



Department of Pediatrics Spring Research Day

Abstracts

Friday, April 11, 2014

Health Sciences Learning Center



Department of Pediatrics Spring Research Day

Abstract Booklet

Table of Contents

Resident Abstracts 2

Fellow Abstracts 13

Faculty/Staff Poster Presentations 17

RESIDENT ABSTRACTS

**AAAAI Poster Presentation

DEVELOPMENTAL ASSESSMENT OF SERUM PERIOSTIN AS AN ASTHMA BIOMARKER IN CHILDREN

Halie Anderson, Robert Lemanske, Joseph R Arron, Cecelia TJ Holweg, Victoria Rajamanickam, James Gern, Daniel Jackson

Background: Increased periostin levels in peripheral blood have been identified as a biomarker of type 2 airway inflammation in adult patients with asthma, which may have important clinical implications for individualized therapy. In children, in vitro studies have demonstrated that airway epithelial cells from children with allergic asthma express greater periostin in comparison to children without asthma.

Objective: We aimed to explore serum periostin as a potential systemic biomarker of asthma in children.

Design/Methods: A total of 288 children from the Childhood Origins of ASThma (COAST) study were followed prospectively from birth. Serum samples were collected at ages 2, 4, 6, and 11 years, and periostin was measured using a proprietary immunoassay developed by Genentech. Relationships among age, asthma, and periostin were assessed.

Results: Serum periostin levels were approximately 2-3 fold higher in children than those previously observed in adults. Levels were highest at 2 years of age ($p < 0.0001$), and did not change significantly between ages 4 years and 11 years. Children who developed asthma by age 6 years had increased serum periostin at ages 2 years ($p = 0.02$), 4 years ($p = 0.002$), 6 years ($p = 0.12$), and 11 years ($p = 0.01$) compared to children who did not develop asthma by age 6 years.

Conclusion: Serum periostin levels are significantly higher in children compared to published adult values and change developmentally, which may be due to bone turnover and growth. Despite this, serum periostin appears to be a predictor of childhood asthma development and warrants further study as a promising biomarker in preschool children.

RECOMMENDATIONS FOR PREVENTION OF DEATH SECONDARY TO SUDDEN CARDIAC ARREST IN STUDENT-ATHLETES

Jessica Babal

Between 1 and 6 in every 100,000 student-athletes suffers from sudden cardiac arrest (SCA) every year. Since most episodes of SCA are preceded by ventricular tachyarrhythmia (ventricular fibrillation or ventricular tachycardia), the greatest chance for survival occurs when CPR and automated external defibrillator (AED) are used in combination. Therefore, proper CPR training for individuals identified as likely first responders is necessary. Since coaches are present nearly 100% of the time during games and practice, and other potentially CPR-trained personnel (such as athletic trainers) may not be present with such consistency, CPR certification of coaches should be highly prioritized. World experts and organizations in the field of sports medicine have also recommended emergency action planning for all schools and venues which host athletic events, which includes CPR training for likely first responders and coordination of response to a cardiac emergency with local EMS. As of February 2014, twenty-four states have mandated CPR certification for coaches. Wisconsin is not one of these states.

Via this policy statement, the Wisconsin AAP advocates for an approach to pediatric SCA that utilizes the combined approach of primary prevention in the pediatrician's office and secondary prevention, specifically recommending that all coaches receive CPR certification and all schools formulate and practice an emergency response plan.

TRANSFUSION COULD COUNTERACT PHLEBOTOMY-INDUCED IRON STORE LOSSES

Adam Bauer, T Zamora, M Georgieff, Don Singer, Pamela Kling

Background: A baby who weighs only 1000g has only 80 mL of blood in the circulation. Transfusions are necessary in premature babies, due to low circulating blood volumes and phlebotomy. Between 0.25-0.4 mg of iron are lost for each mL of phlebotomy losses. About 1 mg of iron is contained per transfusion of packed cells. Due to concerns for safety (blood-borne diseases, necrotizing enterocolitis, iron overload and oxidant stress), the number of babies receiving transfusions have fallen. It is unclear if this translates into less iron available for tissues.

Hypothesis and/or aim: We hypothesized that iron in transfusions have the potential to counteract phlebotomy iron losses. We hypothesize that infants who were born without risk for fetal iron deficiency, but who received phlebotomy and no transfusions would experience depleted tissue stores.

Methods: The three-pronged study was approved by IRBs from the Universities of Wisconsin, Arizona and Minnesota. Aim 1 examined from the electronic medical record for rate of transfusion in VLBW (<1500 g) w at Meriter Hospital NICU from January 2009 to December 2013. Aim 2 examined the effect of transfusion on oxygen-carrying capacity (RBC, plasma lactate), suppression of erythropoiesis (Absolute reticulocytes), iron status (Plasma ferritin), and iron-induced oxidant stress (plasma lipid peroxides). Aim 3 collaborated with the University of Minnesota to study the tissue (brain) iron in ill newborns who have expired.

Results: Compared to baseline, transfusions increased RBCs within 24 hrs ($p<0.05$), decreased plasma lactate with 48 hrs ($p<0.05$), suppressed reticulocyte production within 48 hrs ($p<0.05$) and increased both oxidant stress and iron stores within 24 hrs ($p<0.05$ for both). Twelve tissue samples were sent to University of Minnesota for iron analysis.

Conclusion: Although common, not all VLBW infants receive transfusions before leaving the hospital. Transfusions improve oxygenation are an excellent source of iron, but could promote oxidant stress. It is still not known if phlebotomy losses deplete tissue iron or if iron in transfusions reaches vital tissues such as brain. A multi center collaborative study such as the current one could help address these important questions. In the meantime, thoughtful decisions about which tests are really necessary may minimize both iron losses and transfusions.

FAMILY CENTERED ROUNDS (FCR) SUSTAINABILITY PROJECT

Christina Beaird, Hilary Stempel, Ashley Huth, Tony Wampole, Michelle Kelly, Kristen Shadman, Mary Ehlenbach, Lori Haack

Background: Family engagement during a patient's hospitalization is invaluable to the child's care. Implementing Family Centered Rounds (FCR) at American Family Children's Hospital serves to increase family participation. Creating a checklist for FCR allows for standardization of quality care for all patients involved in FCR. This checklist provides structure to FCR by defining roles and expectations for each interdisciplinary team member. Despite resident checklist training, checklist compliance wavered and became inconsistently followed.

Objective: The purpose of this QI project is implementing a sustainable plan for FCR. We hope to increase the percent of checklist items completed during family centered rounds to > 90%.

Design/Methods: Root cause analysis identified causes of low checklist compliance. Key contributors included: forgetfulness, confusion about definitions of checklist criteria, and lack of buy in or commitment. Checklist definitions were clarified and weekly data collection of components occurred on rounds. The data collection was performed by attendings and was either disclosed or undisclosed. A Resident Dashboard tool was created to provide weekly feedback to the residents regarding their compliance. Trends in overall compliance and read back orders were subsequently analyzed.

Results: Preliminary data indicate checklist compliance increases with observation. Improvement in compliance is sustained in each group, however compliance initially drops with new resident team members.

Conclusion: Intermittent, disclosed observations during rounds appear feasible and likely increase compliance to the FCR checklist. Reporting compliance data on a Resident Dashboard is an effective feedback mechanism for fostering sustainability to the FCR checklist. Utilization of a similar Resident Dashboard tool could be benefit future QI projects looking to increase sustainability.

IMPROVING CHEST X-RAY QUALITY IN THE PEDIATRIC INTENSIVE CARE UNIT

Asaad Beshish, Scott Hagen, Bradley Maxfield, Jill Hammersley, Deborah Soetenga

Background: Chest x-ray (CXR) quality in the Pediatric Intensive Care Unit (PICU) plays an important diagnostic and therapeutic role in the care of critically ill children. A suboptimal CXR may lead to reimaging and exposing patients to unnecessary radiation, or result in a misdiagnosis, the consequence of which could be morbidity or mortality.

Objective: We implemented a multidisciplinary education program to improve the quality of CXRs in the PICU.

Design/Methods: After IRB approval, criteria for defining a quality CXR were agreed upon by experts in pediatric radiology and pediatric critical care. CXR quality was determined using the following criteria: film encompassing entire thorax, removal of overlying equipment, appropriate positioning and labeling, and proper inspiratory film. A retrospective review of all CXRs obtained in the PICU from July 1st – October 31st 2013 was performed. CXR were simultaneously and independently reviewed by two individuals (AB, JH) and the film quality was scored. Following the retrospective review, an on-line education module was developed that contained the criteria for and importance of a quality CXR. Viewing the learning module was mandatory for all PICU nurses and radiology technicians that perform CXRs in the PICU. Completion of the module was monitored through an employee computer based training system to ensure participation. A quality check list was also placed on the portable X-ray machine to remind staff and make sure all criteria were met during CXR acquisition. An ongoing review of all CXRs performed in the PICU during a four-month post-intervention period to monitor CXR quality and assess the effect of the education program.

Results: During the pre-intervention period from July - October 2013, 427 CXR were obtained and reviewed. In most films, the positioning of the patient 97.9% and the labeling of the film 100% were of good quality. A majority of the CXRs 68% had some removable equipment on the chest. In addition, 24% were not aligned or centered, 27% did not have the chin/head in neutral position, and 16% were not inspiratory films. To date, 97.3% of PICU nurses and 96.7% radiology technicians have completed the on-line training. The post-intervention phase of the project, reviewing CXR quality prospectively, is currently under process starting January 15th – May 15th 2014.

Conclusions: We found that the majority of CXR films do not meet an internal standard of quality. By implementing a multidisciplinary and collaborative education module targeting the PICU nurses and radiology technicians we aim to demonstrate improvement in the quality of CXRs in PICU. We plan on measuring this quality indicator over time to determine whether regular refresher training is necessary to maintain the quality.

GLOBAL HEALTH OPPORTUNITIES IN PEDIATRIC HEM-ONC FELLOWSHIPS

Katie Carlberg, Sabrina Butteris

Background: Looking at the past one hundred years of global health initiatives the world's health care resources (human, financial, research, etc.) were largely poured into efforts to stomp out infectious diseases. As a result the threat of communicable diseases has lessened and man's mean life expectancy has risen across the globe. With this, the burden of disease has been gradually shifting to expose the less provocative and often referred to as "neglected" chronic diseases. Perhaps one of the starkest medical contrasts, that exists today, between high- and low-resourced countries is found in childhood cancer outcomes. Simply depending on where a child is born, the chance of survival varies between 20 and 80 percent. The history of the field of pediatric hematology and oncology is distinct from any other. The movement began in the mid 1900's with a few individuals who felt that the outcomes for children with cancer were unacceptable. It has since evolved into an international organization whose collective mindset has allowed the field to progress at an astounding rate over the past 20 years. Those within the field today are starting to respond to the international outcome disparities, similar to the reaction of pioneers like Dr. Sidney Farber and Mary Lasker. Despite this fairly strong undercurrent, the literature has failed to keep abreast of and reflect the work of these current day pioneers.

Objective: To explore opportunities in global health within pediatric hematology-oncology fellowships.

Design/Methods: E-mails were sent to the directors and coordinators of each ACGME-accredited pediatric hematology/oncology fellowship within the United States. The initial survey was intended to determine the prevalence of international work within the field. It asked if a program offered international opportunities to its fellows; and, also inquired if there were any previous or ongoing projects within the department, which cross international borders.

Results: pending

LABORATORY ORDERING PRACTICES FOR FATIGUE AT UNIVERSITY HEALTH SERVICES AT THE UNIVERSITY OF WISCONSIN

Jessica Ferris, Allan Rifkin

Background: Fatigue is a common complaint in primary care offices and can lead to costly diagnostic evaluation.

Objective: To evaluate changes in physician laboratory test ordering practices for complaints of "fatigue", after the presentation of data from an internal chart review, which advocated limiting labs ordered and tailoring labs to pertinent history and exam findings.

Design/Methods: This was a two-part retrospective chart review at the University of Wisconsin – Madison, University Health Services (UHS). Electronic charts were reviewed with "fatigue" coded as the reason for visit or as the final diagnosis. The initial and secondary reviews included visits from 1/4/2012 - 8/30/2012 and 9/24/2012 - 7/1/2013 respectively. Results from the initial chart review were presented to staff physician on 9/21/2012. Data evaluated included the number of labs ordered per patient, the percent of labs that were abnormal, and whether a preliminary diagnosis changed based on laboratory results. The four most ordered labs were further evaluated to assess if labs were ordered based on clinical symptoms, or as a "rule out" lab. Data was analyzed with T-test statistical analysis, with statistical significance represented by $p=0.05$.

Results: Statistical significance was achieved for an increase in the percentage of abnormal CBC ($p=0.05$), TSH ($p<0.001$), monostest ($p=0.002$), and chemistry ($p=0.005$) labs resulted. Statistical significance was also reached for an increase in CBCs ordered based on symptoms ($p=0.005$) and a decrease in CBCs ordered as "rule out" tests ($p=0.05$), as well as a decrease in the number of patients who had four or more lab test ordered ($p=0.01$). There were reductions in the average number of labs ordered per patient, and more patients who had zero lab tests ordered, though this did not reach statistical significance.

Conclusions: These data show that there was a statistically significant increase in the percent of abnormal labs resulted, and that ordering practices of CBCs significantly changed to reflect patient's symptoms and exam findings. Other labs did not have a statistically significant change in ordering practice based on symptoms or "rule out" status. There was also a statistically significant reduction in the instances where four or more labs were ordered for a patient, reflecting a more conservative approach. Overall, labs were more fitted to symptoms, physical exam findings, and pertinent history. Therefore, labs should continue to be tailored, and watchful waiting and close follow up is encouraged, when appropriate.

WILSON DISEASE PRESENTING SHORTLY AFTER INITIATION OF DOXYCYCLINE

Jacob Fish, David Ingram, Dorota Walkiewicz

Wilson disease is a rare autosomal recessive disorder that affects approximately 1 out of every 30,000 live births and is characterized by impaired biliary copper excretion leading to accumulation of copper in multiple organs. The clinical presentation of Wilson disease varies widely, but usually involves clinical manifestations of liver disease, neurologic, and psychiatric symptoms. The severity of manifestations range from asymptomatic to fulminant hepatic failure, renal failure and Coombs-negative hemolytic anemia. Approximately 5% of Wilson disease cases have a very rapid progression to fulminant liver failure with associated hemolytic anemia and renal failure).

Our patient is a previously healthy 17-year-old female with no significant family medical history who presented to American Family Children's Hospital with a five-day history of vomiting, diarrhea, nausea, and dehydration. Twenty-four hours prior to admission she developed jaundice, headaches, myalgia, lightheadedness, and decreased urine output. Five days earlier she had begun a new prescription of doxycycline (100mg BID) for acne. On hospital day 2, a transjugular liver biopsy was performed, which showed evidence of cholestasis, moderate microvesicular steatosis, focal ballooning of hepatocytes, rare glycogenated nuclei and bile ductular proliferation. Trichrome and reticulin stains highlighted pericellular fibrosis and parenchymal necrosis/collapse. Despite full support, her liver failure continued to progress. On day 4 of hospitalization, a successful liver transplant was performed. Of note, final liver tissue copper level came back at 448mcg/g which confirmed the diagnosis of Wilson disease.

We report this case of Wilson disease presenting with acute fulminant hepatic failure, acute on chronic renal failure, and hemolytic anemia shortly after the initiation of doxycycline. We hypothesize that the doxycycline served as a trigger for our patient's acute presentation of underlying Wilson disease.

PEDIATRIC POSTERIOR STERNOCLAVICULAR DISLOCATIONS: A CASE SERIES AND REVIEW

Lise Go, Kara Gill, Michael Kim

Pediatric posterior sternoclavicular dislocations are reported as rare due to late fusion of the medial clavicle epiphysis and its strong posterior ligamentous support. Although reported as uncommon, our institution evaluated and treated a higher frequency of these injuries over the course of a year. Given its challenges in diagnosis and potential for life-threatening complications due to its proximity to thoracic outlet structures, early detection of posterior sternoclavicular dislocations is critical. Hence, in this case series, we review six patient presentations of posterior sternoclavicular dislocations and propose a clinical decision-making algorithm that may enhance clinicians' index of suspicion, leading to earlier diagnosis. To address this topic more comprehensively, review of the "classic" presentation and management of this injury is also included.

SYMPTOMS OF SLEEP-DISORDERED BREATHING AND RENAL FUNCTION IN ADOLESCENTS

David G Ingram

Background: Sleep-disordered breathing (SDB) is common and increasingly found to have deleterious end-organ effects in children. While SDB has previously been shown to be independently associated with renal function in adults, a single small study in children addressing this question did not replicate these findings.

Objective: The purpose of the present investigation was to examine the relationship between symptoms of SDB and renal function in an adolescent population.

Design/Methods: Data were obtained from the National Health and Nutrition Examination Survey (NHANES) survey years 2005-2006. A severity measure of SDB was calculated based on self-reported sleep duration, snoring, snorting, and daytime sleepiness. The two main outcome measures of renal function were glomerular filtration rate (GFR), estimated using the Schwartz equation, and urinary albumin-to-creatinine ratio (UACR).

Results: 751 participants had the requisite data to be included in analysis. The mean age was 17.4 (range 16-19) and 52% of participants were female. SDB severity was not significantly associated with GFR or UACR. Stratifying the sample by c-reactive protein (CRP) level did not significantly alter the results. Stepwise multivariate regression analysis identified body-mass index and systolic/diastolic blood pressures as the most important predictors of UACR; likewise, hemoglobin A1c, CRP, and diastolic blood pressure were the most important predictors of GFR. In contrast, SDB severity was not significantly associated with either UACR or GFR in multivariate analysis.

Conclusion: Symptoms of SDB were not associated with renal function in this sample of adolescents.

GEOGRAPHIC DISTRIBUTION OF COMMON SLEEP DISORDERS: AN INFODEMOLOGICAL STUDY

David G Ingram

Background: Although sleep problems are associated with poor overall health and all-cause mortality, little is known about their geographic distribution in the United States. The only previous study that examined this question found greater sleep disturbance and daytime fatigue in the South, but the study was limited by missing data from several states as well as very broad composite measures that were not specific to any one sleep disorder.

Objective: The purpose of the present investigation was to leverage internet user search data to investigate the geographic distribution of common sleep disorders in the United States.

Design/Methods: Data were obtained from Google Trends. First, the utility of using internet search data as a surrogate for disease prevalence was investigated by comparing search volume and known CDC prevalence of AIDS across states. Next, searches performed between 2004 and 2013 in the categories of obstructive sleep apnea (OSA), restless legs syndrome (RLS), narcolepsy, and insomnia were examined. States were ranked according to the relative number of searches performed for each sleep disorder, and rankings of states in different geographic census regions were compared. Finally, thirty-five state-level measures across demographic, economic, health, and geographic areas were investigated as potential correlates of interstate variability in sleep disorder searches; due to the high number of comparisons, only those relationships with $p < 0.001$ and Spearman's $\rho > 0.6$ were considered significant.

Results: The proof of concept analysis demonstrated good agreement between state search volume and CDC prevalence of AIDS (Spearman's $\rho = 0.84$). For sleep disorders, significant regional variation was found for OSA (Kruskal-Wallis $p = 0.03$), narcolepsy ($p < 0.001$), and RLS ($p = 0.01$), but not insomnia ($p = 0.86$). For both OSA and narcolepsy, searches were highest in the South and Midwest and lowest in the West. For RLS, searches were highest in the Midwest and lowest in the Northeast. The states with consistently high search volumes in all four examined sleep disorders were: Pennsylvania, Ohio, Kentucky, Tennessee, Indiana, and Michigan. Correlates of interstate variability in sleep disorder search volume included: RLS and decreasing median income; narcolepsy and decreasing physical activity, increasing hospital inpatient days, increasing smoking rate, and increasing obesity rate; and no significant correlates for insomnia or OSA.

Conclusion: Analysis of internet search data demonstrated regional differences in common sleep disorders across the United States with an overall concentration in the rustbelt and appalachia. Furthermore, several correlates of interstate variability in sleep disorder search volume were identified.

UNPLANNED TRANSFERS: A RETROSPECTIVE ANALYSIS OF THE ESCALATION OF CARE IN PEDIATRIC PATIENTS

Evan Kemp, Tom Brazelton

Background: Management of illness is a continuous, dynamic process that requires appropriate triage, identification, and treatment of disease. While much research has been done on the response to and management of clinical deterioration, there has been limited research identifying patient and system variables in unplanned PICU transfers that occur within 24 hours of hospital admission.

Objective: To identify patient and system variables associated with unplanned transfer to the PICU within 24 hours of admission to the general care floor.

Design/Methods: This study was a retrospective analysis of patients ≤ 18 years of age that were transferred from general care to the Pediatric Intensive Care Unit (PICU) within 24 hours of admission from January 1, 2010 and December 31, 2012.

Results: There were 186 patients that met criteria for the study. One hundred of the subjects that had unplanned transfer were males (100/186). Subjects most commonly identified their race as "White/Caucasian" (144/186). Forty-eight of the 186 subjects were < 1 year of age. 105 admissions occurred directly from home, clinic or outside hospital. One hundred and twenty five of the admissions with unplanned transfer occurred during the weekday with an average time of admission of 13:27. The Pediatric Hospitalist service admitted 70 of the 186 patients with unplanned transfer. The most common reason for transfer was respiratory issues (i.e. respiratory distress, apnea, RSV, pneumonia). A majority of the patients were transferred during the week (118/186) during workday hours (i.e. average transfer time: 13:42).

Conclusions: Infants < 1 yr, patients who were directly admitted to the hospital, and patients with respiratory diagnoses accounted for a larger proportion of pediatric patients that required unplanned transfer to the PICU. Further data analysis is needed to determine if this patient population is significantly different from the pediatric population admitted to Pediatric General Care.

****PAS Poster Presentation**

IMPACT OF PRENATAL RISK FACTORS ON IRON STATUS OF PRETERM INFANTS AT BIRTH

Patrick McCarthy, Hannah Zundel, Sharon Blohowiak, Pamela Kling

Background: Iron deficiency (ID) is the most common nutritional disorder globally. Eighty percent of fetal iron is obtained in the third trimester, and deficits in iron stores at birth have been associated with impaired cognitive, social-emotional, and neurophysiological development and function. Multiple prenatal risk factors (RF) impede term infant iron stores, but the effect of these RF on preterm infant iron stores is incompletely understood.

Objective: To determine the impact of prenatal RF on ID in preterm infants and to compare the iron status in low (0-1 RF) and high risk (>2 RF) preterm infants.

Design/Methods: Newborns <35 weeks of gestation weighing <2250g were screened for study eligibility. Seven prenatal RF were examined in eligible infants: socioeconomic status, maternal ethnicity, maternal ID, maternal diabetes, maternal obesity, small for gestational age (SGA) status, and multi-fetal birth. Umbilical cord blood was collected at birth. CBC, zinc protoporphyrin/heme (ZnPP/H), reticulocyte-enriched ZnPP/H (RE-ZnPP/H), and serum ferritin were analyzed to assess red cell iron availability, iron incorporation into hemoglobin (Hgb), and total body iron stores. These parameters were analyzed in context of specific RF and low/high risk of ID.

Results: Analyses were done on 54 preterm infants. These data revealed SGA infants had greater red cell distribution width (RDW) (19.7±0.9 vs. 17.3±0.3%; p<0.002, ZnPP/H (255.5±48.3 vs. 162.6±12.0µM/M; p<0.01), and Hgb (15.8±0.1 vs. 14.0±0.5g/dL; p<0.056) than non-SGA infants (p<0.03). SGA infants had lower ferritin (39.9±12.9 vs. 114.7±16.4ng/mL; p<0.025) than non-SGA infants. No differences (p>0.05) between low/high risk groups or with specific RF, except SGA status, were noted.

Conclusions: In contrast to term infants, the effects of prenatal RF in preterm infants are not summative, and SGA status is a dominant RF for ID, indicated by low storage (ferritin) and RBC (ZnPP/H) iron. High RDW and ZnPP/H with increased Hgb in SGA preterm infants may represent iron-deficient erythropoiesis driven by hypoxemia secondary to uteroplacental insufficiency. Preferential iron use for erythropoiesis may impair iron compartmentalization and trafficking to other tissues, increasing risk of poor developmental outcomes in SGA infants. Global nutritional deficiency may also contribute. The impact of other RF may not predominate until later in the third trimester.

PAS DATE/TIME/LOCATION May 4 2014; 4:15 pm- 7:30 pm; Exhibit Hall C. Board number 417.

****PAS Poster Presentation**

FYI, CALL, COME: PERCEPTION OF COMMUNICATION BETWEEN NURSES AND PEDIATRIC RESIDENTS AND ADHERENCE TO TEXT PAGING GUIDELINES

Mary Ehlenbach, Jessica McGee, Laura Ahola, Katherine Baker, Thomas Brazelton

Background: Text paging is a relatively new technology that can potentially save time and decrease workflow interruptions by delivering more information than simply a telephone number. However, communication nuances can be “lost in translation” through text paging. Studies have shown dissatisfaction with text paging often surrounds ambiguity of whether or not messages have been received. There is a paucity of evidence on best practices for text paging.

Objective: To assess compliance with text paging guidelines and the perception of adequate communication between nurses and pediatric residents.

Design/Methods: Guidelines were developed for text paging stating all text pages should contain “FYI,” “Call,” or “Come” and the sender's name and number. Nurses and pediatric residents were surveyed about their perception of adequate communication via text paging before and after implementation. Samples of text pages were audited for compliance with text paging guidelines multiple times after implementation.

Results: Audits of text pages were performed to assess compliance with text paging guidelines. Compliance at 2 weeks, 4 months, 9 months, 13 months, 14 months, 15 months, and 18 months was 59%, 59%, 56%, 49%, 79%, 76%, and 92% respectively. Surveys of nurses and residents were completed. After implementation, the nurses' mean response to “When I page an MD/NP, I receive the response I am looking for” increased from 3.60 (n=25) to 3.89 (n=19), for a mean increase of 0.29 (95% CI -0.002 to 0.59, p=0.051). The mean response to “When I page an MD/NP, I receive a timely response back” increased from 3.36 (n=25) to 3.88 (n=16), for a mean increase of 0.52 (95% CI -0.11-0.92, p=0.01). The residents' mean response to “I receive pages that adequately communicate the patient's acuity” increased from 3.29 (n=28) to 3.53 (n=32), for a mean increase of 0.25 (95% CI -0.099-0.59, p=0.16). The mean response to “I receive pages that adequately communicate what was wanted from me” increased from 3.43 (n=28) to 3.84 (n=32), for a mean increase of 0.42 (95% CI 0.1-0.73, p=0.01). The mean response to “I receive pages that identify the name and call back number of the sender” increased from 3.46 (n=28) to 4.00 (n=32), for a mean increase of 0.54 (95% CI 0.29-0.78, p=0.0001).

Conclusions: Text paging guidelines improved the perception of adequate communication on all measures. Improved perception was noted even when compliance with guidelines was only ~50%. Compliance improved over the 18 months after guidelines initiation.

PAS DATE/TIME/LOCATION May 4 2014; 4:15 pm- 7:30 pm; Exhibit Hall C. Board number 693.

THE DEVELOPMENT OF PRACTICE GUIDELINES FOR MEDICAL STABILIZATION OF PATIENTS WITH EATING DISORDERS ON A GENERAL PEDIATRIC INPATIENT UNIT

Katherine Magnuson, Rachel Bell, Shannon Dean, William Taft, Megan Moreno, Kristin Shadman

Background: Patients with eating disorders may require acute hospitalization to manage consequences of severe malnutrition, monitor and treat potentially fatal consequences of re-feeding syndrome, and facilitate psychiatric evaluation and follow-up. The psychiatric nature of this illness contributes to patient-staff splitting and inefficient medical care when a standard treatment plan is absent. There is a paucity of evidence-based literature detailing step-wise inpatient medical stabilization or patient-staff interaction, creating significant challenges when patients are admitted to a pediatric hospitalist team in a general care setting.

Objective: To develop practice guidelines for patients with eating disorders admitted to a pediatric hospitalist team.

Design/Methods: We convened a multidisciplinary team to develop local guidelines by reviewing national academy position statements of: pediatrics, adolescent medicine, and psychiatry; literature review; and analysis of other institutions' guidelines. Using an iterative process, our team then applied and reviewed the guideline with each admission over two years to refine details, gain consensus, and address challenges.

Results: Our team, including pediatric hospitalists, residents, clinical nutritionists, culinary services, nursing, child psychiatry and adolescent medicine, developed the following: a comprehensive clinical practice guideline detailing admission/discharge criteria, medical monitoring, behavioral/psychosocial guidelines; a nutritional rehabilitation plan of balanced meals and caloric progression; an EMR admission order set; and educational materials. We defined care practices for common challenges including refusal to eat, purging, and inadequate weight gain. Institutional feedback documents decreased confusion among providers, increased consistency and efficiency due to a developed treatment plan, and improved team and patient communication.

Conclusions: Inpatient hospitalizations for medical stabilization of patients with eating disorders can be locally standardized by a multidisciplinary team. In lieu of national guidelines, organizations struggling with standardizing care of such patients could use similar strategies to develop local guidelines. Next steps of this initiative include qualitative and quantitative evaluation of guidelines on provider confidence, length of stay, prevention of medical complications, and weight restoration.

ANTEMORTEM ORGAN DONATION INVOLVING CHILDREN

Laura Sedig, Norman Fost

The need for organ donation continues to rise while the number of donors remains inadequate to meet demand. Currently, donation is limited to living donation from healthy, altruistic individuals and post-mortem donation with consent from family members or advance directives. An overreliance on the problematic "dead donor rule," with fears of litigation, public criticism or loss of accreditation by UNOS, has inhibited changes in policy and practice. The dependence on the dead donor rule undermines the intended purpose of the Harvard Committee on Brain Death report – to increase the number of organs available for donation. In this paper, we report a request for ante-mortem organ donation from a terminally ill child and recommend changes in policy and practice to facilitate such donations.

HENOCH-SCHONLEIN PURPURA NEPHRITIS: WHAT IS THE RIGHT APPROACH?

Samantha Schulz, Jesse Roach

Background: Henoch-Schonlein purpura (HSP) is the most common vasculitis in childhood with a peak incidence of 70 per 100,000 in children ages four and six years. Although largely considered to be a self-limiting disease process, it can manifest with long term renal morbidity. Follow up for the development of renal manifestations is varied and currently no evidence based recommendations for monitoring exists. This may lead to higher healthcare costs and increased parental anxiety.

Objective: To explore the variability in follow up for patients diagnosed with HSP and also assess the level of comfort among practitioners who manage these patients.

Design/Methods: An electronic survey was composed by using Qualtrics software and was distributed among pediatric residents, general pediatricians and pediatric nephrologists at the University of Wisconsin; it was also made available on a listserv of pediatric nephrologists across the United States. The survey addressed eight questions: initial workup for patient with HSP, follow up for a patient with HSP without renal complications, and follow up for a patient with HSP with renal complications. Level of comfort with managing these patients was also addressed, with a score greater than 60 on a scale of 0-100 considered comfortable.

Results: 177 surveys were returned; 168 were fully completed. Respondents included 74% pediatric nephrologists, 12% general pediatricians, 11% pediatric residents, and 2% were pediatric nephrology fellows. For initial workup of a patient with HSP, 53% of non-nephrologists and 48% of nephrologist chose CBC, BMP, urinalysis, and blood pressure, this was also the most common answer for the group. In a patient without renal complications, the most common answer for the group at 33% was urinalysis and blood pressure every two weeks for one month then every other month for 6 months and at next well visit. This selection was the most common among non-nephrologists with 40% choosing this answer. Among pediatric nephrologists, the most common answer at 32% was every week for one month then monthly for 2 months and at next well visit. In a patient with renal complications the results were even more varied. 98% of nephrologists ranked themselves as comfortable managing a patient with HSP nephritis whereas only 28% of non-nephrologists felt comfortable.

Conclusions: In this study, there is consensus around the initial evaluation for a patient with HSP. However, when presented with follow up for a patient with and without renal complications, the responses were more varied and no true consensus prevailed. Not surprisingly, most of the pediatric nephrologists rated themselves comfortable in managing a patient with HSP nephritis. It is interesting, however, that the vast majority of non-nephrologists did not. The results highlight the need for a more standardized approach to manage HSP nephritis.

CULTURE SHOCK IN SHORT-TERM MEDICAL WORK ABROAD

Robert Strait, Sabrina Butteris, Michael Pitt

Culture shock is expected but its effects often underestimated by residents planning rotations in global health abroad. Forging and maintaining a working relationship with institutions in other countries is much bigger than one person's month abroad, and it is incumbent on all participants to contribute towards maintaining open inroads and continuing to pave a smooth path for the many participants who will come after them. Informed expectations are key.

Our residency program offers a global health track for interested residents to prepare them to collaborate more effectively, to represent their home institution more discreetly, and to enjoy their experience more fully during their work abroad. Many pediatric residency programs do not have such a track, yet interest in global health is burgeoning throughout the United States. The Global Child Health Educational Modules Project (GCHEMP) is a multi-institution work group that is creating a series of online modules for use either by established global health tracks or by residents who do not have such a track available to them, and our sub-group is creating the module on culture and culture shock.

The goal of our module is to use adult learning principles to help foster a sense of self awareness and reflection that will assist the learner in identifying their own often unrecognized beliefs, values and reactions to cultures that are different from their own, and to help them develop a skill set that will ease the effects of culture shock during their global health rotation. The module will be published as part of a larger educational program available to residents from anywhere in the country who are seeking to prepare themselves for a rotation abroad in global health.

**SYMPTOMATIC PRESENTATION OF AN ANOMALOUS LEFT
CORONARY ARTERY FROM THE PULMONARY ARTERY
(ALCPA) IN AN 8-DAY-OLD**

Anthony Wampole, Scott Hagen, Amy Peterson

An Anomalous Left Coronary Artery from the Pulmonary Artery (ALCAPA) is a congenital heart disease that is estimated to affect 1 in 300,000 children with some small national cohorts showing a higher incidence. Cases typically present at 4-16 weeks of life with signs and symptoms of heart failure. Here we present a case of an 8-day-old who presented in extremis and was subsequently diagnosed with ALCAPA without typical echocardiogram findings. Her symptomatic presentation is the youngest reported and the failure to demonstrate retrograde coronary flow suggests it is unnecessary in symptomatic presentation.

FELLOW ABSTRACTS

**PAS Oral Presentation

FITNESS EFFECTS OF CDC PHYSICAL ACTIVITY STRATEGIES ARE LIMITED AND VARY BY GENDER

Tasa S. Seibert, MD; Aaron L. Carrel, MD; Jens Eickhoff, PhD, John Bowser, PhD; David B. Allen, MD

Background: Low cardiovascular fitness (CVF), more prevalent in children with low SES and minority status, increases risk for insulin resistance and type 2 diabetes. To reduce childhood obesity, the CDC promotes school-based strategies to increase physical activity (PA). Our pilot data showed that implementing 4 or more CDC PA strategies increased students' mean daily steps from 9,849 to 11,148 ($p < 0.01$). However, the impact of this increased PA on CVF and obesity has not been evaluated.

Objective: Evaluate the impact of school based CDC PA strategies on CVF and BMI. **Design/Methods:** Forty-eight schools with low SES were assigned to either (1) continue routine PA programs ($n=23$, 2691 students, 53.1% boys) or (2) implement 4 or more CDC PA strategies ($n=25$, 3042 students, 51.3% boys). CVF (assessed by PACER, a 20 meter shuttle run) and BMI were obtained at the beginning and end of the school year. Post-study changes in PACER and BMI were assessed. Multivariate analysis evaluated the effect of intervention by ethnicity, location, gender and age.

Results: Mean CVF improved in both intervention and control schools, but there was no difference in CVF (or BMI) between intervention and control school groups. Of interest, in intervention schools, CVF improved in boys ($p=0.019$) but decreased in girls ($p=0.002$). At baseline, Hispanic students were less fit than non-Hispanic students ($p=0.015$) and there was a trend toward decreased fitness in urban compared to rural students ($p=0.058$). There was no intervention effect on CVF or BMI based on ethnicity or location.

Conclusions: Implementation of CDC PA strategies did not significantly change CVF or BMI in intervention schools compared to control schools, but a gender specific effect was noted with improved fitness in boys (but not girls) in intervention schools. Whether this statistically significant change in male CVF is associated with improved metabolic health requires further study. These data suggest that more intensive/effective interventions are needed to achieve positive fitness results for children in general. To address disparities in CVF, specific strategies that effectively increase CVF in at-risk groups (e.g. Hispanic children) and girls are needed.

PAS DATE/TIME/LOCATION May 4, 2014; 8:00 AM-10:00 AM; Obesity and Disordered Eating Section - West 220

**PAS Poster Presentation

GROWTH ATTENUATION THERAPY: PRACTICE & PERSPECTIVES OF PEDIATRIC ENDOCRINOLOGISTS

Allison Pollock, MD, Norman Fost, MD, David Allen MD

Background: Exogenous sex steroid administration before puberty accelerates linear growth and epiphysis closure, decreasing final height. While sex hormones have been used historically to reduce height and improve quality of life in tall-statured girls, treatment of a girl with severe cognitive and physical disabilities in 2006 prompted intense debate. Prescribing growth attenuation therapy (GAT) remains controversial, and there are no reliable data on the prescribing practices and attitudes of today's pediatric endocrinologists.

Objective: This study evaluated the experience, practice and attitudes of pediatric endocrinologists regarding GAT. **Design/Methods:** ~1200 Pediatric Endocrine Society members received an email with a study description and a link to an online anonymous questionnaire. Consent was implied by participating in the survey. Anonymity was assured by data collection via Qualtrics software, which de-identified data; demographic information was not elicited.

Results: 185 responses (122 in academic practice) were analyzed. 119 (64%) responders have been asked to prescribe and 47 (25%) have prescribed GAT. Dates of GAT were not provided. 91% of requests for GAT were prompted by a patient's family. Diagnoses prompting GAT requests included severe cognitive and physical disability (57%), tall stature (36%), spinal muscular atrophy (1%) and scoliosis (1%). Of those with experience prescribing GAT, 47% involved children with severe disability and 51% children with tall stature. Ethics consultation for GAT was requested by 24 (50%) prescribers, of whom 21 (88%) were treating children with severe disability. 86 responders elected not to treat precocious puberty in a severely disabled child for the purpose of reducing height; 4 of these consulted an ethicist. 103 (56%) disagreed with the statement, "GAT is always wrong," while 20 (11%) agreed.

Conclusions: Many pediatric endocrinologists have been asked to offer GAT, most agree that GAT is sometimes appropriate, and 25% of those surveyed have prescribed GAT. Acquiescence to GAT requests appears more common for a diagnosis of tall stature than for severe cognitive and physical disability. Ethics consultation for GAT is most often obtained in cases of severe disability. More data is needed to determine the growth-limiting effectiveness and quality-of-life value of GAT. In addition, more discussion is needed to develop consensus regarding how best to accomplish GAT and when it is in the best interest of the child.

PAS DATE/TIME/LOCATION May 5, 2014; 4:15 pm- 7:30 pm; Exhibit Hall C; Board Number 54; AND PES Presidential Poster Reception Friday night, Sheraton Vancouver Convention Centre Hotel; Grand Ballroom A/B, 7-9pm

****AAAAI Poster**

EVALUATION OF PEANUT ALLERGY IN A BIRTH COHORT

Bashir, H, Tisler, C, Anderson E, Kang T, Salazar, L, Evans M, Gangnon R, Jackson DJ, Lemanske RF Jr, and Gern JE

Rationale: There is relatively little information about longitudinal changes in serum peanut-specific IgE (sIgE) in children with peanut allergy and in children who are sensitized to peanut but not allergic.

Methods: 288 high-risk children were enrolled in the Childhood Origins of Asthma birth cohort and were followed prospectively. Yearly questionnaires related to adverse reactions to foods were completed. Peanut allergy was defined as having an elevated sIgE (>0.35) and an adverse reaction to peanut. Serum peanut-specific IgE (UniCAP, Phadia USA) was also obtained at 1, 2, 3, 5, 6, 9, and 11 years of age. On average, 85% of children had sIgE levels measured at each interval.

Results: 245 children were included in the study at age 6 and 217 remained at age 11. 31 children were sensitized to peanut but not allergic and 11 children had peanut allergy. Group mean sIgE levels at 1, 9, and 11 years were fairly stable for children with peanut allergy (3.96, 4.55, 2.77 kU/L) and for sensitized children (0.6, 0.39, 1.11 kU/L), and overall peanut allergic children had increased sIgE levels compared to those who were sensitized (3.70 vs 0.56 p < 0.0001). In contrast to the group mean data, time-related changes in individual sIgE levels varied widely.

Conclusions: Mean peanut sIgE levels were higher in children with peanut allergy compared to sensitized patients. Analysis of individual patterns of sIgE may yield new insights into personal and environmental factors that modify immune responses to peanut.

American Academy of Allergy Asthma and Immunology, March 3, 2014

****AAAAI Poster**

LONGITUDINAL CHARACTERISTICS OF VIRAL AND NON-VIRAL EXACERBATIONS OF CHILDHOOD ASTHMA

Amaziah T. Coleman, Daniel J. Jackson, Michael D. Evans, Ronald E. Gangnon, Robert F. Lemanske, Jr., James E. Gern

Rationale: Asthma exacerbations secondary to viral illnesses are a known cause of morbidity among children with asthma. Longitudinal characteristics of viral and non-viral exacerbations among children with asthma have not been completely defined.

Methods: Of the 259 children followed prospectively from birth to adolescence in the Childhood Origins of ASThma (COAST) study, 102 met criteria for asthma at age 6 or 11 years. Nasal samples were analyzed for respiratory viruses during exacerbations and for longitudinal patterns and risk factors for viral versus non-viral exacerbations.

Results: Among the children with asthma, 62 (60%) reported at least one exacerbation; 47 (76%) had <3 exacerbations, and 15 (26%) had ≥3. The number of exacerbations was positively associated with total IgE at ages 6 and 11 (p=0.009 and 0.02 respectively) and aeroallergen sensitization at age 11 (p=0.008). Virology was available for 192 of 219 exacerbations, and viruses were identified in 132/192 (69%) exacerbations. Of the 55 children who provided at least one nasal sample during an exacerbation, 42 (76%) had at least one viral exacerbation. When etiology was considered, viral exacerbations were positively associated with higher total IgE at age 6 (p=0.04) and aeroallergen sensitization at age 11 (p=0.03), and non-viral exacerbations were positively associated with higher total IgE at age 6 (p=0.04) and sensitization at age 11 (trend, p=0.11).

Conclusions: In this five-year longitudinal analysis of children with asthma, most children who had exacerbations were susceptible to viral respiratory infections. Indicators of atopy were important risk factors for both viral and non-viral exacerbations.

American Academy of Allergy, Asthma, and Immunology Annual Meeting, March 3, 2014

****AAAAI**

A PATIENT WITH A NOVEL LEUKOCYTE ADHESION DEFICIENCY AND PYODERMA GANGRENOsum-LIKE DISEASE

Jared Darveaux MD, Anna Huttenlocher, MD, Daniel Bennett, MD, Judith Smith, MD, Christine Seroogy, MD, James Gern, MD

Rationale: Macrophage-1 antigen (MAC-1) is an integrin heterodimer composed of CD11b and CD18. Leukocyte adhesion deficiencies (LADs) secondary to CD18 have been well described in the literature. We present a patient with a pyoderma gangrenosum-like disease found to have a novel deficiency of CD11b and normal levels of CD18.

Methods: Cell surface expression of integrins measured by flow cytometry.

Results: A 15 year old girl presents with a 10 year history of multiple lower extremity ulcers, including a non-healing ulcer on her right lower extremity of one year duration. The ulcer began as a pustule and subsequently enlarged to 8x6 cm. Initial workup showed a neutrophil-predominant leukocytosis (12.3 K/uL), anemia (Hgb 9.8), normal quantitative immunoglobulins, and an elevated ESR at 72. Wound cultures were polymicrobial. Coexisting gingivitis prompted testing for LAD, revealing a defect in MAC-1, with near normal levels of CD18 (94%) and nearly absent levels of CD11b (2%) on circulating neutrophils. Lesional biopsies showed suppurative and granulomatous inflammation consistent with pyoderma gangrenosum (PG). Neutrophil oxidative burst testing was normal. Preliminary testing suggests a mild defect in neutrophil motility. The clinical course has been remarkable for intermittent exacerbations and gradual increase in ulcer size despite treatment with corticosteroids, colchicine, IVIG, and antibiotics. **Conclusions:** To the best of our knowledge this is the first case of isolated CD11b deficiency. Unlike previously described MAC-1 deficient cases, this patient presented with PG-like ulcers. This case suggests that MAC-1 is necessary for amelioration of the inflammatory process and/or transition to wound healing. AAAAI, March 2, 2014

Also presented as an oral presentation at the Wisconsin Allergy Society Meeting in October, 2013

****STFM Poster**

COMPARISON OF MEDICAL STUDENT UNDERSTANDING AND RECALL OF STATUS ASTHMATICUS; TRADITIONAL LECTURE VS. INTERACTIVE TEACHING

Jennifer Mosher MD, Scott Hagen MD, Craig Gjerde PhD

Background: In the past 50 years, many universities have focused on ways to make didactic teaching in medical school more interactive. While there has been much focus on problem-based learning, studies are showing equivocal improvement in test scores. In addition to problem based learning, there are other forms of active learning, and there has not been much focus on research looking at other forms of active learning. The purpose of this study is to compare medical student learning from a series of interactive "chalk-talk" lectures and learning from traditional PowerPoint lectures.

Methods: During the third-year pediatric clinical rotation, student groups were alternately assigned to a PowerPoint lecture format or the chalk talk format. In the PowerPoint lecture, students watched a prepared slideshow on the pathogenesis, physical exam, differential diagnosis, and treatment of asthma. For the chalk talk lecture, students were asked to talk through the same information about asthma; their answers were written on a white board and discussed during the lecture. Students received a multiple choice test on three occasions: one test given before the lecture, one given immediately after the lecture, and one given online 6 months after the lecture. Test scores were summarized in terms of means and standard deviations, with a p value of < 0.05 considered significant.

Results: Analysis of the first 4 groups revealed no statistically significant difference in mean baseline scores in the PowerPoint and the "chalk talk" groups. There was no significant difference in the mean post-instruction scores.

Discussion: Preliminary data show that students in both groups learned from the PowerPoint lecture and the chalk-talk lecture. However, with the limited size of our study, we were not able to detect any difference in the amount of learning that was related to the lecture format.

Society of Teachers of Family Medicine, January 1, 2014
My poster earned special recognition for one of the top 10% of posters at the conference.

****AAAAI Poster**

VIRAL ETIOLOGY OF EARLY LIFE WHEEZING ILLNESSES DIFFERENTIALLY PREDICT PERSISTENCE OF ASTHMA IN HIGH-RISK CHILDREN

Rubner FJ, Jackson DJ, Evans MD, Gern JE, Lemanske Jr RF

Rationale: Viral wheezing illnesses in early childhood have been shown to predict development of asthma by 6 years of age. Whether a differential effect on the risk for persistence of asthma out to age 11 years exists based on viral etiology of early childhood wheezing illnesses has not been established.

Methods: 217 children were followed prospectively from birth to 11 years in the COAST (Childhood Origins of ASThma) study. The etiology of viral wheezing illnesses during early childhood was determined using nasal lavage, culture and RT-PCR. Asthma was diagnosed clinically at 11 years. Relationships between the etiology of wheezing illnesses and asthma risk were analyzed.

Results: In univariate analyses, wheezing illnesses in the first 3 years of life with HRV (OR=6.0 95% CI 2.1, 11, $p<0.0001$), RSV (OR=2.9 95% CI 1.6, 5.4, $p=0.0008$) and other viruses (OR=4.8 95% CI 2.6, 9.1, $p<0.0001$) were all associated with an increased risk of asthma at age 11. Using a multivariate model to adjust for histories of wheezing with more than one virus, the risk of asthma at age 11 years was significantly increased in children with HRV wheezing histories (OR=3.7 95% CI 1.7, 7.8, $p=0.0008$), but not in children who wheezed with RSV (OR=1.4 95% CI 0.7, 2.9, $p=0.4$) or other viruses (OR=2.1 95% CI 0.9, 4.7, $p=0.08$).

Conclusion: Viral etiology of wheezing illnesses in the first three years of life confers a differential risk for persistent asthma out to 11 years of age with wheezing due to HRV being the strongest overall predictor of this development.

American Academy of Asthma, Allergy and Immunology National Meeting, March 4, 2014

AAAAI Travel Grant Recipient

****AAAAI Poster**

COMPARISON OF PRE- AND POST-PUBERTAL GENDER DIFFERENCES IN MARKERS OF ANGIOGENESIS AND ASTHMA OUTCOMES

Thomas AO, Devries MK, Tisler CJ, Rajamanickam V, Gern JE, Lemanske RF Jr., Jackson DJ

RATIONALE: Previous studies have demonstrated increased numbers of circulating endothelial progenitor cells (EPCs), defined as peripheral blood mononuclear cells (PBMCs) co-expressing CD34 and CD133, in adults with asthma. However, it is not known whether EPCs are differentially expressed developmentally based upon gender, puberty, and/or asthma diagnosis.

METHODS: A subset (n=42) of children in the Childhood Origins of Asthma (COAST) study were selected for this pilot study based upon pubertal status, defined as tanner stage 4 for males, and menarche for females. Pre- and post-pubertal PBMC samples from 26 females, and 16 males fulfilling these criteria were assessed using flow cytometry to identify the percentage of EPCs (CD34+/CD133+). Relationships among EPC numbers, gender, puberty, and asthma diagnosis were assessed.

RESULTS: Both pre- and post-puberty, females had significantly higher percentages of circulating EPCs (CD34+/CD133+) compared to males (pre-puberty: 0.060% vs 0.041%, $p=0.01$; post-puberty: 0.062% vs. 0.031%, $p=0.0001$). EPC percentages were not significantly higher in children with asthma vs. no asthma (pre-puberty: 0.060% vs. 0.049%, $p=0.13$; post-puberty: 0.052% vs. 0.048%, $p=0.63$). The percentage of circulating EPCs did not differ by asthma severity or the presence of aeroallergen sensitization.

CONCLUSIONS: Circulating EPCs were increased in females compared to males both pre- and post-puberty. In contrast to prior studies in adults, no differences in EPCs were seen in children with asthma. Prospective pubertal follow up in the COAST cohort will help determine if these differences persist or change with the expression and remission of asthma, as well as changes in severity of asthma based on gender and age.

American Academy of Allergy, Asthma, and Immunology, March 2, 2014

FACULTY/STAFF PRESENTATIONS

**PAS Oral Presentation

SIMULATION USE FOR GLOBAL AWAY ROTATIONS (SUGAR): PREPARING RESIDENTS FOR EMOTIONAL CHALLENGES ABROAD, A MULTI-CENTER STUDY

Sabrina Butteris, MD, Sophia Gladding, PhD, Walter Eppich, MD, MEd, Scott Hagen, MD, Amer Al-Nimr, MD, Philip Fischer, MD, Cynthia Howard, MD, Laura Houser, MD, Jacquelyn Kuzminski, MD, Jane Rosenman, MD, Charles Schubert, MD, Tina Slusher, MD

Background: Residents are interested in participating in global health (GH) experiences and while preparation is critical, most is passive. Active preparatory curricula allowing residents to experience and debrief emotional challenges they may encounter abroad is generally lacking. **Objective:** Design and evaluate a simulation curriculum to prepare residents for challenges and emotions they may experience abroad.

Design/Methods: Pediatric GH educators from seven institutions agreed on common challenges and emotional reactions residents experience abroad. They developed cases addressing these themes and trained facilitators to lead and debrief the cases. Residents and facilitators completed evaluations that were analyzed using descriptive statistics and thematic analysis of written comments. **Results:** Program size, degree of fidelity, and facilitator simulation experience varied across institutions. Residents and facilitators completed 160 and 52 evaluations respectively. Respondents found the simulations useful in preparing them for their GH elective with a mean resident score of 4.49 (SD 0.82) and facilitator score of 4.85 (SD 0.36) on a 1-5 scale (1=completely useless, 5=very useful). Residents reported strong emotions in 98% of comments with frustration identified as the primary emotion across all case types. The emotions elicited during the case mirrored the types of emotions residents report as challenging while on their GH electives. After the sessions, 96% of comments reflected anticipated changes to GH rotation preparation plans.

Conclusions: Active preparation for GH electives using standardized, simulated cases appears to be a useful tool that can be implemented across a variety of sites with minimal facilitator training or simulation experience. The curriculum successfully elicited powerful emotions which are often experienced while on a GH elective, and most important, provided an opportunity to debrief these emotions before encountering them abroad. After the simulation and debriefing sessions, nearly all residents reported changing their plans for how to prepare for their elective.

PAS DATE/TIME/LOCATION May 4, 2014, TBD

**PAS Oral Presentation

TRANSITION PRACTICES AND PRIMARY CARE FOLLOW-UP AFTER HOSPITAL DISCHARGE

Ryan J Collier, MD, MPH, Thomas S Klitzner, MD, PhD, Adrianna Saenz, BA, Carlos Lerner, MD, MPhil, Bergen B Nelson, MD, MS, Sungmee Park, Paul J Chung, MD, MS

Background: While follow-up with primary care providers (PCPs) after discharge is assumed to represent high-quality care, little is known about how transition practices influence follow-up rates.

Objective: To examine associations between transition practices and PCP follow-up after hospitalization.

Design/Method: Prospective cohort study enrolling randomly selected children admitted for at least 24 hours to a tertiary children's hospital during 2012-2013. Hospitalizations <24 hours, patients >17 years, NICU/nursery hospitalizations, transfers and deaths were excluded. Questionnaires with families were conducted at admission, 2 and 30 days after discharge, and with PCPs 30 days after discharge. **Results:** Preliminary analyses of the first 442 patients found that 97% reported having a personal provider. Follow-up visits within 30 days of discharge were reported by PCPs after 42% of discharges, with over 80% responding that the follow-up timing was appropriate. After adjusting for complexity (>2 subspecialists, need for home health and durable medical equipment), patient age, and respondent language, the odds of having PCP follow-up were higher when the PCP was notified about hospitalization (AOR 2.1, p=0.03) or received verbal handoff (AOR 3.3, p=0.03), or the discharge summary specified follow-up timing (AOR 4.5, p<0.001). Parents reporting appointments made prior to discharge and PCPs reporting receipt of discharge summaries were not associated with follow-up. Odds of having a follow-up visit were lower among families reporting presence of a Maternal and Child Health Bureau-defined medical home on admission (AOR 0.48, p=0.03). Finally, PCP follow-up was not associated with 30-day readmissions or 7-day emergency department visits.

Conclusions: Higher PCP follow-up after discharge might be achieved through specific transition practices, though whether this is associated with better utilization outcomes remains unclear. Presence of a medical home might reduce perceived need for in-person PCP follow-up after discharge by families, discharging providers or PCPs. Patients with medical homes may also have different forms of contact with PCPs after discharge. Final adjusted analyses will include additional demographic, clinical and severity of illness covariates.

PAS DATE/TIME/LOCATION 5/3/2014; 4:15 PM; East Ballroom C (Vancouver Convention Centre)

****PAS Oral Presentation**

RELATIONSHIP BETWEEN MEDICAL HOME AT HOSPITAL ADMISSION AND READMISSION AFTER DISCHARGE

Ryan J. Coller, MD, MPH, Thomas S. Klitzner, MD, PhD, Adrianna Saenz, BA, Carlos Lerner, MD, MPhil, Bergen B. Nelson, MD, MS, Sungmee Park, Paul J. Chung, MD, MS

Background: Hospital readmissions are a widely used quality indicator. Little is known about the degree to which primary care medical homes may reduce the need for hospital readmissions.

Objective: To test the hypothesis that patients with a medical home will be less likely to have a readmission within 30 days of discharge.

Design/Method: Prospective cohort study enrolling randomly selected children admitted for at least 24 hours to a tertiary children's hospital during 2012-2013. Hospitalizations <24 hours, patients >17 years, NICU/nursery hospitalizations, transfers and deaths were excluded. Questionnaires with families were conducted at index admission, 2 and 30 days after discharge. Medical home was assessed using questions from the National Survey for Children with Special Health Care Needs. Readmissions were defined as any parent-reported admission to any hospital within 30 days of discharge.

Results: Preliminary analyses of the first 442 patients identified 30.7% having a medical home and an overall readmission rate of 13%. Unadjusted readmission odds were 60% lower among those with a medical home (OR=0.40, p=0.012). Having family-centered care and a usual source for sick and well care were the only individual medical home components associated with readmission (OR=0.57, p=0.069, and OR=0.33, p<0.001, respectively). After adjusting for complexity (>2 subspecialists, need for home health and durable medical equipment) and self-efficacy (parent's confidence in avoiding a readmission), patient age, and respondent language, the odds of readmission were still reduced by almost 60% among those with a Maternal and Children Health Bureau-defined medical home on admission (AOR=0.41, p=0.018).

Conclusions: Patients with a medical home prior to hospitalization may have lower odds of 30-day readmission after discharge. Final adjusted analyses will include additional demographic, clinical and severity of illness covariates.

PAS DATE/TIME/LOCATION 5/5/2014; 8:30 AM; East 11 (Vancouver Convention Centre)

****PAS Oral Presentation**

PREDICTORS OF FAMILY ENGAGEMENT IN FAMILY-CENTERED ROUNDS

Elizabeth Cox, MD PhD, Victoria Rajamanickam, MS, Tasha Scott, BS, and Gwen Jacobsohn, MA

Background: Experts endorse family-centered rounds (FCR) to ensure high quality inpatient care. However, some families may not engage optimally in FCR.

Objective: To identify families less engaged in FCR.

Design/Methods: Surveys of demographics and hospitalization characteristics and daily videos of FCR were collected from 151 families of children on our hospitalist, hematology, oncology, or pulmonary services. Trained coders assessed family engagement, coding the number of utterances in 4 key visit tasks (relationship building, information giving and gathering, and decision making) from videos using standard methods. To represent family engagement across the child's stay, the number of utterances for each day of FCR was averaged, for each of the 4 key tasks. Adjusted multivariate negative binomial regression was used to examine associations between engagement and child, parent, and hospitalization factors.

Results: Mothers were often present for FCR (89%); fathers were present for 38%. Parent education varied: 19% had a high school education or less, 34% some college, and 47% college graduates. Children were, on average, 5.6 years old (sd 5.6). Common reasons for hospitalization included breathing problems (31%), fever (19%), or gastrointestinal problems (19%). Intercoder reliabilities were near perfect ($\kappa > 0.8$). In multivariate models, average family engagement in FCR was significantly associated with the proportion of FCR attended by the mother and less so by the father. For a 5-day stay, each day the mother attended FCR resulted in 13.1% more relationship building, 11.4% more information giving and 26.8% information gathering (all p<0.05). Each day the father attended resulted in 4.3% more relationship building, 1.2% more information giving, and 2.6% information gathering (all p<0.05). Compared to parents with a high school education or less, parents with some college or a bachelor's degree had significantly more engagement in information giving (47% and 60% more, respectively; p<0.05) and twice as much information gathering (p<0.01). Compared to families whose children stayed 1 day, family engagement in decision making was double for those staying 2-3 days and almost five times greater for those staying >3 days (p<0.01). **Conclusion:** Support may be needed to optimize engagement for fathers, for parents without any college education, and during short hospital stays. Future work could examine interventions such as peer support or engagement coaches.

PAS DATE/TIME/LOCATION 5/3/2014; 11:00 AM-11:15AM; East 11 (Vancouver Convention Center)

****PAS Oral Presentation**

IRON MAY BE THE CRITICAL LINK BETWEEN MATERNAL OBESITY AND ASTHMA IN OFFSPRING

Natalie C Dosch, Shannon E Murray, Rachel M Weigert, Elyssa F Guslits, Theresa W Guilbert, Christopher L Coe, Pamela J Kling

Background: Maternal pre-pregnancy obesity is associated with asthma diagnosis in offspring, however no clear mechanism for this association has been found. Our lab previously showed that obesity during pregnancy was linked to poorer iron status in offspring. Other work also linked iron deficiency at birth to wheezing in infancy. In combination, these studies suggest iron status plays a key role in this unknown mechanism.

Objective: We analyzed newborn iron status and the stimulation of lymphocyte Th1/Th2 cytokine expression in obese vs. control pregnancies. Our hypothesis was that obese pregnancy depletes newborn iron and alters developmental inflammatory processes, predisposing to asthma.

Design/Methods: UW and Meriter Hospital IRBs approved this study. Eligible subjects included mothers delivering healthy term newborns from routine scheduled caesarean sections. Umbilical cord blood from control and obese pregnancies was analyzed for iron status, including hemoglobin (Hb) and plasma ferritin. WBC counts were obtained and lymphocytes isolated for cell culture, stimulated with phytohemagglutinin, and incubated for 24 hours in normal media or low iron media with deferoxamine. Cytokine expression profiles were examined using a multiple cytokine array.

Results: Cord blood from 23 control and 32 obese pregnancies showed similar white blood cells, lymphocytes, neutrophils and Hb. Ferritin was lower in obesity ($p < 0.04$). When cytokines were analyzed by obesity, IFN-gamma trended lower and IL-12 was higher than control. When analyzed by iron deficiency, IL-1 and IL-10 were higher, compared to those with normal iron status. All cytokines were lower when incubated in low iron conditions, except IL-1, an iron pathway cytokine, which was increased.

Conclusions: In newborns born to obese mothers, iron status was poorer and the Th1 cytokine production downregulated, while other cytokines were upregulated. Data support a relative dysregulation of cytokine profiles in offspring of obese pregnancy that were further disturbed when iron was depleted during incubation. Low iron at birth due to obese pregnancy may therefore contribute to an atopic phenotype that predisposes infants to asthma and allergies.

PAS DATE/TIME/LOCATION May 4, 2014 3:30 pm-5:30 pm
Session: 2865—Obesity & Disordered Eating II Room: West 214

****PAS Oral Presentation**

HYPERANDROGENISM IS ASSOCIATED WITH NAFLD AND METABOLIC RISK IN BOTH NORMAL AND OVERWEIGHT ADOLESCENT GIRLS

Jennifer Rehm, MD, Peter Wolfgram, MD, Ellen Connor, MD, Scott Reeder, MD, PhD, and David Allen, MD.

Background: In adult women, hyperandrogenism connotes increased risk for metabolic syndrome and up to 3 times greater risk of non-alcoholic fatty liver disease (NAFLD) compared to obesity alone, a difference attributed to elevated androgens. It is unclear whether elevation in androgens in adolescents infers a similar increased risk.

Objective: To compare serum androgen levels to markers of metabolic syndrome and NAFLD in both thin and overweight adolescent girls.

Methods: Cross-sectional study of 103 females aged 11 to 14 years, Fasting glucose, insulin, ALT, total testosterone, free testosterone, DHEAS, sex hormone binding globulin (SHBG), body mass index (BMI), and waist circumference (WC) were measured. Hepatic (HFF), visceral (VAT), subcutaneous (SAT), and total (TAT) fat were quantified using MRI proton density hepatic fat fraction.

Results: Demographics: 66% Caucasian, 28% African American & 6% Asian (29% Hispanic, 71% Non-Hispanic). Forty-four percent of subjects were overweight or obese (BMI $> 85\%$). Overall mean age of subjects 12.6 ± 1 , mean BMI 28.5. Mean age of subjects with BMI $\leq 85\%$ (12.6 ± 1) was not different than those with a BMI $> 85\%$ (12.5 ± 1). Correlation analysis shown in tables.

Discussion: In adolescent girls, hyperandrogenism is associated with insulin resistance and increased liver fat. The strong correlation of SHBG with IR and hepatic fat in both normal and overweight adolescents suggests hepatic insulin resistance may develop prior to obesity. However, a correlation with elevation in ALT, which may be associated with hepatocellular injury, and increased hepatic fat is only seen in overweight subjects suggesting that androgens do not play a role in the development of NAFLD in pre-obese adolescents.

Acknowledgements: NIH (RC1 EB010384, R01 DK083380, R01 DK088925, R01 DK096169, & T32 DK077586-01), Wisconsin Alumni Research Foundation Accelerator Program, Genentech Center for Clinical Research, Endocrine Fellows Foundation, and Pediatric Endocrine Society. We thank GE Healthcare for their support.

PAS DATE/TIME/LOCATION May 4, 2014; Session is 3:30-5:30; (4:-4:15); Session: 2865—Obesity & Disordered Eating II, Room: West 214 (Vancouver Convention Centre)

****PAS Poster Symposium**

NTF3 AS A MODIFIER FOR BRACING IN ADOLESCENT IDIOPATHIC SCOLIOSIS

Philip Giampietro, MD, PhD, Alex Stoddard, MSc, MA, Sijian Wang, PhD, Kandice Swindle, BS, Cathleen Raggio, MD, Nancy Hadley Miller, MD, MS, Robert Blank, MD, PhD, Sarah Sund, BS, Praful Aggarwal, MSc and Ulrich Broeckel, MD.

Background: Approximately one in ten patients diagnosed with idiopathic scoliosis (IS) will require active intervention i.e. bracing or surgery. The cost of bracing is approximately \$2000 per brace, which includes adjustment. Identification of a sub group of patients with IS for whom bracing will not be successful would be cost effective and potentially offer patients and their providers a more personalized approach to their treatment.

Objective: To identify genomic region(s) associated with bracing efficacy for IS. **Design/Methods:** Fine mapping of 7 families in which affected members were treated with bracing, with previously demonstrated linkage to 12p13 performed by our group, was performed using the Affymetrix Genome-wide Human SNP Array 6.0, containing >906,600 SNPs. A total of 19 affected subjects were sequenced from families 1, 2, 3, 4, 5, 6 and 7 using Agilent SureSelect whole exome capture with semiconductor sequencing methodology. DNA sequence results from these members were compared with GRCh37 Reference Genome.

Results: Neurotrophin 3 (NTF3) was identified as a candidate gene within the 12p13 region with significant p values in a dominant (.008), continuous (.0091) and recessive mode (.0213). /rs # A freq B freq AB or BB AA>Ab>BB Model free Recessive Model Nearest gene(s) / rs10492095 0.8192 0.1809 0.008 0.0091 0.0024 0.011517609 NTF3 / rs7488279 0.8404 0.1596 0.0165 0.0187 0.0093 0.023363416 NTF3 / rs11063692 0.8404 0.1596 0.0165 0.0187 0.0093 0.023363416 NTF3 / rs7398674 0.8511 0.1489 0.0213 0.0213 0.0226 0.021270698 ANO2

NTF3 (AB or BB associated with scoliosis; AA>AB>BB continuous distribution for scoliosis)

Conclusions: The promoter polymorphism (rs11063714) NTF3 has previously been associated with curve severity for IS in the Chinese Han population. NTF3 is hypothesized to affect proprioception, which may be altered in patients with IS. Our findings, in a separate population provide validation of these results which need to be tested in prospective bracing studies among patients with IS. We anticipate these results will assist with identifying patients with IS who will not be responsive to bracing based on their NTF3 genotype, and provide a rationale for treatment of IS through neurophysiological approaches targeting postural control mechanisms.

PAS DATE/TIME/LOCATION May 6, 2014; 9:45-AM; 4545.689

****PAS Poster Presentation**

VISUALIZATION OF OXYTOCIN SIGNALING MECHANISMS IN A SINGLE CELL

Michelle Chiu, Patrick Halbach, Nathan York, De-Ann Pillers, Bikash Pattnaik

Background: Oxytocin (OXT) is expressed in high levels during parturition, at which point it acts as an endocrine and paracrine signaling molecule of myometrial cells to induce contractions and thus, facilitate birth. A rise in intracellular calcium ([Ca²⁺]_i) is a well characterized result of OXT binding oxytocin receptor (OXTR), most likely through the standard G-protein coupled receptor (GPCR) mediated activation of OXTR.

Objective: We used molecular and live-cell imaging techniques to visualize OXT-OXTR signaling mechanism by real-time fluorescent visualization.

Design/Methods: We generated human embryonic kidney (HEK293) cells stably expressing human OXTR. Intracellular changes in Ca²⁺, in response to OXT treatment, was measured using the standard FURA-2AM ratiometric assay. We used a live-cell fluorescent marker (plekstrin homology domain fused GFP or pH-GFP) for the detection of membrane phosphatidylinositol 4,5-bisphosphate (PIP₂). In the predicted GPCR pathway, upon agonist binding, membrane PIP₂ is hydrolyzed to inositol 1,4, 5-trisphosphate (IP₃) and diacylglycerol (DAG) catalyzed by phospholipase C (PLC). hOXTR stable cells were transiently transfected with pH-GFP using TransIT-LT1 (MirusBio, Madison, WI). GFP positive cells were imaged live within 24-72 hours post transfection. Fluorescent images were acquired every 10 seconds while OXT was applied to activate OXTR.

Results: In response to OXT, cells in the objective field demonstrated a transient increase in [Ca²⁺]_i. pH-GFP has a high affinity for PIP₂, but when PIP₂ hydrolyzes, pH-GFP translocates with IP₃ to the cytoplasm. In our live-cell imaging experiments, cells expressing GFP clearly showed translocation of GFP fluorescence from the membrane location to the cytoplasmic location when the cells were exposed to OXT. The time course of GFP translocation were comparable to the increase in [Ca²⁺]_i.

Conclusions: We confirmed viability of our stable HEK-hOXTR cell culture model. Our experiments demonstrate that OXT-OXTR signaling primarily utilize the standard GPCR mechanism to mobilize intracellular Ca²⁺.

PAS DATE/TIME/LOCATION May 4, 2014; 4:15 PM - 7:30 PM; Exhibit Hall C Board Number: 778

****PAS Poster Presentation**

CHARACTERIZING UNIQUE SUBPOPULATIONS OF CHILDREN WITH SPECIAL HEALTH CARE NEEDS

Ryan J. Coller, MD, MPH, Jens Eickhoff, PhD, Thomas S. Klitzner, MD, PhD, Carlos F. Lerner, MD, MPhil, Mary Ehlenbach, MD, and Paul J. Chung, MD, MS

Background: Children with special health care needs (CSHCN) are a heterogeneous population. It is unclear how different dimensions of medical complexity impact their outcomes.

Objective: To identify complexity subgroups of CSHCN within the US population, and characterize key outcomes.

Design/Methods: Data from the 2009-2010 National Survey of CSHCN were examined to define substantively meaningful subgroups within the CSHCN population.

Following the conceptual frameworks of medical complexity developed by van der Lee and Cohen, multiple indicators in three domains (functional limitations, health care use and characteristic needs) were identified. Latent class analysis was then used to group individuals into otherwise unobservable classes based on these indicators. Outcomes were compared among different latent classes with weighted logistic or negative binomial regression.

Results: Among 40,242 CSHCN, four latent classes emerged according to different combinations of condition impact (broad, across multiple functional domains vs. narrow) and service intensity (high vs. low). Classes with broad impact had significantly worse clinical outcomes and social characteristics. Those with broad impact / high intensity had the highest ED visit rates (RR 3.34, $p < 0.001$) and hospitalizations (AOR 11.97, $p < 0.001$), but only a 20% predicted probability of having a medical home. Those in the narrow impact / high intensity class had the second highest ED visit rates (RR 2.12, $p < 0.001$) despite having the highest overall likelihood of a usual source of care and better social and clinical characteristics (e.g. shared decision making, medical home, family income, insurance status) compared to broadly impacted children.

Conclusions: Complexity of CSHCN can be characterized by different combinations of the extent of the condition's impact and intensity of services, correlating with significantly different outcomes. By understanding the scope of the condition's impact and service intensity, needs and outcomes may be forecasted, irrespective of specific diagnoses. Developing improvement strategies based on class rather than diagnosis could strengthen population management of rare but complex conditions.

PAS DATE/TIME/LOCATION 5/6/2014; 7:00 AM - 11:00 AM; Exhibit Hall C (Vancouver Convention Centre), BOARD NUMBER 509

****PAS Poster Presentation**

"THE EFFECTIVENESS OF BEST PRACTICE GUIDELINES IN IMPROVING RESIDENT PROGRESS NOTES IN AN EHR"

Shannon M Dean, MD, Leigh Anne Bakel, MD and Jens C Eickhoff, PhD

Background: Providers nationally have observed a decline in the quality of documentation after implementing an EHR. Concerns include the over-inclusion of data (note clutter), indiscriminate use of copy and paste, and a perceived loss of cognitive processing when notes are written using an EHR. Despite these concerns, few studies address the need to improve note quality. At our two academic centers, we implemented best practice guidelines with the goal of improving progress notes in the EHR. We also developed an audit tool to examine compliance with our guidelines.

Objective: Our objectives were to examine the effectiveness of implementing guidelines in improving resident progress notes and to establish the reliability of the audit tool used to measure compliance with them.

Design/Methods: At site #1, an entirely new note template was developed to comply with the guidelines. At site #2, a pre-existing template underwent minor changes to achieve compliance. We utilized the audit tool to evaluate progress notes written before and after the development and implementation of the guidelines ($n=25$ in pre- and post-implementation cohorts). Scores were summarized in terms of means and standard deviations. Reliability of the tool was calculated using the intra-class correlation coefficient (ICC) based on multi-level random intercept model. Nonparametric Wilcoxon Rank Sum test was used to compare pre and post-implementation scores. P-values were two sided and considered statistically significant at < 0.05 .

Results: The ICC was 0.96 and 0.78 at sites #1 and 2 respectively, indicating a good to excellent level of reliability among raters. There was a statistically significant improvement in the total score and in questions related to decreasing note clutter at site #1. At site #2, no single question was significantly different, attributed to a nearly compliant pre-existing template. Interestingly, there was a statistically significant decline in the total score at site #2, likely due to use of copy and paste as shown in a trend toward significance for questions related to copy and paste activity. **Conclusions:** Establishing guidelines can lead to improvements in EHR documentation, specifically in the reduction of note clutter. However, as demonstrated at both sites, this intervention alone does not address copy and paste or the loss of critical thinking and writing in the EHR. Interventions for improving the latter require additional investigation.

PAS DATE/TIME/LOCATION May 5, 2014; 4:15-7:30; Vancouver Convention Centre, Exhibit Hall C, Board 530

****PAS Poster Presentation**

UTILITY OF LACTIC ACID LEVELS IN CHILDREN WITH SUSPECTED INTUSSUSCEPTION

Paul T Ishimine, MD, Vanessa L Tamas, MD and P Jamil Madati, MD.

Background: Intussusception is characterized by intermittent abdominal pain, vomiting, and bloody stools. Efforts to risk stratify with history, physical exam and abdominal radiographs can not reliably detect all in need of additional diagnostic testing. Ultrasound is reliable but limited by its availability. Currently, no laboratory screening test exists that can help to define the odds of intussusception. In intussusception, abdominal pain and bloody stools, are postulated to occur from bowel ischemia. Lactic acid is produced when ischemia is present.

Objective: The main objective of this study is to compare mean lactate acid levels in children with and without intussusception. The secondary objective is to correlate lactic acid levels to duration of abdominal pain.

Design/Methods: This was a prospective cohort study of patients, 6 months to 6 years of age, who underwent ultrasound for the diagnosis of intussusception. Subjects were excluded with any of the following disorders: renal disease, metabolic disorder, ventriculoperitoneal shunt placement, seizure disorder, liver disease, history of blunt abdominal trauma, Henoch-Schönlein purpura, and history of abdominal surgery. Serum was obtained as a free flowing sample. A study specific data sheet was given to parents. Lactic acid was analyzed using the VITROS LAC (Ortho Clinical Diagnostics, Rochester, NY) slide method. Student t-test was utilized for continuous variables. Chi square analysis or Fisher's exact test were used for categorical variables.

Results: A total of 42 patients were analyzed: 17 with intussusception (15 positive US, 1 BE, 1 seen on plain films), and 25 without. There were no significant differences between the groups. Mean lactic acid levels did not differ significantly in the two groups (intussusception 1.93 SD 1.13, no intussusception 1.70 SD 0.69). Comparison of mean lactic acid levels between patients with abdominal pain < 24 hours (1.8 SD 0.67) to those with pain > 24 hours (2.5 SD 2.51) was significantly different. One child, with frank rectal bleeding, had a lactic acid level of 5.4 mmol/L. **Conclusion:** Lactic acidemia does not appear to be a useful screening test for intussusception; however, it may indicate disease severity.
PAS DATE/TIME/LOCATION May 4, 2014; 4:15-7:30 pm; Exhibit Hall C (Vancouver Convention Centre)

****PAS Poster Presentation**

MARFAN SYNDROME AND SOCIAL MEDIA: SYMPTOMS, SUPPORT AND CELEBRITIES

Erin F Kelleher, Philip F Giampietro, MD, PhD and Megan A Moreno, MD, MEd, MPH

Background: Marfan syndrome (MS) is a connective tissue disorder that affects thousands of US teens. Some teenage patients with MS may use social media to express their experiences and emotions, but little is known about what patients choose to share online.

Objective: The purpose of this study was to investigate displayed social media content related to Marfan syndrome across six different social media sites.

Design/Methods: The key words "Marfan syndrome" and "Marfans" were searched on six different social media sites including: Instagram, Pinterest, Reddit, Tumblr, Twitter and YouTube. The top five recent and popular posts and related comments for each site were collected and coded weekly for five weeks. A codebook was developed using an iterative process to categorize posts and comments. Posts were excluded if they were reshared content or not in English.

Results: Out of 300 posts collected, 141 were reshared and 4 were in another language, leaving 145 posts (48.3%) to analyze for content. Only 3 (2.1%) posts specified age, gender and location in their profiles. Categories of displayed content included experiences (31.0% of posts) including going to the doctor or having heart surgery. Posts included symptoms (13.8%), most commonly pain and fatigue. A large number of posts (13.7%) referenced Austin Carlile, a celebrity singer with MS as a role model. Posts also included supportive text including offering advice or support to others (9.7%). Examples of supportive posts include #nevergiveup or "Don't let anything stop you from being you either."

Conclusions: Participants post about and often reshare content on social media related to many aspects of living with MS. While little demographic information about individuals was available, physicians and healthcare providers may consider using social media information to understand common concerns and consider new online venues to place health education materials. The frequent posts about a celebrity illustrated the impact that one celebrity patient can have on recognition of a rare disease. It was noteworthy that there were multiple posts about being tired or loss of energy. Future studies aimed at analyzing Facebook profiles in patients with MS may provide additional insight into etiologies for pain and fatigue in patients with MS.

PAS DATE/TIME/LOCATION May 5, 2014; 4:14 PM-7:30 PM; Exhibit Hall C, Board number 305

****PAS Poster Presentation**

EVALUATING THE IMPLEMENTATION OF A FAMILY-CENTERED ROUNDING CHECKLIST

Kelly MM, Cox ED, Xie A, Li Y, Cartmill R, Carayon, P

Background: Checklists are used to standardize processes and improve patient safety; however, implementation challenges still exist in the context of complex healthcare systems. With a multidisciplinary stakeholder team, we developed a family-centered rounding (FCR) checklist aimed at optimizing best practices for family engagement on rounds. To date, evaluating the implementation an FCR checklist across disciplines has not been performed.

Objective: To evaluate the implementation of an FCR checklist across two different inpatient services.

Design/Methods: As part of a larger institutional quality improvement study to improve family engagement on FCR, hospitalist and hematology/oncology physicians (n=27) at a tertiary children's hospital participated in a 90-minute didactic and role-play training on the use of an 8-item FCR checklist. Research assistants then conducted observations of weekday rounds using an observation protocol that identified rounding service, rounding duration and location (bedside or hallway), family presence, and completion of checklist items. Qualitative data on barriers to item completion was recorded. Differences between services were calculated using Chi-squared or t-tests.

Results: Data was collected from 251 individual patient rounding observations over 29 days. Compared with heme/onc, hospitalist rounds were longer (13.3 vs 11.4 minutes per patient, $p<0.02$), and occurred more frequently with the family present (88 vs 71%, $p<0.005$) and in the patient's room (77 vs 2%, $p<0.001$). Hospitalist teams also completed more checklist items in a single rounding session (82 vs 72%, $p<0.001$), and were more likely to do introductions (84 vs 70%, $p<0.01$) and review discharge goals (70 vs 36%, $p<0.001$). Barriers that were more commonly noted on the heme/onc service included, but were not limited to, hallway distractions and limited checklist visibility.

Conclusions: Despite extensive stakeholder involvement in development, implementation of an FCR checklist can still be challenging across different inpatient services. Each service likely faces unique barriers to checklist adherence. Future plan-do-study-act cycles and dissemination efforts will need to carefully consider the context of checklist use. *PAS DATE/TIME/LOCATION May 4, 2014; 4:15-7:30pm; Exhibit Hall C; Poster 708*

****PAS Poster Presentation**

INHIBITING ENDOGENOUS ESTROGEN REDUCES FETAL IRON AND ALTERS FETAL IRON STATUS IN LATE OVINE PREGNANCY

Pamela J Kling, Mary Y Sun, Jason L Austin, Terry M Phernetton, Ronald R Magness.

Background: Estrogen production by the placenta rises dramatically throughout gestation, promoting fetal growth and development. Limited in vitro data show that estrogen modulates iron homeostasis possibly through increasing expression of both endothelial nitric oxide synthase (eNOS) and transporter transferrin receptor (TfR1). Letrozole, a potent clinical aromatase inhibitor, suppresses estrogen production.

Objective: To determine if letrozole which reduces estrogen production also decreases fetal growth rate and fetal iron status.

Design/Methods: Late gestation (120±5d, term=147d) sheep were given prolonged letrozole (20 mg IM loading, then 125 µg/kg/day for 7-8d vs. vehicle control). Fetal and placental morphometrics were measured and TfR1 and eNOS immunoblots performed. We measured maternal and fetal RBC count, hemoglobin, and zinc protoporphyrin (ZnPP/H; a measure of incomplete RBC iron incorporation) and tissue iron.

Results: Letrozole reduced total placental weight per fetus. TfR1 expression was reduced ($P<0.05$), but eNOS trended higher ($0.1 >P>0.05$). Compared to controls, letrozole fetuses were 19% lighter and BMI 12% lower ($P<0.05$). Letrozole also reduced fetal brain, liver, thymus, and spleen weights ($P<0.05$ for all). Letrozole also increased maternal RBC counts and also ZnPP/H, but without elevation of fetal RBC and ZnPP/H. Iron concentration in fetal liver were similar to control, but the letrozole kidneys had higher iron concentration ($P<0.05$) and iron deposition seen.

Conclusions: Inhibiting endogenous estrogen reduced the placental size and produced leaner fetuses. Letrozole also decreased maternal RBC iron incorporation and placental TfR1, but specifically increased fetal kidney iron accretion. These data indicate a role for estrogen in controlling fetoplacental growth and iron metabolism, and fetal body composition. NIH HL49210, HD38843, HL87144. *PAS DATE/TIME/LOCATION May 5, 2014, 4:15 pm- 7:30 pm Exhibit Hall C BOARD NUMBER: 33*

****PAS Poster Presentation**

SIMULATION USE FOR GLOBAL AWAY ROTATIONS (SUGAR): RESIDENT PERCEPTIONS OF THE MOST DIFFICULT AND MOST VALUABLE ASPECTS OF SIMULATED GLOBAL HEALTH EXPERIENCES AT A MULTI-INSTITUTIONAL CURRICULUM STUDY

Michael B Pitt, MD, Sophia P Gladding, PhD and Sabrina M Butteris, MD.

Background: As more residents participate in global health (GH) experiences, educators struggle with how to best prepare them for the challenges of practicing medicine in resource-limited countries. To address this need, pediatric GH educators from 7 institutions collaborated to develop a standardized, peer-reviewed, medical simulation curriculum, which addressed both medical management and emotional challenges often encountered on GH experiences. Over one year, residents across 7 sites participated in 162 simulation cases with 94.4% of evaluation responses indicating the sessions were useful or very useful in preparing them for their GH experience.

Objective: Determine common themes identified by residents regarding the most difficult and valuable aspects of the simulation of GH experiences.

Design/Methods: We conducted a thematic analysis of written responses to the evaluation questions asking what they found to be the most difficult and most valuable parts of the session. Two authors independently coded the written comments using themes initially identified by one author. The two authors compared their coding, discussing areas of disagreement until consensus was reached. We then calculated the frequency of each theme.

Results: For the most difficult part of the session, we identified two dominant themes: working with limited resources (69/161; 43% of comments) and lack of medical knowledge/patient care skills (40%) with additional themes related to cultural context and specific aspects of the cases. For the most valuable part of the session, we identified two dominant themes: learning to work with limited resources (55%) and expansion of medical knowledge (34%) with additional themes related to the debriefing process and specifics of the case.

Conclusions: After participating in the curriculum, residents identified several themes that mirror challenges commonly encountered on GH experiences. Many residents found working with limited resources to be both the most difficult and valuable part of the sessions with the difficulty experienced due to lack of knowledge transformed into a valued expansion of knowledge through the sessions. By having the opportunity to experience and debrief the challenges they may encounter prior to going abroad, residents may have less difficulty navigating them while abroad.

PAS DATE/TIME/LOCATION May 5, 2014; TBD

****PAS Poster Presentation**

SIMULATION USE FOR GLOBAL AWAY ROTATIONS (SUGAR): DESCRIPTION AND FACILITATOR FEEDBACK OF A STANDARDIZED SIMULATION CURRICULUM TO PREPARE RESIDENTS FOR GLOBAL HEALTH EXPERIENCES

Michael B Pitt, MD, Scott Hagen, MD, Walter Eppich, MD, MEd and Sabrina M Butteris, MD.

Background: With increasing numbers of residents participating in GH electives, the need for preparation is crucial. Active preparatory curricula allowing residents to experience and debrief potential emotional challenges are lacking.

Objective: To design a standardized simulation curriculum to prepare residents for possible emotional challenges encountered abroad and solicit facilitator feedback of the case design and efficacy.

Design/Methods: GH educators from a consortium of 7 institutions agreed on the 4 most common challenges residents encounter on GH experiences and developed cases addressing each. Each challenge was paired with a desired adaptive characteristic which would ideally be enhanced after working through the case. Two-page simulation guides and a debriefing script were created and facilitators were trained in their use. Facilitators completed evaluation forms after each case.

Results: Of 52 facilitator evaluations, 100% rated the sessions as useful or very useful in preparing their residents for GH electives. All indicated that the cases elicited the intended challenges, and the simulation guide provided enough information to lead the case effectively. **Conclusions:** Facilitators indicated that the simulation guide provided sufficient information to lead the case and that the desired challenge was attained during the session. By encountering and debriefing these challenges prior to their GH experiences, residents may better navigate these obstacles while abroad.

PAS DATE/TIME/LOCATION 5/5/2014; TBD

****PAS Poster Presentation**

HEMATOPOIETIC ALTERATIONS IN GESTATIONAL IRON DEFICIENCY

Zachary R Smith, Mary Y Sun, Hannah R Zundel, Sharon E Blohowiak, Pamela J Kling

Background: Iron is vital for cell proliferation; therefore, severe gestational iron deficiency (ID) can impair fetal erythropoiesis. In older children, ID increases erythropoietin production, stimulating both erythrocytes and platelets. However, little is known about whether fetal non-erythropoietic hematopoietic cell lineages are susceptible to ID. Additionally, gestational ID may permanently alter the production of hematopoietic cell profiles, leading to clinical implications in adult life. Rats are good models of the hematopoietic lineages.

Objective: To examine the effect of gestational ID on adaptations in newborn rat hematopoietic cell lineages.

Design/Methods: From gestational day 2 to postnatal day (P) 7, dams were fed either iron sufficient (IS) diet (198mg Fe/kg) or ID rat diet (<6mg Fe/kg diet) with the biological lactating dam nursing the pups. At P7, the IS diet was fed to all dams. At P20, pups were weaned to the IS diet. Blood was collected between P2-P10 and again from P30-P45 and analyzed for hemoglobin levels, zinc protoporphyrin/heme (ZnPP/H), reticulocyte counts, WBC counts, platelet counts, and mean platelet volume.

Results: From P2 to P10, hemoglobin levels in ID were 20-25% lower than IS ($P<0.01$ in ID). Erythrocyte iron incorporation was worse in ID, as measured by 2-3 fold higher ZnPP/H in ID ($P<0.01$). At birth, reticulocytes in ID were suppressed ($P<0.004$) but equalized by P7. In the first 10 days, reticulocytes were indirectly related to ZnPP/H ($R^2=-0.09$, $P<0.005$). At birth, WBC was 28% and platelet counts 25% lower in ID; while platelets were 80% larger, ($P<0.005$ for all). Platelet counts were directly related to reticulocytes in the first 10 days ($R^2=0.23$, $P<0.0001$). After weaning, the reticulocytes, WBC and platelets in ID remained lower, while platelet size was larger than in IS ($P<0.003$).

Conclusions: Gestational ID caused short-term and long-term hematopoietic programming alterations in red, white and platelet cell lineages, despite correction of ID and potentially altering function. Because pregnancy complications commonly impair fetal iron delivery, a better understanding of how fetal iron status impacts production and function of all hematopoietic cell lineages is needed.

*PAS DATE/TIME/LOCATION May 5, 2014; 4:15 pm- 7:30 pm Exhibit Hall C SESSION**:* 2927—Neonatology BOARD NUMBER: 416

DISRUPTION IN KIR7.1 CHANNEL LEADS TO BLINDNESS

Pattnaik, Bikash R.; Marino, Meghan J.; Shahi P.; Brar S.; York N.; Pillers, De-Ann M.; Traboulsi, Elias

Purpose: Leber Congenital Amaurosis (LCA) is a rare autosomal recessive disorder caused by the defects in the function of either photoreceptors or Retinal Pigment Epithelium (RPE). Recently, mutations in KCNJ13, an RPE inwardly rectifying potassium channel have been found to be associated with LCA. We describe a patient with a retinal dystrophy compatible with a moderately severe LCA phenotype due to homozygosity for a novel KCNJ13 nonsense mutation.

Methods: A nine year-old male presented with nyctalopia and decreased vision. Clinical studies including a complete eye examination, fundus photography, and OCT were performed. Genetic testing was obtained using PCR-based Next Generation Sequencing (NGS). To study the mutant protein, site-directed mutagenesis was performed on an N-terminal Green Fluorescence Protein (GFP) - fused human KCNJ13 open reading frame insert by Quick-Change Site-Directed Mutagenesis Kit from Stratagene (Agilent Technologies Inc., CA). Chinese Hamster Ovary (CHO) cells were transfected with either the wildtype or mutant plasmid, and cells were studied within 24 to 72 hours post transfection.

Results: Best corrected visual acuity was 20/200 OD and 20/400 OS. Fundus photos showed a pale optic nerve head, attenuated blood vessels, and a pigmented, atrophic macula. Genetic testing detected a novel homozygous G→A transition (c.158G>A) in exon 1 of KCNJ13, which results in a stop codon at position 53 (p.W53X). This is predicted to result in a loss of the transmembrane domain and most of the C-terminal domain. Premature termination of translation was clearly demonstrated when the mutant protein was expressed in a heterologous expression system.

Conclusions: The present report confirms that mutations in KCNJ13 are strongly associated with LCA phenotype. The nature of the present truncating mutation sheds new light on the pathogenesis of the disease process. Kir7.1 is a critical player in vision and may be a candidate gene for other blindness.

International Society for Eye Research Biennial Meeting, July 20, 2014

CHRONIC INTERMITTENT HYPOXIA AUGMENTS BLEOMYCIN INDUCED LUNG FIBROSIS IN RATS

Rudolf K. Braun, PhD; Oleg Broymtman, PhD; David Pegelow, MS; Pei-Ning Hsu; Linda S. Mei; Dhruvangkumar Modi; Marlowe Eldridge, MD; Mihaela Teodorescu, MD, MS.

Rationale: Obstructive sleep apnea (OSA) is common among patients with idiopathic pulmonary fibrosis (IPF), where it has been linked with increased mortality. Chronic intermittent hypoxia (CIH)—its hallmark feature—may be one culprit. We tested the effects of CIH exposure on lung collagen, gas exchange and lung function following intratracheal bleomycin instillation in rats.

Methods: Four groups (n=4/group) of Sprague Dawley rats were instilled with bleomycin (1.5 U/kg) (BLEO) or saline (SAL). Five days after instillation, rats were subjected to CIH (10% FiO₂, 30 episodes/h, 10h/day) vs. normoxia (NORM) for 30 days. Total collagen in the right lung, pO₂ and pCO₂ in the exhaled air, and lung function by body plethysmography were compared between groups.

Results: CIH resulted in: 1) significant increase in total collagen in bleomycin injured lungs compared to BLEO/NORM or the SAL controls; 2) significant exhaled O₂ abnormalities in both SAL and BLEO treated groups compared to the respective NORM groups; 3) a trend of reduced FEV_{0.1}/FVC ratio in CIH treated groups in both the BLEO and SAL compared to the NORM group (0.78±0.10 vs. 0.71±0.14 and 0.67±0.17 vs. 0.61±0.15).

Conclusions: CIH aggravates lung fibrosis and gas exchange abnormalities following bleomycin. These findings underscore the potential of OSA to exacerbate IPF.

Experimental Biology 2014, April 26, 2014

Supported by UW-Madison Department of Medicine Pilot Funding.

CROSSTALK WITH ER α IN TRKB MEDIATED NEUROPROTECTION AFTER NEONATAL BRAIN INJURY

Pelin Cengiz Ulas, Cikla Vishal Chanana, Douglas Kintner, Wenzhu Sun, Peter Ferrazzano, and Jon Levine

Introduction: Hypoxia Ischemia (HI) related brain injury is the leading cause of morbidity and mortality among neonates. Clinical studies indicate that male neonate brains are more susceptible to the effects of HI resulting in more long-term cognitive deficits as compared to females with comparable brain injury. Relative resistance of female neonatal brain to HI suggests that some sex-specific mechanisms afford females greater neuroprotection and/or facilitates recovery. Our recent findings reveal that a brain-accessible tyrosine kinase B receptor (TrkB) agonist, 7,8-dihydroxyflavone (7,8-DHF), exerts a profound neuroprotective effect in the hippocampi of female but not male neonates 3 days after HI on postnatal day (P) 9. Because sex steroid receptors have been linked to neurotrophin signaling and estrogen receptor alpha (ER α) is differentially increased in adult female brain at the ischemia site, we hypothesized that differential TrkB phosphorylation is associated with hippocampal ER α expression post-HI in female neonatal hippocampus. In addition, membrane-associated ER α activation has been shown to be coupled to intracellular signaling via Src-family kinases (SFK) which are known to augment the phosphorylation of TrkB receptors. Therefore, we hypothesize that female-specific responsiveness to 7,8 DHF is linked to increased ER α activity through Src which leads to decreased apoptosis and neuronal survival post-HI.

Methods: Wild type (ER α +/+) and ER α knockout (ER α -/-) P9 pups were subjected to Vannucci's neonatal HI model. The left common carotid artery was cauterized and the pups returned to their dams for two hours. The pups were then placed in a hypoxia chamber and exposed to 10% oxygen at 37°C for 50 min. Pups were either given PBS or 7,8- DHF (5 mg/kg in PBS, ip.) starting at 10 min, then at 24 h, and 48 h post HI. On day 3 following HI, the brains were either fixed for immunohistological staining or the hippocampi dissected out for either immunoblotting or RTPCR. To assess the effects of sex, treatment and HI on immunoblotting band densities [phosphorylated TrkB/full length TrkB, ER α /actin ratios] and RTPCR either separately for the IL or CL sides or for the ratio of IL over CL, 3-way factorial ANOVA was used including all interactions.

Results: Phosphorylated TrkB (p-TrkB) was quantified by immunoblotting in ER α +/+ and ER α -/- mice 3 d post-HI by deriving p-TrkB/full-length TrkB ratios. In ER α +/+ mice, HI and 7,8-DHF preferentially increased p-TrkB in IL female vs male hippocampi 3 d post-HI ($p < 0.0001$). Quantitative polymerase chain reaction (qRT-PCR) and immunoblotting analyses show that at 3 days post HI induces a 2.3 fold increase in ER α mRNA and ER α protein expression in the IL hippocampus of female mice compared to the male mice at 3 d post-HI ($p = 0.002$). However, in ER α -/- mice p-TrkB in IL hippocampi was significantly decreased as determined by immunohistochemical staining and immunoblotting. Thus, HI and 7,8-DHF failed to induce increased phosphorylation of TrkB in ER α -/- female mice 3 d post-HI. Interestingly, immunohistochemistry and immunoblotting revealed that HI results in increased pSrc in ipsilateral dentate gyrus and that the increase is more robust in females.

Conclusion: There is a significant sexually differentiated response to HI and TrkB agonist therapy in neonatal hippocampi. Sexually differential phosphorylation of TrkB is abolished in ER α -/- mice post-HI suggesting an important role for ER α in TrkB phosphorylation and signaling.

AGE-DEPENDENT MICROGLIAL RESPONSES TO HYPOXIA-ISCHEMIA

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Background: The microglial response plays an important role in injury and recovery after hypoxia-ischemia (HI) in the developing brain. We have previously described regional and age-dependent differences in the microglial response to HI. In our previous studies, P9 mice demonstrated a more vigorous microglial activation and proliferation, and increased expression of proinflammatory cytokines after HI compared to P30 mice. The aim of the current study was to assess for differences in the effect of microglial suppression after HI in infant and juvenile mice. We hypothesized that administration of minocycline after HI would result in suppression of microglial activation in both age groups, and would improve brain injury after HI in younger mice.

Methods: HI was induced in P9 and P30 mice using the Vannucci method of carotid artery ligation and subsequent exposure to 10% O₂ for 50 minutes. Mice were administered minocycline (45mg/kg) or vehicle intraperitoneally at 2 hours and 24 hours post-HI. Mice were sacrificed at 2 days and 9 days post-HI. To quantify microglia and assess for microglial activation, flow cytometry was performed on pooled samples of ipsilateral and contralateral hippocampus, striatum and cortex. To quantify brain injury, MAP2 immunostaining was performed at day 2 post-injury and injury score was calculated for the anterior, middle and posterior cortex, CA1, CA2, CA3 and dentate gyrus of the hippocampus, and caudate putamen (0-3) using the contralateral side as a

reference. Iba1 staining was used to characterize microglial responses and morphology.

Results: As seen previously, flow cytometry demonstrated a dramatic increase in CD11b+/CD45+ cells in ipsilateral vehicle treated hippocampus on post-HI day 2 and a delayed increase in CD11b+/CD45+ cells in the cortex and striatum at post-HI day 9. Microglial counts were greater in vehicle treated P9 mice compared to P30 mice in the hippocampus at day-2 post-HI (9.5 fold vs. 5.7 fold increase from contralateral). Both P9 and P30 minocycline treated mice demonstrated a decrease in CD11b+/CD45+ cells in the hippocampus at post-HI day 2. Interestingly, minocycline treated P9 mice demonstrated a significant reduction in CD11b+/CD45+ cells in all ipsilateral brain regions at day 9 post-HI. In contrast, P30 minocycline treated mice demonstrated a rebound increase in CD11b+/CD45+ counts in ipsilateral cortex and striatum on day 9 post-HI. Additionally, minocycline treatment resulted in significant improvement in injury scores in P9 mice but not P30 mice at day 2 post-HI (11.8±1.2 vs 4.0±1.3 in P9, p<0.05; 8.25±5.1 vs. 6.4±3.9 in 30, p=0.78).

Conclusion: Minocycline treatment resulted in a sustained suppression of microglial activation and proliferation in P9 but not P30 mice. Minocycline treatment decreased neurological injury at day 2 post-HI only in P9 mice. Ongoing experiments will assess effect of minocycline treatment on neurological injury at day 9 post-HI. Additionally, we will assess for age-dependent differences in baseline expression of microglial genes associated with M1 phenotype (TNF α , iNos) and M2 phenotype (IL10, arginase), and the effect of minocycline treatment on M1 and M2 microglial responses after HI.

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MEDICATION USE AND POTENTIAL INTERACTIONS IN ADOLESCENTS WITH FRAGILE X SYNDROME

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Background: Fragile X Syndrome (FXS) is one of the foremost genetic causes of intellectual disability. This inherited disorder is X-linked dominant and is prevalent in approximately 1 in 4,000 males and 1 in 8,000 females. Symptoms of FXS vary in composition and strength across individuals and include cognitive delay and behavioral symptoms such as hyperactivity, anxiety and autistic symptoms. Past studies have indicated high rates of co-occurrence of both anxiety and ADHD within fragile X samples. Although there is not a pharmacological treatment available for cognitive dysfunction, medication is commonly used to treat these comorbidities. Medications also may be used to treat other comorbidities including seizure activity, sleep disturbance, and mood regulation.

Objective: We aimed to describe the medication profile in a sample of adolescents with FXS and to investigate possible interactions between medications among those currently taking 2 or more medications.

Design/Method: Participants for the present study were drawn from the larger Family Adaption to the FXS Study funded by the National Institute of Child Health and Human Development (NICHD) as part of the national network of NICHD- funded research centers on fragile X syndrome. This 5 year study focused on adolescents and adults diagnosed with the full mutation of FXS. Criteria for participation in the larger study were that mothers had to live with their son or daughter or have at least weekly contact with them, and documentation confirming the FXS diagnosis was required. The sample for the present project consisted of children with FXS who were at or under the age of 22 years (n=96 at the first wave of data collection). Descriptive statistics in the form of frequency counts and cross tabs were used to describe the medication profile of the sample. The medical website Epocrates was used to determine potential medication interactions for adolescents who were currently taking two or more prescribed medications. The MultiCheck tool allows direct comparison of medications by providing a notification of a potential interaction between two medications. The interactions are organized consistent with the clinical management categorizations: "Contraindicated", "Avoid/Use Alternative", "Monitor/Modify TX" and "Caution Advised".

Results: Results showed that 76.04% of children were currently taking one or more medications while 52.08% were currently on two or more medications. Of the reasons indicated for medication use, anxiety and symptoms of ADD or ADHD were the most frequently reported. Preliminary results suggest that of the children taking two or more medications, 65% are taking a combination of medications that are indicated to have at least 1 potential medication interaction. Concerta, a CNS stimulant drug, was the most common (10.53%) drug indicated as having a potential interaction. Common potential adverse effects of medication interactions included an increased risk of CNS depression and psychomotor impairment.

Conclusions: The present study aimed to identify medication trends and potential medication interactions among adolescents with FXS. Consistent with past research was high comorbidity and overlapping symptoms between FXS and anxiety and ADD/ADHD. Findings indicate the necessity of careful management of the health of children with FXS, as 65% of adolescents in the sample who were taking multiple medications shared a potential adverse interaction between medications, some of which could have severe adverse effects such as CNS depression or psychomotor impairment.

PREVALENCE AND CLINICAL CORRELATES OF OBSTRUCTIVE SLEEP APNEA IN YOUNG INFANTS WITH DOWN SYNDROME

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Background and Objectives: Children with Down syndrome (DS) experience congenital and functional medical issues that predispose them to obstructive sleep apnea (OSA). Research utilizing stringent age criteria among substantial samples of young infants with Down syndrome and OSA is limited. This study examines the prevalence and clinical correlates of OSA among young infants with DS.

Methods: A retrospective chart review was conducted of infants ≤ 6 months of age referred to a Down syndrome clinic based at a large tertiary children's hospital over a five-year period (n=177). Chi-square tests and binary logistic regression models were utilized to analyze the data.

Results: Fifty-nine infants underwent polysomnography, based on clinical concerns. Of these, 95% (56/59) were found to have studies consistent with OSA. Among infants with OSA, 71% experienced severe OSA (40/56). Overall prevalence of OSA among the larger group of infants was 31% (56/177). Significant relationships were found between OSA and dysphagia, congenital heart disease (CHD), prematurity, gastroesophageal reflux disease, and other functional and anatomic gastrointestinal (GI) conditions. Results indicate that odds of OSA are significantly higher among infants with GI conditions in comparison to those without. The combination of dysphagia and CHD predicted the occurrence of OSA in 36% of cases with an overall predictive accuracy rate of 71%.

Conclusion: Obstructive sleep apnea is relatively common in young infants with DS and is often severe. Medical factors including GI conditions, dysphagia and CHD may help to identify infants who are at greater risk and may warrant evaluation.

Down Syndrome Medical Interest Group- USA Annual Symposium 2013, July 19, 2013

USING AN IMMUNIZATION INFORMATION SYSTEM (IIS) TO ESTIMATE THE EFFECTIVENESS OF TDAP IN PREVENTING PERTUSSIS DURING A LARGE OUTBREAK, WISCONSIN, JULY 2011-DECEMBER 2012

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Background: During 2011-2012, a statewide outbreak of pertussis occurred in Wisconsin. We estimated Tdap effectiveness in preventing pertussis among adolescent age cohorts never immunized with whole cell pertussis vaccine.

Methods: We defined the surveillance population (SP) as Wisconsin residents born during 1998-2001 with client records in the population-based Wisconsin Immunization Registry (WIR). A pertussis case was defined as an acute cough illness with onset during 7/1/2011-12/31/2012 in a SP member with laboratory-confirmed *Bordetella pertussis* infection meeting the CSTE definition of confirmed.

Pertussis cases were matched to WIR client records by name and birth date. Tdap brand and date administered were obtained from the WIR. The population unexposed to Tdap was estimated from census data, assuming all Tdap doses received were documented in the WIR. Age-adjusted relative risks and vaccine effectiveness (VE) estimates were calculated using Poisson regression.

Results: Of 1,464 reported cases among the 306,142-member SP, 1450 (99%) were matched to WIR client records. Overall Tdap VE was 68.7% (95% CI: 64.9%-72.0%). VE decreased from 87.4% (84.9%-89.6%) among persons vaccinated 7/1/2011-12/31/2012 to 44.3% (34.8%-52.4%) among persons vaccinated 1/1/2010-6/30/2011 to 12.7% (-6.7%-28.6%) among persons vaccinated 1/1/2008-12/31/2009. During each time interval VE was greater among Boostrix recipients (92.5%, 60.0%, 30.0%) than Adacel recipients (84.3%, 23.7%, -2.0%).

Conclusions: Tdap is effective in preventing laboratory-confirmed pertussis in the short-term, but immunity wanes quickly. Boostrix appeared to induce longer-lasting immunity than Adacel, but these findings should be confirmed in additional studies. We also demonstrated an IIS was useful in examining vaccine effectiveness within a population.

10th Annual International Symposium on Bordetella, September 10, 2013 and platform presentation at IDSA Oct 26, 2013

PULSE OXIMETRY SCREENING FOR CRITICAL CONGENITAL HEART DISEASE

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Design and Objectives: Although the rate of missed diagnosis of critical congenital heart disease (CCHD) is higher in out-of-hospital (OOH) births than in hospital births, no previous study has described the use of pulse oximetry screening for CCHD in this community. This observational study of the Wisconsin OOH births was performed from January to November, 2013. Licensed midwives, Amish birth attendants, and public health nurses were trained in the use of pulse oximetry to detect CCHD, supplied with pulse oximeters, and reported screening results and clinical outcomes.

Results: Results of pulse oximetry screening in 440 newborns were reviewed. 173/440 births were from Amish or Mennonite communities. Prenatal ultrasonography was performed in less than half of the pregnancies, and in only 13% of Amish and Mennonite women. 432 babies passed the screening, 5 babies were incorrectly assigned to have passed or failed, and 3 babies failed the screening. Two of the babies who failed the screening were treated for sepsis and the third had congenital heart disease. There was one false negative result (coarctation of the aorta and VSD).

Conclusions: This study provides the first information on the use of pulse oximetry screening for CCHD in OOH births and shows that pulse oximetry screening can be successfully implemented outside the hospital setting. Although the failure rate in this small sample was higher than reported in studies of hospital births, those babies failing the screening had significant disease processes that were identified more rapidly because of the screening. *2014 Wisconsin Association for Perinatal Care Annual Conference, April 27, 2014, Also submitted to 2014 PAS/ASPR*

This paper is under review with the Journal of Pediatrics

OXYTOCINERGIC SIGNALING VIA GPCR IN A SINGLE HEK293 CELL WITH STABLE EXPRESSION OF THE OXYTOCIN RECEPTOR

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Purpose: We have shown that oxytocin (OXT) localizes to the cone photoreceptor outer segment whereas the oxytocin receptor (OXTR) localizes to the retinal pigment epithelium (RPE). OXT is a neuropeptide hormone traditionally recognized for its role in parturition. A rise in intracellular calcium ($[Ca^{2+}]_i$) occurs as a result of OXT binding to the oxytocin receptor (OXTR), most likely through G-protein coupled receptor (GPCR) mediated activation. We used molecular and live-cell imaging techniques to visualize OXT-OXTR signaling by real-time fluorescence.

Methods: We generated Human Embryonic Kidney (HEK293) cells stably expressing human OXTR (hOXTR-HEK). Intracellular changes in $[Ca^{2+}]_i$ in response to OXT and ATP were measured using a FURA-2AM ratiometric assay. We used a live-cell fluorescent marker (pleckstrin homology domain-fused GFP or PH-GFP) for the detection of membrane phosphatidylinositol 4,5-bisphosphate (PIP₂). In the hypothesized rhodopsin-type class I GPCR pathway, upon agonist binding, membrane PIP₂ is hydrolyzed to inositol 1, 4, 5-trisphosphate (IP₃) and diacylglycerol (DAG) catalyzed by phospholipase C (PLC). hOXTR-HEK cells were transiently transfected with PH-GFP using TransIT-HEK (MirusBio, Madison, WI). ATP binding was used as a positive control. GFP positive cells were imaged within 24-72 hr post transfection. Fluorescence images were acquired every 10 sec.

Results: In response to OXT, hOXTR-HEK cells demonstrated an average ratiometric increase of 0.0738 ± 0.0028 units ($P < 0.005$) corresponding to an increase in ~ 75 nM of free $[Ca^{2+}]_i$. The response to ATP was not significantly different, consistent with the involvement of a GPCR mechanism. PH-GFP has a high affinity for PIP₂ but when PIP₂ hydrolyzes, PH-GFP translocates with IP₃ to the cytoplasm. In our live-cell imaging experiments, resting cells expressing GFP in the sub-membrane domain showed translocation of GFP fluorescence from the membrane to the cytoplasm (an average increase in cytoplasmic pixel density of 512.09 ± 54.27 units, $P < 0.005$) when the cells were exposed to OXT. The time course of GFP translocation correlated with the increase in intracellular $[Ca^{2+}]_i$.

Conclusions: In a HEK293 OXTR expression cell model, we have shown that OXT-OXTR signaling uses a GPCR mechanism to mobilize intracellular $[Ca^{2+}]_i$. These results suggest that intercellular communication may occur in the eye via OXT-OXTR mediated GPCR signaling. *Association for Research in Vision and Ophthalmology, May 6, 2014*

SIMULATION TRAINING TO MAINTAIN NEONATAL RESUSCITATION AND PEDIATRIC SEDATION SKILLS FOR EMERGENCY MEDICINE FACULTY

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Background: Neonatal resuscitations and adverse events in pediatric sedations occur infrequently, thus maintaining skills necessary to manage these children is challenging. As Pediatric Emergency Medicine specialty coverage expands, many Emergency Medicine (EM) physicians have even less exposure to these critical patients. As such, effective training strategies need to be developed. Simulation provides the opportunity to experience a rare event in a safe learning environment, and has shown efficacy in skill acquisition for medical students and residents. Less is known regarding its use for faculty-level learners.

Objectives: To assess the acceptability, efficacy and feasibility of a simulation-based educational intervention for EM faculty on their knowledge, comfort, and perceived competence in neonatal resuscitation and pediatric sedation.

Methods: Eighteen academic EM faculty participated in a four-hour educational intervention with high-fidelity simulation sessions focused on neonatal resuscitation (precipitous delivery of a depressed newborn using Laerdal SimNewB) and adverse events associated with pediatric sedation (laryngospasm and hypoventilation using Laerdal SimBaby). Faculty also practiced umbilical vein catheterization, nasal foreign body removal, and video laryngoscopy skills, as well as, reviewed supplies stocked in our pediatric resuscitation cart. A pre and post-intervention evaluation was completed consisting of knowledge and attitude questions. Paired t-test analysis was used to detect statistically significant change ($p \leq 0.05$).

Results: Results were obtained from 17 EM faculty members. Simulation training was well-accepted pre and post-intervention, and simulation was effective with statistically significant improvement in both knowledge and attitude (Table). This type of event was feasible with 83% of EM faculty participating.

Conclusion: EM faculty have limited opportunities to manage neonatal resuscitations and adverse events in pediatric sedations. Simulation training appears to be an effective educational modality to help maintain these important skills. Table: Comparison of Pre/Post Simulation-based Educational Intervention on Knowledge and Attitude / Pre-Intervention Average Post-Intervention Average % Change P Value / Medical Knowledge Aggregate Test Score (11 questions) 6.83/11 10/11 28.9% <0.0001 / Attitude Questions* / I feel comfortable in managing adverse events that occur in pediatric sedations 3.41 3.88 13.8% 0.0068 / I feel competent in performing emergent pediatric sedations 3.88 4.12 5.9% 0.0413 / I feel comfortable in performing emergent neonatal resuscitations 2.59 3.41 31.7% 0.0061 / I feel competent in performing emergent neonatal resuscitations 3.06 3.65 19.3% 0.0036 / I feel competent in performing umbilical lines 2.18 3.71 70.2% <0.0001 / I feel

competent in performing pediatric airway techniques using a GlideScope 3.71 4.29 15.6% 0.0002 / I feel competent in handling and identifying pediatric airway equipment in the ED 3.71 4.24 14.3% 0.0149 / Participating in this workshop with my colleagues will be (was) anxiety provoking 3.65 3.76 3.0% 0.6959 / Simulation is a good way to update my pediatric critical care skills 4.59 4.71 2.6% 0.1635 / * On a 5-point Likert scale, with 5 indicating "strongly agree", and 1 indicating "strongly disagree" / Statistically significant change ($p \leq 0.05$) in bold

IN VIVO TRACKING OF HUMAN NATURAL KILLER CELLS USING MAGNETIC RESONANCE IMAGING

Erbay Salievsk, Myriam N. Bouchlaka, Kai D. Ludwig, Michael Martinez, Jeremy G. Gordon, Bryan P. Bednarz, Sean B. Fain, Christian M. Capitini

It has been known that natural killer (NK) cells have the ability to kill tumor cells with the aid of several different NK cell receptors, co-stimulatory molecules and cytotoxic granules. However, it is not understood how NK cells mediate their anti-tumor effects by either trafficking to the tumor site and directly killing the tumor or by indirectly stimulating other effector cells. Current methods of tracking immune cells by imaging of 1H contrast agents, such as iron oxide particles, are not ideal as a large part of the 1H signal comes from water in the tissues. We have optimized the non-toxic tracer agent Fluorine 19 using magnetic resonance imaging (MRI) to track human NK cells in vivo. Human NK (hNK) cells were first ex vivo labeled with a commercially available perfluoropolyether (PFPE) tracer. Imaging of hNK cells in vitro and in vivo was performed on a 4.7T small animal MRI system using a 19F volume quadrature coil. Nuclear magnetic resonance (NMR) spectroscopy was performed on a 9.4T spectrometer to verify successful uptake of PFPE agent into hNK cells. In vitro, we show by imaging and spectroscopic analysis that hNK cells highly uptake PFPE within 24 hours of labeling. This 19F signal is dose-dependent and proportionally increases with increasing PFPE concentrations. 19F-labeled hNK cells do not lose their ability to: 1) secrete cytotoxic cytokines and granules (IFN- γ and Granzyme B), 2) express natural cytotoxic receptors (NCRs), and 3) kill K562 leukemia cells in vitro in the same manner as non-labeled hNK cells. Furthermore, in vivo 19F-labeled hNK cells injected subcutaneously or intratumor into a naïve or tumor bearing NOD-SCID-IL-2Ry^{-/-} (NSG) mice, respectively, were nontoxic and detectable by MRI. The 19F signal from the hNK cells stayed localized in the flank or within the human neuroblastoma tumor for at least 48 hours. Overall, 19F labeling of hNK cells represents a successful method to track and quantify the number of apparent cells in a region of interest without altering their cytotoxic function. Further studies for quantification of trafficking patterns are still underway.

BCL-2 EXPRESSION IN ENDOTHELIAL CELLS IMPACTS POSTNATAL RETINAL VASCULAR DEVELOPMENT WITHOUT AFFECTING RETINAL NEOVASCULARIZATION

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Bcl-2 plays an important role in retinal vascular homeostasis. Global lack of Bcl-2 expression results in attenuation of postnatal retinal vascular development and neovascularization during Oxygen-induced Ischemic Retinopathy (OIR). To determine the impact lack of Bcl-2 expression in endothelial cells has during retinal vascular development, remodeling, and neovascularization, we generated mice carrying a conditional Bcl-2 allele (Bcl-2^{Flox/Flox}) and VE-cadherin-cre called Bcl-2^{EC} mice. Bcl-2^{EC} mice displayed decreased numbers of endothelial cells at both 3 and 6 weeks of age compared to wild-type / controls. However, the remodeling of the retinal vasculature proceeded with similar percentage loss of endothelial cells in both wild-type and Bcl-2^{EC} mice. In addition, Bcl-2^{EC} mice had increased pericyte numbers at 6 weeks of age contributing to a lower EC/PC ratio. Retinal arteriogenesis was also decreased in Bcl-2^{EC} mice similar to what we observed in global Bcl-2 knockouts. However, unlike the global knockouts the migrating front of the retinal vasculature proceeded normally and neovascularization during OIR occurred at levels similar to wild-type mice. Therefore, our data suggests that Bcl-2 / expression modulates endothelial cell survival impacting postnatal retinal vascular development with minimal impact on retinal neovascularization during OIR.

Experimental Biology, April 26, 2014

IMMUNOTHERAPEUTIC STRATEGIES TO IMPROVE ALLOGENEIC BONE MARROW TRANSPLANT FOR NEUROBLASTOMA

Kyle D. Terry, Sara E. Kelm, Thomas J. Esposito, Brittany L. Bowen, Paul D. Bates and Christian M. Capitini, MD

For children with high risk neuroblastoma, overall survival is still poor. We wanted to determine if the immunocytokine hu14.18-IL2 can improve the graft-versus-tumor effect of allogeneic bone marrow transplant (alloBMT) against neuroblastoma. On day +0, CD45.2+ Balb/c mice were lethally irradiated and transplanted with CD45.1+ B6 bone marrow and increasing doses of T cells. On day+10, mice were challenged with NXS2 tumor. On days+14-16, mice were injected with hu14.18-IL2 and monitored for GVHD and tumor growth. Hu14.18-IL2 can be safely after alloBMT given with T-cells doses up to 103 without developing lethal GVHD. In addition this T cell dose can control NXS2 growth as well as improve survival. These data demonstrate for the first time that hu14.18-IL2 can be used after alloBMT for neuroblastoma.

IMPROVING ACCESS TO AUTISM DIAGNOSTIC EVALUATIONS

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SPECIFIC AIM STATEMENT We will decrease the number of days from date of referral received to the date initial visit appointment is offered from 59.6 to 53.7 (or by 10%) by September 6, 2013

