



# Department of Pediatrics Research Day

ABSTRACTS FOR POSTERS AND PRESENTATIONS

May 8, 2015



## Department of Pediatrics Research Day Agenda

May 8, 2015  
1335 HSLC  
12:30-4:00 PM

12:30 Lunch

1:00 Introduction and Welcome  
Dr. Jim Gern, Vice Chair for Research

1:30 Oral Presentations

***Predictors of ED Use Shortly after Hospital Discharge***

Ryan Coller, MD, MPH

***Public Or Private? Trends in College Students' Privacy Settings on Facebook***

Kerry Gannon-Loew, MD

***Cluster of Pneumococcal Meningitis with Severe Sequela in a Children's Hospital***

Sarah Webber, MD

***Pbx1/2 are Required in the Lung Mesenchyme for Lung and Pulmonary Vascular Development***

David McCulley, MD

***Does a Lack of Oxytocinergic Signaling in the Alveolar Epithelial Cell Contribute To Development of Respiratory Distress in Preterm Infants?***

Indira Bhagat, MD (*presentation will be given by Bikash Pattnaik, PhD*)

***A Zebrafish Model of Cryptococcosis***

J. Muse Davis, MD, PhD

3:00 Poster Reception (with light hors d'oeuvres)  
Residents, Fellows, and Faculty  
HSLC Atrium



# Resident Abstracts

## UNUSUAL CARDIAC FINDINGS IN A NEONATE WITH CONGENITAL DIAPHRAGMATIC HERNIA

*Adam S. Bauer; John S. Hokanson; Jamie J. Limjoco*

A female infant born at 37 2/7 weeks gestational age with prenatally diagnosed left-sided congenital diaphragmatic hernia (CDH) is found shortly after birth to have left ventricular apical dysfunction. Her mother is 23 years old, and the pregnancy was complicated by oligohydramnios, hypothyroidism, and daily tobacco use. A birthing and surgical plan with possible need for extra-corporeal membranous oxygenation had been discussed with the family. The infant was delivered vaginally and successfully intubated in the delivery room. Apgars were 5, 5 and 6 at 1, 5 and 10 minutes respectively. Initial examination findings were remarkable for meosmelic shortening of the left extremity, with left-sided syndactyly of the third and fourth digits and absence of the fifth digit. The patient was transferred to the NICU on mechanical ventilation and umbilical lines were placed. Due to persistent hypercarbia, the patient was transitioned to the oscillator after surfactant administration. Per protocol, an echocardiogram was obtained 2 hours after birth that showed a patent foramen ovale with left to right shunting, large patent ductus arteriosus with right to left shunting, and biventricular dysfunction with systolic apical ballooning of the left ventricle. These findings were replicated on serial echocardiograms within the next couple of hours. While the patient had normal troponins, the decision was made to delay repair of the CDH until a better understanding the cardiac findings was made. The patient remained stable and echocardiogram at 24 hours of life revealed normalized right ventricular function with improvement of left ventricular function. By the second day of life, the echocardiogram normalized with biventricular function appropriate for a term infant. The infant underwent successful repair of her CDH, and by 10 weeks of life the infant was discharged home with the family without oxygen support and tolerating oral feeds.

The heart findings in this infant are consistent with takotsubo cardiomyopathy, also known as broken heart syndrome. Diagnostic criteria include transient hypokinesis of the left ventricle, absence of obstructive coronary disease as noted by angiography, ST or troponin elevation, and absence of myocarditis or pheochromocytoma. While these criteria have been applied in the adult population, neonatal experience is lacking. The mainstay of treatment is supportive. This case report demonstrates the need for echocardiography in the patient with CDH and shows that takotsubo cardiomyopathy, while typically a disease of postmenopausal women, can be found in the neonatal population.

## DEVELOPMENT OF SYNCOPE GUIDELINE FOR PEDIATRIC PATIENTS IN THE EMERGENCY ROOM

*Gena Cooper; Joshua Ross*

**Background:** Up to 35% of pediatric patients experience at least 1 episode of syncope. Benign causes of syncope, such as neurocardiogenic syncope, account for 71% of cases as they present to the Emergency Department (ED). Rare causes of syncope, such as cardiac arrhythmias, account for less than 5% of the etiology for pediatric syncope. However, the fear of missing rare but serious causes of syncope often drive the performance of invasive and costly evaluations on children in the ED. In one recent study ED-based pediatric study, laboratory testing was obtained in 67% of patients, while another study found electrolyte testing was obtained in 90% of patients while a CBC was performed in 80% of encounters. The median cost of diagnostic testing children in the ED was \$1,055 with electrocardiogram testing most common while the range was \$0 to \$10,686 for additional tests such as serum laboratory studies, brain CT, brain MRI, and echocardiograms. General concerns about widespread variation in diagnostic testing and treatment of children in the ED with syncope in addition to rising health care costs have prompted calls to establish appropriate, safe, efficient, and cost-effective guidelines for the management syncope.

**Objective:** To develop a guideline for the diagnostic evaluation and management of pediatric syncope in the ED.

**Design/Methods:** A literature review was performed to evaluate current guideline development and evidence to support guidelines in use. Next, existing guidelines from both published and unpublished sources for evaluation of pediatric syncope in the ED were reviewed. The current guidelines in conjunction with current research were synthesized into a guideline document for use in the UW and AFCH ED. The guideline was reviewed by Dr. Ross and colleagues for accuracy and applicability in our ED.

**Results:** The guidelines were developed through a collaborative process. They have been reviewed for use in the ED, and implementation will begin when appropriate per ED scheduling.

**Conclusions:** Syncope in children is an often benign event for which ED visits contribute to significant health care cost and invasive testing. No national guidelines exist to help support physician decision-making; however, few institutions have begun this process through the development of guidelines for use in their EDs. The guideline presented here reflects the current evidence for best practices related to pediatric syncope evaluation and management. It will be a tool to support physician decision-making in the ED in an effort to reduce invasive procedures and costs as they relate to pediatric syncope encounters. Further quality improvement evaluation of this intervention would be beneficial to better understand its efficacy in our ED.

## TEEN TIME: A NEW PROGRAM TO SUPPORT ADOLESCENT GIRLS

*Kerry Gannon-Loew; Jenny Cappelle*

**Background:** Accidents, homicides and suicides are the leading causes of death in adolescents. In addition, adolescents are more likely to suffer consequences due to risky behaviors, such as STIs, unwanted pregnancy, school suspensions and legal trouble. Adolescents often feel uncomfortable talking to their parents or physicians about health-related topics and do not know where to look for information. Additionally, health classes in school provide variable information on important health topics.

**Objective:** To provide an opportunity for female adolescents to discuss health-related topics with resident physicians in a casual group setting, as well as to assess the effect of the discussions on the knowledge, attitudes and behaviors of female adolescents.

**Design/Methods:** Adolescent females ages 14-18 were recruited from adolescent clinic, local high schools and by word of mouth to participate in a health discussion group. Monthly 90-minute meetings were held at a local public library. Each meeting was dedicated to one of five specific topics (sexual health, alcohol/drugs, social networking/cyberbullying, mental health, and body image/nutrition) and consisted of a combination of lecture, question & answer, and open discussion. Pre- and post-meeting surveys were distributed to the participants to assess knowledge, attitudes and behaviors about these topics, as well as knowledge about available community resources.

**Results:** A total of six adolescent females participated in the group. The small number of overall participants limits our results. However, nearly every participant rated the usefulness of all the meetings between 8-10 (scale 1-10). Overall, on the post-meeting surveys, participants indicated that their knowledge of the topics and of available resources in the community had increased. Additionally, following the meetings on sexual health and social media, multiple participants indicated that they were planning to make changes in their behaviors (e.g. more likely to use condoms, decrease screen time and change privacy settings on social media). Also, multiple participants expressed a willingness to discuss these topics with their physician, but indicated on the pre-meeting survey that their physician had never asked them questions about these issues.

**Conclusion:** Although it can be a challenge to recruit adolescents to participate in such a group, the participants who did attend were open and willing to discuss sensitive, health-related topics in a group setting. Our participants indicated that adolescent females are willing, and in fact, want to discuss potentially risky behaviors with their physicians in the clinic setting. These discussions are likely to be more beneficial if initiated early (middle school age). The adolescents in our group discussed a willingness to make changes in their behaviors after learning about the potential consequences of their behaviors. Adolescent females also benefit from education about available community resources.

## \*\*\* PAS Poster Presentation

### PUBLIC OR PRIVATE? TRENDS IN COLLEGE STUDENTS' PRIVACY SETTINGS ON FACEBOOK

*Kerry Gannon-Loew; Megan Moreno; Mary Lindstrom*

**Background:** Online privacy is an important issue in adolescent health, as self-disclosure of personal information can put adolescents and young adults at risk. Social networking sites (SNS) allow individuals to share information with a large online audience. Through Facebook, the most popular SNS, young adults share personal information and control who can access that information.

**Objective:** The purpose of this study was to explore how young adults utilize Facebook privacy settings and what factors affect their choice of security settings.

**Design/Methods:** IRB approval was obtained from the University of Wisconsin and University of Washington. Interview data and information from the students' Facebook pages were collected after freshman and sophomore years. Data included gender, type of security settings, the presence of blocking and the number of Facebook friends. Security settings were classified as public, friends of friends, friends only and customizable content. The categories of friends only and customizable were considered more restrictive security settings. Data were analyzed using mixed effects models.

**Results:** Data were collected from 315 students; 56% were female. There was a significant increase in the number of Facebook friends over time ( $p=0.0001$ ), but no significant difference between males and females ( $p=0.38$ ). School, gender and number of friends did not significantly affect the type of security setting or the presence of blocking. Over time, the probability of having more restrictive security settings decreased by a nearly significant amount ( $p=0.054$ ). The likelihood of blocking increased when security was set to more restrictive settings ( $p=0.03$ ).

**Conclusions:** The young adults in this study expanded their social network by gaining more Facebook friends over time. Security settings and blocking on Facebook profiles were dynamic, but were not affected by gender or number of friends. In year two, there was a trend towards less restrictive security settings, indicating that college students may become more willing to share personal information with a larger online audience over time. Profile owners with more restrictive security settings were more likely to block, potentially representing a group of young adults with increased knowledge or concern about protecting their personal information. Future studies should further investigate the individual characteristics that affect self-disclosure online.

\*\*\* PAS Poster Presentation

**FREQUENCY AND NATURE OF MEDICAL ERROR LEADING TO DIAGNOSTIC DELAYS IN CHILDREN WITH CANCER**

*Andrea Carberry; Keith Hanson; Ashley Flannery; Megan Fischer; Jonathan Gehlbach; Carol Diamond; Ellen Wald*

**Background:** Cancer is a rare diagnosis in children, yet malignancy is the leading cause of disease-related death in patients aged 5-18 years. Little has been written regarding medical error leading to diagnostic delay in children with malignancies in developed countries.

**Objective:** This study was undertaken to: 1) determine the frequency of medical error leading to diagnostic delays in pediatric patients with cancer; 2) examine contributing demographic and physician factors; and 3) identify possible causes of physician-related delays.

**Design/Methods:** This retrospective study included pediatric oncology cases presenting to our mid-size tertiary care center between 2007 and 2013. Patient demographics, clinical presentation, timing and location of diagnostic work-up, cancer type, and current patient status were reviewed. A medical error leading to a delay in diagnosis was considered to have occurred if there was: (1) lack of appropriate diagnostic evaluation for persistent symptoms; (2) failure to recognize the presence of a herald sign or symptom; or (3) misinterpretation of diagnostic studies.

**Results:** Medical records of 341 patients were reviewed. 265 cases met inclusion criteria. 28% of patients were classified as having medical errors leading to a delay in diagnosis. When compared to cases without errors, cases with errors experienced more visits before diagnosis, were more likely to have been seen in primary care settings, were more likely to have received inappropriate treatment, and were more likely to have misinterpreted labs or imaging. There were no differences in patient demographics or mortality rate between groups. There was no difference in frequency of delays when stratified by tumor type. However, within the hematologic malignancy group, lymphomas were more likely to have a delay compared to leukemia (56% vs. 22%). The majority of delays were caused by lack of appropriate diagnostic evaluation for persistent symptoms (47%), failure to recognize a herald sign or symptom (45%), and misinterpretation of tests (8%).

**Conclusions:** Twenty-eight percent of children with cancer experienced a delay in diagnosis due to physician-related factors. We propose clinicians initiate diagnostic evaluation if a child presents on multiple occasions for the same complaint or with a herald symptom that does not resolve promptly. While our study showed no difference in mortality rate between groups, future research should evaluate the impact of delay on morbidity, financial expenditures related to healthcare, and the emotional health of families.

**CASE REPORT: NEWBORN WITH VESICULAR LESIONS WITH NEGATIVE HSV TESTING FOUND TO HAVE INCONTINENTIA PIGMENTI**

*David Holz; Kristin Eastman; Daniel Sklansky*

**Background:** Incontinentia pigmenti (IP), also known as Bloch–Sulzberger syndrome, is an X-linked dominant neurocutaneous disorder with a characteristic cutaneous presentation that can also have neurologic, ophthalmologic and dental manifestations. IP is an ectodermal dysplasia resulting from a mutation in the inhibitor of nuclear factor (NF) kappa-B kinase subunit gamma/NF-kappa beta essential modulator gene (IKBKG/NEMO gene), which encodes a regulatory protein.

**Case Report:** A 15 day-old female was admitted from outpatient clinic for further evaluation of vesicular lesions concerning for primary herpes simplex virus (HSV) infection. She was born at 41 weeks to a 35 year old G1P1001, O negative/antibody positive, Rubella immune, Hepatitis B negative, Group B Streptococcus positive mother. Patient was discharged home in good health with erythema toxicum rash. At her 2-week well child visit her mother raised concern about a 2-3 day history of vesicular rash that initially developed on her arms and progressed to involve her trunk and legs. Her mother reported that lesions had the appearance of fluid-filled blisters. Skin exam revealed vesicles and crusted papules on erythematous bases in a linear blaschkoid arrangement on the right greater than left lower legs, and the right upper arm. A few vesicles were also noted on the right anterior chest and upper back. The remainder of her exam was unremarkable.

**Hospital Course:** Due to concern for primary HSV infection, the Pediatric Infectious Disease team was consulted. The patient was started on intravenous acyclovir for presumptive primary HSV infection pending studies. The CBC was remarkable for eosinophilia, and the CSF and CMP were unremarkable. PCR samples from all sites were negative for HSV. Further evaluation of the vesicular lesions showed evidence of progressive crusting with distribution of lesions in a blaschkoid distribution concerning for Incontinentia Pigmenti (IP). Dermatology was consulted and agreed that the lesions were suspicious for IP. A single 3.5 mm punch biopsy of one of the lesions was performed on the right thigh, showing eosinophilic spongiosis with necrotic keratinocytes consistent with Incontinentia Pigmenti.

**Discussion:** We report a case of neonatal Incontinentia Pigmenti (IP), a rare X-linked dominant neurocutaneous disorder that can mimic other vesiculopustular skin lesions on initial presentation. This report serves to demonstrate that IP should remain in the differential diagnosis for well-appearing neonates presenting with vesicular lesions. Expedient determination of IP could shorten the duration of empiric treatments and testing, thus saving cost and preventing harm. It is also important for pediatricians to be aware of the need for multidisciplinary evaluation and management of IP involving genetics, dermatology, ophthalmology, neurology, and dentistry teams.



## COVERT *TOXOCARA* INFECTION PRESENTING AS ACUTE RESPIRATORY DISTRESS

Emilie Korn; Sheryl Henderson

*Toxocara canis* and *Toxocara cati* are common parasites present throughout North America. They produce a range of clinical manifestations including asymptomatic, visceral larvae migrans, ocular migrans and covert toxocariasis. The systemic symptoms arise from larvae migrating from the intestinal lumen via hematologic spread into various organs where the larvae transpire. The human immune response to the larvae outside of the GI tract can cause significant eosinophilia and degranulation of the eosinophils cause the systemic symptoms. Covert *Toxocara* infections present as asthma exacerbations and are defined by eosinophilia, wheezing, and pulmonary infiltrates.

Our patient is a previously healthy 25 month-old with no history of wheezing who presented to the ER via ambulance from an outside hospital with persistent fever and respiratory distress. His illness began about 6 weeks prior to presentation with cough, rhinorrhea, intermittent fever, and intermittent wheezing. His fever occurred about every 3 days with max temperatures of 101. The day prior to admission, his fever increased to 103.2 and he developed rhinorrhea, cough, tachypnea and retractions. He was brought to an outside ER where he received additional albuterol nebulizers without improvement, IV ceftriaxone, IV clindamycin and Tylenol and was transferred to our ER via ambulance. Initial blood work was significant for WBC 39.3, hemoglobin 11.8, hematocrit 35.6, platelets 517, eos 45.1%. Additional blood work was significant for hypergammaglobulinemia with IgG 2250, IgM 736, IgE 521, *Toxocara* antibody IgG elevated to 2.54, lead level 9.9. Chest x-ray was significant for mild sporadic opacities. He was diagnosed with covert *Toxocara* infection and treated with albendazole and methylprednisone. His symptoms improved within 24 hours of started medications.

*Toxocariasis* has many different clinical presentations including acute asthma exacerbation or viral induced wheezing, and is a significant cause of morbidity in North America. It has been theorized as a cause of persistent asthma, epilepsy, and poor cognition. As of yet there is no protocol for identifying individuals at risk for significant disease.

## THE IMPORTANCE AND INFLUENCE OF PRE-CLINICAL WILDERNESS MEDICINE EDUCATION

Andrew Lewandowski; Mark Brownson; Benjamin M Ho; Marlowe Eldridge

**Background:** The field of Wilderness Medicine was established to improve scientific and medical knowledge of matters related to wilderness environments and, thus, to lead to better diagnosis and management of patients in austere environments. It is now a rapidly evolving field as a result of research efforts and collaboration by medical professionals, scientists, outdoor experts, and teams of first responders. It is multifaceted, and includes concepts from Disaster Medicine, Global Health, Emergency Medicine, and Primary Care. Despite its multidisciplinary involvement and applicability to patients in both emergency medicine and now primary preventative medicine settings, Wilderness Medicine is not routinely taught or available to pre-clinical medical students.

**Objective:** To assess the benefits of Wilderness Medicine course for medical and physician assistant students.

**Design/Methods:** A Wilderness Medicine elective course, taught by faculty and residents, was established through the University of Wisconsin School of Medicine and Public Health in 2013 to expose medical and physician assistant students to this field. Students were administered a survey to assess the influence of the course on career/specialty choice.

**Results:** Of the respondents, 7.69% replied that the elective “definitely” influenced or changed their specialty or career interests, 38.46% replied “somewhat,” and 53.85% replied “not really.” Enrollment has increased from 47 students in 2013 to 60 students in 2015. Lecture evaluations have shown positive scores.

**Conclusion:** Wilderness Medicine is an important field to which medical professionals should be exposed. This course meets those needs, and has reported impacts on student career choice.

\*\*\* PAS Poster Presentation

**UNIVERSAL VS SELECTIVE PEDIATRIC LIPID SCREENING IN THE DIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLEMIA**

*Hilary Stempel; Ann Dodge; Erin Marriott; Amy Peterson*

**Background:** Familial hypercholesterolemia (FH) is a common autosomal dominant disorder of lipid metabolism characterized by marked LDL cholesterol elevation from birth and premature cardiovascular disease (CVD). Once a proband is identified, cascade screening of family members can identify at-risk family members. Studies demonstrate that limiting pediatric lipid screening to those considered at high CVD risk would fail to detect at least 30% of pediatric dyslipidemias. In 2011, the American Academy of Pediatrics modified their lipid screening guidelines and endorsed universal lipid screening of all children 9-11 and again between 17-21 years old.

**Objective:** To evaluate trends of universal versus selective pediatric lipid screening in identifying patients with FH presenting to a pediatric dyslipidemia clinic.

**Design/Methods:** A retrospective chart review was performed on all patients diagnosed with FH during 2/2011 to 10/2014 from a pediatric dyslipidemia clinic.

**Results:** FH was identified in 39 individuals (56% male), between the ages of 6.1-22.2 years (mean 11.8 years), at clinic presentation. Mean LDL at presentation was 226 mg/dL (range: 160-437 mg/dL). Documented indications for performing initial lipid screen included the following: universal screening (18%), family history of CVD (55%), patient risk factor (17%), and other (10%). Selective screening (family history and patient risk factor) only identified 72% of children with FH. Cascade lipid screening of first degree family members was performed on the 21 patients who were the proband FH diagnosis in their family. Subsequently, 18 family members (from 13 families) received a diagnosis of FH. Statin therapy was prescribed in 31 patients and resulted in an average LDL reduction of 50% from baseline.

**Conclusions:** Universal screening, as recommended per expert guidelines, is becoming a more common method of identifying pediatric patients with FH. Universal screening added an additional 18% children identified to have FH not previously identified with selective screening. Further, 10% of children were diagnosed based on parent request and not by provider-driven selective screening. Family members with FH were identified in 62% of families screened via cascade screening. Children with FH were successfully treated with statin therapy with an average reduction in LDL of 50% from baseline.

\*\*\* PAS Poster Presentation

**PNEUMOCOCCAL MENINGITIS IN THE PCV13 ERA: A CLUSTER OF CASES WITH INCREASED MORBIDITY & MORTALITY**

*Sarah Webber; Gena Cooper; Gregory DeMuri; Ellen Wald*

**Background:** The thirteen-valent pneumococcal conjugate vaccine has reduced overall rates of invasive pneumococcal disease (IPD); however, the effect on incidence of pneumococcal meningitis (PM) is less clear. Our children's hospital has had infrequent admissions of children with pneumococcal meningitis during the past ten years.

**Objective:** To present a cluster of cases of pneumococcal meningitis with unexpectedly high morbidity and mortality.

**Design/Methods:** Patients aged 0-18 years admitted to American Family Children's Hospital from January 2004 until December 2014 with culture proven IPD were identified through a retrospective review of medical records and by direct patient care. IPD was defined as a positive culture for *S. pneumoniae* from any sterile site except cerebrospinal fluid (CSF). Meningitis was defined as a positive culture for *S. pneumoniae* from CSF with the exception of a single patient with a positive blood culture for *S. pneumoniae* who presented with clinical signs of meningitis and brain herniation in whom CSF was not obtained. Organisms were identified using traditional methods and serotyping was performed by a commercial laboratory.

**Results:** A total of 14 cases of PM and 12 cases of non-meningitis IPD during the study period were noted with an average of 0-2 cases of PM each year. Between July 2013 and December 2014, we identified 7 cases of PM in children age 5 months to 6 years. Two children died from their infection. All five surviving cases of PM were complicated by hearing loss and developmental regression. Additionally, two developed seizures, two developed pneumococcal hemolytic uremic syndrome (HUS), two had transient cranial nerve palsy, and one suffered persistent cranial nerve II palsy.

**Conclusions:** We report a cluster of PM in the PCV13 era associated with a high degree of morbidity, especially deafness and HUS, correlating with pneumococcal serotypes not contained in PCV13. This series reflects important deviation from literature-based expected outcomes. All patients in this cluster experienced neurologic sequelae in contrast to rates of 40-63% reported in the recent literature. Mortality in pneumococcal meningitis is expected to be approximately 8-13% of cases in well-resourced healthcare settings; however, the mortality rate in this small series was 29%. Our case series is consistent with recent reports suggesting rates of pneumococcal meningitis may not be decreasing as rapidly as other manifestations of invasive pneumococcal disease following PCV13. The cases may reflect serotype shifting following the thirteen-valent pneumococcal conjugate vaccine with increased propensity to infect the central nervous system.

\*\*\* PAS Poster Presentation

**DEVELOPMENT AND EVALUATION OF A SIMULATION-BASED PEDIATRIC CURRICULUM FOR ECUADORIAN FAMILY MEDICINE RESIDENTS**

*Sarah Webber; Sabrina Butteris; David Gaus; Carlos Troya Altamirano*

**Background:** A new rural residency program at Hospital Hesburgh in Ecuador aims to expand beyond the traditional linear communication methods used in Ecuadorian medical education by providing simulation-based education. Simulation-based education during residency has had variable implementation Ecuador and other resource limited settings. Resultantly, faculty at Hospital Hesburgh have requested assistance in developing simulation-based curricula for use by their Family Medicine residents.

**Objective:** To pilot and evaluate a simulation-based pediatric curriculum in a Family Medicine residency program in rural Ecuador.

**Design/Methods:** With the faculty at Hospital Hesburgh we developed a 2-day curriculum for first year Family Medicine residents on the basics of caring for ill pediatric patients. The course combined didactic sessions, case discussions and deliberate practice through simulation. Specific emphasis was placed on developing a systematic approach to evaluating seriously ill pediatric patients, teamwork and communication. After the course, participants completed an anonymous written evaluation consisting of questions with both Likert scales and space for open-ended comments. Open-ended responses were grouped into large categories.

**Results:** 14 of the 16 participants (88%) completed the evaluation. All participants rated the course as either good (n=10) or excellent (n=4) (with 1=not satisfactory and 4=excellent). The most common recommendations from participants were to provide material prior to the course (n=11) and allocate more time to deliberate practice (n=10). Aspects of the course that were identified as valuable were the simulated cases (n=7), working in a team (n=7) and specific medical content (n=7). All fourteen surveyed stated they would change the way they care for ill infants and children after the course.

**Conclusions:** This simulation-based curriculum was well received and was perceived by participants as effective in teaching Ecuadorian Family Medicine residents about caring for ill pediatric patients. It provided the residents with medical content and concepts of teamwork and closed loop communication. Learners reflected the benefits of learning to participate in medical teams and defining leadership in a team setting despite its divergence from the hierarchical medical education structure with which many were familiar. The participants engaged in self-reflection and peer-to-peer feedback, supporting the applicability of de-briefing in this setting. The successful implementation of simulation based pediatric curriculum demonstrated here may have implications for broader utility in other traditional linear communication education environments.



# Faculty/Fellow Abstracts

**\*\*PAS Poster Presentation**

**DOES A LACK OF OXYTOCINERGIC SIGNALING IN THE ALVEOLAR EPITHELIAL CELL CONTRIBUTE TO DEVELOPMENT OF RESPIRATORY DISTRESS IN PRETERM INFANTS?**

*Indira Bhagat; Bikash Pattnaik; De-Ann Pillers*

**Background:** Oxytocin (OXT), a ubiquitously acting neuropeptide hormone, likely regulates the function of diverse tissues in the body by cell signaling that occurs via the oxytocin receptor (OXTR). Throughout the first two trimesters of gestation, the OXT level is consistently low. As the OXT level increases significantly during the last trimester in preparation for birth, infants born preterm may miss out any potential beneficial effect of OXT on the fetal lung provided OXTR signaling occurs within the human alveolar epithelial cells. We hypothesize that OXTR signaling occurs within the human alveolar epithelial cells, and that the lack of exposure of the alveolar epithelial cells in premature babies (born before the third trimester) to the usual fetal levels of maternal OXT hormone increases the risk of subsequent development of respiratory distress in such preterm infants.

**Objective:** To determine if OXTR signaling occurs within the human alveolar epithelial cell.

**Design/Methods:** The human lung epithelial cell line A549 (American Type Culture Collection, VA) which is commonly used as an in vitro model for type II pulmonary alveolar epithelial cells, that was derived from lung adenocarcinoma tumor explants, was cultured. Immunohistochemistry was used to localize OXTR in the cultured cells by incubation of the cells with primary (anti OXTR mouse mAb), and then secondary antibodies (Goat anti mouse Alexa 488). RT-PCR was done to look for OXTR mRNA expression in the harvested A549 cells.

**Results:** Immunopositive cells showed OXTR localization to the cell membrane. RT-PCR showed OXTR DNA bands of 452 bp in size, consistent with the presence of OXTR mRNA transcripts in the A549 cells.

**Conclusions:** We demonstrated OXTR localization (protein) on the membrane of the human alveolar epithelial cells (A549). OXTR mRNA expression was confirmed using RT-PCR. These results suggest that OXTR signaling occurs within the human alveolar epithelial cells and support our hypothesis that OXT may play a role in the maturation of fetal lung. Further confirmation of our study outcome through Western blot analyses for protein and cellular signaling pathway is planned.

**MEANINGFUL OUTCOMES FOR YOUTH WITH CHRONIC ILLNESSES AND THEIR FAMILIES**

*Eliza Blanchette; Elizabeth Cox*

**Background:** Approximately 15–18% of the pediatric population has a chronic disease. Each chronic disease requires self-management on the part of the child and their parents to improve health and well-being. For many families, optimal self-management is challenging. Understanding parent and child views of the outcomes that matter most to them (meaningful outcomes) informs future development of family-centered interventions to improve pediatric chronic disease self-management. Knowledge of these outcomes will enable providers to effectively engage with these youth and their families to develop positive and sustainable self-management behaviors.

**Objective:** 1. To establish meaningful outcomes for youth with type 1 diabetes or chronic kidney disease and their parents. 2. To assess parent and child perceptions of provider-identified meaningful outcomes for these two chronic diseases.

**Design/Methods:** Using items from the literature and prior work on topics of concern to teens with type 1 diabetes, an open-ended survey was developed. The survey includes open-ended questions inquiring about what is meaningful to youth and families of youth with type 1 diabetes or chronic kidney disease. Likert scale questions (n=4-5) to assess perceived importance of provider-identified meaningful outcomes for these diseases was also included. Surveys will be provided either via mail or online through the UW secure site Qualtrics to patients 12-17 years old with either type 1 diabetes or chronic kidney disease and to a parent or guardian of these youth. Subjects with type 1 diabetes will be recruited through the UW Diabetes Center registry. Subjects with chronic kidney disease will be identified in clinical practice by a member of their primary clinical team or will be identified in clinic. Each participant will be offered \$10 for participation in the form of a gift card.

**Results:** IRB approval has been obtained and surveys will be provided as above. Survey data will be analyzed using open-coding techniques with standard qualitative methods as well as standard descriptive methods or ordinal and interval measures for the Likert scale items.

## RHINOVIRUS A AND C WHEEZING ILLNESS IN INFANCY AND THE DEVELOPMENT OF ASTHMA

*Amaziah Coleman; Kristine Grindle; Tressa Pappas; Fue Vang; Daniel Jackson; Michael Evans; Ronald Gangnon; Robert Lemanske, Jr.; James Gern.*

**Background:** Rhinovirus (RV) wheezing illness in early life is a risk factor for subsequent childhood asthma. Whether the species of rhinovirus causing the wheezing illness differentially affects asthma risk is unknown. We hypothesized that RV-C wheezing would be the best predictor of asthma development.

**Design/Methods:** Children participating in a high-risk birth cohort (Childhood Origins of ASThma) were followed prospectively to determine wheezing illnesses with specific RV species in the first year of life. A total of 259 children were followed at year 6, 238 at year 8, and 217 at year 11. Asthma was defined by physician diagnosis, the use of SABA, daily ICS, step-up therapy and/or oral corticosteroids. Nasal samples were collected during wheezing illnesses and analyzed for respiratory viruses using multiplex PCR, partial sequencing for RV typing.

**Results:** Children who wheezed with RV-C in the first year of life had significantly higher rates of asthma at age 6 [OR 3.5 (1.3, 9.7)], but not at ages 8 [OR 1.8 (0.6, 5.2)] or 11 [OR 2.6 (0.9, 7.3)]. Wheezing with RV-A was not associated with asthma at year 6 [OR 1.3 (0.6, 3.1)], year 8 [OR 2.3 (1.0, 5.4)] or year 11 [OR 1.7 (0.7, 4.1)]. There were no wheezing episodes associated with RV-B infections.

**Conclusions:** This longitudinal analysis suggests that wheezing with RV-C in the first year of life is an indicator of increased risk for the subsequent development of asthma. Additional studies are needed to confirm this observation.

## \*\*PAS Platform Presentation

### PREDICTORS OF ED USE SHORTLY AFTER HOSPITAL DISCHARGE

*Ryan J. Collier; Shannon M. Dean; Paul J. Chung*

**Background:** Factors leading to early ED visits after hospital discharge are not well-known and may be distinct from factors leading to readmissions.

**Objective:** Identify predictors of ED visits within 7 days of hospital discharge and compare them to 30-day readmission predictors.

**Design/Methods:** Administrative data were assembled from all encounters for 0-21 year olds at a children's hospital during 2007-2014. Labor/delivery, neonatal and encounters ending in death, transfer, discharge against medical advice or to hospice were excluded. Outcomes were ED visit within 7 days or all-cause readmission within 30 days of discharge. Bivariate and multivariate logistic regression clustered by patient tested relationships between outcomes and demographic and clinical characteristics. Severity of illness was evaluated by the Pediatric Medical Complexity Algorithm categorizing non-chronic, non-complex chronic, or complex chronic diseases.

**Results:** 15,046 patients had 25,151 discharges followed by 970 ED visits (3.9%) within 7 days. In clustered multivariate logistic regression, lower odds of 7-day ED visits were observed for older children (e.g., OR 0.74 [0.55-0.99] for 6-10 vs <2 year olds), parent non-English preference (OR 0.34 [0.18-0.64]), and PCPs external to the health system (OR 0.79 [0.64-0.98]). Higher odds were observed for public insurance (OR 1.25 [1.00-1.55]), >2 ED visits in the prior year (OR 1.81 [1.35-2.42]), length of stay >8 days (OR 1.41 [1.03-1.24]), and >3 medications at discharge (OR 1.64 [1.10-2.43]). 30-day readmissions, however, showed no relationship with PCP affiliation or number of discharge medications, and showed strong associations with parenteral nutrition dependence (OR 1.95,  $P=0.005$ ) and complex chronic disease (OR 3.38,  $P<0.001$ ).

**Conclusions:** 7-day ED visits and 30-day readmissions appear to have different clinical antecedents, suggesting these outcomes might have different underlying causes. Understanding unique risk factors for early post-discharge ED visits may be useful for care transitions improvement efforts.

## A ZEBRAFISH MODEL OF CRYPTOCOCCOSIS

*J. Muse Davis*

Cryptococcal meningitis is an often fatal disease which rose to prominence with the advent of the HIV epidemic. Currently, nearly one million HIV patients are affected per year, two thirds of whom do not survive [1]. Airborne cryptococcal spores initially establish infection in the lung, but subsequently disseminate to the brain to cause meningitis. The mechanisms by which the fungus establishes infection, survives immune resistance and ultimately disseminates to the brain are not well understood. I have developed a model using larval zebrafish which allows direct, live visualization of host-pathogen interactions from the initial encounter with phagocytes to CNS-specific spread. As seen in other models, spores are readily phagocytosed by macrophages. Those that survive intracellularly rapidly germinate and persist. Over the course of a few days, these escape from inside the host phagocytes and disseminate to the CNS as free yeast in the blood stream. Subsequently they can be seen in the perivascular spaces of the brain. This localization is strikingly similar to that seen in human pathology. With the availability of host and cryptococcal mutant strains and molecular tools, this model promises to become very useful for probing the mechanisms of cryptococcal meningitis.

## \*\*PAS Poster Presentation

### TRENDS IN U.S. HOSPITAL STAYS FOR LISTERIOSIS IN INFANTS

*Bruce Edmonson; Angela Veessenmeyer*

**Background:** *Listeria monocytogenes* infection in infants is exceedingly rare but can cause serious illness and death. Although *Escherichia coli* and group B *Streptococcus* are the most common causes of serious bacterial illness in neonates, young infants with febrile illness are commonly treated empirically for listeriosis. No population-based studies have been performed to determine the incidence of listeriosis in infants in the U.S.

**Objective:** We used a multi-year, U.S. hospital discharge database to: (1) characterize hospital stays of infants with listeriosis; (2) estimate the population incidence of listeriosis in infants; and (3) estimate the absolute number of discharges for listeriosis expected annually in discrete age groups during infancy.

**Design/Methods:** This study was a retrospective analysis using 6 sample years of the Kids' Inpatient Database from 1997-2012. Discharges with a principal or secondary diagnosis code for listeriosis (027.0) were analyzed according to infant age group (0-6 days, 7-28 days, 29-89 days, and 90+ days) and to whether additional diagnosis codes indicated bacteremia, meningitis, or both. We estimated population incidence by excluding from the numerator discharges associated with a transfer out to a different hospital.

**Results:** During the 6 study years, there was a cumulative total of 344 (95% Confidence Interval [CI]: 290-397) hospital discharges for listeriosis in infants. The mean annual incidence of listeriosis (per 100,000 births) was 0.53 (95% CI: 0.37-0.68) in the 0-6 day age group and 0.49 (95% CI: 0.29-0.69) in the 7-28 day group. In contrast, the incidence dropped to 0.07 (95% CI: 0.02-0.12) and 0.06 (95% CI: 0.07-0.11) in infants 29-89 days and 90+ days old, respectively. Notably, over 90% of discharges for listeriosis in infants 7 days or older were also coded for meningitis as compared with only 24% of discharges in infants younger than 7 days. The expected absolute number of discharges for listeriosis without meningitis is < 2 per year in U.S. infants 7-28 days of age. This decreases to < 1 after the first month of life.

**Conclusions:** *L. monocytogenes* is an exceedingly rare cause of serious bacterial illness in infants, particularly in infants over a week of age who have no evidence of meningitis. Therefore, the practice of prescribing ampicillin for the empiric treatment of presumed listeriosis in febrile infants without evidence of meningitis should be reconsidered.



## RHINOVIRUS SPECIES AND ASTHMA EXACERBATIONS IN INNER-CITY CHILDREN

*Ann Esquivel*

**Background:** In case-control studies of acute asthma, infections with rhinovirus-C (RV-C) and less so RV-A can cause acute wheezing, while RV-B is seldom associated with exacerbation. We conducted an outpatient cohort study of inner-city asthmatic youth with recent exacerbation requiring parenteral steroids or hospitalization, and hypothesized that RV-C would be the RV strain most strongly associated with exacerbations.

**Design/Methods:** The Preventative Omalizumab or Step-up Therapy for Severe Fall Exacerbations (PROSE) study included 513 asthmatic children, ages 6-17 years, from low income census tracts in 8 cities for a randomized trial of guidelines-based asthma care vs. add-on fluticasone boost vs. add-on omalizumab. Nasal mucus samples were collected weekly over a 4-month period during the fall seasons of 2012 or 2013. Viral exacerbations were defined as virus detection via PCR within 7 days on either side of an acute exacerbation. RV-positive samples were then sequenced to determine species.

**Results:** 6,096 samples were analyzed. Viruses were detected in 66.7% of the 150 samples obtained during 86 exacerbations compared to 38.0% of the 5,946 other samples (OR=3.27,  $p<0.001$ ). RVs were detected in 85/150=56.7% of exacerbation samples and 2,140/5,946=36.0% of non-exacerbation samples (OR=2.33,  $p<0.001$ ). RV-C was most likely associated with exacerbation (OR=2.15,  $p<0.001$ ), followed by RV-A (OR=1.84,  $p=0.003$ ). RV-B was not significantly associated with exacerbation (OR=1.28,  $p=0.35$ ).

**Conclusions:** RV species influenced the risk for asthma exacerbation in this outpatient study; RV-C and RV-A were most strongly associated with exacerbations. Frequent RV detection in non-exacerbation samples suggests that there are additional factors that contribute to the risk of virus-induced exacerbations.

## PATIENT-DERIVED IPS-RPE AS A SUITABLE MODEL OF LCA16

*Dalton Hermans; Nathaniel York; Pawan Shahi; DeAnn Pillers; David Gamm; Bikash Pattnaik*

**ABSTRACT:** Leber Congenital Amaurosis (LCA) is an autosomal recessive genetic disorder which causes severe vision impairments including blindness, photophobia, and nystagmus. It is caused by mutations to genes in the retina and retinal pigment epithelium (RPE). In order to model a particular patient's LCA-causing mutation, we use human-induced pluripotent stem cells (hiPSCs) derived from the patient that are then differentiated into RPE cells. Here, we demonstrate the proper characterization of these cells through molecular marker expression, genomic sequencing, western blot analysis, immunocytochemistry, and electrophysiological traits.

## RADIATION REDUCTION CAPABILITIES OF A NEXT-GENERATION PEDIATRIC IMAGING PLATFORM

Luke Lamers; Martine Moran; Jenna Torgeson; John Hokanson

**Background:** Cardiac catheterization plays a vital role in the clinical management of patients with congenital heart disease (CHD). Any technology shown to improve image quality at lower x-ray dose is beneficial to CHD patients and staff performing the procedures. Recent years have seen concerted efforts to reduce the interventional radiation exposure through technological process. In this regard, systems have moved from image intensifiers to flat panel detectors (FD) with increased acquired image bit depth, as well as employing crystalline silicone instead of amorphous silicon. In addition, novel x-ray tubes have been introduced that changed from classic coil filaments for photon generation to flat emitters. A novel next-generation pediatric imaging platform now available for commercial use implements the above technologies and is proposed to significantly decrease radiation exposure. The extent of radiation reduction is yet to be studied in pediatric CHD patients.

**Objectives:** 1. Document the degree of x-ray dose reduction for a single interventional procedure, patent ductus arteriosus (PDA) occlusion, occurring with transition from a standard catheterization lab imaging system to a next-generation system with pediatric specific settings. 2. Compare radiation dose data from the next-generation system to currently published benchmarks [1,2] for PDA occlusion.

**Design/Methods:** Retrospective case review of patient radiation exposure data for all consecutive patients < 20 Kg who underwent PDA closure at the University of Wisconsin between 1/1/2013 and 1/10/2014. All procedures were performed by a single cardiologist (LL) with no variation in procedural technique. Procedures from 1/1/13-12/31/13 were performed in the adult catheterization laboratory with a bi-plane imaging system (ALLURA FD 10/10, Philips Medical Systems, Best, Netherlands) with standard settings (Group 1). Procedures from 1/1/14-1/10/14 were performed in a dedicated pediatric laboratory on a bi-plane imaging system (Q.zen, Siemens Healthcare, Forchheim, Germany) optimized for pediatric patients (Group 2). Parameters of exposure studied include the following: 1. Total Fluoroscopy time (AP and lateral imaging combined) 2. Number of AP and lateral cine-angiograms performed 3. Cumulative Air Kerma (milligray; mGy) 4. Dose-area product (DAP;  $\mu\text{Gym}^2$ )

System settings and imaging techniques varied considerably in the two laboratories and are summarized in Table 1. For Group 1 the FDs were positioned to minimize the source to detector distance. Magnification and collimation was utilized to window the thorax. For Group 2 the Air Gap technique was utilized (Anti-scatter grid removed; largest field of view selected at FD, source to image distance is maximum to achieve desired magnification). The FDs utilized are mid-size detectors measuring 29 x 26 cm. Magnification was uniformly set at 26 cm and due to the air gap shutters and collimation was utilized extensively to window the thorax. Additional

information recorded included patient's age and weight, minimal PDA dimension and type of occlusion device.

**Results:** Demographic data are summarized in Table 2. PDA minimal angiographic diameters and ranges were similar: Group 1 – mean PDA diameter 2.2 mm with a range of 1-4.5 mm, Group 2 – mean PDA diameter 2.9 mm with a range of 1.2-6 mm (p-value 0.2). Closure devices for Group 1 included: 5/4 Amplatzer duct occlude (ADO) (n=7), 6/4 ADO (n=1), 6 mm Amplatzer Vascular plug II (n=2) and Gianturco coil 38-5-3 (n=1). Closure devices for Group 2 included: 5/4 ADO (n=4), 6/4 ADO (n=2), 8/6 ADO (n=2), 10/8 ADO (n=1) and MReye coil 38-4-3 coil (n=1).

Fluoroscopy times, patient cumulative air Kerma and DAP are presented in Table 2 and graphically represented. The number of angiograms performed for Group 1 patients approached statistical significance (p value=0.06) when compared to Group 2. Results of ANCOVA, where the dose outcome measures (Kerma and DAP) were log-transformed are shown in Table 3. The adjusted analysis confirms that dose outcome measures are significantly lower for Group 2 patients (p=0.0001).

Table 4 compares dose data for Group 2 patients to recently published benchmarks [1,2]. Glatz et al [2] data reflects Air Gap technique with removal of anti-scatter grid during PDA closure for all patients < 12.5 kg. Ghelani et al [1] describes pooled data for ninety six PDA closures from seven congenital catheterization laboratories for patients < 1 year of age. Group 2 procedural dose exposure data for air Kerma is 50-75% and DAP 30-60% less than the documented benchmarks.

**Conclusions:** Decreasing patient and operator radiation exposure during congenital cardiac catheterizations should be a goal for all pediatric interventionists. This is the first data characterizing the dose reduction capabilities of a next-generation imaging system in clinical practice. When paired with removal of the anti-scatter grids and air gap technique we documented dose savings of greater than 50% when compared to standard imaging systems and published benchmarks.

The true benefit of this dose reduction capability is most applicable to patients with complex CHD exposed to significant cumulative radiation during repeat prolonged procedures.

**\*\*PAS Platform Presentation**

**PBX1/2 ARE REQUIRED IN THE LUNG MESENCHYME FOR LUNG AND PULMONARY VASCULAR DEVELOPMENT**

David J. McCulley; Mark D. Weinhold; Elizabeth A. Hines; Licia Selleri; Xin Sun

**Background:** Congenital diaphragmatic hernia (CDH) affects 1 in 3000 live births and is associated with among the highest mortality rates (20-40%) of all developmental anomalies. In addition to the diaphragm defect, patients with CDH have a significant risk of mortality due to abnormal lung and pulmonary vascular development. Previously it was believed that defects in the lung and pulmonary vasculature result from inadequate space in the thorax caused by the diaphragmatic hernia. Clinical data and early research suggest that the lung and pulmonary vascular abnormalities can arise independently from the diaphragm defect. The etiology of CDH remains poorly understood and the relationship between the diaphragm defect and abnormal development of the lungs and pulmonary vasculature is unclear. Although several chromosome abnormalities have been reported in patients with CDH, only a few individual gene mutations have been found. Recently, it was shown that global inactivation of a homeobox-containing transcription factor, *Pre-B-Cell leukemia factor 1 (Pbx1)*, results in CDH in mice, however the role of Pbx1 in the developing lung and pulmonary vasculature has not been explored.

**Objective:** To study the role of *Pbx1/2* in the developing lung mesenchyme and pulmonary vasculature focusing on mechanisms that affect lung hypoplasia and pulmonary hypertension.

**Design/Methods:** Using a conditional knockout approach in a mouse model, we inactivated the expression of *Pbx1/2* in the developing lung mesenchyme. We characterized the lung and pulmonary vascular defects of *Pbx1/2* mutant mice at embryonic and early postnatal stages. We also analyzed the expression of genes important for alveologenesis, vascular development, and regulation of vascular tone.

**Results:** Loss of PBX1/2 in the developing lung mesenchyme results in mice that have abnormal postnatal lung and pulmonary vascular development. PBX1/2 mutant mice die within the first 28 days of life and have simplified lung and pulmonary vascular architecture with severe pulmonary hypertension. Loss of PBX1/2 also results in changes in gene expression causing impaired pulmonary vascular development and abnormal regulation of vascular tone.

**Conclusions:** PBX1/2 is required for normal lung and pulmonary vascular development. Loss of PBX1/2 results in primary lung and pulmonary vascular defects including lung hypoplasia and pulmonary hypertension similar to that seen in human patients with CDH.

**\*\*PAS Poster Presentation**

**VALIDATION OF FILTER PAPER HBA1C MEASUREMENT FOR SCREENING APPLICATION IN NEWBORNS**

Allison Pollock; Gregory Kopish; David Allen; Michael MacDonald; Mei Baker

**Background:** Degree of glycosylation of hemoglobin at birth may reflect intrauterine exposures that predict risk for future metabolic disease including type 2 diabetes. Normal ranges of HemoglobinA1c (HbA1c), which measures glycosylation of hemoglobin A, are available for older children and adults, but have not been established in neonates. Validation of HbA1c measurement on dried blood spots (DBS) is needed before potential application to statewide newborn screening population studies.

**Objective:** Establish a reliable method to measure HbA1c on dried newborn screening (NBS) specimens.

**Design/Methods:** The ion-exchange HPLC Tosoh G7 HbA1c assay was selected for its demonstrated lack of interference from elevated HbF found in newborn samples. Control DBS were prepared using de-identified residual blood from the University of Wisconsin Hospital and Clinic Laboratory of Chemistry. Multiple assay trial runs were conducted to examine 1) stability of HbA1c in DBS; 2) optimal elution time; and 3) stability of eluted HbA1c.

**Results: Stability of HbA1c in DBS:** During the interval of 3, 4, 5 and 6 days of DBS, there was substantial but consistent overestimation of the true A1c values (bias and 95% CI for each respectively 0.83 (0.78-0.89), 0.87 (0.81-0.92), 0.83 (0.66-0.99), 0.87 (0.81-0.92)).

**Optimal elution time:** 60 minutes of elution produced the satisfactory results on 1 day old DBS with a "within assay" standard deviation of 0.058 and an average bias of 0.02%. **Stability of eluted HbA1c:** The bias and reproducibility of the HbA1c assay results did not vary significantly between days 0, 1 and 2 after DBS elution (bias -0.06, 0.07, 0.03, % total variability 34.29, 35.34, 30.36 respectively) using 1 day old DBS with 60 minutes elution.

**Conclusions:** Bias and reproducibility of DBS HbA1c assessment using Tosoh BioScience G7 HPLC assay is optimized by utilization of DBS < 3 days post-sample application and elution time > 60 minutes. Eluted HbA1c value are not significantly affected by stored at 40C up to 2 days after elution. These results show that obtaining reliable results from large population DBS using this HbA1c assay may be feasible.

## \*\*PAS Poster Presentation

### SEVERE AND PERSISTENT THYROID DYSFUNCTION ASSOCIATED WITH TETRACYCLINE ANTIBIOTICS

Allison Pollock; Tasa Seibert; David Allen

**Background:** Tetracycline antibiotics, including minocycline and doxycycline, are commonly prescribed to adolescents to treat acne vulgaris. Concentration of minocycline in thyroid tissue is suggested by incidental findings of black pigmentation in adult autopsies. The thyroid dysfunction related to minocycline described in 2 pediatric case reports was transient and/or associated with autoimmune thyroiditis.

**OBJECTIVE:** This study reports a series from one institution of pediatric cases of non-immune thyroid dysfunction associated with tetracycline class antibiotics.

**Design/Methods:** Cases were selected for this series from patients seen by Pediatric Endocrinology providers at the University of Wisconsin since January 2000. Inclusion: Age < 18 yrs with both a tetracycline prescription and abnormal TSH result in the electronic medical record. Exclusion: autoimmune thyroid dysfunction, congenital thyroid disease.

**Results:** 4 patients met criteria; 1 was removed due to potentially confounding valproate therapy. The remaining 3 patients are summarized in the Figure. All patients had acne and presented at age 16 with hyperthyroidism, negative anti-thyroid antibodies, low uptake on radioiodine thyroid uptake scan.

Case	Age (yrs) at presentation	Sex	Tetracycline class medication, dose (Total mg/day)	Minimum TSH (reference range in uIU/ml)	Maximum free T3 (reference range in pg/ml)	Antibodies TPO, T3I, T4I, * Thyroglobulin	Radioiodine thyroid scan and uptake (reference range 10-30%)	Methimazole + propranolol treatment	Subsequent persistent hypothyroidism
1	16.0	Female	minocycline 200mg <sup>†</sup> doxycycline 150mg	0.009 (0.5-5.5)	3.7 (2.44-5)	negative	2.9%	no	no
2	16.5	Male	minocycline 200mg	<0.03 (0.364-0.7)	23.9 (0.04-6)	negative	0.30%	yes	no
3	16.2	Male	minocycline 200mg	<0.01 (0.364-2)	15.9 (0.34-6)	negative	0.5%	yes	yes

\* TPO = Thyroid peroxidase antibody, T3I = Thyroid stimulating immunoglobulin, T4I = Thyroid stimulating hormone receptor antibody. † Patient switched from minocycline to doxycycline 2 months prior to presentation.

2 patients had severe hyperthyroidism and required short-term treatment with methimazole and propranolol. 1 patient subsequently developed persistent hypothyroidism, with elevation in TSH after discontinuation of minocycline (maximum TSH level of 19.3mIU/ml).

**Conclusions:** Tetracycline antibiotic induced thyroid dysfunction may be more common, serious, and persistent than previously realized. Minocycline and doxycycline can cause a non-immune chemical thyroiditis leading to severe hyperthyroidism which, following removal of offending antibiotics, may evolve into persistent hypothyroidism. Minocycline and doxycycline should be considered as possible etiologies in pediatric cases of non-autoimmune thyroid dysfunction. Prospective study of children on tetracycline antibiotics could determine the utility of screening thyroid function in these patients.

### TRKB SIGNALING AND HYPOTHERMIC NEUROPROTECTION AFTER NEONATAL HYPOXIC ISCHEMIC ENCEPHALOPATHY

Yashica Seymour; Ulas Cikla; Stephanie Marquez; Eshwar Udho; Douglas Kintner; Vishal Chanana; Peter Ferrazzano; Pelin Cengiz

**Background:** Cerebral ischemia resulting from hypoxic ischemic encephalopathy (HIE) affects over 20,000 neonates every year in the US. Interestingly, female neonates are more resistant to the effects of HIE than males, a phenomenon that is poorly understood. The neurotrophin receptor, tyrosine kinase B (TrkB), plays an important role in neuroprotection and improving the long-term functional recovery following HIE by increasing neuronal survival. Therapeutic hypothermia is now considered the standard of care for neonates with HIE. However, the effects of hypothermia on TrkB phosphorylation are unknown. This fact would make it difficult for 7,8-DHF therapy to be translated to the term human neonates who get treated with hypothermia. In addition, experimental data suggests that hypothermic male neonates have better neuroprotection compared to females post-HIE.

**Objective:** To establish the hypothermia model in neonatal mice post-HIE and ask the questions; 1) whether there are sex differences in early neurological damage at different temperatures 2) whether hypothermia induces hippocampal TrkB phosphorylation or not.

**Design/Methods:** After isoflurane anesthesia, P9 mice underwent Vannucci's neonatal HIE model by electro-cauterizing left common carotid artery and exposing the mice to hypoxia (10% oxygen) for 50 minutes. Following hypoxic/ischemic insult, mice were stratified to seven different target temperatures ranging from 31.0C to 38.0C by 1.0C increments for five hours. To monitor core temperatures, rectal temperature of a sentinel mouse was measured. After five hours the animals were returned to dams. Three days after HI, animals were sacrificed and the brains harvested for immunostaining for MAP2 (for neurological injury scoring) and p-TrkB with tyramine amplification. To semi-quantitate p-TrkB staining, whole brain images were imported into Image J software. The mean pixel values for the CL and IL region of interests were subtracted from Background pixel values and expressed as the IL/CL ratio from 3 hippocampal slices per mice.

**Results:** Our results show that average MAP2 neurological injury scores increase in both male and female neonate brains as the temperature increases [from  $8 \pm 2$  (31-32.0C) up to  $25 \pm 2$  (37-38.0C)]. Male brains seem to be more susceptible to hyperthermia as indicated by the MAP2 neurological injury scores. Interestingly, there is a higher % change in IL/CL hippocampal p-TrkB ratio in hypothermic male mice (32-33.0C) compared to female mice at 3 days post-HIE ( $30 \pm 5$  versus  $18 \pm 4$ ).

**Conclusions:** Once completed, these studies will help us determine the role of hypothermia in p-TrkB mediated neuroprotection in both sexes after HIE related brain injury.

## MESENCHYMAL STEM CELL-EDUCATED MACROPHAGES ROLE IN GVHD AND RADIATION INJURY PROTECTION

*Lauren Reil; Myriam Bouchlaka; Mike Martinez; Peiman Hematti; Christian Capitini*

**Abstract:** Total body irradiation is typically used to condition patients for allogeneic hematopoietic stem cell transplant, leading to release of inflammatory cytokines from damaged tissues. After transplant, many patients develop graft-versus-host disease (GVHD) resulting from donor T cells attacking host tissues leading to further inflammation. Mesenchymal stem cells (MSCs) have immunosuppressive and tissue repair properties, but clinical trials using MSCs to treat GVHD have shown mixed results. Macrophages (MQs) are important regulators of immunity and can promote tissue remodeling. We have previously shown that MSCs can educate MQs toward a unique anti-inflammatory phenotype, however the implications for in vivo models of inflammation have not been studied. Using flow cytometry, we found that in comparison to MQs, mesenchymal stem cell-educated macrophages (MEMs) have increased expression of the inhibitory molecules PD-L1 ( $p=0.039$ ), PD-L2 ( $p=0.0002$ ), and markers of alternatively activated macrophages: CD206 ( $p=0.04$ ) and CD163 ( $p=0.0004$ ). MEMs also show increased expression of TGF- $\beta$  ( $p<0.0001$ ), Arginase-1 ( $p<0.0001$ ) and IL-6 ( $p=0.0006$ ), and decreased expression of IL-12 ( $p=0.004$ ) and TNF- $\alpha$  ( $p<0.0001$ ) by RT-PCR. In two xenogeneic mouse models, we show that MEMs significantly enhance survival from lethal GVHD ( $p=0.028$  vs MSC) and from lethal radiation ( $p=0.0044$  vs MSC). MEMs could be a novel cellular therapy for the management of GVHD and protection from radiation-induced injury.

## READ-THROUGH OF LCA16 (KCNJ13) NONSENSE MUTATIONS W53X AND R166X BY RTC-14

*Pawan Shahi; Vladime Bakhutashvili; Simran Brar; Katherine Umhoefer; Richard Gatti; De-Ann Pillers; Bikash Pattnaik*

**Background:** The inwardly-rectifying potassium channel Kir7.1 is present in the apical processes of retinal pigment epithelial (RPE) cells. Several mutations in the gene that encodes Kir7.1 (KCNJ13) cause blindness in the allelic disorders of Snowflake Vitreoretinal Degeneration (SVD) and Lebers Congenital Amaurosis (LCA16). In this study, we treated two Kir7.1 nonsense mutations that result in LCA16 (W53X and R166X) with the read-through compounds Ataluren (PTC-124; AdooQ Biosciences) and a novel small molecule, RTC-14.

**Design/Methods:** Chinese Hamster Ovary (CHO-K1) cells were transfected with N-terminal GFP-fused W53X and R166X mutant plasmids. The cells were then treated with two different concentrations, 5  $\mu$ M and 10  $\mu$ M, of the read-through compounds PTC-124 or RTC-14 after eight hours of transfection, and the cells were incubated with these drugs for 36 hours. Whole-cell patch clamp electrophysiology was performed on the transfected cells. Function of the Kir7.1 channel was measured in the presence of Cs<sup>+</sup> to block function, or the highly permeant Rb<sup>+</sup> to enhance current. The students T-test was used and significance was determined at the  $P<0.05$  level.

**Results:** Both W53X and R166X transfection resulted in non-measurable Kir7.1 current as compared to the wild-type Kir7.1 channel, and the cells were depolarized. Upon treatment of cells with PTC-124 we detected no measurable difference in either the current amplitude or the resting membrane potential ( $V_m$ ). In contrast, RTC-14 showed partial rescue of both the current amplitude and  $V_m$ . R166X expressing cells responded to RTC-14 treatment by a 15 mV hyperpolarizing shift in  $V_m$  ( $-25.92 \pm 2.7$  to  $-40.16 \pm 4.05$  mV;  $P<0.02$ ) and an increase in current amplitude measured at -150 mV from  $-98.5 \pm 24.7$  to  $-122.8 \pm 28.15$  pA,  $P = 0.52$ . W53X, however, showed a 33 mV hyperpolarization shift in  $V_m$  ( $-29.37 \pm 3.55$  to  $-61.94 \pm 2.9$  mV;  $P<0.001$ ). We also noticed a four-fold augmentation in both inward ( $-80.4 \pm 11.2$  to  $-316.16 \pm 60.8$  pA at -150 mV;  $P<0.01$ ) and outward ( $-7.4 \pm 2.4$  to  $33.3 \pm 11$  pA at -40 mV;  $<0.02$ ) current amplitude.

**Conclusions:** RTC-14 is effective in the abrogation of both  $V_m$  and current amplitude in the LCA16 nonsense mutations W53X and R166X. W53X was more amenable to read-through by RTC14 as compared to R166X. Our studies clearly demonstrate the potential of the small-molecule RTC-14 as a therapeutic agent for treating LCA16 due to Kir7.1 channel nonsense mutations.

**\*\*PAS Poster Presentation**

**TRENDS IN US HOSPITAL DISCHARGES FOR RETROPHARYNGEAL ABSCESS IN CHILDREN**

*Daniel Sklansky; Tony Kille; Bruce Edmonson*

**Background:** Single institution studies indicate that hospitalizations for retropharyngeal abscess (RPA) in children have been increasing over the past ten years.

**Objective:** To describe national trends in the hospitalization of children diagnosed with RPA.

**Design/Methods:** We used information from all 6 samples spanning the period from 1997 to 2012 in the Kids' Inpatient Database to generate national estimates for hospital discharges of patients aged 0-18 years for whom a principal or secondary diagnosis code indicated RPA. For this study, we defined RPA to also include coding for parapharyngeal abscess. Discharges for peritonsillar abscess (PTA) were also identified and served as a comparison group. Population rates for RPA and PTA were estimated using census denominators for each sample year.

**Results:** In 2012 there were an estimated 3401 (95% CI: 2974-3828) discharges with RPA. Most discharged patients were male (61%, 95% CI: 58%-62%), 46% (95% CI: 44%-48%) were aged 1-4 years, and 70% (95% CI: 66%-74%) were seen in an emergency department. There were no patient deaths and 83% (95% CI: 79%-86%) of discharges were from an urban teaching hospital. From 1997 to 2012, annual discharge rates for RPA more than doubled from 2.0 (95% CI: 1.8-2.3) to 4.4 (95% CI: 3.8-4.9) per 100,000 population. During the same period, discharge rates for PTA fluctuated within the range of 6.9 to 8.4 without any trend. RPA accounted for an increasing proportion of total discharges for RPA and PTA, increasing stepwise from 21% in 1997 to 41% in 2012 ( $p < 0.001$  for trend). Over the same period, there were stepwise declines in the proportion of RPA discharges associated with a procedure code for surgical drainage (52% to 44%) and in length of stay (5.2 days to 3.7 days) ( $p < 0.001$  for each trend).

**Conclusions:** U.S. hospital discharges for RPA in children have increased rapidly. Possible explanations include changes in the true incidence of RPA, the threshold for hospitalization, imaging practices, and diagnostic criteria. The decreasing use of drainage procedures and shorter lengths of stay suggest an evolution in medical practice and/or in the characteristics of children admitted.

**\*\*PAS Poster Presentation**

**TYPE 1 DIABETES MELLITUS IN A PATIENT WITH KNOWN MCADD**

*Robert Strait; Ellen Connor; Gregory Rice*

**Background:** Striving to maintain blood glucose in the normal range in type 1 diabetes can lead to brief periods of hypoglycemia, which are well tolerated by most patients. A child who also has medium chain acyl dehydrogenase deficiency (MCADD), however, is at higher risk of neurologic damage from hypoglycemia because of the inability to produce ketones as a secondary source of energy. Lack of ketoacidosis despite significant insulin deficiency also alters the clinical presentation of new-onset type 1 diabetes with MCADD.

To report a child with known MCADD who developed hyperosmolar dehydration without ketoacidosis as the presentation of type 1 diabetes, and to describe modification of post-diagnosis blood glucose parameters to minimize the occurrence of non-ketotic hypoglycemia.

**Case Report:** A 4 year old girl with MCADD presented with polyuria, polydipsia, vomiting and dehydration. Abdominal pain and mental status changes were absent. Labs: glucose 1373 mg/dL, bicarbonate 23 mmol/L, anion gap 19 mmol/L, sodium 120 mmol/L, HbA1c 11.1%, serum osmolality 295 mOsm/kg, small urine ketones. Zinc transporter, IA-2, and GAD antibodies were positive. EKG and telemetry showed no arrhythmia. Ketones and anion gap were not useful parameters to monitor, so osmolality, electrolytes and blood glucose were followed.

Management after discharge included a treatment threshold of 100 mg/dL for hypoglycemia, a limit of 8 hours fasting when well, and a sick-day plan of admission for IV 10% dextrose if not tolerating at least 15 kcal/kg every 4 hours orally.

Diagnosis of type 1 diabetes, assessment of illness severity, and sick-day care are all complicated by the absence of ketosis in MCADD. Absence of DKA should not distract from the diagnosis, and subsequent treatment is modified from the standard approach to further minimize the risk for hypoketotic hypoglycemia. Presence of even trace ketones indicates severe insulin deficiency and catabolism. Glucagon is effective for incidental hypoglycemia, but accumulation of fatty acids in the liver and deficiencies in gluconeogenesis in MCADD make oral or IV glucose necessary when glycogen is depleted by prolonged illness. Elevated free fatty acids are arrhythmogenic and can produce cardiomyopathy, so telemetry is recommended during severe illness.

**\*\*PAS Poster Presentation**

**NATIONAL TRENDS IN HOSPITAL DISCHARGE RATES FOR LOWER RESPIRATORY TRACT INFECTION IN NATIVE AMERICAN CHILDREN**

*Bethany Weinert; Bruce Edmonson*

**Background:** Children enrolled in the Indian Health Service (IHS) are known to have higher rates of hospitalization for lower respiratory tract infection (LRTI) than other children in the U.S. Many Native American (NA) children receive some or all of their medical care outside the IHS, and there is little information available about LRTI hospitalization rates in NA children in the general population.

**Objective:** To describe and compare rates of LRTI discharges from non-Federal hospitals in NA and white children.

**Design/Methods:** We used Kid's Inpatient Database samples from 1997 to 2012 to identify discharges in children ages <5 years who had a principal or secondary diagnosis code for LRTI. To address systematic underreporting and misclassification of race/ethnicity in administrative databases, we estimated population rates by using hospital births to derive race-specific denominators.

**Results:** Among children with a hospital discharge diagnosis of LRTI in 2012, Native American children were more likely than white children to be covered by Medicaid insurance (76% vs. 49%) and to live in a western state (55% vs. 17%), in a rural county (52% vs. 28%), or in a zip code area with mean household income in the lowest quartile (52% vs. 30%) with  $P<0.001$  for each comparison. LRTI rates in 2012 were higher for NA children (22.5/1000, 95% CI: 17.5/1000-27.6/1000) than for white children (11.0, 95% CI: 10.2-11.8). For NA infants, rates were particularly high in western states (72.8, 95% CI: 45.8-99.8) and these rates were much higher than for white infants (22.2, 95% CI: 18.1-26.4). From 1997 to 2012, national rates declined for white children (from 14.8 to 10.9,  $p<0.001$  for trend) but not for NA children (19.7 to 22.5,  $p=0.45$ ).

**Conclusions:** Based on information in hospital discharge databases that exclude IHS hospitals, hospital discharges for LRTI occur in Native American children nationally at rates that are high and comparable to rates reported for children enrolled in the IHS. Further, while LRTI hospitalization rates have been declining for other ethnic groups, this has not occurred for Native American children.

**OUTCOMES THAT MATTER TO TEENS WITH TYPE 1 DIABETES**

*Clara Yanglei Ye; Thor Jeppson; JM Schopp; Ellen Kleinmaus; Elizabeth Cox*

**Background:** The teenage years are a critical period in which teens with type 1 diabetes take on more disease management responsibilities in preparation for adulthood. Diabetes control is often sub-optimal for teenagers. Understanding the outcomes that matter to teens could support successful interventions to improve diabetes care. This study examined outcomes that mattered to teens with diabetes who posted on two public forums for type 1 diabetes.

**Objective:** To gain an understanding about the outcomes that matter to teens with type 1 diabetes using posts from online communities.

**Design/Methods:** 72 publicly-available posts from 2011-2013 were randomly selected from the "teen" sections of two major diabetes online forums. Twenty-two posts were eliminated from the initial sample due to 1) although posted in the "teen" section, the poster was not 13-17 years of age ( $n=13$ ) or 2) lack of relevant content ( $n=9$ ). From each selected post, the content and descriptive data (e.g., duration of diabetes and age) were collected. Standard open coding techniques were used to analyze content and identify outcomes found in the posts. An outcome was defined as impacts or consequences as a result of type 1 diabetes. Researchers independently examined and recorded their interpretation of each post and then met to discuss the coding. A codebook was jointly developed to facilitate the identification of meaningful outcomes from the posts.

**Results:** 50 posts written by 36 unique teens were examined for outcomes. The average age of teens was 15.7 years old (16 specified their age). From the 18 teens who specified how long they have had type 1 diabetes, the average duration was 6.3 years, with a median of 5 years. The three most common outcomes mentioned in forum posts were 1) control of blood glucose, 2) emotional wellbeing, and 3) positive interactions with peers. Other outcomes mentioned included 4) physical wellbeing, 5) family interactions, 6) education and motivation of others, 7) interactions with others such as school personnel and 8) academics.

**Conclusions:** Results suggest that teens who post within online diabetes forums convey many outcomes that matter beyond the control of their blood sugar. Healthcare providers and family members may want to consider these outcomes when motivating teens with type 1 diabetes to improve blood glucose control.

**\*\*PAS Poster Presentation**

**OXYTOCIN INHIBITS THE FUNCTION OF KIR7.1 ION CHANNELS**

*Nathaniel York; Michelle Chiu; De-Ann M. Pillers; Bikash Pattnaik*

**Background:** Kir7.1 is an inwardly rectifying K<sup>+</sup> channel expressed in the retina, heart, brain, and uterus. Inhibition of Kir7.1 results in increased organization and force of uterine contractions. Reduced expression of Kir7.1 occurs towards the end of gestation resulting in greater membrane depolarization. Thus, Kir7.1 is important for uterine contraction. Oxytocin (OXT) is a hormone well known for its role during the initiation of myometrial contractions via the activation of the oxytocin receptor (OXTR), a G-protein coupled receptor. Our primary interest is in the retina, where Kir7.1 channels are regulated by PIP<sub>2</sub>, which is a substrate of the OXTR signaling cascade. In this study, we explored the fundamental question of whether Kir7.1 is inhibited in vitro by OXT-mediated stimulation of the OXTR.

**Objective:** Determine whether OXT activation of OXTR can inhibit Kir7.1 current via the GPCR mechanism.

**Design/Methods:** Both human embryonic kidney (HEK-293), and Chinese Hamster Ovary (CHO) cell lines are commonly used in electrophysiological studies, due to the lack of endogenous ion channel expression. We created a HEK cell line with stable OXTR expression (HEK-OXTR). EGFP fused Kir7.1 was transiently expressed by transfection. Kir7.1 current was measured by the whole-cell patch clamp technique during treatment with HEPES Ringer (HR) solution supplemented with either 100nM OXT or Ba<sup>2+</sup>, a Kir channel inhibitor. We used the cholinergic GPCR M1 (CHO-M1, ATCC) cell line as an experimental control. These cells also transiently expressed EGFP-Kir7.1 and were stimulated by carbachol. We used paired T-test for comparison.

**Results:** Current recording revealed a Ba<sup>2+</sup> sensitive inwardly rectifying Kir7.1 channel in transfected cells. In the HEK-OXTR cells treatment of OXT resulted in the decrease in Kir7.1 current amplitude by 67% (n=9; P< 8.34x10<sup>-7</sup>). While Ba<sup>2+</sup> treatment resulted in the depolarization of the cells from -70mV as part of complete Kir7.1 channel inhibition, OXT had no effect on membrane potential. In our control CHO-M1 cells Ba<sup>2+</sup> blocked Kir7.1 completely and carbachol inhibited 66% of current.

**Conclusions:** We have shown that oxytocin inhibits Kir7.1 current via activation of the OXTR. This observation could have significant implications for our understanding of the events related to labor and for potential interventions to prevent premature birth. We propose that reduced Kir7.1 expression in late gestation allows for OXT mediated depolarization and the initiation of contractions.



