19-101 (Platform)


**Allen, Kelsey,** K. Thomas Hardy, Terry Dixon, Katherine E. Twombley, Amy Wahlquist, Heidi J. Murphy

**Background:** Many patients in neonatal intensive care units (NICU) are exposed to antibiotics known to cause acute kidney injury (AKI). Antibiotic exposure may be a modifiable risk factor for renal morbidity; however, the association between exposure and development of AKI in a general NICU population is understudied.

**Objective:** Our study aims to quantify exposure to nephrotoxic antibiotics and characterize its association with AKI in a general NICU population.

**Methods Used:** Retrospective chart review of medical records from infants admitted within 48 hours of life to a single NICU between 7/1/17 and 12/31/17 that underwent >1 sepsis evaluation with antibiotic receipt. Demographic, laboratory, and clinical care data were collected. Comparisons were made between those who developed AKI (defined by neonatal, modified Kidney Intervention: Improving Global Outcomes serum creatinine-based criteria; n= 15) and those who did not develop AKI (n=146). Fisher’s exact and Wilcoxon rank sum tests were used to compare characteristics; the relationship between antibiotic exposure and AKI was examined using logistic regression models.

**Summary of Results:** Medical records of 364 infants were reviewed, 164 (45%) met inclusion criteria; 3 (<1%) infants were excluded due to lack of creatinine values. Neonates with AKI were younger, smaller, and had lower APGAR scores. Those with AKI experienced a greater number of sepsis evaluations and received more cumulative doses of antibiotics compared to infants who did not develop AKI. Univariate logistic regression analysis showed that each additional antibiotic dose was associated with a significantly higher risk of developing AKI (OR 1.053, 95% CI 1.028-1.078, p<0.0001). After adjusting for presence of patent ductus arteriosus, hypoxic ischemic encephalopathy, small for gestation age status, indomethacin or vasopressor receipt, the increased risk of AKI remained (aOR 1.045, 95% CI 1.013-1.079, p=0.006) (Table 1). When examining only doses of ampicillin, nafcillin, and gentamicin, the risk of AKI again increased with increased doses (OR 1.063, 95% CI 1.011-1.118, p=0.04).

**Conclusions:** In a general NICU population, patients who develop AKI are more premature, have lower birthweights, lower APGAR scores, experience a greater number of sepsis evaluations, and are exposed to a larger number of antibiotic doses. In this population, we observed an incremental relationship; as the number of antibiotic doses increases, the risk of AKI increases.
Utilization of Early Intervention Services among Children with Congenital Cardiac Disease

Hannah Hollon, Mary C. Kral, PhD, Andrea Boan, PhD, Jennifer Poon, MD, and Sinai Zyblewski, MD

**Background.** Congenital heart defects are the most common birth anomaly, affecting 1% of births each year in the United States (CDC, 2018). With advancements in cardiac surgery, a larger number of children born with critical heart conditions are surviving into adulthood. With this increase in survival, it is necessary to focus on long-term outcomes because research indicates that these patients show increased neurodevelopmental impairments as compared to the general pediatric population (Marino et al, 2012).

**Objectives.** To examine the relationships between utilization of early intervention (EI) services and demographic, cardiac, and neurodevelopmental variables in pediatric patients with congenital cardiac disease.

**Methods.** The sample comprised 159 children with congenital cardiac disease who were followed in the MUSC Cardiac Neurodevelopment Clinic. Demographic, medical, and neurodevelopmental data were gathered via IRB-approved retrospective medical record review. Data were analyzed by Chi square and Wilcoxon t-approximation.

**Results.** Patient characteristics appear in Table 1. There were no statistically significant group differences (i.e., patients who received EI services versus patients who did not) in terms of insurance type, two ventricle status, Norwood procedure, neurologic injury, or prolonged opiate or benzodiazepine use. Patients diagnosed with a genetic condition were 2.7 times more likely to use EI services (OR 2.67, 95% CI 1.22-5.87, p=0.0126). Patients with a history of G-tube feeding were 3.1 times more likely to use EI services (OR 3.10, 95% CI 1.55-6.22, p=0.0011). Patients who utilized EI services had significantly longer lengths of hospital stay (mean difference of 2.82±4.04, p=0.0003). There were no statistically significant group differences in terms of performance on developmental screeners (see Table 2).

**Conclusions.** Our retrospective chart review revealed that patients with greater medical complexity were more likely to utilize EI services. However, use of EI services did not differentially influence neurodevelopmental outcomes, as indicated by performance on

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**Table 1. Logistic regression models of acute kidney injury during antibiotic exposure**

<table>
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<th>HIE</th>
<th>SGA</th>
<th>Indomethacin pressor</th>
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<td></td>
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<tr>
<td>OR†</td>
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<td>95% CI</td>
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<td>1.032-1.088</td>
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**Total Doses of Ampicillin, Gentamicin, and Nafacillin**

<table>
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<th>PDA</th>
<th>HIE</th>
<th>SGA</th>
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<tr>
<td>OR†</td>
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</table>

PDA, patent ductus arteriosus; HIE, hypoxic ischemic encephalopathy; SGA, small for gestational age; Pressor, vasopressor/inotropic receipt.
†Odds ratio for each one unit increase in dose, after adjusting for SGA, HIE, PDA, and indomethacin or vasopressor/inotropic receipt.
neurodevelopmental screeners. It is likely that patients lost to follow up resulted in far fewer screenings than expected. In the future, it would be useful to study ways to increase family awareness of EI services with the results of screening tests that can identify those patients at risk for neurodevelopmental delays.

| Table 1. Patient demographic, medical, and neurodevelopmental characteristics. |
|-------------------------------------------------|-------------------|------------------|
| **Demographics characteristics**                | n (%)             |
| Gender, female                                  | 73 (45.90)        |
| Insurance type, Medicaid                        | 94 (59.10)        |
| **Cardiac characteristics**                     | Mean (SD)         |
| Gestational age, weeks                          | 37.84 (2.158)     |
| Birth weight, grams                             | 2977.68 (676.666) |
| Length of stay in ICU, weeks                    | 4.25 (3.714)      |
| Primary cardiac diagnosis:                      |                   |
| Single ventricle, ductal dependent for systemic | 59 (37.10)        |
| Single ventricle, ductal dependent for pulmonary| 61 (38.40)        |
| Single ventricle, not ductal dependent           | 6 (3.80)          |
| Two ventricle                                   | 30 (18.90)        |
| Indeterminate                                   | 1 (0.60)          |
| Primary cardiac surgery type:                   |                   |
| Norwood, Sano                                    | 29 (18.20)        |
| Norwood, modified Blalock-Taussig               | 13 (8.20)         |
| Hybrid                                          | 29 (18.20)        |
| Shunt                                           | 62 (39.00)        |
| Other                                           | 23 (14.50)        |
| Neurologic injury during hospitalization        |                   |
| Cerebrovascular accident                        | 3 (1.90)          |
| Hemorrhage                                      | 23 (14.50)        |
| Seizure(s)                                      | 2 (1.30)          |
| Multiple types                                   | 2 (1.30)          |
| None                                            | 129 (81.10)       |
| Genetic condition, yes                          | 33 (20.80)        |
| Prolonged opiate use, yes                       | 66 (41.5)         |
| Prolonged benzodiazepine use, yes               | 24 (15.10)        |
| Mode of feeding at discharge, oral              | 80 (50.30)        |
| **Neurodevelopmental characteristics**           | Mean (SD)         |
| Utilized early intervention services, yes       | 53 (33.30)        |
| PLS Auditory Comprehension (SS)                 | 92.00 (20.851)    |
| PLS Expressive Communication (SS)               | 92.45 (20.808)    |
| CAT (SS)                                        | 78.42 (25.757)    |
| CLAMS (SS)                                      | 94.50 (26.239)    |

Note: Prolonged opiate use = greater than 7 days of continuous opiate infusion necessitating Methadone; Prolonged benzodiazepine use = greater than 7 days of continuous benzodiazepine infusion necessitating Ativan; PLS = Preschool Language Scales; CAT = Clinical Adaptive Test; CLAMS = Clinical Linguistic and Auditory Milestone Scale; SS = Standard Score.
Title: Mitochondrial Dynamics Modulation Delivers Protective Effects in Organ Transplantation
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Medical University of South Carolina, Charleston, SC

Background: As semi-professional antigen-presenting cells to a recipient’s memory T-cells, microvascular endothelial cells (mECs) are central to a donor organ’s immunogenicity. Organ preservation-associated injuries increase mEC immunogenicity, leading to a cascade of immunological events and ultimately resulting in allograft rejection. Mitochondrial dynamics in the form of fusion & fission can regulate the phenotype of an immune cell and has been shown to play a role in dendritic cell differentiation, migration, and T-cell effector/memory interchange. However, whether mitochondrial fusion/fission plays any role on the immunological phenotype of mECs is unknown.

Objective: In the present study, we modulate mitochondrial fusion/fission in mECs and assess their immunophenotype and impacts on transplant outcomes in vivo. Methods: Mouse cardiac endothelial cells (MCECs) were pre-treated with M1, a fusion promoter, and Mdivi1, a fission inhibitor, before being subjected to cold storage/warm reperfusion and subsequently co-cultured with sensitized allogeneic CD8+ T-cells for 7 days. Supernatant granzyme B and interferon gamma levels were determined after co-culturing. MCEC surface expression during the first 24 hours after warm reperfusion was also evaluated. Using a murine transplant model, Balb/c donor hearts were pre-treated with M1/Mdivi1 for 3 hours, followed by heterotopic transplantation into C57BL/6 recipients, and the transplanted cardiac allografts’ survival rates were assessed.

Results: In vitro, pre-treated MCECs with M1/Mdivi1 decreased granzyme B and interferon gamma release from co-cultured allogeneic CD8+ T-cells. In addition, on MCEC surface, expression of the co-inhibitory ligand PD-L1 was increased while expression of the adhesion molecule VCAM-1 and the antigen-presenting molecule MHC-I was decreased. In vivo, pretreating donor hearts with M1/Mdivi1 significantly delays their rejection by the recipients.

Conclusions: Promoting mitochondrial fusion/inhibiting fission delivers protective effects both in vitro and in vivo in organ transplantation.

Infantile Hemangiomatosis Masquerading as Congenital Hypothyroidism

Cahill, John

Case Report: An eight-week-old premature female presented with feeding intolerance and abdominal distension relieved by intermittent bowel movements. She had been unable to
tolerate human milk fortifier and various formula trials, including elemental formula. She was otherwise well with two normal newborn screens, obtained at two and thirty days of life. Her physical exam was notable for a distended abdomen with normal bowel sounds and no organomegaly. Abdominal radiographs revealed gaseous distension throughout her gastrointestinal tract. A contrast enema was notable for redundant sigmoid colon without colonic strictures. A rectal biopsy ruled out Hirschsprung's disease. New onset mild hypothermia coupled with constipation led to a clinical concern for hypothyroidism. Screening thyroid stimulating hormone was high while free thyroxine was normal. The patient was immediately started on levothyroxine with suspected congenital hypothyroidism missed by newborn screen. A later plain film suggested hepatomegaly, and a subsequent ultrasound identified innumerable hypoechoic lesions throughout the liver concerning for hemangiomas. Her skin exam revealed numerous very small hemangiomas. Echocardiography and bronchoscopy were unremarkable. The dermatologic and ultrasound findings prompted initiation of propranolol for infantile hemangiomas (IH). Her feeding intolerance has improved and she continues to follow with endocrinology and dermatology as an outpatient.

Discussion: Infantile hemangiomas occur in roughly 5% of the population with premature infants at higher risk than term infants. Complications include ulceration, sensory impairments, congestive heart failure due to arteriovenous shunting, airway obstruction and hypothyroidism. Hypothyroidism is specifically found with diffuse hepatic IH, secondary to excess production of type 3 iodothyronine deiodinase by the hemangiomas, which catalyzes the conversion of thyroxine to reverse triiodothyronine, and triiodothyronine to 3’3’-diiodothyronine; both are biologically inactive. Despite two normal newborn screens this patient was profoundly hypothyroid most likely from widespread hepatic IH. Providers should be aware of the associations between IH and prematurity and the relationship between diffuse hepatic hemangiomas and clinical hypothyroidism.

19-105 (Poster)
Developmental origins of adult disease: Persistent adiposity, inflammation, metabolic disruption and dyslipidemia in adult offspring of Docusate treated C57BL/6 dams.

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Background: Evidence indicates that obesity can be promoted by chemical ‘obesogens’ that drive one or more processes: adiposity, hunger, inflammation or suppress metabolism. Dioctyl sodium sulfosuccinate (DOSS), a lipid emulsifier and candidate obesogen in vitro, is widely used in processed foods, cosmetics, ear drops, and as stool softener medicines (e.g. Colace/Docusate sodium) commonly used during pregnancy.

Objective: To determine whether Docusate/Colace use during pregnancy is prudent.
Methods: In vivo testing of DOSS was performed in a developmental origins of adult obesity model. Pregnant mice were orally administered vehicle control or DOSS at times and doses comparable to stool softener use during human pregnancy. All weaned offspring consumed only standard diet without DOSS up to 16 weeks of age.

Results: Adult male but not female offspring of DOSS-treated dams showed significantly increased body mass, overall and visceral fat masses, and decreased bone area, with fat mass/bone area changes consistent with a stem cell differentiation paradigm. They also exhibited significant decreases in plasma adiponectin and increases in leptin, glucose intolerance and hyperinsulinemia. Inflammatory IL-6 was elevated, as was adipose Cox2 and Nox4 gene expressions, which may be associated with promoter DNA methylation changes. Multiple significant plasma phospholipid/sterol lipid increases paralleled profiles common to long-term high-fat diet induced obesity in males.

Conclusion: Collectively, developmental DOSS exposure leads to increased adult adiposity, inflammation, metabolic disorder and dyslipidemia in offspring fed a standard diet, suggesting that pharmaceutical and other sources of DOSS taken during human pregnancy might contribute to long-term obesity-related health concerns in offspring.

19-106 (Poster)

Endothelin Receptor B Shapes Glomerular Function through Sympathetic Synapse Formation

Makita, Takako

Background: During embryonic development, the kidneys become innervated by sympathetic nerves, which ultimately control renal blood flow and glomerular filtration rate, sodium and water reabsorption, and renin release. Sympathetic nerve extends their axons along blood vessels to reach their targets, in what is called “neurovascular congruency”, but virtually nothing is known of how these axons communicate with vasculatures during establishment of functional circuitry in developing kidneys. New observations described in this study lead to the model by which endothelin signaling plays crucial roles in renal sympathetic synapse formation, and further address how sympathetic nerves influence renal glomerular morphogenesis.

Objective:
This study is to address critical role of endothelin signaling in establishment of functional sympathetic synapse at the end-organs.

Methods:
We used mouse genetic approach to generate sympathetic neuron-specific ETB (ThCre;ETB) mutant mice. Using histochemical and immunohistochemical visualization techniques, we evaluated anatomical consequences of lacking ETB expression in developing sympathetic neurons and their axons. Furthermore, we assessed renal function of sympathetic neurons-specific ETB mutant mice by measuring urine (total protein, creatinine) and serum (creatinine, BUN, albumin) chemistry.
**Results:**

$ET_B$-deficient sympathetic neurons exhibited normal projection and innervation of the kidneys. However, in the kidneys of these $ThCre; ET_B$ mutant mice, the synaptic marker synaptophysin was substantially reduced, and the lack of functional synapses resulted in dysmorphic glomeruli. We observed dysmorphic glomerular capillary endothelium which failed to sustain physical interaction with podocytes, resulting in vascular breakdown and glomerular disintegration. Urine and blood chemistry confirmed the physiological consequences of these defects.

**Conclusions:**

We found that $ET_B$ is essential for the post-guidance step of synapse formation at sympathetic nerve endings, which ultimately results in glomerular dysmorphia. This exemplifies a new mode of neurovascular congruence in which the nerve controls organ morphogenesis. This has crucial ramifications for therapeutic strategies to pediatric kidney disease.

19-107 (Poster)

**Echocardiographic Predictors of Hospital Outcomes in Preterm Neonates: A Preliminary Report**

Kirsten Graff, MD; Julie Roach Ross, MD; Kristen Morella, MPH; Shahryar Chowdhury, MD, MSCR

Background The response of the right ventricle (RV) to increased afterload likely significantly influences outcomes in preterm neonates with pulmonary hypertension. However, most studies investigating the clinical utility of echocardiography in preterm neonates with pulmonary hypertension have focused on echocardiography’s accuracy in estimating RV pressure. Fewer studies have investigated echocardiography’s ability to predict hospital outcomes in this population. Our objective was to investigate the association between measures of RV function and hospital outcomes in preterm neonates with pulmonary hypertension. We hypothesized that measures of RV function, and not estimates of RV pressure, would be associated with hospital outcomes in this population.

Methods We retrospectively identified premature neonates (<37 weeks gestational age) with a diagnosis of pulmonary hypertension born at our institution or transferred within 48 hours of life. Patients with a major congenital abnormality or with congenital heart disease other than a patent ductus arteriosus were excluded. Patients’ initial echocardiograms were identified. Two-dimensional measures of ventricular size and function, spectral and tissue Doppler measures, and measures of pulmonary hypertension severity were assessed. Our primary outcome was in-hospital mortality or need for extracorporeal membrane oxygenation (ECMO). Secondary outcomes included ventilator days and hospital length of stay.

Results A total of 39 total patients were assessed, 20 males and 19 females. Six patients (15.4%) had the primary outcome of ECMO or death. There was no difference in sex, gestational age, race or ethnicity between the infants who lived and those who went on to ECMO or death. Patients who reached the primary outcome had a lower median birth weight [680 (IQR 628, 810) versus 547 (IQR 451, 659) grams, $p = 0.011$] and lower TV inflow doppler A [53 (IQR 44, 69) versus 42 (IQR 24, 50) $p = 0.047$] between the groups. In univariable logistic regression analysis, only birth weight ($p = 0.03$) was associated with ECMO or death. No echocardiographic variables of right ventricular function or pulmonary hypertension severity were associated with the primary outcome. In terms of secondary outcomes, days on the ventilator was correlated with gestational age ($p = 0.006$) and tricuspid annular systolic plane
excursion (p = 0.038). There were no echocardiographic associations with hospital length of stay.

Conclusion The preliminary results of our study suggest that commonly used echocardiographic parameters of right ventricular function and estimates of pulmonary hypertension severity have no significant association with in hospital morbidity and mortality in the preterm neonatal population. These findings support continued research into novel echocardiographic measures that may predict outcomes in preterm neonates with pulmonary hypertension at high risk for morbidity and mortality.

**DIFFERENCES IN ECHOCARDIOGRAPHIC MEASURES**

19-108 (Poster)

**Generation of a new mouse to model pancreatic cancer-induced cachexia**

**Erin, Talbert**, Maria C. Cuitiño, Gustavo W. Leone, Cynthia D. Timmers, Daniel S. Eiferman, David C. Evans, Mary E. Dillhoff, Carl R. Schmidt, Denis C. Guttridge

Cachexia is a wasting syndrome that occurs in patients with chronic illnesses and is characterized by pronounced loss of skeletal muscle and adipose tissue. In cancer patients, cachexia associates with increased morbidity and mortality and decreased treatment tolerance. Although advances have been made in understanding the mechanisms of tumor-induced tissue loss, two recent unsuccessful Phase III clinical trials suggest that gaps remain in translating pre-clinical findings to the clinic. The reasons for these gaps are being evaluated, but one possibility may be the limitations of current animal models to recapitulate the etiology of human cancer-induced wasting.

To address this concern, we engineered a genetic mouse model of cancer cachexia based on
pancreatic cancer patients who commonly suffer from weight and muscle loss. We called this model the KPP mouse, because of the postnatal induction of the oncogene Kras and depletion of the tumor suppressor Pten specifically in the pancreas. KPP mice progressively lose skeletal muscle and adipose mass as a consequence of their tumors. Fiber typing demonstrated that muscle wasting resulted from specific atrophy of glycolytic Type IIB/IIX muscle fibers. Functionally, KPP mice exhibited decreased total muscle force production, but maintained specific force. Although KPP mice exhibited defects in muscle regeneration similar to the common C-26 and LLC mouse models of cachexia, they only expressed modest changes in the ubiquitin proteasome and autophagy pathways, which is more similar to muscle from cachectic pancreatic cancer patients. Globally, we found that muscle from KPP mice exhibits a gene expression pattern that more closely resembles muscles from cachectic pancreatic cancer patients. We envision that KPP mice will be a useful resource in advancing our mechanistic understanding of cancer cachexia as well as in identifying more effective anti-cachexia therapies.

19-109 (Poster)

Biomarkers of Calcium Homeostasis at Birth and Primary Tooth Opacities

S.G. Reed, C.S. Miller, A.B. Lawson, B.W. Hollis, C.L. Wagner

Objective:
To assess the relationship of biomarkers for calcium homeostasis from cord blood samples and enamel opacities (OP) of the primary maxillary central incisor teeth.

Methods:
Secondary analyses were conducted using longitudinal data from a randomized controlled trial of maternal prenatal vitamin D3, birth data and dental data from a follow-up study of the children. OP was scored for each of the incisal, middle and cervical facial regions of the 2 teeth using the Enamel Defects Index. Key biological covariates of calcium homeostasis were assayed from cord blood and included hormones 1,25-dihydroxyvitamin D (1,25(OH)2D), 25(OH)D precursor to 1,25(OH)2D; and parathyroid hormone (iPTH); and calcium (Ca) and phosphorus (P).

Results:
Of the 144 children, 45 (31%) had opacities. For the binary outcome of child OP, the logistic regression model, adjusted for median maternal serum 25(OH)D during pregnancy, showed a statistically significant 5% decrease in odds of OP for each pg/mL 1,25(OH)2D increase. Results for 25(OH)D, iPTH, Ca, and P were not significant (NS). For OP extent scores, 10 children had OP=1 region, 31 children OP>1, and 4 children were excluded for missing data. Opacities were evenly distributed amongst regions and teeth. Using OP extent score as the outcome, the truncated Poisson regression model, adjusted for median maternal serum 25(OH)D during pregnancy, showed statistical significance for a 6% decrease in number of expected regions of OP for each pg/mL 1,25(OH)2D increase; a 58% increase of OP for each mg/dL Ca increase; and a 30% decrease in number of expected regions of OP for each mg/dL P increase. Results were not adjusted for scales of units. Results for 25(OH)D and iPTH were NS.
Conclusions:
Preliminary results support additional longitudinal studies specifically designed with a focus on factors during pregnancy, at birth and early infancy for OP to contribute to the frontier of knowledge regarding sound tooth development.

Support funding Agency/Grant Number – Abstracts: Thrasher Research Fund, AADR Student Research Fellowship, NIH Grant Awards R03 DE025082, R01 HD043921, T35 DE007337, P20 RR017696, P30 GM103331, UL1 TR000062, UL1 TR001450, UL1 RR029882

Financial Interest Disclosure: Dr. Hollis had previous support from DiaSorin Inc. for serving as an academic consultant.

19-110 (Poster)
Dexamethasone Alters Tracheal Aspirate T-cell Phenotype in Ventilated Preterm Infants
Pediatrics-Neonatology and *Otolaryngology, Medical University of South Carolina, Charleston, SC, United States

Introduction
Postnatal corticosteroids are used in preterm infants with bronchopulmonary dysplasia (BPD) to improve respiratory status and facilitate weaning of respiratory support. Corticosteroids have anti-inflammatory effects and alter immune responses that may explain their benefits in ventilator-dependent preterm infants. We previously demonstrated that T-cells are present in the tracheal aspirates (TA) of ventilated preterm infants. We hypothesized that postnatal dexamethasone (dex) would not only reduce respiratory severity score (RSS), but also alter expression of T-cell surface markers in ventilated preterm infants.

Methods
TA samples were collected from a convenience sample of preterm infants born between 23 0/7 weeks and 28 6/7 weeks who were mechanically ventilated. Institutional Review Board approval and informed consent were obtained prior to collection. Samples were obtained during routine or clinically-indicated suctioning by the bedside nurse or respiratory therapist. Initially, samples were obtained for a nonsteroid-related study. Retrospectively, we identified infants who received dex clinically for respiratory management. Infants were included if they had a TA sample obtained within 72 hours of the start of a ten-day dex course and a subsequent TA sample within 72 hours after dex initiation. Infants were excluded if they had received previous steroids in the prior 14 days. Immune cell phenotyping was conducted by intracellular immunostaining with flow cytometric analysis. Standard statistical analysis was conducted using GraphPad Prism (GraphPad Software, La Jolla, California USA).

Results
We collected samples from 43 infants, nine of whom received dex; five infants had samples meeting inclusion criteria for dex timing of samples obtained. We confirmed a significant reduction in RSS with dex treatment (p=0.05, paired t-test, data not shown) as well as a significant decrease in percent of CD4+ cells also expressing IL-6 (p =0.02, paired t-test, Figure 1), CXCR3+ cells expressing IL-2 (p <0.05, paired t-test, data not shown) and CXCR3+ cells expressing IL-6 (p <0.001, paired t-test, data not
Conclusions
Preterm infants with BPD who received dex have a reduction in RSS and altered T-cell phenotypes that may represent the beneficial anti-inflammatory effects of dex. These findings are limited by the number of patients enrolled. Increasing the sample size with a prospective collection of TA samples pre- and post-steroids to create a more homogeneous sampling will improve this study.

![Graph showing CD4+ and IL-6+ live cells.](image)

Figure 1. Five mechanically ventilated premature infants of at least 14 days of age were treated with dexamethasone to improve respiratory status. Flow cytometry was performed on tracheal aspirates taken from these infants before and after the dexamethasone course, demonstrating a significant reduction in the number of CD4+ cells expressing IL-2 (P = 0.02 by paired t-test, n=5).

19-111 (Poster)
Outcomes Using Narrow Band UVB Phototherapy for Acute Skin Graft Versus Host Disease (GVHD) in Pediatric Allogeneic Hematopoietic Stem Cell Transplant Recipients

Snyder, Alan, Lara Wine Lee, MD2, Jennifer Joi Jarosckak, MD3, Lori Burton Donahoo, MSN, APRN, CPNP3 and Michelle Hudspeth, MD3

Acute graft-versus-host-disease (aGVHD) is a significant complication of pediatric allo-BMT. Narrow band UVB (nbUVB) therapy allows targeted treatment without systemic immunosuppression, but data is limited for pediatric patients. We retrospectively reviewed the charts of all pediatric allo-BMT patients from July 1, 2007- July 1, 2018.

Seven patients (1 female, 6 male) with a median age of 12.9 years (range 3-20) received nbUVB therapy. Diagnoses included ALL (4), MDS (2), and NHL (1). Preparative regimens were TBI-based (5) or Bu/Cy (2). Donor sources included MSD (1), MUD (1), MMUD (4), and haplo (1). Three of the patients had unrelated female donors. All patients failed topical steroids prior to nbUVB. Treatment with nbUVB was initiated at a median of 48 days (range 44-77) post-BMT, requiring a median of 26 treatments (range 4-36) over a median of 11.5 weeks (range 3 - 17). One patient underwent a second trial of nbUVB due to recurrence. Complete response was
noted in 75% of the 8 total nbUVB treatment courses with a mean cumulative dose of 364.5 J·cm⁻² (range 234 - 1557). Partial response and no response each occurred in one treatment course (12.5%). Only two patients had aGVHD of other organs prior to nbUVB; however, all seven received IV/PO steroids during a portion of nbUVB treatment. Five patients remain alive without cGVHD at a median of 7 years (range 0.8-10) post-BMT. One patient with a TBI-based preparative regimen developed poikilodermatous radiation dermatitis 4 years post-BMT. No other additional treatment-related skin complications to date. Two patients developed overlap syndrome and cGVHD and died.

There is scant published data regarding nbUVB use in pediatric aGVHD treatment. These results suggest that nbUVB is a highly effective second-line therapy for treatment of pediatric cutaneous aGVHD, and further research should be completed to elucidate its efficacy.

<table>
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<th>Patient</th>
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<th>Disease</th>
<th>Prep Regimen</th>
<th>Donor</th>
<th>GYHD PPX &amp; Peak Cutaneous Stage</th>
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<th># nbUVB Sessions</th>
<th>Cumulative Joules</th>
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<td>M</td>
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<td>TBI/CY/TIHO</td>
<td>Haplo-SD</td>
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<td>2 (d)</td>
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<td>M</td>
<td>MDS</td>
<td>BUCY/ATG</td>
<td>MMUD 9/10</td>
<td>- CSA/MTX/ATG - Stage III</td>
<td>(a) 15 (b) 15</td>
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19-112 (Poster)

**Postoperative Calcium Chloride Infusions in Neonates Undergoing Cardiac Surgery**

Laura Murray, Holly Alford, BS, A. Lauren Haney, PharmD, Marc Hassid, MD, Shahryar Chowdhury, MD, Jacob Strelow, MPH, Eric M. Graham, MD, Minoo N. Kavarana, MD, FACS, Jason R. Buckley, MD

Background- Neonatal cardiac performance is highly dependent on calcium delivery to the myocardium. There has been little research on the use of calcium chloride infusions in the neonatal population to treat low cardiac output syndrome after cardiac surgery. Inotropic medications such as dopamine, epinephrine, and milrinone have long been used to support post-operative myocardial function. We hypothesized that the use of calcium chloride infusions would decrease the doses required of traditional inotropic and vasoactive medications by supporting cardiac output in this patient population.
Methods - We performed a single-institution, retrospective, cohort study. All neonates (≤30 days old) undergoing cardiac surgery from 03/01/2016 through 02/28/2018 were included. Infants who returned from the operating room on Extracorporeal Membrane Oxygenation (ECMO) were excluded. Our institution began using postoperative calcium chloride infusions in neonates undergoing cardiac surgery in January 2017. Our primary outcome was to compare the number of patients with a maximum Vasoactive Inotropic Score (VIS) >15 in the first 24 hours following surgery between those who received calcium chloride infusions and those who did not.

Results - Eighty-two patients met inclusion criteria. Forty patients received postoperative calcium infusions and 42 patients did not. Gestational age, weight at surgery, age at surgery, surgical complexity and cardiopulmonary bypass times were similar between groups. There was no difference in frequency of maximum VIS > 15 between groups. Twenty-three (56%) patients receiving calcium had a postoperative VIS > 15 compared with 27 (68%) patients not on a calcium infusion (p = 0.36). Patients receiving calcium infusions had higher ionized calcium values in the early postoperative period (1.33 vs 1.24, p = 0.01). Six-hour postoperative lactate levels were higher in the calcium infusion group (p=0.004) but were similar at 12 and 24 hours. All other postoperative hemodynamic parameters including heart rate, blood pressure, and cerebral oximetry were similar between groups at 6, 12, and 24 hours. There was a higher rate of postoperative cardiac arrest in the group that did not receive a calcium infusion (0 vs 12.2%, p = 0.03). There were no differences in postoperative length of ventilation, time to enteral feeding, hospital LOS, or operative mortality between groups.

Conclusions - This analysis failed to show that calcium chloride infusions in neonates who underwent cardiac surgery decreased exposure to other inotropic and vasoactive agents in the first 24 post-operative hours. Further study is needed to understand if calcium infusions decrease the risk of postoperative cardiac arrest.

19-113 (Poster)
C3 and C3a in Tracheal Aspirates is Associated With Successful Decannulation from Extracorporeal Membrane Oxygenation (ECMO) in Pediatric Patients: A Pilot Study

Ekta Patel, DO; Price Ward, MD; Cara Slagle, MD; S. Zaki Yazdi, MD; Dennis Delany, MD; Bethany J Wolf, PhD; Jennifer Mulligan, PhD; Rita M. Ryan, MD

Introduction: Exposure of a patient's blood to the extracorporeal membrane oxygenation (ECMO) circuit incites an inflammatory response characterized by elevated inflammatory markers in the plasma. Our objective was to identify biomarkers within tracheal aspirates (TA), rather than plasma, associated with successful decannulation, defined as improvement in heart or lung function prompting decannulation (not as part of withdrawal of support). Specifically, we aimed to determine if the inflammatory profile in TA obtained at ECMO initiation can predict successful decannulation from ECMO.

Methods: We prospectively enrolled a convenience sample of pediatric patients receiving ECMO for respiratory indications between March 1, 2016 and August 31, 2018 at a single institution. IRB approval and informed consent were obtained. Baseline samples were TA obtained prior to or within 24 hours of ECMO initiation. We quantified TA inflammatory cytokines and complement proteins, which were corrected for total protein by bicinchoninic acid assay.
The primary outcome was the association between the baseline cytokines/complement concentrations and time to successful decannulation. Analyses were conducted in R v3.5.0 using base and survival packages (R Foundation, Vienna, Austria).

Results: We analyzed tracheal aspirates from 14 ECMO patients: 11 neonatal (78.6%) and 3 pediatric (21.4%). Patients with higher C3 and C3a at baseline had a greater probability of earlier successful decannulation compared to patients with lower levels ($p=0.03$, HR: 1.03, 95% CI: 1.00-1.05 and $p=0.03$, HR: 1.04, 95% CI: 1.00-1.09, respectively, by likelihood ratio test from a cox regression model). Lower baseline levels of interleukin (IL)-6 were possibly associated with higher chance of successful decannulation earlier than those with higher levels ($p=0.05$). Kaplan-Meier “survival” curves for high versus low (above or below the median) levels of C3, C3a and IL-6 are shown (Figure) depicting time to successful decannulation. Additionally, 5 of the 14 patients enrolled had an infectious indication for requiring ECMO; total protein (0.2 mg/mL vs 8.8 mg/mL, $p=0.01$), IL-6 (474 pg/mg vs 13166 pg/mg, $p=0.01$), IL-10 (5.4 pg/mg vs 15.8 pg/mg, $p=0.02$) were all significantly higher. However, these cytokine levels did not correlate to chances of successful decannulation.

Conclusions: Our results suggested an early higher measurement of complement activation may be a useful prognostic indicator for successful decannulation from ECMO. Further studies should be conducted to better evaluate this association.

Figure: Kaplan-Meier “survival” analysis curves comparing subjects above or below the median values for C3, C3a, and IL6. Solid black lines represent the curves for subjects below the median for each cytokine and dashed black lines are for subjects above the median. Tick marks on the curves represent censoring times for the 4 subjects that did not successfully decannulated from ECMO.

19-114 (Poster)
Early Introduction of Enteral Feeds after Necrotizing Enterocolitis Decreases Recurrence or Stricture: A New Meta-Analysis
Ekta Patel, Rita M. Ryan, Dulaney A. Wilson, Aaron P. Lesher
Background
There is currently no recommendation for when to re-initiate enteral feedings after non-surgical necrotizing enterocolitis (NEC). Two prior studies (Bohnhorst 2003, Brotsci 2009) reported experiences with earlier feeding (<5 days or median 4 days) and found there was little harm and a few advantages to earlier refeeding. While our recent retrospective study (Arbra 2018) was under journal review, a meta-analysis of the two prior studies was published (Hock 2018). The present meta-analysis increases the cohort of patients by 40 patients in the earlier feeding group (<7 days) and 98 patients in the later feeding group (≥7 days).

Objective
By combining our 138 patients with the previously analyzed 91 patients, we hypothesized that earlier introduction of enteral feeds after diagnosis of non-surgical necrotizing enterocolitis would not result in an increase in NEC recurrence or stricture.

Design/Methods
A search of Cochrane, Pubmed, Scopus, Google Scholar and clinical trials.gov database was performed. The same two publications were found as well as our new publication and the recent meta-analysis. No randomized control trials (RCT) were found. An aggregate data meta-analysis was performed of the three studies now available to examine the occurrence of intestinal stricture, NEC recurrence or both (STATA, Stata Corporation, State College, TX).

Results
A total of 229 patients were available: 96 in the earlier feeding group (<5-7 days or median 4 days) and 133 in the later feeding group (≥5-7 days or median 10 days). NEC recurrence (pooled OR=0.56; 95% CI=0.19-1.60; p=0.276) or post-NEC stricture (OR=0.28; 95% CI=0.08-1.02; p=0.053) did not differ between earlier and later groups. The composite negative outcome (recurrence or stricture) showed a significant benefit (OR=0.32; 95% CI=0.13-0.78; p=0.013) to earlier refeeding (Figure). The weighted mean time to full feeds after re-initiation was significantly lower in the earlier group compared to the late group (11.0 ± 2.1 days vs. 12.9 ± 3.5, p<0.001, paired t-test).

Conclusion
There was no increase in negative outcome with earlier refeeding after NEC. In fact, earlier refeeding resulted in a significantly lower risk for the combined outcome of NEC recurrence or stricture. However, the evidence is based on three single institution retrospective studies; thus, a RCT should be performed to confirm these results.

19-115 (Platform)

Combination of Low Grade Radiation with 4-1BB Monoclonal Antibody to Target Group 3 Medulloblastoma
Presenting Author: Mohammed Alshareef, MD Arabinda Das, Mohammed Alshareef, David Cachia, Charlotte Delbarba, Jennifer Oletsky, Daniel McDonald, Samuel L Cooper, Kenneth Vanek, Joseph M. Jenrette III, Sunil J. Patel, Samuel Cheshier, Ramin Eskandari

Introduction  Group 3 Medulloblastoma (MB) subtype has the worst prognosis amongst the MB subtypes. Despite aggressive treatments, survival of patients with Group 3 MB remains below 50% over 5 years. A limitation of therapeutic success is cancer cellular mechanisms suppressing immune responses, enabling escape of detection. We previously identified tumor-associated micoglias (TAMs) as important in T-cell-excluded tumor phenotype. The goal of our study was to reprogram intratumoral TAMs to allow T-cell infiltration into Group 3 MB tumor, improving efficacy of immunotherapy. We examine the immunobiologic rationale for treating with low-dose radiation treatment (LDRT) followed by 4-1BB monoclonal antibody (mAB) treatment.

Methods  Brain tissue was obtained from patients with Group 3 MB at MUSC and Group 3 MB cell line MP1 and were implanted over the occipital bone in C57BL/J mice. We examine treatment with 1 Gy LDRT followed by 4-1BB-targeting mAB and evaluate conversion of M2 microglia into the M1 phenotype, enhancement of MB cell death in ex vivo human and mice. We evaluate post-treatment tumoral size, cell death, and survival in mice.

Results  TAMs were activated with LDRT followed by 4-1BB antibody and converted from M2-like microglia to M1-like microglia, confirmed by ELISA SPOT. Total number of TILs following treatment were significantly increased. In vivo mice models reacted similarly, with increased tumoral cell death in response to LDRT and 4-1BB mAb. There was reduction of tumor size by 60% and increased survival when compared to untreated controls. We also determined that cell death occurred within malignant tumor cells but not healthy neuronal cells following LDRT plus 4-1BB mAb treatment.

Conclusions  We propose a novel treatment using LDRT followed by 4-1BB antibody to increase TAMs activation, conversion of T-cells and result in significant increase in intra-tumoral cell death, reduction in in vivo tumor size and increased overall survival in a mouse model.

Das, Arabinda

Figure 1.
The Modified Rib Construct: An Alternative to Managing Severe Pediatric Spinal Deformity

Mohammed Alshareef, Richard Gross.

**Introduction** Conditions associated with higher complication rates while treating pediatric spinal deformity include poor bone quality, larger deformities (especially hyperkyphosis), neuromuscular and congenital scoliosis. Progressive spinal deformity in childhood leads to abnormal lung development with compromised pulmonary function and reduced life expectancy. Current methods of treatment include dual growing rods (GR), magnetically controlled GR (MCGR). In this study, we describe the basic science and clinical rationale for the usage of the 4-rib upper thoracic fixation rib construct (RC) for medically fragile children with severe deformity.

**Methods** An RC was developed by necessity in 2 cases of early onset scoliosis (EOS) with severe kyphosis and osteoporosis. We had a total of 21 medically-fragile patients with adequate follow-up, 6 died of unrelated causes, and the other 15 had >5 year follow-up (average of 86 months). Biomechanical testing of a porcine model was performed with applied kyphotic loads to compare traditional pedicle screw fixation to the RC. We then performed successful thoracic kyphosis creation on a porcine model via an anterior transthoracic approach. This was followed by posterior corrective instrumentation using the RC. Post-operative x-rays were obtained at 2 week intervals until necropsy was performed at 6 weeks. CT and histologic imaging were performed at necropsy.

**Results** With biomechanical testing, 6 pedicle screw constructs all failed at a remarkably constant deflection angle. There were no failures with the 6 rib constructs. Corrective instrumentation applied to a 25-kg pig with a fixed thoracic kyphotic deformity resulted in remodeling of the instrumented spine adjacent to the deformity. Histology was compatible with the effect of the Hueter-Volkmann law. We evaluated 21 patients with complex EOS treated with the RC and had 86-month average follow-up period. We present results for blood loss, operative time, post-operative complications, and degrees of correction for the subtypes of EOS. No complications had permanent effect on final result and none of the subjects had proximal junctional kyphosis (PJK) as a complication.

**Conclusions** The rib construct is a safe and effective method for management of severe deformity in medically fragile pediatric patients. Complications related to failure of fixation are common but treatable. There were no permanent complications and no proximal junctional kyphosis (PJK). This method can also be used to improve chin brow angle in patients with pre-existing PJK.
Efficacy of a risk stratification system for newborns with a prenatal diagnosis of congenital heart disease

Jacqueline Doyle, Shahryar M. Chowdhury, Alison Chapman, and Sinai C. Zyblewski

Background
Advancements in fetal echocardiography have improved prenatal diagnosis of complex congenital heart disease (CHD) and the identification of fetuses at risk for hemodynamic instability at birth. In January 2017, a high-risk cardiac delivery stratification system was implemented at MUSC to improve multidisciplinary delivery planning and to reduce postnatal hemodynamic instability in infants with complex CHD.
Objectives
The objective of this study was to determine if the implementation of a risk stratification system improved delivery planning and care coordination for infants with a prenatal diagnosis of d-transposition of the great arteries (d-TGA) or hypoplastic left heart syndrome (HLHS) with a restrictive or intact atrial septum (IAS). The primary outcome studied was the duration of time between birth and initial cardiac intervention. Secondary outcomes included length of stay in the pediatric cardiac intensive care unit (PCICU), total length of hospital stay, and survival to discharge.

Methods
This was a single-institution retrospective chart review. Inclusion criteria included all neonates born at MUSC with a prenatal diagnosis of d-TGA or HLHS with a restrictive or IAS between January 1, 2015 and June 30, 2018. The subjects were categorized into two groups - pre- and post-implementation of risk stratification system. Perinatal and clinical data were obtained from electronic medical records. Descriptive and comparison statistics were performed within and between the groups.

Results
There were 9 infants in the pre group and 11 infants in the post group. The average time to cardiac intervention was 111 minutes (range 103-122) in the pre group and 65 minutes (range 40-81) in the post group (p<0.01). Nine infants (100%) survived to discharge in the pre group and 8 (73%) survived to discharge in the post group (p=0.22). Average length of PCICU stay was 16 days (range 14-30) in the pre group and 17 days (range 13-20) in the post group (p=0.93). The total length of hospital stay was 22 (range 19-49) in the pre group and 27 (range 16-39) in the post group (p=0.93).

Conclusions
Implementation of a high-risk cardiac delivery stratification system decreased the time between birth and initial cardiac intervention for infants with d-TGA or HLHS with a restrictive or IAS. There was no significant difference between length of ICU stay, total length of hospital stay, or survival to discharge between the pre- and post-implementation groups. Further study is required to determine if earlier cardiac intervention improves patient morbidity.

19-118 (Poster)

RANKL Increases Resistance to TRAIL Induced Cell Death in Oral Squamous Cell Carcinoma Tumor Cells

Purushoth Ethiraj1, Yuvaraj Sambandam1, Jessica D. Hathaway-Schrader1,2, Azizul Haque3, Chad M. Novince1,2 and Sakamuri V. Reddy1*

1Dept. of Pediatrics/Endocrinology, Darby Children's Research Institute, 2Dept. of Oral Health Sciences, College of Dental Medicine, 3Department of Microbiology & Immunology and Hollings Cancer Center, Medical University of South Carolina, Charleston, SC 29425, USA.

Oral squamous cell carcinoma (OSCC) is the most common malignancy among oral cancers. OSCC has potent osteolytic activity, resulting in local bone invasion. Tumor necrosis factor
(TNF) family member, RANK ligand (RANKL) is a critical osteoclastogenic factor that resorb bone. We have recently shown that OSCC tumor cells express RANKL and the RANK receptor. We have also identified that RANKL expression is autoregulated in OSCC tumor cells. Furthermore, RANKL significantly increases OSCC tumor cell proliferation. TNF-related apoptosis inducing ligand (TRAIL) has been shown to induce apoptosis in a variety of tumor cells. However, OSCC cells are relatively resistant to TRAIL-induced apoptosis. Therefore, we hypothesized that RANKL increases resistance to TRAIL-induced cell death in OSCC tumor cells. TRAIL interacts with receptors DR4, DR5, DcR1 and DcR2. Real-time RT-PCR analysis showed high-level of DR4, DR5 and relatively low levels of DcR1 and DcR2 mRNA expression in OSCC cells. Further, SCC1 and SCC74A tumor cells stimulated with TRAIL (100 ng/ml) for 24 h showed increased levels of RANKL expression. In addition, we analyzed apoptosis in OSCC cells by labeling DNA strand breaks (TUNEL assay) by fluorescence microscopy. Interestingly, RANKL stimulation of SCC1 tumor cells treated with TRAIL showed increased resistance to TRAIL induced cell death. We further confirmed these results by analyzing apoptotic marker protein expression in OSCC tumor cells. These data suggest that blockade of RANKL expression in OSCC tumor cells may enhance the therapeutic potential of TRAIL to control OSCC tumor growth/progression.

![Immunohistochemical analysis of RANKL and RANK expression in primary human OSCC tumor and adjacent normal tissues. Immunostaining was performed using anti-RANKL & RANK antibodies.](image)

19-119 (Poster)
**Prophylactic use of Recombinant rFVIIa in Patients with Glanzmann Thrombasthenia**

**Noisette N. Laurence**, Shayla Bergmann

**Background**
Glanzmann's thrombasthenia (GT) is rare autosomal recessive disorder, consisting of a platelet surface receptor disorder of glycoprotein (GP) IIb/IIIa (integrin αIIbβ3), resulting in faulty platelet aggregation and diminished clot retraction.(1) GT may be classified by flow cytometry using monoclonal antibodies for αIIb and β3. Bleeding phenotype most commonly presents with menorrhagia, purpura, epistaxis, gingival and gastrointestinal (GI) bleeding. (2,4) Epistaxis is
particularly common in children, and may respond to compression, topical thrombin, anti-
fibrinolytics and nasal packing. Further treatment with platelet transfusion, rFVIIa and/or nasal cautery has shown success in controlling nasal hemorrhage.(1)

Objective
We present a boy with Glanzman's thrombasthenia with multiple pediatric intensive care admissions (PICU) for hemorrhagic shock secondary to severe epistaxis and GI bleeding, refractory to platelet transfusions and local control, treated with prophylactic rFVIIa. He does not qualify for bone marrow transplant.

Design/Method
A 12 yo male with GT presented in hemorrhagic shock following one day of epistaxis. Intravenous aminocaproic acid, normal saline boluses, packed red blood cell transfusions (pRBC) and platelets were administered. The patient was admitted to the PICU. Bleeding was controlled with intravenous aminocaproic acid every 6 hours, one dose of intravenous rFVIIa and nasal packing. Bilateral internal maxillary artery ligation followed. During the next 4 years, he was admitted 29 times, 10 of which were to the PICU due to hemorrhagic shock. His various bleeding presentations included combinations of epistaxis, hematemesis, melena/hematochezia and telangiectasias. Two central lines were required for management of resuscitation. As a last-ditch effort to control severe acute bleeding, we initiated prophylactic intravenous rFVIIa at 65µg/kg per day 3 times a week.

Results
Since the start of prophylactic rFVIIa, he has been admitted once in a 7-month period for an elective procedure. His severe bleeding episodes are controlled. He has not required pRBC or platelet transfusional support. There has been no thrombosis formation.

Conclusion
rFVIIa has been reported to be effective with a good safety profile in patients with GT. Unlike platelet transfusions, rFVIIa poses no infectious risk nor does it cause antibodies production to HLA and/or αIIbβ3.(2) Despite the short half-life of rVIIIa, we show significant improvement in the quality of life of our patient, supporting our prophylactic use. Our hope is data from the GT registry will contribute toward continued development of clinical "recommendations" for the management of GT using rFVIIa until a higher level of evidence may become available from randomized clinical trials.

19-120 (Poster)

High flow nasal cannula: too much flow for the floor?

Genereux M, Sims M, Wolf B, Kane I

Objectives
Children with bronchiolitis often require hospital admission for supportive care. In many hospitals, patients requiring high flow nasal cannula (HFNC) must be admitted to an intensive care unit. The purpose of our study was to evaluate whether HFNC could be safely used on the
general hospital floor. A secondary aim of the study was to determine whether clinical characteristics were different among children admitted to our ICU and our step down unit.

Methods
This is a retrospective cohort study at a tertiary children’s hospital of patients aged 1 month through 2 years admitted with bronchiolitis on either standard nasal cannula or HFNC. Incidence of adverse outcomes was defined as a medical emergency team response, code, intubation, or death.

Results
The incidence of adverse outcomes was low. There was not a significant difference in adverse outcomes between patients on HFNC compared to those conventional nasal cannula. Additionally, escalation of care was not different between groups admitted to the ICU and the step down unit, despite the variations in age and initial support.

Conclusions
While clinicians are able to identify children who need HFNC, risk stratification within that group based on gestalt may not be accurate. HFNC, when used to treat children without history of prematurity or serious cardiac or respiratory co-morbidities, is safe for use on the floor. However, further investigation involving patients with significant pre-existing conditions is
required to fully elucidate the safety profile of HFNC on the floor.

Table 1

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Table 2

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<td>White</td>
<td>9 (34.6)</td>
<td>14 (40.0)</td>
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<tr>
<td>African American</td>
<td>11 (42.3)</td>
<td>16 (45.7)</td>
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<tr>
<td>Other</td>
<td>6 (23.1)</td>
<td>5 (14.3)</td>
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<td>Sex, Male, n (%)</td>
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<td>19 (54.3)</td>
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<td>Age, Months, median (IQR)</td>
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<td>9.8 (13.6)</td>
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<td>29 (82.9)</td>
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<td>Documented Retractions, yes, n (%)</td>
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<td>33 (94.3)</td>
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<td>IV Fluids Started in ED, yes, n (%)</td>
<td>24 (92.3)</td>
<td>32 (91.4)</td>
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No difference observed in time to full oral feeds between late preterm IDM and late preterm non-IDM newborns

Harley, Kelley D., Newman, Jill C.; Taylor, Sarah N.

Background: Late preterm (LP) patients often have difficulty with oral feeding. Oral feedings may be more pronounced in the LP Infant of Diabetic Mothers, possibly due to leptin effects. Adipose tissue and the placenta produce Leptin, a hormone that plays a key role in controlling energy balance by inhibiting food intake. Leptin production in term IDM (type I exposure), has been found to be 3-4 times higher. This leads us to postulate that LP IDM have more difficulty with oral feeds than LP non-IDMs.

Hypothesis: LP IDMs have longer time to full oral feeds than LP non-IDMs.

Design/Methods: A retrospective cohort study of LP infants (34 0/7 - 36 6/7 weeks post-menstrual age) admitted to the neonatal intensive care unit at a single academic center was conducted. Data obtained from the electronic health record was compared for time until full oral feeds and initial weight gain trajectories. Time to full oral feeds was assessed using Cox Proportion regression analysis.

Results: 471 subjects (120 IDM and 351 non-IDM) were included. The two groups were similar when comparing gestational age, gender, race, NICU level of admission (II or III), length of stay and respiratory support. The IDM group had a significantly higher mean birth weight [2723g vs. 2254g; p<0.0001], a higher incidence of being LGA [27.5% vs. 2.0%; p<0.0001] and higher incidence of hypoglycemia [51.7% vs. 27.6%; p<0.0001]. Overall, LP infants in this cohort reached full oral feeds at a median of 91 hours with interquartile rage (IQR) at 40 and 218 hours. LP IDM and non-IDM did not differ in duration to obtain full oral feeds. For the LP IDM group oral feeds were reached at a median of 95 hours (IQR= 44, 225). The LP non-IDM cohort reached full oral feeds at a median of 90 hours (IQR= 39, 218). The IDM group has 0.93 (95% CI 0.75, 1.14) the hazard of the non-IDM group when comparing time to full oral feeds (p= 0.4873).
Conclusion(s): LP IDM in our cohort had higher birth weights, higher incidence of being LGA and higher incidence of hypoglycemia. There is no significant difference in time to full PO feeds between LP IDM vs. LP non-IDM. Moving forward, we will attempt to identify the underlying reason for this clinical misperception. Furthermore, we will compare initial growth trajectories for LP IDM as compared to established growth charts.

**Figure 1.** Time to Full Oral Feeds Kaplan-Meier Survival Curve

There was no difference in time to full oral feeds between late preterm IDM (LP IDM) and late preterm non-IDM (LP non-IDM) newborns

- All LP infants in this cohort reached full oral feeds at a median of 91 hours (IQR= 40, 218)
- LP IDM reached full oral feeds at a median of 95 hours (IQR= 44, 225)
- LP non-IDMs reached full oral feeds at a median of 90 hours (IQR= 39, 218)
- LP IDMs have 0.93 (95% CI 0.75, 1.14) the hazard of LP non-IDMs when comparing time to full oral feeds (p= 0.4873)

**19-122 (Poster)**

**Monitoring Tumor Drug Uptake from Thermosensitive Liposomes by in Vivo Fluorescence Imaging**

**Motamarry, Anjan**, Ayele H. Negussie, Christian Rossman, James Small, Amber Marissa Wolfe, Bradford J. Wood and Dieter Haemmerich

Background: Pediatric cancer patients treated with chemotherapeutics such as anthracyclines are at risk of developing late-term morbidities due to systemic drug exposure, and targeted delivery to tumors via drug delivery systems could reduce such toxicities. Thermosensitive liposomal doxorubicin (TSL-Dox) is a drug delivery system that rapidly releases the contained
drug in response to localized hyperthermia (HT) (>40ºC). TSL-Dox allows highly localized delivery (~10-30x local dose compared to free Dox). We hypothesized that 1) fluorescence imaging during HT could be used to visualize drug delivery in real time. 2) In vivo tumor fluorescence is predictive of tumor drug uptake. 3) The locally delivered dose can be modulated by adjusting the duration of HT.

Methods: Nude mice carrying subcutaneous tumors (Lewis lung carcinoma) were anesthetized and injected with TSL-DOX at a dose of 5mg/kg. Localized HT was induced by heating tumors for either 0, 15, 30 or 60 min by a custom-designed heating probe, heated to 50ºC, and placed on the skin above the tumors. In vivo fluorescence imaging (excitation 550 nm, emission 610 nm) was performed before, during, and for 6 min after HT. After imaging, tumors were extracted and drug uptake quantified by HPLC. Serum samples were obtained before and after the HT to analyze the pharmacokinetics of the drug.

Results: Local drug uptake could be visualized in real-time during HT, and fluorescence intensity correlated with amount of drug delivered to the tumor. Compared to unheated tumors, in vivo fluorescence of heated tumors increased by 4.6 (15min HT), 9.3 (30min HT) and 13.2 fold (60min HT). Tumor drug concentration increased by 1.9 (15min HT), 2.9 (30min HT) and 5.2 (60min HT) fold compared to tumors not exposed to HT, demonstrating the effect of HT duration on drug uptake. We also found a strong correlation ($R^2 = 0.67$) between in vivo fluorescence intensity of the target tumor area and the drug delivered.

Conclusions: We demonstrated that in vivo fluorescence imaging allows real-time monitoring of local drug delivery, and is predictive of delivered dose. Modulating the HT duration allows control of locally delivered dose.
Croup Patient Admission Following Multi-Dose Racemic Epinephrine in the Pediatric Emergency Department

Dincman, Savannah, Simpson, Annie; Saef, Steven; Price, Amanda

Background
Croup is an illness frequently encountered in the pediatric emergency department (PED). Nebulized racemic epinephrine (RE) treatments are often used to treat patients who present to the PED with stridor at rest (moderate to severe croup). Patients may remain asymptomatic after a first RE treatment or may require additional treatments. Variation exists in the management of croup patients who require two or more RE treatments in the PED.

Objective
To identify factors associated with patients who are admitted to an inpatient hospital unit after receiving two or more RE treatments for croup in the PED and to describe interventions during hospitalization.

Design/Methods
This is a retrospective observational single center study performed at a tertiary care pediatric hospital. Institutional Review Board (IRB) approval was obtained. We identified patients...
presenting to the PED from 2014 to 2017 who had a diagnosis of "croup," "stridor," or "laryngotracheobronchitis" and received two or more treatments of RE while in the PED. Bivariate analyses were completed using the Wilcoxon Two-Sample and Chi-Square tests.

Results
Of 44 patients identified, 32 (72.7%) were admitted to the hospital. Longer duration of illness prior to PED presentation was associated with inpatient hospital admission (2.0 vs 1.0 d; p < 0.05). Admission was not associated with longer length of stay in the PED, patient age, the length of time between RE doses, or severity of illness at time of PED presentation and disposition. Of patients who presented to the PED during daytime hours (n = 24, 7am-7pm), 83% were admitted vs. 60% of patients during nighttime hours (n = 20, 7pm-7am). The increased frequency of admissions during daytime approaches significance (p = 0.084). Subgroup analysis of admitted patients demonstrated 34% (n = 11) received additional RE doses while inpatient. Otherwise no additional interventions (i.e. supplemental oxygen, transfer to higher level of care, intubation) were implemented. Patients who received RE during admission had longer hospital stays (32.0 vs. 16.3 h; p < 0.01).

Conclusions
The majority of croup patients who received two or more RE treatments in the PED were admitted. In this study, the only factor associated with hospital admission was longer duration of illness. Among those admitted, RE treatment was the only inpatient intervention performed, which was associated with longer duration of hospitalization.

19-124 (Poster)

Methotrexate and Metronidazole: A Bad Combination?

Allison Uber, MD; Andrew Picca, DO; Shayla Bergmann, MD; Michelle Hudspeth, MD

Medical University of South Carolina, Charleston, South Carolina, USA

Background: High-dose (HD) methotrexate (MTX) and intrathecal (IT) methotrexate (MTX) are associated with acute leukoencephalopathy with a wide range of neurologic presentations. The risk of Clostridium difficile infection (CDI) is highest among pediatric patients with hematologic malignancies. Metronidazole is typically used as first-line treatment, but it also carries a risk of encephalopathy that is not well known among medical providers. Encephalopathy is associated with newly initiated metronidazole therapy as well as prolonged use.

Objective: Present two cases of encephalopathy after concurrent methotrexate and metronidazole administration. Increase awareness of potential metronidazole encephalopathy in a vulnerable patient population and consideration for alternative treatment for CDI.

Design/Method: Retrospective chart review.
**Results:** Case 1 is an 11 year old female with high risk B-Cell Acute Lymphoblastic Leukemia who presented with aphasia, inappropriate laughter, and excessive drooling on day 24 of Interim Maintenance I, ten days after HD MTX with delayed clearance. She also received two days of metronidazole for CDI prior to presentation. Brain MRI demonstrated areas of restricted diffusion in the bilateral posterior frontal lobes. She returned to her baseline neurologic state with supportive care approximately 48 hours after her admission and discontinuation of metronidazole. She was changed to oral vancomycin to complete CDI treatment. Case 2 is a 16 year old female with high risk B-Cell Acute Lymphoblastic Leukemia who presented with right sided weakness and slurred speech on day 23 of Interim Maintenance I, nine days after HD methotrexate and completed the metronidazole course six days prior to presentation. Brain MRI demonstrated prior known findings of unchanged periventricular leukomalacia due to history of prematurity. She returned to baseline with supportive care within 15 hours apart from minor residual right sided weakness, which persisted for approximately 36 hours.

**Conclusion:** Metronidazole induced encephalopathy is an obscure phenomenon in pediatric medicine. HD MTX and IT MTX are associated with neurotoxic events that are well reported. As metronidazole remains the recommended agent for CDI, it is important to consider it as a source of encephalopathic events for pediatric patients undergoing concurrent MTX therapies and metronidazole treatment. It is plausible to hypothesize that methotrexate and metronidazole may have a cumulative effect and potentiate neurotoxic side effects. Further, it may be appropriate to consider prioritizing use of oral vancomycin for CDI in this select patient population.

**19-125 (Poster)**

**Improved student BMI with a school-based obesity prevention initiative that targets policy, systemic and environmental changes to improve nutrition and increase physical activity**

**Key, Janice,** Martin, Coleen; Morella, Kristen

**BACKGROUND AND PURPOSE:**
Childhood obesity has more than tripled since the 1970s, such that currently 1 out of 5 children and adolescents are now obese. Underlying causes include inadequate physical activity and nutrition. To address this issue, school-based programs have been developed to make policy, systemic and environmental changes (PSE) targeting nutrition and exercise. Evaluation has found no single program is adequate but that effective school-based programs must include a combination of strategies addressing both physical activity and nutrition using the Whole School, Whole Community, Whole Child approach. However, despite recommendations, schools have been slow to implement these evidence-based programs and policies.

**DESCRIPTION:**
The Docs-Adopt© School Health Initiative was developed in 2010, based upon several community-generated pilot programs, as a method to increase school implementation of evidence-based obesity prevention / wellness PSE programs. This implementation model is unique in that it (1) recruits local physicians/health professionals to join school wellness
committees, and (2) incentivizes schools to strategically address their specific needs through selection of evidence-based programs from a wellness checklist. The online protected School Wellness Checklist© awards points for specific activities, the scores of which are used in an annual wellness contest. The Initiative has been readily and rapidly adopted by schools, spreading to now include 12 districts/communities with 193 participating schools, thereby reaching 135,000 children.

LESSONS LEARNED:
Evaluation of the Initiative has found that schools with increased implementation of PSE changes (as measured by a higher score on the School Wellness Checklist©) had lower student BMI. Student BMI data was obtained through the Fitnessgram© data for 2 school years, 2016-2017 and 2017-2018. This preliminary analysis evaluated BMI score and has not yet evaluated categories of BMI, i.e. obesity and overweight. Evaluation of BMI among schools participating in the Initiative found that those with higher checklist scores had lower student BMI, with a linear relationship between score and mean BMI. This reduction in BMI was consistent for every age group, from 5-year-old kindergarteners to seniors in high school. Overall for every 70 points higher on the checklist there was a 1-point decrease in absolute BMI value (p = 0.005).

CONCLUSIONS AND IMPLICATIONS:
This simple school-based intervention is an effective implementation model that motivates and assists schools to make many PSE changes. Use of this Initiative appears to have an impact on improving student BMI. This model may be used to promote implementation of proven programs and policies, thereby reaching a greater number of schools and more children.

SUPPORT/FUNDING SOURCE: Boeing SC, The Duke Endowment, Baldwin Foundation, Coastal Community Foundation, Pottstown Area Health and Wellness Foundation
Sources:
Ramesh, SI; et al. Medication Neurotoxicity in Children. Pediatric

19-126 (Poster)
GSNO Pre- and Post-conditioning Blocks Blood-Brain Barrier Disruption and Improves Endothelial Function in a Mouse Model of Cerebral Ischemia and Reperfusion

Inderjit Singh, Avtar K. Singh, Hamza Khan, Jasdeep S. Dhindsa, Fei Qiao, Pavan Kumar, Mushfiquddin Khan

Background: Endothelial dysfunction is a major risk factor of stroke, and stroke injury itself causes endothelial dysfunction leading to vascular dementia. Endothelial pathology following stroke blocks the mechanisms of neuroprotection and neurorepair. Aberrant endothelial nitric oxide synthase (eNOS) activity and disturbed nitric oxide (NO) metabolome are mainly responsible for endothelial dysfunction. The major NO metabolite S-nitrosoglutathione (GSNO) maintains endothelial function via S-nitrosylation and invokes neuroprotection via activation of Akt. We investigated whether exogenous administration of GSNO targets beneficial functions of eNOS-derived NO in protecting the neurovascular unit using wild-type and eNOS-deficient mouse models of stroke.

Methods: Transient cerebral ischemic injury was induced by middle cerebral artery occlusion (MCAO) for 60 minutes in male adult wild-type and eNOS-null mice. GSNO (0.1 mg/kg body weight, iv) and GSNO reductase inhibitor N6022 (5mg/kg body weight, iv) were administered 30 minutes before MCAO in pre-injury studies and at reperfusion in post-injury studies. Brain infarctions, edema, and neurobehavioral functions were evaluated 24 h after reperfusion. Akt activity was determined by western blot and immunohistochemistry.

Results: eNOS-null mice had a higher degree (p<0.05) of injury than wild-type. Pre-MCAO treatment with GSNO significantly reduced infarct volume, decreased edema and improved neurological score, and increased tactile strength in both wild-type and eNOS-null mice compared with untreated, injured animals. Post-ischemic injury GSNO treatment also significantly reduced infarct volume and improved neurological score. N6022 also had effects similar to exogenously administered GSNO.

Conclusions: Reduced brain infarction and edema, and improved neurobehavioral function by pre-injury exogenous/endogenous GSNO treatment indicate that GSNO-mediated pre-conditioning protects against IR, likely by targeting the eNOS-derived NO-dependent functions involving Akt activity. Neurovascular protection by GSNO and N6022 in both pre- and post-ischemic injury events support GSNO and/or N6022 as a promising candidate to be evaluated for prevention and protection of humans from stroke and stroke-induced dementia.

19-127 (Platform)
Role of Asymmetric Dimethyl Arginine (ADMA) in Brain Microvascular Pathology:
Potential Implication in Vascular Cognitive Impairment and Dementia

Choi, Seungho1, Carroll, Steven L.2, Singh, Avtar K.2, 3, Singh, Inderjit1, 4, *, and Won, Jeseong2, *.  
1 Department of Pediatrics and 2 Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, SC, USA.  
3 Pathology and Laboratory Medicine Service and 4 Research Service, Ralph H. Johnson Veterans Administration Medical Center, Charleston, SC, USA.  

* Corresponding authors: Inderjit Singh, Ph.D. and Jeseong Won, Ph.D.

ABSTRACT

Recently, asymmetric dimethyl arginine (ADMA) has gained attention as an endogenous nitric oxide synthase (NOS) inhibitor and risk factor and biomarker for metabolic syndrome and cardiovascular diseases. In this study, we investigated the role of ADMA in the microvascular pathology in the brain of animal model of Alzheimer’s disease (AD) with microvascular pathology (APPswDI transgenic mice: Tg-SwDI). Tg-SwDI mice showed age dependent increase in ADMA levels in the serum as well as decreased serum L-arginine levels, compared to age matched wild type controls. To investigate the role of ADMA in AD and microvascular associated brain pathologies, Tg-SwDI received daily ADMA for 6 weeks. ADMA treatment promoted loss of spatial learning and memory performance and brain Aβ40/Aβ42 deposition in Tg-SwDI mice. In addition, ADMA treatment exacerbated brain microvascular pathology in Tg-SwDI mice as observed by increased blood-brain barrier (BBB) disruption (increased Evans blue extravasation and loss of tight junction proteins ZO-1 and claudin-1), increased endothelial stress fiber marker (increased phosphorylation of myosin light chain: MLC), and decreased microvessel density. The similar observation was also made in cultured human brain microvessel endothelial cells that ADMA treatment induced endothelial cell signaling for F-actin stress fiber (nitrotyrosine production and activation of RhoA) and endothelial barrier disruption. Overall these data document the potential role of ADMA, an endogenous NOS inhibitor and uncoupler, in the brain microvascular pathology associated with AD and vascular cognitive impairment and dementia (VCID).

19-128 (Platform)

TITLE: High Risk Opioid Prescribing and Dispensing to Children 0-18 Years Old

AUTHORS: Basco, William; Zhang, Jingwen; Mauldin, Patrick; Ball, Sarah; Simpson, Kit

Purpose of Study: Previous studies demonstrated declines in overall opioid prescribing and dispensing for children, but less detail is known about high risk prescribing. This study evaluated three CDC-defined state level opioid outcomes that we considered “high risk:” a) the percentage of children receiving ≥ 90 morphine mg equivalents/day; b) the rate of patients receiving opioid prescriptions from multiple providers; and c) the percentage of extended-release opioid prescriptions dispensed to opioid-naïve children (CDC state-level opioid indicators #23, 24, and 25).

Methods Used: Using 2010-2017 South Carolina (SC) Prescription Drug Monitoring Program (PDMP) data, we identified dispensed prescriptions for opioid analgesic preparations to children 0-18 years old, excluding cough and cold opioid preparations, tramadol, and propoxyphene. We
calculated the frequency of high-risk prescribing. Measures #23 and 25 are expressed as percentages, while measure #24 is an expression of opioid prescriptions per population. The SC Dept of Health and Environmental Control and the Institutional Review Board of MUSC approved this study.

Summary of Results: Dispensing of opioid analgesics to children 0-18 decreased 32% overall from 80/1,000 children/year in 2010 to 54/1,000 children/year in 2017. Each high-risk measure declined over time. The percentage of subjects receiving ≥ 90 morphine mg equivalents/day (Measure #23) declined from 3.8% in Q1 of 2010 to 2.9% in Q4 of 2017, a 24% decline (p<0.01). For Measure #25, the percentage of subjects who received an extended-release opioid who were opioid naïve was 65.9% in Q1 of 2010, peaked at 81.8% in Q1 of 2015, and declined back to 64.6% by Q4 of 2017. Receipt of opioids from multiple providers (Measure #24) peaked at 9.59/million children/6 months in 2014, declining to 0.85/million children/6 months by 2017.

Conclusions: Among children 0-18, receipt of ≥ 90 morphine mg equivalents/day and receipt of opioids from multiple providers declined during the years 2010-2017. However, fully 2/3 of the children who received extended-release opioid analgesics were opioid naïve and should not have received extended-release products intended for opioid-tolerant individuals. In addition to reducing opioid prescribing for children overall, efforts are needed to specifically reduce high risk prescribing.

19-129 (Platform)

Regulation of endothelial barrier integrity by redox-dependent nitric oxide signaling: Implication for traumatic and inflammatory brain injuries

Seungho Choi 1, Nishant Saxena 1, Tajinder Dhammu 1, Mushfiquddin Khan 1, Avtar K. Singh 2, 3In, derjit Singh 1, 4, *, and Jeseong Won 2, *.

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* Corresponding authors: Inderjit Singh, Ph.D. and Jeseong Won, Ph.D.

Abstract:
Nitric oxide (NO) synthesized by eNOS plays a key role in regulation of endothelial barrier integrity but underlying cell signaling pathway is not fully understood at present. Here, we report opposing roles of two different redox-dependent NO metabolites; peroxynitrite (ONOO−) vs. Snitrosoglutathione (GSNO), in cell signaling pathways for endothelial barrier disruption. In cultured human brain microvessel endothelial cells (hBMVECs), thrombin induced F-actin stress fiber formation causes barrier disruption via activating eNOS. Thrombin induced eNOS activity participated in cell signaling (e.g. RhoA and calcium influx mediated phosphorylation of myosin light chain) for F-actin stress fiber formation by increasing ONOO− levels. On the other hand, thrombin had no effect on intracellular levels of S-nitrosoglutathione (GSNO), another cellular NO metabolite. However, exogenous GSNO treatment attenuated the thrombin-induced cell
signaling pathways for endothelial barrier disruption, thus suggesting the role of a shift of NO metabolism (GSNO vs. ONOO\(^-\)) toward ONOO\(^-\) synthesis in cell signaling for endothelial barrier disruption. Consistent with these *in vitro* studies, in animal models of traumatic brain injury and experimental autoimmune encephalomyelitis (EAE), ONOO\(^-\) scavenger treatment as well as GSNO treatment were effective for attenuation of BBB leakage, edema formation, and CNS infiltration of mononuclear cells. Taken together, these data document that eNOS-mediated NO production and following redox-dependent NO metabolites (ONOO\(^-\) vs. GSNO) are potential therapeutic target for CNS microvascular disease (traumatic and inflammatory) pathologies.
19-130 (Platform)

A Novel Examination of a Preterm Lung: Unexpected Predominance of Man9 N-glycan

Baatz, John, R.M. Ryan, H. Kelley, P. Ward, D. Spyropoulos, R. Drake, P. Angel

Under IRB exclusion we had an opportunity to obtain fresh post-mortem human lung tissue from a baby who was a premature infant with abnormal kidneys, oligohydramnios and a concern for pulmonary hypoplasia. A piece of tissue was obtained at the time of autopsy and placed in a new cryopreservative (SolxMNX, Cryogenix, USA) that allows for long-term preservation of live tissue with the ability to procure later stem cells and isolated living cells such as type II alveolar epithelial cells. We wished to test our ability to measure glycans in this tissue using matrix-assisted laser desorption/ionization imaging mass spectrometry MALDI-IMS.

Using MALDI-IMS (Figure 1) we noted that multiple N-glycan species could be measured across the tissue including bi-antennary core fucose N-glycan, Man9 N-glycan, and bi-antennary sialic acid. Surprisingly, there were high levels of Man9 N-glycan, which is uncommon in healthy adult lung, but is consistent with a growing lung. Man9 N-glycan is an oligomannose N-linked oligosaccharide found in both mammalian and plant glycoproteins.

N-linked glycosylation is the attachment of a sugar molecule oligosaccharide (glycan) to an asparagine residue of a protein. Glycosylation of proteins can significantly alter their structure and therefore their function. Simple study of changes in gene and/or protein expression may not be adequate to fully understand biological systems in general and lung development in particular. BPD is likely an abnormal repair response to lung injury, specifically occurring while the lung is still developing. Further understanding of glycan changes during normal development may inform us of important changes in the disease process of BPD.

Figure 1. Mass Spectrometry Imaging of N-glycans on cryopreserved pediatric lung tissue. A) Hematoxylin and eosin stain. B) bi-antennary core fucose N-glycan; C) Man9 N-glycan; D) Bi-antennary sialic acid. Data demonstrates mapping multiple N-glycan types across tissue.
SARM1 MEDIATES DOPAMINERGIC NEURODEGENERATION IN A MOUSE MODEL OF PARKINSON’S DISEASE

Ammal Kaidery N., Banerjee R., Yang L, Calingasan NY, Rinvik E, Ottersen OP, Nathan C. F, Ding A, Beal M.F., Morgan J., Starkov AS, Thomas B.

Introduction: Activation of stress signaling pathways in conjunction with mitochondrial dysfunction play a key role in selective degeneration of dopaminergic neurons in Parkinson’s disease (PD). Here we show that Sarm1 (sterile alpha and Toll interleukin 1 receptor (TIR) motif), a neuronally expressed mitochondria associated adaptor protein mediates nigrostriatal dopaminergic neurodegeneration by modulating stress activated protein kinase signaling and mitochondrial calcium capacity.

Methods: Dopaminergic neurotoxicity in wild type and SARM1 knockout (KO) mice using the acute and sub-acute regimens of parkinsonian neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) was determined by tyrosine hydroxylase-positive (TH+) cell counts. Wild type (WT) and Sarm1 siRNA knockdown (KD) N2A cells were assessed for mitochondrial activity and calcium measurements. Immunobloting and realtime PCR were used for gene expression analysis.

Results: KO mice were resistant to both acute and sub-acute MPTP-neurotoxicity than wild type analyzed by stereological counts of TH+ neurons of substantia nigra pars compacta (SNpc). SARM1 mediated MPTP-neurotoxicity was associated with coimmunoprecipitation of SARM1 with stress activated protein kinase JNK3 on the mitochondria. Assessment of JNK3 mediated signaling pathways by immunoblot and confocal microscopy showed that phosphorylation of c-jun in SNpc dopamine neurons were significantly reduced in MPTP treated KO and MPP+-treated KD cells compared to wild types. SARM1 deletion caused inhibition of MAPK/JNK3 signaling both in vivo and in vitro and reduced translocation of JNK3 to mitochondria during MPTP/MPP+ toxicity compared to wild types. Mitochondrial functional analysis showed significantly higher oxygen consumption rates, increased mitochondrial calcium capacity and reduced caspase-3 activity in the presence of MPP+ in brain mitochondria from SARM1 null mice and in KD cells when compared to WT controls.

Conclusion: Our findings suggest SARM1 mediates dopaminergic neurodegeneration by serving as a mitochondrial adaptor to recruit cytosolic JNK3 and modulating mitochondrial calcium capacity.

Translational impact: Sarm1 could serve as a therapeutic target for PD.

Acknowledgements: Supported by NIH grant NS060885, NS062165, Par fore Parkinson, National Parkinson Foundation (CSRA) Chapter.

19-132 (Poster)

Role of S-nitrosoglutathione (GSNO) homeostasis in subset specific CD4+ cell mediated immunomodulation in experimental autoimmune encephalomyelitis

Won, Jeseong 1, *, Saxena, Nishant 2, Choi, Seungho 2, Singh, Avtar K. 2, 3, and Singh, Inderjit 2. ** Corresponding authors: Inderjit Singh, Ph.D. and Jeseong Won, Ph.D.
Abstract:
Our laboratory recently has reported that S-nitroso-glutathione (GSNO) and inhibitor of its catabolic enzyme (GSNO reductase) play key roles in Th17 and Treg mediated immune modulation of experimental autoimmune encephalomyelitis (EAE, an animal model of multiple sclerosis). In immune and inflammatory cells, GSNO homeostasis is primarily regulated by its synthesis mediated by inducible nitric oxide synthase (iNOS) and catabolism mediated by GSNO reductase (GSNOR) and EAE pathogenesis involves increased expressions of these enzymes in the CNS.

To assess the roles of iNOS and GSNOR in the pathogenesis of EAE, EAE was induced in C57BL/6 (WT), GSNOR knockout (KO), and iNOSKO mice. GSNORKO-EAE mice showed very mild clinical symptoms of EAE with no obvious demyelination in the spinal cord as compared to WTEAE mice. However, iNOSKO mice had more severe clinical EAE disease and greater demyelination in the spinal cord as compared to WT. Consistent with our previous data with GSNO or N6022 (GSNOR inhibitor) treated EAE mice, GSNORKO-EAE mice showed milder pro-inflammatory (Th1 and Th17) but greater anti-inflammatory (Th2, FOXP3+ Treg, and FOXP3- Treg) CD4+ T cell immune responses in the spleens and spinal cords as compared to the WT-EAE mice. Conversely, iNOSKO-EAE mice showed greater pro-inflammatory but milder anti-inflammatory CD4+ T cell immune responses in the spleens and spinal cords as compared to the WT-EAE mice. Taken together with data from exogenous GSNO and N6022 studies, these studies with genetic models document that cellular GSNO homeostasis is critical in subset specific immunomodulation of EAE disease (Th1/Th17 vs. Th2/Treg) and thus identifies a novel target and potential treatment option for multiple sclerosis and EAE.

19-133 (Poster)

Opioid Prescribing Habits in Sickle Cell Disease: An International Survey of Providers
Nadirah El-Amin, DO1, Paul Nietert, Ph.D2, Julie Kanter, MD3

Background: Vaso-occlusive pain crisis (VOC) are the hallmark of sickle cell disease (SCD) and the main reason for healthcare utilization. National and international guidelines recommend aggressive IV opioids, IV fluids and anti-inflammatory therapy as the mainstay of treatment for acute pain. However, many pain crises are managed at home with oral agents. There are no guidelines on medications for home pain management, likely due to lack of clinical trials comparing the efficacy and safety of oral agents for use at home. Amplifying these issues is the growing concern for opioid abuse and misuse in the US and internationally.

Objective: This study aimed to describe the opioid prescribing habits among providers treating individuals with SCD in the US and internationally.

Methods: A thirty-question REDcap survey was sent electronically. Recruitment techniques included purposive and snowball sampling.
Results: There were 127 responses and 17 countries represented. Over half of the respondents were from the US (59%). Most of the respondents were Hematologist/Oncologists both pediatric (43%) and adult (34%). Of the pediatric responses, US providers were more likely to prescribe opioids than non-US physicians (100% vs 67%, p<.004) and were more likely to be “very comfortable” prescribing opioids than non-US physicians (90% vs 29%, p<.001). Of those physicians who prescribe opioids, most (79%) prescribed 30 doses or less at a time. However, non-US physicians were more likely to prescribe less than 10 doses at a time (50% vs 13%, p <.05). Overall, the five most commonly prescribed medications for pain management were: acetaminophen (96%), ibuprofen (76%), short acting morphine (52%), oxycodone (46%) and combination products (41%). However, US physicians were more likely to prescribe oxycodone (70% vs 10%, p< .001), dilaudid (52% vs 10%, p<.001), long acting morphine (51% vs 19%, p<.05), combination products (61% vs 10%, p<.001). Non US physicians were more likely to report never being concerned that patients were misusing opioids than non-US physicians (48% vs 12%, p<.05).

Conclusions: VOC’s are the most common reason for healthcare use in SCD. While many countries used opioids for outpatient pain management, non-US prescribers are more likely to prescribe less potent opioids in lower quantities. As concerns have increased for complications of long term opioid use, alternative disease-modifying agents for the prevention of SCD related pain are an unmet need. But, identifying optimal home pain management strategies is also necessary to improve care in SCD.
Pernicious anemia presenting with pancytopenia: A rare pediatric diagnosis.

Robinson, Mayra, MD; El-Amin, Nadhira, MD; Bergmann, Shayla, MD; Hudspeth, Michelle, MD; Lazarchick, John, MD.

Background: Pernicious anemia (PA) is the most frequent cause of severe vitamin B12 deficiency. Its prevalence is 0.1% in the general population and 1.9% over the age of sixty. It is a multifactorial autoimmune disease characterized by the presence of intrinsic factor and parietal cell antibodies against the gastric H/K–ATPase; decreasing B12 uptake in the GI tract. Megaloblastic anemia represents the most common clinical manifestation of B12 deficiency. Additional findings described include thrombocytopenia, neutropenia, hemolysis and pancytopenia. Given its multiple clinical characteristics, diagnosing PA in the pediatric population may be challenging with only a few proven cases reported.

Objective: To describe a unique presentation of PA in a pediatric patient.

Design/Methods: We present a 15 year old male with PA referred to rule out malignancy. His initial presentation included a 10 pound weight loss over 3 months, post-prandial abdominal pain, fatigue, mouth ulcers and newly diagnosed pancytopenia. Laboratory values at his initial presentation included macrocytic anemia with Hemoglobin of 7.6 gms/dL and MCV 110.9 fl, reticulocytes 2.24%, LDH 7,489U/L, neutropenia (ANC 1.0K/CUMM) and thrombocytopenia (65K/CUMM). AST 189 U/L, ALT 124 U/L and total bilirubin 2.4 mg/dL. Direct Coombs test was negative. Peripheral smear showed occasional hypersegmented neutrophils with normal WBC morphology.

The differential diagnosis included hematologic malignancy, an autoimmune hemolytic process or a gastrointestinal etiology.

Results: CT scan of his neck, chest, abdomen and pelvis was negative for a mass. A bone marrow biopsy appeared hypercellular with megaloblastic changes suspicious for megaloblastic anemia and negative for malignancy.

Esophagogastroduodenoscopy reported autoimmune atrophic gastritis with focal metaplasia of the stomach body. RBC folate and B12 levels were low at 20.4 and 146 respectively with elevated methylmalonic acid at 3.50 MOL/L. Subsequent antibody testing was positive for the presence of intrinsic factor antibodies and elevated parietal cell antibodies, confirming the diagnosis of pernicious anemia.

Our patient received treatment with vitamin B12 injections and folate supplementation. Four weeks later his hemoglobin improved to 10.6 Gms/dL and platelets to 351K/CUMM.

Conclusion: Juvenile PA is a rare and challenging diagnosis due to the wide variation of its clinical presentation, which can often be confused with a malignant process. Although it is not specified in the pediatric population, surveillance of elderly individuals showed that they are at increased risk of gastric adenocarcinoma and gastric carcinoid tumors. PA is associated with other autoimmune disorders making the diagnosis of PA imperative for appropriate patient care, treatment and surveillance.
19-135 (Poster)

Role of Asymmetric Dimethylarginine (ADMA) in Vascular Pathology Associated with Experimental Autoimmune Encephalomyelitis (EAE)

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3 Pathology and Laboratory Medicine Service and 4 Research Service, Ralph H. Johnson Veterans Administration Medical Center, Charleston, SC, USA.
* Corresponding authors: Inderjit Singh, Ph.D. and Jeseong Won, Ph.D.

Abstract:
Recently, asymmetric dimethylarginine (ADMA), an endogenous nitric oxide synthase (NOS) inhibitor, has gained attraction for its role in vascular pathology. Vascular pathology is an important factor causing neuronal dysfunction/degeneration in multiple sclerosis (MS), yet the role of ADMA in MS remains elusive. MS patients are known to have elevated blood ADMA level. Accordingly, mice with experimental autoimmune encephalomyelitis (EAE, an animal model of MS), which were generated by myelin autoimmunization and blood-brain barrier (BBB) breakdown by pertussis toxin, also had increased blood ADMA level with decreased ADMA catabolism in liver and kidney. To explore the role of ADMA in EAE pathogenesis, EAE mice were treated with daily ADMA. ADMA treatment promoted Th1 and Th17 immune responses in the spleen, increased peripheral mononuclear cell infiltration and demyelination in the spinal cord, and exacerbated the clinical EAE disease. ADMA treatment also increased BBB disruption and induced EAE disease even without pertussis toxin treatment for BBB disruption in MOG immunized mice. These data document that elevated blood ADMA level correlate with clinical, immunological, neurological, and BBB pathologies of EAE. ADMA induces BBB pathology, thus facilitating CNS infiltration of peripheral immunocytes for development of EAE, hence pointing to the potential of ADMA-mediated mechanisms in clinical disease of EAE and MS.

19-136 (Poster)

Inter-hospital Variation of Inpatient versus Outpatient Pediatric Burn Treatment After Emergency Department Evaluation

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Affiliations:
1 Division of Pediatric Surgery, Department of Surgery, Medical University of South Carolina, Charleston, South Carolina 2 Quality Department Medical University of South Carolina Children’s Hospital, Charleston, SC

Pediatric burns are significant source of injury with an estimated 160,000 pediatric burns per year treated in the United States. Approaches to burn care in the pediatric population are highly variable and can be targeted as a potential measure in quality improvement. We hypothesized that institutions vary significantly in their allocation of treatment of non-severe burns to either inpatient or outpatient care. We performed a query of the PHIS database for fiscal year 2017 to
quantify small pediatric burn admissions and Emergency Department visits (ED) and analyze associated charges. The ICD-10 code T31.0 was used to identify burns involving less than 10% of total body surface area (TBSA). The PHIS database query yielded a total of 39 children’s hospitals which delivered burn care. Of those centers, only 7 provided exclusively outpatient management. 35 centers were included based on burn volume per year. In centers that provided ED care, an average of 83±87 ED evaluations were performed per hospital (range: 0-371). While 72% of all burns across institutions were treated as outpatients after initial ED evaluation, the management across institutions was uneven with inpatient admission rates ranging from 0-100%. Median inpatient charge per patient was greater than 33-fold compared to outpatient burn treatment (p<0.001).

Significant variation was observed in regard to inpatient versus outpatient pediatric burn management in small burns. Compared to outpatient burn care, inpatient care is significantly more costly. Implementing protocols and personnel to provide adequate attention to small burns in the ED could be an important cost-saving measure.

19-137 (Platform)

Can We Predict Who Will Need a Feeding Gastrostomy in Babies Discharged from the NICU?

Background: Some premature babies are unable to achieve full oral feeding and require a gastrostomy tube (GT) for safe discharge. If we know earlier that a GT is required, we may be able to achieve earlier discharge, potentially leading to decreased hospital length of stay and attendant benefits of feeding and development in the home.

Objective: To identify factors for building a predictive model for GT at discharge.

Methods: We determined that the population of non-anomaly-related GTs was <30 weeks' (w) gestation (GA) and collected data retrospectively on all babies <30w (n=283) admitted to the NICU in 2015 and 2016; 47 had G-tubes and 236 did not. After exclusions for being non-contributory to developing the model (e.g. died before 36w), we collected full data on 204 infants; 41 with GT, 163 were discharged on full oral feeds with no GT (NGT). A forward stepwise selection method was applied in a logistic regression analysis to obtain a parsimonious model to predict G-tube use.

Results: In univariate analyses, factors significantly different between < 30w GT vs. NGT babies included various demographics and NICU factors as well as respiratory parameters at 30d, 32w GA, and 36w GA (Table). GA at last CPAP (47.8w vs. 32.7w), rapidity of oral feeding increase, and GA at which oral feedings were first attempted (38.8w vs. 34.1w) were also significantly different. Based on the univariate analyses and clinical input, the model selection method applied selected five variables to be adequate predictors. The variables selected are: NEC, use of HFV ever, FiO2 at 32w, PDA treated, and PMA at first feed. Approximate thresholds at which the prediction diagnostics were most useful were also obtained and corresponding diagnostics were performed using AUC under ROC curves. The AUC values ranged above 0.894 suggesting that certain thresholds developed could be useful in practice.

Conclusion: There are many factors that are associated with the need for a feeding gastrostomy at discharge. We are refining a prediction model and planning a validation cohort with which to test the model. After a validation cohort, these data could be used to facilitate earlier GT placement, earlier discharge, lower healthcare costs, and possibly improved neurodevelopmental outcome based on earlier family interaction rather than longer NICU stay.

<table>
<thead>
<tr>
<th></th>
<th>All babies N=204</th>
<th>G-tube babies N=41</th>
<th>Non-G-tube babies N=163</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (wks, mean (SD))</td>
<td>27.4 (1.8)</td>
<td>26.0 (1.9)</td>
<td>27.5 (1.6)</td>
<td>0.0000 (t-test)</td>
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<tr>
<td>Birth weight (g, mean, SD)</td>
<td>962 (274)</td>
<td>751 (218)</td>
<td>1015 (261)</td>
<td>0.0000</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>67 (33%)</td>
<td>10 (24%)</td>
<td>57 (35%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>119 (58%)</td>
<td>26 (63%)</td>
<td>93 (57%)</td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
<td></td>
<td>5 (12%)</td>
<td>13 (8%)</td>
<td>NS 0.367</td>
</tr>
<tr>
<td></td>
<td>18 (9%)</td>
<td>100 (49%)</td>
<td>26 (63%)</td>
<td>74 (45%)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>---------</td>
<td>-----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>100</td>
<td>26</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>104</td>
<td>15</td>
<td>89</td>
</tr>
<tr>
<td>Inborn</td>
<td>176 (86%)</td>
<td>38 (93%)</td>
<td>138 (85%)</td>
<td>176 (86%)</td>
</tr>
<tr>
<td></td>
<td>Outborn</td>
<td>30 (14%)</td>
<td>3 (7%)</td>
<td>25 (15%)</td>
</tr>
<tr>
<td>Maternal Drug Use</td>
<td>15 (7%)</td>
<td>4 (10%)</td>
<td>11 (7%)</td>
<td>NS (0.51)</td>
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<td>NAS</td>
<td>4 (2%)</td>
<td>1 (2.4%)</td>
<td>3 (1.9%)</td>
<td>NS (0.84)</td>
</tr>
<tr>
<td>SGA</td>
<td>36 (18%)</td>
<td>12 (29%)</td>
<td>24 (15%)</td>
<td>0.029 (chi2)</td>
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<tr>
<td>Multiple gestation</td>
<td>60 (30%)</td>
<td>46 (28%)</td>
<td>14 (34%)</td>
<td>NS (0.603)</td>
</tr>
<tr>
<td>PDA tx with meds</td>
<td>66 (33%)</td>
<td>22 (55%)</td>
<td>44 (27%)</td>
<td>0.001 (chi2)</td>
</tr>
<tr>
<td>PDA ligation</td>
<td>24 (12%)</td>
<td>13 (32%)</td>
<td>11 (7%)</td>
<td>0.000 (chi2)</td>
</tr>
<tr>
<td>NEC (any stage)</td>
<td>19 (9%)</td>
<td>9 (22%)</td>
<td>10 (6%)</td>
<td>0.003 (chi2)</td>
</tr>
<tr>
<td>NEC w/surgery</td>
<td>9 (4.4%)</td>
<td>8 (19.5%)</td>
<td>1 (0.6%)</td>
<td>0.000 (exact)</td>
</tr>
<tr>
<td>IVH (any grade)</td>
<td>62 (30%)</td>
<td>22 (54%)</td>
<td>40 (25%)</td>
<td>0.000 (chi2)</td>
</tr>
<tr>
<td>IVH Gr 3-4</td>
<td>14 (7%)</td>
<td>7 (17%)</td>
<td>7 (4%)</td>
<td>0.009 (exact)</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td>9 (4%)</td>
<td>6 (15%)</td>
<td>3 (2%)</td>
<td>0.002 (Fisher’s exact)</td>
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<tr>
<td>Reservoir</td>
<td>3 (1.5%)</td>
<td>2 (5%)</td>
<td>1 (0.6%)</td>
<td>NS 0.10 (exact)</td>
</tr>
<tr>
<td>VP shunt (VPS)</td>
<td>4 (2%)</td>
<td>2 (5%)</td>
<td>2 (1%)</td>
<td>NS 0.18 (exact)</td>
</tr>
<tr>
<td>Any maternal milk at 32w</td>
<td>137 (67%)</td>
<td>28 (68%)</td>
<td>109 (67%)</td>
<td>NS 0.862</td>
</tr>
<tr>
<td>FiO2 at 30d</td>
<td>27.9 ± 10.5</td>
<td>36.2 ± 14.1</td>
<td>25.7 ± 8.2</td>
<td>0.000 (t-test)</td>
</tr>
<tr>
<td>MAP at 30d</td>
<td>5.2 ± 4.2</td>
<td>8.3 ± 3.5</td>
<td>4.4 ± 4.0</td>
<td>0.0000</td>
</tr>
<tr>
<td>Resp mode at 30d</td>
<td>No RS/ NC)/ VT (vapotherm)</td>
<td>79 (39%)</td>
<td>5 (12%)</td>
<td>74 (45%)</td>
</tr>
<tr>
<td></td>
<td>CPAP/NIPPV/CV/HFV</td>
<td>125 (61%)</td>
<td>36 (88%)</td>
<td>89 (55%)</td>
</tr>
<tr>
<td></td>
<td>FiO2 at 32w PMA</td>
<td>27.5 ± 11.1</td>
<td>33.3 ± 15.1</td>
<td>26.0 ± 9.4</td>
</tr>
<tr>
<td></td>
<td>MAP at 32w PMA</td>
<td>4.6 ± 3.7</td>
<td>7.7 ± 3.3</td>
<td>3.8 ± 3.4</td>
</tr>
<tr>
<td>Resp mode at 32w</td>
<td>No RS/ NC)/ VT (vapotherm)</td>
<td>84 (42%)</td>
<td>4 (10%)</td>
<td>80 (49%)</td>
</tr>
<tr>
<td></td>
<td>CPAP/NIPPV/CV/HFV</td>
<td>119 (59%)</td>
<td>36 (90%)</td>
<td>83 (51%)</td>
</tr>
<tr>
<td></td>
<td>FiO2 at 36w PMA</td>
<td>25.5 ± 12.4</td>
<td>30.3 ± 10.4</td>
<td>24.2 ± 12.5</td>
</tr>
<tr>
<td></td>
<td>MAP at 36w PMA</td>
<td>2.0 ± 3.4</td>
<td>1.1 ± 2.2</td>
<td>6.0 ± 4.6</td>
</tr>
<tr>
<td>Resp mode at 36w</td>
<td>No RS/ NC)/ VT (vapotherm)</td>
<td>154 (77%)</td>
<td>16 (39%)</td>
<td>138 (87%)</td>
</tr>
<tr>
<td></td>
<td>CPAP/NIPPV/CV/HFV</td>
<td>45 (23%)</td>
<td>25 (61%)</td>
<td>20 (13%)</td>
</tr>
<tr>
<td></td>
<td>MAP at time of first oral feeding</td>
<td>34.9 (3.2)</td>
<td>38.8 (4.4)</td>
<td>34.2 (2.3)</td>
</tr>
</tbody>
</table>
A Case of Post-Renal Transplant Sirolimus-Induced Colitis in a Pediatric Patient with Cystinosis.

Garcia DI, MD, Nadig SN, MD PhD, Murty P MBBS, Fernandes A, Lewin DN, MD, Twombley KE, MD

Cystinosis is a lysosomal storage disorder in which more than 90% of patients progress to end-stage renal failure by 20 years of age and ultimately require renal transplantation. Sirolimus is an anti-proliferative agent often used in post-transplantation immunosuppression regimens whose mechanism of action is to inhibit mammalian target of sirolimus (mTOR) thereby blocking cell cycle progression from G1 to S phase. As with many immunosuppressive medications, sirolimus carries a complex side-effect profile, however the effect of colitis, to date has not been reported with this medication. We describe the first reported case of pediatric sirolimus-induced colitis following renal transplant for nephropathic cystinosis.

The patient underwent colonoscopy following onset of symptoms in which several colonic biopsies were taken. Histology with hemotoxylin and eosin staining was performed and evaluated by GI pathology fellowship board-certified pathologists at our institution. In addition to testing for inflammatory, autoimmune and infectious etiologies, donor-derived DNA and chimerism testing was run to assess for Graft Versus Host Disease (GVHD). Repeat colonic biopsies were performed following resolution of symptoms.

We describe the first reported case of pediatric sirolimus-induced colitis following renal transplant for nephropathic cystinosis. The patient was a twelve-year-old female who, three months post-transplant, developed symptoms of colitis following a change in immunosuppressive drug regimen to sirolimus and prednisone after an adverse reaction to mycophenolate mofetil. Histology from colonic biopsies showed gland drop out with crypt atrophy and focal apoptosis initially concerning for a gastrointestinal manifestation of GVHD. Donor-derived DNA and chimerism testing, however, ruled out GVHD as a diagnosis. Following sirolimus discontinuation, the patient’s symptoms completely resolved and repeated colonic biopsy showed normal histology.

Serologic and histologic testing proved to be negative for other etiologies of the patient's colitis symptoms. The temporal relationship of colitis symptoms following commencement of sirolimus as well as the resolution of symptoms following discontinuation of sirolimus led us to conclude that the patient’s colitis was drug-related.
TITLE: Early Parenteral Electrolyte Delivery in Extremely Low Birth Weight Infants

AUTHORS: Glenn, Stephanie R1; Finch, Carolyn3; DellaValle, Diane M4; Taylor, Sarah N2

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3. Clinical Nutrition, Virginia Commonwealth University Medical Center, Richmond, VA, United States.
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ABSTRACT:
Purpose of Study: To determine if increased parenteral phosphorus delivery and early parenteral potassium delivery resulted in fewer IV replacements required for hypophosphatemia and hypokalemia.

Methods Used: This study retrospectively reviewed extremely low birth weight (ELBW) infants who received increased parenteral nutrition (PN) phosphorus (1.2 mmol/100 mL; calcium-to-phosphorus molar ratio 1:1) and potassium (1.4 mEq/100 mL) by 24 hours of life (increased-
electrolyte (IE) group; born 2016). PN electrolytes, serum electrolyte lab values, and number of IV phosphorus and potassium replacements were compared with a standard-electrolyte (StE) group (born 2015) given 0.97 mmol/100 mL PN phosphorus (calcium-to-phosphorus ratio 1.2:1) and no potassium in the first 24 hours of life. Data analysis used descriptive statistics and repeated measures ANOVA. P value <0.05 was considered statistically significant for main effects and P value <0.2 for interaction effects.

**Summary of Results:** Thirty-three ELBW infants were included in this study (IE n=13, StE n=20). There were no significant differences between groups in birth weight, gestational age, or gender. There were no differences between groups in the number of IV phosphorus and potassium replacements. The IE group did receive more PN potassium without subsequent hyperkalemia. A significant effect of time was observed for PN phosphorus and calcium intakes in the IE group (P <0.001) compared to the StE group. A significant group by time interaction was observed for PN phosphorus (P=0.018). Significant time effects were observed for both serum calcium and potassium (P <0.001 and P=0.03, respectively).

**Conclusions:** Early delivery of PN phosphorus and potassium was safe for ELBW infants receiving early PN protein and frequent monitoring for deficiency was needed. In our unit, PN phosphorus was increased to 1.2 mmol/100 mL, and PN potassium safely provided by 24 hours of life.
19-140 (Poster)

Surfactant Regulation by the Natriuretic Peptide Pathway: A New Mechanism for Steroid Effects

Rita M. Ryan, Paintlia M, Newton D, a Kemp M, b Jobe AH, Baatz JE.

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Rationale: Premature babies who have inadequate surfactant at birth develop respiratory distress syndrome (RDS). Maternal antenatal steroids decrease the risk of RDS by improving endogenous surfactant availability. Atrial Natriuretic Peptide (ANP) and C-ANP (a specific agonist of natriuretic peptide receptor (NPR) -C) are recently discovered regulators of surfactant secretion. ANP stimulates surfactant release when it stimulates NPR-A, its classic receptor. But ANP or C-ANP stimulation of NPR-C inhibits beta-adrenergic stimulation of surfactant release; glucocorticoids blunt this inhibitory effect. Dexamethasone decreases NPR-C mRNA expression in alveolar epithelial type II cells (ATIIs) in vitro. We wished to examine antenatal steroid effects on the NP system as well as further examine the specific effects of NPR-C. Specifically, we wished to test the hypothesis that antenatal steroids will decrease ANP in fetal lung fluid in sheep in vivo and the hypothesis that siRNA knockdown of NPR-C will block the inhibitory effect of ANP on terbutaline-induced upregulation of SP-B mRNA in vitro.

Methods: Pregnant ewes were given betamethasone (beta, Celestone, 0.25mg/kg) or placebo at 121±1 days of gestation and then delivered 2 or 5 days later. Fetal lung fluid was collected and ANP was measured by ELISA in ten animals. To further understand the effect on surfactant production in ATIIs we used NPR-C silencing RNA (siRNA). SiRNA and control RNA were incubated with a surfactant-producing mouse lung epithelial (MLE-15) cell line. Surfactant production induced by ANP and/or terbutaline (TER) was assessed by measuring SP-B mRNA in MLE-15 cells.

Results: Fetal lung fluid ANP was significantly lower in maternal beta-treated offspring compared with control (mean ± standard deviation; control 54.3 ± 2.6, beta 2 days before birth 29.1 ± 10.0, beta 5 days 18.5 ± 11.5, P= 0.007, by one way ANOVA). In addition, siRNA for NPR-C eliminated the effect of ANP to inhibit TER-induced SP-B mRNA expression in MLE15 cells (Figure), P<0.05 by ANOVA.

Conclusions: The effects of steroids on type II cell surfactant secretion are mediated by ANP and effected through the NPR-C. Blocking NPR-C mRNA expression alters the normal inhibitory effect of ANP on beta-adrenergic receptor stimulated surfactant production. This pathway may offer a unique target to alter surfactant secretion or production.
Roles of an Nkx2-5 Target Gene in the Developing Heart


Congenital heart disease (CHD) is the most common congenital defect in newborns, occurring in approximately 20,000 live births per year in the US. It is also the leading cause of death due to congenital defect. While the underlying genetics are complex, significant progress has been made in understanding key genes involved in its genesis. Nkx2–5 is a critical homeobox transcription factor that is associated with approximately 4% of all CHD. Nkx2-5 is highly expressed in the second heart field (SHF) region, a pool of cardiac progenitor cells present in the anterior pharyngeal arch during mid-gestation. Expression of Nkx2–5 is vital for formation of the right ventricle (RV) and outflow tract (OFT) from SHF cells, with Nkx2–5 knockout mice manifesting severe OFT and RV hypoplasia resulting in essentially a single ventricle phenotype due to decreased proliferation of SHF cells. However, definition of the precise role of Nkx2-5 in facilitating SHF expansion is incomplete.

We have found that Nkx2-5 positively and directly regulates a novel target gene, Ccdc117, in cells of the SHF at these stages. Furthermore, we have shown that the nuclear and mitotic spindle associated protein, Ccdc117, interacts with the MIP18/MMS19 cytoplasmic iron- sulfur (FeS) cluster assembly (CIA) complex, which transfers critical FeS clusters to several key enzymes with functions in DNA repair and replication.

Additionally, we have shown that loss of cellular Ccdc117 expression results in decreased rates of DNA synthesis, unresolved DNA damage, and reduced cellular proliferation rates associated with a delay at the G1-S transition. These results suggest a novel role for Nkx2-5 as a cell-cycle regulator in the developing heart, via Ccdc117’s interaction with elements of the CIA pathway and the facilitation of DNA replication during SHF expansion. Ongoing experiments are geared...
toward determining the precise role of Ccdc117 in iron sulfur cluster delivery, and its integration with related cellular pathways regulating redox balance and iron metabolism.

19-142 (Poster)

A Single Sugar Tong Splint is Equivalent to a Long Arm Cast for Maintenance of Acceptable Reduction of Midshaft and Proximal Pediatric Forearm Fractures

Davis Osborn BS; Robert Murphy MD; Brian Thomas Sleasman MD; William R Barfield PhD; James F Mooney MD

Background: Displaced pediatric forearm fractures frequently are treated with closed reduction and external immobilization, most commonly in a long arm cast. However, a single sugar tong splint (SSTS) may limit potential complications associated with casting and is technically easier for resident physician trainees to learn and replicate. Existing literature reveals no difference in maintenance of alignment or need for repeat intervention in patients immobilized with either a SSTS or a LAC, but most series contain many patients with distal fractures. No data exists comparing these immobilization types in a series of only midshaft or proximal forearm fractures.

Objective: The purpose of this study was to compare the efficacy of SSTS as compared to LAC for maintenance of reduction and need for repeat intervention for midshaft or proximal forearm fractures.

Methods: Patients aged 3 to 15 years who underwent closed reduction and immobilization of a displaced or angulated midshaft or proximal forearm fracture at a single tertiary care pediatric hospital over a 6-year period were included. Medical records were used to determine patient demographics. Radiographs from the time of injury, post reduction and at four weeks follow-up were reviewed for coronal and sagittal plane angular alignment. Secondary intervention (either repeat manipulation and/or surgical stabilization) was recorded and compared according to the method of index external immobilization.

Results: 121 patients qualified for inclusion (70 LAC, 51 SSTS). The groups were matched in terms of age (p=0.95), gender (p=0.41), BMI (p=0.12), and angular deformity prior to reduction in the sagittal (p=0.78) and coronal planes (p=0.83). There was a significant improvement in sagittal (p=0.003) and coronal (p=0.002) alignment in all patients immediately following closed reduction. At 4 weeks follow-up, there were no significant differences in residual sagittal (p=0.15) or coronal (p=0.68) alignment comparing LAC to SSTS. Nine patients underwent secondary intervention after the index reduction (LAC 7/70, SSTS 2/51) with no statistical difference between groups (p=0.30).

Conclusion: There were no statistically significant differences between patients managed with LAC or SSTS in regard to residual sagittal or coronal plane angular deformity at 4 week follow up or incidence of secondary intervention. Based on this finding, both SSTS and LAC appear to be acceptable and equivalent methods of immobilization for displaced midshaft and proximal pediatric forearm fractures that undergo closed reduction.
**19-143 (Poster)**

*Case-Control Study of Pneumatosis Intestinalis in Pediatric Allogeneic HSCT Patients*

*Mamatha Mandava M.D, Amy Wahlquist M.S., Jennifer Jarosck M.D, Michelle Hudspeth M.D*

**Background:** Pneumatosis intestinalis (PI) is a complication with potential for significant morbidity and mortality. Limited information is known regarding risk factors and outcomes.

**Methods:** We conducted a retrospective case-control study of all pediatric allo-HSCT at our institution from July 2007 – July 2018. Comparisons of categorical variables and continuous variables between cases (PI) and controls (no PI) were done via Fisher’s exact tests and a two-sample t-test. OS was compared between cases and controls via a log-rank test.

**Results:** We identified a total of 117 HSCT events for 113 patients. PI occurred in 6 (5.1%) transplants. For the entire cohort, median age at HSCT was 7.85 years (range 0.39-22.82) with 60.68% (n=71) HSCT events for males. Malignant disease was the predominant indication for HSCT (76.92% n=90). Donor sources varied, including 28.21% (n=33) MRD, 36.75% (n=43) MUD/MMRD/matched CBU, 29.06% (n=34) MMUD/mismatched CB, and 5.98% (n=7) haplo. Predominant graft source was BM at 71.79% (n=84), followed by CB 23.08% (n=27) and PBSC 5.13% (n=6). MAC regimens were most common with TBI-based in 43.59% (n=51) and Bu-based in 39.32% (n=46). The remainder of conditioning regimens were RIC in 11.11% (n=13) and Cy/ATG based in 5.98% (n=7). aGVHD and cGVHD were noted in 38.46% (n=45) and 12.82% (n=15), respectively. During the first 100 days, 52.99% (n=62) had a documented infection. There was no statistically significant association between sex, race, age, diagnosis, HLA match, graft source, or GVHD and PI. While there was also no statistically significant association between conditioning regimens or infections and PI, there was a possible trend for clinical significance. TBI-based regimens were less common in cases (16.7% versus 45% p=0.4), and more infections were seen in the cases (83.3% versus 51.4% p=0.2). All cases recovered from PI with medical management alone. No deaths were attributable to PI and 66.67% (n=4) cases remain alive at last follow up. Median survival time could not be estimated as both groups had more than 50% of patients still alive at the time of analysis.

**Conclusion:** We did not identify any clear association of PI with factors such as HLA match, graft source, underlying diagnosis, or GVHD which may be due to the limited number of cases. Future multi-institutional studies with larger cohorts may be able to identify risk factors for this rare complication.

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**19-144 (Poster)**

*TO GIVE OR NOT: RASBURICASE IN TUMOR LYSIS SYNDROME AND GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY*

*Mamatha Mandava M.D, Laurence Noisette M. D, Michelle Hudspeth M.D, Jennifer Joi Jarosck M.D, Sandeepkumar Kuril M.D.*

**Background:** Tumor lysis syndrome (TLS) is a life-threatening complication occurring in certain malignancies causing multi-organ dysfunction and dyselectrolytemia due to tumor cytolysis. The classic triad of hyperuricemia, hyperkalemia and hyperphosphatemia can evolve rapidly into clinical TLS. Patients are at risk for TLS based on tumor burden, tumor grade, renal impairment...
and age. In addition to active monitoring and hydration, prophylaxis with Rasburicase is recommended for high-risk patients. Rasburicase, a recombinant urate oxidase, can cause both methemoglobinemia and hemolytic anemia due to increase oxidative stress especially in patients with Glucose-6-phosphate dehydrogenase (G6PD) deficiency.

**Objective:** To present a case report of a 15-year-old African American male with Acute Myeloid Leukemia (AML), FLT3-ITD+, at high risk for TLS, who developed severe methemoglobinemia post-Rasburicase treatment due to mild G6PD deficiency.

**Design/Method:** The medical record was reviewed, and the case is presented. One week before presentation, patient was symptomatic with headaches, vomiting, malaise and anorexia. Physical examination showed right conjunctival hemorrhage and wet petechiae. Laboratory work up revealed hyperleukocytosis with total white blood count (WBC) of 421K/cumm, hemoglobin (Hb) 7.3gm/dl, platelets 133k/cumm, lactate dehydrogenase 4615 IU/L, uric acid 9.2 mg/dl and prothrombin time 19.5sec/INR 1.6. Diagnosis of AML was made on peripheral blood flow cytometry. He began hydration and received 6 mg Rasburicase due to signs of leukostasis and high risk for TLS. He underwent leukapheresis but was placed on mechanical ventilator within 12 hours due to persistent hypoxia despite supportive care most likely due to pulmonary leukostasis and infection. Subsequently, he was started on standard AML chemotherapy regimen.

**Result:** At 36 hours, the methemoglobin level was elevated at 13.3 % (normal, 0.4-1.5). No hemolysis was noted. Pre-transfusion quantitative G6PD level, upon finding methemoglobinemia, was elevated at 26.9 U/g Hb (normal, 9.9-16.6). However, the confirmatory molecular testing showed A376G/G202A, a class III mutation in the G6PD gene. Patient was managed conservatively as methylene blue would have worsened methemoglobinemia and caused hemolysis in G6PD deficiency.

**Conclusion:** Screening for G6PD with routinely used quantitative spectrophotometry test has a long turnover as most laboratories batch samples and interpretation requires expertise. Rapid diagnostic tests like qualitative fluorescence spot test, if available, can be valuable before administering Rasburicase in high risk settings. Blood transfusion, hemolysis and leukocytosis can give spurious G6PD levels warranting confirmatory molecular testing. If G6PD status is unknown especially in high risk ethnic groups, patients should be warned about the risk of developing methemoglobinemia and hemolytic anemia with Rasburicase therapy.

**19-145 (Poster)**

**Bach1 inhibition, a novel therapeutic strategy for Neurodegenerative disorders**

**Ahuja, Manuj,** Navneet Ammal Kaidery, Irina Gaisina, Kazuhiko Igarashi, Otis C. Attucks, Bobby Thomas

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative movement disorder characterized by loss of nigrostriatal dopaminergic neurons. Except for the palliative treatment, there is no cure available for PD. Based on pathophysiological findings, aberrant oxidative stress and inflammation are extensively targeted for developing PD therapies. The most promising cellular target is the nuclear-factor-E2-related factor 2 (Nrf2)/anti-oxidant re-sponse element (ARE) sig-nal-ing pathway which regul-atates the ex-pres-sion of battery of genes encoding anti-oxi-dative, anti-inflam-matory, and cyto-pro-tective genes. However, all known
Nrf2 activators are electrophilic and thus, may potentially result in oxidative stress on chronic usage. Transcription factor Bach1 [BTB and CNC homology 1] binds to ARE-like sequences, functioning as a transcriptional repressor, thus antagonizing the activator function of Nrf2 and hence, potentially be aimed to develop better non-electrophillic ARE activators.

Methods: We investigated the effects of Bach1 inhibition (both genetic and pharmacological) on Nrf2/ARE signaling both in vitro and in vivo and its ability to block 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced dopaminergic neurotoxicity, associated oxidative damage, and inflammation in mice.

Results: We observed that both genetic (Bach1 null mice) and pharmacological inhibition (oral administration of non-electrophillic Bach1 inhibitor) of Bach1 attenuated MPTP-induced nigrostriatal dopaminergic neurodegeneration. The neuroprotective effects in Bach1 null and Bach1 inhibitor treated wild type mice against MPTP was not due to differences in conversion of MPTP to MPP+. Assessment of mRNA and protein levels of Nrf2 pathway target genes in Bach1 null mice and Bach1 inhibitor treated wild type mice exhibited marked induction of both antioxidant and anti-inflammatory genes.

Conclusion: Our results suggests that Bach1 inhibition is a promising target against dopaminergic neurodegeneration owing to its ability to activate neuroprotective Nrf2/ARE genetic program. Translational Impact: Genetic and pharmacological inhibition of Bach1 could serve as a novel non-electrophillic target for therapeutic intervention in PD.

19-146 (Poster)

Reaching Children from Low-Income Families Through a School-Based Obesity Prevention Initiative

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Medical University of South Carolina, Charleston, SC, United States.

Purpose: Children in low-income families are more likely to become obese and are more difficult to reach by traditional health care means. School based obesity prevention programs that impact all children enrolled may be an effective way to intervene. However, Title 1 schools with a high percentage of children from low-income families tend to have fewer resources and parental support. Thus, Title 1 schools may be less likely to participate or may participate at a lesser level in school-based wellness programs compared to schools enrolling children from higher income families. The purpose of this study was to determine participation of Title 1 schools in the South Carolina Docs Adopt School Health Initiative© (DASHI), an evidence-based program that motivates schools to make changes in policies, environments, and systems, while competing in a wellness “contest” with other schools, earning points for implementing items on the School Wellness Checklist© (SWC).

Methods: This outcome evaluation of DASHI examined Title 1 versus non-Title 1 schools in 3 comparisons: (1) participation in DASHI, (2) achievement of Wellness Awards and (3) overall SWC scores and subscores. Data included SWC scores for the 2017-18 school year. Analysis used chi-square and ANOVA.

Results: 11 school districts participated in DASHI in 2017-18, with all schools in each district eligible for participation. 87 of 123 non-Title 1 schools (70%) and 100 of 126 Title 1 schools (79%)
participated (p =.115). Of participating schools, 74 of 87 non-Title 1 schools (85%) and 93 of 100 Title 1 schools (93%) earned Wellness Awards (p=.079). Mean SWC points for Title 1 schools totaled 94.4 versus 93.8 points for non-Title 1 schools (p=.935). There was no significant difference between Title 1 and non-Title 1 subscores in the 7 subcategories of the SWC.

**Conclusions:** DASHI is as successful in Title 1 schools enrolling students at higher risk of obesity as in non-Title 1 schools. Title 1 schools are as likely to participate in DASHI and they implement the same number of wellness changes as non-Title 1 schools enrolling students from higher income families. This indicates that school-based obesity prevention programming may be an effective method to reach at-risk children.

**19-147 (Poster)**

**Identification of the Ste20-Like Kinase as a Novel regulator of Pediatric Neuromuscular Disease**

**Benjamin R. Pryce,** Dounia Hamoudi, John About-Hamad, Khalid N. Al-Zahrani, Jonathan J. Hodgins, Antoine Boulanger-Piette, Sabrina Bossé, Jérôme Frenette, Michele Ardolino, Denis C. Guttridge, Luc A. Sabourin

**Abstract**

Pediatric neuromuscular disorders include a broad range of inherited disorders. These disorders are often lethal, with little to no therapy available for treatment. One such disorder is Duchenne Muscular Dystrophy (DMD), which is caused by the loss of dystrophin and is characterized by progressive loss of muscle function. Children suffering from DMD experience significant muscle wasting and loss of ambulation by their early to mid-teens. Patients with DMD rarely live beyond their 20s with cardiac and respiratory dysfunction being the primary cause of death. Patients with advanced DMD show increased expression of inflammatory cytokines, which decreases the capacity for muscles to regenerate, further worsening the disease. Despite an increase in our understanding of the pathology of DMD, treatment options remain limited. Therefore, the identification of novel therapeutic targets is essential in order better treat DMD patients. In this study, we demonstrate that dystrophic muscle increases the expression of the Ste20-Like Kinase (SLK). SLK has been previously implicated in playing a role in functioning downstream of TGF-β, a cytokine that has been found to be enriched in dystrophic muscle. Similarly, deletion of SLK from dystrophic mice resulted in increased regeneration, blunted muscle inflammation, and restored some aspects of muscle function. Furthermore, we have identified the molecular mechanism that is responsible for this effect, which may provide more alternatives for therapeutics for the treatment of DMD.

**19-148 (Platform)**

“QRS Fragmentation versus QRS Prolongation in Predicting Right Ventricular Enlargement and Dysfunction in Children and Adults with Repaired Tetralogy of Fallot”

**Stephanie Gaydos MD,** Anthony Hlavacek MD, Susan Evenhouse MD, Jacob Strelow MPH, Shahryar Chowdhury MD, Lanier Jackson MD
Introduction: Patients with repaired Tetralogy of Fallot (rTOF) remain at risk for late life-threatening sequelae, including right ventricular (RV) dilation and failure, ventricular arrhythmias, and sudden death. QRS prolongation is a well recognized ECG predictor of these outcomes. QRS fragmentation (fQRS), a marker of myocardial scar and electrical instability, has been studied for similar prognostication in adults with rTOF with recent association with mortality. The goals of this study are to compare QRS prolongation with fQRS as markers of RV dilation and dysfunction by MRI in children and adults with rTOF, and to determine the prevalence of fQRS in youth with rTOF.

Methods: This was a single institution retrospective review of rTOF patients who had a cardiac MRI at age ≥10 years and a 12-lead ECG within 1 year of MRI. MRI measurements of biventricular size and ejection fraction (EF) were recorded. A single blinded observer analyzed ECGs for fQRS and QRS duration. fQRS was defined as ≥3 R-waves/notches in the R/S complex (more than 2 in RBBB) in ≥2 contiguous leads. QRS prolongation was defined as ≥160ms.

Results: 138 subjects were included after identification of cardiac MRI and EKG per above. Median age at MRI was 21.7 years (range 10 to 58.5) with 41% of subjects age ≤18. The average time from TOF repair to MRI was 22.3 ± 11.6 years. No deaths were identified. fQRS was found in 46% of subjects. Patients with fQRS had lower RV EF (p <0.001) and larger RV end-diastolic volume index (RVEDV) (p= 0.011). QRS prolongation was noted in only 25% of subjects; this group had lower RV EF (p <0.001), larger RVEDV (p= 0.002), and lower LV EF (p= 0.019). Stepwise linear regression revealed that both QRS prolongation (p= 0.001) and fQRS (p= 0.004) were independent predictors of RV EF. Only QRS prolongation had independent associations with RVEDV and LV EF. fQRS was seen in 42.1% of pediatric subjects.

Discussion: While fQRS was significantly associated with RV dysfunction in children and adults with rTOF, QRS prolongation was a superior predictor of MRI abnormalities. Results suggest that QRS prolongation is a stronger marker than fQRS for late structural RV and LV sequelae in rTOF. fQRS was frequently seen in pediatric subjects with rTOF, which has not been described.

19-149 (Poster)

Taking Aim at Gun Safety Education for Pediatric Residents: Utilizing the BeSMART program to increase resident comfort with gun safety principles

Kelsey Gastineau, Laura Lowrey, MD; Barbra Giourgas, MD; Amy Clark, MD; Annie Andrews, MD

Introduction
Firearm injuries are a threat to children’s health with America representing 91% of firearm-related deaths in children among all high-income countries. As pediatricians, we must systematically incorporate gun safety education into our interactions with families, regardless of the clinical area in which we work.

Objective
To measure the effect of educational interventions on comfort with gun safety topics and self-reported discussion rates among pediatric trainees. Additionally, we sought to identify barriers to discussing gun safety in our primary care clinic.

Methods
We developed an anonymous survey to quantify trainee comfort with and frequency of gun safety discussions during primary care visits. We began with a baseline survey prior to any intervention. We then rolled out the BeSMART (Secure guns in the home, Model responsible behavior, Ask about the presence of guns in other homes, Recognize the role of guns in suicide, Tell your friends to BeSMART) program in the clinic. This included a trainee lecture, signage in clinic, informational handouts and gun locks for interested families. Follow up surveys were distributed at two separate intervals between interventions to track changes in trainee comfort and reported rate of gun safety discussion. Chi-square tests evaluated for significant differences in trainee comfort and reported frequency of discussions.

Results
Twenty-seven Pediatric trainees completed our baseline survey. Baseline results revealed that the majority of trainees (59%) reported discussing gun safety with only 0-10% of patients. The most common barriers to discussion were time, difficulty integrating the topic into the visit and cultural stigma. We saw a non-significant increase in the proportion who discussed gun safety >50% of the time (from 7% to 13% to 15%). Additionally, the proportion of trainees who discussed gun safety < 10% of the time decreased from 59% to 56% then 15% (overall chi-square p=.07). The proportion of trainees who reported feeling very uncomfortable or uncomfortable decreased from 22% to 19% to 15% (overall chi-square p=0.67). The BeSMART program was identified as the most effective intervention increasing gun safety discussion.

Discussion/Conclusion
In this single center study we determined trainees report multiple barriers to discussing gun safety during clinic visits and although we saw an overall increase in reported discussion frequency, educational interventions alone have left room for continued improvement. As we work to optimize our interventions for the clinic, we plan to test strategies for incorporating the BeSMART program into inpatient workflow.

19-150 (Platform)
Predictive Value of Reported Last Oral Intake as Measured by Point-of-Care Gastric Ultrasound

Matthew M Moake MD PhD, Bradley C Presley MD, & Benjamin F Jackson MD

Background
Procedural sedation and analgesia (PSA) is a common procedure in the Pediatric Emergency Department (PED) for patients requiring urgent noxious interventions. There is debate regarding the optimal timing of PSA in relation to patient-reported last oral intake, or nil per os (NPO) status. Gastric point-of-care ultrasound (POCUS) provides the ability to directly measure the stomach content of an individual patient and is being used with increasing frequency as a surrogate for aspiration risk in general anesthesia planning.

Objectives
We sought to evaluate the accuracy of reported last oral intake in predicting measured gastric content as determined by gastric POCUS in PED patients.

**Methods**
We performed a prospective observational study of a convenience sample of English-speaking patients age six months and greater presenting to the MUSC PED between June 1 and December 31, 2018. Participants underwent a brief history including reported last oral intake and had gastric content measured using POCUS in both supine and right lateral decubitus (RLD) positions. Patients were then asked to remain NPO unless contraindicated by their care, and repeat POCUS examination was repeated every 2 hours until ED disposition. Measured gastric content was subsequently compared to expected content based on last reported oral intake as determined by American Society for Anesthesiology (ASA) fasting guidelines.

**Results**
We enrolled 99 patients during this 6-month period. Gastric content was successfully measured by POCUS in 95 of 99 (96%) patients. Of the 99 patients enrolled, only 17 were considered to be NPO per ASA guidelines at the time of POCUS evaluation. Amongst this group, 5 patients (29%) demonstrated gastric content inconsistent with NPO status. Of the 82 patients not considered to be NPO, 11 (13%) demonstrated content consistent with being NPO. 15 of the original 99 patients were able to be evaluated approximately 2 hours after their initial evaluation. Of these, only 4 patients were considered NPO, and 3 of these 4 were found to have content inconsistent with NPO status.

**Conclusions**
Reported last oral intake correctly predicted measured gastric content in 83% of patients. Only a small fraction of patients was considered NPO at the time of evaluation. Amongst these almost a third were found to have gastric content inconsistent with their NPO status. Further research will be required to determine the significance of this finding and identify predictors of patients with both expedited and delayed gastric emptying in the PED.

19-151 (Poster)

**Not Just Functional Abdominal Pain: Constipation and Pediatric Solid Tumors**

**Charyse Diaz, MD, Jennifer Jaroscak, MD, and Jackie Kraveka DO, Division of Pediatric Hematology-Oncology, Medical University of South Carolina, Charleston, SC 29425.**

**Background:** Constipation is a common pediatric diagnosis with benign functional constipation as the most common cause. Occasionally, it can herald a more insidious diagnosis particularly if constipation is an acute problem with associated severe abdominal distension, vomiting and/or a mass palpable by the child’s caregiver.

**Materials and Methods:** We present 4 cases of new oncologic diagnoses that originally presented to the ED with complaints of constipation. We will review their clinical presentation and physical exam findings at time of admission to illustrate the overlap between constipation and abdominal tumor presentations.

**Table 1. Patient 3y Characteristics and 5Presentationy**

**Results:** From December 2017 to February we identified 4 new oncology patients that had a similar presentation for constipation. We diagnosed neuroblastoma, Wilms tumor, rhabdomyosarcoma, and hepatoblastoma.
Discussion:
Constipation is a common childhood diagnosis. It is important to distinguish characteristics that can help differentiate function constipation from a pathologic cause of constipation. The diagnostic yield is greatest from answering these questions:
- Constipation: acute or chronic?
- Did adherence to a bowel regimen improve symptoms?
- Are there other associated symptoms such as fever, emesis or diarrhea?
- Is the abdominal distension so severe that it would not be simply explained by functional constipation?

Conclusions:
- Careful physical exam is most useful in diagnosing abdominal tumors
- Acute constipation in previously continent children warrants further investigation
- Consider imaging with severe abdominal distension that does not resolve with a bowel regimen

Future directions:
We would like to work with our ED residents on a diagnostic questionnaire that can help differentiate functional constipation from constipation due to a pathologic cause.
Prevalence of Gastroesophageal Reflux and Anti-Reflux Medication Use in a Nutrition NICU Graduate Clinic

Jessina Thomas1, Xiaoyi Tina- Zhang1, Brynn Donnelly1, Lauren Sams2, Sarah Taylor3, Ricardo Arbizu1,4, and Candi S. Jump1,4

1Department of Pediatrics, 2Division of Pediatric Nutrition, 3Division of Neonatology, 4Division of Pediatric Gastroenterology. Medical University of South Carolina, Charleston, SC.

Gastroesophageal reflux is a common symptom in preterm infants, but when reflux contributes to respiratory symptoms, feeding intolerance, or poor weight gain, medical therapy is often started.1-3 Anti-reflux medication use in these infants needs to be weighed against potential risks such as increased risk of necrotizing enterocolitis and infection.4,5 The use of these medications has been described in a large population based study.6 In our hospital, we have established a Nutrition Neonatal Intensive Care (NICU) Graduate Clinic to follow infants deemed to be at high risk for feeding intolerance or poor growth at time of discharge.

We retrospectively reviewed 202 patients seen for their initial Nutrition NICU Graduate Clinic visit between December 2016 and March 2018. Data was collected on demographics, growth, medical and nutritional interventions. The mean gestational age of our patients was 30 weeks, mean birthweight was 1.3 kg, and mean time to initial follow up was 4.9 weeks. Of all patients, 41 (20%) were discharged from the NICU on anti-reflux therapy (51% H2 blocker, 63% PPI). At the time of discharge from the NICU, 30 (73%) of the patients on anti-reflux medication had gastrostomy tubes. At initial follow-up, the average growth velocity for this population from time of discharge was 15.3 g/day, with 17% of patients with adequate weight gain (>30 g/d), 32% with moderate growth failure (20-29 g/d), and 54% with severe growth failure (<20 g/d). Despite scheduled early follow up, 7 out of the 41 (17%) patients on anti-reflux medications were admitted to the hospital prior to initial follow up and 4 of those were due to symptoms related to feeding intolerance or poor growth.

This data represents a unique cohort when compared to infants in previous studies.6 Our cohort should be considered higher risk based on number of patients with gestational age <28 weeks (34.2%), Medicaid as primary insurance (70.3%), and race demographics (53.5% African-American). Our patients have earlier follow up and detailed growth and readmission data. Overall, NICU patients discharged on anti-reflux therapy had similar birthweights and gestational ages as those not on anti-reflux therapy but they were more likely to have gastrostomy tubes (p<0.05), poor interval weight gain (p<0.05), and be admitted for symptoms related to feeding or growing difficulties (p=0.15). The presence of anti-reflux medications at time of discharge from NICU can help to identify those patients at high risk for readmission and growth failure and which patients should, therefore, have follow up earlier than the mean of 5 weeks.
Adequate Growth After Discharge

Brynn Donnelly, MD, X. Tina Zhang, MD, PhD, Jessina Thomas, MD, Lauren Sams, MS, RD, LD, Sarah Taylor, MD, Candi S. Jump, DO, MSEd

Early growth failure can have long-term effects on growth and neurodevelopment, and patients discharged from the Neonatal Intensive Care Unit (NICU) are at especially high risk. At time of discharge from the NICU there are obstacles to continuing to provide appropriate nutrition that include: coexisting medical conditions, maternal milk supply and ability to provide expressed breast milk, and difficulties with fortification of feeds.

We describe a cohort of patients discharged from our institution’s Level II & III nurseries with outpatient follow-up in a designated “Nutrition NICU Graduate Clinic” with a pediatric gastroenterologist and dietitian. Patients discharged from the NICU can be referred to the clinic based on birth weight, feeding regimen, and/or practitioner concern and are typically seen 4-8 weeks after discharge from the NICU. The common interventions at visits include: adjusting caloric density and volume of feeds, managing reflux and constipation, changing formula, educating family on feed preparation and managing gastrostomy tube feeds.

Data was retrospectively reviewed for 202 patients seen for their initial clinic visit between December 2016 and March 2018. The caloric density of feeds at the time of discharge varied from 19 kilocalories per ounce (kcal/oz) to 30kcal/oz with 50% percent of infants receiving breastmilk as a part of their feeding regimen. At the first visit, 84 of the 202 patients (46.1%) were no longer on the feeding regimen prescribed at the time of NICU discharge because of improperly mixed formula (42.9%) or other feeding variations. In these patients, 60.7% were receiving feeds below calorie goal and 15.5% were receiving feeds above calorie goal. There was no significant difference in mean growth velocity between patients receiving feeds inconsistent compared to consistent with discharge instructions (24.3 g/day vs. 27.8 g/day), but there was a significant difference in those patients whom had lost weight (8.3% vs 1.7%, p<0.05). Intervention was required to increase caloric density of feeds of 40.4% of patients who were not following discharge instructions and in 11% of patients whom were following instructions (p<0.05) (Table 1).

These results highlight the importance of education and timely intervention in this high-risk population. The high percentage of patients receiving feeds inconsistent with discharge regimen, despite formula mixing education prior to discharge, emphasizes the need for re-evaluation of our educational methods. We plan to study this area further with a quality improvement project.
Table 1. Patients receiving feeds consistent with discharge feeding instructions at time of follow up

<table>
<thead>
<tr>
<th></th>
<th>Consistent</th>
<th>Inconsistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n, %)</td>
<td>118 (58.4%)</td>
<td>84 (41.6%)</td>
</tr>
<tr>
<td>Readmission for poor weight gain (n, %)</td>
<td>2 (1.7%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Patients that lost weight after discharge (n, %)</td>
<td>2 (1.7%)</td>
<td>7 (8.3%)*</td>
</tr>
<tr>
<td>Growth velocity after discharge (g/d)</td>
<td>27.8</td>
<td>23.4</td>
</tr>
<tr>
<td>Clinic nutrition intervention (n, %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase nutrition</td>
<td>13 (11.0%)</td>
<td>31 (40.4%)*</td>
</tr>
<tr>
<td>Decrease nutrition</td>
<td>17 (14.4%)</td>
<td>19 (22.6%)</td>
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</tbody>
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*p<0.05

19-154 (Poster)
Title: Development of a Nursery Protocol for the Management of Prenatally-Diagnosed Pyelectasis

Amy M Clark, MD, Jessica Hook, MD, Missy Lalich, MD, Mia Amaya, MD, MPH, Claire A MacGeorge, MD, MSCR

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Background: Abnormalities of the urinary system are the most common congenital anomalies detected on routine prenatal ultrasound and should be followed up postnatally to prevent chronic kidney disease and end stage renal disease. There are no consensus guidelines for postnatal management of urinary anomalies such as pyelectasis (dilation of renal pelvis). Creating a management protocol may improve consistency in management and follow up.

Methods: A survey was created with questions regarding management choices in a step-wise fashion for newborns with prenatally-diagnosed pyelectasis. The survey was then distributed to all the pediatric nephrologists at MUSC and their results informed the decision points in the protocol. A retrospective chart review was then performed to gather baseline data from April to October 2018.

Results:
The following recommendations were endorsed by all nephrologists:
1. Obtain postnatal renal ultrasound for prenatal pyelectasis prior to discharge from nursery.
2. Consult pediatric nephrology for postnatal renal ultrasound result of grade 2 hydronephrosis or higher regardless of laterality or gender.
3. All patients with normal or grade 1 hydronephrosis and higher regardless of laterality should follow up with pediatric nephrology one month from discharge with a repeat RUS the same day.
A total of 18 patients were identified as having prenatal pyelectasis in the study period. Seven patients had resolution of pyelectasis prior to delivery based on prenatal ultrasound. Of the 11 patients who had persistent pyelectasis, 55% had a RUS done prior to discharge. Four patients had grade 2 hydronephrosis or higher on postnatal ultrasound and 50% had an inpatient consult to nephrology. Only 55% of patients received a referral to nephrology and order for follow up.
renal ultrasound upon nursery discharge. Of the 11 patients, 10 had follow up with pediatric nephrology. The range of time to nephrology follow up was 6 days to 5 months from hospital discharge (average: 1.8 months).

**Conclusions:** All pediatric nephrologists at MUSC had similar views regarding management of pyelectasis, allowing for a cohesive, streamlined protocol. This protocol will aid with identifying infants with major GU anomalies, as well as improve our inpatient management and outpatient follow up compliance.

19-155 (Platform)

**Effect of different hyperthermia methods on drug delivery with thermosensitive liposomes**

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**Abstract**

Background: Anthracyclines like doxorubicin are used in pediatric cancer patients, but are associated with cardiotoxicity leading to cardiac dysfunction and other morbidities. To prevent this, targeted drug carriers like thermosensitive liposomes (TSLs) are being developed. TSLs are nanoparticles that encapsulate a drug and release it when exposed to hyperthermic temperatures (>40 ºC), thus, achieving a targeted drug delivery.

Objective: The goal of this study was to quantify and explain the impact of different hyperthermia methods on tumor drug uptake with TSL encapsulated doxorubicin (TSL-Dox).

Methods: We developed a 3-D coupled computer model that simulated both tissue heating and drug delivery. The drug delivery model simulated intravascular release from TSL-Dox, drug extravasation into tissue interstitium, and cellular uptake. A mouse hind limb was scanned by a 3-D scanner and the resulting geometry was imported into finite element modeling software. Three heating devices were simulated considering parameters used in prior in vivo studies: (1) water bath (42ºC temperature), (2) thermistor probe (45 ºC temperature), and (3) infrared (IR) laser (43 ºC maximum tissue temperature). We simulated an infusion of TSL-Dox at a dose of 5 mg/kg over 30 s. 15 min post infusion, hyperthermia was applied for 15 min, followed by 10 min of cooling. We report the tumor temperature at the end of hyperthermia, TSL plasma half-life, and tumor drug concentration 10 min after hyperthermia conclusion.

Results: Water bath hyperthermia achieved uniform heating of the hind limb and tumor with an average tumor temperature of 40.3 ºC (range 40.0-40.8ºC). The thermistor produced highly localized heating but did not achieve adequate release temperatures throughout the tumor (average 38.8ºC, range 37.6-42.7ºC). The IR laser produced localized heating with adequate tumor temperatures (average 40.3 ºC, range 39.3-40.7 ºC). The TSL Dox plasma half-life was 18.1, 31.3 and 23.1 min for water bath hyperthermia, thermistor and IR laser, respectively. Tumor drug concentrations for water bath, thermistor probe, and IR laser were: 10.9 μg/g (range 10.6-11.3 μg/g), 11.5 μg/g (range 7.0-16.2 μg/g), and 15.2 μg/g (range 14.6-15.6 μg/g). The large-volumetric heating via water bath resulted in rapid depletion of encapsulated doxorubicin in the systemic circulation, which explains the lesser tumor drug uptake. The thermistor caused higher tumor drug concentration than water bath due to smaller heating volume, but likely
underdosed some tumor regions due to inadequate temperatures. The laser device exposed the whole tumor to a drug concentration higher than the earlier heating methods and achieved adequate temperatures while limiting hyperthermia outside the target volume.

Conclusions: For optimal TSL-based drug delivery, localized hyperthermia is important to avoid rapid depletion of available encapsulated drug in systemic plasma as observed in the commonly used water bath method. Overheating larger tissue volumes will decrease the drug available for TSL based delivery to tumors resulting in a poor therapeutic outcome.

Keywords: hyperthermia, computer model, thermosensitive liposomes, drug delivery
Penicillin Allergy in the MUSC Pediatric Emergency Department

Mason Ruthford MD, Matthew Moake MD PhD, Scott Russell MD

Background
Penicillin (PCN) allergy is commonly reported among Pediatric Emergency Department (PED) patients. Although antibiotics (ABX) can be a cause of life-threatening immune-mediated drug reaction, studies have shown many reported allergies to be inaccurate, with subsequent testing revealing no true allergy. PCN allergy displaces use of appropriate first-line treatments with broad-spectrum and non-beta-lactam ABX. This exposes patients to increased side effects, adverse events, and cost, and can lead to ABX resistance. Identification and testing of patients with inaccurate PCN allergy present an opportunity to address these issues and improve overall patient care.

Objectives
As part of a quality improvement initiative to address PCN allergy, we sought to define the overall burden of PCN allergy within the PED. With this data we hope to design an intervention to address PCN allergy for PED patients, with emphasis on identifying and testing patients with likely inaccurately-listed allergy.

Methods
We performed an EPIC query of current pediatric patients to determine the overall prevalence of PCN allergy; our needs population. We identified patients with PCN allergy who had a PED visit in the past year, our convenience group, as well as those patients with prior Allergy encounters as a surrogate for potential prior PCN allergy evaluation. We further reviewed listed PCN allergy symptoms to estimate those with likely low-risk symptoms that may be amenable to ED-based testing.

Results
2,239 current pediatric patients with listed PCN allergy were identified. Among these, allergy severity was listed as high in 566 (25.3%), medium in 279 (12.5%), and low in 730 (32.6%). Closer evaluation of reported symptoms demonstrated potentially low-risk symptoms in as many as 1,295 patients (57.8%), with only 213 patients (9.5%) listing anaphylaxis, angioedema, or shortness of breath. Of all patients with listed PCN allergy, only 113 (5.0%) had a prior listed Allergy clinic encounter. 213 (9.5%) had a PED visit within 2018.

Conclusions
A large number of pediatric patients within the MUSC system have a listed PCN allergy. Of these, only a small fraction has established care with the MUSC Allergy department, indicating their PCN allergy has likely not been addressed. The PED saw approximately ten percent of these patients in the past year, and as such could serve a valuable role in closing this differential. Of those patients with PCN allergy, over fifty percent had potentially low-risk symptoms that may be amenable to an ED-based screening and testing initiative.
MATERNAL VITAMIN D STATUS AFFECTS HEPATITIS B VACCINE RESPONSE IN BREASTFEEDING INFANTS

Danforth A. Newton PhD, John E. Baatz PhD, Judy R. Shary MS, Carol L. Wagner MD
Dept. of Pediatrics/Neonatology, MUSC

Background/Hypothesis: Vitamin D (VitD) affects immune function across the lifespan, which includes pregnancy and lactation. We hypothesized that the response of fully breastfeeding infants to HBV would differ as a function of maternal and/or infant's vitD status as measured by circulating 25-hydroxyD (25-D) concentration.

Methods: Plasma 25-D concentration and HBV titers were measured in a subset of mothers and exclusively breastfeeding infants (n=56 pairs) participating in a lactation vitD supplementation clinical trial. Mothers were randomized to receive either 400 vs. 6400 IU vitD3/day and infants 400 IU/day or placebo (if mother was in 6400 IU group). An additional 14 infants were exclusively formula-fed. 25-D concentration (RIA) and infant anti-HBV IgG titers (ELISA) after 3 vaccinations (7 months of age) were measured. The association between maternal vitD treatment group, circulating 25-D, and HBV IgG titers was explored using Spearman's correlation and ANOVA.

Results: Though still considered immune, exclusively breastfeeding infants of vitD-sufficient mothers had significantly lower titers of plasma anti-HBV IgG compared to infants of vitD-insufficient/deficient mothers (p<0.001). Statistical correlation of infant titer was much more strongly linked to mother's vitD status than to infant’s own, and this relationship was not seen in vitD-sufficient, formula-feeding infants.

Conclusions: HBV IgG titers of breastfeeding infants differed at 7 months of age by maternal vitD treatment and not on the basis of infant vitD status. These findings suggest that effects of vitD on breastmilk composition results in regulation of an infant’s immune response. A currently ongoing lactation pilot study continues to collect samples to confirm and expand these findings.

19-158 (Poster)

HLA-DR Upregulation in Pediatric Kidney Transplant Biopsies

Omar Moussa, Sally Self, Evelyn Bruner, Katherine Twombley

Introduction Renal tubular epithelial cells do not typically express human leukocyte antigen DR (HLA-DR). It’s expression has been associated with different types of tubular injury in adult renal transplant patients including rejection, CNI toxicity and viral infections. This has not been studied in children, and considering that children have different immune systems that adults, it’s significance is unclear. Our center routinely stains for HLA-DR presence in all transplant biopsies.

Objective Determine which types of injuries in pediatric kidney transplant patients were associated with HLA-DR expression.

Design/Methods A retrospective chart review was conducted of children receiving a kidney transplant biopsy between January, 1st of 2011 to October, 31st of 2016. Inclusion required
recipients to have at least received one kidney transplant biopsy and be under the age of 18 at the time of transplant. Data was collected using medical records.

**Results** There were 41 pediatric kidney transplant recipients with 117 biopsies eligible for review (table 1). There was an increased HLA-DR expression with ACR and mixed AMR/ACR. Interestingly, the GFR was lower and there was more fibrosis in the HLA-DR positive group. These results suggest that HLA-DR expression in renal tubular epithelia cells was associated with ACR and mixed ACR/AMR. HLA-DR expression was also seen more in biopsies with longer times from transplant and was associated with lower GFR and more fibrosis suggesting it might be more associated with later rejection episodes.

<table>
<thead>
<tr>
<th>Histologic findings:</th>
<th>HLA-DR all (n=117)</th>
<th>HLA-DR positive (n=28)</th>
<th>HLA-DR negative (n=89)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>bACR</td>
<td>7 (6%)</td>
<td>4 (14.3%)</td>
<td>4 (4.5%)</td>
<td>0.09</td>
</tr>
<tr>
<td>ACR</td>
<td>10 (8.5%)</td>
<td>7 (25%)</td>
<td>3 (3.4%)</td>
<td>0.0017</td>
</tr>
<tr>
<td>AMR</td>
<td>7 (6%)</td>
<td>3 (10.7%)</td>
<td>4 (4.5%)</td>
<td>0.35</td>
</tr>
<tr>
<td>ACR/AMR</td>
<td>10 (8.5%)</td>
<td>9 (32.1%)</td>
<td>1 (1.1%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Isometric vaculization</td>
<td>2 (1.7%)</td>
<td>0</td>
<td>2 (2.2%)</td>
<td>1</td>
</tr>
<tr>
<td>BK</td>
<td>2 (1.7%)</td>
<td>1 (3.6%)</td>
<td>1 (1.1%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Pylonephritis</td>
<td>3 (2.6%)</td>
<td>2 (7.1%)</td>
<td>1 (1.1%)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

**Conclusions**
These results suggest that HLA-DR expression in renal tubular epithelia cells was associated with ACR and mixed ACR/AMR. HLA-DR expression was also seen more in biopsies with longer times from transplant and was associated with lower GFR and more fibrosis suggesting it might be more associated with later rejection episodes.

19-159 (Poster)

**Isradipine or hydralazine: Which is more cost effective and safer for the treatment of hypertension**

**Kathleen Sprott1, Elizabeth Mack1, Oana Nicoara1, Katherine Twombley1.**

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**Background:** Isradipine is commonly used for the treatment of acute hypertension in transplant patients in many hospitals but was not on formulary in our facility. There were several IV options for treatment of acute HTN, but limited PO options. Most of the PO options have undesirable side effects in many of our patients: 1) Hydralazine, PO commonly not used in peds for acute HTN 2) Minoxidil, hypertrichosis, edema, pericardial effusion in infant at our center, would need
to be compounded 3) Clonidine, sedation (not ideal in setting of HTN when monitoring mental status) and rebound HTN with discontinuation.

Objective: To compare the cost and safety of PO Isradipine verses IV Hydralazine for the use of acute HTN in children. We hypothesize that Isradipine use is as safe as Hydralazine and results in decreased costs.

Methods: We conducted a 6-month temporary addition of Isradipine to our hospital formulary with a follow-up evaluation to see cost and safety of Isradipine use compared to historical Hydralazine use. Historical Hydralazine data was collected from February 2015 to July 2015. Prospective Isradipine data was collected from February 2016 to July 2016. Safety data was collected from patient safety information forms and clinical record review.

Results: Cost of Isradipine: 2.5 mg capsule: $1.36, 5 mg capsule: $1.99

<table>
<thead>
<tr>
<th>Time</th>
<th>IV doses for hydralazine</th>
<th>Hydralazine cost</th>
<th>Nicardipine cost</th>
<th>Nitroprusside orders</th>
<th>Isradipine doses</th>
<th>Isradipine cost</th>
<th>Total cost</th>
<th>PSIs/other isradipine safety concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb-July 2015</td>
<td>496</td>
<td>$6768 + dilution doses</td>
<td>$4064</td>
<td>19</td>
<td>0</td>
<td>0</td>
<td>$0</td>
<td>10,832</td>
</tr>
<tr>
<td>Feb-July 2016</td>
<td>218</td>
<td>$2,361 + dilution doses</td>
<td>$2464</td>
<td>20</td>
<td>206</td>
<td>180</td>
<td>5005</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusion: Isradipine use resulted in a 50% reduction in injectables based on current use. There were no safety concerns reported. Isradipine is a safe alternative to IV medications when used for acute hypertension in both transplanted and non-transplanted children.

19-160 (Poster)

Iron Sulfur Transport as a Regulator of Placental Growth

Brill-Edwards, Madeline, Brooker, John, Sutton, Kim, Lee, Kyu-Ho

OBJECTIVES: The cardiac homeobox transcription factor, Nkx2--5, has roles in both normal heart development and placental development during pregnancy. In mouse placentae, Nkx2--5 is expressed in multiple trophoblast lineages during placental development. We have recently shown that Nkx2--5 positively and directly regulates the gene for a novel protein known as Coiled-coil domain containing (Ccdc) 117. Ccdc117 interacts with the CIA2B component of the MIP18/MMS19 cytoplasmic iron sulfur cluster assembly complex which is crucial for DNA replication and repair. Following depletion of either Ccdc117 or CIA2B protein in HeLa cells, there is a reduction in the rate of DNA synthesis and cellular proliferation, with an associated delay at the G1--S transition, and
significantly increased DNA damage. As part of an overall investigation of the role of Nkx2-5 and Ccdc117 in placental development, this project seeks to define the effects of decreased expression of Ccdc117 and CIA2B in HTR8 extravillous trophoblast cells, placental trophoblasts that become endovascular cytotrophoblasts that remodel spiral arteries essential for nourishing the placenta and the developing fetus.

METHODS: We used siRNA transfection to accomplish depletion of Ccdc117 and CIA2B protein as confirmed by Western blot. Using propidium iodide staining and flow cytometry we obtained cell cycle profiles of HTR8 cells following knockdown. Using immunofluorescence assay, we examined the expression of DNA damage markers, apoptosis markers, and mitosis markers in HTR8 cells that had undergone siRNA knockdown of Ccdc117 and CIA2B.

RESULTS AND CONCLUSION: We have found that siRNA mediated knockdown of Ccdc117 in HTR8 extravillous trophoblast cells results in cell cycle delay at the G1/S transition or early S phase, with evidence of increased DNA damage and decreased proliferation. Ongoing experiments will determine if CIA2B siRNA knockdown in HTR8 extravillous trophoblast cells has similar effects.

19-161 (Poster)

Endoscopic pharmacobezoar removal in a patient with intractable serotonin syndrome

Cummings, Quinn, Allen Kelsey, Kane, Ian

Serotonin syndrome generally resolves with supportive care within 24 hours. We describe a case of medication-induced serotonergic toxicity refractory to supportive care and antidotal therapy that resolved after removal of a pharmacobezoar by EGD. Our patient was a 14 year-old male prescribed 40 mg fluoxetine daily for depression who was transferred to our hospital with altered mental status. He was brought by EMS to an outside hospital after having bizarre behavior and seizure-like activity at school. At this facility, he had a normal CBC and CMP, and a CT head which was reported as unremarkable. On arrival to our ED, he was combative and had generalized tonic-clonic seizure activity for which he was admitted to the PICU. Vital signs were HR 135, BP 130/56, T 36.7 C, and RR 21 with SaO2 of 99% on room air. He was agitated with sustained clonus of his lower extremities, dry mucous membranes and axillae, normal bowel sounds and symmetric briskly reactive 5 mm pupils. He was oriented to person only. ECG showed sinus tachycardia but was otherwise normal. In the PICU, he was on a midazolam infusion and q12h cyproheptadine; despite addition of morphine and dexmedetomidine over the next 2 days, he still had signs of serotonin syndrome. He developed respiratory failure on day 3 and was subsequently intubated. The next day he had an EGD wherein a drug-eluting pharmacobezoar of bupropion and fluoxetine was removed from the stomach. After removal of these pill fragments and subsequent WBI, the patient’s mental status returned to baseline, and he was extubated the next day. Pharmacobezoars in the GI tract generally have an obstructive component and rarely cause prolonged toxicity. Drug-containing bezoars are more likely to form in enteric-coated medications, as the capsule prevents dissolution in gastric acid, though they have been reported in extended-release and immediate-release preparations and even liquid preparations. Even in massive overdose, isolated fluoxetine ingestion rarely results in serotonin syndrome, and seizures are rare. Our patient's fluoxetine level was 320 ng/ml on day 3 of
illness, suggesting that a co-ingestant (bupropion as described earlier) was responsible for the severity of his presentation. Bupropion has proconvulsant properties and can increase serum SSRI levels due to CYP450 2D6 pathway inhibition. Pharmacobezoar formation is an underrecognized clinical entity with sparse data to guide management. We believe it is prudent to consider endoscopy in a patient with drug toxicity that persists beyond expected toxicokinetic parameters.

19-162 (Poster)

Sam68 Alternative Splicing of sFlt1 mRNA in the Genesis of Preeclampsia

Wagener, Quentell, Sinkway, James, Coley, Kymbreana, Awe, Oyindamole, Lee, Kyu-Ho

OBJECTIVES: Preeclampsia is a condition that occurs in 3--5% of pregnant women. Symptoms include hypertension, proteinuria, and is associated with high levels of the antiangiogenic factor sFlt1, produced in the placenta, in the circulation. In previous work, we found an association between high placental mRNA levels of sFlt1 and an RNA binding protein, Sam68. Sam68 mediates alternative RNA processing events like those responsible for generating sFlt1. In preliminary mouse studies, induced expression of placental Sam68 results in elevated levels of sFlt1 in the circulation.

The objective of this study was to define the mechanism by which Sam68 regulates sFlt1 in preeclampsia. Specifically, we wished to confirm the physical interaction between sFlt1 precursor RNA transcripts and Sam68. Defining the mechanism that regulates sFlt1 can lead to
more targeted therapies; for example, small molecule screening, that can be directed towards inhibiting the generation of sFlt1 by interaction with Sam68.

METHODS: We used plasmid transfection to express HA--tagged wild--type Sam68, or Sam68 isoforms containing a deletion of or a point mutation in the RNA--binding KH domain, in HTR8 placental trophoblast cells. We then performed RNA immunoprecipitation followed by qPCR to determine if sFlt1 could be recovered with the Sam68 protein.

RESULTS: Immunoprecipitation experiments confirmed the recovery of sFlt1 precursor RNA transcripts with wild--type Sam68 protein. Recovery with wild--type Sam 68 was approximately 16x more efficient as compared to recovery with either mutated isoforms.

CONCLUSIONS: Preliminarily, these data support our hypothesis that Sam68 is directly involved in the alternative splicing of Sam68 to produce and regulate sFlt1 production in placental trophoblast cells. Ongoing and future experiments are focused on further validation of the precise interactions of Sam68 with consensus splice recognition sequences in the precursor RNA, and on the effect of varying Sam68 protein levels on splicing efficiency.

19-163 (Poster)

Piece It Together: Balance Assessments in Youth with ASD and NDD in a Novel Wellness Program

Holly Knapp, SPT, Carrie Papa; Conner McDonald, MS3; Martina Mueller PhD; Mary Ashley Mercer, MD; Carolyn Peterseim, MS2; Janis Newton; Cynthia Dodds PhD, PT, PCS; Eve Spratt MD, MSCR

Piece It Together (PIT) is a community-based comprehensive wellness program designed for transitional age youth with Autism Spectrum Disorder (ASD) or other mild neurodevelopmental disabilities (NDD). The program focuses on exercise, nutrition, stress management, and socialization. The USDHHS recommends that adolescents participate in at least 60 minutes per day of moderate-to-vigorous intensity physical activity. In a study by Stanish et al., adolescents with ASD engaged in significantly less moderate-to-vigorous physical activity than their typically developing peers, with only 14% meeting the Physical Activity Guidelines for Americans [1]. Additionally, research findings have documented balance and coordination impairments in individuals with ASD [2], with improvements seen following balance and flexibility training programs [3]. While additional outcomes, such as flexibility, depression and anxiety, were collected as part of the larger PIT program, the purpose of this pilot study was to assess balance as measured by the mini-Balance Evaluations Systems Test (miniBEST) and strength as measured by the MicroFit and the InBody 570 Analyzer©2014, before and after a fitness intervention in youth with ASD or other NDD. The miniBEST [4] has shown good interrater and, test-retest reliability, and good correlation with other balance assessments. It is scored on a 0-2 scale; score 0 is physically unable to perform the action, 1 is some imbalance, and 2 is performing the action without difficulties. The MicroFit measures biceps muscle strength and the InBody 570 measures skeletal muscle mass. In 2017 and 2018, 32 participants (64.3% male; mean age 19.4 years +/- 3.9) completed the 6-week PIT program consisting of 90-minute classes two times per week. Each class incorporated balance activities and 45 minutes of activity such as spinning, Tae Bo, or circuit training. Results from the miniBEST pre and post
testing included small trend improvements from pre to post in the Reactive Postural Control (p=0.078) subscale. In addition, measures of strength showed improvements, bicep muscle strength (p=0.024) and skeletal muscle mass (p=0.028). Balance deficits in this population can improve within a short amount of time with regular physical exercise interventions.

19-165 (Poster)

Title: Loss of social motivation predicts atypical deletion size in Williams syndrome

Authors: Lugo, M., Parrish, P., and Kozel, B.A.

Abstract:
Williams-Beuren Syndrome (WBS) is a multisystem disorder produced by the hemizygous deletion of 1.5-1.8 Mb on chromosome 7q11.23. Encompassing 26-28 genes, manifestations include characteristic facies, vascular abnormalities, hypercalcemia, and a predictable pattern of neurodevelopmental and cognitive strengths and weaknesses. Small numbers of patients with longer deletions, extending in the centromeric or telomeric direction from the WBS critical region have been described, with varying consequences. To elucidate clinical differentiators between these uncharacteristic deletions as compared to typical ones, we evaluated nine individuals with atypical WBS deletions – four extending in the centromeric direction, four telomeric, and one bi-directionally. We found a history of infantile spasms and refractory seizures, profound developmental delays (including significantly delayed gross motor skills and no apparent speech or communicative abilities), and sex hormone differences in the patient with a bi-directionally larger deletion; however, these clinical phenotypes were more variable in the 8 individuals with centromeric or telomeric-only deletions, with the most notable finding being the absence of infantile spasms or seizure history in any of these individuals. Lastly, given the well-known neurocognitive profile of hyper-sociality juxtaposed with autistic features in WBS, we sought to determine how the social phenotypes of individuals with an atypical deletion compared to those with a more typical deletion. Utilizing the Social Responsiveness Scale-2 (SRS2), a frequently utilized measure to assess dimensions of autism-spectrum disorder, we found that individuals with atypical deletions had significantly higher (more abnormal) social motivation scores (p=0.002) when compared to their counterparts with typical WS deletions. In recognizing this distinction, physicians can better identify patients with atypical WS deletions who may benefit from additional diagnostic testing including chromosomal microarray (CMA) evaluation, screening, and therapeutics aimed at manifestations not commonly seen in typical WS. Comparisons of our cohort to individuals with atypical deletions in the literature will be presented.

19-166 (Poster)

Uncovering novel Hoxc8 functional roles in vivo through CRISPR/Cas9 genome editing in mice

Diana Fulmer1, Jan Guz1, Mary Ann Baybo1, Russell Norris1, Andy Wessels1, Michael Kern1, Richard Visconti1, Alexander Awgulewitsch2,1

1Department of Regenerative Medicine & Cell Biology, Medical University of South Carolina (MUSC), Charleston, SC; 2 Department of Medicine, MUSC.
BACKGROUND. Members of the phylogenetically conserved Hox family of transcription factors typically have multiple functional roles in different developmental scenarios and in adult tissues and organs. This is illustrated by Hoxc8 with its documented roles in patterning the axial skeleton, motoneuron specification, and mammary gland development, as well as its involvement in different types of cancers. However, raw data from gene expression databases (Genepaint, Allen Brain Atlas) as well as preliminary data of our own suggest additional and hitherto unknown functions in lung, heart, and brain that have yet to be uncovered.

OBJECTIVE. Based on these preliminary Hoxc8 expression data, the goal of this study was to assess whether loss specifically of the Hoxc8 homeodomain DNA binding function might affect lung and heart development.

METHODS. Through CRISPR/Cas9-mediated genome editing in C57BL/6J mice, a new Hoxc8Δhb mutant allele was created in which the homeodomain DNA binding function was disrupted by a single nt exchange. Potential abnormalities in lung and heart development were determined by preliminary histopathological analyses.

RESULTS. Homozygous Hoxc8Δhb/Δhb mice suffer from a high degree of early postnatal lethality (>50%), similar to the previously reported Hoxc8-/- null mice, the causes for which had not been determined. At E16.5, Hoxc8Δhb/Δhb mutants seem indistinguishable from their Hoxc8+/+ littermates with respect to size and overall appearance, and initial histopathological analysis of lung and heart sections (H&E staining) did not indicate obvious structural defects. However, an overtly sick Hoxc8Δhb/Δhb mouse sacrificed at 10d post natum (P10) that was about half in size and weight compared to its littermates showed severe abnormalities in pulmonary architecture as well as possible histopathological abnormalities of the heart. The lungs showed thickened alveolar walls and enlarged interstitial regions. These pathological changes were mirrored by changes observed in a rare adult (≈3 months) Hoxc8Δhb/Δhb mouse. Potential cardiac defects in the mutant mouse at P10 included disorganization of the right ventricular wall and aberrant mitral valve morphology.

CONCLUSIONS. By introducing a single nt exchange, we generated novel Hoxc8 mutants whose apparent developmental defects suggest previously unknown roles for Hoxc8 in lung and heart development. In general, this type of approach of introducing small changes in critical functional domains appears greatly suitable for modeling certain SNP-associated human diseases.

19-167 (Platform)

Microstructural diffusion MRI changes from DKI following taVNS treatment

H. Moss, J. Jensen, B.W. Badran, M. George, D.D. Jenkins

Background: Premature or hypoxic ischemic (HIE) birth is associated with significant impairment of motor skills, which may manifest as poor oromotor skills involved in feeding. Transcutaneous auricular vagus nerve stimulation (taVNS) paired with oromotor feeding training, is being tested as a novel therapy that may lead to remodeling of motor cortex and improved feeding skills. Non-invasive neuroimaging via diffusional kurtosis imaging (DKI) provides quantitative biomarkers of white matter (WM) tract integrity, injury and perhaps response to therapy. DKI captures greater complexity within the tissue microenvironment than
standard clinical diffusion tensor imaging. Therefore, microstructural changes with taVNS treatment may be better quantified with DKI.

**Objective:** To determine if taVNS enhances plasticity involved in a learned feeding task through microstructural changes in specific WM tracts from DKI before and after a 2-3-week course of taVNS-paired feeding.

**Design/Method:** We obtained consent in this IRB approved study to enroll preterm or HIE infants (n=12, mean 44±5 weeks GA). Unsedated DKI (3T Siemens Skyra) was performed before and after the 2-3-week taVNS-paired feeding sessions. DKI parameters: 3mm3 voxels, TE/TR 141/6000ms, with in-plane image acceleration of 2. Raw DKI data were denoised; Rician noise bias and Gibbs artifact ringing corrected with smoothing, and diffusion and kurtosis tensors calculated using Diffusional Kurtosis Estimator (DKE) for mean diffusivity (MD), fractional anisotropy (FA), and mean kurtosis (MK) parametric maps. Bilateral regions of interest (ROI) from the Johns Hopkins neonatal WM brain atlas were transformed into each subject’s image space and binarized as masks for voxel-wise averaging. Paired t-test compared pre- and post-treatment FA, MD and MK for right and left posterior limb of internal capsule (PLIC) and inferior frontal orbital fasciculus (IFOF). Parameters for infants who attained full oral feeds were compared to those who did not and required G-tube placement in a general linear model (GLM) with GA (birth, pre and post-scan) as covariates.

**Results:** DKI identified significant changes in WM tract microstructure over the taVNS treatment period. FA and MK in L & R PLIC and IFOF were significantly different from pre to post-taVNS (all p< 0.05). Feeding outcome significantly contributed to the GLM in predicting FA of R IFOF.

**Conclusion:** This pilot data suggests that 2-3 weeks of taVNS treatment stimulates microstructural maturation observable over a short time-span in DKI diffusivity and kurtosis parameters.

19-168 (Poster)

**Very Low Birth Weights (VLBW) Infants Reaching Full Enteral (EN) Feeds Within Two Postnatal Weeks—Implementation and Outcomes of an Enteral Nutrition Protocol**

**A Fenin 1, J Ross1, JC Newman 1, S Taylor 2 1Medical University of South Carolina, Charleston, SC, Yale University School of Medicine, New Haven, CT**

Background: Debate continues regarding early initiation and rapid advancement of VLBW infants EN despite evidence of safety and known risks of parenteral nutrition (PN) and central venous lines (CVL). Recent guidelines recommend full EN by 7 postnatal days for infants born 1-1.5 kg and by 14 postnatal days for infants born <1 kg to optimize gastrointestinal health and decrease exposure to PN and CVL.

**Objectives:** Identify whether new EN goals (reach full EN by 7 postnatal days for infants 1-1.5 kg and by 14 postnatal days for infants <1kg) were achieved, tolerated, and associated with positive or negative outcomes.

**Methods Used:** After IRB waiver, VLBW infants admitted in first postnatal day data was abstracted from a clinical nutrition database and categorized as either 6 months prior to revised
EN protocol (Epoch 1) or after implementation (Epoch 2). The implemented protocol included feed initiation 6-24 hours post-birth, decrease in trophic feed days, discontinuation of gastric residual monitoring with a schedule to 1) reach full EN by postnatal day 7 with CVL removal by postnatal day 5 for infants born 1-1.5 kg and 2) reach full EN by day 14 with CVL removal on day 12 for infants born <1 kg.

**Summary of Results** Epoch 1 had 50 infants [(31 1-1.5 kg and 19 < 1 kg) and Epoch 2 had 117 (75 1-1.5 kg and 42 < 1 kg)]. Infants 1-15 kg reaching full EN by 7 days were 36% in Epoch 1 and 83% in Epoch 2 (p<0.0001). Infants <1kg reaching full EN by 14 days were 32% in Epoch 1 and 78% in Epoch 2 (p=0.0005).

Median (interquartile range) CVL days from Epoch 1 to Epoch 2 decreased, for infants 1-1.5 kg, from 9 (8,11) to 6 (5,7) and, for infants <1kg, decreased from 17 (14,32) to 9 (7,9) (p<0.0001 for both). Median (interquartile range) parenteral nutrition (PN) days from Epoch 1 to Epoch 2 decreased, for infants 1-1.5 kg, from 8 (6,10) to 5 (5,6) and, for infants < 1 kg, decreased from 17 (14,26) to 8 (8,10) (P<0.0001 for both).

**Conclusions** In this study, with the implemented protocol, ~80% of infants born 1-1.5 kg/ and <1 kg reached full EN by 7 and 14 postnatal days, respectively, with a significant decrease in CVL and PN days. Further study to ensure safety and sustain these improvements is warranted, but the observed decreased risk and likely cost has potential for a significant improvement in neonatal care.

**19-169 (Poster)**

Effects of mavoglurant on visual attention and pupil reactivity while viewing photographs of faces in Fragile X Syndrome.

**Hessl, D. / Berry-Kravis, E. / Hagerman, RJ, Harvey, D. Sansone, S. Joshi, R. / Chin, J. / Crestodina, C.**

**BACKGROUND:**
Numerous preclinical studies have supported the theory that enhanced activation of mGluR5 signaling, due to the absence or reduction of the FMR1 protein, contributes to cognitive and behavioral deficits in patients with fragile X syndrome (FXS). However multiple phase 2 controlled trials in patients with FXS have failed to demonstrate efficacy of compounds that negatively modulate mGluR5, including two phase 2b randomized controlled trials (RCT) of mavoglurant (AFQ056, Novartis Pharma AG), when the primary measures of interest were behavioral ratings. This has cast some doubt onto the translation of the mGluR5 theory from animal models to humans with the disorder.

**METHODS:**
We evaluated social gaze behavior—a key phenotypic feature of the disorder—and sympathetic nervous system influence on pupil size using a previously-validated eye tracking paradigm as a biobehavioral probe, in 57 adolescent or adult patients with FXS at baseline and following three months of blinded treatment with one of three doses of mavoglurant or placebo, within the context of the AFQ056 RCTs.

**RESULTS:**
Patients with FXS treated with mavoglurant demonstrated increased total absolute looking time and number of fixations to the eye region while viewing human faces relative to baseline, and compared to those treated with placebo. In addition, patients had greater pupil reactivity to faces relative to baseline following mavoglurant treatment compared to placebo.

DISCUSSION:
The study shows that negative modulation of mGluR5 activity improves eye gaze behavior and alters sympathetically-driven reactivity to faces in patients with FXS, providing preliminary evidence of this drug’s impact on behavior in humans with the disorder.

![Number of Fixations](image)

**Number of Fixations.**

Average change in number of fixations to the eye region of faces by adolescent and adult patients with fragile X syndrome following 3 months of treatment with placebo vs. 25 mg, 50 mg, or 100 mg of the mGluR5 negative modulator mavoglurant. Dots reflect the model estimated
change for each group in standard deviation units. Bars reflect 95% confidence intervals. Horizontal line at zero reflects no estimated change. *Those treated with 25 mg or 100mg of mavoglurant experienced more change on average than the placebo group (p<0.05).

19-170 (Poster)
Febrile Ulceronecrotic Mucha-Habermann Disease in a Pediatric Patient: A Case Report

Warner, Tessa, Monroe, Alexandra

Background
Febrile ulceronecrotic Mucha-Habermann disease is characterized by the sudden onset of ulceronecrotic skin lesions and is potentially life threatening. It can occur de novo or in the setting of pityriasis lichenoides et varioliformis acuta (PLEVA), which is an uncommon cutaneous inflammatory disorder more frequently affecting young adults and children.

Objective
We report a case of a 7-year-old male in whom the disease started as PLEVA and evolved to febrile ulceronecrotic Mucha-Habermann disease (FUMHA).

Methods
The patient's medical chart was reviewed. A review of case reports was also completed and compared to the care of our patient.

Results
A 7-year-old male presented to our pediatric emergency department with rash and fever. Symptoms began roughly three weeks prior to presentation. The rash was originally thought to be guttate psoriasis. The rash worsened and the patient was started on prednisolone and triamcinolone. A few days after initiation of steroids he presented to the emergency department with rash and fever. His skin exam showed widespread pink to red papules and plaques, many of which are ulceronecrotic. The densest areas of rash were on the trunk, neck, groin and proximal extremities. The rash spared the palms, soles, conjunctiva, oral mucous membranes and urethra (Figure 1). While in the emergency department the patient was given one fluid bolus. A CBC, BMP, LFTs and blood cultures were obtained in ED and were unremarkable. The patient was seen by Dermatology who recommended the patient be admitted and treated with solumedrol and triamcinolone due to concern for FUMHA. Dermatology also performed a punch biopsy that later proved to be PLEVA. He stayed in the hospital two days. He was placed on weekly methotrexate one week after discharge as recommended by Dermatology and had significant improvement in his rash. He was also switched to PO prednisone from solumedrol once he had no new lesions developing. Five months later the patient is stable and without new lesions and continues on methotrexate, PO steroids and triamcinolone ointment.

Conclusions
Given the high mortality rate of about 20%, FUMHA is important to recognize since early treatment provides decreased mortality. Prior case reports have shown the benefit of using methotrexate for treatment of FUMHA and this was once again seen in the case of our patient.
Neuroimaging predicts performance on the Specific Test of Early Infant Motor Performance (STEP)

Laurel Gower Wolf, BA, Hunter Moss, BS, Truman Brown, PhD, Viswanathan Ramakrishnan, PhD, Patty Coker-Bolt, PhD, Dorothea Jenkins, MD

Background: The Specific Test of Early Infant Motor Performance (STEP) is a novel infant

Figure 1: Patient's skin exam showing widespread pink to red papules and plaques, many of which are ulceronecrotic. The densest areas of rash as seen are the trunk, neck, and proximal extremities.
motor skills test that has been introduced as an efficient developmental screening assessment for preterm infants that correlates with 12-month Bayley-III outcomes. Neuroimaging with MRI provides a non-invasive means to quantify the neurodevelopmental status of infants through metabolic and structural measures. These measures may predict future neurodevelopmental outcomes such as functional motor and/or cognitive deficits. Further validation of the STEP via neuroimaging will therefore provide support that the STEP is assessing functions that are closely related to CNS structures.

Objective: To determine the relationship of the STEP to neuroimaging through Magnetic Resonance Spectroscopy (MRS) metabolite ratios and Fractional Anisotropy (FA).

Methods: Prospective cohort study of 16 preterm infants with STEP outcome measures at 0-3 months corrected gestational age (GA), MRS and Diffusion Tensor Imaging (DTI) at term GA, and Bayley-III at 12 months. Generalized linear models were created using MRS metabolite ratios or white matter (WM) tract FA value averages as covariates to predict STEP. Additionally, generalized linear models were created using the metabolite ratios or average FA values and STEP score at term or 3 months to predict Bayley gross motor (GM) and cognitive scores at 12 months.

Results: Ratios of N-acetyl aspartate to creatine (NAA) in both frontal WM and basal ganglia (BG) significantly contribute to a model predicting STEP scores at both term and 3 months. NAA and myoinositol ratios in the BG both significantly predict Bayley cognitive scores at 12 months. Additionally, NAA in the WM and BG interacts with STEP scores to contribute to a model predicting Bayley GM at 12 months. FA values in the posterior thalamic radiations (PTR) and rostral limb of the internal capsule (RLIC) predict scores on STEP at both time points. Multiple, distinct WM tracts also contribute to STEP models predicting Bayley cognitive and gross motor scores at 12 months.

Conclusion: Performance on the STEP is related to MRS metabolite NAA and multiple WM tract FA values. Additionally, neuroimaging data in a model with STEP scores strongly predict 12-month Bayley outcomes. These findings suggest that performance on the STEP relates to CNS structural and metabolic integrity and that both neuroimaging and early motor performance can be used to better predict later development.

19-172 (Poster)
Acute Flaccid Myelitis: Polio of the West...With a Twist in the Tale!
Bhatia, Sonal

INTRODUCTION: AFM affects the anterior horn cell of the spinal cord resulting in an acute onset of upper and/or lower extremity weakness. Although, a definite cause is unknown, viruses are implicated. Most patients have a viral prodrome. Diagnosis is clinical with broad differentials and ancillary tests [lumbar puncture (LP) and a magnetic resonance imaging (MRI)] can be helpful. No definite treatment is available. Long-term outcomes range from complete recovery to permanent deficits.

AIMS AND OBJECTIVES: To highlight this rare but devastating condition through a pediatric
patient who presented with acute onset weakness. Till date, only two cases of AFM have been reported in our state.

CLINICAL CASE: A 5 year old healthy boy presented with acute onset right arm weakness preceded by upper respiratory symptoms. No bladder or bowel or sensory symptoms were noted. Neurological examination revealed a flaccid right arm with absent motor function proximally but relatively preserved strength distally. Cervical and thoracic spine MRI showed non-enhancing T2 hyperintensity extensively affecting the central gray matter. LP showed mildly elevated protein and mild pleocytosis. Given anecdotal reports of benefit with steroids in AFM, he was treated with 5 doses of methylprednisolone without any improvement and ultimately discharged. Unfortunately, 2 weeks later, he was admitted for new left lower extremity weakness/spasticity and gait difficulty. MRI then showed symmetric thickening and enhancement of the anterior cauda equina nerve roots suggestive of Guillain-Barre syndrome (GBS). He was treated with intravenous immunoglobulins (IVIG) with significant improvement of the new symptoms; however, the right arm remained flaccid and weak and was unchanged at the 6-week follow-up.

DISCUSSION: Due to the considerable overlap of clinical features, differentiating AFM from other causes of acute flaccid paralysis, like GBS, is difficult during the early course of the illness. Attention should be given at an accurate and early diagnosis given the differences in acute treatment and long-term outcomes.

CONCLUSION: Hallmark features of AFM include rapid onset of extremity weakness with a proximal predominance. GBS typically presents as an ascending paralysis with a distal predominance. While there is no definite treatment for AFM, GBS is treated with IVIG. This case is unique as GBS like illness followed AFM. To the best of my knowledge, this has not been reported in the medical literature.

19-173 (Platform)

Role of neuro-inflammation in the pathophysiology of pediatric hydrocephalus: Measuring pro-inflammatory cytokines in an ex vivo model of pediatric hydrocephalus.

Michael Smith, Kim Sutton, Ramin Eskandari

Background: Pediatric hydrocephalus (HCP) afflicts nearly 400,000 new children annually causing progressive neurological disabilities over their lifetime. Hallmark features of HCP include pathological elevation of intracerebral pressure (ICP) and abnormal enlargement of the cerebral ventricles due to an imbalance between cerebrospinal fluid (CSF) production and absorption. Elevated ICP is a primary injury mechanism present at diagnosis and each recurrence of HCP treatment failure. Despite surgical intervention, secondary injury mechanisms contribute to lifelong cognitive and motor deficits. While the mechanisms of secondary injury to brain tissue resulting from sustained elevated ICP are not fully understood,
neuro-inflammation likely contributes to the pathophysiology of HCP. Inflammation in the CNS is characterized by an upregulation of cytokines in the brain, secreted by microglia, astrocytes and neurons. In fact, several previous studies have reported elevated levels of pro-inflammatory cytokines in the CSF of patients with HCP.

Objective: Using a previously describe ex vivo model of neonatal HCP, the goal of this study was to determine if pressure alone is sufficient to modulate the secretion of cytokines from mono-cellular constructs of human neurons and astrocytes, which could be used to target/determine cell specific neuro-inflammatory mechanisms related to HCP pathologies.

Methods: To simulate pressure induced brain injury, we developed an ex vivo model of neonatal hydrocephalus, which combines 3D neural cell cultures and the previously described Pressure Controlled Cell Culture Incubator (PC$^3$I). Human cells were maintained in a 3D peptide-conjugated alginate hydrogels were subjected to pathologic pressure (30 cmH$^2$O) of untreated hydrocephalus for up to 48 hr. Culture media bathing of the cell-laden hydrogels was analyzed for pro-inflammatory biomarkers using inflammatory multiplex assays, while cellular viability was determined using an assay that measured intracellular esterase activity and plasma membrane integrity.

Results: Using cytokine multiplex assays revealed a time-dependent increase in the concentration of pro-inflammatory cytokines released by neurons, but not astrocytes when compared to their time-matched controls. Specifically, a time-dependent release of IL-6 and IL-8 from 3D neuron cultures, but not from astrocyte cultures following sustained pressure exposures.

Conclusions: Using a novel ex vivo model of pathologic elevated ICP, this data suggest that the signaling of pro-inflammatory cytokines are involved in the signal associated with elevated ICP, and may be a key in the early secondary injury response to elevated ICP in the developing neonatal brain. Future experiments using this model will be valuable to further determine how individual cellular phenotypes responded to pathological ICP.

19-174 (Platform)

N-Acetylcysteine Mitigates Acute Opioid Withdrawal and Enhances Neuroprotection in Neonatal Rats

Ward, Price, Moss, Hunter; Brown, Truman; Kalivas, Peter; Jenkins, Dorothea

There has been a dramatic increase in the number of infants experiencing neonatal abstinence syndrome (NAS). During opioid withdrawal, there is a disruption to glutamate homeostasis resulting in an increase in synaptic glutamate, oxidative stress, and increased neuronal firing. In adult addiction models, N-Acetylcysteine (NAC) restores glutamate homeostasis and mitigates the oxidative stress of withdrawal via conversion to glutathione, a potent antioxidant and neuroprotective substrate.

We hypothesized that NAC administered before acute opioid withdrawal in neonatal rats would increase CNS glutathione (GSH) and normalize glutamate-glutamine (GLX) and N-Acetylaspartate (NAA) concentrations, thus providing neuroprotection and reducing withdrawal symptoms.
Osmotic minipumps containing methadone (opioid dependent, OD) and saline (SHAM) were implanted into Sprague Dawley dams 7 days prior to delivery. We randomized OD rat pups to receive either naloxone + saline or NAC (50-100mg/kg), administered on PND7 to precipitate acute withdrawal. Serial magnetic resonance spectroscopy (MRS) was done on PND6-7 before, 30 and 120 min after withdrawal. On PND7 we assessed withdrawal behaviors at 5-min intervals for 90 min after naloxone, and summed scores over 45-90 min (the peak withdrawal period). Higher scores indicate more severe withdrawal. Statistical analysis was done using one-way ANOVA with Tukey post-hoc test and Pearson correlation coefficient.

Mean summed behavioral scores were significantly different between SHAM, saline OD and NAC OD pups (F=8.37, p=0.002). By post-hoc test, saline OD scores (17.2±4.2, n=10) were significantly different than SHAM (6.5±0.6, n=4, p=0.003), and NAC OD scores (11.3±5.6, n=9, p=0.029). Scores were not significantly different between NAC OD and SHAM rats (p=0.21). Scores were negatively correlated with MRS metabolite concentrations 30 min after naloxone for [GSH] (r= -0.602, p=0.033, n=10) and [NAA] (r= -0.770, p=0.005), but not for [GLX] (r= -0.392, p=0.131). No significant correlation was noted for behavior scores and MRS metabolites at 120 min after naloxone.

In an antenatal model of OD, NAC mitigates acute opioid withdrawal in rat pups. Higher withdrawal scores in rat pups related to lower CNS [GSH] and [NAA], markers of oxidative stress and neuronal health. This is the first study to demonstrate in vivo neurochemical changes during acute opioid withdrawal in a neonatal OD model, and shows NAC as a potential novel treatment for NAS.

**Impact of Gastroesophageal Reflux Disease on Childhood Hearing and Otologic Outcomes**

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**Abstract:**

Impact of Gastroesophageal Reflux Disease on Childhood Hearing and Otologic Outcomes

Introduction: While gastroesophageal reflux disease (GERD) is associated with the pathogenesis of middle ear disease in children, hearing outcomes in this population are poorly understood.

Objectives: To determine the relation between GERD in the first year of life and hearing outcomes in early childhood.

Methods: Retrospective cohort study of children with GERD and/or reflux esophagitis (RE) before age 1. Demographic, otologic, and medical data were extracted from the AudGen Database. Available audiograms were analyzed for prevalence, severity, and progression of hearing loss (HL) by age 5. Results: Compared to the control group of 20515 children, the 6695 children with GERD had a lower rate of HL (OR 0.89, 95% CI 0.84-0.94), while children with RE
had a higher rate of HL (OR 1.51, CI 1.17-1.95). The median severity, as measured by pure-tone average, was 25.0 dB, and median improvement by age 5 was 5.0 dB. The difference in severity and progression of HL between groups was less than 3 dB. Among children with GERD, fundoplasty or fundoplication (FF) was associated with an increased odds of HL (OR 7.65, CI 2.74-29.6). Children with FF or RE were more likely to have tympanoplasty tubes placed (OR 6.77, CI 3.92-11.69; OR 5.51, CI 4.48-6.78, respectively) and more likely to have eustachian tube dysfunction (OR 2.64, CI 1.51-4.65; OR 1.68, CI 1.31-2.15, respectively). Neither children with FF or RE had a higher incidence of cholesteatoma.

Discussion: GERD has been implicated in the pathogenesis of disorders of the middle ear in children. We show that more severe features of GERD such as RE and FF were associated with an increased prevalence of hearing loss. Furthermore, these severe features were associated with higher rates of eustachian tube dysfunction and need for tympanostomy tube placement.

19-176 (Poster)

A Scalable Loan Program to Promote Equal Access to Personal Tele-Electrocardiogram Devices

Baker GH, Ferguson B, Jackson L, Cain N

Purpose: The purpose of this study was two-fold. Firstly, we sought to evaluate pediatric arrhythmia detection using a novel telehealth device. Secondly, to test a scalable, loan-based program to lower financial access barriers for novel wearable/peripheral telehealth devices in the pediatric population.

Design: We provided Kardia tele-electrocardiogram (ECG) devices on a loan basis to patients at no charge in our outpatient pediatric cardiology clinics. The Kardia device is a small, wireless ECG monitor that pairs to a smartphone via an app. ECG recordings are taken by placing two fingers on two magnetic plates of the small device. Data can be easily and quickly transmitted via the app. This pilot project tests a model designed to eliminate the economic barriers for utilization of direct-to-consumer medical peripheral/wearable devices and ensure a more equitable distribution across all socio-economic strata. Currently, the device is only available to providers when purchased by patients or their families, limiting it to the population willing and able to purchase it ($100). If our loan-based model is successful in eliminating economic barriers other providers/institutions may adopt this model. This problem is not unique to this device and therefore the solution could be scalable to a multitude of current and future devices.

Results: Over a four-month period, 39 patients were given the Kardia monitor. The age range of patients was from 1 month-49 years with an average age of 14.5 years. A total of 371 tracings were recorded by patients. Patients transmitted between 1-71 EKG tracings over the 30 day enrollment. There were 9 abnormal recordings (2.4%) with 8 showing premature ventricular beats and one showing supraventricular tachycardia. No EKGs were uninterpretable. Of the 28 devices expected to be returned, 14 devices have been returned to clinic (50%) over the four month period. Of the 32 patients who completed their enrollment period, eleven returned the survey (34%) and all patients felt the device was easy or very easy to use.
Conclusions. Our initial experience suggests the Kardia is an effective and convenient method for outpatient pediatric arrhythmia detection. Additionally, a loan based program is a viable option to improve access to reusable direct-to-consumer peripheral/wearable devices in the pediatric population. Further improvement in this model should focus on methods to increase levels of device and survey return.

19-177 (Poster)

Transfusion Practices Among Hematology/Oncology Healthcare Professionals

Majd Ghanim, Jennifer H. Voeks, and Julie Kanter

Introduction/Background:

There are no evidence-based guidelines for optimal transfusion practices for patients undergoing chemotherapy and stem cell transplant. There are minimal low-quality studies regarding transfusion thresholds as well as the efficacy of pre-transfusion medications (to reduce febrile non-hemolytic transfusion reactions) for these patients. To pursue a prospective quality improvement study, it is important to know the current transfusion standards used by practitioners regarding: 1) transfusion thresholds for platelets and red blood cells and 2) routine use of pre medications prior to transfusions. Additional research questions included differences in the above standards by region or by pediatrics vs. adult providers.

Study Design and Methods:

Expedited IRB approval was obtained. We conducted a REDCap survey from 3/1/18-4/12/18 targeting hematology oncology providers of both pediatric and adult providers. The survey was emailed through multiple databases with members from several countries that included both adult and pediatric hematology/oncology practitioners.

Results:

One hundred and nineteen hematology/oncology practitioners completed the survey: 94 attending physicians, 19 fellows and 6 nurse practitioners. Most respondents practiced in United States (90%, 107/119), the rest practiced in Canada, India, Italy and Iran. The majority of participants were pediatric hematology/oncology providers (84%, 100/119). Of the remaining providers 10 treated only adults and 9 treated both adults and children. The vast majority (97%, 115/119) of participants did not utilize a standard policy for premedication prior to red blood cell transfusions. Similarly, 95% (111/117) of participants made individual decisions on premedication with platelet transfusions rather than using an institutional policy. When asked about the threshold to transfuse blood products, 71% (75/105) of those who treated patients undergoing chemotherapy said they would transfuse red blood cells when patients had a hemoglobin of \( \leq 7 \) g/dL, and 79% (82/104) would transfuse platelets when patients had a platelet count \( < 10 \) K/mL. Practitioners treating bone marrow transplant (BMT) patients had more variability and used higher transfusion thresholds. Fifty-two percent (33/64) of them would transfuse red blood cells for patients undergoing BMT with a higher threshold of hemoglobin of 8 g/dL while only 36% used the lower threshold of 7 g/dL. Similarly, for platelet transfusions for patients undergoing BMT, 47% (31/66) would use a 20K/mL threshold, and 45% would transfuse platelets at a threshold of 10 K/mL.
Conclusion:

There is currently no routine practice of utilizing pre-medications prior to transfusions of red blood cells or platelets. Instead, practitioners surveyed indicated a preference for individualizing the use of pre-medications only if patients had a previous transfusion reaction. As the use of these medications is not evidence-based, additional studies are needed to determine their efficacy. Transfusion thresholds are relatively consistent among providers with the majority aiming for more liberal thresholds in patients undergoing chemotherapy and more conservative for those undergoing BMT. More studies are needed to evaluate the risks and benefits of using different transfusion thresholds.

19-178 (Poster)
Donor Specific Antibodies and Antibody Mediated Rejection within the 1st Year Post Transplant in Pediatric Heart Transplant Recipients is Associated with Delay in Achieving Therapeutic Tacrolimus Levels

Ali Burnette, Kathryn Wray, Heather Corbo, Kathleen Sprott, Heather Henderson, Nicole Pilch, Andrew Savage, Vanessa Adams

Introduction: Early antibody mediated rejection (AMR) can contribute to shorter graft survival in pediatric heart transplant (tx) recipients. The use of induction therapy varies among centers as does timing for initiation of maintenance immunosuppression. We have noticed a possible increase in the development of donor specific antibodies (DSA) and AMR within the 1st year post-tx at our center. We therefore initiated a quality improvement project to study our recent era of clinical practice and patient (pt) outcomes with respect to development of DSA and/or AMR.

Methods: A single center retrospective cohort study of heart tx pt from March 2015 to March 2018 was completed using our center's electronic medical record and United Network for Organ Sharing (UNOS) data. Baseline demographics, induction history, and early tacrolimus levels were reviewed and compared with post-tx rejection history and DSA data.

Results: 14 pt aged 8 months to 20 years, received a heart tx between 3/2015 and 3/2018. Seven pt (50%) developed DSA within the 1st year post-tx. The pt's that developed DSA tended to be older (4 pt >10 yr of age) and African American race (n=5). Five pt had dilated cardiomyopathy and 2 pt had palliated congenital heart disease. Four of the 7 pt were treated for AMR based on pathology and/or graft dysfunction by echo or invasive hemodynamics. All 4 of these pt were African American and had a delay of greater than one week in achieving a therapeutic tacrolimus level of > 8. Nine of 14 pt received 1-5 doses of anti-thymocyte globulin (ATG), 4 of which developed DSA and 3 pt had AMR. Two episodes of acute cellular rejection (ACR) greater than 1R occurred in two of the pt that were also treated for AMR.

Conclusion: In this small single center sample we discovered that half of the patients developed DSA in the first year post-transplant, but only a few them developed clinical or hemodynamic
concern for antibody mediated rejection. The development of AMR was associated with African American race and delay in achieving a therapeutic tacrolimus level. Therefore we have become more aggressive with getting tacrolimus levels to goal sooner and/or using additional doses of ATG induction when levels remain less than goal greater than 5 days post-tx.