Department of Pediatrics Research Day

RESEARCH POSTERS AND PRESENTATIONS

May 12, 2017

School of Medicine and Public Health
UNIVERSITY OF WISCONSIN-MADISON

RESEARCH DAY
FRIDAY, MAY 12, 2017
HSLC 1345

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12:00 – 12:30 PM HSLC 1220-1222	**Research Grants 101** *Department of Pediatrics Grants Team*
12:30 – 1:00 PM HSLC 1345	**Lunch**
1:00 – 3:00 PM HSLC 1345	**Oral Presentations** *(see below)*
3:00 – 5:00 PM HSLC Atrium	**Poster Reception (with light hors d'oeuvres)** *Residents, Fellows, and Faculty*

ORAL PRESENTATIONS

1:00 – 1:30 PM	**Introduction and Welcome from Keynote** *Robert Lemanske, MD*
1:30 – 1:45 PM	**Predictors of Time-Intensive Care Coordination Needs Among Patients in One Pediatric Complex Care Program** *Mary Ehlenbach, MD*
1:45 – 2:00 PM	**Physician Identification and Documentation of Pediatric Admission Danger Signs at Mbale Regional Referral Hospital: Effect of Refresher Training** *Amanda Becker, MD; Kathleen Miller, MD*
2:00 – 2:15 PM	**Automatic Stop in NICU Admit Order Set: Antibiotic Stewardship Initiative** *Cora Astorga, MD*
2:15 – 2:30 PM	**Methylxanthine Exposure Reduces Acute Kidney Injury in Preterm Neonates - Results from the Awaken (Assessment of Worldwide Acute Kidney Injury Epidemiology in Neonates) Study** *Matthew Harer, MD*
2:30 – 2:45 PM	***Potentially Modifiable Variables Associated with Extubation Success in Neonates*** *Allison* *Allison Taber, MD*
2:45 – 3:00 PM	**Differentiating Zika and Dengue Virus Infections with a Linear Eptide Array** *Emma Mohr, MD, PhD*
3:00 – 5:00 PM	**Poster Reception (with light hors d'oeuvres)**

Resident Abstracts

PHYSICIAN IDENTIFICATION AND DOCUMENTATION OF PEDIATRIC ADMISSION DANGER SIGNS AT MBALE REGIONAL REFERRAL HOSPITAL: EFFECT OF REFRESHER TRAINING

Amanda Becker; Kathleen Miller; Erin Chung; Peter Oluput-Oluput

Background: Appropriate triage and recognition of danger/ priority signs in critically ill children during the first 24 hours of admission is necessary to reduce child mortality, particularly in settings with limited resources. We hypothesized that a quality improvement project at Mbale Regional Referral Hospital (MRRH) to improve provider recognition of danger signs would result in increased documentation of danger signs and indirectly decrease mortality.

Methods: An educational refresher course was held for members of the medical team reviewing paediatric "danger signs" and effective triage. Handouts were given to all participants and posters were placed in the triage area and acute care ward listing defined danger signs. A retrospective chart review was performed to identify documentation of danger signs on admission to the pediatric acute care ward at MRRH for the 2 week period prior to the educational intervention. Data points included the number of danger signs, patient outcome, diagnosis, and length of stay. An additional retrospective chart review assessing the same data points was performed for the 2-week period after the intervention.

Results: 25 clinical staff attended the refresher training. 210 charts were reviewed prior to the intervention and 179 post-intervention. The mortality rate in the pre-intervention group was 10%; of these patients, 76% died within the first 24 hours of admission. The average number of positive danger signs identified was 1.0 among patients who survived and 1.8 among patients who died, which was statistically significant (p-value 0.0015). There was a statistically significant association between the presence of positive danger signs and death (p-value 0.0048). In the post-intervention group, 179 charts were reviewed in the two weeks following the intervention. 8% of patients had zero danger signs identified. The average number of danger signs identified among patients who survived was 1.7, and 2.7 among those who died (p-value 0.0196). There was a statistically significant increase in the average number of danger signs documented in the pre-vs post intervention group, which averaged of 1.0 in the pre- group and 1.7 in the post-intervention group. Mortality decreased from 10% to 6%, but this was not statistically significant (p-value 0.058).

Conclusions: There was a statistically significant increase in the number of danger signs identified on admission after the educational intervention and placement of visual reminders in the work environment. There was a difference in mortality, although not statistically significant, which may have been related to the number of patients in the study. Refresher trainings for identification of pediatric danger signs lead to increased identification and documentation of danger signs, which could be associated with a decreased mortality over time.

NON CELIAC GLUTEN SENSITIVITY

Jeff Clark

Background: While celiac disease (CD) has become a wellknown disease entity, understanding and acceptance of its counterpart, non-celiac gluten sensitivity (NCGS) has lagged behind. We sought to compare NCGS diagnosis rates within pediatric and family medicine practices in south central Wisconsin with national prevalence estimates. Celiac disease is known to be an immune-mediated disordertriggered by exposure to gluten in genetically predisposed individuals including HLD-DQ-2 and DQ-8 mutations, which has established histologic features. No genetic, auto-immune or other etiologies for NCGS have yet been found, but diagnosis is currently made following symptomatic improvement on a gluten free diet in the setting of normal range TTG and serum IgA to rule out celiac disease and negative RAST testing to rule out wheat allergy. Difficulties in recognition and/or diagnosis of NCGS are lead by the lack of specific serologic tests or histologic findings as are found in celiac disease. Also, there does not exist unified, consistent clinical diagnostic criteria, which leaves substantial room for interpretation between providers. A further challenge to diagnosis is that symptoms of NCGS, like CD, can appear contradictory or nonspecific - as known symptoms include constipation or diarrhea, and extra-intestinal findings such as "foggy mind", lack of wellbeing, and tiredness. Lastly, there may be reluctance among providers to confer a diagnosis if they are not sure it is widely legitimized within medical literature. More accurate understanding of NCGS prevalence is needed, but this cannot be obtained without first developing consistent diagnostic parameters among individual practitioners.

Methods: We conducted a single center, retrospective review of charts from pediatric and family medicine clinics in south-central Wisconsin, among patients with age range from 2 to 18 years who were diagnosed with ICD-9 and ICD-10 codes as follows: Non-celiac gluten sensitivity: ICD 10 = Z91.018, ICD 9 = V15.05, Non-celiac gluten enteropathy: ICD 10 = K90.89 IDC 9 = 579.8; History of gluten intolerance: ICD 10 = Z87.19 ICD 9 = V12.79 and Gluten-sensitive enteropathy/Celiac disease ICD 10 = K90.0 ICD 9 = 579.0. Study period was July 1st 2006-June 30th 2016 (10 years). *IRB request has been filed.*

Results: Results are pending. We expect to compare UW system results with national prevalence rates of CD and NCGS, both of which are around 1:133.

Conclusions: We anticipate that we will provide education to Pediatric and Family Medicine providers in the UW community regarding the existing diagnostic criteria of NCGS

ECHOCARDIOGRAPHY IN THE NORMAL NEWBORN NURSERY

Michael E. Fenster; John S. Hokanson

Background: In the era of improved prenatal detection and universal congenital heart disease screening, we aimed to evaluate the utility of echocardiograms in the normal newborn nursery (NNN).

Methods: This chart review was performed on all newborn echocardiograms performed at one hospital from January 2008 through December 2015. Only the first echocardiogram done on each patient was studied. The studies were screened based on birth weight, ordering provider, and documented indication for study to exclude tests performed in the intensive care unit. The study reports were reviewed to categorize the indication for study, impact on patient care, and primary lesion identified. In addition, nursery physicians were surveyed to determine their specialty, management of murmurs in the NNN, and whether their evaluation of murmurs has changed since completing residency.

Results: 26,565/30,430 infants born at Meriter received their care in the NNN, of which 499 (1.88%) had echocardiograms. The most common indication for echocardiogram was for a murmur (71%), followed by findings on fetal ultrasound (9%). Fifty percent of studies were normal, 42% showed incidental findings, the most common being small VSDs, 6% had abnormalities that may need treatment in the future, but did not change management before discharge, and 2% resulted in some change in care before hospital discharge. Of the 11 infants with a change in management, 3 required transfer to a surgical center and 8 needed only increased monitoring or supplemental oxygen. One of the three requiring surgery was diagnosed on fetal ultrasound, and the other two had loud (3/6 or 4/6) murmurs. The surgical patients included two cases of aortic stenosis and one coarctation of the aorta.

Sixty three of 135 (47%) physicians completed the survey. In otherwise asymptomatic infants with a murmur, 30% of respondents order echocardiograms before discharge, 24% would schedule early outpatient follow-up, and 24% would provide routine follow-up with the primary care provider.

Conclusions: In a modern normal newborn nursery, critical congenital heart lesions are rarely identified by echocardiograms. Infants with benign murmurs who are otherwise asymptomatic could safely be followed as an outpatient.

THE DIAGNOSTIC CHALLENGES OF PEDIATRIC BLASTOMYCOSIS OSTEOMYELITIS: A CASE SERIES

Daniele Gusland; Andrew Livermore; Jie Nguyen; Alana K. Sterkel; James Conway

Backgroud: Blastomyces dermatitidis is a dimorphic fungus endemic to the United States and Canada. Though both Histoplasma and Blastomyces are found in similar geographic regions, blastomyces is many times more likely to cause dissemination in the immunocompetent host. Disseminated infection frequently involves the bone. However, given the indolent nature of this fungal infection and the prevalence of more common infectious etiologies of osteomyelitis, diagnosis and treatment is often significantly delayed.

Case Report: We review two pediatric cases which initially presented with isolated orthopedic symptoms without documented fever or pulmonary complaints, though both had signs of pulmonary infection on imaging.

Discussion: These cases demonstrate the importance of a high level of suspicion as well as appropriate diagnostic work-up, including surgical pathology with fungal stains, when evaluating osteomyelitis in patients exposed to a blastomyces-endemic region.

COMPLETION ANGIOGRAM MAY BE SUPERIOR TO TRANSESOPHAGEAL ECHOCARDIOGRAM FOR DETECTION OF PULMONARY ARTERY RESIDUAL LESIONS IN CONGENITAL HEART DISEASE SURGERY

Erick Jimenez; Petros Anagnostopoulos; Catherine C. Allen; Derek B. Hoyme; Luke J. Lamers

Background: Evaluate if completion angiography is more effective than transesophageal echocardiography at detecting of residual pulmonary artery lesions.

Methods: Retrospective review of 19 surgical cases involving the pulmonary vasculature that had postoperative transesophageal echocardiography and completion angiography from February 2014 to February 2017. Transesophageal echocardiograms were interpreted by two physicians blinded to surgical and completion angiography results. Transesophageal echocardiograms were categorized as adequate repair, inadequate requiring revision or unable to assess. Transesophageal echocardiograms data was compared to results of the completion angiography and to operative notes to determine the ability of each method to detect significant residual lesions.

Results: Mean age 5.4 months and mean weight 5.9 kg. Diagnosis included single ventricle variants (n=14), tetralogy of Fallot variants (n=4) and corrected transposition (n=1). Surgeries included: Glenn operation (n=8), pulmonary artery reconstructions (n=4), main pulmonary artery banding (n=4) and bilateral pulmonary artery banding (n=3). Surgical revision was indicated in 2 of 19 cases by TEE results versus 6 of 19 by completion angiography. Sensitivity of TEE to detect residual lesions of the pulmonary arteries was 40% (95% CI: 12-77%), specificity 100% (95% CI: 78-100%). Positive predictive value was 100% (95% CI: 34-100%) and negative predictive value was 80% (95% CI: 55-93%). Intraoperative angiography related complications included arrhythmia and staining.

Conclusions: Completion angiography may be more effective at detecting post-operative pulmonary artery lesions compared to transesophageal echocardiography. Documentation of pulmonary artery lesions with completion angiography allows immediate surgical revision potentially limiting necessity for future interventions.

THE EFFECT OF A CANCER CELL VACCINE IN A MURINE ALLOGENEIC HSCT-MODEL OF NEUROBLASTOMA RELAPSE

Tyce Kearl; Christian Capitini

Background: Cancer cell vaccination is a type of immunotherapy in which cancer cells are altered and transferred into a patient in the hope that the patient will develop a potent immune response to the vaccine and also to the patient's own cancer cells.

Methods: We examined cancer cell vaccination in a murine allogeneic HSCT-model of neuroblastoma relapse with transfusion of ex vivo-expanded NK cells as a potential synergistic treatment for neuroblastoma, a pediatric cancer with poor survival.

Results: First, we determined if in-vitro expansion of NK cells could be augmented by co-culture with AGN2a cells (a murine neuroblastoma). Unfortunately, AGN2a is known to suppress T cell expansion and our results suggest that it suppresses NK cell expansion as well. Because of this result, subsequent in vivo experiments did not involve transfusion of NK cells. Other laboratories have shown that expression of T cell co-stimulatory molecules on AGN2a cancer cell vaccines greatly enhances anti-tumor T cell-dependent responses following syngeneic hematopoietic stem cell transplant (HSCT). Our study was designed to test AGN2a cancer cell vaccine in an allogeneic HSCT model. Allogeneic, rather than syngeneic, HSCT generally allows for increased anti-tumor responses and better represents clinical HSCT from one person to another. A/J strain mice received a transplant from B6 strain mice and were challenged 11 days later with an A/J-derived neuroblastoma cell line, NSX2, to simulate the clinical scenario of tumor relapse post-HSCT. Mice subsequently were injected at various time points with the AGN2a cancer cell vaccine (also originally derived from A/J mice) and with the immunocytokine hu14.18-IL-2, which is used in this model to augment the anti-tumor response.

Conclusions: Administration of the cancer cell vaccine did not prolong survival, but actually worsened it. Subsequent studies are needed to determine the reason for this result; in particular, the function of T cells in this experimental model requires further attention.

EPISODES OF STIFFENING AND APNEA IN A SIX-WEEK OLD FEMALE

Allison L. Lindell; Vanessa Tamas

Case Report: A six week old term female with a history of choanal atresia status post endoscopic repair and dilations, normal newborn screen, and patent foramen ovale is transferred from outside hospital to the emergency room for evaluation of multiple episodes of apnea with stiffening. On arrival in the emergency room, she is fussy but alert. Vital signs are notable for a heart rate of 167 bpm and a respiratory rate of 82 rpm on 0.5 L nasal cannula. Findings from the physical exam are normal except for mildly dysmorphic features and increased tone in all four extremities. While being examined, infant has an episode of stiffening with desaturation to 70%. Initial laboratory evaluation is notable for calcium <5.0 mg/dL, ionized calcium 2.75 mg/dL, phosphorus 11.3 mg/dL, and magnesium and albumin within normal limits. An EKG shows normal sinus tachycardia with prolonged QTc at 477 ms. A head CT scan is obtained and shows no acute intracranial process. She is treated with calcium gluconate and phenobarbital for suspected seizures secondary to hypocalcemia.

The infant is admitted to the pediatric intensive care unit for further management where her calcium corrects on a calcium chloride infusion. Parathyroid hormone is found to be 6 pg/mL and she is also started on calcitriol. Genetic and immunologic testing is sent including FISH, microarray, flow cytometry, quantitative immunoglobulins and oxidative burst. Microarray shows a 10p15.3p14 deletion.

Discussion: Partial chromosome 10 deletion is rare chromosomal abnormality. It is associated with a DiGeorge-like syndrome, including hypoparathyroidism, genitourinary anomalies, developmental delay, and choanal atresia. The initial presentation of these infants may be seizures due to hypocalcemia, and acute management focuses on correction of electrolyte abnormalities.

USE OF AN ONLINE EDUCATION MODULE IMPROVES PEDIATRIC RESIDENT OBJECTIVE KNOWLEDGE OF THE INPATIENT ASTHMA EXACERBATION ALGORITHM AT AFCH

Mitchell Luangrath; Qianqian Zhao; Kristin Shadman

Background: The clinical practice guideline for diagnosis and management of asthma at the American Family Children's Hospital (AFCH) includes a delegation protocol (the pediatric inpatient asthma exacerbation algorithm) that enables respiratory therapists (RTs) to provide respiratory assessments and subsequent bronchodilator therapy for children with wheezing. However, care team members have expressed concern that the protocol is poorly understood, which leads to discontinuation and/or deviation from the protocol. Our aim was to increase objective knowledge of the inpatient asthma exacerbation algorithm among pediatric residents through an online education module.

Methods: The asthma protocol education module was created using Prezi, an online presentation platform. Identical pre and post-module assessments were created. Residents were asked to rate their understanding and perception of the asthma protocol and answer objective questions regarding the content of the inpatient asthma exacerbation algorithm. All pediatric residents were e-mailed links to the pre-module assessment and the education module. Residents who completed the module were provided a link to the post-test one week later. No assessment was made of residents who did not complete the module.

Results: 35/43 pediatric residents completed the pre-module assessment and 26 completed the post-module assessment. There was overall improvement of correct responses from pre to post-module among all residents ($p < 0.0001$), as well as interns alone ($p = 0.0003$). Residents demonstrated specific improvement in the following: patient age inclusion ($p = 0.0021$), recommended emergency department therapy prior to admission ($p = 0.0204$), modified pediatric asthma severity score (mPASS) needed to indicate bronchodilator treatment ($p < 0.0001$), and the maximum number of puffs of albuterol given per treatment bundle ($p = 0.0003$). Intern recognition of mPASS score indicating bronchodilator treatment also demonstrated improvement ($p = 0.0002$). There was a trend towards improvement for the remaining individual questions among all residents and interns alone, including questions pertaining to resident perceptions and perceived understanding of the protocol.

Conclusions: Pediatric residents' knowledge of the inpatient asthma exacerbation protocol improved following use of an online education module. Further research is needed to assess impact on protocol usage and patient outcomes.

COMPARISON OF FREQUENTLY USED GROWTH CHARTS WITH INFANTS BORN IN MADISON, WISCONSIN

Rachel Petro; Elizabeth Goetz

Background: At the time of birth an infant's weight is used to classify the infant as small for gestational age (SGA), average for gestational age (AGA), or large for gestational age (LGA). This classification is important to know, as those that are SGA or LGA are at higher risk for complications shortly after birth, including hypoglycemia, ineffective thermoregulation, birth trauma, and respiratory distress. Two common growth charts used to plot birth weight include the World Health Organization (WHO) and the Fenton, which were created using different populations. The goal of this project was to compare these charts with infants born in Madison, Wisconsin.

Methods: Gestation age, birth weight, and sex were collected from 3,260 infants admitted to the newborn nursery at Meriter Hospital in Madison, WI between January and November of 2016. 10 infants were excluded from further analysis due to incomplete data or inappropriate encounter type. Each infant was categorized as either SGA, AGA, or LGA based on WHO and Fenton definitions, and difference between these classifications was tallied.

Results: 471 of 3,250 (14%) differed in classification of SGA/AGA/LGA. 77.5% (365 of 471) were classified as AGA using Fenton criteria and SGA or LGA using WHO criteria. 22.5% (106 of 471) were classified as AGA using WHO criteria but SGA or LGA using Fenton criteria. Scatter plots of weight for gestational age were created for both male and female infants born at Meriter. The 10th, 50th, and 90th percentiles were calculated for each gestation age available from this data, which was then compared graphically with the same percentiles from the WHO and Fenton charts.

Conclusions: Graphically, the data from the Meriter cohort appears to fit more closely with the Fenton chart than the WHO, however further analysis is required to determine if this is a statistically significant difference. 77% of the time when there was a classification difference the infant would've been classified as AGA when using Fenton criteria and SGA or LGA via WHO. If a hospitalize utilizes SGA or LGA status to identify infants who require closer monitoring, this means that a large percentage of infants would be subjected to unnecessary or possibly invasive monitoring when it may not be indicated if the WHO chart is used.

CASE REPORT OF THE NATURAL HISTORY OF INCIDENTALLY FOUND MEDULLOBLASTOMA FOLLOWED RADIOGRAPHICALLY IN A YOUNG ADULT WITH CHRONIC HEADACHES

Nicholas Pytel; Mariah Bashir; Shahriar Salamat; Rishi Lulla; Neha Patel; Diane Puccetti

Background: Medulloblastoma is a malignant tumor diagnosed in 12-25% of pediatric brain tumors, 77% before the age of 19. In adulthood, the rate sharply declines with increasing age to be only diagnosed in 0.4-1% of adult brain tumors. These tumors are diagnosed typically after symptoms are noted consistent with increased intracranial pressure.

Case Report: We present a case of a young adult who was followed with serial MRI scans due to history of headaches and over time developed a lesion in the cerebellum that was later diagnosed as a medulloblastoma. We present this case as a natural history of medulloblastoma and will include a review of the literature. Patient AG had the original MRI brain scan for chronic headaches yielding only a right posterior fossa arachnoid cyst. Four years later, persistent headaches warranted another scan showing a new lesion with T2 FLAIR hyperintensity in the left cerebellar hemisphere. Serial scans over two years showed progression in size and complexity of this new lesion originally thought benign. AG underwent craniotomy with mass resection that resulted in cytoplasmic beta-catenin positive medulloblastoma without anaplasia on neuropathology. It was also without metastasis or CSF involvement. Post-operative imaging showed a small suspicious area near the resection cavity which biopsies later proved positive for residual medulloblastoma greater than 1.5 cm, thus placing this patient into the high-risk treatment category. AG elected proton therapy (36 in the craniospinal region with posterior fossa boost) with vincristine following protocol ACNS0331 with maintenance therapy afterward. AG has since been followed with serial MRI scans without evidence of residual disease.

Discussion: After reviewing the literature, low occurrences of incidental CNS tumors have been found in trauma and research cases. It is rare to have radiographic evidence of the onset of a malignant brain tumor.

****PAS Poster Presentation**

EXPANDING THE FRAME - OUTCOMES FOLLOWING EXTREMELY PREMATURE BIRTH BEYOND NEURODEVELOPMENTAL IMPAIRMENT

Matthew A. Rysavy; Tarah T. Colaizy; Carla Bann; Susan R. Hintz; Sara B. DeMauro; Andrea F. Duncan; Betty R. Vohr; Myriam Peralta-Carcele; Edward F. Bell

Background: Neurodevelopmental impairment (NDI) is frequently used in studies of prognosis and therapy following extremely preterm birth. However, it is unclear what this outcome might mean to families in terms that are most meaningful to them. We compared the designation of NDI with other medical, functional, and social outcomes of potential importance to families and clinicians.

Methods: We analyzed data for infants born at 22 0/7 through 26 6/7 weeks at hospitals participating in the NICHD Neonatal Research Network between 5/2006 and 6/2012. Infants with congenital anomalies were excluded. NDI was defined by commonly used cut-offs based on the Bayley-III cognitive score, Gross Motor Functional Classification System score, and presence of cerebral palsy, blindness, and/or hearing impairment at 18-22 months' corrected age. We calculated the proportion of children with medical, functional, and social outcomes by NDI category. Chi-square tests were conducted to compare outcomes by NDI category. Subgroup analyses using Cochran-Mantel-Haenszel tests were conducted to account for gestational age in weeks.

Results: Of 6,562 children eligible for inclusion, complete outcome data were available for 6,101. Prior to follow-up, 2,618 children died. Of the remaining 3,483 children, 825 (24%), 1,576 (45%), 657 (19%), and 425 (12%) had no, mild, moderate, and severe NDI at follow-up, respectively. Rates of outcomes by severity of NDI are shown in the table. The observed trends persisted after accounting for gestational age at birth.

Conclusions: Severity of NDI was correlated with several outcomes of interest to families and clinicians. However, many infants with no or mild NDI had significant medical, functional, and social needs. Non-NDI outcomes such as these warrant further attention in prognostic research and studies of therapeutic interventions.

RESIDENT AND ATTENDING SUCCESS AT LUMBAR PUNCTURE IN TERM NEONATES

Derek R. Spindler; Sadie J. Skarloken; Sarah A Webber; Daniel Sklansky

Background: It is important for physicians to perform successful lumbar puncture (LP) in order to obtain cerebral spinal fluid (CSF) in the workup of febrile neonates. Recent studies indicate that opportunities for residents to perform LP are decreasing and a corresponding decline in resident success with LP1. Furthermore, simulation practice may not improve success rates. We sought to determine if resident LP success rate is indeed lower than that of attending physicians. We hypothesize that because attending physicians have more experience and likely trained in an era with more LP opportunities, their success rates are higher than recent residents. To our knowledge no prior studies have compared attending and resident LP success rates.

Methods: Charts of infants <30 days old admitted from 2001 through 2015 were identified in our electronic database using institutional coding for lumbar puncture, CSF lab studies, and blood cultures. Blood culture was queried to capture children with failed LPs who subsequently did not have LP billing or CSF results to trigger identification for the study. We recorded success in obtaining CSF in the first LP session, number of needle insertions required per session, and training status of the procedure provider. Success was defined by any lab report of CSF. Success rates based on training status were compared using a Chi-square test.

Results: We identified 184 patients undergoing LP during the study period, with a first-session failure rate of 27.2%. Residents were successful 70.1% of sessions vs. 87.1% for attendings (Chi-square P-value = 0.050). For LP sessions in which the number of spinal needle insertions was reported, there were a mean of 2.14 insertions with median of 2 insertions per session.

Conclusions: Over the study period, resident physicians were less likely than attendings to have a successful LP attempt. Further analysis of success rate trends over time, and specific patient and provider characteristics may reveal reasons for lower resident success other than lack of experience. This data may provide insight into future interventions to increase resident LP success rate.

INCIDENCE OF BRADYCARDIA AND HYPOTENSION DURING CONTINUOUS DEXMEDETOMIDINE INFUSION IN PEDIATRIC PATIENTS FOLLOWING CARDIAC CATHETERIZATION

Shannon J. Summers; Cari L. Meyer

Background: Dexmedetomidine acts as an agonist on alpha-2 receptors in the brain and spinal cord, producing anxiolytic, sedative, analgesic, and sympatholytic effects. Due to its sympatholytic activity, bradycardia and/or hypotension are common side effects. Dexmedetomidine is frequently used as a continuous infusion to sedate children following cardiac catheterization. The incidence of sympatholytic side effects in children receiving dexmedetomidine following cardiac catheterization is unknown and it is possible that children with cardiac disease may be more sensitive to decreased sympathetic activity.

Methods: Medical records for pediatric patients aged from birth to 18 years who underwent cardiac catheterization at American Family Children's Hospital between 1/2/2013 and 2/26/2016 were analyzed. The dose of dexmedetomidine, duration of infusion, and incidence of hypotension and bradycardia were recorded. Definitions of bradycardia and hypotension were based on Pediatric Advanced Life Support (PALS) guidelines.

Results: During the study period, 297 patients underwent a cardiac catheterization. Of these patients, 125 received a continuous dexmedetomidine infusion during the immediate postoperative period. Five patients were excluded due to the use of additional intravenous sedative infusions. Of 120 patients, bradycardia occurred in 10 patients (8.3%) and hypotension occurred in 11 patients (9.2%). One patient (0.8%) had both hypotension and bradycardia. No patients suffered adverse events due to bradycardia or hypotension and no additional medications were needed to correct the hypotension or bradycardia. Incidence was not associated with infusion rate or duration.

Conclusions: Dexmedetomidine is associated with a low incidence of hemodynamically insignificant bradycardia and/or hypotension when used postoperatively as a continuous infusion in pediatric patients following cardiac catheterization.

FACTORS ASSOCIATED WITH EXTUBATION FAILURE IN A NEONATAL COHORT

Allison E. Taber

Background: To identify variables which are associated with extubation success or failure in all neonates requiring intubation at Unity Point Health Meriter in a 36 bed, level III NICU.

Methods: Retrospective data was gathered on all neonates who required intubation from January 2015 to October 2015. Failure was defined as needing reintubation within 72 hours of extubation.

Results: 53 neonates required intubation during the study period. 7 were not included in the analysis as they died or were transported prior to extubation. Of the 46 neonates included, 34 (76%) had successful extubations and 11 (24%) had extubation failure. In a multivariate logistic model examining all study variables caffeine use (p=0.0286) and supplemental oxygen (p=0.011) were the factors that resulted in a statistically negative effect on extubation success. Adjusting for supplemental oxygen the odds ratio of caffeine use versus no use on extubation success is 0.038 (0.002,0.710). Adjusting for caffeine usage, the odds ratio for each unit of oxygen increase is 0.768 (0.627,0.941).

Conclusions: In this cohort oxygen supplementation and caffeine use had a statistically significant negative effect on extubation success. Supplemental oxygen is currently used as criteria for extubation readiness and failure increases with each unit of FiO2. The association between caffeine use and extubation failure (although with very small odds ratio) is likely secondary to the fact the younger neonates receive caffeine supplementation and these neonates had more extubation failure rather than caffeine use itself contributing to extubation failure. Some variables included on the extubation checklist did not have significant effect on extubation success (pH, PCO2 and ET-CPAP trial) and leads to the question if those guidelines are being followed properly or if the parameters should be adjusted. Ongoing analysis of neonates requiring intubation and the factors surrounding extubation is needed to optimize timely extubation success.

EVALUATION OF INDOOR MICROBIOTA IN WISCONSIN FARM VS. NON-FARM HOMES USING ELECTROSTATIC DUST COLLECTORS

Mariam Wahidi; Rose F. Vrtis; Kei E. Fujimura; Susan V. Lynch; DJJ Heederik; Matthew C. Keifer; Iris A. Reyes; Casper G. Bendixsen; Christine M. Seroogy; James E. Gern

Background: European studies show that farm environmental exposures reduces the risk for development of atopic diseases. We examined whether electrostatic dust collectors (EDCs) are an effective method for assessing airborne microbial material, and evaluated the microbiota of settled dust between Wisconsin farm- and non-farm home environments.

Methods: The Wisconsin Infant Study Cohort (WISC) project includes examination of settled dust from ~200 family homes-half on dairy farms and the other half on surrounding non-farm homes-in Marshfield, WI. DNA was extracted from the first 88 EDC samples, along with negative control samples. 16S bacterial rRNA V3-V4 region amplicon sequencing was performed via MiSeq. Sequences were processed and chimera-checked using the USEARCH pipeline and normalized with DESeq2. Alpha- and beta-diversities were calculated in QIIME.

Results: 83 of the 88 samples had sufficient DNA for sequencing, and there was no amplification from the blank controls. Comparison of settled dust revealed greater diversity of bacterial microbiota in farm homes than non-farm homes, as measured by Shannon's index (t-test, $p<0.001$) and Faith's Phylogenetic diversity (t-test, $p<0.001$). Bacterial taxa were more evenly distributed in farm homes (Welch's t-test, $p=0.006$). House classification (farm home vs. non-farm home) explained 12% of the variation in community composition (PERMANOVA; weighted UniFrac, $R2=0.12$; $p<0.001$). In farm homes, Firmicutes and Actinobacteria were enriched and Bacteroidetes and Proteobacteria were underrepresented ($q<0.05$).

Conclusions: EDCs are an effective method for assessing airborne microbiota. Settled dust in Wisconsin farm homes has greater bacterial alpha- and beta-diversities than non-farm homes, and composition is remarkable for increased enteric bacteria.

FACULY/FELLOW ABSTRACTS

INCREASED RHINOVIRUS-INDUCED INNATE IMMUNE RESPONSE IN PERIPHERAL BLOOD DURING INFANCY IS ASSOCIATED WITH IMPROVED LUNG FUNCTION AT SCHOOL AGE

***Halie Anderson**; Ronald Sorkness; Victoria Rajamanickam; Ronald Gangnon; James Gern; Robert Lemanske Jr.; Daniel Jackson*

Rationale: Previous studies have examined relationships between early life peripheral blood immune responses and the development of wheezing and atopy and have suggested low innate immune responses in early life are associated with increased risk for persistent wheeze. However, little is known about early-life immune response profiles and relationships to lung function later in life.

Methods: Peripheral blood mononuclear cell samples collected at birth and 1 year from children in the Childhood Origins of Asthma (COAST) study were stimulated with rhinovirus (RV), and interferon-α (IFN-α) responses were measured using multiplex ELISA. Spirometry was obtained between 6-16 years, and standardized using Global Lungs Initiative (GLI) equations to calculate z-scores. Relationships between RV-induced IFN-α and lung function across pubertal development were assessed using mixed models adjusted for gender.

Results: There was not a significant relationship between cord blood RV-induced IFN-α and school-aged lung function. However, increased RV-induced IFN-α at 1 year was associated with significantly greater lung function between 6 and 16 years. [Post-bronchodilator forced expiratory volume 1 (FEV1) pre-puberty [(z-score increase 0.61 (95% confidence interval (CI) 0.28-0.93) for each log10 increase in IFN-α $p<0.001$); peri-puberty [(z-score 0.53 (95% CI 0.17-0.88); $p=0.004$)]; post-puberty [(z-score 0.49 (95% CI 0.14-0.84); $p=0.01$)].

Conclusion: Increased RV-induced IFN-α in peripheral blood at age 1 year is associated with improved lung function into adolescence, although this relationship is not present at birth. This suggests that development of more robust innate anti-viral responses during the first year of life may enhance lung function throughout childhood and adolescence.

****PAS Poster Presentation**

MESENCHYMAL STROMAL CELL (MSC) EXTRACELLULAR VESSICLES ENHANCE ANGIOGENESIS IN VITRO

Vivek Balasubramaniam; Gretta Nelson; C. Chetty, R. Braun

Background: Chronic lung disease of infancy is characterized by impaired lung growth secondary to prematurity and subsequent treatment. It has recently been demonstrated that impaired lung function as a consequence of premature birth persists into adulthood. At this time there are no therapies that can restore lung structure and function. We have previously shown that the treatment of neonatal rats with mesenchymal stromal cell (MSC) extracellular vesicles (EV) protects neonatal mice from exposure to hyperoxia. We hypothesize that EV protection of lung structure is through the preservation of angiogenesis.

Objective: To determine the effect on MSC derived EV on endothelial cell growth and function in vitro.

Design/Methods: We exposed rat bone marrow derived MSCs to serum free media for 24 hours and collected the media. An aliquot of conditioned media (MSC-CM) was centrifuged at 20,000xg to remove cell debris and then centrifuged at 100,000xg to remove EV. This media was EV depleted CM (EVdCM). Four types of media, Media with Serum (Control), MSC-CM, EVdCM and serum free media (SFM) was then plated on top of HUVEC cells. Cells were plated on matrigel for 24 hours to assess tube formation. To assess migration, a confluent layer of HUVEC were scratched and plated with above conditions and after 24 hours the width of the scratch was measured. All of these were done with an n=4 in each condition.

Results: Treatment with MSC-CM resulted in a 77% decrease in cell front (scratch width) and total tube length of 23840 um. Treatment with SFM only resulted in a 23% decrease in cell front and 617 um total tube length. treatment with EVdCM only resulted in a 44% decrease in cell front and a 4019 um tube length. This represents a significant difference ($p<0.01$) difference in all three tests as compared to Control. EV treatment also resulted in an significant increase in eNOS protien expression.

Conclusion(s): Treatment with MSC EV results in an increase in markers of angiogensis that include tube formation, migration and increased eNOS protein expression. This suggests that EV could be a therapeutic option for the preservation of lung angiogenesis and lung growth after prematurity

****PAS Poster Presentation**

PRIORITIES FOR CHILD HEALTH ADVOCACY: RESULTS FROM A NATIONAL SURVEY OF CHILD HEALTH RESEARCHERS

S. Shah; H.L. Brumberg; L. Sanders; **Vivek Balasubramaniam**

Background: Recent political and policy events have significant implications for child health in the US. The perspectives and priorities of child health researchers have not yet been identified.

Objective: To identify priorities for a national child-health advocacy agenda, from the perspective of child-health researchers.

Design/Methods: A 14-item, web-based survey was administered to all US members of the Society for Pediatric Research in June 2016. Response rate was 16% (N=571); compared with non-respondents, respondents were more likely to be members of the AAP and other pediatric societies. Primary outcomes were ranked responses for policy priorities in two domains: Research and Child Health. Outcomes were assessed overall and by respondent characteristic (sex, geographic region, years from training, research type, research funding, and clinical practice). Sequential logit analysis was used to produce a final model for each list, adjusting for these characteristics.

Results: For research priorities, highest rank was NIH funding (69% rank 1, mean rank 1.61), followed by reversing the ban on gun violence research (17% rank 1; mean rank 2.93). For child-health priorities, highest priority was health care access (opposing Medicaid block grants) (44% rank 1, mean rank 2.10), followed by Medicaid payment parity with Medicare (26% rank 1, mean rank 2.56). In unadjusted analyses, geography (South) and setting (outpatient) were associated with likelihood of ranking health care access or Medicaid parity. In unadjusted and adjusted analyses, receiving federal research funding was associated with likelihood of ranking NIH funding (AOR 1.55).

Conclusion(s): Among child-health researchers, the priority areas for national policy advocacy are NIH funding, Medicaid block grants, and Medicaid payment parity. These priorities were consistent across geography, care setting, and type of research.

DYNAMIC CARDIAC PET/MR IMAGING OF GLUCOSE UTILIZATION AND CONTRACTILE FUNCTION UNDER HYPOXIC STRESS

***Gregory P. Barton**; Alan McMillan; Niti Aggarwal; Kara Goss; Marlowe Eldridge*

Purpose: In the setting of heart disease, cardiac metabolic changes precede overt pump dysfunction. However, in most clinical scenarios, metabolism and function are not typically assessed together. Moreover, cardiac contractile function and metabolism are typically measured under resting conditions. The purpose of this study was to develop novel methodology to study the dynamic relationship between contractile function and metabolism in a rest-stress scenario in a preclinical model. The induction of a physiological stressor, such as hypoxia or exercise, can elicit subclinical changes in cardiac function which are not typically observed under resting imaging conditions. Finally, to determine the relationship between cardiac metabolism and contractile function the two must be measured together, which requires the use of simultaneous PET and MR imaging.

Methods: Following an overnight fast, healthy pigs (45-50kg) were anesthetized using telazol (5mg/kg)/xylazine (1mg/kg IM). An endotracheal tube was inserted and a mechanical ventilator connected to 21% oxygen, and maintenance anesthetization was maintained with isoflurane. After an overnight fast, 10 pigs (5 male, 5 female) were anesthetized and mechanically ventilated prior to a cardiac PET/MRI study. We used normoxic gas (21% O_2) as rest and hypoxic gas (12% O_2) as a cardiac stress. In order to determine dynamic changes in glucose utilization, ^{18}F-fluorodeoxyglucose (FDG) was continuously infused at a rate of 0.01 ml/s during 25-30 minutes of normoxia exposure and during 25-30 minutes of hypoxia exposure. Cardiac MRI was performed simultaneously with PET imaging, allowing for coregistration of cardiac structures with FDG metabolism. Cardiac function was measured with ECG-gated, cine two-dimensional (2D) steady state free precession (SSFP) techniques to calculate left ventricular (LV) and right ventricular (RV) volumes.

Results: Following hypoxic stress there was an increase in heart rate (HR), cardiac output (CO), LV ejection fraction (EF), and rate pressure product ($p < 0.05$) as shown in Figures 3 and 4. Arterial saturation decreased from 99% to ~70% SpO_2 ($p<0.05$) due to hypoxia exposure. There were no changes in RV volumes or RV EF. The ratio of the LV to BP slope of the PET data increased 3-fold ($p<0.05$) suggesting increased LV glucose utilization as a result of hypoxic stress, as shown in Figure 5.

Discussion: The purpose of this study was to explore a novel methodology utilizing dynamic cardiac PET/MR techniques to simultaneously assess contractile function and metabolism in a serial rest-stress protocol. Hypoxic stress induces a significant change in contractile function as measured with MRI, which is coupled with an increased rate of LV FDG uptake relative to BP as measured with PET. Interestingly, the BP slope decreased under hypoxic stress in all but one animal, suggesting a global increase in glucose uptake. These findings are similar to what has been observed in humans hearts exposed to hypoxia using non-dynamic PET methods. Currently, conventional cardiac PET studies use a bolus injection of FDG to measure glucose utilization. The use of a continuous infusion of FDG allows dynamic imaging to perform a serial rest-stress protocol within a single study, which may help elucidate changes that are not measurable at rest. We have demonstrated the capability of performing this study in healthy animals, and our results suggest that these same techniques may further elucidate more subtle functional and metabolic abnormalities in the presence of heart disease. Further work to refine this methodology includes extension of the PET infusion model to full kinetic modeling and the integration of more advanced MR imaging such as 4D flow to assess hemodynamic and kinetic energy changes under stress.

PULMONARY VASCULAR RESPONSE TO EXERCISE AND HYPOXIA IN ADULT SURVIVORS OF PRETERM BIRTH

***Arij Beshish**; Kristin Haraldsdottir; Greg Barton; Laura Tetri; Rudolf Braun; David Pegelow; Mari Palta; Luke Lamers; Kara Goss; Marlowe Eldridge*

Introduction: An estimated 15 million neonates are born preterm every year in the United States, 10% of all live births. Premature birth disrupts pulmonary vascular growth and initiates a cascade of events that can result in abnormal pulmonary vasoreactivity and vascular remodeling, which may ultimately lead to pulmonary hypertension. In this study, we evaluate the long term effects of prematurity on pulmonary vascular function and vasoreactivity in adults during rest and exercise both in normoxia and hypoxia. We hypothesize that adults born premature will have elevated pulmonary arterial pressures and increased pulmonary vasoreactivity in response to exercise and hypoxia.

Methods and Measurements: To date, five preterm-born adults (born in 1988 - 1991, Gestational age ≤ 32 weeks) and five age matched healthy controls have completed this study. A Millar catheter was inserted into the pulmonary artery and pulmonary arterial pressures were measured at rest and during exercise while breathing both 21% and 12% O_2. Each subject performed two bouts of exercise on a supine stepper at 70% of their maximal power, as determined from a maximal exercise test done during a screening visit. Values are presented as mean ± SD.

Results: Preterm subjects demonstrated elevated resting mean pulmonary arterial pressure (mPAP) and systolic pulmonary arterial pressure (sPAP) compared to controls in both normoxia (mPAP 26.67 ± 2.17 mmHg vs. 14.22 ± 3.77 mmHg, p = 0.009; sPAP 36.56 ± 4.51 mmHg vs. 23.82 ± 2.28 mmHg, p = 0.03) and hypoxia (mPAP 32.93 ± 3.40 mmHg vs. 16.82 ± 4.11 mm Hg, p = 0.008; sPAP 42.11 ± 2.90 mmHg vs. 26.48 ± 4.83 mmHg, p = 0.005). Normoxic exercise demonstrated a similar degree of elevation in mPAP and sPAP in preterm subjects compared to controls (mPAP 31.32 ± 1.74 mmHg vs. 20.25 ± 5.60 mmHg, p = 0.001; sPAP 47.52 ± 5.86 mmHg vs. 35.36 ± 5.47 mmHg, p = 0.01 respectively). Hypoxic exercise also showed an elevation in mPAP and sPAP among preterm subjects when compared to control (mPAP 40.09 ± 1.36 mmHg vs. 24.26 ± 5.04 mmHg, p = 0.002, sPAP 56.46 ± 2.73 mmHg vs. 39.08 ± 4.68 mmHg, p = .004). These results are a part of an ongoing study.

Conclusion: This data suggests that individuals born preterm have resting pulmonary hypertension and increased pulmonary vascular reactivity to hypoxia.

PERSONALIZING IRON DEFICIENCY SCREENING IN PEDIATRIC PRIMARY CARE

***Nicholas Bohrer**; Carol A Diamond; Jeffrey S Sleeth; Caroline Paul; Scott Hebbring; Amy Plumb; Pamela J Kling*

Introduction: Untreated iron deficiency and iron deficiency anemia (ID/IDA) in infancy can impair neurocognitive development. Universal screening of hemoglobin concentration (Hb) is recommended at one year of age, or earlier if risk factors are present. Although easier to obtain as a screen, Hb is neither sensitive nor specific as a sole marker of body iron status. Initiation of a best practice alert in 2014 improved UW Health screening rates at one year of age. This project has two aims. The Enhanced Screening aim is to assess need for and then create and implement an ID learning module for pediatric nursing staff and/or providers, to improve screening and treatment of high-risk infants. The Familial Hemoglobin aim is to further discredit Hb as a sole iron screen by characterizing familial and environmental influences on Hb, while also supporting more personalized Hb reference ranges.

Methods: Enhanced Screening: qualitative data was collected from both observation of infant health supervision visits at five UW Health pediatric clinics, as well as a verbal needs assessment of several nurses at the clinics. An online learning module is being developed based on the American Academy of Pediatrics (AAP) 2010 iron screening guidelines, that discusses infant iron deficiency risk factors and nutrition/supplementation. Familial Hemoglobin: patient Hb/hematocrit data from two population-based datasets from the Marshfield Clinic are being analyzed at 9 months-3 years and 16-18 years of age, comparing Hb between twin-twin and parent-child pairs, to assess the relative influences of heritable and environmental factors on Hb over time.

Results: Enhanced Screening: variability exists between nurses' and providers' attention to ID screening and nutrition, and between screening practices in pediatric clinics. High-risk infants, especially neonatal intensive care graduates, are not being evaluated earlier than 1 year, as per AAP recommendation. Familial Hemoglobin: initial data summaries suggest that the distribution of Hb values are similar between male and female twins at 9 months-3 years, while at 16-18 years of age a gender difference emerges with non-normal distributions, especially for males. Values between twins are strongly related in early life. Although less robustly related in adolescence, even twins of the opposite sex are related, a finding that we were not anticipating.

Conclusion: Despite improvements in screening rates for identification of ID/IDA, there is need to further improve standardization of screening practices, especially in high-risk infants who would benefit from earlier screening. We will further proceed with both development of the learning module, and analysis of the Hb data. Familial Hb may predict Hb values, and using Hb as the sole test screen for ID/IDA may not be advised.

IMPLEMENTATION OF A PEDIATRIC IV TO PO PROTOCOL AT AN ACADEMIC CHILDREN'S HOSPITAL AUGMENTED BY CLINICAL DECISION SUPPORT

***Randy Braun**; Monica Bogenschutz; Jill Strayer; Jessica Poehls; Amy Crawford; Josh Vanderloo; Sheryl Henderson; Daniel Sklansky; Sara Pivovar; Lucas Schulz*

Purpose: Implementation of an antimicrobial stewardship program (ASP) is a required condition for participation by The Joint Commission. Interventions, such as parenteral to enteral (IV-to-PO) interchange, are key to early success when starting a stewardship program. These interventions can reduce venous access, decrease costs, and improve patient care. This project developed a new pediatric IV-to-PO guideline and delegation protocol, implemented a novel clinical decision support (CDS) tool to support guideline and protocol implementation, and created a framework for continuous improvement of the guideline and protocol, along with a CDS tool.

Methods: The ASP began in May 2016 and an IV-to-PO Interchange was identified as a core element by the ASP committee. The pediatric guideline was created by combining resources from a national pediatric stewardship collaborative with the existing adult guideline and review by an interdisciplinary committee. A delegation protocol was developed along with the guideline, to allow pharmacists as physician delegates to perform IV-to-PO interchange in patients who meet approved criteria. A clinical decision support tool was developed in the electronic medical record (EMR) to aid pharmacists in identifying appropriate patients for route interchange based on the guideline. The CDS tool also allows inline clinician feedback to facilitate a quality improvement cycle for the guideline and tool itself. Impact of the route interchange guideline, associated protocol, and CDS tool will be measured using days of therapy (DOT) per 1000 patient days as defined by the National Healthcare Safety Network (NHSN), antimicrobial costs, and central line days.

Results: The guideline and protocol were created and approved by an interdisciplinary workgroup, the organizations Pharmacy and Therapeutics committee and medical board. The CDS tool was implemented in EMR with pediatric clinical pharmacist assistance during development. It identifies patients eligible for IV-to-PO interchange based on diet order and an active order for an intravenous medication in the guideline. Feedback data from the tool is exported from the EMR and reviewed on a monthly basis by ASP team members. Findings from the review process will be used to update the associated guideline, protocol and CDS tool when necessary.

Conclusions: Pediatric patient characteristics create unique challenges for practice standardization, but it is still possible to implement hospital wide guidelines and protocols to decrease cost and improve patient care. Clinical pharmacists augmented with clinical decision support tools can improve patient outcomes and decentralize stewardship efforts. Real-time and continuous feedback frameworks can assist in maintaining up to date and relevant clinical practice guidelines.

ADOLESCENT CHILDREN BORN PRETERM HAVE ALTERED CARDIAC REGULATION DURING AND IMMEDIATELY FOLLOWING MAXIMAL EXERCISE.

***Melissa Brix**; Kristin Haraldsdottir; Mari Palta; Arij Beshish; Laura Tetri; Andrew Watson; Kara Goss; Marlowe Eldridge*

Introduction: Heart rate recovery (HRR) after maximal exercise has been shown to be a marker of fitness and disease status. Individuals born prematurely exhibit increased left ventricular mass and reduced end systolic and end diastolic volume. It has been shown that slower HRR is correlated with a higher risk for cardiovascular diseases. Oxygen (O_2) pulse is defined as the total volume of oxygen consumed per heartbeat and a low O_2 pulse has been associated with pulmonary hypertension (PH) and other cardiovascular (CV) diseases. It is correlated with stroke volume and overall cardiovascular efficiency during exercise. The purpose of our research was to investigate the long-term effects of preterm birth on HRR immediately following maximal exercise, and we hypothesized that it would be slower in adolescents born preterm.

Methods: Fifteen children 12-13 years old, 8 born preterm (birthweight <;1500g, gestational age <32 weeks) and 7 children born full term (gestational age 38-40 weeks) underwent progressive maximal exercise testing on a cycle ergometer, with continuous measurement of O_2 consumption (ml/kg/min), as well as cardiac output (Q), stroke volume (SV), and heart rate (HR) using thoracic bioimpedance. SV and Q were indexed to body surface area (BSA (m^2)). HR was recorded for 2 minutes of rest following maximal exercise and HRR was the absolute drop in HR at 2 minutes from maximal HR (HRR_{2min}). Statistical analysis was done using multiple t-tests and linear regression.

Results: HRR_{2min} following maximal exercise was lower in preterms than controls (54.4 ± 4.2 v 63.5 ± 5.9, p=0.01, respectively). Preterm subjects had lower relative maximal oxygen consumption (VO_{2max}) compared to control subjects (39.6 ± 9.3 v 52.8 ± 7.3 ml/kg/min, p=0.03). The increase in O^2 pulse from rest to maximal exercise was greater in controls compared to the preterms (8.8 2 ± 1.1 v 4.8 ± 3.0 ml O^2/beat, p=0.02). SV did not increase significantly in preterms from rest to maximal exercise (51.7 ± 9.0 v 53.3 ± 8.3 ml/m2, p=0.77), but SV significantly increased in controls (47.4 ± 4.0 v 51.3 ± 8.4 ml/m2, p=0.01). Furthermore, the change in SV (ΔSV) from rest to maximal exercise was significantly smaller in preterms than in controls (0.0 ± 7.2 v 20.3 ± 17.0 ml/m^2, p=0.012). A simple linear regression showed a positive relationship between ΔSV and HRR (p=0.03, r2=0.39).

Discussion: We found that multiple measurements associated with cardiac regulation were significantly different in preterms compared with controls. A slower HRR has been correlated with PH risk and CV disease that could lead to future complications. The inability to augment SV during exercise is uncommon, and has been noted in patients with CV disease. Finally, the linear regression showed that there is a positive relationship between ΔSV from rest to maximal exercise and HRR after exercise, indicating that there may be a direct relationship between the two variables. We have demonstrated that multiple cardiac parameters are altered in adolescent children born preterm during and immediately following exercise. There appears to be an altered cardiac regulation mechanism in adolescent children born preterm, and this will be an important area of study in the future.

USE OF PROTEOMIC AND FLOW CYTOMETRY ASSAYS TO CHARACTERIZE INNATE ANTI-VIRAL IMMUNE RESPONSES USING CORD BLOOD IN A BIRTH COHORT STUDY

***Jamee Castillo**; Amanda Barlow; Amy Dresen; Brent Olson; Tamara Koepel; Iris Reyes; Jennifer Meece; Michael Evans; Casper Bendixsen; Matthew Keifer; James Gern; Christine Seroogy*

Rationale: Farm exposure is protective against asthma and our preliminary findings suggest viral respiratory illnesses (VRIs). Type I interferon responses are immature in neonates, however the relationship between varied immune maturation markers has not been studied. Proteomic and flow cytometry assays were used to characterize neonatal immune responses to rhinovirus (RV-A16) and viral-associated TLRs, and the results of these two assays were compared. We hypothesize that Type I IFN secretion will positively correlate with pDC maturation and pDC IFN function and farm children will have increased anti-viral activity at birth compared to non-farm children.

Methods: In a prospective birth cohort study, cord blood was collected from farm and non-farm neonates. 53 study subjects (26 farm and 27 non-farm) were analyzed. Blood mononuclear cells were isolated and stimulated with RV-A16 and viral-associated TLR agonists (R848 & CpGA). Multi-parameter flow cytometry and multiplex, bead-based assays were used to determine innate and adaptive immune responses. Spearman's rank coefficient was calculated to determine correlation between assays. Differences between farm and non-farm IFNa2 secretion and pDC function were analyzed.

Results: For R848 agonist, IFNa2 supernatant levels were positively correlated with plasmacytoid dendritic cell IFN mean fluorescence intensity (pDC IFN gMFI, rs=0.33, p=0.04) and pDC IFN integrated mean fluorescence intensity (pDC IFN igMFI, rs=0.36, p=0.02). IFNa2 was not correlated with pDC IFNa expression (pDC IFNa+) and pDC maturation (pDC CD40+CD86+). There was no difference between IFNa2 secretion in cord blood supernatant between farm and non-farm neonates. There was also no difference between farm and non-farm neonates in pDC IFN function and pDC maturation.

Conclusion: Proteomic and flow cytometry assays provide a detailed characterization of neonatal anti-viral responses. In interrogating anti-viral immune responses, proteomic and flow cytometry data, in general, demonstrated weak correlations. This suggests that other mononuclear cells, in addition to pDCs, are significant sources of IFN. Preliminary analysis found similar anti-viral immune responses in cord blood from farm and non-farm neonates. Post-natal exposures may be responsible for the observed reductions in the frequency of VRIs in farm infants.

AEROBIC CAPACITY LIMITATION IN ADOLESCENT CHILDREN BORN PREMATURE IS DRIVEN BY BLUNTED CARDIAC OUTPUT RATHER THAN ACTIVITY LEVEL OR STRENGTH

***Ryan Centanni**; Kristin Haraldsdottir; Arij Beshish; Kara Goss; Mari Palta; Marlowe Eldridge*

Purpose: One in 10 children in the United States are born preterm. Young adults born preterm have been shown to have impaired gas exchange and diminished aerobic capacity, but very little is known about the effects of prematurity on fitness and cardiovascular function in adolescent children. The intent of this study is to identify possible explanations to why preterm birth has negative effects on exercise through measurements of fitness (hand grip strength, vertical jump displacement, VO2max), cardiac output (Q) measurements using bioimpedance, with pubertal development (Tanner stage), and physical activity assessment data.

Methods: Eight children born preterm (PT) (age 12-13, birth weight <1500g, gestational age 24-31 weeks) and 7 age-matched children born full term (CT) (gestational age 38-40 weeks) completed maximal hand grip strength (HG) using a dynamometer and vertical jump displacement (VJ). Subjects underwent progressive maximal exercise on a cycle ergometer, with continuous measurement of O2 consumption (ml/kg/min), as well as Q using thoracic bioimpedance. Q was indexed to body surface area (BSA (m2), Qi). Subjects completed pubertal (Tanner Stage) and physical activity questionnaires (PAQ-C). Statistical analysis was done using multiple t-tests.

Results: There was no difference in PT compared to CT in combined HG (112.1 ± 9.6 v 115.3 ± 11.5 kg, p=0.79), VJ (29.5 ± 5.0 v 33.5 ± 4.7 cm, p=0.23), Tanner Stage (3.3 ± 0.6 v 2.9 ± 0.7, p=0.19), or PAQ-C (2.05 ± 0.5 v 2.15 ± 0.4, p=0.72). PT had lower relative maximal oxygen consumption (VO2 max, ml/kg/min) compared to CT (38.3 ± 9.3 v 51.5 ± 7.3 ml/kg/min, p=0.03). Qi significantly increased in PT from rest to maximal exercise (6.7 ± 1.6 v 10.4 ± 3.4 L/min/m2, <0.01) and significantly increased in CT (5.9 ± 0.9 v 14.2 ± 3.4 ml/m2, <0.01). The change in Qi from rest to maximal exercise was significantly smaller in PT compared to CT (5.6 ± 1.1 v 9.0 ± 2.6 ml/dL, p=0.02). By calculating SVi from Qi and HR, it was found that SVi did not increase in PT from rest to maximal exercise (51.7 ± 9.0 v 53.3 ±8.3 ml/m2, p=0.04), while SVi significantly increased in CT (47.4 ± 4.0 v 67.7 ± 14.4 ml/m2, p=0.01). The change in SV from rest to maximal exercise was significantly smaller in PT compared to CT (1.6 ± 6.5 v 13.2 ± 2.3 ml/dL, p=0.98).

Conclusion: Adolescent children born preterm exhibit lower maximal aerobic capacity and significantly smaller maximal Qi than age-matched controls. PTs do not have decreased hand grip strength or vertical jump displacement compared to CTs. PTs have similar levels of physical activity as CTs. This data suggests that PTs may not be able to adequately increase Q in response to increasing metabolic demand, and this may reduce their ability to exercise at higher intensities. These differences are not due to differences in lifestyle or puberty, and are localized to systemic cardiac differences.

SOCIAL FACTORS AFFECTING IMMUNIZATION STATUS OF POPULATIONS IN BORDER AREAS OF CHIANG MAI PROVINCE, THAILAND

Jessica S. Chung; *Stephanie Koning; James H. Conway*

Background: Recent Northern Thailand border outbreaks of previously controlled diseases suggest that childhood immunization coverage in the region may be an issue. This area includes a highly mobile marginalized population who face barriers to medical care and prevention programs. This study focuses on border regions in Thailand that have served as major entry and resettlement sites for displaced populations from the conflict-ridden Shan state in Myanmar.

Objective: Immunization status of children in these communities was collected, to examine social factors that affect timeliness and completeness.

Design/Methods: This study utilized pilot data collected in 2015 and 2016 through an ongoing research study on the Myanmar border in Thailand. Information was obtained from 342 face-to-face interviews with mothers of children five years and younger in two village clusters in Chiang Mai Province. Women were asked to provide documentation of immunizations. Paper questionnaire data were entered into Microsoft ACCESS databases and descriptive analyses were performed using STATA. Timeliness was examined by assessing rates for recommended vaccines within relevant age groups. Social factors were studied by comparing age-specific rates with socio-demographics and access indicators (Table 1).

Results: Of children surveyed, 79.4% had all newborn vaccinations documented, with decreasing rates until receiving MMR (Table 2), Timeliness in vaccinations appeared to decline with age as well, with the exception of 3-5 year-olds (Table 1). Maternal ethnicity and education did not correlate with differences in immunization coverage. However, maternal language other than Thai or Shan was associated with a lower rate of timely immunization. Lack of child health insurance had the most marked effect, with approximately 30 percent lower immunization rates in the uninsured.

Conclusion(s): This study provides valuable pilot data regarding factors affecting immunization coverage for a vulnerable population of children in the Thai-Myanmar border region. Immunization uptake around delivery benefited from births being primarily in health facilities, but there was significant dropout over time. Improvement in immunization coverage at 3-5 years suggests school entry is an impetus for catch-up. Health insurance status appears to be more significant than maternal social factors such as ethnicity, educational levels and language use for ensuring immunization coverage. Factors that determine health insurance availability need to be explored further.

****PAS Platform Presentation**

CONCEPTUALIZING 'A HEALTHY LIFE FOR A CHILD WITH MEDICAL COMPLEXITY'

Ryan J. Coller, *Elizabeth S. Barnert, Bergen Nelson, Lindsey Thompson, Thomas Klitzner, Moira Szilagyi, Abigail Breck, Paul J. Chung*

Background: What constitutes health for children with medical complexity (CMC) and how to measure it are largely unknown, and may differ from other pediatric populations. While previously developing candidate domains of population health for CMC from systematic literature review and in-depth interviews with experts, we identified important measurement gaps.

Objective: To first generate and then synthesize a comprehensive list of concepts describing health and potential health outcomes for CMC from a diverse national sample of respondents.

Design/Methods: Snowball sampling from previous in-depth interviews identified 159 US participants in the following 3 groups: (1) Child and Family Advocates (including parents); (2) CMC Healthcare and Social Work Providers; and (3) CMC Healthcare Systems, Research, and Policy Leaders. In the first stage of Group Concept Mapping (GCM), respondents participated in internet-based idea generation by answering the focus prompt, "A healthy life for a child or youth with medical complexity includes: _". Each respondent provided an unlimited number of short free-text responses. Through inductive content analysis, statements were synthesized and reduced through investigator consensus to 72 unique ideas for sorting and rating.

Results: 110 participants completed the brainstorming phase (69.2%), with broad national representation. Respondents submitted 879 individual statements. Response items were preliminarily organized by the research team into 48 different categories, encompassing diverse domains of health. While many of the domains included traditional CMC focus areas including medical home and family-centered care attributes, most involved affective (e.g., comfort), family well-being (e.g., sibling health, financial security), and community-integration (e.g., education, participation in social activities) outcomes that have not been routinely or well measured by healthcare systems.

Conclusion(s): GCM identifies important outcomes missing from most existing work. This process may lead to a better, more comprehensive population health framework for CMC and perhaps children more generally. The final GCM step will sort items into final domains and rate their measurement feasibility and perceived impact.

****PAS Platform Presentation**

HEALTHCARE COSTS ASSOCIATED WITH USE OF RESPIRATORY MEDICAL EQUIPMENT AND SUPPLIES

***Ryan J. Coller**; Jay Berry, D Goodman; M Hall; A Houtrow; D Kuo; R Agrawal; E Cohen; J Thomson; D DeCourcey; N DeJong; A Melwani; M Coquillette; A Agan*

Background: Most tools that categorize medical complexity to assess healthcare use and cost in children focus predominately on chronic diagnoses, with little attention to complex healthcare needs, including use of respiratory medical equipment and supplies (RMES). Our objective was to assess the healthcare costs associated with RMES use at home.

Methods: Case control analysis of 11,306 children using and 21,192 children not using RMES [propensity matched by age and complex chronic conditions (CCC)] age 0-to-21 years and continuously enrolled in Medicaid in 2013 from 10 states in the Truven Health Medicaid MarketScan Database. RMES use at home was identified with Healthcare Common Procedure Coding System (HCPCS), billed by medical supply companies, and International Classification of Diseases, 9th Revision (ICD9), codes billed by clinicians and hospitals. RMES included oxygen (47%), suctioning (28%), apnea monitor (23%), CPAP/BiPAP (22%), tracheostomy (17%), mechanical ventilator (8%), cough assist (5%), and vest (4%). We regressed RMES use on total annual per member per year (PMPY) Medicaid payments, adjusting for enrollment reason, gender, age, race/ethnicity, and number of chronic conditions (of any complexity).

Results: Of children using RMES, 5% were identified with ICD9 only, 80% with HCPCS only, and 15% with both ICD9 and HCPCS. Most (87%) children using RMES had a chronic condition (of any complexity); 71% had a CCC. Neuromuscular (32%) was the most common CCC. PMPY payments in propensity-matched children using vs. not using RMES were $45,892 vs. $15,036, p<0.001. In adjusted analysis, payment increased significantly (p<.001) for children using oxygen (+$3,525), suctioning (+$8,569), apnea monitor (+$13,747), CPAP/BiPAP (+$1,117), ventilator (+$32,323), tracheostomy (+$11,977), cough assist (+$6,342), and vest (+$11,999). Of children using RMES, most payments were for hospitalization (57%), specialty care (24%), and medications (6%); < 3% was for RMES or home nursing.

Conclusions: RMES use may identify additional projected healthcare costs in children beyond consideration of chronic diagnoses alone. Most of the cost of children using RMES is due to increased inpatient and specialty care and not due to the equipment itself, thus RMES is likely an indicator of underlying health instability and fragility. Population health initiatives of children with medical complexity may benefit from consideration of RMES use in risk assessment.

****PAS Poster Presentation**

HOSPITAL AND EMERGENCY DEPARTMENT USE DUE TO DEVICE COMPLICATIONS FOR CHILDREN WITH MEDICAL COMPLEXITY

***Ryan J. Coller**; Mary Ehlenbach; Gemma Warner; Paul J. Chung*

Background: Many children with medical complexity (CMC) depend on devices to support essential functions; however, complications can lead to unplanned hospital or emergency department (ED) use. Understanding patient and device characteristics conferring greatest risk could guide interventions.

Objective: Identify predictors of ED and hospital use for medical device complications in a newly enrolled cohort of CMC at a complex care program.

Design/Methods: Retrospective cohort study of patients enrolled in a pediatric complex care program between 4/1/2014 and 12/1/2016. Program criteria include ≥3 body systems affected by chronic conditions, ≥3 subspecialists, and ≥5 hospital days or ≥10 clinic visits in the prior year. Demographic and severity of illness characteristics (numbers of devices, affected body systems, subspecialists, hospital and ED visits in prior year), presence of 23 distinct medical devices, and hospital or ED visits due to device complications in year before enrollment were assessed. Logistic regression identified associations between ED or hospital use due to device complications and demographic, clinical, and device characteristics.

Results: Among 199 CMC, 176 used medical devices (88.4%), with median 2/patient (IQR 1-4). The most common devices were gastrostomy tubes (61.9%), nebulizer (39.7%) and suction machines (34.1%). ED visits and hospitalizations from device complications in the prior year occurred for 18.2% and 9.7% of patients, respectively, accounting for 20.8% of all ED visits and 11.6% of all hospitalizations in the sample. CMC with a ventricular shunt, jejunostomy tube, or central venous catheter had the highest percentage of hospitalizations from device complications (25.0%, 37.5%, 50.0%, respectively). CMC with NG/NJ tubes had the highest percentage of ED visits from device complications (50.0%). Clinical and demographic characteristics, meanwhile, were poor predictors of device-related ED or hospital use. After adjusting for types and number of devices, demographics, and severity of illness, having a jejunostomy (AOR 11.3, p=0.003) or ventricular shunt (AOR 9.2, p=0.015) remained significantly associated with hospitalization from device complications.

Conclusion(s): ED and hospital visits due to device complications, some of which may be preventable, are common among CMC enrolled in our complex care program. If confirmed at other programs, interventions should target these devices and complication rates should be incorporated into cost-benefit analyses.

****PAS Platform Presentation**

TRANSITIONING TO ADULT-ORIENTED INPATIENT CARE: CURRENT STATE WITHIN US CHILDREN'S HOSPITALS

***Ryan J. Coller**; Sarah Ahrens; Mary Ehlenbach; Kristin Shadman; Paul J. Chung; Debra Lotstein; Andrew LaRocque; Ann Sheehy*

Background: Hospital charges and lengths of stay appear to be substantially greater when adults with child-onset chronic conditions are admitted to children's rather than adult-hospitals. Despite multiple efforts to improve pediatricadult healthcare transition, little guidance exists for transitioning inpatient care.

Objective: This study sought to characterize current pediatric-adult inpatient care transition practices across US children's hospitals.

Design/Methods: National survey of inpatient general pediatric service leaders at US children's hospitals during January-July 2016. Questionnaires assessed institutional characteristics, presence of an inpatient transition initiative (i.e., specific process and/or leader), and 22 inpatient transition activities organized by the Got Transition / Six Core Elements framework. Bivariate associations among institutional characteristics, specific transition activities, and presence of a specific process and/or leader were explored with logistic regression.

Results: Ninety-six of 195 children's hospitals responded (49.2%). A transition initiative existed at 38% of children's hospitals, significantly more often when there were dual-trained internal medicine-pediatrics providers or outpatient transition processes. Specific activities were infrequent and varied widely from 2.1% (tracking youth in inpatient transition) to 42.2% (identifying children overdue for transition). Institutions with an initiative were more likely to perform 10 of 22 activities, including proactively identifying patients needing transition, using transition checklists, and creating patient-centered transition care plans. Of the other 12 activities, half involved transition planning, the essential step between readiness and actual transfer of care.

Conclusion(s): Relatively few children's hospitals have leaders or dedicated processes to shepherd the transition from US children's hospitals to adult-oriented inpatient care. Across institutions there is wide variability in performance of activities to facilitate this transition. Feasible process and outcome measures are needed.

USING STAKEHOLDER ENGAGEMENT TO OPTIMIZE RECRUITMENT AND RETENTION OF CHRONICALLY ILL CHILDREN AND TEENS IN A CLINICAL TRIAL

***Elizabeth D. Cox**; Thor C. Jeppson; Tosha B. Wetterneck; Natalie DeCheck; Nancy Pandhi; Alex Binder*

Introduction: Children, teens, and the chronically ill are often hard to reach as participants in research studies. This work uses interviews and advisory boards of parents, teens, children, and other stakeholders to identify barriers and solutions to support participation of these hard-to-reach populations in a multi-site randomized controlled trial of behavioral interventions in type 1 diabetes.

Methods: Before the trial, semi-structured interviews were conducted with 20 families and 23 staff members from two participating clinics. During the study's first 18 months, notes were taken at nine advisory board meetings of parents, children, teens, and other stakeholders. These interviews and meeting notes were open-coded to identify barriers and solutions to participation of children and teens with type 1 diabetes. Through an iterative process of coding and discussion, these barriers and solutions were organized into themes.

Results: Stakeholder participation was high for interviews (64% of those invited) and the advisory board meetings (91% attendance). Of the barriers identified, 50% arose from interviews while the other 50% arose from stakeholder advisory board meetings. Seven themes arose as barriers to research participation for children and teens with type 1 diabetes: 1) study logistics, 2) costs of participating, 3) communication, 4) other commitments, 5) negative perceptions of research participation, 6) fear of study procedures, and 7) control group disappointment. Stakeholders also identified innovative and effective solutions to these barriers. For example, to minimize the impact of study participation on children and teens' other commitments such as schoolwork, stakeholders suggested working with teachers to create study activities that could also count for academic credit. As another example, to minimize disappointment with being randomized to the control group, teens suggested explaining to participants that "a computer," not study staff, decides who receives the intervention. Ultimately, the trial recruited 73% of eligible participants. After 15 study months, 99.5% of participants were retained and data completion rates exceed 80%.

Dissemination and Implementation Implications: Using family and clinic staff interviews in tandem with input from ongoing stakeholder advisory boards facilitated identification and resolution of seven types of barriers to research participation for chronically ill children and teens. Engaging key stakeholders facilitates the identification and resolution of barriers to research participation for hard-to-reach populations. The barriers and solutions identified can be used by other researchers to support participant recruitment and retention, ultimately improving representativeness of findings.

****PAS Platform Presentation**

NASAL BACTERIAL COLONIZATION AND DENSITY INCREASES DURING ASYMPTOMATIC VIRAL UPPER RESPIRATORY INFECTION (URI)

***Greg DeMuri**; James Gern; Jens Eickhoff; Ellen Wald*

Background: Colonization with pathogenic respiratory bacteria is a necessary condition for the development of the bacterial complications of URI – otitis media, sinusitis and pneumonia. Previous studies have shown that symptomatic viral URI is associated with an increase in density of *Streptococcus pneumoniae*,(Sp) *Haemophilus influenzae(*Hi) and *Moraxella catarrhalis* (Mc).

Objective: The aim of this study was to compare the density and rate of detection of Sp, Hi and Mc in nasal samples obtained both during episodes of asymptomatic viral infection and episodes without viral infection.

Methods: Children 4-7 years of age were followed prospectively for 1 year. Nasal washes were obtained during well-surveillance visits conducted quarterly after confirming patients were asymptomatic for at least two weeks. Multiplex PCR was used to detect respiratory viruses and quantitative PCR for Sp, Hi and Mc was performed on the same nasal sample.

Results: From February 2012 to September 2015, 279 subjects were enrolled. One subject, who refused all nasal washes following enrollment, was excluded. 205 subjects completed one full year of follow up. A total of 847 surveillance samples were obtained. When a respiratory virus was not detected 33%, 37%, 23% and 7% of samples had 0, 1, 2 or 3 respiratory pathogens detected respectively. When a respiratory virus was detected 21%, 37%, 30% and 12 % of specimens had 0, 1, 2 or 3 respiratory pathogens detected. Any bacterial pathogen was detected significantly more often when a virus was detected. ($p<0.01$)

When a respiratory virus was not detected the mean (95% confidence intervals) densities for Sp, Hi and Mc were 1.6 (1.4-1.7), 0.7(0.6-0.8) and 1.2 (1.0-1.4) colony forming unit equivalents (CFUe)/ml respectively. When a virus was detected the mean densities were 2.3(2.0-2.5), 1.0(0.8-1.2) and 1.6 (1.3-1.8) CFUe/ml, respectively; the differences between densities when virus was detected vs not detected were significant ($p<0.01$) for all three bacterial species.

Conclusions: Nasal samples obtained from asymptomatic children during quarterly surveillance visits were more likely to have detectable bacterial pathogens (*Sp, Hi and Mc*) and in higher density when a virus was detected compared to when virus was not detected. This may provide an explanation for the development of acute otitis media or bacterial sinusitis in children without an apparent antecedent viral URI.

****PAS Platform Presentation**

PREDICTORS OF TIME-INTENSIVE CARE COORDINATION NEEDS AMONG PATIENTS IN ONE PEDIATRIC COMPLEX CARE PROGRAM

***Mary Ehlenbach**; Gemma Warner; Ryan J. Coller*

Background: Pediatric complex care programs aim to improve outcomes of children with medical complexity through medical management and care coordination. Little is known, however, about which patients will be the most timeintensive to manage. Such information could inform program planning.

Objective: To identify pre-enrollment characteristics that predict more care coordination time among patients in a complex care program.

Design/Methods: Retrospective cohort study of patients enrolled in a pediatric complex care program from October 2015-September 2016. Program criteria include ≥3 body systems affected by chronic conditions, ≥3 subspecialists, and ≥5 hospital days or ≥10 clinic visits in the prior year. Pre-enrollment clinical characteristics (numbers of affected organ systems, subspecialists, medications, emergency department visits, hospitalizations, and medical devices) and demographics (age, gender, race/ethnicity, insurance, primary language, and distance from program) were assessed.

Program staff recorded time spent on patient care. Patients were categorized as new (enrolled during the study period, n=76) or established (enrolled prior, n=71). Using the full year for established patients or first two months for new patients, negative binomial regression identified clinical and demographic characteristics associated with care coordination time. Regressions for established patients were adjusted for duration in the program.

Results: New patients required median 7.5 (IQR 4.5-11.6) hours/patient/month; while the top 10%ile required median 20.9 (IQR 16.8-33.9) hours. Established patients required median 2.1 (IQR 1.3-3.2) hours/patient/month; while the top 10%ile required median 6.6 hours (IQR 5.7-11.0). Demographics were poor predictors of care coordination time.

Patients with more pre-enrollment hospitalizations or ED visits required significantly more care coordination time, whether new or established (hospitalizations IRR 1.12, p=0.016 and IRR 1.13, p=0.008, respectively; ED IRR 1.07, p=0.019 and IRR 1.10, p=0.004, respectively). Care coordination time in the first two months after enrollment also increased 7% for each additional subspecialist seen (IRR 1.07, p=0.035).

Conclusion(s): The top 10 percent of patients required three-fold more care coordination time in one complex care program. Clinical instability measured by hospital and ED use prior to enrollment may predict time-intensive care coordination needs. Demographics were not helpful in predicting time-intensive needs.

****PAS Poster Presentation**

GETTING TO KNOW YOU: NON-FACE-TO-FACE TIME SPENT ON NEW VERSUS ESTABLISHED PATIENTS IN A PEDIATRIC COMPLEX CARE PROGRAM

***Mary Ehlenbach**; Gemma Warner; Ryan J. Coller*

Background: Pediatric complex care programs spend substantial but poorly defined time on non-face-to-face coordination of care for children with medical complexity. Understanding time needs of new and established patients could inform program planning.

Objective: To define non-face-to-face care coordination time spent on new and established patients at a pediatric complex care program.

Design/Methods: Retrospective cohort study of patients enrolled in a pediatric complex care program from October 2015 through September 2016. Program criteria include ≥3 body systems affected by chronic conditions, involvement of ≥3 subspecialists, and either ≥5 hospital days or ≥10 clinic visits in the prior year. Patients were categorized as "new" (enrolled during the study period, n=76) or "established" (enrolled prior to the study period, n=71). Program staff (physicians, advance practice providers, nurses, social workers) recorded time spent caring for patients. Total and non-face-to-face time was aggregated per patient per month. Using t-tests, we identified the point after enrollment at which there was no significant difference in time spent for new and established patients.

Results: Clinical and demographic characteristics were not different between new and established patients. For established patients, 2.1 hours (78%) of the mean 2.7 hours/patient/month were spent in non-face-to-face care coordination. For new patients in the first two months after enrollment, 6.2 hours (66%) of the mean 9.4 hours/patient/month were spent in non-face-to-face care coordination. Significantly more time was spent in non-faceto-face care coordination for new compared to established patients (6.2 vs 2.1 hours/patient/month respectively, $p<0.001$). At 3 months after enrollment, new patients continued to require significantly more time (3.1 vs 2.1 hours, $p=0.04$). After 3 months, however, non-face-to-face time each month was no longer significantly different from established patients (1.8-2.9 hours vs 2.1 hours, $p>0.05$).

Conclusion(s): Up to three-quarters of time spent on patients in a complex care program is dedicated to non-face-to-face care coordination. The first 3 months after enrollment is highly time-intensive, after which non-face-to-face time may stabilize. This initial investment of time should be considered when planning staffing for complex care programs. Payment mechanisms that acknowledge non-face-to-face time are needed for financial sustainability.

MRI BIOMARKERS OF FUNCTIONAL OUTCOME AFTER SEVERE PEDIATRIC TBI: A FEASIBILITY ASSESSMENT

*Benjamin Yeske; Andrew Alexander; Michael Bell; **Peter Ferrazzano***

Purpose: Establish the feasibility of conducting a neuroimaging study of severe pediatric TBI as an ancillary study to the ongoing ADAPT Trial, with adequate power to identify biomarkers of specific neurocognitive dysfunctions.

Methods: We conducted a survey of ADAPT site-PIs to determine imaging practices in severe TBI patients and interest in participating in an ancillary neuroimaging study. We subsequently determined the incidence and timing of MRI scan in subjects enrolled in the ADAPT Trial at 10 sites.

Results: 25/48 ADAPT sites completed the survey. Most respondents (22/25) indicated that they obtain an MRI scan in over half of children with severe TBI, with 9/25 sites reporting MRI scanning in >95% of their severe TBI patients. Regarding timing of MRI, 20/25 respondents reported that severe TBI patients typically have an MRI obtained during the first 2 weeks post-injury. In addition to standard anatomic imaging, MR sequences obtained "often or always" included: diffusion-weighted (22/25), susceptibility-weighted (17/25), T2*-weighted gradient recall echo (16/25), diffusion tensor imaging (9/25), and perfusion-weighted imaging (7/25). Only 8/25 sites reported use of a standardized MRI protocol for pediatric TBI patients. In a retrospective analysis at 10 ADAPT sites, we found that 90/130 ADAPT subjects received an acute MRI within 30 days post-injury. Fifteen ADAPT sites, accounting for over 50% of ADAPT enrollment, committed to recruit ADAPT subjects for a non-sedated MRI scan at one year post-TBI.

Conclusion: Collection of 400-600 acute MRI scans from the 1000 subjects enrolled in ADAPT to study associations between acute MRI findings and functional outcome is potentially feasible. Allowing for 20% mortality and 50% recruitment rate, recruitment of 100-150 ADAPT subjects from 15 ADAPT sites for a follow-up MRI to study relationships between advanced MRI measures and neurocognitive function is potentially feasible and would represent the largest such study conducted to date.

AGE-DEPENDENT DIFFERENCES IN MICROGLIA GENE EXPRESSION AND MORPHOLOGY IN RESPONSE TO HYPOXIA ISCHEMIA IN THE DEVELOPING BRAIN.

Becca Novak; Jayadevi Chandrashekhar; Dila Zafer; Vishal Chanana; Pelin Cengiz; ***Peter Ferrazzano***

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: infant mice (P9) demonstrated a more vigorous microglial activation and proliferation compared to juvenile mice (P30). The aim of the current study was to assess for age-related differences in microglia morphology and gene expression during normal brain development and in response to hypoxic-ischemic injury.

Methods: Immunostaining was performed in naïve P2, P9, P30, and P60 mice. Microglia were isolated from P2, P9, P30 and P60 mice and quantitative rt-PCR was performed. HI was induced in P9 and P30 mice by unilateral carotid artery ligation and exposure to 10% O2 for 50 minutes and immunostaining and rt-PCR was performed 2 days post-injury.

Results: During normal brain development, microglia are seen to progress from an ameboid morphology to a highly ramified morphology. Expression of the TGFbeta receptor and the Mer Tyrosine Kinase receptor significantly increased. HI resulted induced an increase in TGFbeta receptor expression in P9 mice which remained significantly less than the expression seen in P30 mice.

Conclusions: Microglia morphology and gene expression evolves during normal brain development. Hypoxia ischemia results in different microglial responses depending on the age at which the injyr occurs. TGFbeta receptor signaling and MerTK signaling may play a role in age-dependent differences in microglial responses to HI.

INTEGRATED RHYTHM AND PACEMAKER SIMULATION SYSTEM: A CONFIGURABLE TOOL FOR REAL WORLD TRAINING OF HEALTHCARE PERSONNEL

Quan Chen; Zachary Bower; Nicholas Von Bergen; Joshua Medow; ***Scott Hagen***

Background: Arrhythmias can occur as many as 40% of patients after cardiac surgery. Temporary pacemakers are an important treatment modality for many of these arrhythmias, but requires training to utilize safely and effectively. The current model of pacemaker training involves the supervision of learners at the patient's bedside as the pacemaker is manipulated. This model of training has potential risk to the patient as the learner adjusts the pacemaker in response to the patient's rhythm. The purpose of this project is to develop a temporary pacemaker training device and reduce the risk to patients needing a temporary pacemaker after cardiac surgery.

Methods: A team of clinicians (Pediatric ICU, Adult ICU, Pediatric Cardiac Electrophysiology) and biomedical engineers sought to develop a rhythm generator with adjustable waveforms to resemble common arrhythmias. The rhythm generator will also interact with a temporary pacemaker in the same manner as a patient's heart. The output of the rhythm generator and the pacemaker should be displayed on a monitor for the student and instructor. Finally, we sought to develop a curriculum for learners to evaluate a displayed rhythm and respond appropriately with the temporary pacemaker in such a way that will benefit a patient.

Results: An android tablet based rhythm generator* was programmed to create normal and abnormal cardiac rhythms and to output the rhythm to a microcontroller via Bluetooth technology. Through integration of the tablet, microcontroller, temporary pacemaker and hospital monitor, the device is capable to generate continuous ECG with variable options to adjust the rhythm. The students will be able to see how the heart will respond to different pacemaker settings. A training curriculum is based on the most common arrhythmias encountered in the post-operative cardiac surgical patient. (*The android tablet used in this project is a Samsung SM-T550 with latest Android operating system version 6.0.1. The android integrated development environment used is Android studio version 2.2.3. The I/O interface is based on an Arduino Mega 2560 board and HC-05 Bluetooth module.)

Conclusions: A team of clinicians and biomedical engineers collaborated to develop a simulation training device and teaching curriculum for a temporary pacemaker. Use of the pacemaker simulator trainer may decrease the risk to patients. Future development will be directed at the usability of the device in training and investigating the impact of the device on the learners understanding of temporary pacemaker use in post-operative cardiac arrhythmias.

****PAS Poster Presentation**

ARE ADOLESCENTS BORN PREMATURE AT INCREASED RISK FOR LEFT VENTRICULAR DIASTOLIC DYSFUNCTION? A CARDIAC MRI STUDY.

***Kristin Haraldsdottir**; Laura Tetri; Arij Beshish; Mari Palt; Oliver Wieben; Christopher Francois; Jacob MacDonald; Kara Goss; Marlowe Eldridge*

Background: Greater left ventricular (LV) mass, lower LV ejection fraction (EF), blunted gas exchange during exercise, and lower exercise capacity have been reported in young adult survivors of prematurity. With the advancements in neonatal care in the past three decades, the cardiac and lung function of children born in in the 21st century is largely unknown.

Objective: We sought to determine resting LV volumes and function in children born premature compared to age matched term-born controls.

Design/Methods: Seven children born preterm (PT) (age 12-13, birthweight <1500 g, gestational age 24-31 weeks) and 6 age-matched children born full term (CT) (gestational age 38-40 weeks) participated in this ongoing study. Cardiac magnetic resonance imaging was performed in both groups at rest. Quantification of end diastolic volume (EDV), end systolic volume (ESV), EF, SV, maximal expansion velocity (MEV, an index of diastolic relaxation), and global fractional wall thickening (FWT) were analyzed using short axis images and Segment software (Lard, Sweden). All cardiac volumes were indexed to body surface area. Statistical analysis was performed by t-tests.

Results: EDVi is lower in preterms compared to controls, (62.8 ml/m^2 ± 8.7 v 74.9 ± 8.2 ml/m^2, respectively, p=0.03). ESVi is lower in preterms compared to controls, (19.0 ± 6.7 ml/m^2 v 27.1 ± 4.0, respectively, p=0.03). Ejection fraction trends higher in preterms compared to controls, (70.5 ± 7.4 v 64.0 ± 2.7, respectively, p=0.06). Resting SVi is not significantly different between preterms and controls (43.8 ± 3.2 ml/m^2 v 47.8 ± 5.0 ml/m^2, respectively, p=0.11). Three subjects per group were analyzed for maximal expansion velocity and fractional wall thickening. MEV trends lower in preterms compared to controls (10.2 ± 3.3 cm/s v 13.2 ± 0.5 cm/s, respectively, p=0.18). FWT trends higher in preterms compared to controls (94.6 ± 33.2% v 80.1 ± 10.1%, respectively, p=0.19).

Conclusion(s): Adolescent children born premature exhibit lower EDV and ESV at rest, while there is no difference in SV. Interestingly, preterms exhibited greater EF compared to controls, which can indicate increased contractility or LV hypertrophy. Our previous research in this population suggests that there may be a diastolic limitation in this population, which will require further analysis of maximal expansion velocity and fractional wall thickening. In conclusion, adolescent children born preterm may be at increased risk for impaired LV function due to diastolic dysfunction.

****PAS Poster Presentation**

METHYLXANTHINE EXPOSURE REDUCES ACUTE KIDNEY INJURY IN PRETERM NEONATES - RESULTS FROM THE AWAKEN (ASSESSMENT OF WORLDWIDE ACUTE KIDNEY INJURY EPIDEMIOLOGY IN NEONATES) STUDY

***Matthew Harer**; Louis J. Boohaker; J. Bryan Carmody; David T. Selewski; Ronnie Guillet; Jonathan R. Swanson; David Askenazi; Jennifer R. Charlton*

Background: Acute kidney injury (AKI) occurs frequently in preterm infants and is independently associated with increased morbidity and mortality. Previous small single-center observational studies and randomized clinical trials have shown that adenosine antagonists such as caffeine and theophylline reduce the severity of AKI. Although both of these methylxanthines (MX) are used frequently in preterm infants to treat apnea of prematurity, their role in prevention of AKI remains under investigation.

Objective: We sought to determine whether MX exposure was associated with reduced incidence of AKI in a multi- center cohort of preterm neonates during the first week following birth.

Design/Methods: We reviewed the medical records of all neonates born <36 weeks' gestation from the AWAKEN database (international, retrospective cohort study of neonates admitted from 1/1/14-3/31/14 from 24 institutions). Neonates admitted >2 d and those with severe congenital renal anomalies were excluded. MX exposure was defined as any dose of theophylline or caffeine within the first 7 days after birth and prior to the AKI occurrence. AKI was defined by the neonatal modified KDIGO definition and limited to 7 days after birth.

Results: A total of 1176 neonates were reviewed. AKI occurred in 180 (15.3%) and 492 (41.8%) were exposed to MX (Table 1). AKI severity (stages 1-3) and AKI definition criteria (serum creatinine (sCr) alone, urine output (UOP) alone, sCr or UOP) were assessed and 18 neonates met the AKI classification by both sCr and UOP criteria. Of the 492 neonates who received MX, 478 (97.1%) received caffeine and 15 (3.0%) received theophylline. Among the neonates who received a MX, AKI occurred in 47/492 (9.5%) as compared to 133/684 (19.4%) who did not receive a MX (χ^2, p<0.001, RR 0.44, NNT 11). Group characteristics listed in Table 2.

Conclusion(s): In the AWAKEN cohort â€“ the largest multicenter study of preterm neonatal AKI reported to date - the incidence of AKI in neonates who received MX was about half the rate of those who did not receive MX. This study supports the growing body of evidence suggesting that MX may reduce the burden of AKI in premature infants. While further anaylsis of this data set is ongoing, a prospective study to evaluate the effect of MX on AKI is warranted.

****PAS Poster Presentation**

URINE STRUCTURAL BIOMARKERS CAN IDENTIFY RENAL DYSFUNCTION IN CHILDREN BORN PRETERM

***Matthew Harer**; Brian Halloran; David Askenazi; Jennifer R. Charlton*

Background: Children with acute kidney injury (AKI) and former preterm neonates are at risk of developing chronic kidney disease (CKD). Classic diagnostic methods to estimate glomerular filtration rate (eGFR) are insufficient, limited by sensitivity and invasiveness. Previous studies have shown that urinary biomarkers reflective of structural changes in the kidney may precede functional changes. However, to our knowledge, these urinary markers have not been evaluated as an early detection tool for CKD in former preterm neonates with a history of AKI.

Objective: Evaluate differences in urinary biomarkers of kidney damage that may be related to AKI in former preterm infants.

Design/Methods: Children between the ages of 2-7 years born <1500 grams with and without a history of neonatal AKI (KDIGO definition using serum creatinine alone) were evaluated for signs of CKD (reduced eGFR, proteinuria, or hypertension). Fourteen urinary biomarkers were analyzed by electrochemiluminescent multi-array ELISA's (Meso Scale Discovery, human kidney injury panels 3 & 5, QuickPlex SQ 120) normalized to urine creatinine.

Results: The median age of the cohort was 5 years (n=33) and 15 subjects (45%) had at least one sign of CKD (eGFR < 90 mL/min/1.73m2 (n=9), urine protein/creatinine > 0.2 (n=4), blood pressure >95th%tile (n=2)). In the CKD group, beta-2-microglobulin (B2M) was significantly higher as compared to the control group (Table 1). The area under the curve (AUC) to detect renal dysfunction with B2M alone was 0.73 (CI 0.54-0.91, p=0.03) and improved to 0.80 (CI 0.64-0.96, p<0.01) when combined with epidermal growth factor (B2M/EGF). Of the subjects who had a history of neonatal AKI (n=22), 13 had a sign of CKD at follow-up. Compared to children without a history of neonatal AKI, those with AKI had significantly higher values of B2M, cystatin C and uromodulin (Table 2). A comparison of biomarkers with relation to CKD status and AKI history can be seen in Figure 1.

Conclusion(s): In this cohort of former preterm children, urine structural biomarkers differentiate children by CKD status as well AKI history. The increase in cystatin C and decrease in EGF seen in children with a history of neonatal AKI are comparable to a published study of urinary biomarkers at the time of neonatal AKI – suggesting the injury caused by AKI may result in persistent structural changes. Further studies are required to determine if these biomarkers can provide mechanistic insights between AKI and CKD and their role in CKD diagnostic and outcome markers.

ABDOMINAL ADIPOSITY ASSESSED BY WAIST CIRCUMFERENCE IS NOT PREDICTIVE OF HYPERANDROGENISM IN ADOLESCENT GIRLS

***Lauren A Kanner**; Jennifer L Rehm; M Tracy Bekx; Jens Eickhoff; David B Allen; Ellen L Connor*

Background: Hyperandrogenism in PCOS has been directly associated with abdominal fat accumulation. Waist circumference (WC), in contrast to BMI, preferentially assesses visceral, intraperitoneal and abdominal subcutaneous fat to give an estimate of global abdominal adiposity. Therefore, WC might be expected to be tightly associated with degrees of hyperandrogenism in addition to its correlation with insulin resistance (IR). While excess abdominal adiposity has been positively correlated with total and free testosterone levels in women with and without PCOS, WC has not been evaluated as an independent and clinically feasible predictor of hyperandrogenism in adolescents. We hypothesized that targeted testing of obese adolescent females based upon WC facilitates detection of hyperandrogenism and IR.

Study Design: Retrospective cross-sectional chart review of adolescent girls aged 13-20 years (median age 16 years) who met Androgen Excess-PCOS Society diagnostic criteria for PCOS presenting to a multidisciplinary clinic between 2011-2016 (1). Those on oral contraceptives or Metformin at initial visit were excluded. BMI, WC, WC/BMI and weight for age z-scores were analyzed compared to free (FT) and total testosterone (TT), fasting insulin (FI), and fasting glucose (FG) levels.

Results: Forty-six subjects met inclusion criteria. Multivariate analysis confirmed that weight-for-age was an independent predictor for FG. Weight-for-age z-score was positively correlated FG (rho=0.43, p= 0.005), FI (rho=0.47, p= 0.003) and FT (rho=0.39, p=0.010). BMI z-score was moderately correlated with FG (rho=0.34, p= 0.034) and strongly correlated with FI (rho=0.55, p= 0.0005). WC was positively correlated with FI (rho=0.44, p=0.0005). WC was moderately positively correlated with FI (p=0.005). There was no significant association between BMI z-score or WC with TT or FT.

Conclusions: Multiple studies in adult women report an association between abdominal adiposity and hyperandrogenism. In this group of adolescents with PCOS BMI and WC were non-significant predictors of testosterone levels and thus this study does not support this association. Although results could be secondary to WC being an inaccurate indicator of abdominal adiposity in this group, this seems unlikely given extensive prior experience demonstrating validity of WC correlations with markers of IR which were confirmed in this study. A more likely explanation is that the relationship between abdominal adiposity and hyperandrogenism is still evolving during adolescence.

****PAS Poster Presentation**

PARENT EXPERIENCES ACCESSING THEIR HOSPITALIZED CHILD'S ELECTRONIC HEALTH RECORD

***Michelle M. Kelly**; Peter L.T. Hoonakker*

Background: Web-based portals provide parents access to their child's electronic health record (EHR), enhancing engagement by providing healthcare information and a way to communicate with their child's providers. Currently limited to ambulatory use, portals may also be used as a tool to engage parents in their child's care in the hospital.

Objective: To evaluate parent experiences using a portal application on a tablet computer to access real-time information about their child's hospitalization and communicate with hospital providers.

Methods: We conducted semi-structured interviews with 12 parents of hospitalized children <12-years old who received a portal application on a tablet computer to use throughout their child's hospital stay. Linked to their child's inpatient EHR, the portal included real-time vitals, medication information (dosing, times, routes), lab results, daily schedule, education, provider pictures/roles, and the ability to send secure-messages to hospital providers (Figure). Qualitative content analysis of interview transcripts was performed in an iterative process.

Results: All but one parent used the portal, with an average use of two logins/day/parent. All reported benefits, such as: checking medications to ensure accuracy, viewing lab results in preparation for rounds and using the schedule to feel more in control of their child's care. No parent sent a secure-message using the portal; many stated they would rather speak face-to-face with hospital providers. All but one parent felt comfortable potentially receiving lab results through the portal before their child's provider. Many were willing to use the portal to answer admission questions, report care satisfaction and/or give hospital feedback upon discharge. Parents were also interested in accessing daily physician notes using the portal for reasons such as: improving care plan recollection and understanding, ensuring documentation accuracy, and communicating with and/or handing off care to other family members.

Conclusions: Parent participants were very positive about using a portal to receive real-time information about their child's hospitalization. Parents were enthusiastic about accessing physician notes through the portal, but were less interested in using secure-messaging to communicate with hospital providers. Results suggest portals may play a role in engaging parents in the identification of medical errors and improving the quality and safety of hospital care.

CAFFEINE EFFECTS ON HYPEROXIA-ALTERED EXPRESSION OF EPITHELIAL-MESENCHYMAL TRANSITION (EMT) GENES IN LUNG ALVEOLAR EPITHELIAL CELLS (AEC)

***Wenxiang Luo**; Bikash R. Pattnaik; De-Ann M. Pillers*

Background: Caffeine is a medication routinely prescribed to treat apnea of prematurity. However, recent research has shown an association between caffeine treatment and a reduction in bronchopulmonary dysplasia (BPD). Fibrosis is an important feature in the lungs of BPD infants. EMT has been shown to contribute to pulmonary fibrosis caused by recurrent lung injury. Hyperoxia is a major causative factor of BPD. Our previous research showed that hyperoxia caused alteration in expression of EMT genes in AEC. Here we hypothesized that caffeine treatment counteracts EMT alteration caused by hyperoxia, thereby to alleviate BPD.

Objective: To determine the effects of caffeine on hyperoxia-caused alteration towards EMT in AEC.

Methods: Hyperoxia cells were incubated in 95% O2/5% CO2 whereas control cells were in room air with 5% CO2. Quantitative real-time PCR was used to measure mRNA expression in responses to hyperoxia and caffeine treatments in human A549 AEC and non-tumorigenic C10 mouse AEC. Data were analyzed by ANOVA and t-test. A P vale of <0.05 was deemed significant.

Results: Experimental results showed that in human A549 cells, caffeine suppressed hyperoxia-induced expression of alpha-smooth muscle actin (alpha-SMA) and serpin peptidase inhibitor clade E member1 (SERPINEl), the two EMT Marker genes. Caffeine also reduced induction of interleukin-8 (IL-8), an inflammatory marker, but treatment with caffeine did not change hyperoxia-diminished expression of occludin (OCLN). The effects of caffeine on hyperoxia-altered expression of EMT genes were further conducted in mouse C10 cells. Caffeine reduced induction of alph-SMA and Serpinel in hyperoxia-treated C10 cells. The diminished expression of OCLN was not changed by caffeine. In C10 cells, caffeine did not affect the increased expression of IL-6, a well-known inflammatory marker. However, further experiments showed that caffeine suppressed induction of Tnfsf-18, another inflammatory gene.

Conclusions: Our results demonstrated that caffeine counteracted alterations caused by hyperoxia in transcription of EMT and inflammatory pathway genes in AEC. This could be part of the mechanism underlying the beneficial effect of caffeine on BPD. Our data also indicated that caffeine may affect various targets in multiple pathways involved in BPD, which warrants further exploration.

****PAS Poster Presentation**

ATTITUDES SURROUNDING THE SURGICAL AND MEDICAL MANAGEMENT OF NEONATES WITH SEVERE NECROTIZING ENTEROCOLITIS

*Gillian C. Pet, **Ryan M. McAdams**, Lilah Melzer, Assaf P. Oron, Adam Goldin, Patrick Javid*

Background: Recent advances in the management of pediatric short bowel syndrome (SBS) have resulted in improved long-term survival. However, there is still widespread disagreement as to whether comfort care or aggressive surgical management should be offered to neonates with impending severe SBS. Our aim was to define management strategies used by both neonatologists and pediatric surgeons and explore physician decision making for severe SBS in the neonate.

Design/Methods: Members of the American Pediatric Surgical Association and American Academy of Pediatrics Section on Neonatal-Perinatal Medicine were surveyed online. We asked whether respondents would recommend comfort care or bowel resection for infants with impending SBS and a variety of gestational ages, lengths of residual bowel, and comorbidities. Additional items evaluated respondents' capability to discuss issues surrounding SBS in the premature infant and queried opinions regarding long-term outcomes in infants with SBS.

Results: 288 neonatologists and 316 pediatric surgeons responded, for response rates of 10% and 28% respectively. Neonatologists were more likely to recommend comfort care across all scenarios ($p<0.02$). Neonatologists felt more capable of discussing comfort care ($p=0.001$) and neurodevelopmental outcomes with families ($p<0.001$), while surgeons felt more capable of discussing long-term quality of life for the child and family ($p<0.01$), long-term care needs ($p<0.001$), and the likelihood of achieving enteral autonomy ($p<0.001$). Neonatologists were more likely to answer "I don't know" when asked about the probability of a premature infant with minimal residual bowel surviving until kindergarten ($p<0.001$) and were less likely to agree that a good neurodevelopmental outcome was probable in this population ($p=0.001$).

Conclusion(s): Our results suggest that neonatologists and pediatric surgeons strongly differ in their recommendations regarding management of premature infants with impending severe SBS. Neonatologists were much more likely to recommend comfort care in this population and less likely to agree that long-term survival and good neurodevelopmental outcomes were possible. Given their complementary perspectives, it is important that both groups be involved in the decision-making process for critically ill premature infants with SBS. Interdisciplinary education on new advances in pediatric SBS may be beneficial.

****PAS Poster Presentation**

WHOLE BLOOD VOLUMES ASSOCIATED WITH MILKING INTACT AND CUT UMBILICAL CORDS IN TERM NEWBORNS

***Ryan M. McAdams**; Emily Fay; Shani Delaney*

Background: Umbilical cord milking (UCM) is a method of providing placental-to-newborn transfusion at birth that has gained popularity. Various methods of intact (I-UCM) and cut UCM (C-UCM) have been reported in the literature, including varying the cord length that is milked and the number of times the cord is milked. However, limited information is available regarding the amount of whole blood transfused to the newborn with C-UCM or I-UCM.

Objective: To compare placental transfusion whole blood volumes (BV) associated with UCM of intact and cut umbilical cords in term newborns.

Design/Methods: Women aged 18-55 years old admitted to a single tertiary care center and delivering at ≥37 weeks' gestation were assigned to receive either I-UCM or C-UCM. After delivery of the infant, the cord was clamped and cut to separate the newborn. The clamped cord underwent milking while still attached to placental circulation (I-UCM), or a segment was cut separate from the placenta prior to milking (C-UCM). To determine BV associated with I-UCM, the cord was milked 3 or 4 times prior to delivery of the placenta. To determine BV associated with C-UCM, umbilical cord segments were cut at 3 different lengths (10, 20, and 30 cm) and milked 4 times. Total BV were compared between IUCM and C-UCM. Written informed consent was obtained from all participants in this study as approved by the University of Washington Institutional Review Board.

Results: 60 women (≥ 37 weeks' gestation) met inclusion criteria. For C-UCM, total milked BV increased proportional to umbilical cord length, whereas volume/cm of umbilical cord decreased with UC length. C-UCM with 30 cm long cord segments delivered an average total BV of 24.8±4 ml or 8.0±1.3 ml/kg. With each cut umbilical cord segment length (10, 20, and 30 cm; n=10 for each length) most of the total placental transfusion BV was delivered with the 1st cord milking (90.1±11%), with 98.1±4.5% of total BV delivered after cord milking x2. Total BV was not significantly different after I-UCM x3 (n=15; 46.3 ±24.1 ml) vs x4 (n=15; 48.5 ±19.0 ml), but I-UCM x3 and x 4 was associated with increased BV compared to the 30 cm length C-UCM technique ($p<0.05$).

Conclusion(s): I-UCM (x3 or x4) provides a greater placental transfusion total BV than C-UCM. Milking the cord more than twice when using the C-UCM technique offers no advantage. Further studies are need to clarify short- and longterm outcomes associated with different UCM techniques.

ABC, 123… ASP: ANTIMICROBIAL STEWARDSHIP PROGRAM IMPLEMENTATION AT A TERTIARY CHILDREN'S HOSPITAL

***Erin McCreary**; Jodie Ritchie; Lucas Schulz; Monica Bogenschutz; James Conway; Nicole Lubcke; Joseph McBride; Jill Strayer; Josh Vanderloo; Meghann Voegeli; Sheryl Henderson*

Background: The Joint Commission (TJC) recently announced a medication management standard for antimicrobial stewardship. An effective antimicrobial stewardship program (ASP) involves a multidisciplinary team making coordinated interventions to optimize antimicrobial use and educating providers and patients. Successful programs reduce unnecessary antimicrobial use, decrease antimicrobial-associated toxicities and secondary infections, and prevent the emergence of treatment-resistant pathogens. Additionally, ASPs reduce antimicrobial drug spend, decrease rates of hospital-acquired infections and improve overall quality of care.

Purpose: The purpose of this project is to ensure compliance with TJC standard at the American Family Children's Hospital (AFCH) in order to provide the safest, most effective and judicious antimicrobial care to pediatric patients.

Methods: This project received Institutional Review Board exemption as a quality improvement initiative. A multidisciplinary ASP team, including an ID trained physician, pharmacist, and ancillary support staff was formed. A survey was sent to providers pre-ASP implementation to gather data on antimicrobial prescribing. An internal database using National Healthcare Safety Network logic was used to report antimicrobial days of therapy per 1000 patient days. The ASP team conducted prospective audit and feedback for all patients receiving antimicrobial therapy three times weekly. Clinical practice guidelines were developed to standardize treatment of neutropenic fever and antimicrobial prophylaxis for pediatric hematopoietic stem cell transplant recipients, and to facilitate IV to enteral route interchange.

Preliminary Results: A 1.0 FTE pharmacist and 0.2 FTE physician was approved. The survey was sent to 386 providers with 21.6% inpatient response rate. No respondents had major concerns regarding the initiation of an ASP. Over 60% of providers stated that correcting dosages, drug-bug mismatches, susceptibility mismatches, and de-escalation are always helpful stewardship initiatives. Fifty-one percent were mostly comfortable prescribing empiric antimicrobials, whereas only 29% were very comfortable. Twenty percent reported some level of discomfort with antimicrobial prescribing. The mean ADOT/1000PD in the pre-ASP implementation period for all antimicrobials was 648 days. Prospective audit and feedback identified 52% of the AFCH census receive antimicrobial therapy each day, with a mean daily census of 67 patients. A total of 45 interventions have been identified in a six-week period. Of these, 34 (76%) of the interventions were accepted by the primary team within 48 hours. Accepted interventions included: decreased duration of therapy (16%), dose adjustment or dose rounding (16%), de-escalation or discontinuation of antimicrobials (13%), intravenous to oral therapy (9%), drug-bug mismatch or therapy escalation (4%), or other (42%). Other interventions involved laboratory monitoring, formulation interchanges, and recommending an ID consult.

Conclusions: A recently established pediatric antimicrobial stewardship program has successfully identified several opportunities for education and intervention and is expected to decrease antimicrobial use and improve overall quality of patient care.

****PAS Platform Presentation**

A GENETIC MODEL OF PULMONARY HYPERTENSION ASSOCIATED WITH CONGENITAL DIAPHRAGMATIC HERNIA

***David McCulley;** M. Wienhold; M. Brix; X. Sun*

Background: Congenital diaphragmatic hernia (CDH) is a common and severe developmental anomaly. In addition to the diaphragm defect, infants with CDH have significant risk of mortality due to abnormal lung and pulmonary vascular development resulting in severe lung hypoplasia and pulmonary hypertension. The developmental basis for the lung defects in patients with CDH is poorly understood. Furthermore, many infants with CDH do not respond to medications that treat pulmonary hypertension. Genetic analysis in patients with CDH is now standard and there is a growing list of gene defects implicated in CDH, however the functional consequences of these genetic abnormalities and their implications for pulmonary hypertension are not clear. Recently Pre-B-Cell Leukemia (Pbx) transcription factors were found to be required for diaphragm development, however their role in lung and pulmonary vascular development has not been determined.

Objective: To study the role of Pbx transcription factors in the developing lung and pulmonary vasculature.

Design/Methods: Using a tissue specific gene deletion approach in a mouse model, we inactivated the expression of Pbx genes in the developing lung mesenchyme. We characterized the lung and pulmonary vascular defects in Pbx mutant mice at embryonic and early postnatal stages. We also analyzed the physiological effects of Pbx deletion and the downstream genetic consequences implicated in postnatal pulmonary vascular smooth muscle relaxation. Using these data we devised a pharmacological treatment approach to reverse pulmonary hypertension in Pbx mutant mice.

Results: Lung mesenchyme-specific deletion of Pbx in mice results in failure of postnatal alveologenesis and lethal pulmonary hypertension. Pulmonary hypertension in Pbx mutant mice is due to failure of normal pulmonary vascular smooth muscle relaxation after birth. Deletion of Pbx expression results in mis-regulation of multiple downstream factors that control the balance of pulmonary vascular smooth muscle contraction and relaxation. Abnormal pulmonary vascular smooth muscle contraction, pulmonary hypertension, and lethality in Pbx mutant mice were reversed by treatment with the Rho-kinase inhibitor, Y-27632.

Conclusion(s): Pbx genes are required for normal postnatal lung development and vascular smooth muscle relaxation. Analysis of the downstream effects of Pbx gene deletion led to a pharmacological strategy that reversed pulmonary hypertension and reduced mortality in this genetic model of pulmonary hypertension associated with CDH.

LONG-TERM RETINAL VASCULAR EFFECTS OF TRKB AGONIST (7,8-DHF) THERAPY AFTER NEONATAL HYPOXIC ISCHEMIC ENCEPHALOPATHY

***Olachi Mezu-Ndubuisi**; Dila Zafer; Thao Adams; Ayse Canturk; Damla Hanalioglu; Pelin Cengiz*

Objective: Hypoxia ischemia (HI) related brain injury secondary to perinatal asphyxia leads to long-term neurodevelopmental disabilities. There are no clinically effective pharmacological treatments to decrease neurological damage post-HI. Neurotrophin activation has been shown to repair retinal neurovascular diseases. We hypothesize that highly selective tyrosine kinase B receptor (TrkB) agonist, 7,8-dihydroxyflavone (7,8-DHF), rescues retinal vascular injury after neonatal HI. This study investigates the long-term effects of 7,8-DHF post-HI on the retinal vascular injury, cognitive and visual outcome.

Method: After exposing P9 mice to Vannucci's neonatal HI model, mice were randomly assigned to get phosphate buffered saline (PBS) or 7,8-DHF (5 mg/kg) i.p. daily starting from 10 mins for 7 days. In this model L retina/hemisphere is exposed to HI, while R retina/hemisphere is exposed to hypoxia only. After anesthesia, retinal imaging is done with fluorescein angiography (FA) at early (P24-L, P28-R retina) and late (P38-L, P42-R-retina) time points post-HI. Retinal artery width (RAW) and retinal vein width (RVW) were measured with MATLAB program. Mice were tested for vision and cognition at P60 using flagged MWM and NOR. ANOVA and student t-test were used for analysis.

Results: At P24 L RAW were significantly higher in 7,8-DHF treated vs. PBS-treated mice (38.66 ± 4.54µm vs. 28.40 ± 3.31µm, p=0.02) and unchanged compared to left RAW of P38 mice (p=0.09). 7,8-DHF treatment resulted in higher RAW on the L compared to R retina (38.66 ± 4.54µm vs 30.93 ± 0.79µm, p=0.013). No differences were detected in the R RAW or in RVWs among the groups.

Conclusion: These observations suggest that L RAW in PBS treated mice were smaller compared to L RAW in 7,8 DHF treated mice 2 weeks and 4 weeks post-HI. This is likely due to facilitated recovery of retinal ischemia with 7,8 DHF treatment. Further studies are underway to correlate RAW with vision and cognitive function.

SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY CORRELATES RETINAL THINNING TO RETINAL VASCULAR DEVELOPMENT IN AN IN VIVO MOUSE MODEL OF RETINOPATHY OF PREMATURITY

***Olachi Mezu-Ndubuisi**; Lauren Taylor; Jamee Schoephoerster*

Background: Retinopathy of Prematurity (ROP) is a condition of abnormal retinal vascular development affecting premature infants, exacerbated by exposure to hyperoxia due to lung immaturity. Fluorescein angiography in live anesthetized mice has been used to depict various phases (Early, Mid, Late, and Mature) of retinal vascular development (RVD). Spectral domain optical coherence tomography (SD-OCT) allows *in vivo* cross-sectional visualization of retinal structures; but retinal structural abnormalities have not been well elucidated in ROP. In this study, simultaneous *in vivo* FA and SD-OCT were used to study changes in retinal structure in the different phases of RVD.

Method: 63 mice were exposed to 77% oxygen from postnatal (P) day 7-P12 to precipitate oxygen-induced retinopathy (OIR), while 63 mice were raised in room air (RA). Simultaneous FA and SD-OCT were performed using the Micron IV retinal imaging device. Boundaries of the inner and outer retina was delineated with a semi-automated software program, and the mean total retinal thickness (TRT), inner retinal thickness (IRT), and outer retinal thickness (ORT) calculated in RA and OIR mice at progressive phases of retinal vascular development: Early (P19), Mid (P24), late (P32), and Mature (P47).

Results: At P19, the TRT was higher in RA (197.57±3.49µm, n=14) compared to OIR mice (162.66±17.75µm, n=13,p<0.001). There was no difference between the ORT in RA(94.51±1.81µm) and OIR mice (91.06±6.44µm,p=0.08), while the IRT was significantly reduced in OIR (71.60±17.14µm) compared to RA (103.07±3.47µm, P<0.0001) mice. From P19 to P24, there was no change in IRT in OIR mice (> 0.9999), while RA mice had a significant decrease in IRT (p<0.0001). The inner retinal thickness was significantly reduced in OIR (P<0.0001) and RA mice (P=0.02) going from P24 to P32, consistent with the physiologic transition in retinal vascular development going from mid to late phase. There was no change in inner retinal thickness in both OIR (P>0.9999) and RA mice (P=0.061) from P32 to P47. At P47, the IRT was still thinner in OIR compared to RA mice (P<0.0001). There was no change in ORT with increasing age from P19 up to P47 in both RA mice (P>0.5) and OIR mice (P>0.5) .

Conclusion: We have elucidated the natural progression of retinal structural changes in OIR using simultaneous *in vivo* SD-OCT and FA. Retinal thickness was significantly decreased in the OIR mice compared to room air, specifically in the inner retina with increasing postnatal age; while RA mice had preserved retinal thickness with increasing age. Our study suggests likely apoptosis or atrophy of inner in ROP, which persists into maturity despite revascularization of the capillary network. Further in vivo structural studies will aid understanding of the patho-physiology of ROP, the mechanisms of its disease progression, and aid the future correlation of structural changes to functional implications.

DIFFERENTIATING ZIKA AND DENGUE VIRUS INFECTIONS WITH A LINEAR PEPTIDE ARRAY

***Emma L. Mohr**; John C. Tan; Adam Bailey; Adam Ericson; Connor R. Buechler; Dawn M. Dudley; Christina M. Newman; Mariel S. Mohns; Meghan E. Breitbach; Laurel M. Stewart; Sarah J. Barilovits; Jigar Patel; David H. Connor*

Background: Identifying women at risk of congenital Zika virus (ZIKV) transmission is complicated by the lack of sensitive, specific, and scalable diagnostic tools. Conventional serologic assays, which are necessary to identify at-risk pregnancies in women who have already cleared viremia, cannot distinguish between ZIKV and closely related, co-endemic flaviviruses such as Dengue virus (DENV). In order to develop ZIKV-specific serologic assays, ZIKV-specific epitopes that do not cross react with DENV-specific epitopes must be identified.

Design: We utilized rhesus macaque serum from pre-ZIKV challenge, post-primary ZIKV challenge and post-secondary ZIKV challenge timepoints to identify linear B cell epitopes unique to ZIKV. We designed a high density peptide array containing peptides representing a library of multiple Flavivirus polyproteins and measured the reactivity of pre-ZIKV challenge and post-ZIKV challenge rhesus macaque sera to the peptides.

Results: We identified two linear epitopes in the ZIKV envelope glycoprotein region that demonstrate reactivity with post-ZIKV challenge sera in three animals challenged with Asian lineage ZIKV at both the post-primary challenge and post-rechallenge timepoints. The pre-ZIKV challenge sera from these animals did not react with these linear peptides. Importantly, this ZIKV-immune sera did not cross react with the corresponding peptides in the envelope glycoprotein of DENV serotypes 1, 2, 3 or 4. These unique linear epitopes may be utilized to develop diagnostic serologic assays for ZIKV infection.

DIETARY THERAPY COMPLIANCE OF OBESE CHILDREN IS IMPROVED BY USE OF SPECIALLY DESIGNED WEBSITE

***Yashoda G Naik**; Cassandra M Vanderwall; David B Allen; Jennifer Rehm*

Objectives: Success in changing lifestyle is the first step in preventing and reversing metabolic syndrome in youth. In tightly controlled settings, a low-fructose diet improves insulin resistance and hepatic steatosis. Whether fructose-restriction can be effective in the real-world setting remains unclear.

Purpose: To determine whether provision of a tailored, interactive website enhances 6-month compliance with low-fructose (LF) and standard healthy diets (SH) in obese adolescents.

Methods: Adolescents ages 11-17 years with BMI >95th%tile, were stratified by sex and ethnicity and randomized to intervention (LF) or control (SH) diets. LF diet: limit fructose to < 25 grams/day. SH diet: standard healthy diet. Adolescents and adult guardians were instructed to log in weekly to a healthy eating website to view daily dietary tips, recipes, blog entries, discussion groups and LF and SH diet resources and to complete a food frequency questionnaire. A registered dietitian assessed compliance at baseline and 6 months using 24-hour recall. Primary outcome measure was percentage of subjects who met dietary goals. Web usage was measured by page hits for each login over the course of the study.

Results: Twenty subjects (8 LF, 12 SH) completed the study. No significant difference in BMI change between LF and SH. The LF group demonstrated both improved dietary compliance and higher overall web use (Table 1). Website usage was higher in those who met dietary goals, but decreased over time. (Fig 1a, 1b).

Conclusions: Provision and usage of an interactive healthy eating website improved long-term compliance with dietary recommendations, particularly when subjects who were asked to follow a difficult intervention such a LF diet. However, while the LF group had a higher compliance rate, this group also had higher drop out. Family participation had significant impact on both the web use as well as compliance. These findings suggest that provision of an interactive website may be a helpful addition to institution of long-term lifestyle-altering diets in adolescents.

Characteristics and Web Use in Study Subjects

	Control	Intervention
Age (years)	14.3 (11.5-16.5)	14.2 (11.7-16.7)
Sex (% Female)	66%	88%
Average change in BMI-Z score over 6 months	-0.1	-0.1
Met Dietary Goal (%)	58%	75%
Average Child Total Web Use (# Hits Over 6 months)	97.1	270.1
Average Parent Total Web Use (# Hits Over 6 months)	87.6	191.6

Table 1: There was no statistical difference in age, BMI change or overall web use between intervention and control groups. Sex was statistically different between groups.

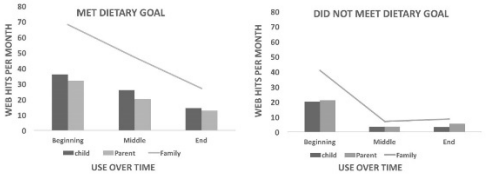

Figure 1: In both the intervention and control groups, average website use by individual subjects, parents and combined (family) was higher compared to website use in subjects that did not meet their dietary goal.

****PAS Workshop**

ACCELERATING MEDICAL EDUCATION SCHOLARSHIP: FROM IDEA TO PUBLICATION

Caroline Paul*; Jean Petershack; Margarita Vasquez; Janet Fischel; Su-Ting Li; Janet Serwint; Erika Abramson; Patti Hicks; Meghan Treitz; Tai Lockspeiser; Mary Rocha; Heather McPhillips; Jennifer Trainor; Amy Quinn*

Description: Producing scholarship from educational research is important for academic pediatricians. This workshop is designed to advance participant knowledge and skills in producing quality educational research and scholarship. Presenters will begin with a review of Boyer's and Glassick's conceptual models of scholarship and discuss the value of contextualizing the research question in a theoretical framework. Participants are strongly encouraged to bring with them a project idea (at any level of development). Using an educational scholarship planning tool and guidance from expert facilitators, participants will further develop their idea. Presenters will review the components of a SMART (Specific, Measurable, Achievable, Relevant and Timely) research question and the strategies of an effective literature review. In small groups with peers and facilitators, participants will use these concepts to refine their research question and convert that question into a set of specific aims. Workshop leaders will then review both quantitative and qualitative study designs and present strategies for choosing a study design to match specific aims. Working again in small groups, participants identify study designs and outcome variables best suited to their individual project and obtain feedback on project proposals from peers and facilitators. The workshop will conclude with specific examples for dissemination of scholarship including alternatives to traditional journals. Participants will leave this workshop with a completed planning worksheet for their project, resources including a primer on common study designs and basic statistics used in educational research, and annotated references. Trainees at all levels as well as faculty are welcome regardless of prior experience conducting educational scholarship.

****PAS Workshop**

COLLECTING VALIDITY EVIDENCE: A HANDS-ON WORKSHOP FOR YOUR INSTRUMENT OF CHOICE

Caroline Paul*; Mary Rocha; Gary Beck Dallagan; Amal Khidir; Jean Petershack; Pattie Quigly; Teejay Jirasevijinda; Jan Hanson*

Description: Many medical educators lack the skillset to develop or select instruments with validity evidence. This hands-on interactive workshop will equip participants with the skills needed for a systematic approach to demonstrate evidence of validity. Participants will apply these concepts to evaluating a pre-existing instrument or designing an instrument of their own. The workshop provides an overview of validity as defined by Messick (1989) and the APA Standards (2014) and then offers a novel conceptual model to make the abstract nature of validity more accessible to participants. Numerous examples of validity evidence in selected domains are presented. Participants will work individually and in pairs to clarify the construct for their instrument. Then, consequences of validity evidence will be highlighted to the participants before they embark on a highly interactive series of mini-didactics followed by individual work and pair-sharing. After each mini-didactic, participants will use a developed worksheet to outline specific steps to collect validity evidence in the corresponding domain for their selected instrument. Expert facilitators will consult closely with participants during these exercises. The session concludes with a report out to the large group, a summary of pearls from the audience, and anticipated next steps. Participants should bring a pre-existing instrument or an idea for an instrument they would like to develop. The instrument may be currently in use or intended for future use. By the end of this workshop, participants will take home a step-by-step guide on collecting validity evidence for an instrument and will gain skills to further develop and appraise an instrument for validity evidence to take back to their own institutions for implementation.

****PAS Platform Presentation**

TOLL-LIKE RECEPTOR 1 (TLR1) SNPS N248S, H305L AND S602I ASSOCIATE WITH PRETERM BIRTH IN WISCONSIN INFANTS

*Wenxiang Luo, S. Tokarz, **De-Ann Pillers;** Tarjani Ranade; Jens Eickhoff; Mei Baker; Bikash Pattnaik*

Background: Preterm birth (PTB) occurs in 11% of US births, causing significant morbidity and mortality. A subset of PTB occurs in pregnancies complicated by infection. The first line of defense against infection is the innate immune system via the Toll-like receptor (TLR). Activation of TLRs by pathogens initiates an inflammation cascade of signaling moieties and cytokines. Genetic variation in these pathways leads to diseases with chronic and deregulated inflammation. Inflammation is known to be associated with preterm birth, and TLR single nucleotide polymorphism (SNP) alterations have been described. We have previously reported results for SNPs in three TLRs (1, 2, and 4) in Wisconsin infants, with only TLR1 SNP rs4986791 (N248S) associated with preterm birth.Objective: TLR1 had not been associated with PTB previously, so we sought to validate our results with additional SNPs in discrete gene positions. We hypothesized that SNPs rs3923647 (H305L) and rs5743618 (S602I) would similarly mark an increased risk for preterm birth, and that the combined effects of TLR1 SNPs (N248S, H305L and S602I) may provide clarity regarding the importance of an association of TLR1 with **PTB.Design/Methods:** Residual newborn screening DNA from Wisconsin infants of gestational ages (GA) 23-42 wks was tested with IRB approval. 3000 samples were used for TLR1 SNP N248S analysis, with 1616 and 1176 samples adequate for subsequent H305L and S602I testing, respectively. SNP genotype was by TaqMan SNP Genotyping Assay (Lifetechnologies, CA). Ancestral background was by maternal declaration.

Results: The H305L minor allele T associated with PTB: gestational age (GA) < 34 wks, Odds Ratio (OR) 1.62 (P = 0.0002522); GA< 28 wks, OR 1.56 (P = 0.0023896). The S602I minor allele T also associated with PTB: GA< 34 wks, OR 1.72 (P<0.00000001); GA< 37 wks, OR 1.34 (P= 0.0004450). The minor allele combined effects of 305 (T) and 248 (C) showed a significant association with PTB (GA < 34 and <28 wks) (P < 0.00004), as well as low birth weight (< 1250g) (P < 0.0000015). The combined effects were most prominent in the Wisconsin Black cohort (GA<34 wks; OR for Whites is 1.81 vs. 3.27 for Blacks). SNP 305 heterozygotes were under-represented, but also favored an association with PTB.

Conclusion(s): TLR1 SNPs support an association with PTB in a Wisconsin cohort. TLR1 is part of a tightly linked cluster of TLR genes that act as co-receptors with TLR2, a key step in the inflammation cascade. Aberrant TLR1 may lead to PTB via an altered inflammation response.

EFFECT OF SEX AND PUBERTY ON MANNITOL AIRWAY RESPONSIVENESS

***Sima Ramratnam**; Robert Lemanske, Jr.; Ronad Sorkness, Victoria Rajamanickam, James Gern, Daniel Jackson*

Rationale: Airway hyperresponsiveness is associated with the presence of asthma. Puberty results in a shift in asthma prevalence between sexes, with post-pubertal males having a lower prevalence of asthma. Furthermore, methacholine responsiveness has been shown to decrease in pubertal boys with asthma. Our objective was to examine the association of sex and puberty on mannitol airway responsiveness in a high-risk birth cohort.

Methods: Childhood Origins of ASThma birth cohort study children were followed prospectively from birth and assessed annually. Mannitol bronchoprovocation, an indirect airway challenge test, was performed in children pre-puberty (n=144) and post-puberty (n=72). Repeated measures analysis was used to examine the relation of sex and pubertal status on mannitol airway hyperresponsiveness.

Results: Among all study children, there was a significant reduction in the rate of positive mannitol challenge post-puberty (OR=0.38, 95% CI 0.19-0.75, p=0.01). We next examined impact of sex on airway responsiveness. Post-pubertal boys had a reduced rate of positive mannitol challenge (OR=0.26, 95% CI 0.10-0.67), while girls did not have a significant reduction in mannitol responsiveness post-puberty (OR 0.7, 95% CI 0.24-1.98).

Conclusion: Our results demonstrate that there is a reduction in airway hyperresponsiveness as assessed by mannitol challenge post-puberty that appears to be most prominent in boys. This loss of responsiveness may contribute to fewer asthma symptoms among boys during this time frame.

COMBINED INHIBITION OF JAK/STAT AND BCL2 DURING EX VIVO NK CELL EXPANSION ENRICHES A HIGHLY CYTOTOXIC NK CELL SUBSET

***Katie R. Seibold**; Kirsti L. Walker; Sabrina A. Kabakov; Christian M. Capitini*

Ex vivo expansion of human NK cells with CD137L and IL-15 is being explored both preclinically and clinically as a means of increasing the number and activation of NK cells for a variety of cancers, but results to date have not shown consistent efficacy. JAK1/2 inhibition impairs NK cell maturation, activation and cytotoxicity. However, the absence or mutation of STAT1/3 molecules which are typically phosphorylated by JAK1/2 enhance NK cytotoxicity. We hypothesize that inhibition of the JAK/STAT pathway in CD137L/IL-15 activated NK cells stimulate NK cell activation and increase more potent effectors if combined with a BCL2 inhibitor. NKs were ex vivo expanded with CD137L/IL-15 for 12 days, then exposed to increasing concentrations of Ruxolitinib (0.313 - 10μM) and/or Venetoclax (6.25 - 200nM) for 24 hours before analysis. Ruxolitinib and Venetoclax enriched a CD56dim cytotoxic subset and decreased a CD56bright cytokine-producing subset in a dose-dependent manner. Ruxolitinib alone increased CD16 and CD69 expression which indicates NK cell activation. Importantly, both drugs did not induce markers associated with senescence (CD57) or exhaustion (PD-1/Tim-3) or decrease NK cell viability. Western blot analysis confirmed the inhibitory actions of Ruxolitinib on STAT1, pSTAT1, STAT3, pSTAT3 in a dose-dependent manner. However, Bcl-2 did not indicate inhibition from Venetoclax, which suggests the need to repeat the experiment with modified dosages in order to confirm the efficacy of the inhibitor. Further, cytokine levels of TNF-, TFG-, and IFN- will be analyzed via ELISA assays to identify the effects of Ruxolitinib and Venetoclax on inflammation. We expect to see both pro-inflammatory cytokines, IFN- and TNF-, decrease with treatment.

****PAS Poster Presentation**

MANAGING EATING DISORDERS ON A GENERAL PEDIATRICS UNIT: REMOTE VIDEO MONITORING PILOT

***Kristin Shadman**; Ryan Coller; Windy Smith; Daniel Sklansky*

Background: Children with eating disorders (ED) are often admitted to general care units for medical stabilization. Close surveillance, often in the form of one-to-one direct supervision, is used to reduce unwanted behaviors; however it is costly, reduces availability for other patient care, and may allow counterproductive conversations with the patient about weight, food, or exercise.

Objective: To evaluate the cost and feasibility of remote video monitoring (RVM) supervision of ED patients admitted to a general pediatric unit for medical stabilization.

Design/Methods: Beginning with the introduction of an ED clinical protocol in September 2013, this pilot retrospective cohort study assessed monitoring cost, length of stay (LOS) and days to weight gain of patients 12-17 years old admitted for medical stabilization of an ED. Prior to RVM implementation in July 2015, all patients had one-to one nursing assistant (NA) supervision. Since then RVM has been used unless a patient expressed suicidal ideation (SI). RVM staff monitored up to eight video feeds simultaneously, communicating with patients through the monitor to correct behaviors, and alerting unit nurses as necessary. Feasibility was assessed by family refusal of RVM, conversion from RVM to NA for SI, technology failure, complaints and unplanned discontinuation. Wilcoxon rank sum assessed differences in median monitoring cost, LOS, and days to weight gain for patients receiving NA vs RVM.

Results: 26 patient admissions were included (NA=16 and RVM=10). Median monitoring cost for the NA group was significantly more expensive at $4256/admission vs $542/admission for the RVM group ($p<0.001$). Median LOS was 13 days for the NA group, and 9 days for the RVM group ($p<0.01$). Median days to weight gain were 3 for both groups ($p=0.24$). No patients converted from RVM to one-to-one NA supervision. One patient with SI was converted to RVM after SI resolved. Two patients required ongoing one-to one NA supervision during post-implementation period due to continued SI. There were no reported patient complaints, technology failures or unplanned discontinuations of RVM.

Conclusions: Use of RVM in this pilot study appeared feasible and less costly, without significant difference in time to weight gain. Larger samples in multiple centers are needed to affirm RVM safety, acceptability, and efficacy.

KCNJ13 GENE AUGMENTATION THERAPY TO TREAT BLINDNESS DUE TO KIR7.1 DEFECTS

***Pawan K. Shahi**; Sabrina Stulo; Dalton J. Hermans; De-Ann M. Pillers; Bikash R. Pattnaik*

Purpose: Mutations in the KCNJ13 gene, encoding the inwardly rectifying potassium Kir7.1 ion-channel in the RPE, cause autosomal dominant snowflake vitreoretinal degeneration (SVD) and autosomal recessive Leber's congenital amaurosis (LCA16). Molecular and biophysical analysis of the mutant protein revealed a non-functional protein product. With a goal of restoring retinal function via gene augmentation therapy, we tested the efficacy of Kir7.1 channel functional rescue using an in vitro model of CHO cells expressing disease-associated mutations.

Methods: We cloned human Kir7.1-WT (wild-type) and W53X (mutant) into Flip-In^{TM} expression vector (ThermoFisher Scientific) and transfected them into Chinese Hamster Ovary (CHO) cells to express the protein products. Expression of Kir7.1 was verified through PCR and Restriction fragment length polymorphism (RFLP) analysis. Whole-cell configuration of patch-clamp technology was used to measure Kir7.1 current. Protein expression was confirmed by Western Blotting. N-terminal GFP-fused Kir7.1 wildtype was cloned into an AAV serotype 2 gene expression vector, packaged, transduced to CHO cells expressing the W53X mutant channel with a MOI of 100 for 6 hrs and analyzed within 1-2 weeks.

Results: Sequencing and RFLP analysis confirmed stable integration human Kir7.1-WT and W53X into CHO-K1 lines. We measured 9.6 ± 0.94 fold (n=10) increase in inward current on replacing the extracellular K+ with Rb+ in Kir7.1-WT expressing cells. Higher Rb+ conductivity is a known feature of the Kir7.1 channel. The W53X stable cell line, in contrast, registered only 1.84 ± 0.04 fold increase (n=9, P=3.32E-07) in Rb+ conductance, due to the truncated Kir7.1 protein. When W53X CHO cells were transduced with the AAV carrying the GFP fused functional Kir7.1 gene, a distinct Kir7.1 inward current was observed as the current was amplified 9.64 ± 3.62 fold after Rb+ treatment (n=7, P= 3.37E-08).We observed a complete recovery of membrane potential from -35 mV to -54 mV. We also visualized GFP expression on the cell membrane by confocal microscopy and identified a 70 kDa Kir7.1 protein band through Western Blot analysis.

Conclusions: We showed successful functional restoration of the Kir7.1 channel in an in vitro CHO stable cell model expressing the W53X LCA16 mutant channel. This proof-of-principle approach shows the potential of augmenting a normal gene into cells with diseases caused by KCNJ13 mutations.

****PAS Platform Presentation**

CORRELATION BETWEEN ATTENDING PHYSICIAN AND RESIDENT MEAN MILESTONES-BASED ASSESSMENT SCORES OF PEDIATRIC RESIDENTS

***Daniel Sklansky**; Grant Syverson; Melissa Cercone; Kenneth Desantes; John Frohna*

Background: Milestones-based end-of-rotation assessments by faculty may be used to help Clinical Competency Committees (CCCs) assign summative resident sub-competency milestone levels. Resident assessment of residents provides CCCs a potentially valuable source of information, especially when the numbers of attending assessments are low, although the reliability of milestones-based assessments by residents is unknown.

Aims: To determine correlation between attending assessments and 1) senior assessments of interns, and 2) intern assessments of seniors.

Methods: All residents at our institution receive end-of-rotation milestones-based assessments from faculty and residents outside of their class. Each intern and senior was assigned an aggregate mean milestone score based on weighted sub-competency assessments for the 2015-2016 academic year from residents and attendings, respectively. Second-year trainees were excluded due to having infrequent assessments by residents. Linear regression was used to analyze the relationships between attending-assessed mean milestone scores and peer-assessed mean milestone scores for the intern and senior classes.

Results: Over the 2015-16 academic year interns (n=15) had 1313 and 1693 sub-competency assessments by attendings and seniors, respectively. Seniors (n=15) had 1053 and 822 sub-competency assessments by attendings and interns, respectively. Attending and senior resident mean milestones scores of interns were strongly correlated (r2=0.70). Attending and intern assessments of senior residents were only weakly correlated (r2=0.23).

Conclusion: Senior residents may provide reliable milestones-based assessments of interns. Stronger correlation to attending assessments from seniors suggests that residents may acquire assessment skills as part of their professional development during residency. Future studies will examine assessment correlation within specific core competencies.

****PAS Poster Presentation**

THE IMPACT OF A CLINICAL PATHWAY ON THE EMERGENCY DEPARTMENT LENGTH OF STAY IN CHILDREN WITH APPENDICITIS

***Joohee Son**; Chris Ford; Michael K. Kim; Scott Hetzel*

Background: Despite the availability of advanced imaging technology and diverse diagnostic tests in the emergency department (ED), the evaluation of appendicitis remains complicated. To address this issue, appendicitis clinical pathways have been recommended to standardize and streamline the evaluation process. It has not yet been fully described whether the implementation of an ED appendicitis clinical pathway results in decreased length of stay.

Objective: To evaluate the impact of a clinical pathway on ED length of stay in patients diagnosed with appendicitis before and after the implementation of a clinical pathway.

MethodsS: A chart review was performed on all pediatric ED patients diagnosed with appendicitis (age < 18 years) at a tertiary academic pediatric emergency department before and after the implementation of an appendicitis clinical pathway. Time stamps were extracted for the following times: first MD assigned, first labs ordered, imaging ordered, antibiotics ordered, disposition determined, and ED departure. First MD assigned was used as the start of the clinical evaluation process and time intervals were calculated going forward. An adjustment period of three months was allowed after the clinical pathway was implemented. Differences in time intervals were analyzed using chi-squared test, t-test, or Wilcoxon-Rank sum test, and p-values were adjusted using the Holm-Bonfferoni method.

Results: A total of 139 patients were analyzed during the study period. There were 66 patients with a diagnosis of appendicitis before implementation of the clinical pathway (5/1/2014 – 1/31/2015) and 73 patients after the implementation (5/1/2015 – 1/31/2016). Gender proportions (62.1% vs 58.9% male) and mean ages (11.3 vs 11.5 years) were similar between the pre- and post-implementation groups. Time interval from first MD assigned to first imaging started (103 min vs 70 min, p=0.039) and time to departure (305 min vs 248 min, p=0.009) decreased from pre-implementation to post-implementation. Additionally, use of U/S increased (59.1% vs 98.6%, p<0.001) while the use of CT decreased after implementation of the clinical pathway (71.2% vs 13.7%, p<0.001).

Conclusion: The implementation of a pediatric appendicitis clinical pathway, which includes performing an ultrasound before a CT scan, resulted in significant reduction of length of stay for children diagnosed with appendicitis in the ED.

REDUCED RISK OF ATOPIC DERMATITIS IN INFANTS FROM WISCONSIN FARM VERSUS NON-FARM FAMILIES

*Matthew Keifer; Casper Bendixsen; Iris Reyes; **Christine Seroogy***

Rationale: Exposures on traditional European dairy farms reduce the risk of atopic dermatitis (AD) in young children. Whether dairy farm environments in the United States have similar effects is unknown. The Wisconsin Infant Study Cohort (WISC) in Marshfield, Wisconsin is a birth cohort with prenatal enrollment of participants stratified into dairy farm and non-farm groups. Based on European findings, we hypothesize that children born into farm families in the WISC cohort will be less likely to develop AD compared to non-farm children.

Methods: Parents reported by questionnaire if a health care provider had diagnosed the child with AD. Parents completed between 1 to 8 questionnaires at clinic visits (2, 9, 12, 18, 24 months) and phone calls (6, 15, 21 months). The target enrollment is 100 per group, and to date there are 170 subjects (farm n=73; non-farm n=97) and 686 subject visits (farm n=324; non-farm n=362). Fischer's exact test was used to evaluate group-related differences in AD.

Results: Median follow-up time was similar for the two groups (farm=13.44 months; non-farm=11.25 months). Cumulative prevalence of AD in farm subjects was 11% (n=8) and 23% (n=22) in non-farm (p<0.036). Percent of visits with current AD reported in farm subjects was 7% (n=23) and 12% (n=43) in non-farm (p<0.022).

Conclusions: Wisconsin farm children are about half as likely to develop AD during infancy compared to non-farm children. These findings suggest that environmental factors found in Wisconsin dairy farms reduce the risk of developing AD.

IMPROVING ALLOGENEIC BONE MARROW TRANSPLANT FOR OSTEOSACRCOMA USING IMMUNOCYTOKINE

***Keven J. Stonewall**; Paul D. Bates, and Christian M. Capitini*

Osteosarcoma is the most common bone tumor usually diagnosed in children and young adults. It is found in areas of bone with rapid growth. Hu14.18-IL-2 is an immunocytokine that promotes anti-tumor activity due to its ability to recognize the disialoganglioside, GD2, on expressing tumors. The objective of this project is to investigate if hu14.18-IL-2 can safely be infused after an allogeneic bone marrow transplant. BALB/C were irradiated and injected with bone marrow and T cells from C57BL/6 donors respectively on Day +0. On Day +10, the BALB/C recipients were challenged with K7M2 osteosarcoma to mimic tumor relapse. On Days +14-16, mice were treated with hu14.18-IL-2 and followed for graft versus host disease clinical scores, tumor growth, and overall survival. Tumors were also examined for GD2 expression and NK cell infiltration by immunohistochemistry. We expect that hu14.18-IL2 will be well tolerated and enhance graft-versus-tumor effects against osteosarcoma.

CORTISOL AWAKENING RESPONSE (CAR) AND FASTING MORNING CORTISOL MAKE DISCORDANT PREDICTIONS ABOUT MARKERS OF METABOLIC SYNDROME.

***Robert B Strait**; David B Allen*

Background: Chronic amplification of the hypothalamic-pituitary-adrenal axis (HPAA) from psychological stress may predispose to ectopic fat (EF) deposition and metabolic syndrome (metS). The relationship of self-reported stress, chronic HPAA activation, EF, and biochemical indicators of metS in overweight children remains unclear.

Objective: This study examines whether salivary measures of HPAA activity correlate with self-reported stress, increased EF, insulin resistance (IR), and dyslipidemia in overweight children.

Methods: Cross-sectional study of 28 ethnically diverse, pubertal (i.e. LH > 0.5 mIU/mL) girls and boys, ages 10-18 years, with BMI > 85th percentile. Exclusion criteria: chronic glucocorticoids or medication for diabetes, IR or dyslipidemia. Stress was assessed by the Perceived Stress Scale (PSS) and the Positive and Negative Affect Schedule (PANAS-C). Chronic HPAA activation was assessed by salivary fasting morning cortisol upon first waking, and by the 30-minute cortisol awakening response (CAR: rise in cortisol in the first 30 minutes after waking). MetS was assessed by HOMA-IR, fasting glucose, triglycerides, HDL and non-HDL cholesterol. EF was assessed by DXA scan.

Results: Morning waking cortisol and CAR showed no correlation with any biochemical measures of metS, with DXA measures of EF, or with subjective psychological stress as measured by PSS and PANAS-C scores.

Comparison	Correlation Coefficient (95% CI)	P-value
CAR vs. fasting morning HOMA-IR	+0.59 (-0.20 – 0.78)	0.14
CAR vs. fasting morning triglycerides	+ 0.00 (-0.66 – 0.66)	1.00
CAR vs. PANAS-C score	+ 0.11 (-0.56 – 0.69)	0.77
CAR vs. PSS score	+ 0.26 (-0.45 – 0.76)	0.48
MWC vs. fasting morning HOMA-IR	+ 0.35 (-0.41 – 0.69)	0.37
MWC vs. fasting morning triglycerides	- 0.59 (-0.89 – 0.16)	0.10
MWC vs. PANAS-C score	+ 0.16 (-0.53 – 0.72)	0.66
MWC vs. PSS score	- 0.06 (-0.66 – 0.59)	0.87

Conclusion: In overweight children, salivary CAR and salivary waking cortisol fail to show the expected correlation with markers of metabolic syndrome and with survey assessments of psychological stress. This calls into question the use of salivary cortisol measures to assess chronic stress and HPAA activation in children. Further study is needed to validate measures of perceived stress and HPAA activation in children before determining whether interventions to reduce chronic stress might reduce the risk of metS.

NEURALLY ADJUSTED VENTILATORY ASSIST WEANING OF NEONATES WITH CONGENITAL DIAPHRAGMATIC HERNIA

***Adam Szadkowski**; Michael Wilhelm; Jamie Limjoco; David McCulley; Charles Leys; Yousef Al Ali; Awni Al-Subu*

Case report: Neurally adjusted ventilator assist (NAVA) has been shown to improve synchrony by adjusting inspiratory pressures in response to the electrical activity of the diaphragm (EAdi) during mechanical ventilation. Neonates with congenital diaphragmatic hernia (CDH) are at increased risk for ventilator asynchrony and worsened respiratory function as a result, and would appear to be ideal candidates for NAVA for this reason. However, there is limited data about NAVA in this setting and potential concerns about the ability to obtain good EAdi signals. Herein we report on three cases of CDH in which NAVA was used both invasively and non-invasively. The mean gestational age was 37 weeks and 100% were males. One patient had right-sided anterior CDH, while the other two were large left-sided CDHs. All patients were intubated immediately after birth and started on SIMV pressure control. Mean time to surgery was 7 $\pm$ 1 days. All patient were repaired via open laparotomy with either a gortex patch closure or muscle flap. Patients were transitioned to invasive NAVA 15 $\pm$ 7 days post operatively as weaning was underway. EAdi signals were consistently strong with a median of 9.5 µvolts and a range of 6 -17 µvolts. The median NAVA starting level was 2.1 cm $\pm$ 1 H2O/µvolt. Patients were extubated with a NAVA range 1.1-1.6 cm H20/uvolt to noninvasive NAVA 3 + 2 days after initiation of invasive NAVA. Patients were successfully weaned to room air 9 $\pm$ 5 days after extubation. In this series, NAVA was tolerated without deleterious effects. EAdi signals were consistently strong and patients were easily transitioned from conventional pressure control ventilation strategies. The major barrier to weaning appeared to be the novelty of NAVA to staff and lack of familiarity. However, the ability to transition to non-invasive ventilation may have shortened the period of intubation. NAVA appears to be a useful mode of ventilation both invasively and non-invasively in CDH patients, particularly given the primary focus on minimizing ventilator-induced lung injury.

HIGH FLOW NASAL CANNULA IMPACT ON BRONCHIOLITIS SCORES IN THE PICU

***Adam Szadkowski**; Rhonda Yngsdal-Krenz; Michael Wilhelm*

Background: Bronchiolitis is a frequent cause of inpatient admission for children and many require PICU monitoring. Therapy for bronchiolitis is primarily supportive and high flow nasal cannula (HFNC) has recently emerged as a treatment to possibly reduce the duration and severity of disease. Little data exists to determine how to apply and wean HFNC leading to wide variability between practitioners.

Purpose: To develop a clinical score-based system for initiating, titrating and weaning HFNC in patients with bronchiolitis. Using this system we want to determine whether it is most efficient and effective to wean HFNC slowly or more rapidly in patients with bronchiolitis.

Design: A minimal risk/exemption IRB was obtained. Patients less than 2 years old with a diagnosis of bronchiolitis admitted to the PICU from Oct 2015 to March 2016 were included. Patients were scored simultaneously by PICU fellows and respiratory therapists using one of two validated clinical scoring systems. We initially used the validated Modified-Tal bronchiolitis scoring system and then switched to the Cincinnati Children's bronchiolitis WARM score, which was implemented in our ED and inpatient ward. Scores were obtained every 4 hours until patients were weaned off from HFNC. Management of HFNC was independent of score and based on attending clinical judgement. Primary outcomes included the score at each wean and discontinuation of HFNC. Secondary measures included need for escalation or resuming HFNC after being weaned off.

Findings: 21 patients with bronchiolitis were placed on HFNC. Scores had an inter-rater reliability of 83%. At initiation of HFNC, flow rates and FiO2 varied widely and were not correlated with the clinical score. There was wide variability in scores for which HFNC was weaned and/or discontinued, but 85% of the time the score was the same or lower at a wean. Of those that weaned off HFNC, no patients required escalation to HFNC or intubation within 24h.

Conclusions: Clinical application of HFNC in bronchiolitis in our PICU varied widely and was not correlated with an objective clinical scoring system. Both steady and rapid weans did not correlate with the need for restarting HFNC or adverse events.

Implications for Practice: HFNC is often used for bronchiolitis in the PICU, but its impact on the clinical severity and the duration of ICU stay is unclear. Further studies will help determine if a standardized approach using scores to guide HFNC management and weaning can decrease duration of PICU stay for bronchiolitis.

MILRINONE EFFECTS ON CONTRACTILITY IN HUMAN STEM CELL DERIVED ENGINEERED CARDIAC TISSUE

***Andrea Talukdar**; Jonathan Hernandez; Willem de Lange; J. Carter Ralphe*

Background: Milrinone, a bipyridine compound that inhibits phosphodiesterase III isoenzyme, is used to treat or prevent low cardiac output syndrome in the pediatric intensive care unit (PICU). Inhibition of PDE III increases cyclic adenosine 3',5'-monophosphate, leading to phosphorylation of calcium handling and sarcomere contractile proteins in cardiomyocytes. Animal studies demonstrate an increasing positive effect of milrinone on contractility with increasing age, with little effect on contractility seen in fetal animals. Limited studies in human pediatric patients indicate that milrinone increases cardiac output in neonates and lowers the incidence of LCOS. It is not clear whether these effects are due to reduced afterload or increased contractility. No studies have examined the direct effects of milrinone on cardiomyocyte force production in immature human myocardial tissue.

Objective: To determine the effect of milrinone on contractility and twitch kinetics in immature human cardiac tissue.

Methods: Human induced pluripotent stem cell (hiPSC) (line DF19-9-11) was differentiated using the small molecule protocol into cardiomyocytes (CM) followed by formation into a 3D engineered tissue construct (ECT) using a fibrin and Matrigel matrix. After two weeks of maturation, during which the cardiomyocytes form a compact tissue with intracellular connections, the ECTs were attached to a force transducer in a perfusion chamber with oxygenated 1.8 mM Ca^{2+} Krebs solution. Response to electrical pacing and an intact Frank-Starling relationship verified ECT suitability for further testing. The twitch force amplitude and kinetics were then recorded at frequencies of 0.25Hz-3Hz. The solution was then perfused with 1 mM isoproterenol to provide background adrenergic stimulation, and twitch force recordings repeated. Then the ECT was perfused and tested with a solution with 1 mM isoproterenol and 10 uM milrinone. The protocol was repeated with 0.6 mM Ca^{2+} Krebs solution.

Results: The total twitch force of the ECTs (n=8) was significantly increased with the addition of isoproterenol (1.590 $\pm$0.00641 mN to 1.743$\pm$0.00898 mN, $p<0.05$ ANOVA, N=8), however, there was a significant decrease with the addition of milrinone to (1.662 $\pm$0.00688 mN, $p<0.05$). The time to maximum force was decreased with isoproterenol (0.260 $\pm$0.00641ms to 0.239 $\pm$0.00898 ms, $p<0.05$) and further decreased with milrinone (0.223$\pm$0.00688 ms, $p<0.05$). The time to 50% decay in force was significantly decreased with the addition of isoproterenol (0.163$\pm$0.0160 ms to 0.123$\pm$0.0160 ms, $p<0.05$), and trended towards a further decrease with milrinone (0.112$\pm$0.0097 ms)

Conclusion: Milrinone decreases time to maximum contraction in the setting of pre-treatment with isoproterenol, but did not affect relaxation kinetics. Paradoxcally, while isoproterenol increased twitch amplitude, the addition of milrinone decreased the amplitude. These data suggest that while the beta adrenergic signalling is intact and responsive, the hiPSC CM ability to respond to milrinone is blunted and incomplete. One explanation for our lack of effect is that the hiPSC-CM ECT is more consistent with a fetal myocardium, as animal studies in the past demonstrated no inotropic effect of milrinone on fetal hearts. Further studies are needed to determine whether the lack of effect is due to properties intrinisic to the maturity of the hiPSC-CM ECT, or an artifact of the experimental protocol.

PROPAGATION MAPPING TO IMPROVE SLOW-PATHWAY VISUALIZATION IN ATRIOVENTRICULAR NODAL REENTRY TACHYCARDIA

***Amy Van Aartsen**; Jennifer Lampe; Ian Law; Nicholas Von Bergen*

Background: Voltage mapping has previously been demonstrated to allow a guided ablation of the slow pathway in atrioventricular nodal reentrant tachycardia (AVNRT). However there continues to be substantial subjectivity in the approach, and at times, voltage mapping does not adequately define the site of successful ablation. This retrospective study aimed to evaluate the use of propagation mapping used in conjunction with voltage mapping for guided ablation of AVNRT in pediatric and young adult patients.

Methods: A retrospective study evaluated all patients 30 years of age or younger who underwent voltage mapping at two institutions with AVNRT. Patients were excluded if they had congenital heart disease or inadequate voltage point density within the triangle of Koch (TK). Patient and procedural demographic were collected. The voltage map was evaluated, and data points were checked for accuracy, excluding them if they were artifact or a non-consistent atrial driven rhythm. The Propagation map was constructed utilizing these voltage points and an atrial propagation "wave collapse" was marked on the map. The location of the wave collapse, the successful lesion, and the appearance of the voltage map were evaluated.

Results: Thirty-Five patients with adequate point density for evaluation of propagation mapping were evaluated. There was success in 100% of patients with a recurrence rate of 2.8%. There were no long term complications. The median number of lesions to success was 1 (range 1-16). The age ranged from 4 to 20 years. The median fluoroscopy time was 0s, and median procedure time of 118min. There was a low voltage area present in all patients, and a wave collapse in all patients. The majority of the successful lesions were just above superior to the wave collapse within the triangle of Koch over a low voltage area.

Conclusion: This was the first study to retrospectively evaluate propagation mapping as an aid in the identification of the slow pathway for AVNRT ablation. The successful ablation site was typically a few millimeters superior to the wave collapse over a low voltage area.

SEX DIFFERENCES IN GLOBAL AND REGIONAL CARDIAC FUNCTION IN RESPONSE TO ACUTE HYPOXIA

Lauren Vildberg*; Gregory Barton; Alan McMillan; Niti Aggarwal; Kara Goss; Marlowe Eldridge*

Introduction: It is widely known that physiological differences between males and females result in differences in cardiac mass and volumes. There are conflicting results on whether differences in cardiac mass and volumes result in functional differences between males and females, with some reports suggesting increased or no difference in contractile function in females as compared to males. Moreover, very little information exists on whether cardiac sex differences exist under conditions of stress, such as hypoxia. Therefore, we hypothesized that females would demonstrate greater systolic and diastolic function during acute hypoxia. Using cardiac magnetic resonance imaging (MRI) we assessed global and regional cardiac functional response of males and females exposed to acute hypoxia.

Methods: Ten healthy pigs (5-female) (45-50kg) were anesthetized, intubated and placed on mechanical ventilation (21% oxygen). After 25 minutes of normoxic breathing the inspired gas was switched to 12% oxygen to induce a hypoxic stress for 25 minutes. Cardiac MR imaging was performed to assess global and regional differences in cardiac function during normoxia and hypoxia. MR images were analyzed to determine left ventricular (LV) and right ventricular (RV) volumes and regional LV radial velocities in the same basal, midmyocardial and apical slice from each pig.

Results: There were no differences in body weight, blood pressure or LV mass between sexes ($p > 0.05$). Other cardiac measures such as heart rate (HR), LV and RV volumes, cardiac output (CO) and fractional wall thickening were similar during normoxia ($p > 0.05$). In hypoxia, both sexes showed increases in HR, CO, apical fractional wall thickening (Fr WT) and LV ejection fraction (EF) ($p < 0.05$). A significant difference between the sexes was revealed, as females showed increased LVEF during hypoxia as compared to males (70.2 ± 2.4 vs 61.7 ± 2.6 $p = 0.039$, respectively). Additionally, radial expansion velocity at peak-filling rate (PFR) was greater in females as compared to males during normoxia (-13.1 ± 1.2 cm/s vs -10.6 ± 0.3 cm/s $p = 0.04$, respectively) and hypoxia (-13.2 ± 0.4 cm/s vs -10.3 ± 1.8 cm/s $p = 0.04$, respectively).

Discussion: No differences were seen between male and female cardiac measures in normoxic conditions. LVEF increased despite no change in LV end diastolic volume and mean arterial pressure (MAP). This increased LVEF could have been due to our finding that LV apical Fr WT increased during hypoxia. Interestingly, under hypoxia, LVEF increased to a greater extent in females as compared to males, which may be explained by the finding that basal Fr WT decreased in males during hypoxia while females showed no changes. Additionally, we found that females demonstrated greater LV radial expansion velocity at PFR as compared to males under both conditions, suggesting increased diastolic function in females. These findings suggest that females exhibit increased cardiac function under hypoxic stress. Future work using 4D flow MRI during rest and stress scenarios is likely to further elucidate sex differences in cardiac function.

OXYTOCIN RECEPTOR ONTOGENY IN THE RPE

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Purpose: We have previously localized oxytocin receptor (OXTR) to the retinal pigment epithelium and oxytocin (OXT) to the cone photoreceptors, and have shown that RPE cells exposed to oxytocin activate OXTR signaling that may modulate the function of the RPE Kir7.1 channel. To further elucidate the role of OXTR signaling in the retina, and whether it is key during eye development or at maturity, we sought to determine the ontogeny of OXTR expression in the postnatal mouse RPE.

Methods: We considered the mouse eye at birth equivalent to 25 weeks of human gestation and each day thereafter to represent a week of gestation based on published vascular development studies. C57BL6/J mice were used, with eyes obtained from newborn (p0), p5, p10 p15, p20 and adult mice (7 weeks). We adopted the simultaneous RPE isolation and RNA stabilization method previously described by Wang et al. to isolate mRNA from RPE cells. Superscript III first scribe transcription kit (Thermo-Fisher) was used to synthesize cDNA and PCR was performed using MyTaq Red Mix (Bioline) with primers designed for mouse OXTR and RPE-65 (control to verify RPE cell lineage). Following agarose gel electrophoresis relative expression in RPE was determined by comparing OXTR band intensity with RPE65 (I-OXTR/I-RPE65) using Image Studio Lite (Li-Cor Bioscience).

Results: mRNA isolated from RPE cells showed OXTR expression in 1 animal at p10 (n=4, 25%) and 3 animals at p15 (n=5, 60%) and all animals by p20 (n=5, 100%). No animal showed OXTR expression prior to p10. The average expression level was 0.06 at p10, 0.23 Â± 0.04 for p15, 0.48 ± 0.22 for p20 and 0.36 ± 0.18 for the adult mice (average ± SEM). Despite a trend towards higher expression the difference was not significant, likely as a result of the large variation in the expression levels within each time point. We investigated whether gender was predictive of expression level in adult mice but found no correlation as both genders demonstrated variable expression.

Conclusion: OXTR expression appears in some mice at a developmental stage in mice that is comparable to late gestation in the human fetus, with all mice expressing OXTR when the eye reaches developmental maturity. Combined with our previous observation of oxytocinergic inhibition of the RPE Kir7.1 channel and localization of OXT in the cone photoreceptors, we suggest that retinal OXT-OXTR signaling plays a role in communication between photoreceptors and RPE in the fully developed retina.

****PAS Platform Presentation**

STAFF EXPERIENCES WITH AND INTERPRETATIONS OF DO-NOT-RESUSCITATE ORDERS IN THE NICU

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Background: Studies of adult populations have demonstrated that do-not-resuscitate orders (DNRo) are often variably interpreted by clinical staff. DNRo are associated with increased risk of patient death, independent of other clinical factors. Experiences with and interpretations of DNRo by neonatal intensive care unit (NICU) staff remain largely unknown.

Design/Methods: This multicenter study surveyed NICU staff experiences with and interpretations of DNRo. The survey, created de novo, underwent iterative review and cognitive pretesting by a group of experts. Questions covered 3 domains: clinical experience discussing DNRo with families or caring for patients with DNRo; beliefs about meanings of DNRo relating to patient care; and prior education on this topic.

Results: Two hundred fifty-seven surveys were completed at 4 academic NICUs. Respondents were registered nurses (59%), respiratory therapists (12%), residents/fellows (11%), neonatologists (9%), and mid-level providers (7%). Forty-five percent had >10 years of clinical experience; 88% were female. Table 1 shows the frequency that respondents discussed DNRo with families or cared for patients with DNRo. Over the preceding 5-years, those who had >10 years of experience were more likely to have had discussions ($p<0.001$) or cared for patients ($p=0.003$) compared to those more junior. Prior education about discussing DNRo with families and caring for patients with DNRo varied by clinical role ($p<0.0001$ and $p=0.0001$, respectively) (Figure 1). There were no differences based on institution of practice or clinical experience. Figure 2 shows respondents' beliefs about withdrawing or withholding medical interventions from patients with DNRo, including when such actions had not been discussed with patients' families. Respondents with previous experience caring for patients for whom interventions had been withheld or withdrawn were significantly more likely to agree that withholding or withdrawing interventions without a family discussion is acceptable ($p=0.0001$ and $p<0.0001$, respectively). Other respondent demographics, including prior education, did not significantly affect these beliefs.

Conclusion(s): NICU staff have experience with DNRo, yet many lack formal education in discussing or managing DNRo. Broad interpretations of DNRo exist amongst staff, with those who have previous experiences withholding or withdrawing medical interventions for patients with DNRo believing this practice is acceptable, even in the absence of a discussion with families.

TRKB PHOSPHORYLATION MEDIATED HIPPOCAMPAL NEUROPROTECTION IS DEPENDENT ON ESTROGEN RECEPTOR ALPHA IN FEMALE HIPPOCAMPAL NEURONS AFTER IN-VITRO ISCHEMIA

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Background: Perinatal asphyxia resulting in hypoxia-ischemia (HI) related brain injury is an important cause of life-long mortality and morbidity(Fatemi, Wilson et al. 2009). Female newborn brains are relatively resistant to the detrimental effects of perinatal asphyxia while male newborn brains are more susceptible (Hill and Fitch 2012). Our recent findings reveal that 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 neonate mice through phosphorylation of the TrkB post-HI (in-vivo) (Uluc, Kendigelen et al. 2013; Cikla, Chanana et al. 2016). The observed neuroprotection appears to be related to phosphorylation of TrkB in hippocampal neurons.

Hypothesis: We hypothesize that sexually differentiated neuroprotection mediated by TrkB phosphorylation is ERα dependent in hippocampal neurons after in-vitro ischemia.

Results: Sexed hippocampal primary neurons were cultured from P1 ERα+/+ and ERα-/- C57BL/6J mice. At DIV 7, cells were treated with either normoxic media or 7,8-DHF following normoxia or OGD. Cells were stained, imaged (confocal microscopy) and analyzed (Image J) for ERα cell survival (Calcein, PI), p-TrkB and MAP-2 at 24 h REOX. ERα mRNA and aromatase expressions detected using RT-qPCR after 4 h OGD - 3 h REOX. ANOVA with a Bonferroni post-hoc test was used for analysis. OGD/REOX and OGD/REOX+7,8-DHF increased ERα mRNA expression by 2 ($p= 0.06$) and 4 ($p=0.004$) folds, respectively at 3 h REOX only in ERα+/+ female neurons. 7,8-DHF treatment significantly increases p-TrkB expression only in ERα+/+ female neurons after OGD/REOX ($p=0.0023$). OGD/REOX decreased cell survival by 30% in both ERα+/+ and ERα-/- male and female neurons ($p=0.003$) whereas, 7,8-DHF rescued cell survival up to normoxic levels only in ERα+/+ female hippocampal neurons ($p=0.048$). ANA-12 (TrkB antagonist) administration following OGD/REOX and 7,8-DHF treatment, abolished the increased ERα mRNA expression ($p=0.023$). Aromatase mRNA expression was similar among the groups ($p=0.62$) suggesting similar estradiol content. Daily administration of testosterone starting with 24 h after the preparation of neuronal culture results in decrease of Erα expression in females with expression level similar to male after OGD/REOX.

Conclusion: In conclusion, 7,8-DHF enhances neuroprotection only in ERα+/+ female hippocampal neurons following in-vitro ischemia in an ERα dependent but estradiol independent way. We will attempt to identify the expression of demethylation enzymes following in-vitro ischemia to investigate the effect of epigenetic factors on ERα expression.