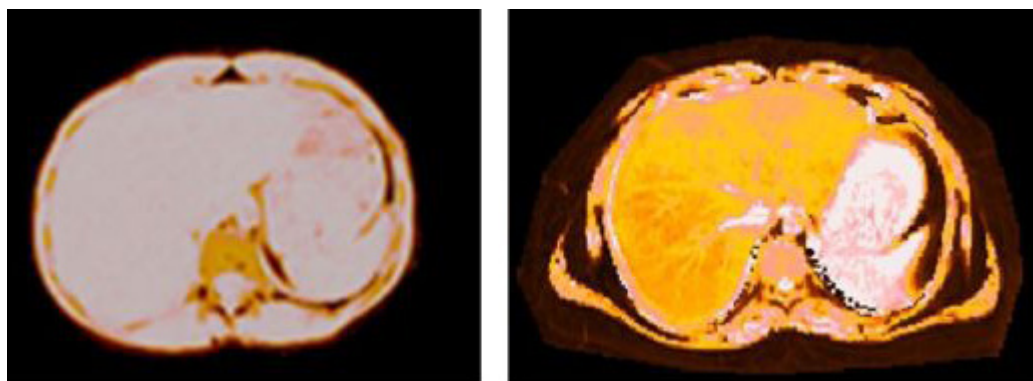
Design: This study included parents or caretakers of children aged 6 to 17 years who were evaluated by hepatic MRI for fat quantification to confirm diagnosis. Each participant received a printed report containing an MR image of their child's liver (post-processed to yellow hue) with coinciding fat fraction contrasted to an adjacent image of a normal liver (pinkish hue). A nurse educator included these images as a resource for educating parent and child on NAFLD, emphasizing consequences (cirrhosis) and cause (obesity). Parent comprehension and recall was assessed by 9 open-ended questions at clinic visit and 2 to 4 weeks later by telephone. Health literacy assessment was performed using NVS (newest vital sign), a quick 6-item tool.

Results: Twenty-two subjects were enrolled and 19 subjects completed the study. Best comprehension was associated with liver color and the amount of fat in liver. Poorest comprehension was identification of associated liver injury. Best recall was color of normal liver. Worst recall was identification of associated liver injury. NVS (n=22) indicated adequate literacy (36.4%), possibility of limited literacy (36.4%), and high likelihood of limited literacy (27%).

Conclusion: The personalized color images of the liver were useful tools to contrast fatty liver from normal liver. However, other features of fatty liver disease including fat content and associated liver injury were not comprehended or recalled as well. These factors, including poor health literacy, are likely to contribute to the refractoriness of NAFLD and obesity in this population.

Comprehension and Recall

		Correct response	Initial (n=22) % correct	Follow-up (n=19) % correct
Q1	Type of machine used to measure fat	MRI	84	89
Q2	Color of normal liver	Pink	100	95
Q3	% fat in normal liver	5% or less	95	74
Q4	Color of child	Yellow	100	84
Q5	% fat in child	Value under image	100	53
Q6a	List liver injury not seen in MRI	Inflammation/scarring	47	21
Q6b	List liver injury not seen in MRI	Inflammation/scarring	74	47
Q7	Condition that can result from fatty liver	Cirrhosis or permanent scarring	79	58
Q8	Recommended way to lower fat in liver	Lose weight	95	79
Q9	What does change from dark yellow to light yellow over time mean	Liver has decreased fat	63	63



Normal liver (pink) and fatty liver (yellow, 36.4% fat)

724 **IBD & CRYPTOSPORIDIUM.** Patricia Bierly. *GI, The Children's of Phila, Willow Grove, PA*

Inflammatory Bowel Disease is an umbrella term for both Crohn's Disease and Ulcerative Colitis. IBD is a condition in which the intestines become inflamed. The factor that triggers the immune system to produce an inflammatory response in is unknown. Genetic, infectious, and immunologic factors all have been implicated. IBD can have periods of remissions and flares. The cause of an IBD flare may not always be identified; stool studies for infections have been often identified including C. Diff and bacterial. The following case confirms that stools for parasites including cryptosporidium should be obtained in patients with IBD.

Case studies: BG is a 13 year old male who was healthy until 6 months ago when he developed abdominal pain and bloody diarrhea. Initial infection work up was negative. Hospitalized and placed on Pentasa and IV steroids. There was no improvement after 4 days- started on Inflixamab with significant improvement. With 2nd and 3rd infusions had an anaphylactic reaction, remained on Prednisone with bloody diarrhea. Plan was to start Humira therapy but he required re- hospitalization, did not respond to IV prednisone therefore underwent a diverting ileostomy. BG was started on Humira which maintained him with occasional blood in from the ostomy. BG had reanastomosis surgery and while in the hospital had vomiting, frequently bloody bowel movements up to 8 per day. Stools studies were obtained that were positive for Cryptosporidium.

Cryptosporidium: Cryptosporidium was first identified in 1910. It was known for infection in 1970. In humans cryptosporidium involves the jejunum and ileum resulting in watery diarrhea lasting up to 2 weeks with potential for re-infection. Cryptosporidium is found in contaminated drinking water, fresh vegetables, seafood and spread person to person. Illness usually resolves in 10-14 days in immunologically healthy people, this can relapse. Cryptosporidium is not usually tested for in routine stool studies for Ova and Parasites. The rate of oocytes shedding and stool consistency may affect the results and multiple samples are requested over several days. Stool specimens are examined microscopically using different techniques (e.g., acid-fast staining, direct fluorescent antibody [DFA], and/or enzyme immunoassays for detection of *Cryptosporidium* sp. antigens).

Treatment: Nitazoxanide- FDA approved for children over the age 1 years old

Summary: BG was treated with Nitazoxanide, BG had 4-5 loose bowel movements per day with no blood. Two months later BG was having one formed stool without blood. Patients with IBD on therapy that alter immune system are at increased risk of developing serious infections and should obtain stool studies for parasites including cryptosporidium.



725 **A HOSPITAL WIDE QUALITY IMPROVEMENT PROJECT TO OPTIMIZE MATERNAL BREAST MILK SUPPLY IN MOTHERS WITH INFANTS IN THE NEONATAL INTENSIVE CARE UNIT.**

Nancy Murray^{1,2}, Mel Buman³, Jill Kigler-Owens¹. ¹NICU, Methodist Women's Hospital, Omaha, NE; ²Neonatal Care PC, Omaha, NE; ³Labor and Delivery, Methodist Women's Hospital, Omaha, NE

Maternal breast milk (MBM) is the best nutrition for infants, especially for premature infants. MBM has been shown to reduce the incidence of serious complications in premature infants. Ensuring an adequate MBM supply is the first step in assuring that infants are provided the protective benefits of MBM. Mothers, who are unable to directly breast feed due to the infant's condition, must utilize an electric breast pump to initiate and maintain their milk supply. Evidence suggests mothers who are separated should begin pumping within 2 or 4 hours (depending on delivery method) after birth to promote lactogenesis and to achieve optimal breast milk volumes. "Pump early, pump often (PEPO)" is often the phrase used to describe the evidence based strategies to initiate and maintain a milk supply in mothers who cannot directly breast feed.

In January of 2016, the new practice of PEPO was initiated on the Neonatal Intensive Care (NICU), Labor and Delivery (L&D), and Postpartum (PP) units. A voice over power point was viewed by all nurses. Nurses in L&D and PP demonstrated setting up a breast pump and hand expression during their annual competencies. The hospital wide policy was updated to reflect the change and electronic medical records were changed to capture pumping times. 14 new breast pumps were purchased, so that there are 54 pumps in the hospital, 2 in L&D, 42 in NICU and 10 in PP. The expectation was to have mothers initiate pumping within 2 hours post vaginal delivery or 4 hours post caesarean delivery (C-section). Previous policy recommended pumping within 6 hours after delivery. Mothers would then be instructed and encouraged to pump 8 times a day. The volume of MBM at day 7 was targeted to be above 500 ml/infant.

The intervention was initially successful after the staff education. Success was defined as the number of mothers, who met the target initiation times for first pumping and then pumping 8 times a day. After initial success, there was a drift to longer times for the first pumping session. In October of 2016 the implementation and monitoring of the first pumping time was transferred from the NICU staff to the L&D staff. PEPO became the unit goal for 2017 for L&D and PP.

Following implementation the average time to first pump for vaginal deliveries decreased from 10 hours pre-intervention to 1.8 post-intervention. Average time to first pump for cesarean section deliveries decreased from 12.9 hours pre-intervention to 3.5 post-intervention. 74% of the mothers are producing 500 ml/day of breast milk on day 7.

After initiation of audits, staff follow-up and unit goal setting, the PEPO project was effective. This successful practice change required more than education. Modification in work flow, cooperation between units and frequent monitoring was needed to achieve the goal of establishing and maintaining maternal milk supply; thus assuring the infants in the NICU received MBM.

726 EFFECTS OF IMPLEMENTATION OF INFANT DRIVEN FEEDING (IDF) PROTOCOLS WHICH INCLUDED PRE AND POST BREAST FEEDING WEIGHTS IN 35 WEEK GESTATIONAL AGE INFANTS IN THE NEONATAL INTENSIVE CARE UNIT (NICU).

Nancy Murray^{1,2}. ¹NICU, Methodist Women's Hospital, Omaha, NE; ²Neonatal Care PC, Omaha, NE

Nipple feeding is a complex, highly coordinated activity, and the preterm infant has to reach a certain level of developmental maturity to be successful in the oral feeding process.

Traditional feeding practices or volume driven feeding involve the clinician ordering the number of nipple feedings the infants can attempt each day, which are primarily based on an infant's weight and gestational age. In this model of care, successful feeding is often defined as the volume taken by an infant. After successfully consuming the desired volume, additional opportunities to feed are ordered. This was the model utilized at Methodist Women's Hospital NICU in 2014.

In 2015 the NICU instituted Ludwig & Waitzman's infant driven feeding program. Utilizing this program, the infants are allowed nipple attempts only if he shows certain readiness cues. This may give infant shorter, but more frequent oral feeding opportunities. A successful feeding in the IDF model includes the achievement of the following major goals: the feeding is safe, functional, nurturing, and individually, as well as developmentally appropriate. This type of practice is considered to be more physiologically appropriate compared to the traditional practice and has been shown to accelerate feeding advancement and shorten the time of hospital stay.

One component of IDF is the accurate assessment of the infant's breast feeding attempts. Historically this has been done by the number of minutes the infant breast feeds. Utilizing the mother's assessment, the infants feeding is then supplemented by a prescribe amount of breast milk and/or formula. Using pre and post breast feeding weights the actual amount of milk consumed by the infant is obtained and then the infant is gavage or bottle fed the remaining amount.

An evaluation of these changes was undertaken to determine if LOS and weight gain were impacted by the implementation of IDF. A chart review of infants admitted to NICU with gestational age at birth between 35 weeks to 35 weeks and 6 days was conducted. The exclusively bottle fed infants fed following the volume protocol (n=18) had an average LOS of 15.1 days and gained 1.03 grams during their hospitalization. The exclusively bottle fed infants who were fed using IDF (n=19) had a LOS of 11.4 days and had a weight gain of 8.9 grams during their hospitalization. The reduction in LOS is clinically significant and reflects the results seen by other hospitals utilizing IDF.

Infants who were fed by both breast and bottle had similar LOS regardless of the feeding protocol. The volume driven group had a LOS of 11 days vs LOS of 12 days in the IDF group. This LOS is similar to the bottle fed group in 2015 that were fed with IDF protocol. However, the weight gain between the two groups differed with the implementation of pre and post breast feeding weights. The infants whose mothers "estimated" their breast feeding intake based on minutes of active nursing (n=58) were below birth weight at discharge (-9 grams) whereas the group that had pre and post feeding weights (n=85) had gained 4 grams by time of discharge.

Implementation of IDF was a positive change, decreasing LOS and improving weight gain in 35 week gestation infants.

727 BODY COMPOSITION IN CHILDREN WITH CYSTIC FIBROSIS IN THE INSTITUTO NACIONAL DE PEDIATRIA, MEXICO CITY. *Miriam Bautista^{1,2}. ¹Gastroenterología Y Nutrición, Instituto Nacional De Pediatría, Ciudad De Mexico, Mexico, Mexico; ²Cancer Center, The American British Cowdray Medical Center, Mexico City, Mexico*

We reviewed in the literature studies about body composition in children with cystic fibrosis (CF) and we found few studies made in the world and none made in Mexico so we wanted to assess it because a low free fat mass (FFM) and poor clinical outcome has been associated so the aim of this study was to evaluate the body composition by air displacement plethysmography through the BOD POD Body Composition System, in children with cystic fibrosis (CF).and also compare it with the physical activity using questionnaires (PAQ-C) and (PAQ-A).

Methods: We included 17 pediatric patients with CF at the Instituto Nacional de Pediatría in Mexico, City. and we measured the body composition, dietary and physical assessment.

The statistics analysis was made through descriptive statistic for the demographic variables and in order to compare the questionnaire of physical activity and body composition we used Wilcoxon signed rank test.

Results: Ten patients had low FM, five medium FM and two of them had high FM. Regarding FFM 15 had normal mass and 2 were depleted. The girls scores were significantly better (53.3%) against the boys (46.7%). In fact 2 boys had depleted FFM. Even though children did mild or moderate physical activity they had low FM in both groups but if the physical activity was moderate they tended to have more FFM. The 58,8 % did not have an adequate intake of their caloric requirement according to the physical activity. None of our patients had an adequate protein intake (p,000). The 98% of the patients had an iron intake in the diet above the recommended dietary allowance (RDA) in 51%. (p.003) versus the zinc dietary intake that had negative intakes regarding RDA in 38.5% p (.001) as selenium was below 44% of the RDA. The vitamin B complex and vitamin A were also below the RDA in the 53% (p,000).

Conclusion: The study shows that the children with CF had low FM. The BMI (body mass index) is not a good indicator of body composition. The patients have inadequate diets, and therefore, need nutritional guidance to foster adequate dietary intake and the resulting improvement in better body composition, guaranteeing better quality of life for the patients.

728 TO DETERMINE THE EFFECT THAT FREEZING AND THAWING HAS ON THE VISCOSITY OF HOMEMADE BLENDERIZED FORMULA TO BE FED BY GASTROSTOMY TUBE. Sharon Weston, Lauren Sorel, Tracie Clarke, Wendy Elverson. Center for Nutrition, Boston Children's Hospital, Boston, MA

Homemade blenderized formula by gastrostomy tube is an alternative approach to traditional formula feeding, and has been indicated to improve tolerance compared to commercially prepared formula in patients experiencing gagging, retching, vomiting, volume intolerance, constipation, and diarrhea. The viscosity of the blenderized formula tends to be thicker than commercialized formula, and may help reduce reflux related symptoms. Registered dietitians can provide important guidance to the families by providing education regarding preparing the formula, analyzing the nutrient composition of the formula, and monitoring patient tolerance and growth. Recipes are typically developed with goals for caloric density, viscosity, and nutrient composition. Recipes include ingredient lists and amounts that will be blended using a high powered blender. For practical reasons, prepared formula may be frozen and then thawed before administering by gastrostomy tube. Differences in viscosity may impact the delivery of the formula as it is administered by syringe or by pump, and also may impact the effectiveness of reducing reflux symptoms. In this study, standard blenderized formula recipes were prepared using a Ninja high powered blender. The viscosity of each sample was measured in centipoise using a Brookfield viscometer. All samples were measured at the same temperature (21 C). Samples were then frozen for 72 hours (-18 C) and then thawed in water (25 C). After completely thawing and brought back to temperature (21 C), the viscosity of the samples were then measured and compared to the original sample values. Results indicated that freezing and thawing homemade blenderized formula does change the viscosity of the blend (Table1). Frozen and thawed blends had significantly lower viscosity measurements as compared to the freshly prepared blends (1652 cP +451 and 7430 cP ± 144, respectively). This difference in viscosity may impact delivery of the formula and also may result in clinical tolerance differences.

729 NUTRITIONAL SUPPORT IN THE CARDIOVASCULAR INTENSIVE CARE UNIT AT THE INSTITUTO NACIONAL DE PEDIATRIA - MEXICO DURING 2012 – 2015. Beatriz Pinzon Navarro^{1,2}.
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Background: The Congenital heart disease is the most important group of congenital malformations. Approximately one quarter of these children require surgery or therapeutic catheterization during the first year of life. Nutritional support is one of the greatest challenges in the evolution of these patients; the objective is to describe the nutritional support of the patients in the Cardiovascular Intensive Care Unit during the period from January 1st 2012 to December 31th 2015.

Material and Methods: We included hospitalized patients in the Cardiovascular Intensive Care Unit from January 1st 2012 to December 31th 2015 who according to the criteria of the attending physician required Nutrition Support. The information was obtained from the physical and electronic records and sheets data collection by the Team of Nutrition Support wich included general patient data, clinical diagnosis, daily prescription data and outcome of the Nutrition Support. In order to estimate the energy requirements, we used two methods: Schofield formula adding correction factors such as growth, physical activity, underlying pathology, sepsis, etc., and for enteral or mixed feeding we used daily energy recommendations (FAO-WHO) plus stress factors.

Results: 57 patients (19 girls and 38 boys). The nutritional assessment was made within the first 48 hours of the patients admission to the Intensive Care Unit and was made in 39 patients (68.4%). The nutritional support was lasted from 1 to 316 days with an average of 27.2 days.

The energy requirement at the beginning was covered in 69%, at the third day 79%, 86.6% at seven days and in the fourteen day they reached 102% adequacy.

Conclusions: In our population, we found that they are at high risk of deteriorating nutritional status. Poor nutritional status has been associated with length of stay, mortality, risk of infections and costs. It has been reported after eight days of stay in the Pediatric Intensive Care Unit, there is a deficit of energy and protein supply, compromising the growth and development of children.

Cardiovascular Surgery Team and Nutritional Support Service must combine efforts to prevent patients undergoing heart surgery from entering better nutritional conditions.

**Table 1. Homemade Blended Formula:
Viscosity Measurements of Freshly Prepared Versus Frozen and Thawed Formula**

Freshly Prepared HBF			
	Viscosity (cP)	Torque (%)	Temperature ©
sample 1	7570	63.10	21
sample 2	7438	62.00	21
sample 3	7282	60.70	21
N (sample size)	3.00	3.00	3.00
Mean	7430	61.93	21
Std Dev	144	1.20	0
S E (Standard Error in the Mean)	83	0.69	0

Frozen and Thawed HBF			
	Viscosity (cP)	Torque (%)	Temperature ©
sample 1	1416	11.80	21
sample 2	1368	11.40	21
sample 3	2172	18.10	21
N (sample size)	3	3.00	3
Mean	1652	13.77	21
Std Dev	451	3.76	0
S E (Standard Error in the Mean)	260	2.17	0

730 PANCREAS CARE CENTER SUCCESS: PRE-VISIT PLANNING AND QUALITY IMPROVEMENT PROCESS IN CHILDREN WITH PANCREATIC DISEASE. Angela Turner¹, Jennifer Jacob¹, Tom Lin¹, Jaimie Nathan², Maisam Abu-El-Haija¹. ¹Gastroenterology, Hepatology And Nutrition, Cincinnati Children's Hospital, Cincinnati, OH; ²Pediatric Surgery, Cincinnati Children's Hospital, Cincinnati, OH

Issue/Background: Pre-visit planning (PVP) is a process used in the management of chronic illnesses. Pediatric pancreas disorders are often lifelong and can lead to poor quality of life, pain requirements, nutritional concerns and other health related complications. The process of collecting and processing patient information can delay visits and reduce the amount of time providers and care team members spend with patients. This disruption in patient flow can result in inefficiencies and may lead to patient/family dissatisfaction. PVP addresses each individual patient's needs and processes data for decision making and ensures standards of care are followed with the goal of improving outcomes. There is a need to standardize care for outpatient pancreas disease management and this becomes critical when patients see multiple subspecialists, need imaging studies, and lab tests all within a day or two.

Objective: To create a PVP process that is consistent and highly reliable. To develop a shared and standardized understanding of the review prior to the patient appointment. Team members include physicians, care managers, social worker, registered dietitian, intake coordinator and data analyst. **Our smart aim defined in the Key Driver Diagram was to Increase Review of PCC Patient's PVP Elements from 0% to 90% by end of the six months. Increase Completion of PCC Pts' PVP Bundle Elements from 0% to 70% by end of that period.**

Improvement Model/Methods: We utilized the improvement model known as Continuous Improvement which involves planning and designing, implementing, evaluating, assessing, and reassessing. We created a model for pre-visit planning in August 2016 which involved monitoring for nutritional risk and vitamin deficiencies, pain and endocrine needs, current patient status and subspecialty appointments. Using the model, the team performed weekly review and made care coordination recommendations so that visits were well planned and standards of care maintained. Feedback from the PCC team were incorporated into the model as well.

Findings: A process map was generated. By implementation of the process, and performing multiple Plan Do Study Act (PDSAs), we refined the process, until it was smoothly followed, and consistently applied. We were able to accomplish our goals by developing a process and increased review of Patient's PVP from 0% to 90% by end of the six months. We accomplished completion of PVP Bundle Elements from 0% to 70% by end of that period.

Conclusion/Implications for Practice: Pre-visit planning supports providing efficient patient care and is important when patients and families are traveling long distance to a specialty care center. A model of PVP has the potential to improve care and clinical outcomes.

CONCURRENT SESSION V – ENDOSCOPY

Saturday, November 4

2:00pm – 3:30pm

731 UNSEDATED IN-OFFICE TRANSNASAL ENDOSCOPY IS SAFE AND EFFECTIVE IN MONITORING DISEASE ACTIVITY IN PEDIATRIC EOSINOPHILIC AND NON-EOSINOPHILIC ESOPHAGEAL DISEASE. *Nathalie Nguyen^{1,2}, William Lavery^{3,2}, Kelley Capocelli^{4,2}, Emily DeBoer^{5,2}, Robin Deterding^{5,2}, Jeremy Prager^{6,2}, Clint Smith^{1,2}, Krystal Mesebrink^{1,2}, Robert Kramer^{1,2}, Glenn Furuta^{1,2}, Joel Friedlander^{1,2}.* ¹*Pediatric Gastroenterology, Hepatology & Nutrition, Children's Hospital of Colorado, Aurora, CO;* ²*University of Colorado, Aurora, CO;* ³*Department of Pediatrics, Children's Hospital of Colorado, Aurora, CO;* ⁴*Department of Pathology, Children's Hospital of Colorado, Aurora, CO;* ⁵*Breathing Institute, Section of Pulmonary Medicine, Children's Hospital of Colorado, Aurora, CO;* ⁶*Department of Otolaryngology, Children's Hospital of Colorado, Aurora, CO*

Background: Methods to monitor esophageal disease in children include sedated endoscopic visualization and assessment of mucosal biopsies. Although effective, traditional esophagoduodenoscopy (EGD) is time consuming, expensive, and carries short-term and potential long-term risks associated with general anesthesia. Recently, we reported the use of unsedated transnasal esophagoscopy (TNE) in a small cohort of children to survey the mucosa of children with EoE. The aim of this study was to evaluate the completion rate, adverse events, and quality/adequacy of pathology specimens obtained during TNE in children with esophageal pathology.

Methods: We performed a retrospective chart review on all children undergoing TNE between June 2014 and February 2017. Children underwent TNE in an outpatient clinic room as previously described. In a standard clinic room, subjects sat upright in a chair and were given 2-6 sprays of 4% aerosolized lidocaine to nares for topical anesthesia. Subjects were given video goggles to view a movie of their choice in order to aid in tolerance of the procedure. Unsedated TNE was performed and biopsy specimens were obtained with either 2.8 mm endoscope with 1.2 mm channel (small TNE scope) or 4 mm endoscope with 2 mm channel (large TNE scope). Twenty-one subjects were previously reported (Friedlander J et al. 2016). Number of TNE, completion rate, visual findings, histology results, and adverse events were recorded. Significant adverse events were defined as Grade 2 (requiring referral to emergency department or unanticipated evaluation by a physician) or above (Kramer RE et al. 2016).

Results: One hundred seventy-eight TNEs were performed on 120 subjects (5-18 years old, mean age 12 years, 122 males, 56 females) using either a 2.8 mm (small TNE) or 4 mm (large TNE) endoscope. TNE comprised of 4.2% (109 TNEs/ 2620 EGDs) of all diagnostic EGDs in 2016 at our center. Fifty-eight subjects underwent TNE with small TNE scope (ages 5-17 years) and 120 subjects underwent TNE with large TNE scope (ages 6-18 years). Twenty-nine subjects had undergone >1

TNE. All adverse events were grade 1: vomiting (6.2%), spit up (1.7%), epistaxis (1.1%), nasal irritation (2.2%), pre-syncope (0.6%), and anxiety (0.6%). Of the 23 subjects with grade 1 adverse events, 17 of 120 subjects (14%) had undergone TNE with large scope and 6 of 58 subjects (10%) had undergone TNE with small scope. There were no adverse events classified as grade 2 or higher. Visual findings reported with small and large TNE included normal mucosa, tracheoesophageal fistula anastomosis, exudate, rings, edema, and linear furrows. Histological findings included esophageal eosinophilia (Table 1), basal cell hyperplasia, rete peg elongation, dilated intercellular spaces, lamina propria fibrosis, unspecified esophagitis, and normal histology. All biopsy specimens from both endoscope models were adequate for evaluation by pathology.

Conclusion: Unsedated TNE is well-tolerated and safe in children ages 5-18. Mucosal inspection and histological sampling obtained from both small and large TNEs are adequate to visualize key features of esophagitis.

Histological Findings	Number of Subjects (%)			
	Small TNE Scope (N=58)		Large TNE Scope (N=120)	
	Proximal	Distal	Proximal	Distal
Eosinophils/HPF				
0 eos/HPF, normal	28 (48.3%)	24 (41.4%)	66 (55%)	57 (54.7%)
1-15 eos/HPF	10 (17.2%)	10 (17.2%)	28 (23.3%)	25 (20.8%)
>15 eos/HPF	20 (34.5%)	24 (41.4%)	26 (21.7%)	38 (31.7%)
Lamina Propria Presence	21 (36.2%)		56 (46.6%)	

732 NASPGHAN Endoscopy Prize

ENDOSCOPIC VACUUM SPONGE THERAPY FOR THE TREATMENT OF ESOPHAGEAL PERFORATIONS IN PEDIATRIC PATIENTS.

Michael Manfredi¹, Susannah Clark², Peter Ngo¹, C Smithers², Thomas Hamilton², Shawn Medford¹, Russell Jennings². ¹Medicine, Boston Children's Hospital, Boston, MA; ²Surgery, Boston Children's Hospital, Boston, MA

Background: Negative pressure wound therapy, commercially known as V.A.C. therapy, was developed in the early 1990s and is now standard of care therapy for chronic wounds, ulcers and burns. Adapting vacuum sponge therapy for use intraluminally for perforations of the esophagus was first reported in 2008. We report the first pediatric experience on endoscopic vacuum sponge therapy (EVST) for closure of esophageal perforations.

Aim: To evaluate the technical feasibility, safety and efficacy of EVST in a pediatric population with esophageal perforations.

Methods: We performed a retrospective chart review on all patients who underwent EVST for esophageal perforations from (October 2013 to May 2017) at our institution (IRB-P00004344). Our primary aim was to look at success, which was defined as closure of esophageal perforation requiring no additional therapy. We also looked at complications from EVST and technical issues with EVST placement.

Technique: A sump tube was passed through the nares and pulled out the mouth. The tube was then driven lengthwise through a custom-made vacuum sponge fashioned from a V.A.C. granufoam™ dressing (KCI USA, San Antonio) until the end of the tube was protruding by about 5 to 10 mm and tied in place very close to the ends of the sponge using a silk tie. A prolene suture was driven through the end of the tube and tied into a short loop to help with endoscopic placement (see picture). The sponge was then advanced into the esophageal lumen under endoscopic and fluoroscopic guidance. The sump end was connected to a V.A.C. therapy pump (KCI USA, San Antonio), which was turned on to a continuous negative pressure of 125 mm Hg. Further modifications that were made with in time, were changing tubing from a sump to a Jackson-Pratt Drain tube. This tubing has more circumferential holes to increase suction and minimized tube clogging.

Results: A total of 13 patients underwent therapy for esophageal perforation. Six patients had placement for post-surgical perforation and seven were placed secondary to post-endoscopic therapy perforation. Overall success rate was 85% (11/13). The mean duration of treatment with each sponge was 6 days (range 1-9); the mean number of EVST sessions per patient was 2 (range 1-4). The mean total duration of therapy was 11 days (range 4-21.) There were no technical failures with placement. The one complication was due to the devices failure to obtain a negative suction for over 12 hours, leading to worsening of the perforation.

Conclusion: EVST is a novel, promising technique for the treatment of esophageal perforations in a pediatric population. Further improvement in device customization could improve success rate further.

Endoscopic Vacuum Sponge Results	
Number of VAC Patients	13
Female	7
Mean Age in Months (range)	28 (3 to 107)
Mean number of VAC sessions (range)	2 (1 to 4)
Mean days per Sponge Duration in days (range)	5.9 (1 to 9)
Mean days total per patient in days (range)	11 (4 to 21)
Post-Anastomotic Perforations Patients	6
Post Endoscopic Perforation	7
Sealing of all esophageal perforation	11/13 (85%)
Sealing of Post Anastomotic Perforations	5/6 (83%)
Sealing of Post Endoscopic Perforations	6/7 (86%)



CONCURRENT SESSION V – GLOBAL HEALTH

Saturday, November 4

2:00pm – 3:30pm

- 733 TESTING ENGINEERED BACTERIOPHAGE AS AN INNOVATIVE TREATMENT APPROACH AGAINST ENTERIC PATHOGENS.** *Alejandro Llanos-Chea^{1,2}, Robert Citorik³, Stefania Senger^{1,2}, Shanmugapriya Sothiselvam³, Sebastien Lemire³, Kourtney Nickerson^{1,2}, Timothy Lu³, Alessio Fasano^{1,2}, Christina Faherty^{1,2}.*
¹Pediatric Gastroenterology, MassGeneral Hospital for Children, Boston, MA; ²Harvard Medical School, Boston, MA; ³Massachusetts Institute of Technology, Cambridge, MA

Background: Environmental enteropathy (EE) is an acquired subclinical condition of the intestine among children of developing countries that leads to mucosal inflammation, villous blunting, altered barrier integrity, and reduced intestinal absorptive capacity. EE leads to chronic malnutrition and stunting in children, further causing cognitive and physical deficits. EE is thought to be a result of chronic exposure to enteropathogens such as *Shigella flexneri*, enteropathogenic *Escherichia coli*, and *Salmonella enterica*, which are Gram-negative bacterial pathogens of the gastrointestinal tract. Phage therapy is routinely used for enteric infections in Eastern European countries. A single phage particle can target a specific bacterial species or a subset of the same species. Nevertheless, the exact mechanism of phage killing is unknown, the microbiota may be targeted, and the development of bacterial resistance to the phage may occur. To address these concerns, we are developing engineered pathogen-specific phages to specifically target enteric bacteria while preserving commensal organisms as a practical treatment option for EE.

Methods: Engineered phages are being developed at the Massachusetts Institute of Technology that will deliver single-guide RNA CRISPR-Cas9 genetic circuits targeting essential genes of *Shigella* and *Salmonella*, leading to chromosomal degradation and bacterial cell death. As a proof of concept, we have tested bacteriophages enriched from Intesti-bacteriophage (Eliava Institute, Georgia) as a *S. flexneri* 2a 2457T-specific antibacterial agent. Phage killing was assessed through broth kill curves, infection assays in HT-29 cells, and on a novel cecum-derived organoid monolayer infection model. Organoids are reproduced from human biopsy samples in which stem cells are collected from the intestinal crypts, expanded in culture, and subsequently seeded onto transwells to establish three-dimensional monolayers that differentiate into intestinal tissue following treatment with DAPT, an inhibitor of the γ -secretase complex.

Results: We have demonstrated an efficient killing effect of the prototype phage on *S. flexneri* through kill curve analyses in multiple types of culture media and during infections with HT-29 cells and cecum-derived organoid monolayers as determined by recoverable bacterial titers. Imaging techniques, such as immunofluorescence and transmission electron microscopy, were used to support our findings. Additionally, we found other strains of *Shigella* were susceptible to the phage, while the phage did not kill commensal bacteria, as demonstrated in our co-culture analysis with the human commensal *E. coli* HS. As a result of these experiments, this prototype phage is being used as a basis for development of a *Shigella*-specific engineered phage following design techniques already initiated for a candidate *Salmonella*-specific phage.

Conclusions: Our ongoing work demonstrates that phage-mediated killing of bacteria is a successful and feasible alternative to antibiotics for elimination of enteric pathogens. Furthermore, application of the organoid monolayer model has given us unprecedented insight into the pathogenesis and related phage-dependent intervention strategies for *Shigella*. Future work will evaluate the efficacy of the engineered phages being developed for *Shigella* and *Salmonella*-specific clearance. This work could lead to the clinical development of engineered phage to target pathogenic bacteria while minimizing off-target effects on the human microbiome.

CONCURRENT SESSION V – MALABSORPTION

Saturday, November 4

2:00pm – 3:30pm

- 734 **LIPID MALABSORPTION AND AN INFLAMMATORY RESPONSE IN INTESTINAL ARX LOSS OF FUNCTION MOUSE MODELS.** Natalie Terry^{1,2}, Lucie Ngaba¹, Benjamin Wilkins^{1,2}, Danielle Pi¹, Nishi Gheewala¹, Klaus Kaestner². ¹Pediatrics/Gastroenterology, The Children's Hospital of Philadelphia, Philadelphia, PA; ²Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

Background/Aims: Children born with congenital diarrheal disorders have high morbidity and mortality. Total parenteral nutrition, or intravenous nutrition, is a life-saving intervention though is accompanied by significant risks. Thus, therapeutic options must be developed to treat the underlying malabsorption. One cause of congenital diarrhea is enteroendocrine cell dysgenesis, where the loss of intestinal endocrine cells leads to a severe malabsorptive diarrhea (Cortina et al Hum Pathol 2007). Aristaless-related homeobox, ARX/Arx, is specifically expressed in the intestinal endocrine cells. Both loss of function and polyalanine expansion mutations have been described in human intestinal disease. We investigated the phenotypes of intestinal-specific *Arx* deletions to further understand the mechanism of malabsorption in enteroendocrine dysgenesis.

Methods: We developed an intestinal-specific model of *Arx* deficiency using male villin-Cre; *Arx*^{loxP} (*Arx*^{int}) mice where *Arx* is deleted from the intestinal epithelial starting in embryonic stages. In order to also study the role of *Arx* in maintenance of the endocrine lineage, we created an inducible knockout mouse with *Arx* deficiency using villin-CreER; *Arx*^{loxP} (*Arx*^{iKO}) mice where tamoxifen induction leads to loss of *Arx* in the adult mouse. Histology was assessed with both hematoxylin/eosin stains and electron microscopy while immunohistochemistry and quantitative RT-PCR were performed to assess the lineage allocation of the enteroendocrine cells. *Arx*^{iKO} mice were treated with standard chow, high fat diet, pancreatic enzymes, and a low fat diet. Growth curves were closely followed with serum triglyceride and fatty acid determination. To identify the signaling cascades underlying the diarrheal phenotype, microarray profiling was executed. Finally, enteroids were cultured in EGF/Noggin/R-spondin supplemented media after crypt isolation from the epithelium.

Results: Intestinal *Arx* is required for the specification of the cholecystokinin (CCK), glucose-dependent insulinotropic peptide (GIP), secretin (Sct), glucagon-like peptide 1 (GLP-1) and GLP-2 lineages, though the Chromogranin A (CgA) is not reduced. Loss of *Arx* also leads to an upregulation of somatostatin (SST). The *Arx*^{int} mice have significant failure to thrive and high mortality in the first few weeks of life with evidence of lipid malabsorption. Microarray profiling demonstrates strong upregulation of antimicrobial peptides, such as Reg3 β . In the adult *Arx*^{iKO} mice, diarrhea, weight loss, and lipid malabsorption

are also present on standard chow and a high-fat diet but can be reversed with pancreatic enzyme supplementation and a low-fat diet. Using *Arx*^{KO} enteroids, we are developing an *ex vivo* system of lipid absorption.

Conclusions: Intestinal *Arx* is required for proper lineage allocation in development and maintenance of the enteroendocrine lineage subtypes. A primary feature of these mouse models is lipid malabsorption that can be reversed with dietary treatment and pancreatic enzyme supplementation. Understanding how the hormones communicate with the enterocytes to mediate specific lipid passage will direct dietary treatments for patients with enteroendocrine cell dysgenesis.

735 NASPGHAN Pancreas Award

EVALUATION OF PH INTERFERENCE AND ACCURACY OF PANCREATIC ENZYME ACTIVITY BY DIRECT PANCREATIC FUNCTION TESTING.

Jonathan Beri¹, Heidi Hagerott¹, Zhaoping He², Zarela Molle-Rios¹. ¹Gastroenterology, A.I. duPont Hospital for Children/Thomas Jefferson University, Wilmington, DE; ²Biomedical Research, Nemours/Alfred I DuPont Hospital for Children, Wilmington, DE

Background: Testing pancreatic enzyme activities in pancreatic fluid collected via endoscopic stimulation is the gold standard to evaluate exocrine pancreatic dysfunction. There is no standardization on how to determine if a sample is adequate for pancreatic enzyme testing. Two factors influence sample integrity and enzyme activities, proper alkalization from bicarbonate secretion of pancreas and acidification from gastric contamination. We hypothesize that pH is a simple marker to determine the sample reliability for enzyme testing. Our goal was to evaluate the effects of pH on the enzyme activities and identify factors influencing pH in pancreatic fluid.

Methods: Children (N=465; <18 year age) who underwent exocrine pancreatic stimulation testing at Alfred I duPont Hospital for Children and Nemours Children Hospital between 2010 and 2016 were identified via electronic medical records. Demographic and clinical data included age, diagnosis, pancreatic stimulation drug and presence of catheter used. Pancreatic testing included pancreatic fluid pH and enzyme activities of amylase, lipase, chymotrypsin, trypsin and elastase. The abnormal enzyme was defined by the reference value and pH was categorized into pH>7.0 as normal, ≤7 to ≥4.0 and <4.0 as abnormal. The comparison was assessed by t test and chi-square contingency. P-value less than 0.05 was used to indicate statistical significance.

Results: Prevalence of abnormal pH ≤7 to ≥4 was 33% and pH <4.0 was 1% (Table 1). Samples in acidic pH groups (≤7 to ≥4.0 and <4.0) had a significantly higher percentage of abnormal enzyme activities and a lower mean activity compared with samples with normal pH >7.0 (Table 1). Complete deficiency with all 5 abnormal enzymes was 76% (19/25) in pH <4.0 samples and 29% (165/561) in pH ≤7 to ≥4 which was significantly higher than 9% (98/1130) in normal pH (>7.0) samples (p<0.001).

Patients in acidic pH ≤ 7.0 group (at least one sample) had statistically greater % of abnormal enzymes (at least one abnormal enzyme in sample/samples) compared to patients in pH >7.0 group, 72 % vs 58%, respectively (P < 0.001). Correlation between acidic pH and specific factors including age, use of a catheter and drug used for pancreatic stimulation were analyzed. Patients with catheters were older than without (mean age 6.4 vs 5.6 yr) however not statistically significant (P=0.095). Percentage of abnormal pH (# abnormal pH sample/total samples) was 37.3% with catheter and 31.8% without (P=0.126) and % of abnormal enzymes (# of abnormal enzymes/total enzymes tested) was 31.0% with catheter and 33.3% without (P=0.492). Patients who received Sincalid were significantly older than those who received Secretin, 6.4±5.1 vs 5.3±5.6 respectively (P = 0.029) and were more likely to have a higher % of abnormal pH, 38.3% vs 29.4% (p=0.012) and abnormal enzymes, 35.0% vs 29.7% (p=0.107).

Discussion/Conclusion: Our data shows that pancreatic fluid samples with an acidic pH had a significant effect on the outcome of enzyme activity potentially leading to a false exocrine pancreatic insufficiency diagnosis. The use of a catheter and age had no effect on the pH of samples whereas the drug used for pancreatic stimulation may have an effect on pH. Further research needs to be completed to corroborate these findings.

Total N = 1721	>7 (n=1130)*		≤7 to ≥4 (n=561)*		<4 (n=25)*	
% of total	66%		33%		1%	
	% Abnormal	Mean ± SD	% Abnormal	Mean ± SD	% Abnormal	Mean ± SD
Amylase	25.5	43.2±65.5	49.4	29.1±45.7	100.0	0.6±1.1
Lipase	21.7	475.7±452.8	46.0	318.6±392.0	100.0	22.6±14.5
Chymotrypsin	34.3	10.4±10.7	51.9	8.2±11.6	92.0	1.5±1.6
Trypsin	22.1	816.8±747.8	40.6	654.0±771.1	84.0	141.1±181.8
Elastase	18.2	39.0±43.6	36.2	28.5±34.8	100.0	0.4±0.6

*Comparisons between pH groups had P

CONCURRENT SESSION V – NEUROGASTROENTEROLOGY AND MOTILITY

Saturday, November 4

2:00pm – 3:30pm

736 **ENTEROCHROMAFFIN CELLS ARE GUT CHEMOSENSORS THAT COUPLE TO SENSORY NEURAL PATHWAYS.**

James Bayrer^{1,5}, Nicholas Bellono², Stuart Brierley^{3,4}, Holly Ingraham⁵, David Julius².

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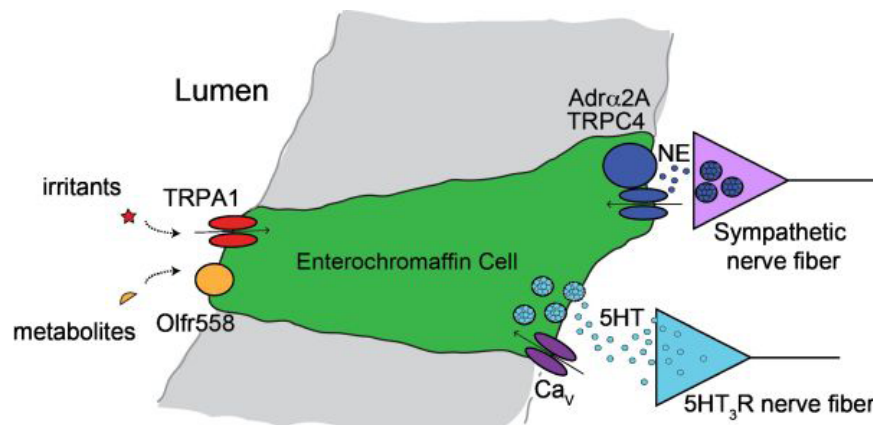
Background. Dietary, microbial, and inflammatory factors modulate the gut-brain axis and influence physiological processes ranging from metabolism to cognition. The gut epithelium is a principle site for detecting such agents, but precisely how it communicates with neural elements is poorly understood. Serotonergic enterochromaffin (EC) cells are proposed to fulfill this role by acting as chemosensors, but understanding how these rare and unique cell types transduce chemosensory information to the nervous system has been hampered by their paucity and inaccessibility to single cell measurements.

Methods: We employed intestinal organoids expressing a fluorescent marker under control of the Chromogranin A promoter (ChgA-GFP) to selectively mark EC cells, enabling single cell measurements and the elucidation of intrinsic biophysical, pharmacological, and genetic properties. We accomplished this using a combination of single-cell patch clamping, fluorescent calcium imaging, immunohistochemistry, and RNA expression profiling. We next extended our intestinal organoid culture findings through the structural delineation of EC cell-sensory afferent nerve fiber synaptic-like connections using a 5HT₃R-GFP reporter mouse and imaging of synaptic markers. Finally, we interrogated the functionality of the identified EC-afferent nerve fiber synapse using an *ex vivo* gut-nerve system to record epithelial stimulus-evoked single nerve fiber activation.

Results: EC cells express an array of receptors and voltage-sensitive ion channels that integrate separate stimulatory pathways to control serotonin release. Using a combination of pharmacological and gene expression profiling we identified three primary classes of EC cell stimulants that trigger serotonin release: irritants, volatile short chain fatty acid microbial metabolites, and catecholamines. We further demonstrate using CRISPR-mediated gene knockout, pharmacological blockade, and immunohistochemistry that these agents act via specific receptors expressed selectively in EC cells. In the intestine, sensory afferent nerve fibers as marked by 5HT₃R expression co-localize with EC cells and form synapse-like connections. Moreover, we show proximity of sympathetic nerve fibers to EC cells suggesting one local source for stimulatory catecholamine production. Finally, we demonstrate that sensory afferent nerve fiber activity can be potentiated via selective EC cell activation including the induction of hypersensitivity to mechanical stimulation.

Conclusions: We demonstrate that EC cells express specific chemosensory receptors, are electrically excitable, and modulate serotonin-sensitive primary afferent nerve fibers via synaptic connections, thus enabling them to detect and transduce environmental, metabolic, and homeostatic information from the gut directly to the nervous system. The pathways outlined here have to potential to be modulated for the treatment of visceral hypersensitivity syndromes.

Support: K12 HD072222, K08 DK106577



737 EXAMINING THE LINK BETWEEN CONSTIPATION AND DEPRESSION: A NOVEL ROLE FOR SEROTONIN IN THE GUT-BRAIN-MICROBIOME AXIS. Narek Israelyan¹, Tara Lorimer^{1,3}, Yeji Park^{1,3}, Albert Xing¹, Zi Shan Li^{1,2}, Ruth Ann Luna⁵, Alamelu Venkatachalam⁵, Marc Caron⁴, Jacob Jacobson⁴, Michael Gershon², Kara Gross Margolis¹. ¹Pediatrics, Columbia University, NEW YORK, NY; ²Pathology, Columbia University, New York, NY; ³Institute of Human Nutrition, Columbia University, New York, NY; ⁴Department of Cell Biology, Duke University School of Medicine, Durham, NC; ⁵Children's Hospital Microbiome Center, Baylor College of Medicine, Houston, TX.

Irritable bowel syndrome (IBS) affects 14% of the US population and 11% of people worldwide. Half of IBS patients also suffer from depression and this association is stronger with constipation-predominant IBS (IBS-C) than with diarrhea-predominant IBS. Despite the prevalence of these co-occurring conditions, there are no therapies that optimally treat both the brain and gut manifestations. GI-focused therapies for IBS (i.e., linaclotide) do not treat depression. Though selective serotonin reuptake inhibitors (SSRIs) can alleviate pain in IBS and treat depression, chronic SSRI therapy often causes constipation. There is thus a critical need for effective therapies that target the gut-brain axis in IBS. Such treatments, however, require a greater understanding of brain-gut connections.

Reciprocal interactions between the gut, brain, and microbiome, termed the gut-brain-microbiome (GBM) axis, have increasingly been found to play roles in human disease. Serotonin (5-HT), a neurotransmitter classically known for its roles in sleep and mood, is also critical for central (CNS) and enteric nervous system (ENS) development, GI motility, and enteric microbiome modulation. Tryptophan hydroxylase 2 (Tph2), the rate-limiting enzyme in CNS and ENS 5-HT biosynthesis, could thus be a brain-gut link.

A variant in the Tph2 gene (R441H) was identified in a cohort of patients with unipolar depression. Transgenic mice containing a similar variant (R439H; equivalent to human R441H) display an 80% decrease in CNS 5-HT levels and a predisposition to depression-like symptoms.

We sought to determine whether this abnormality in Tph2 could underlie the co-occurrence of depression and constipation by evaluating the R439H mouse for defects in ENS development and GI function. Immunocytochemical examination of bowel wall revealed that

the ENS was hypoplastic in R439H mice with a decreased number of total neurons in the submucosal and myenteric plexuses ($p < 0.005$ vs WT; Fig 1) and an exaggerated hypoplasia in 5-HT-dependent neuronal populations (TH- and GABA-expressing, $p < 0.005$). Further, total GI transit ($p < 0.05$), small intestinal transit ($p < 0.02$) and gastric emptying ($p < 0.03$) were slower in R439H mice than WT. To evaluate whether the slowed motility resulted from abnormal ENS development, in vitro peristaltic contractions (a direct measure of ENS function without CNS input) were quantified. The frequency and velocity of contractions were significantly lower in R439H mice ($p < 0.001$ vs WT; Fig 2). An additional measure of ENS function, growth of enteric villi, was also less in R439H than WT ($p < 0.0001$). Finally, enteric microbiota anomalies were observed in R439H mice

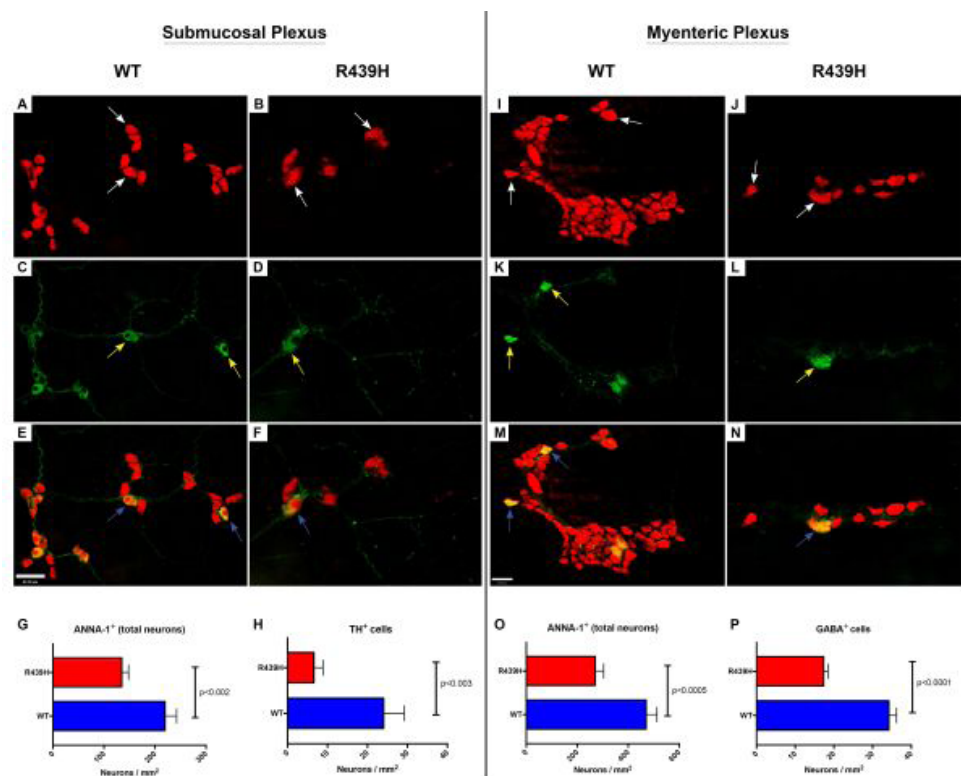


Figure 1. Numbers of total and late-born enteric neurons are lower in Tph2 R439H than in WT mice. $n = 3-4$ /group. (A and B) Submucosal ANNA-1 immunoreactive neurons [white arrows]: (A) WT; (B) Tph2 R439H. (C and D) Submucosal TH-immunoreactive neurons [yellow arrows]: (C) WT; (D) Tph2 R439H. (E and F) Merged images of submucosal ANNA-1 and TH-immunoreactive neurons; note that TH-immunoreactive cells contain coincident ANNA-1 immunoreactivity [blue arrows]: (E) WT; (F) Tph2 R439H. (G) Total neurons in submucosal plexus. (H) Dopaminergic neurons (TH-immunoreactive) in submucosal plexus. Scale bars: 60 μ m in submucosal plexus. (I and J) Myenteric ANNA-1 immunoreactive neurons [white arrows]: (I) WT; (J) Tph2 R439H. (K and L) Myenteric GABA-immunoreactive neurons [yellow arrows]: (K) WT; (L) Tph2 R439H. (M and N) Merged images of myenteric ANNA-1 and GABA-immunoreactive neurons; note that GABA-immunoreactive cells contain coincident ANNA-1 immunoreactivity [blue arrows]: (M) WT; (N) Tph2 R439H. (O) Total neurons in myenteric plexus. (P) GABAergic neurons in myenteric plexus. Scale bars: 32 μ m in myenteric plexus.

that mimic those seen in patients with IBS. In conclusion, we examined a mouse model (R439H) that contains a variant in Tph2 that is also overexpressed in patients with depression. In addition to an increased propensity to depression, these mice exhibit ENS hypoplasia, abnormalities in ENS-regulated GI functions, and an enteric dysbiosis. The R439H SNP in Tph2 may therefore link GI and CNS co-morbidities in disorders of the gut-brain-microbiome axis, such as IBS-C.

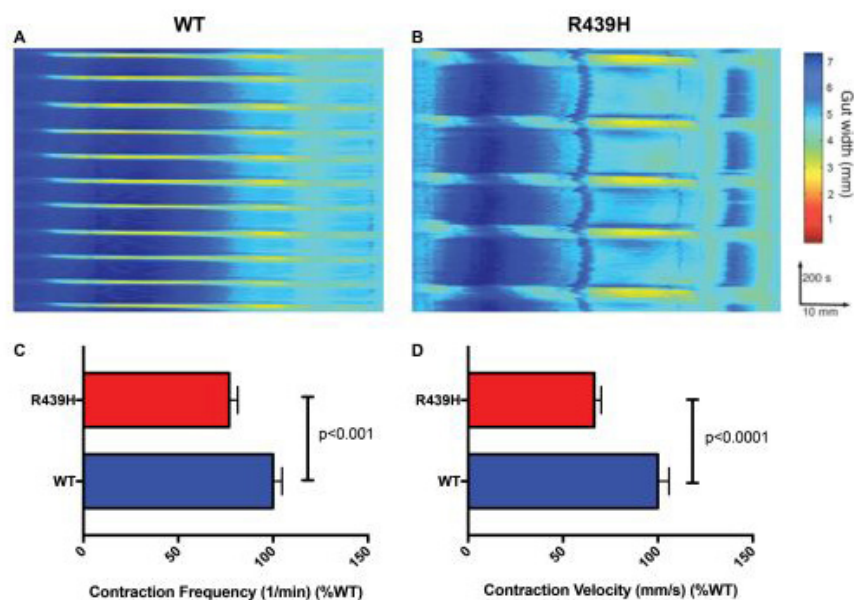


Figure 2. In-vitro intestinal motility is abnormally slow in Tph2 R439H mice. $n = 6-8/\text{group}$. (A and B) Typical spatiotemporal maps showing peristaltic contractions in isolated preparations of colon. The ordinate represents time, and the abscissa represents oral-to-anal distance. The width of the gut (mm), indicative of contractions, was pseudocolored: (A) WT; (B) Tph2 R439H. (C) Contraction frequency. (D) Contraction velocity. Data represents the mean \pm SEM.

CONCURRENT SESSION VI – INFLAMMATORY BOWEL DISEASE

Saturday, November 4

3:45pm – 5:15pm

- 738 THE EPIGENETIC COMPLEX PRC1 MAINTAINS REGULATORY T CELL LINEAGE STABILITY.** Michelle Gonzalez^{1,2}, Phyllis Svingen², Mary Sagstetter², Olga Sarmento², Adebowale Bamidele², Zhifu Sun³, Asha Nair³, Thomas Smyrk⁴, Angela Mathison², Raul Urrutia², William Faubion². ¹Pediatric Gastroenterology, Mayo Clinic, Rochester, MN; ²Epigenetics and Chromatin Dynamics Laboratory, Division of Gastroenterology and Hepatology and Translational Epigenomic Program, Mayo Clinic, Rochester, MN; ³Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN; ⁴Division of Anatomic Pathology, Mayo Clinic, Rochester, MN

Introduction: We have previously identified a deregulated gene network driven by the transcription factor FOXP3 in T cells isolated from Crohn's Disease (CD) lesions. Subsequent bioinformatics analysis of this gene set indicates a role for the epigenetic complex Polycomb Repressive Complex 1 (PRC1) in the co-repression of FOXP3 gene targets. In this study, we use cell lines, primary T cells, and mouse models to characterize the function of BMI1, a core protein of PRC1, in FOXP3+ Treg cell biology.

Methods: Bioinformatics analysis was performed using edge R 3.8.6 and the Enrichr gene set analysis web server. BMI1 was quantified by qPCR and immunoblotting. BMI1 function was assessed by target gene (IL-2) activation by flow cytometry and inhibited using pharmacologic and genetic approaches. Treg cellular phenotyping was performed by flow cytometry for signature proteins and cytokines. BMI1 in vivo function was assessed by conditional KO.

Results: Our prior work identified a signature gene set for Crohn's disease notable for loss of FOXP3 gene regulation ($n=260$ genes). To gain further biological information and guide subsequent mechanistic studies, we performed gene-list enrichment

analyses using the web-based interactive application, Enrichr (Ma'ayan laboratory, Mt Sinai Hospital). Our gene list was highly enriched within gene sets regulated by polycomb group proteins ($p=2.1e-36$, ChEA2016 database). Furthermore, the PRC1 complex ($p=0.003$, CORUM database) and specifically the BMI1-containing PRC1 complex ($p=0.005$, CORUM database) emerged as two lead candidate complexes functionally related to our gene list. We subsequently turned to in vitro analyses to assess the functional role of BMI1 in FOXP3+ Treg cells. We discovered that PRC1 is present in Treg cells shown by the interaction of BMI1 and RING1B proteins. In FOXP3-expressing T cell lines, BMI1 inhibition using PTC-209, a specific inhibitor of BMI1 leads to marked de-repression of IL-2, an established FOXP3 gene target (5.73 vs 17.87% cells). These data suggest that maintenance of FOXP3 repression of the IL-2 gene requires BMI1. Generalizing this mechanism to Treg signature genes, we confirmed loss of expression of the key immunoregulatory protein CTLA4 in primary Treg cells treated with PTC-209. Finally, we generated a mutant mouse line with conditional BMI1 KO in FOXP3-expressing T cells. Pups of a high CRE expressing cell line with BMI1 deletion displayed evidence of systemic Treg dysfunction, as they were grossly runted, did not survive beyond 18 days, and displayed marked elevation of the proinflammatory cytokines IL6 (924.10 vs 1.29 pg/mL) and TNF α (19.90 vs 2.37 pg/mL). At the tissue level, necropsy suggests that the likely cause of death in this mouse line was pneumonitis. Due to significant toxicity, a low CRE expressing cell line was bred. At the level of cytokine expression, they expressed higher levels of serum IFN γ than paired wild type mice (2.5-fold increase, $p=0.048$). Additionally, at the single cell level we showed generalized deregulation in Treg gene expression profiles.

Together these data suggest that the epigenetic complex PRC1, identified through gene network analysis of lymphocytes isolated from CD patients, maintains Treg signature genes and inactivation of the complex leads to systemic immune mediated disease.

106 **BACH2-RELATED IMMUNE DEFICIENCY AND AUTOIMMUNITY (BRIDA) A NOVEL MONOGENIC DISEASE CAUSED BY HAPLO-INSUFFICIENCY OF BACH2**

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The etiology of autoimmune disease is regarded as multifactorial, involving interplay between genetic and environmental factors. There is an association between single nucleotide polymorphisms (SNPs) at/near gene loci with disease susceptibility. How most SNPs impart genetic risk remains unknown, but one mechanism is via interference with binding of transcription factors (TFs) to critical regulatory elements. Monogenic causes of disease (ie in cases of primary immune disease (PID) and early onset intestinal inflammation) on the other hand by contrast can be due to disrupt protein structure or function. In some cases they are caused by haplo-insufficiency, where only a single functional copy of the gene exerts influence. In the cases of PID and intestinal inflammation there has been associated defects in T and/or B cell development and/or function. BTB And CNC Homology 2 (BACH2) is a regulator of T and B lymphocyte differentiation and genetic polymorphisms in BACH2 have been observed in a variety of autoimmune diseases (ie asthma, coeliac disease, vitiligo, multiple sclerosis, IBD). Although these associations point to a shared mechanism, a function for BACH2 in the maintenance of immune homeostasis has not been established.

Herein, we report three patients with heterozygous hypomorphic mutations in BACH2 in two unrelated kindreds with evidence of autoimmunity, immunodeficiency, and early onset intestinal inflammation associated with B and T cell defects. Patients had marked reduction of total and class-switched memory B cells, defective production of class-switched immunoglobulins in vitro and B cell lymphopenia. In addition studies, BACH2 appears to play an important role in suppressing the myeloid gene program in developing B cells as it controls terminal B cell maturation by repressing expression of the Prdm1 gene. Furthermore, these patients expressed reduced percentage of suppressor regulatory FoxP3+ T cells with increased expression of Th1 pro-inflammatory transcription factors (i.e. T-bet). Thus, BACH2 functions as a regulator of

immune activation that stabilizes immunoregulatory capacity while repressing the programs of inflammatory cell lineage. The two distinct BACH2 missense mutations identified in these patients resulted in reduced BACH2 protein expression. Mutant (L24P) was insoluble and unable to form dimers; the second mutant (E788K) formed cytoplasmic aggregates. Transfection experiments revealed that mutant alleles did not exert a dominant-negative effect but effects were secondary to haplo-insufficiency, through influence of a single functional copy of the gene.

Thus, BACH2 haploinsufficiency was associated with a new monogenic disease characterized by immunodeficiency (hypogammaglobulinemia), recurrent infections, immune dysregulation, and occurrence (in some instances) of early onset intestinal inflammation; which we have termed BRIDA (BACH2-related immune deficiency and autoimmunity). These findings identify BACH2 as an additional gene that requires screening for early onset intestinal inflammation as it appears to be a key regulator of B and T-cell differentiation that controls inflammatory disease by the careful balance between immunity and tolerance.

CONCURRENT SESSION VI – LIVER

Saturday, November 4

3:45pm – 5:15pm

739 **RESULTS OF ITCH, A MULTI-CENTER RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF MARALIXIBAT, AN ILEAL APICAL SODIUM-DEPENDENT BILE ACID TRANSPORTER INHIBITOR (ASBTI), FOR PRURITUS IN ALAGILLE SYNDROME (ALGS).**

Benjamin Shneider¹, Cathie Spino², Binita Kamath³, John Magee⁴, Peter Whittington⁵, Kenneth Setchell⁶, Alexander Miethke⁷, Jean Molleston⁸, Cara Mack⁹, Robert Squires¹⁰, Karen Murray¹¹, Kathleen Loomes¹², Philip Rosenthal¹³, Saul Karpen¹⁴, Daniel Leung¹, Stephen Guthery¹⁵, Danny Thomas¹⁶, Averell Sherker¹⁷, Ronald Sokol^{18,19}. ¹Pediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Houston, TX; ²Department of Biostatistics, University of Michigan, Ann Arbor, MI; ³Division of Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children and University of Toronto, Toronto, ON, Canada; ⁴University of Michigan Medical School, Ann Arbor, MI; ⁵Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, IL; ⁶Department of Pediatrics – Pathology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ⁷Division of Pediatric Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH; ⁸Pediatric Gastroenterology, Hepatology and Nutrition, Indiana University School of Medicine /Riley Hospital for Children, Indianapolis, IN; ⁹Section of Pediatric Gastroenterology/Hepatology/Nutrition, Children's Hospital Colorado, Aurora, CO; ¹⁰Children's Hospital of Pittsburgh, Pittsburgh, PA; ¹¹Division of Gastroenterology and Hepatology, University of Washington Medical Center, Seattle Children's, Seattle, WA; ¹²Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital of Philadelphia, Philadelphia, PA; ¹³Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, University of California, San Francisco, San Francisco, CA; ¹⁴Pediatric Gastroenterology, Hepatology and Nutrition, Emory University School of Medicine/Children's Healthcare of Atlanta, Atlanta, GA; ¹⁵Pediatric Gastroenterology, Hepatology and Nutrition, University of Utah, Salt Lake City, UT; ¹⁶Department of Gastroenterology, Children's Hospital Los Angeles, Los Angeles, CA; ¹⁷Liver Diseases Research Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD; ¹⁸Section of Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital Colorado, Aurora, CO; ¹⁹for the Childhood Liver Disease Research Network (ChiLDRen), DCC, Ann Arbor, MI

Background: Medically refractory, severe, cholestasis-induced pruritus in ALGS may be improved by surgical interruption of the enterohepatic circulation (biliary diversion or ileal exclusion). This trial tested the hypothesis that pharmacologic interruption of the enterohepatic circulation of bile acids (BA), using the ASBTi maralixibat (previously LUM001; SHP625), would reduce pruritus in ALGS (NCT02057692).

Methods: 37 children with ALGS (age 6.8 ± 4.5 yr) were randomly assigned to 1 of 4 treatment groups: once daily placebo, 70, 140 or 280 $\mu\text{g}/\text{kg}$ of maralixibat for 13 weeks. Pruritus was assessed using a novel pediatric, observer version of the Itch Report Outcome (ItchRO™[Obs]), range 0 – 4 [severe], entry criteria ≥ 2) and by clinician report (clinician scratch scale, CSS, range 0 – 4 [severe]). Liver chemistries, serum BA (sBA) and 7- α -hydroxy-4-cholesten-3-one (C4, a bile acid biosynthesis marker) were measured serially. The primary outcome was the mean change from baseline to wk 13 in ItchRO™(Obs). A priori, the first statistical test of efficacy pooled subjects with the two highest tolerated doses (140 + 280 $\mu\text{g}/\text{kg}/\text{d}$ indicated by*) compared to placebo.

Results: Primary outcomes are in the Table. The % of subjects with change from baseline to wk 13 of ≤ -1 was higher in maralixibat* vs placebo for ItchRO (65% vs. 25%, p=0.06) and CSS (76% vs. 25%, p=0.01). Of those with baseline CSS of ≥ 3 , improvement of ≥ 3 occurred in 6/11 maralixibat* and 0/9 placebo subjects. Maralixibat* yielded statistically non-significant decreases in total and direct bilirubin (-0.7 [0.39] and -0.4 [0.21] mg/dL, p=0.09 and 0.06, respectively) and an increase in ALT (+33 [18.6] IU/L, p=0.08). sBA changed minimally, presumably due to a compensatory increase in C4, supporting the biological activity of maralixibat (% Δ sBA* -37% (48%) p = 0.44, % Δ C4* +401% (199%) p=0.15). Adverse events were similar between maralixibat and placebo.

Conclusions: Although the pre-specified primary analyses of ItchRO were not all statistically significant, the data suggest that maralixibat was safe and may reduce pruritus in ALGS. Determination of optimal dosing and further assessments of safety and efficacy in children with cholestasis are warranted.

Supported by the NIDDK and in part by Shire via a Collaborative Research and Development Agreement with the NIDDK

	Placebo N=12	maralixibat dose (μ g/kg/day)				
		70 N=8	140 N=11	280 N=6	140+280* N=17	All active N=25
ItchRO[Obs], Wk 13 - baseline [^]	-0.58 (0.24)	-1.47 (0.30)	-1.49 (0.26)	-0.62 (0.36)	-1.05 (0.21)	-1.19 (0.18)
Difference from placebo [^] p-value (ANCOVA)	-----	-0.89 (0.40) 0.032	-0.91 (0.35) 0.014	-0.04 (0.44) 0.930	-0.47 (0.33) 0.159	-0.61 (0.31) 0.055

[^]mean or mean difference (SE)

CONCURRENT SESSION VI – UPPER GI

Saturday, November 4

3:45pm – 5:15pm

740 APFED Outstanding EGID Abstract Award

INCREASED MAST CELL DENSITY AND DEGRANULATION IS ASSOCIATED WITH POST-TREATMENT ENDOSCOPIC ABNORMALITIES AND SYMPTOMS DESPITE HISTOLOGIC REMISSION IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS.

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Background: Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease characterized by symptoms of esophageal dysfunction and eosinophil-predominant inflammation. Consensus guidelines for diagnosis in children are 6-8 weeks of high dose proton pump inhibitor (PPI) followed by esophagogastroduodenoscopy (EGD) with biopsy demonstrating at least 15 eosinophils per high powered field (eos/hpf). Remission is currently defined by a post-treatment endoscopy with less than 15 eos/hpf. Despite histologic improvement, both abnormal endoscopic findings as well as clinical symptoms of esophageal dysfunction can persist. Mast cells have been shown to be elevated in patients with active EoE and thought to have a role in the pathogenesis of smooth muscle contractility and fibroblast activation. In this study, we evaluated the role of mast cells in patients with histologic remission in a prospective pediatric cohort. The aim of this study was to evaluate whether mast cell density and degranulation is increased in children with EoE in histologic remission with endoscopic abnormalities and/or symptoms.

Methods: We performed a secondary analysis of prospective data collected in children undergoing post-treatment upper endoscopy at Ann & Robert H. Lurie Children's Hospital of Chicago, IL, USA from 2011 to 2015. EoE cases were previously

diagnosed based on 2011 consensus guidelines. Patients were treated with either elimination diet or topical steroids. Only EoE patients with histologic remission, defined by an eosinophil count of less than 15 per hpf, were included along with non-EoE controls, defined as patients with symptoms of esophageal dysfunction and diagnostic EGD demonstrating less than 15 eos/hpf. Patients with other inflammatory disorders, transplant, connective tissue disease or non-EoE eosinophilic disease were excluded. Archived unstained slides were obtained from the mid and distal esophagus and immunohistochemistry for tryptase was performed. Peak mast cells per high powered field (MC/hpf) and degranulated MC/hpf were quantified in all epithelial regions. Demographics were collected at enrollment; symptom surveys and endoscopic findings were recorded at the time of endoscopy. Clinical remission was defined as the absence of any symptoms or endoscopic abnormalities.

Results: 92 EoE patients (mean age 10, 71% male, 92% Caucasian) and 24 control patients (mean age 11, 50% male, 88% Caucasian) were evaluated. Mast cells were significantly elevated in EoE patients in remission compared to controls (16.6 vs 5.2, $p < 0.001$). Patients with basal zone expansion had higher mast cell density (19.5 vs 14.3, $p = 0.04$). Mast cell density was increased in patients with edema ($p = 0.0025$), furrows ($p = 0.002$), and rings ($p = 0.012$) but not exudate. Furrowing was independently associated with elevated mast cell density and basal zone expansion in regression modeling ($p = 0.035$, $p = 0.041$). Degranulated mast cells were increased in patients with furrows and rings. Patients in clinical remission ($n = 15$), with no endoscopic abnormalities or symptoms, had lower mast cell density and degranulation compared to non-clinical remission (10.7 vs 18.1, $p = 0.01$) but no difference from control (10.7 vs 5.4). There was no difference in eosinophilia, type/duration of treatment, or atopy between clinical remission and non-clinical remission. Patients with abdominal pain, early satiety, odynophagia, and reflux/regurgitation had increased mast cell density compared to patients in clinical remission.

Conclusions: Mast cell density and degranulation is increased in children with EoE in histologic remission compared to controls. Those patients with histologic remission but ongoing endoscopic abnormalities or symptoms had increased mast cell density and degranulation when compared to patients in clinical remission. Mast cells are additionally increased in biopsies with persistent basal zone hyperplasia despite histologic remission. These findings are independent of eosinophilia, type/duration of treatment and atopy. This pediatric cohort suggests an independent role for mast cells in EoE as a potential outcome metric associated with a poor clinical response, and perhaps necessitating a role for mast cell targeted therapy.

