RESEARCH RETREAT 2023

VANDERBILT UNIVERSITY
MEDICAL CENTER

Department of Pediatrics

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2023 Research Retreat

11:00am – 11:50am	**Boxed Lunch Pick-up and Poster Registration/Set-up** Monroe Carell Theater Lobby
12:00pm – 1:00pm	**Keynote Speaker: Lisa A. Robinson, MD, FRCP(C), FASN, FCAHS** Vice Dean, Strategy & Operations, Professor, Department of Paediatrics Temerty Faculty of Medicine, University of Toronto Full Member, Institute of Medical Science, School of Graduate Studies, University of Toronto Senior Scientist, Cell Biology Program, Research Institute, The Hospital for Sick Children Staff Physician, Division of Nephrology, The Hospital for Sick Children Canada Research Chair (CRC) Tier 1 in Vascular Inflammation and Kidney Injury *"A Career as a Pediatric Clinician-Scientist: Challenges and Opportunities"* Wadlington A&B (Virtual option available)
1:00pm – 1:15pm	**Break**
1:15pm – 3:00pm	**3rd Year Fellow Data Blitz Presentations** Wadlington A&B (Virtual option available) Michael R. DeBaun, MD, MPH – Moderator Professor of Pediatrics and Medicine, Division of Pediatric Hematology/Oncology J.C. Peterson Chair in Pediatrics, Department of Pediatrics Vice Chair for Clinical and Translational Research, Department of Pediatrics Director, Vanderbilt-Meharry Center of Excellence in Sickle Cell Disease *4-Minute Presentations* Matthew Buendia, MD; Rohini Chakravarthy, MD; Benjamin Crawford, MD; Doel Dhar, MD, MS; Chiara Foster, MD; Margaret Free, MD; Blake Gruenberg, MD; Hope Hendricks, MD; Sandra Kikano, MD; Mary Killian, MD; Andy Liu, MD; Alexandra Muhar, MD; Meghan Murphy, MD; Prashant Raghavendran, DO; Meaghan Ransom, MD, MPH; Derica Sams, MD; Shikha Saxena, MD; and Megan Shea, DO, MPH
3:00pm – 4:00pm	**Fellow and Faculty Poster Session & Reception** Monroe Carell Theater and Boardroom (*No virtual option)
4:00pm – 4:30pm	**2023 Research Retreat Awards Ceremony** Wadlington A&B (*No virtual option) 2023 Turner-Hazinski Award Winners 2023 Research Retreat Abstract Award Winners

Keynote Speaker

"A Career as a Pediatric Clinician-Scientist: Challenges and Opportunities"

Lisa A. Robinson, MD, FRCP(C), FASN, FCAHS

Vice Dean, Strategy & Operations,
Professor, Department of Paediatrics
Temerty Faculty of Medicine, University of Toronto
Full Member, Institute of Medical Science,
School of Graduate Studies, University of Toronto
Senior Scientist, Cell Biology Program,
Research Institute, The Hospital for Sick Children
Staff Physician, Division of Nephrology, The Hospital for Sick Children
Canada Research Chair (CRC) Tier 1 in Vascular Inflammation and Kidney Injury

Dr. Lisa Robinson is the Vice Dean of Strategy & Operations at Temerty Faculty of Medicine at the University of Toronto. She leads the Faculty's academic strategic planning, oversees academic affairs, and serves as the Vice Dean lead for the Faculty's Offices of Inclusion and Diversity, Indigenous Health, and Access and Outreach. She is a Professor in the Department of Paediatrics and Institute of Medical Science, and a Staff Physician and former Head of the Division of Nephrology at The Hospital for Sick Children.

Dr. Robinson is a Senior Scientist in the Program in Cell Biology at The Hospital for Sick Children Research Institute and holds a Canada Research Chair (CRC) Tier 1 in Vascular Inflammation and Kidney Injury. Her research program integrates molecular biology, cell biology, advanced microscopic, and biochemical approaches with experimental models of inflammation, cardiovascular disease, and kidney injury. She is also the President of the American Pediatric Society.

Data Blitz Presentations

Data Blitz Presentations

DBP – 1	Matthew Buendia
DBP – 2	Rohini Chakravarthy
DBP – 3	Benjamin Crawford
DBP – 4	Doel Dhar
DBP – 5	Chiara Foster
DBP – 6	Margaret Free
DBP – 7	Blake Gruenberg
DBP – 8	Hope Hendricks
DBP – 9	Sandra Kikano
DBP – 10	Mary Killian
DBP – 11	Andy Liu
DBP – 12	Alexandra Muhar
DBP – 13	Meghan Murphy
DBP – 14	Prashant Raghavendran
DBP – 15	Meaghan Ransom
DBP – 16	Derica Sams
DBP – 17	Shikha Saxena
DBP – 18	Megan Shea

N-ACETYLCYSTEINE ATTENUATES HISTOPATHOLOGICAL FINDINGS OF EOSINOPHILIC ESOPHAGITIS BY REDUCING STAT6 ACTIVATION

Matthew A. Buendia[1,5], Justin Jacobse[2,3,5], Aaron Kwag[3], Mae Wimbiscus[3], Christopher S. Williams [3,4,5], Girish Hiremath[1], Yash Choksi [3,4,5]

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[4]Program in Cancer Biology, Vanderbilt University School of Medicine, Nashville, TN, USA [5]Veterans Affairs Tennessee Valley Healthcare System, Nashville, TN, USA

Objective: Increased oxidative stress is thought to contribute to the pathophysiology of Eosinophilic Esophagitis (EoE). Thus, our aim was to determine whether N-acetylcysteine (NAC), an antioxidant known to reduce oxidative stress, could reduce esophageal inflammation in experimental EoE.

Study Design: Immortalized human esophageal epithelial cells (EPC2-hTERT) were pre-treated with NAC for 1 hour and then with IL-13, a known activator of STAT6, (except for control) for 30 minutes. Cells were collected for immunoblot of phosphoSTAT6 (pSTAT6) and total STAT6. This experiment was repeated but IL-13 and NAC remained on the cells for 24 hours, and quantitative real-time PCR (qPCR) was done to assess relative gene expression of *CCL26,* a known target of STAT6 activation. In the absence of cells, recombinant IL13Rα1 was mixed with control and increasing doses of NAC and assayed on a Nanotemp Tycho to assess for qualitative structural changes. For *in vivo* experiments, eosinophilic esophagitis was induced in C57/BL6 mice with 1 µg recombinant IL-33 intraperitoneal (IP) injections daily for 7 days with or without NAC. Five groups of adult mice were tested: 1) Sucrose water with saline IP; 2) 3% NAC/Sucrose water with saline IP; 3) Sucrose water with IL-33 IP; 4) 3% NAC/Sucrose water with IL-33 IP; 5) 300 mg/kg NAC topical suspension with IL-33 IP. At the end of the 7 days, esophageal tissue was collected for histology.

Results: Pre-treatment of EPC2-hTERT cells with NAC prior to IL-13 led to a significant reduction in pSTAT6/STAT6 in a dose-dependent manner as compared with IL-13 alone (vs 1 mM, 47%, $P<0.05$; vs 10 mM, 76%, $P<0.01$). After 24 hours, *CCL26* expression was significantly reduced with NAC + IL-13 as compared with IL-13 alone (1- mM, 54%, $P<0.05$; 10- mM 45%, $P<0.01$) As previously reported, IL-33 induced esophageal basal cell hyperplasia (BCH) in mice compared to controls (20.72 ± 0.45 vs. 9.07 ± 0.35 vs 10.56 ± 0.33, $P<0.0001$). Consumption of NAC in drinking water or the administration of a NAC topical suspension reduced IL-33 induced BCH (20.72 ± 0.45 vs. 14.37 ± 0.21, $P<0.01$; vs. 13.86 ± 0.53, $P<0.01$). Furthermore, 3% NAC in drinking water significantly reduced relative MBP counts (1.00 ± 0.08 vs 0.51 ± 0.07, $p<0.05$) with a similar trend when administering NAC topical suspension (1.00 ± 0.08 vs 0.56 ± 0.11, $p=0.19$). When recombinant IL13Rα1 was mixed with NAC, inflection temperatures measured on the Nanotemp Tycho were lowered in a dose-dependent fashion compared to IL13Rα1 alone.

Conclusions: NAC reduces STAT6 activation and *CCL26* expression induced by IL-13. NAC consumption via drinking water or by administration of an esophageal topical suspension attenuates IL-33 induced BCH and esophageal eosinophilia in mice. Targeting oxidative stress may serve as a novel pharmacologic pathway for the treatment of EoE.

Mentor: Yash Choksi, MD (yash.a.choksi@vumc.org)

HOSPITAL READMISSIONS FOLLOWING PEDIATRIC ALLOGENEIC HEMATOPOETIC STEM CELL TRANSPLANT

Rohini Chakravarthy, MD[1], Justin A. Godown, MD[2], Tatsuki Koyama, PhD[3], Lili Sun, PhD[3], Carrie L. Kitko[1], MD, Debra L. Friedman, MD, MS[1]

[1]Department of Pediatrics, Division of Pediatric Hematology/Oncology, Vanderbilt University Medical Center, Nashville, Tennessee; [2]Department of Pediatrics, Division of Pediatric Cardiology, Vanderbilt University Medical Center, Nashville, Tennessee; [3]Department of Biostatistics, Vanderbilt University Medical Center, Nashville, Tennessee

Background: Survival rates for pediatric patients who receive an allogeneic hematopoietic stem cell transplant (HSCT) for both malignant and non-malignant conditions continue to improve. However, hospital readmissions post-HSCT remain common. There is a paucity of data regarding timing and indications for these readmissions, particularly beyond the first 180 days post-transplant.

Objective: Ascertain rates, indications, and risk factors for hospital readmissions in the first year following HSCT in pediatric, adolescent, and young adult (AYA) patients.

Study Design: All patients 0-25 years who received a first HSCT between 2008 and 2020 and survived to initial hospital discharge were identified via the Pediatric Health Information System (PHIS) administrative database using procedural and APR-DRG codes. Data was collected on all hospital readmissions one-year post-HSCT discharge. Primary ICD diagnosis codes were categorized using Clinical Classification Software (CCS) to identify indications for readmission. The Kaplan-Meier method was used to assess time to first readmission. A multivariable Cox proportional hazard model identified independent risk factors for hospital readmissions.

Results: 6,917 patients met inclusion criteria, and 4,873 patients (70%) required at least one readmission during first year post-HSCT discharge. The median time to first readmission was 51 days (interquartile range [IQR] 48-54). Multiple readmissions occurred in 3,130 patients (45%). The most common indication for readmission was infection. Independent risk factors for a first readmission included complications during the initial HSCT admission such as longer initial HSCT admission (Hazard Ratio [HR] 1.11; 95% Confidence Interval [CI] [1.05,1.17]; p<0.001), graft vs host disease (GVHD) (HR 1.26; CI [1.15,1.37]; p<0.001), infection (HR 1.08; CI [1.02,1.16]; p=0.016) and patient characteristics such as African American race (HR 1.11; CI [1.01,1.21]; p=0.024) and Asian race (HR 1.19; CI [1.03,1.37], p-value 0.019). GVHD (HR 1.23; CI [1.11,1.36]; p<0.001) and longer initial HSCT admission (HR 1.12; CI [1.03,1.23]; p=0.002) were also risk factors for a second readmission. Non-Hispanic ethnicity (HR 0.88; CI [0.8,0.97]; p<0.013) and HSCT for aplastic anemia (HR 0.86; CI [0.76,0.98]; p<0.023) are associated with a decreased risk of both first and second readmission, while HSCT for hemoglobinopathies (HR 0.85; [CI 0.75,0.96]; p-value 0.008) was associated with a decreased risk for only a first readmission.

Conclusion: The majority of pediatric and AYA patients undergoing HSCT will require at least one readmission within one-year post-HSCT discharge. Patients who undergo HSCT for certain non-malignant conditions, such as aplastic anemia and hemoglobinopathies, appear to have a lower risk of readmissions, possibly reflecting eligibility criteria for HSCT or the intensity of the preparative regimens. Infection represents the most common indication for readmission. GVHD during the initial HSCT encounter is a risk factor for both an initial and subsequent readmission. Racial minorities may have a higher risk of readmission; however, further studies are needed to validate and determine the reasons underlying this. Continued efforts aimed at GVHD and infection prevention may help decrease risk of readmission throughout the first-year post HSCT.

Mentors: Debra Friedman, MD, MS; Carrie Kitko, MD; and Justin Godown, MD

MESENCHYME-DERIVED INFLAMMATION RECRUITS MACROPHAGES AND ALTERS SACCULAR STAGE LUNG DEVELOPMENT

Benjamin C. Crawford[1], Reit Van Der Meer[1], Shivangi Dave[1], Wei Han[2], Charles Shissias[1], Dawn Newcomb[2], Wei Shi[3], Jennifer Sucre[1], Timothy S. Blackwell[2], and John T. Benjamin[1]

Departments of Pediatrics[1] and Medicine[2] at Vanderbilt University Medical Center, Developmental Biology and Regenerative Medicine Program at the Children's Hospital of Los Angeles[3]

Objective: Fibroblasts in the lung mesenchyme direct organization of future airspaces during the saccular stage of lung development. Inflammation in preterm infants alters critical components of this process leading to reduced alveolar formation and bronchopulmonary dysplasia (BPD). Therefore, we sought to model the effects of inflammatory signaling initiated by fibroblasts in the mouse lung mesenchyme and, thereby, better understand how inflammation contributes to BPD pathogenesis.

Study Design: To model the effect of lung mesenchyme-specific inflammation, we used a transgenic mouse model in which human IKKb (an upstream activator of NF-kB) is expressed in Tbx4-positive lung fibroblasts in a doxycycline (Dox) inducible manner (referred to as IKKb^{Tbx4}). We activated the transgene in neonatal IKKb^{Tbx4} mice during the saccular stage from postnatal (PN) day 0-5 by placing lactating dams on Dox (2g/L) and evaluated the effects on the lung at PN5 and PN60. Additionally, we investigated the effect of transgene activation in lung fibroblast cultures generated from IKKb^{Tbx4} mice.

Results: Transgene activation in IKKb^{Tbx4} mice resulted in lung inflammation with increased mRNA expression of cytokines and chemokines and recruitment of macrophages (% macrophages/viable cells: 7.6% $\pm$ 0.5, IKKb^{Tbx4}: 33.2% $\pm$ 0.6; $P < 0.05$) into the lung. Dox treatment of lung fibroblast cultures from IKKb^{Tbx4} mice also demonstrated similarly increased transcription of macrophage chemokines. Conditioned media from these cells stimulated chemotaxis of macrophages *in vitro*. IKKb^{Tbx4} mice had altered saccular stage lung development with abnormalities in fibroblast differentiation, increased interstitial thickening, and decreased distal airspace area (distal airspace area [% of total distal lung]: control: 41.2% $\pm$ 2.7, IKKb^{Tbx4}: 26.2% $\pm$ 0.3; $P < 0.05$). Depletion of macrophages with daily injections of intraperitoneal (IP) clodronate from PN 1-4 rescued the saccular lung phenotype in IKKb^{Tbx4} mice. Importantly, saccular stage macrophage recruitment also had long term consequences. Adult IKKb^{Tbx4} mice at PN60 demonstrated an emphysematous lung phenotype with alveolar simplification (mean linear intercept: control: 22.5 uM $\pm$ 0.7, IKKb^{Tbx4}: 39.9 uM $\pm$ 2.1; $P < 0.05$) and altered tissue elastance.

Conclusions: Our findings suggest fibroblast-macrophage interactions have an important role in the inflammatory cascade leading to abnormal saccular lung development. Delineating mediators of reciprocal fibroblast-macrophage crosstalk and the downstream effects of macrophage-dependent inflammation are needed to better understand BPD pathogenesis.

Mentor: John Benjamin, MD (john.benjamin@vumc.org)

EOSINOPHILIA IS NOT SIGNIFICANTLY PRESENT IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS PATIENTS EXPOSED TO IL-1 AND IL-6 BLOCKING BIOLOGIC MEDICATIONS

Doel Dhar MD MS[1], Rachel Dickey[2], Srushti Gangireddy, MS[3], Henry H. Ong, PhD[3], Wei-Qi Wei, MD, PhD[3], Anna E. Patrick, MD, PhD[1*]

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[2] Lipscomb University College of Pharmacy and Health Sciences, Nashville, TN
[3] Vanderbilt University Medical Center, Department of Biomedical Informatics, Nashville, TN

Objective: Systemic juvenile idiopathic arthritis (sJIA) is characterized by arthritis, fevers, rashes. In some patients, sJIA can progress to a hyperinflammatory state known as macrophage activation syndrome (MAS) that is associated with high morbidity and mortality. Biologic medications that block the IL-1 and IL-6 pathways involved in SJIA pathogenesis are critical life-saving therapeutics that have revolutionized sJIA treatment and dramatically improved clinical outcomes. Emerging data suggests an association between IL-1 and IL-6 blocking biologics and a severe drug hypersensitivity including drug reactions with eosinophilia and systemic symptoms (DRESS) that can include lung involvement. It is unclear if early recognition of eosinophilia could be used to identify this severe reaction and allow for medication changes before the development of irreversible organ damage. In this study, we determine the frequency of eosinophilia in sJIA patients and investigate the relationships between eosinophilia and IL-1 and IL-6 blocking biologic medications in a cohort with extensive longitudinal clinical data.

Study Design: Patient charts were identified from the electronic health record (EHR) that contained JIA-associated International Classification of Diseases, Ninth Revision (ICD-9) or International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes, finding 3462 charts. These charts underwent manual review for inclusion criteria, which required at least two rheumatology encounters documenting sJIA onset prior to the age of 18. Demographics, medications, laboratory results, and ICD codes from the sJIA charts were extracted from the EHR. Eosinophilia was identified using a definition of one count of an absolute eosinophil count ≥ 1500 cells/μl or two consecutive absolute eosinophil counts ≥ 500 cells/μl within a three-month timespan. The exposure to IL-1 blocking biologics (anakinra, canakinumab) or IL-6 blocking biologics (tocilizumab) was determined by documentation in prescribing data and validated by drug use in clinical notes. Chi-squared testing was used to analyze categorical variables with a p-value of 0.05 considered significant.

Results: In the EHR, 166 sJIA patients were identified that met inclusion criteria. The sJIA cases were 54% female and 74% Caucasian. The median age of sJIA diagnosis was 7 years old (IQR 3-11). Of these patients, 123 (74%) were exposed to anakinra, canakinumab or tocilizumab during their disease course, with 92 (55%) exposed to anakinra, 25 (15%) exposed to canakinumab, and 66 (40%) exposed to tocilizumab. We identified 48 sJIA patients who met our definition of eosinophilia. The patients meeting criteria for eosinophilia were 54% female, 79% Caucasian, and had a median age of sJIA diagnosis of 6 years old (IQR 2-9). The demographics for sJIA patients with eosinophilia were not significantly different from total sJIA case demographics. Of sJIA patients with eosinophilia, 16 (33%) developed eosinophilia while on IL-1 or IL-6 blocking biologics. The number of sJIA cases with eosinophilia exposed to biologics was not significantly different from the number of sJIA cases with eosinophilia not exposed to biologics by Chi-square test.

Conclusions: A sJIA patient cohort was identified and validated using ICD-9 and ICD-10-CM codes and chart review in the EHR. We identified an overlap between patients with eosinophilia and patients exposed to an IL-1 or IL-6 blocking biologic medications. Further investigation is needed to fully characterize the relationships between eosinophilia & biologic medications and to understand how these relationships intersect with drug reactions that cause long-term organ damage & MAS. The potential impact of these studies is to identify biomarkers and risk factors that can be used for early identification of clinically severe outcomes in sJIA.

Mentor: Anna Patrick, MD, PhD (anna.e.patrick@vumc.org)

THE IMPACT OF CLONIDINE ON TACHYCARDIA, HYPERTENSION, AND AGITATION POST DEXMEDETOMIDINE INFUSION

Chiara Foster, MD, Capt, USAF, FAAP[1,2]; Jessica Anderson, PharmD[2]; Kristina Ann Betters, MD, FAAP[1,2]

[1]Vanderbilt University School of Medicine
[2]Monroe Carrell Jr. Children's Hospital at Vanderbilt

Objective: Dexmedetomidine is frequently used as a sedative in the pediatric intensive care unit (PICU) despite limited data on the risk factors, manifestations, and treatment of withdrawal. Clonidine is often utilized to treat withdrawal based on its similar mechanism of action, but data showing efficacy is lacking. We hypothesized that patients treated with clonidine would have fewer symptoms of withdrawal- specifically less agitation, hypertension, and tachycardia- in the first 24 hours after discontinuation of a dexmedetomidine infusion.

Study Design: This retrospective observational cohort study took place in a 30-bed PICU over a 2-year period. Data was collected on all intubated patients receiving dexmedetomidine infusions except patients on clonidine prior to admission and those receiving end of life care. Variables of interest collected via electronic medical record included maximum infusion rate, days on infusion, drip wean duration, exposure to other sedatives, treatment with clonidine during weaning, Withdrawal Assessment Tool 1 (WAT-1) scores, heart rate and blood pressure changes from pre-wean baseline, and presence of agitation, as measured by Richmond Agitation Sedation Scores greater than 0. The study cohorts were compared using medians with interquartile ranges and Fisher exact tests and 2 tail t tests where appropriate.

Results: While there was a significant difference in the maximum infusion rate of dexmedetomidine in the clonidine group (n=17, median 1.6 mcg/kg/hr, IQR 1.2-2.0) compared to the no clonidine group (n=13, median 1.0 mcg/kg/hr, IQR 0.8-1.4; p= 0.02), there was no statistically significant difference in days on infusion (median 9.0 days, IQR 7-11 vs. 5.0 days, IQR 5.0-11.5; p=0.17) or drip wean duration (both medians of 1.0 day, IQR 1.0-2.0 vs. 1.0-2.5). For symptoms of withdrawal, there was no difference in presence of agitation (8 [47%] vs. 7 [54%], p= 0.71), delirium (6 [35%] vs. 5 [39%], p= 0.93), WAT-1 scores greater than 3 (8 [47%] vs. 7 [54%]), a heart rate elevation >15 bpm (14 [82%] vs. 10 [77%]), or at least two episodes of a systolic blood pressure increase above 10 mmHg over baseline (10 [59%] vs. 11 [85%]) in the first 24 hours post infusion.

Conclusions: In this small cohort of patients treated with prolonged dexmedetomidine infusions, treatment with clonidine did not reduce agitation, WAT-1 scores, or heart rate and/or blood pressure changes post infusion.

Mentor: Kristina Ann Betters, MD (kristina.betters@vumc.org)

EVOLUTION OF INVASIVE AND COLONIZING STAPHYLOCOCCUS AUREUS ISOLATES

Margaret Free, Nicole Soper, Buddy Creech, Isaac Thomsen

Vanderbilt University Medical Center, Monroe Carell Jr. Children's Hospital at Vanderbilt.
Vanderbilt Vaccine Research Program

Objective: *Staphylococcus aureus* is the most common bacterial pathogen isolated in children with invasive bloodstream and musculoskeletal infections. A major barrier to vaccine and novel therapeutic development against *S. aureus* is its continuous evolution. Many recent vaccine candidates have targeted antigens that once appeared crucial to the pathogenesis of *S. aureus*, only to see these factors recede from circulating invasive strains. Characterization of clinically relevant *S. aureus* isolates over time is necessary to find targets for novel therapeutics. Efforts toward new interventions should target factors that remain prevalent in invasive isolates over time.

Study Design: We obtained 131 invasive *S. aureus* isolates from children admitted to the Monroe Carell Jr. Children's Hospital at Vanderbilt from 2010 to 2022, and 246 colonizing isolates. Whole genome sequences were obtained using the Illumina sequencing platform. Virulence factors and multi-locus sequence type (MLST) were determined using Geneious software and through PubMLST, an open-access curated database.

Results: There were 10 unique clonal complexes (CC) identified among 320 isolates. CC8 remains the most common invasive clonal complex, though CC8 is significantly less frequent now than in 2010-2012. Diversity of invasive strains has increased substantially, with the emergence of CC5 and CC121 lineages causing invasive disease in children. CC1 was found exclusively in colonization strains.

Virulence factor prevalence has changed significantly over time. Panton-Valentine leucocidin (PVL), enterotoxins K and Q (SEK/SEQ), and the pathogenic arginine catabolic mobile element (ACME), have decreased significantly in invasive *S. aureus* strains since 2010, from 53-70% to 21-35% of current isolates. Leukocidin ED (LukED) and surface protein staphylokinase (Sak) are strongly associated with invasive strains compared to colonization strains. Conversely, toxic shock toxin (TST) and Staphylococcal enterotoxin B (SEB) were seen more commonly in colonization strains (12-15%) compared to invasive strains (5-7%). The genes encoding for gamma hemolysins (HlgA-C), leukocidin AB (LukAB), iron-regulated surface proteins (IsdA, IsdB), staphylococcal binding immunoglobulin protein (sbi), extracellular fibrinogen-binding protein (Efb), and clumping factors A and B (ClfA, ClfB) were identified in all strains tested.

Conclusions: Significant shifts have occurred over the past decade in the predominant circulating *S. aureus* strains and their virulence factor repertoire. The once-dominant CC8 (USA300 clone) has receded, and with that has come a significant reduction in some factors once thought crucial for pathogenesis. These findings also have implications for infection prevention and control practices, as eradication of colonizing strains with low potential for pathogenicity may inadvertently allow for replacement by more virulent strains.

Mentor: Isaac Thomsen, MD, MSCI (isaac.thomsen@vumc.org)

PILOT STUDY TO DEVELOP A CLINICAL PREDICTION RULE FOR INTUSSUSCEPTION

Blake Gruenberg, MD[1], Gabriella Crane, MD[2], Marla Levine, MD[1], Noah Harrison, MMSc[3], Don Arnold, MD, MPH[1]

[1] Department of Pediatric Emergency Medicine, Vanderbilt University Medical Center
[2] Department of Pediatric Radiology, Vanderbilt University Medical Center
[3] Vanderbilt University Medical School of Medicine

Background/Objective: Intussusception is the most common cause of intestinal obstruction in infants and young children. The classic intussusception triad (spasmodic abdominal pain, palpable abdominal mass, and red currant jelly stool) is rarely reported, and presenting symptoms often have significant overlap with other diagnoses. Because of the ambiguity of presentation, it is difficult for clinicians to determine who should receive a workup for intussusception and those who have more benign abdominal processes. We set out to model and internally validate a clinical prediction rule for intussusception in young children.

Design/Methods: We performed a retrospective chart review of all patients under the age of 6 years who had imaging ordered in the PED for evaluation of possible intussusception over a three-year period (2018-2020) in an academic children's hospital ED with annual volume of around fifty thousand patient encounters. Demographic, historical, and exam findings were recorded. Variables with $p < 0.20$ in univariate logistic regression were included in a multivariable logistic regression model with intussusception diagnosed by ultrasound as the dependent variable. We used robust standard errors and applied shrinkage of adjusted odds ratios (aOR) to mitigate optimism using penalized maximum likelihood estimation (PMLE). We internally validated this model using 300 bootstrap replications with replacement.

Results: A total of 1,115 patient encounters met our inclusion criteria. In the final multivariable model using PMLE, signs and symptoms most strongly associated with presence of intussusception included bilious emesis (aOR, 11.54; 95% CI, 3.65-36.52), bloody stool (aOR, 4.67; 95% CI, 2.65-8.24), abdominal pain (aOR, 4.16; 95% CI, 2.47-7.00), emesis not specified as bilious (aOR, 3.36; 95% CI, 1.96-5.80), intermittent fussiness (aOR, 1.74; 95% CI, 1.07-2.85), and diarrhea (aOR, 0.14; 95% CI, 0.06-0.34). Bootstrap internal validation yielded a c-index of 0.784.

Conclusions: This pilot clinical prediction rule for children with suspected intussusception internally validated very well, as it correctly predicted and assigned 78% of patients to the intussusception or no intussusception groups. Future prospective studies are needed to refine and further validate this model.

Mentor: Donald H. Arnold, MD, MPH (don.arnold@vumc.org)

USING WHOLE GENOME SEQUENCING AND CLINICAL RISK FACTORS TO INVESTIGATE CARBAPENEM RESISTANT ENTEROBACTERALES TRANSMISSION

Hope Hendricks[1], Lili Tao[2], Ritu Banerjee[1], Romney Humphries[2]

Vanderbilt University Medical Center Divisions of Pediatric Infectious Diseases[1]; Department of Pathology, Microbiology and Immunology[2] in Nashville, Tennessee, USA

Objective: The rising prevalence of carbapenem resistant Enterobacterales (CRE) is a global public threat. To characterize relatedness and transmission of CRE strains through a hospital system, we retrospectively performed whole genome sequencing (WGS) on sequentially collected CRE at an academic medical center and analyzed WGS data using the web-based software application EPISEQ CS (bioMerieux, Marcy l'Etoile).

Study Design: Included subjects with CDC-defined CRE isolated from clinical specimens from Sept. 2021 to Feb. 2022 were identified through the laboratory information system. Clinical data were collected to evaluate risk factors for CRE infection and potential transmission events. Isolates were sequenced by Miseq. Genomic characterization and phylogenetic analysis were performed using EPISEQ CS (bioMerieux, Marcy l'Etoile). The relatedness of isolates of the same species was analyzed by whole genome multilocus sequencing typing (wgMLST) and categorized by percent similarity, which was pre-defined by bacterial species.

Results: Fifty-five CRE isolates from 52 patients were evaluated. Clinical and laboratory details are listed (Table 1). Most patients were >50 years old, had ≥1 preexisting chronic disease (34 of 52), had prolonged hospital admissions (mean 41 days) and were critically ill (56% received ICU care). Thirty-four patients (65%) received antibiotics in the 7 days prior to incident culture, including vancomycin (31%), cefepime (27%), and piperacillin-tazobactam (21%). Carbapenemase encoding genes *bla*$_{KPC}$ and *bla*$_{VIM}$ were identified in 9 and 8 isolates, respectively. In addition, *bla*$_{CTX-M}$ was detected in 11 isolates. Phylogenetic analysis suggested 5 VIM-producing *K. pneumoniae* isolates from patients in a burn unit were identical, confirming the hospital transmission of VIM-producing *K. pneumoniae.* Two possibly related *K. pneumoniae* isolates were also identified from 2 subjects without epidemiologic links and in specimens collected 47 days apart (Fig. 1).

Conclusions: We demonstrate the potential for real-time WGS to identify related, resistant pathogens, to better understand their intra- and inter-facility transmission and to rapidly interrupt outbreaks.

Mentor: Ritu Banerjee, MD, PhD (ritu.banerjee@vumc.org)

NONINVASIVE ASSESSMENT BY CARDIAC MAGNETIC RESONANCE OF ACUTE REJECTION AND CARDIAC ALLOGRAFT VASCULOPATHY IN PEDIATRIC HEART TRANSPLANT PATIENTS

Sandra Kikano MD, Simon Lee MD, Debra Dodd MD, Justin Godown MD, David Bearl MD, Maryanne Chrisant MD, Kak-Chen Chan, MD, Deipanjan Nandi, MD, Kimberly Crum BS, RN, Kristen George-Durrett BS, Lazaro Hernandez MD, Jonathan H. Soslow MD

Objective: To determine if cardiac magnetic resonance (CMR) can non-invasively detect acute rejection (AR) and cardiac allograft vasculopathy (CAV) in pediatric heart transplant (PHT) patients.

Study Design: Patients were enrolled at three tertiary care children's hospitals. Prospective enrollment occurred as part of a funded multicenter research study at 2 sites; retrospective data collection was performed at all 3 sites to supplement enrollment. Data were collected from surveillance EMB or EMB at the time of clinical concern for a unique episode of AR. AR was defined as an abnormal EMB necessitating a change in immunosuppressives. CAV diagnosis was determined based on coronary angiography. Patients were excluded if they had a diagnosis of AR and CAV simultaneously, had CMR obtained >7 days from AR diagnosis, had EMB negative AR, or if they could not undergo contrasted, unsedated CMR. CMR data included standard volumes, global longitudinal and circumferential strain (GLS, GCS) measured using feature tracking, native T1, T2 and extracellular volume (ECV) mapping, and left ventricular (LV) filling curves to assess diastology. Normative values from each magnet were obtained to generate native T1 and T2 z-scores. Kruskall-Wallis testing was used to compare groups: 1. No AR or CAV (Healthy) 2. AR 3. CAV. Wilcoxon rank sum testing was used to compare subgroup analyses for significant values.

Results: Fifty-nine patients met inclusion criteria (mean age 17 years [15-19]) with 10 (17%) having AR, and 11 (19%) with CAV. Patients with CAV were older in age and had increased time since transplant; there were otherwise no significant demographic differences between the groups. Patients with AR had worse left ventricular ejection fraction (LVEF) ($p=0.001$) and larger left ventricular (LV) end systolic and diastolic volumes. Global circumferential strain (GCS) was worse in patients with AR ($p=0.054$) and CAV ($p=0.019$), compared to Healthy patients. ECV and T2 z-scores in all locations were elevated in patients with AR when compared to CAV and Healthy. Native T1 z-scores were also elevated in AR compared with the other groups. Diastolic markers were not significantly different between the groups.

Conclusions: CMR findings can differentiate CAV and AR from Healthy PHT patients. In this cohort, CAV subjects have normal global function (LVEF) but abnormal GCS which may suggest early subclinical dysfunction. CAV subjects also have normal parametric mapping. AR patients have abnormal function (LVEF and GCS) and tissue characteristics consistent with edema, with elevated ECV, native T1 and T2 z-scores. Characterization of these patterns may assist in informing standardization of CMR findings and help determine diagnostic differences in PHT patients.

Mentor: Jonathan Soslow, MD, MSCI (jonathan.h.soslow@vumc.org)

TRANSCATHETER PDA CLOSURE: A RETROSPECTIVE ANALYSIS OF OUTCOMES AND NEED FOR LONG-TERM FOLLOW-UP.

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Objective: Transcatheter closure of patent ductus arteriosus (PDA) is well-described for managing those patients who fail medical therapy and have hemodynamically significant PDAs. Various techniques have been reported and the procedure has become increasingly common even in extremely low birth weight premature infants. The procedure is believed to have fewer long-term adverse outcomes than a surgical approach or expectant medical management. However, to date, studies have included only small cohorts of patients, reporting varying rates of successful closure, adverse outcomes, and length of follow-up. The aim of this study was to conduct a retrospective review of a large cohort of patients in order to identify rate of successful closure, frequency of adverse outcomes, and to determine need for long-term follow-up in these patients.

Study Design: We conducted a retrospective review of 300 children ≤18 years old who underwent transcatheter PDA closure between 2010 and 2018 at our institution. We collected demographic data, closure indication(s), echocardiographic findings, hemodynamic data, PDA measurements, device used, procedure complications, and follow-up echocardiographic findings.

Results: Mean age at time of closure was 3.4 ± 3.8 years. The primary indications for closure included presence of a murmur (37.3%), cardiomegaly (32.7%), risk of endarteritis (18.7%), pulmonary overcirculation (5.0%), pulmonary hypertension (4.3%), failure to thrive (1.3%), and failed medical therapy (0.7%). 299 patients (99.7%) underwent successful PDA closure. 8 (2.7%) had procedural complications, which included thrombosis (n = 2, overall risk 0.7%) and device embolization (n = 6, overall risk 2%). 2 patients had branch pulmonary artery obstruction with associated gradients >2m/s but did not require additional intervention with resolution by 1 year follow-up. 16 patients (5.3%) had residual PDA shunt that resolved within 48 hours post-procedure; 0 patients had associated hemolysis. Follow-up times varied among providers, and 158 (52.8%) patients were followed by cardiologists outside of our institution. Of those who had follow-up in our system, no patient developed a late complication, specifically branch pulmonary artery stenosis, aortic arch obstruction, device embolization, or thrombosis.

Conclusions: In this large cohort of patients who underwent transcatheter PDA closure, there was a high rate of successful closure with low risk of adverse events. Complications that did occur were peri-procedural. Those patients that had residual PDA shunt or branch pulmonary artery obstruction had improvement and/or resolution within 1 year of closure. No late complications were seen in follow-up, including branch pulmonary artery stenosis, aortic arch obstruction, device embolization, or thrombosis. This study demonstrates that patients who undergo successful PDA device closure may not require long-term follow-up past 6-12 months post-procedure.

Mentor: Jonathan H. Soslow, MD, MSCI (jonathan.h.soslow@vumc.org)

COMMUNICATION DURING RAPID RESPONSES USING SBAR PRESENTATION

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Introduction: During a rapid response, when the pediatric critical care team is called to assess a decompensating patient, clear and concise communication is key. Presentations with excessive and unnecessary information delay patient assessment and care. This quality improvement project aimed to educate residents to present a patient in the situation, background, assessment, and recommendation (SBAR) format, with the goal of promoting effective communication during rapid responses.

Methods: Critical care providers (nurse practitioners, fellows and attendings) were surveyed on baseline quality of communication during rapid responses using a survey that rated communication in several domains. Plan, Do, Study, Act (PDSA) cycle interventions were initiated to educate on SBAR communication. The first PDSA cycle consisted of in-person teaching in small groups during weekly mock codes. The second PDSA cycle was monthly didactic lectures during resident noon conferences. The third PDSA cycle had residents practice SBAR presentation at those mock codes. During the study period, a weekly survey was sent to critical care providers and asked respondents to rate communication during rapid responses using a five-point Likert scale. A one on the Likert scale represents strong disagreement and a five represents strong agreement with a survey statement. Survey question results were plotted over time using a statistical process control chart.

Results: A total of 119 responses were recorded, 22 pre- and 97 post-interventions. Responses to the survey statement “SBAR was used for communication during the rapid response” improved from a median of 1.5 on the Likert scale pre-intervention, with 0% of the responses agreeing to the statement, to 4 and 53% respectively post-intervention. For the survey statement “I was presented an appropriate amount of information about the patient,” responses improved from a median of 3 pre-intervention, with 23% of the responses agreeing to the statement, to 4 and 70% post-intervention.

Conclusion: Implementation of an SBAR curriculum increased the use of SBAR communication during rapid responses and improved perceived communication. Subsequent PDSA cycles could include real-time communication feedback at rapid responses and expanding the SBAR curriculum to surgical trainees and bedside nurses.

Mentor: Katharine Boyle, MD (katie.boyle@vumc.org)

ASSOCIATION BETWEEN MATERNAL USE OF MEDICATIONS FOR OPIOID USE DISORDER (MOUD) DURING PREGNANCY AND CHILD WELFARE OUTCOMES

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Objective: Over the last two decades there was a fourfold increase in the number of pregnant women with opioid use disorder (OUD) in the U.S. Concurrently, there was a rise in the number of infants entering the foster care system, most due to parental substance use, leading to family separation and strain on the child welfare system. Nationwide, infants are the fastest growing age group entering foster care, accounting for 20% of annual foster care placements. Medications for OUD (MOUD) are recommended for use during pregnancy and are associated with improved outcomes for both mothers and infants, including decreased risk of overdose and preterm birth; however, the extent to which use of MOUD during pregnancy is associated with reductions in family separation remains understudied. This study seeks to determine if use of MOUD during pregnancy is associated with higher rates of infant discharge home from their birth hospitalization with their biological mother, compared to infants of mothers not receiving MOUD.

Study Design: Data were collected prospectively using a standardized collection tool to capture maternal and neonatal characteristics, neonatal treatment, and neonatal discharge disposition for infants with opioid exposure at a single center born between March 2018 and January 2022. Infants were included if they were exposed to an opioid and born $\geq$ 35 weeks without critical illness. A multivariate logistic regression model was constructed, with potential confounders chosen a priori, to evaluate the association of MOUD with discharge home with biological mother.

Results: Among 459 maternal-infant dyads meeting our inclusion criteria, 362 mothers (78.9%) received MOUD during pregnancy and 350 infants discharged home with their biological mother (76.2%). Mothers who received MOUD were more likely ($p<0.001$) to be white vs. non-white (93.1% vs. 71.1%), covered by Medicaid (90.6% vs. 73.2%), have infants born at higher gestational age (39 vs. 37 weeks) and were more likely to be discharged home with their infants (82.9% vs. 51.6%) [Figure 1]. After accounting for potential confounders, infants of mothers who received MOUD during pregnancy were 5.8 times more likely to be discharged home with their biological mother (aOR 5.81, 95% CI 3.34-10.27).

Conclusions: Maternal use of MOUD during pregnancy was associated with higher rates of infant discharge from birth hospitalization with the biological mother, suggesting that treatment of OUD with medication is a potentially important intervention for reducing family separation and the stress of the opioid crisis on the foster care system.

Mentor: Stephen Patrick, MD, MPH, MS (stephen.patrick@vumc.org)

PATIENT CHARACTERISTICS ASSOCIATED WITH OPIOID PATIENT-CONTROLLED ANALGESIA PUMP (PCA) USE DURING CANCER TREATMENT, A SINGLE INSTITUTION REVIEW

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Objective: To identify pediatric cancer patients at risk for requiring use of an opioid patient-controlled analgesia pump (PCA) during therapy.

Study Design: Patients were screened for eligibility through an electronic medical record (EMR) database. Pediatric patients diagnosed with cancer and treated with systemic chemotherapy at Vanderbilt Children's Hospital between 2010 and 2019 were included in this study. Patient demographics, diagnosis and treatment history, baseline psychosocial data, as well as documented pain symptoms and management were abstracted from the EMR and recorded in a REDCap database. Patients were censored at completion of therapy, death, admission for allogeneic stem cell transplant, first cycle of anti-GD2 antibody, or when lost to follow-up. Nominal variables were compared using Chi square/Fishers exact test and multivariable logistic regression was performed.

Results: Six hundred eighty-five patients were followed for a median of 194 days. Diagnoses include 48.9% hematologic malignancies (with 5.7% having non-Hodgkin lymphoma), 19.4% localized solid tumors, 13.6% metastatic solid tumors, 12.4% localized CNS tumors, and 5.7% metastatic CNS tumors. The cohort is predominantly white and non-Hispanic. There is a slight male predominance (56%). The median age of the overall cohort was 7 years. At the time of diagnosis, 74.5% of patients were living in a 2-caregiver household.

A PCA was required for pain control in 18.5% of patients (n=127). There was no statistically significant difference in PCA use based on gender, race/ethnicity, use of government assistance, or pre-existing history of anxiety/depression. On univariate analysis, older age (median of 12 years vs 7 years), exposure to anthracyclines or alkylating agents, diagnoses of metastatic solid tumors and non-Hodgkin lymphoma, and autologous stem cell transplant were significantly associated with PCA use, whereas living in a 2-caregiver household appeared to be protective against needing a PCA. On multivariate analysis, factors independently associated with PCA use include a metastatic solid tumor diagnosis (odds ratio [OR] 2.37, 95% Confidence Interval [CI] 1.4-4.2; p=0.003), a diagnosis of non-Hodgkin lymphoma (OR 2.96, CI 1.5 – 5.7; p=0.001), autologous stem cell transplant (OR 11.7, CI 4.4-31.1; P<0.001), and increased age (OR 1.08, CI 1.0-1.1; p<0.001) when controlled for type of household as well as exposure to anthracyclines or alkylating agents. This model yielded a c-statistic of 0.75 (CI 0.70-0.80). Mucositis was the most common indication for PCA use (48%), followed by abdominal pain (15%) and musculoskeletal pain (11%). The median duration of PCA use was 7 days. Common side effects associated with PCA use include constipation (33%), pruritis (23%), and sedation (10%). Of the patients admitted on a PCA, 19.7% had a subsequent admission requiring a PCA with a median duration of 42 days between admissions.

Conclusion: PCA use is common in pediatric oncology, particularly in older patients with metastatic solid tumors, non-Hodgkin lymphoma, and those requiring high dose chemotherapy with autologous stem cell transplant. Additional research is needed with a focus on these high-risk groups to determine if earlier supportive care interventions can decrease the need for PCA use during cancer therapy.

Mentor: Adam Esbenshade, MD, MSCI (adam.esbenshade@vumc.org)

EVALUATING NEW ASSAYS FOR BIVALIRUDIN MONITORING

Raghavendran P, Tillman B, Wheeler A, Gailani D

Background: Direct Thrombin Inhibitors (DTIs) are becoming important anticoagulants in pediatric and adult patients. DTIs are monitored with the activated partial thromboplastin time (aPTT) and the activated clotting time (ACT), both complex assays, and performance may be altered by clinical conditions including inflammation, thrombosis, bleeding diathesis and others. More accurate assays for monitoring therapeutic anticoagulation are required for safe use. A clot-based diluted Thrombin Time (dTT) assay and chromogenic anti-IIa assays show preliminary promise in correlating with increasing doses of DTI, but more data is needed on how these assays relate to each other and to the aPTT in diverse patient populations.

Methods: Patients of any age who received bivalirudin between March 2020 and April 2022 were analyzed. Medical records were reviewed demographic data as well as adverse outcomes (bleeding, thrombosis, death) while on the medication. Plasma samples from patients drawn for aPTT standard of care clinic monitoring were analyzed using the chromogenic anti-IIa and dTT assays and were compared to aPTT measurements as well as bivalirudin dosing documented in the medical record.

Results: 32 patients were analyzed, from which 136 samples were tested with the chromogenic assay and 120 with the dTT. All samples also had aPTT tested simultaneously. Correlation between aPTT and the chromogenic and dTT assays was poor (Spearman coefficient 0.56 and 0.62, respectively). There was strong positive correlation between chromogenic and dTT assays when compared against each other (Spearman coefficient of 0.9239). When comparing the assays bivalirudin dose, there was much better correlation between chromogenic and clot-based assays to dose than aPTT to dose (Spearman coefficient of 0.22 for aPTT versus dose, 0.51 for chromogenic assay versus dose, 0.63 for dTT versus dose). When examining median chromogenic anti-IIa and dTT levels correlating to varying aPTT levels (60-70 seconds, 70-80 seconds, 80-90 seconds), there was incremental increase in median for each tier in both assays (median levels were 0.46, 0.53 and 0.59 µg/mL for chromogenic assay; median levels were 0.59, 0.75 and 1.26 µg/mL for dTT).

Conclusion: There is good correlation between the chromogenic and dTT assays as well as poor correlation between those assays and aPTT. There is also better correlation between bivalirudin dose and both the chromogenic and dTT assays compared to aPTT. This indicates newer tests have more stability with different clinical presentations and critical illness across the age spectrum for appropriate medication monitoring. Though more data is needed to assess how certain assay levels relate to clinical outcomes, data shows these newer tests can serve as more reliable monitoring for bivalirudin in adult and pediatric patients with varying clinical presentations.

Mentor: David Gailani, MD (dave.gailani@vanderbilt.edu)

DEVELOPMENTAL TRAJECTORY OF EXTRACELLULAR VESICLE CHARACTERISTICS FROM THE LUNGS OF PRETERM INFANTS

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Background: Extracellular vesicles (EVs) have been identified as important mediators of cellular communication. Because lung development requires vast cellular and structural changes that rely on cellular communication, EVs may be both markers and mediator of normal development and of bronchopulmonary dysplasia (BPD) after preterm birth.

Objective: To characterize EVs across lung development.

Study Design: TAs were collected from infants born between 22- and 35-weeks gestation intubated for in/out surfactant or respiratory failure. TA were analyzed for EVs with electron microscopy (EM), nanoparticle tracking analysis (NTA), and bead-based flow cytometry with the MACSPlex Exosome Kit. We queried a single-cell transcriptomic atlas of mouse lung development for EV marker expression.

Results: TAs were collected from 34 patients, with 27 samples containing detectable EVs. For analysis, patients were divided into two groups based on developmental stage, late canalicular (22w0d to 26w6d) and saccular (27w0d to 34w6d). EM showed EVs of varying sizes in TAs. NTA revealed infants in the late canalicular stage had larger mean and median EV diameter. Bead-based flow cytometry found an abundance of the EV-enriched tetraspanins CD9, CD63 and CD81 across GA and particularly high levels of EVs carrying CD326 (*EpCAM)* and CD133 (*Prom-1*), consistent with the detection of abundant EVs derived from epithelial cells. Higher levels of $CD24^+$ EVs were detected in samples from the late canalicular vs. saccular stage (p=0.0095). There also appeared a trend towards higher levels of $CD14^+$ in EVs in the late canalicular stage (p=0.0664). Among infants that went on to develop BPD, higher levels of $CD24^+$ (p=0.0186) and $CD14^+$ (p=0.0372) EVs were detected. Query of epithelial cells from a developmental atlas revealed abundant levels of EV marker gene expression in epithelial cells across analogous stages in mouse lung development.

Conclusions: We have identified a developmental trajectory of enriched $CD24^+$ EVs during early lung development and an association of $CD24^+$ EVs with developmental stage and BPD and $CD14^+$ EVs with risk of BPD, independent of GA. This work lays a foundation to query the biologic function of EVs during lung development, with the overall goal of identifying therapeutic agents for restoring lung development in premature neonates.

Mentor: Jennifer Sucre, MD (jennifer.sucre@vumc.org)

WEIGHING IN ON THE RESULTS FROM EFFECTIVE SURVEY SCALES: A CROSS-SECTIONAL ANALYSIS OF THE ASSOCIATION BETWEEN FAMILY RESILIENCE AND FAMILY FUNCTIONING AMONG FAMILIES OF INFANTS ENROLLED IN AN EARLY CHILDHOOD OBESITY PREVENTION STUDY

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Objective: Across the United States, there are emerging efforts to identify the variables within well-functioning families that are associated with improved resilience and promote the healthy development of children. This study examined the association between parent-reported family resilience and family functioning among parents of young children enrolled in a randomized trial, Greenlight Plus, which focused on obesity prevention.

Study Design: We conducted a cross-sectional analysis of survey data collected at baseline of the Greenlight Plus, which enrolled parents and children shortly after birth from six medical centers around the country. Family Resilience was assessed by the 11-item Social and Economic Resources Subscale of the Family Resilience Assessment Scale (FRAS), with higher subscale scores indicating greater utilization of resources. Family functioning refers to the ways in which a family operates as a system, including how family members interact with one another, how decisions are made, and how roles and responsibilities are distributed. This was assessed by the Family Assessment Device (FAD), which consists of 12 items that measure the structural, organizational, and transactional characteristics that distinguish between healthy and unhealthy families, with higher scores reflective of worse family functioning. We assessed the association between the FRAS and the FAD using a proportional odds logistic regression model, adjusting for study site, child age, child sex, child race, family size, parent education and COVID-19 Exposure and Family Impact Scale (CEFIS).

Results: We had complete data on 596 families. The average age of children was 24.6 weeks (21.5 SD). The parent reported race and ethnicity of participants was Hispanic 272 (45.6%), Non-Hispanic white 123 (20.6%), Non-Hispanic Other 111 (18.6%) and Non-Hispanic Black 88 (14.8%). The average number of adults in the home was 2.30 (0.963 SD) with 132 (22.1%) of the caregivers having less than high school education. The average score on the FRAS was 3.02 (0.42 SD). The average score on the FAD was 1.72 (0.51 SD). In the adjusted proportional odds regression model, FRAS was associated with FAD (OR 1.18, 95% CI 1.14, 1.22, $p<0.001$). This indicates that each increasing value of family resilience was associated with an 18% (14-22%) increase in the odds of a higher family functioning.

Conclusion: Increasing levels of family resilience are associated with higher levels of family functioning. Our findings suggest that promoting family resilience through interventions aimed at improving communication, problem-solving, and support may be an effective means of enhancing overall family functioning. These findings have important implications for medical providers and policymakers interested in promoting family well-being.

Mentor: William J. Heerman, MD (bill.heerman@vumc.org)

EFFECT OF EARLY-LIFE HOUSEHOLD EXPOSURE TO LIPOPOLYSACCHARIDE ON CHILDHOOD ASTHMA IS MODIFIED BY 17Q12-Q21 GENOTYPE

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Objective: Lipopolysaccharide (LPS), a major component of Gram-negative bacteria, is a ubiquitous microbial exposure that strongly stimulates the immune response. Past studies have shown a protective, null, or even detrimental effect of early-life household LPS exposure on childhood asthma. Because childhood asthma onset is determined by complex gene-by-environment interactions, we hypothesized that the conflicting LPS results may be explained by such an interaction. To test this hypothesis, we explored whether the effect of early-life household LPS exposure on childhood asthma is modified by genetic variations in the 17q12-q21 region, a widely replicated locus for childhood wheezing phenotypes.

Study Design: The study population included healthy term infants enrolled in a population-based prospective birth cohort (INSPIRE). LPS concentrations were measured in household dust samples collected at age one year using ELISA. Five-year current asthma was defined as parental report of ever physician-diagnosed asthma and current asthma-related symptoms at age 5 years. A single nucleotide polymorphism (SNP) in the 17q region, rs2305480, was characterized using a TaqMan assay. A logistic regression model was used to test the association of household LPS concentration in the first year of life with 5-year current asthma while adjusting for infant's sex, age at the time of LPS collection, secondhand smoke exposure, maternal asthma, and insurance type. In a model stratified by race and ethnicity, we included an interaction term between LPS concentration and genotype.

Results: LPS measurements in household dust samples were available for 935 infants. The median (interquartile range) LPS concentration was 1.11 (0.25-2.51) endotoxin units per milliliter. In the 704 children (75.3%) with 5-year outcome data, the 5-year current asthma rate was 122/704 (17.3%). There was no association between early-life household LPS exposure and 5-year current asthma in this cohort (OR 1.04, 95%CI 0.80-1.36, p=0.77). However, in 238 non-Hispanic white children with genetic data, we detected effect modification of early-life household LPS exposure on 5-year current asthma by rs2305480 (p=0.018 for the interaction term). For children with the GG genotype, increased LPS exposure was associated with increased odds of 5-year current asthma, whereas for children with the AA genotype, increased LPS exposure was associated with decreased odds of 5-year current asthma.

Conclusions: Our study suggests that the impact of early-life household LPS exposure on childhood asthma risk is modified by genetic variations in the 17q region, demonstrating a novel gene-by-environment interaction. Our short-term goal is to replicate our findings in other large birth cohorts with more diverse heritages. Ultimately, these results could be used to develop personalized asthma prevention strategies for children with high-risk genotypes.

Mentor: Christian Rosas-Salazar, MD, MPH (c.rosas.salazar@vumc.org)

RESIDENT VIEWS ON LEARNING TO COMMUNICATE SERIOUS NEWS

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Background: Communication in pediatric medicine is unique due to the triadic relationship between the patient, their caregivers, and the medical team. While the American College of Graduate Medical Education and American Academy of Pediatrics recommend incorporating communication skills into program requirements and milestones, neither endorse specific curricula or experiential learning opportunities. This results in an overreliance on informal curriculum and varied experiences for the learner that makes it difficult to draw conclusions on how best to teach and evaluate communication skills to pediatric residents. This study aims to describe the state of communication skill development in pediatrics at a single-center academic institution and create recommendations for future educational opportunities.

Methods: Email invitations for semi-structured Zoom interviews were sent to third-year pediatric residents in Fall 2021 and to second-year residents in Spring 2022 (IRB #211163); medicine-pediatric residents were excluded to eliminate confounding from their experiences in adult medicine. Thematic analysis was done by the same person who conducted the interviews. Results were compared using a 2-tail t-test to determine statistical significance. The interviews all began with a prompt to discuss a time when the participants discussed serious news, which was described as news that was potentially surprising, life-altering, or that could change a patient's clinical trajectory. The interviews also included questions on experiences with communication education and barriers to participating in conversations where serious news was discussed. The interviews all concluded with the same prompt on an idealized communication curriculum during pediatric residency.

Results: Twenty-one residents participated: 12 third year, 9 second year. One third year resident was a pediatric neurology resident, and the rest were categorical pediatric residents. 7 of 21 (33%) recounted telling patients serious news during their intern year. 12 of 21 (57%) recalled having a more senior physician present during one of these discussions. 13 of 21 (62%) endorsed that observing more senior physicians deliver serious news was how they learned to deliver serious news, with 1 respondent stating that they did not like this education modality. 14 of 21 (67%) stated that they wanted more real or simulated opportunities to deliver serious news, and 14 of 21 (67%) viewed family-centered rounds as a time when a resident could be tasked with delivering serious news. There were some differences between the cohorts. 2nd year residents were more likely to feel confident in delivering serious news if a senior physician invited them to be present at the conversation (89% vs. 58%, p=0.07), and were more likely to endorse a lack of medical knowledge (78% vs. 58%, p=0.17) and a lack of self-confidence (89% vs. 67%, p=0.13) as a barrier to their involvement. 3rd year residents felt that they needed to advocate for themselves to be included more (67% vs. 33%, p=0.07), and were more likely to view a prebrief with a senior physician as beneficial (75% vs. 44%, p=0.082).

Conclusion: These results offer suggestions for crafting experiential learning at both the senior and junior physician levels. More intentional preparation by senior physicians, including prebriefing, physical placement, and immediate feedback could allow residents to better recognize opportunities for developing their communication skills. Being able to practice these skills in a variety of clinical settings and for non-end-of-life scenarios is also viewed favorably by residents. This study is limited to the experiences of residents at a single institution, and statistical significance is likely hampered by small sample sizes.

Mentor: Tracy Hills, DO (tracy.hills@vumc.org)

Poster Abstracts

Poster Abstracts

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INTRAVENTRICULAR HEMORRHAGE AMONG VERY LOW BIRTH WEIGHT INFANTS IN A SOUTH AFRICAN COHORT: TRENDS & SHORT-TERM OUTCOMES

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Objectives: Neonatal mortality accounts for nearly half (47%) of under-5 deaths with the highest mortality rate in sub-Saharan Africa. Globally, preterm births are among the leading causes of most neonatal deaths. In South Africa (SA), prematurity accounts for 47.9% of neonatal deaths. The incidence of intraventricular hemorrhage (IVH) in very low birth weight (VLBW) infants in South Africa from 2013-2015 was 26.7%. The sequalae of IVH is severe and irreversible and management is mainly supportive and hence prevention is key. We hypothesize that infants born in SA may have different modifiable risk factors and outcomes of IVH compared to infants in higher resource settings. Our study aims to characterize the incidence of IVH, associated risk factors and outcomes in VLBW infants in a SA hospital to further guide modification of existing neonatal management protocols for management and prevention of IVH.

Study Design: This study will be a retrospective cohort study of infants born with a birth weight ≤1500 grams diagnosed with IVH at Charlotte Maxeke Academic Hospital in Johannesburg (CMJAH), South Africa from 2016 to 2020.

Results: Preliminary data from 2016 to 2020 from a pre-existing database identified 490 VLBW infants with IVH. 146 of them had Grade 3 or 4 IVH. Total sample size of at least 450 for all grades, and 110 for severe IVH will be included in the analysis. Secondary data analysis will be completed pending approval of full access to database by the CEO of CMJAH.

Conclusion: We hypothesize that infants born in South Africa may have different modifiable risk factors and outcomes of IVH compared to infants in higher resource settings.
Conclusion pending secondary data analysis.

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INTEGRIN α3β1 REGULATES ALVEOLAR BASEMENT MEMBRANE FORMATION DURING POSTNATAL LUNG DEVELOPMENT AND ASSEMBLY

Annica Alwine, Pete Gulleman, Dawn Newcomb, Erin Plosa.

Objective: Cell-extracellular matrix interactions are essential for lung development. Alveolar epithelial cells (AECs) connect to the matrix through integrins, transmembrane heterodimeric αβ receptors. We previously reported that β1 integrin is required for lung branching morphogenesis and alveolarization. While Integrin α3β1 is essential for basement membrane formation in both skin and kidneys, the role of integrin α3β1 in the lung is undefined. We hypothesize that α3β1 integrin is required for alveolar basement membrane formation by regulating collagen IV localization and developmentally precise laminin isoform expression.

Study Design: We deleted the α3 integrin subunit in lung epithelium at embryonic day 9.5 (E9.5) using Shh-Cre, ($\alpha3^{Shh.Cre}$ mice), thereby targeting α3β1 specifically. Histological analysis was quantified using ImageJ. FlexiVent assessed pulmonary function. Frozen sections were stained by immunofluorescence (IF) for laminin and collagen subunits to delineate the regions of matrix disorganization. ECM component gene expression was measured by qPCR.

Results: P3 $\alpha3^{Shh.Cre}$ lungs exhibited thickened alveolar septa and decreased airspace number compared to $\alpha3^{f/f}$ control littermates, indicating impairment in saccular stage lung development. P28 $\alpha3^{Shh.Cre}$ lungs exhibited increased mean linear intercept, increased type 2 AEC number/ hpf (64±5 in $\alpha3^{Shh.Cre}$ vs. 40±3 in $\alpha3^{f/f}$, p <.05). Pulmonary function testing demonstrated increased resistance ($\alpha3^{Shh.Cre}$ 1.11 vs. $\alpha3^{f/f}$ 0.58 cmH2O/ml/s, p <.05) and decreased compliance ($\alpha3^{Shh.Cre}$ 0.02 vs. $\alpha3^{f/f}$ 0.04 ml/cmH_2O, p <.05) in P28 $\alpha3^{Shh.Cre}$ lungs compared to controls. In addition, P28 $\alpha3^{Shh.Cre}$ lungs exhibited increased collagen deposition compared to $\alpha3^{f/f}$ lungs by hydroxyproline assay ($\alpha3^{Shh.Cre}$ 17.69 vs. $\alpha3^{f/f}$ 47.90 µg/mL, p <.05). Immunostaining demonstrated increased deposition of specific collagen IV α1 and α2 chains, mislocalized to the alveolar interstitium rather than the expected location in the basement membrane. P28 $\alpha3^{Shh.Cre}$ type 2 AECs exhibited significantly decreased expression of ECM components *Lama5*, *Lamb1*, *Lamc2*, and *Lamc1* (p <.05). In contrast, the embryonic laminin-1 isoform persisted at increased protein levels in the developing alveolar septa of saccular stage $\alpha3^{Shh.Cre}$ lungs compared to control littermates, suggesting failed developmentally programmed laminin isoform switching in $\alpha3^{Shh.Cre}$ mice.

Conclusion: Epithelial α3β1 is required for sacculation, basement membrane formation, and proper ECM component expression. Failure of α3β1 integrin-mediated expression of alveolar basement membrane components during sacculation impairs lung development and restricts adult lung function.

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PREDICTIVE MODELLING AND POSTNATAL MANAGEMENT OF NEONATES WITH SUSPECTED COARCTATION OF THE AORTA WITH A PDA: A SINGLE CENTER STUDY OF TWO ERAS

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Introduction: Coarctation of the aorta (CoA) is difficult to diagnose pre- and postnatally due to the presence of a patent ductus arteriosus (PDA). Consequently, many infants with prenatal concern for CoA are admitted to the ICU for observation while awaiting PDA closure. Our prior work created and validated a coarctation prediction model (CPM) to differentiate neonates with and without CoA in the presence of a PDA, with the CPM calibrated for maximum sensitivity. This resulted in a postnatal management algorithm for these neonates (Figure 1). The objective of this study was to characterize difference between two eras at our center: before and after implementation of this postnatal treatment plan. We hypothesized that these measures would decrease length of stay, ICU length of stay, prostaglandin administration, central line use, and increase breastfeeding incidence.

Methods: This is a retrospective study of 143 infants with prenatal concern for CoA who did not require surgical intervention at a single quaternary academic children's hospital in Nashville, Tennessee from 2006-2020. 63 neonates in the preintervention group, 80 in the postintervention group. The CPM was implemented in September of 2014, which divides the two eras. Neonates <35 weeks post-menstrual age and <2 kg were excluded from the study. Infants with simple congenital heart disease (atrial septal defect, ventricular septal defect) were included but patients with all other types of congenital heart disease were excluded. Demographic data was collected as well as length of stay, ICU length of stay, time to first feed, prostaglandin administration, central line utilization, number of echocardiograms, breastfeeding rates, and inflation adjusted hospital costs. Variables were analyzed using Wilcoxon rank sum for continuous variables and Chi squared analysis was used for discrete variables. Infants were followed one year from discharge to collect data on readmissions and readmission diagnoses.

Results: Time to first feed (p value <0.001), prostaglandin administration (p value <0.001), and central line utilization (p value 0.027) all were reduced in the postintervention cohort (Table1). Length of stay, ICU length of stay, number of echocardiograms, breastfeeding rates, and inflation adjusted hospital costs did not reach statistical significance between the two eras. In the postintervention era, 16 infants represented to the ED after discharge, all unrelated to cardiac disease. Two deaths occurred in the postintervention cohort during the first year of life but none due to cardiac disease. 28 infants in the postintervention era were able to be discharged from the newborn nursery or general pediatrics floor as opposed to the NICU.

Conclusions: The postintervention era had less CVL and PGE utilization but not difference was noted between LOS, ICU LOS, breastfeeding rates, or inflation adjusted cost. Over a 14-year period, we found that use of a postnatal management plan incorporating CPM resulted in no adverse cardiac outcomes. This appears to be a safe and reliable method for managing neonates with suspected CoA with a PDA using a novel predictive model.

Mentor: Jonathan Soslow, MD, MSCI (jonathan.h.soslow@vumc.org)

A COMPARISON OF TELEBURN TO IN-PERSON CONSULTATIONS OF PEDIATRIC PATIENTS IN A CHILDREN'S EMERGENCY DEPARTMENT

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Objective: Pediatric Burn Care is an essential component to pediatric emergency care. Regional Burn Centers provide burn care but unfortunately there are disparities in access to regional burn centers for pediatric patients. Teleburn is a tool that enables providers without a certified burn center to provide photos of a burn to experts and receive recommendations on burn care. The purpose of this study is to evaluate the effectiveness of a Teleburn system to the gold standard in-person consultation in regard to burn infection rate, clinic follow up rate, post-burn admission rate, and 72-hour bounce back rate.

Design/Methods: Data was collected from December 2019-March 2022 through the electronic medical record. A total of 416 patient encounters that met criteria were analyzed. The criteria for a Teleburn encounter are displayed in Fig. 1 and this was the criteria applied to the in-person burn consults. A non-inferiority study was designed comparing proportional outcomes of telemedicine burn initial visits to emergency department visits in regard to burn infection rate, clinic follow up rate, post-burn admission rate, and 72-hour bounce back rate. The data were compared with a difference of greater than 10% being considered inferior.

Results: Amongst the patient encounters 45.6% were female and ages ranged from 7 weeks to 19 years. Most common burn type was scald at 47.5%, with thermal being second at 43.7%. No differences were identified in rates of readmission - 1.67% difference (95% CI -27%< x< 23.8%) and return within 72 hours – 0.7% difference (-18.4%< x< 19.7%). Teleburn patients were 12.6% less likely to follow up (2.7%< x< 22.40%). Only one infection was identified, which is insufficient to conclude non-inferiority in terms of infection events.

Conclusion: While convenient, Teleburn consult could not be demonstrated to be non-inferior to in-person consultation. No differences in infection rates were identified, and difference in readmission and return were clinically insignificant. Efforts to improve follow-up may prove successful in raising the standard to that of in person visits given the large geographic areas covered by most regional burn centers. This research advocates for more enhancement of Teleburn consult systems for pediatric acute minor burns and presents easily surmountable limitations. This study demonstrates that telemedicine may be effective and feasible to regional burn centers if follow up can be improved.

Mentor: Ronnie Mubang, MD (ronnie.mubang@vumc.org)

DECIPHERING SETD2 CONTRIBUTIONS TO GENOMIC INTEGRITY AND HOW FUNCTIONAL LOSSES LEAD TO CANCER DEVELOPMENT

Sandra Baril, MD; Peds Heme/Onc Fellow PGY5

Objective: SETD2 is a tumor suppressor that is mutated and deleted across a wide range of malignancies, including relapsed and refractory cancers. Our research aims to resolve the SETD2 functional domain(s) responsible for cell viability and genomic instability as well as target a synthetic approach to selectively target cancer cells harboring SETD2 mutations.

Study Design: To test which SETD2 domains are required for viability, I will use HeLa TetOn-Cas9 cells to create SETD2-knockout cells and re-introduce variable SETD2 mutations that target functional domains. I will use these constructs measure viability and quantify mitotic errors to relate SETD2 mutation to genomic stability. In order to explore mechanisms for clonal fitness, I have used a variety of chemotherapeutics to create dose response curves with SETD2-knockout HeLa cells compared to wild-type. I will seek to identify mechanisms of chemoresistance by using CRISPR screens to identify differences in enrichment or depletion of DDR genes in SETD2-knockout versus wild-type cells.

Results: Preliminary results have revealed an increased sensitivity to mitotic inhibitor, Vincristine, for SETD2-knockout cells compared to wild-type (EC50 7.934e-9 vs 5.278e-8). There has been no difference observed for purine analogues, Thioguanine and Mercaptopurine, or to topoisomerase II inhibitor, Doxorubicin. There has not been a consistent difference observed for folate antagonist, Methotrexate.

Conclusions: Our results suggest that replication stress applied by exposure to Vincristine leads to increased death for SETD2-knockout cells. Since it has been shown that SETD2 mutations are amplified in relapsed Pediatric ALL, where Vincristine is a mainstay of therapy, additional research must be done to investigate the ability of SETD2-knockout cells to develop resistance over time. Further studies are to be performed on multiple ALL cell lines.

Mentor: Kimryn Rathmell, MD, PhD (kimryn.rathmell@vumc.org)

ULTRASOUND FOR SPINAL ANATOMY IN INFANTS

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Background: Lumbar puncture is often performed for diagnostic purposes in infants. A safe and successful lumbar puncture demands a good understanding of anatomy. Specifically, lumbar puncture site, patient positioning, and depth of needle insertion should be all be optimized. Height and weight have been shown to influence needle insertion depth for lumbar punctures in children and adults. However, there is a knowledge gap regarding the optimal site and depth of needle insertion in infants.

Objectives:

- To determine a formula that predicts optimal needle depth insertion as measured by ultrasound for lumbar puncture in infants aged 0-6 months of age based on patient characteristics.
- To determine if there is a difference in optimal needle depth for interspaces L2/L3 to L5/S1.
- To determine if there is a difference in subarachnoid fluid volume for interspaces L2/L3 to L5/S1.

Study Design: We are recruiting a convenience sample of patients aged 0-6 months old in the MCJCHV Emergency Department. Patients are ineligible for enrollment if they have known spinal pathology, have had a prior lumbar puncture within twenty-four hours, or are deemed too ill to tolerate an ultrasound.

We collect demographic and clinical information via chart review, caregiver interview, and physical examination. Information includes age, gestational age at birth, gender, race, height, weight, chief complaint, and hydration status.

A Sonosite PX ultrasound machine with linear 12MHZ transducer is used to obtain images of a participant's spine in the left lateral decubitus position. The lumbo-sacral junction is used to confirm landmarks. Images are uploaded to Q-path for review and measurements. All information is stored in Redcap. Statistical analysis will include descriptive statistics and multivariable regression models to develop formulas that predict optimal needle depth and fluid volume. Covariates for these models will include age, gender, BMI, and hydration status.

Results: We have enrolled 42 participants of a planned cohort of at least 62 with alpha set at 0.05 to achieve 90% power to detect a correlation coefficient (r)of at least 0.4 in a linear regression model in which BMI is the independent variable and needle insertion depth is the dependent variable.

Conclusion: We hypothesize that BMI predicts optimal needle insertion depth, there will be a difference in needle depths at different spinous process interspaces, and there will be a difference in subarachnoid fluid volume at different spinous process interspaces.

Mentor: Marla Levine, MD (marla.levine@vumc.org)

INCIDENT ASTHMA IN THE ELECTRONIC HEALTH RECORD: A LANDMARK APPROACH ASSESSING OBESITY AND METABOLIC DYSREGULATION

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Objective: Obesity adversely impacts asthma prevalence, severity, morbidity, and therapeutic response. The increasing prevalence of obesity necessitates clarifying the role of obesity and metabolic dysregulation (MetD) in incident asthma.

Study Design: We performed a landmark analysis to compare time-to-asthma diagnosis after a 3-year run-in period (t0-t3) using a retrospective, longitudinal cohort of subjects from the Vanderbilt CardiOvascular and Multiple MetabOlic Disease in Obesity Resource (COMMODORE). Incident asthma was defined as two International Classification of Diseases (ICD) codes plus one asthma medication within six months. Those with a diagnosis of asthma before t3 were excluded. Components of MetD were: hypertension or diabetes diagnosis, low high-density lipoprotein, and high triglycerides. We tested the association between individual MetD components and 10-year asthma-free probability using Kaplan-Meier tests. Cox proportional hazards models were used to assess the incident asthma risk with other variables including weight.

Results: 106,365 electronic records met inclusion criteria with 1,029 (1%) cases of incident asthma (median 2,462 + 1229 days to development). Individuals with incident asthma were younger, female, more likely to develop chronic obstructive pulmonary disease (COPD), and without a history of smoking or diabetes. Patients who developed COPD during the run-in period who subsequently developed asthma demonstrated a distinct clinical phenome compared to those who did not subsequently develop asthma. Diabetes present at t0 or developed by t3 was a protective independent predictor of incident asthma (-0.65 and -0.46, respectively, $p<0.0001$). No other components of MetD were significant predictors. Weight at t3 was associated with a significant increase in the 10-year cumulative risk assuming population median age, weight, height and no MetD.

Conclusions: Weight gain, but not MetD, is a modifiable risk factor for asthma development. Understanding factors which modify asthma development offers targets for preventing asthma development.

Mentor: Katherine Cahill, MD (katherine.cahill@vumc.org)

SPECIFIC CLINICAL FEATURES MAY DIFFERENTIATE EARLY CHILDHOOD ONSET FROM LATE CHILDHOOD ONSET PEDIATRIC EOSINOPHILIC ESOPHAGITIS

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Objectives: Eosinophilic esophagitis (EoE) is a chronic, allergen-mediated clinicopathologic disease affecting all ages. While the differences between pediatric and adult onset EoE have been well documented, little is known about the differences within the pediatric onset EoE. Herein, we investigated if clinical features are distinct for early childhood onset EoE (eo-EoE; < 5 years) when compared to late childhood onset EoE (lo-EoE; 5-18 years).

Study Design: We reviewed medical records of 269 children (≤18 years) newly diagnosed with EoE at Monroe Carell Jr. Children's Hospital at Vanderbilt between May 2017 and October 2022. EoE was defined per the 2011 Consensus Guidelines. Their socio-demographic data, growth parameters, clinical presentation, allergic comorbidities, family history, esophagogastroduodenoscopy (EGD) findings rated per the endoscopic reference scoring system (EREFS), and esophageal histology (peak eosinophil count, and presence or absence of basal zone hyperplasia, eosinophilic microabscess, and lamina propria fibrosis) were extracted for analysis. The eo-EoE and lo-EoE groups were matched for gender, race, and ethnicity. Chi-squared and Fisher Exact tests were used for categorical data and paired t-tests for continuous variables.

Results: In all, 50 children were in the eo-EoE group, and 58 children were in the lo-EoE group. The mean (SD) age of the eo-EoE group was 1.86 (1.16) years and the lo-EoE group was 12.4 (3.33) years of age. Z-score for age (weight/length if age < 2 years or body mass index if age ≥ 2 years) was significantly lower for eo-EoE compared to lo-EoE [0.01 (1.48) vs. 0.80 (1.25); $P < 0.004$]. The eo-EoE group had significantly higher rates of eczema (54.0% vs. 17.2%; $P<0.001$), weight concerns (36.0% vs. 10.3%; $P = 0.002$) and feeding difficulties (30.0% vs. 0.0%; $P < 0.001$) compared to lo-EoE group. On the other hand, children in the lo-EoE group were more likely to present with abdominal pain (3.0% vs. 21.0%; $P < 0.001$) compared to children in the eo-EoE group. The total EREFS scores were lower in the eo-EoE group compared to the lo-EoE group [1.34 (0.96) vs 2.00 (1.28); $P=0.006$], and they were less likely to have edema (24.0% vs. 50.0%, $P = 0.009$). There were no differences between the groups with regards to family history of EoE or atopy and histologic findings.

Conclusions: Clinical features such as feeding difficulties, atopic co-morbidities, growth faltering, and EoE-relevant endoscopic abnormalities can distinguish children with eo-EoE from lo-EoE even after accounting for gender, race, and ethnicity. These results deepen our understanding of the pediatric EoE. Further investigation is needed to understand why the presentation of eo-EoE differs from lo-EoE and why the endoscopic findings are relatively mild in eo-EoE, despite no difference in histologic findings.

Mentor: Girish Hiremath, MD, MPH (girish.hiremath@vumc.org)

RSV INFECTION RATES AND RISK FACTORS IN A POPULATION-BASED US COHORT OF TERM HEALTHY INFANTS

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Objective: Respiratory syncytial virus (RSV) is a leading cause of respiratory morbidity in infants worldwide. Most prior research has focused on severe RSV illness, and few studies have conducted population-based surveillance to determine rates of RSV infection and risk factors for infection in the general pediatric population.

Study Design: In a population-based birth cohort of term healthy infants (INSPIRE), RSV infection was determined during the first year of life by 1) active and passive biweekly surveillance using RSV RT-PCR to identify RSV during each infant's first RSV season, and 2) serum RSV antibody testing at 1 year of age. Rates of infection, upper and lower respiratory tract infection (URI and LRTI), and hospitalization were calculated during infancy. The adjusted association and relative contribution of risk factors for RSV infection in the first year of life was estimated using multivariable logistic regression analyses. The relative contribution of the regression variables was estimated by computing the proportion towards explaining the likelihood of the outcome (RSV detected vs not detected).

Results: Among 1680 infants in whom RSV infection status was ascertained, 897 (53%) had RSV detections in the first year of life and 783 (47%) did not. 36% of detections were among symptomatic infants, and 64% were detected by serology alone. Among symptomatic RSV infections, 83% were URI and 16% were LRTI. Among those infected, 32% sought healthcare. There were 30 hospitalizations due to RSV, which accounted for 3.3% of those infected or 1.8% of the total birth cohort. Risk factors with highest relative contribution for first year RSV detection, in order, were infant birth month, daycare attendance, presence of siblings, and neighborhood percent below poverty. Study year, infant sex, secondhand smoking exposure, and maternal asthma were not significantly associated with risk of infant RSV detections. Ever breast feeding trended toward protecting from infection but was not statistically significant.

Conclusion: RSV infects more than half of infants in the first year of life. The rates of symptomatic disease, LRTI, and healthcare utilization demonstrate the considerable burden of respiratory morbidity. Additionally, the risk factors we identified may provide opportunities for infection prevention. As new vaccines and extended half-life monoclonal antibodies may soon be available for severe illness prevention, these data provide important US estimates of the burden of RSV disease and risk factors for infection in healthy term infants.

Mentor: Tina V. Hartert, MD, MPH (tina.hartert@vumc.org)

THE UTILITY OF NASAL NITRIC OXIDE IN THE DIAGNOSTIC EVALUATION OF PRIMARY CILIARY DYSKINESIA

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Objective: Diagnosing primary ciliary dyskinesia (PCD) involves recognition of the unique clinical phenotype combined with genetic evaluation, ciliary biopsy, and nasal nitric oxide (nNO) testing. In this study, we evaluate the hypothesis that nNO testing has improved our ability to diagnose PCD.

Study Design: Since nNO testing was established in 2017, 131 patients were referred to the PCD Center at MCJCHV for evaluation. Clinical and diagnostic data were collected from the medical record. Per PCD Foundation standards, a nNO value of ≤ 77 nl/min is suggestive of PCD, but diagnosis must be confirmed by genetic testing or ciliary biopsy.

Results: nNO testing was completed in 121 of 131 (92%) PCD consultations and was the only PCD test performed in 67 (51%) patients. The 10 (8%) participants who didn't complete nNO were under age 5 or already had a confirmed PCD diagnosis on genetic testing. When nNO was completed, it was performed once in 95 (78%) participants and ≥2 times in 26 (21%) participants.

nNO Once with Value <77 nL/min:

10 (10%) of the 95 patients who completed nNO once had a value ≤77 nL/min. 5 (50%) were diagnosed with PCD by genetic testing, 2 (20%) were lost to follow up and 3 (30%) are under age 5 and completing ongoing evaluation.

nNo Once with Value >77 nL/min:

85 (90%) of the 95 patients who completed nNO once had a value >77 nL/min. The median result was 262.8 nL/min. 32 (38%) patients had additional PCD diagnostic testing. 2 (2%) patients were diagnosed with PCD by genetic testing. 11 (13%) patients are completing ongoing evaluation. 72 (85%) patients were given a negative PCD diagnosis and 67 (93%) of these patients were given an alternative diagnosis.

nNO >2 Times:

26 patients completed nNO ≥2 times. 2 (8%) patients were ultimately diagnosed with PCD based on genetic testing. 14 (54%) patients had nNO values that remained low without confirmatory PCD testing. 6 (23%) patients had nNO values that normalized (increased over time) and were given a negative PCD diagnosis. 4 (15%) additional patients had nNO values that remained consistently elevated and were given a negative PCD diagnosis.

Genetic testing was sent in 49 (37%) consultations overall. The genetic testing positivity rate for PCD was 12% when performed without nNO or prior to nNO testing and was 31% when performed after nNO testing.

Conclusions:

While nNO testing is not intended to be a stand-alone test, our diagnostic trends show that nNO has great utility at an accredited PCD center. Initially high nNO values prevent additional costly diagnostic testing and facilitates expedited diagnosis of alternative sinopulmonary conditions. Repeated low nNO values without positive confirmatory testing suggests probable PCD diagnosis and results in the initiation of PCD-targeted therapies. The genetic testing positivity rate for PCD is higher when nNO testing is performed first.

Mentor: Michael O'Connor, MD (michael.g.oconnor@vumc.org)

PREVALENCE OF NASOPHARYNGEAL CARRIAGE OF MACROLIDE RESISTANCE-ASSOCIATED *ERM* GENE AMONG HEALTHY CHILDREN AND ADULTS IN A PERI-URBAN COMMUNITY IN PERU

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Objective: Erythromycin ribosome methylase (*erm)* genes, which confer macrolide resistance, are commonly detected in healthcare settings. Yet, their prevalence among healthy individuals in the community is unknown. Here we provide an initial assessment of *erm* carriage in healthy children and adults.

Study Design: Nasopharyngeal swabs were systematically obtained at enrollment and weekly thereafter from children and adults enrolled in a household-based prospective cohort study in Lima, Peru. Samples were sequenced using the Illumina Respiratory Pathogen/ID AMR Panel to detect common respiratory bacteria and antimicrobial resistance genes. We defined 'any *erm* gene' (*erm*) as the detection of at least one of the specific *erm* gene classes. We compared the prevalence of *erm* colonization at enrollment among age groups (ages 0-4, 5-17, 18-44, and >45 years) using the Fisher's exact test.

Results: 63 individuals were included in this analysis; 68% were female and median age was 14 years (IQR 4.8, 37.0). An *erm* gene was detected in 32 (50.8%) of individuals, most commonly *ermC* (40%) and *ermB* (25%). The prevalence of *erm* gene detection was similar among age groups: [0-4 years (10/18, 55.6%), 5-17 years (10/17, 58.8%), 18-44 years (9/19, 47.4%) and >45 years (3/9, 33.3%) (p=0.625)].

Conclusions: These preliminary results indicate that *erm* genes were commonly detected in healthy community-dwelling children and young adults in Lima, Peru. Future analysis will assess changes in *erm* carriage over time, transmission among household members, and its clinical relevance.

Mentors: Leigh Howard, MD, MPH (leigh.howard@vumc.org), Carlos G. Grijalva, MD, MPH (carlos.grijalva@vumc.org)

THE EFFECT OF AUTOMATED INSULIN DELIVERY SYSTEMS ON BULLYING IN PEDIATRIC PATIENTS WITH TYPE 1 DIABETES

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Objective: Pediatric patients with chronic diseases experience high rates of bullying, and youth with type 1 diabetes (T1D) may be at even higher risk than those with other chronic health conditions. Because diabetes management requires visible self-care tasks, including frequent blood glucose monitoring, carbohydrate counting with meals, and multiple daily subcutaneous insulin injections (MDI), children with diabetes may be identified as "different" and therefore a possible target for bullying. While previous studies identified associations in youth with T1D between bullying, poorer diabetes management, and suboptimal glycemic control, treatment modalities have never been evaluated as a risk factor. Diabetes technology is rapidly evolving, and new devices have the potential to improve glycemic control and decrease the burden of management. While wearable diabetes devices reduce the need for some of the more visible tasks of self-management (e.g., finger sticks, injections), they may still draw attention to the child's health condition with alarms and devices worn on the body. We propose to evaluate perceived bullying, psychosocial outcomes (i.e., diabetes distress, depressive symptoms, quality of life), and glycemic control in adolescents with T1D related to the use of automated insulin delivery (AID) systems.

Study Design: For the proposed study, 60 dyads (a patient and his/her parent) will be enrolled. Eligibility criteria include: 1) patient age between 10–14 years old; 2) patient diagnosed with type 1 diabetes for at least 1 year; 3) planning to start an AID system; 4) both the patient and their parent must identify English as their primary language, with the ability to read and write. Dyads will be recruited from the Vanderbilt Eskind Diabetes Clinic when they present for a previously scheduled appointment to transition from multiple daily injection (MDI) therapy to an AID system. The patient and parent will complete surveys evaluating perceived of bullying, bullying related to diabetes-management tasks, diabetes distress, quality of life, depressive symptoms, diabetes management, and general demographic information. These surveys will be completed at the time of recruitment and repeated 6 months after initiating an AID system to compare pre- and post-data. Additionally, glycemic control and automation utilization will be assessed.

Data analyses will be done using paired t-tests with data before and after initiation of the AID system. We will calculate effect sizes by comparing the mean differences over time on our secondary outcomes: diabetes distress, depressive symptoms, quality of life, and glycemic control. We will also examine the bivariate correlations between bullying and glycemic outcomes, as well as adjusting for cofounders.

Preliminary Results: At this time, six parent/adolescent dyads have been recruited with a mean age of 12.8 years and mean hemoglobin A1c of 9.9% prior to the initiation of an AID. This cohort is 83% male, 50% Black/African American, and 100% of the students are enrolled in public school.

Conclusions: The ongoing study will assess the effects of automated insulin delivery systems on bullying, psychosocial outcomes, and glycemic control in adolescents with T1D and their parent.

Mentors: Sarah Jaser, PhD (sarah.jaser@vumc.org), Jill Simmons, MD (jill.h.simmons@vumc.org)

NON-INVASIVE DETECTION OF GASTRIC SLOW WAVES USING HIGH RESOLUTION ELECTROGASTROGRAM IN CRITICALLY ILL CHILDREN

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Objective: Enteral nutrition (EN) is a crucial priority in pediatric critical care, associated with lower 90-day mortality, shorter length of stay, and less organ dysfunction.[1,2,3] Feeding intolerance, defined as inadequate enteral intake with gastrointestinal (GI) symptoms, has a multifactorial pathophysiological basis and is a barrier to EN.[4,5] Gastric motility is mediated by slow-wave (3 cycles per minute) electrical activity produced by the interstitial cells of Cajal. Diseases affecting the GI system can alter normal slow-wave activity and lead to dysmotility.[6] To date, no clinically validated tool exists to quantify gastric motility, and there exists a critical knowledge gap regarding how to optimally advance EN in critically ill children. High resolution electrogastrography (HR-EGG) uses a non-invasive multi-electrode array to analyze spatiotemporal slow-wave characteristics.[7] We seek to characterize gastric signaling in critically ill patients and assess its association with feeding intolerance.

Study Design: We will identify patients ages 7-18 admitted to the Pediatric Intensive Care Unit (PICU) with acute respiratory failure who are expected to receive continuous EN with standard calorie formula. With caregiver consent, a 25-electrode array will be applied to the abdomen and connected to an amplifier to obtain HR-EGG recordings. HR-EGG recordings will be obtained for 30 minutes prior to initiation of EN, at 0-25% goal EN intake, and at 25-50% goal EN intake. Patients will be assessed for GI symptoms with a Feeding Intolerance Score (FIS, table below).[5] We will compare pre-prandial and post-prandial dominant frequency, percent power distribution and gastric slow wave propagation patterns using HR-EGG.

Points	0	1	2	5
Abdominal Distention/Pain	None	Mild distention	Moderate distention or transient abdominal pain	Severe distention or persistent abdominal pain
Nausea/Vomiting	None	Nausea only	Nausea and vomiting	Vomiting requiring gastric decompression
Diarrhea	None	Loose stools ≥ 3 times/day with volume 250-500ml	Loose stools ≥ 3 times/day with volume 500-1500ml	Loose stools ≥ 3 times/day with volume >1500ml

Total Score = Abdominal distention/Pain + Nausea/Vomiting + Diarrhea

Results: In healthy adolescent subjects (n = 10, age 11-17), we identified normal gastric slow wave activity with a frequency of 2.6 ± 0.4 cycles per minute (cpm) preprandial and 2.8 ± 0.3 cpm postprandial. Dominant normal anterograde propagation patterns (slow wave activity moves from subject's left to right) was also observed in both pre/post-prandial recordings. Mean EGG propagation speed did not change from preprandial to postprandial (12.9 ± 3.4 mm/s and 12.5 ± 3.1 mm/s; $p = 0.80$) in healthy subjects.

Conclusion: In future studies (IRB pending), we hypothesize that critically ill patients have abnormal gastric slow wave activity [tachygastria (4-9 cpm) or bradygastria (<2.5 cpm)] compared to healthy controls. We will investigate if introducing enteral feeds alters gastric slow wave activity. We hypothesize that there will be an association between abnormal HR-EGG signals and presence of gastrointestinal symptoms as measured by increased FIS as a marker of feeding intolerance.

Mentor: Michael Wolf (michael.wolf@vumc.org)

ERYTHROPOIETIN USE IN PEDIATRIC VENTRICULAR ASSIST DEVICE PATIENTS

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Objective: Anemia has been found to be common in pediatric ventricular assist device (VAD) patients. There is thought that avoidance of transfusions in patients awaiting heart transplant may minimize the risk of allosensitization. Erythropoietin can be used to stimulate red blood cell production and has been utilized to reduce the number of blood transfusions in children following placement of a VAD. One study in the adult population showed erythropoietin use after left ventricular assist device implantation is associated with significantly higher rates of suspected pump thrombosis. Pump thrombosis can lead to pump failure and hemodynamic collapse. This has led to some hesitation to utilize this therapy in pediatric patients. No studies have evaluated the use of erythropoietin in pediatric patients receiving VAD support. In this study, we aim to assess erythropoietin use, including frequency and timing, in all pediatric patients admitted to a Pediatric Health Information System (PHIS) center from 2010 - 2020 who undergo placement of a VAD. We will also assess differences in the need for blood transfusions post-VAD, the incidence of stroke and the need for re-operation due to device complications.

Methods: Using the Pediatric Health Information System (PHIS) center, we will identify patients that underwent VAD placement from 2010-2020. Variation in the use of erythropoietin will be described across all sites. A propensity score matched analysis will be performed based on the probability of receiving erythropoietin. Cohorts will be compared to assess differences in the need for blood transfusions post-VAD and the need for reoperation due to device complications.

Results: 1260 patients underwent VAD placement. 336 patients received erythropoietin post-VAD placement. Further results pending additional statistical analysis.

Conclusion: Conclusion pending statistical analysis. We hypothesize that there is no increased risk of reoperation for device complications or stroke in patients who received erythropoietin post-VAD placement compared to those who did not.

Mentor: Justin Godown, MD (justin.godown@vumc.org)

MITRAL VALVE HYPOPLASIA AND STRUCTURAL ABNORMALITIES ARE ASSOCIATED WITH UNIVENTRICULAR PALLIATION IN THE FETUS WITH POSTNATAL COARCTATION OF THE AORTA

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Introduction: Reliably predicting which fetuses with borderline left heart structures and coarctation of the aorta (COA) can undergo postnatal biventricular repair (BVR) versus univentricular palliation (UVP) remains challenging for fetal cardiologists. Fetal echocardiographic measurements that predict surgical outcomes are not well defined, particularly in relation to the mitral valve. The purpose of this study was to determine whether mitral valve hypoplasia or structural abnormalities, which can be difficult to diagnose prenatally, influence surgical outcomes for fetuses with postnatally confirmed COA.

Methods: Neonates with a fetal echocardiogram and a postnatal diagnosis of COA at a single institution between 2010 and 2020 were retrospectively reviewed. Neonates with complex congenital heart disease, including certain diagnosis of hypoplastic left heart syndrome, were excluded from the study. Maternal and pregnancy history, fetal and neonatal echocardiograms, and postnatal surgical outcomes were reviewed. Data were compared between two outcomes groups, BVR or UVP, to determine differences in fetal echocardiograms.

Results: Sixty-seven neonates with COA were eligible for inclusion (52% male, gestational age at birth 37.9 ± 1.9 weeks). COA was suspected by fetal echocardiogram in 60 of these neonates (90%). UVP was performed in three (4%) of the patients. Postnatal UVP was associated with an initial fetal mitral valve z-score of -4.40 (-4.44, -3.85) vs -2.10 (-2.65, -1.40), $p = 0.007$, and left to right flow across the foramen ovale (100% vs 6%), $p = 0.001$, (gestational age at first fetal echo 29.9 ± 4.6 weeks). Postnatal mitral valve hypoplasia or structural abnormalities were also associated with UVP (100% vs 23%), $p = 0.017$.

Conclusion: UVP for newborns with COA are associated with lower fetal mitral valve z-scores and fetal left to right flow across the foramen ovale. These findings may help guide prenatal counseling about the postnatal surgical course for fetuses with borderline left heart structures and COA.

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QUALITY IMPROVEMENT TO IDENTIFY AND ADDRESS FOOD INSECURITY DURING INPATIENT ADMISSIONS

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Objective: Childhood Food Insecurity (FI) is associated with worse physical, mental, and developmental health outcomes. Connection to food resources has been shown to improve family food security as well as children's health outcomes. Hospitalized children represent a vulnerable population, with higher FI rates and inconsistent primary care, that is important to target in efforts to identify and address FI. We aimed to improve FI screening for eligible English-, Spanish-, and Arabic-speaking families from 0% to 60% and provide location-based food resource information to >80% of families with a positive FI screen.

Study Design: In February 2021 our multidisciplinary team began testing routine FI screening, which was not previously done, among a subset of PHM patients on one unit. After numerous PDSA cycles (Figure 1), we expanded screening to patients on all services on the unit in January 2023. Our process measure was the overall percentage of eligible families screened for FI. To monitor for inequity in the screening process we also followed the percentage of eligible families screened by language. Our primary measure was the percentage of families with FI who received food resource information. To monitor for a substantial increase in social work consults due to the desired consult for high-risk screens the balancing measure was the percentage of screened patients with a social work consult. Statistical process control charts were used to analyze the impact of our interventions.

Results: The percentage of eligible families screened for FI increased from zero to a current mean of 31.65% in association with this initiative, with special cause variation noted by two centerline shifts and three most recent data points above the upper control limit (Figure 1). There was no statistical difference in screening rate by language. 13.4% of families screened positive for FI. Provision of resources increased from 56% to 100% with special cause variation associated with automated EHR resource provision for positive screens. There was no significant impact on volume of social work consults among screened patients.

Conclusion: Small tests of change, starting with a single nursing role on a single unit, were used to establish a process for routine FI screening without significantly increasing social work consults. Automation of the resource provision process based on patient answers increased provision of appropriate food resource information. Work is ongoing to spread screening more broadly across the hospital and equitably increase the percentage of families screened.

INFANT SAFE SLEEP SURVEY: ASSESSING PARENTAL KNOWLEDGE AND PRACTICE

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Objectives: Sudden Unexpected Infant Death (SUID) remains a leading cause of mortality, with about 3,400 sudden unexplained infant deaths per year in the United States. To our knowledge, no study has been conducted in a pediatric emergency department to evaluate parents' knowledge and practices regarding safe sleep. Nor has one assessed both parents' knowledge and practice of all American Academy of Pediatrics (AAP) A-level recommendations related to placing an infant to sleep.

Methods: Infants less than 12 months of age will be identified by key personnel of the research team in the pediatric emergency department. Surveys will be orally administered to parents of those patients in their self-identified preferred language of English or Spanish. Participants will be surveyed regarding safe sleep knowledge pertaining to sleep position, sleeping surfaces, surface sharing, objects in bed, cardiopulmonary monitors, and pacifier use at bedtime. They will then be asked about their sleep practices regarding infant sleep position, sleeping surfaces, surface sharing, objects in bed, cardiopulmonary monitor use, and pacifier use at bedtime. Finally, participants will identify sources from which they have learned about safe sleep, including various medical providers, online resources, print resources, family, and friends.

Results: Data is currently being collected, with 100 surveys completed at time of submission. The accrual goal for this study is 200 participants. Responses to knowledge questions about safe sleep will be dichotomized into "correct" and "incorrect" responses based on the 2022 AAP recommendations on safe sleep. Statistical methods used in analysis will include chi square tests and odds ratios.

Conclusions: Analysis of data is pending completion of data collection and statistical analysis. This study may identify needed areas of education, gaps between knowledge and practice, and where parents are obtaining information about safe sleep. Investigators hypothesize that there are disparities in both safe sleep knowledge and practices by race-ethnicity, parental age, number of children, and level of education.

Mentor: Donald Arnold, MD, MPH (don.arnold@vumc.org)

INVOLVEMENT OF PART C EARLY INTERVENTION PROVIDERS IN TELE-ASSESSMENTS FOR AUTISM: IMPACT ON CAREGIVER SATISFACTION

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Objective: Telemedicine offers a convenient and accurate way of diagnosing autism spectrum disorder (ASD) in toddlers. While caregiver acceptability of tele-assessments for ASD has been demonstrated in past work, specific factors contributing to caregiver satisfaction needs to be investigated further. Our institution has partnered with the state Part C early intervention system (the Tennessee Early Intervention System; TEIS) to provide ASD tele-assessments to toddlers. As a part of this model, a child's TEIS early intervention (EI) provider is often included in the diagnostic evaluation. We sought to examine caregivers' perspectives of this model of ASD evaluation and to determine whether the presence of an EI provider led to higher caregiver satisfaction.

Study Design: Participants included 291 children under age 3 who received telemedicine ASD evaluations from December 2021 through October 2022 using the TELE-ASD-PEDS (TAP) following referral by TEIS. EI providers were encouraged to join their clients' appointments virtually or in-person and participated in various capacities (e.g., preparing for and assisting in administration of the TAP, providing information about autism and next steps). Afterwards, families received surveys inquiring about their experience with various aspects of the appointment.

Results: Of the 291 children who completed tele-assessments, 102 caregivers filled out post-evaluation surveys. 76 of these 102 caregivers had an EI provider in attendance for their child's appointment. Survey responses were scored along a Likert-type scale (ranging from 5 = Strongly agree to 1 = Strongly disagree). Mean scores were calculated for questions designed to capture satisfaction. Broadly, caregiver ratings were very positive. Between-group comparison using Mann-Whitney U tests yielded no significant differences (p values > 0.05) in mean caregiver ratings as a function of the presence or absence of an EI provider. However, the majority of caregivers who had an EI provider present indicated that they agreed or strongly agreed that it was important that the provider was able to participate (93%), that the assessment was better because the provider was able to participate (82%), and that they felt more comfortable because the provider was present (82%).

Conclusions: Caregivers gave positive feedback about this model of delivering ASD assessments. Though caregiver satisfaction with tele-assessments did not significantly differ based on participation of an EI provider, families whose providers were included identified that they were an important part of their child's remote ASD evaluation.

Mentor: Laura Corona, PhD (laura.l.corona@vumc.org)

ASSOCIATION OF ECHOCARDIOGRAPHIC INDICES WITH MYOCARDITIS AND PRESENCE OF MYOCARDIAL DELAYED ENHANCEMENT BY CARDIAC MAGNETIC RESONANCE IMAGING IN MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN

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Objective: Myocarditis and myocardial delayed enhancement (MDE) are common cardiac magnetic resonance (CMR) findings in multisystem inflammatory syndrome in children (MIS-C). We hypothesized that laboratory markers and echocardiographic indices in the acute presentation would associate with the presence of myocarditis and MDE by CMR.

Study Design: We performed a retrospective study of all patients admitted to our institution with MIS-C who underwent follow-up CMR, which became part of our institution's MIS-C protocol early in the pandemic. Clinical characteristics and laboratory values were collected via chart review. Inpatient echocardiogram with lowest left ventricular ejection fraction (LVEF) was analyzed for area/length LVEF, shortening fraction (SF), and global longitudinal and circumferential strain (GLS, GCS). CMR reports were reviewed for right and left ventricular volumes and ejection fraction as well as for presence of myocarditis (as defined by modified Lake Louise Criteria) and MDE. Association of inpatient laboratory markers and echocardiographic indices with presence of myocarditis and MDE was assessed with logistic regression.

Results: Fifty-four patients with median age 9.6 years (IQR 7.2-14.5) were included; 31 required admission to the intensive care unit. Summary of inpatient laboratory values and echocardiographic indices are presented in Table 1. Myocarditis was present in 24 (44%) patients, and MDE was present in 30 (56%) patients (Table 1). There was no association between echocardiographic LVEF, SF, GLS, or GCS and presence of myocarditis or MDE by CMR (Table 2). Admission erythrocyte sedimentation rate (ESR) associated with presence of MDE and maximum brain natriuretic peptide (BNP) associated with presence of myocarditis and trended toward association with MDE (Table 2).

Conclusions: Echocardiographic indices in the acute presentation do not associate with presence of myocarditis or MDE by CMR in MIS-C patients; serum ESR and BNP may be predictive of abnormal CMR findings.

Mentor: Joshua Chew, MD (joshua.d.chew@vumc.org)

ANTIBIOTICS AT DISCHARGE: HOW OFTEN DO WE GET IT RIGHT?

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Background: An estimated 1 in 8 patients discharged from the hospital are prescribed at least one antibiotic;[1,2] between 25-70% of those antibiotic prescriptions are incorrect in some way.[1,3,4] Our quality improvement project characterizes the type and frequency of errors in antibiotics prescribed upon discharge from Monroe Carell Jr Children's Hospital at Vanderbilt.

Study Design: Retrospective review of antibiotic prescriptions written at discharge for patients hospitalized at a pediatric tertiary care center, May 19 to September 19, 2022. All enteral antibiotics prescribed to patients discharged from the pediatric emergency department (ED) or inpatient units were evaluated by provider-selected indication specified on the antibiotic order. Prescriptions were evaluated for appropriateness using national and local clinical practice guidelines to define correct antibiotic selection, dose, frequency, and duration.

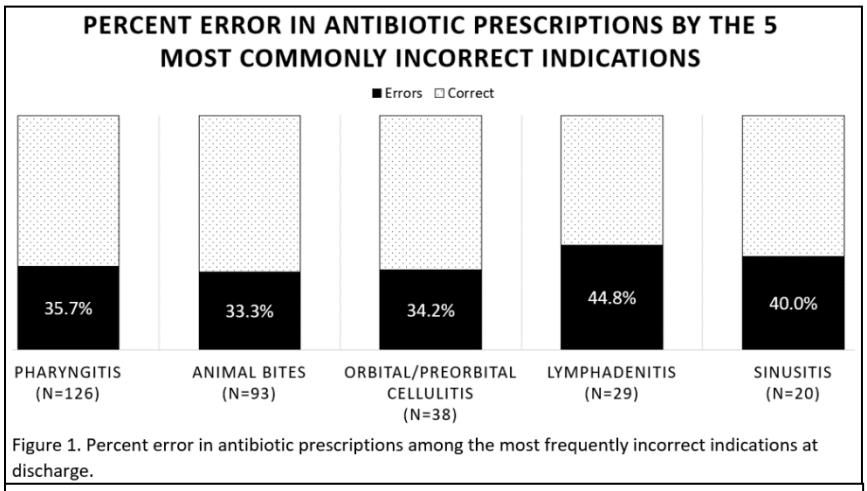

Figure 1. Percent error in antibiotic prescriptions among the most frequently incorrect indications at discharge.

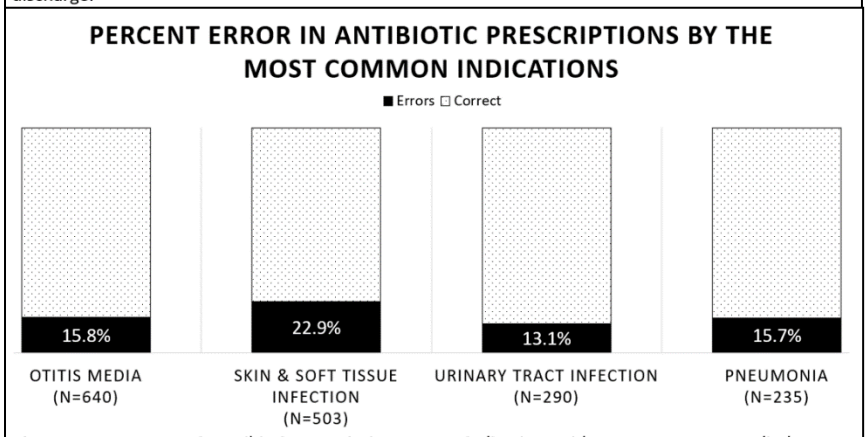

Figure 2. Percent error in antibiotic prescriptions among indications with >200 encounters at discharge.

Results: Among 3059 antibiotic prescriptions evaluated, 701 (22.9%) contained at least one error. Inappropriate dosing (329/3059; 11%) was the most common error. Comparing all indications, lymphadenitis had the highest percentage of errors (13/29; 44.8%) (Figure 1), but among indications with >200 encounters, antibiotic prescriptions for skin and soft tissue infections had the most errors (115/503; 22.9%) (Figure 2). By provider type, prescriptions written by surgeons had more errors those written by non-surgeons (184/622 [30.0%] vs. 511/2406 [21.2%]).

Conclusions: Errors were noted in nearly one quarter of antibiotics prescribed for patients being discharged from the pediatric ED or inpatient units. These findings can inform design of interventions to decrease discharge prescription error rate, such as bolstering provider education and incorporating clinical decision support within the electronic medical record.

Mentors: Sophie E. Katz, MD (sophie.e.katz@vumc.org) and Ritu Banerjee, MD, PhD (ritu.banerjee@vumc.org)

FAMILY INCOME, ANXIETY, AND QUALITY OF LIFE IN PEDIATRIC PATIENTS WITH ADVANCED CANCER

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Background: Pediatric patients with advanced cancer and their caregivers have an increased burden of stress and anxiety. Financial hardship adds to this burden and can lead to diminished quality of life and poorer outcomes. While increased parental anxiety in relation to familial financial difficulty has been described, fewer studies have focused on associations of family income with anxiety and with quality of life in pediatric patients with advanced cancer.

Objective: To evaluate the association of family income with anxiety and quality of life in pediatric patients with advanced cancer and their caregivers.

Study Design: This study is a secondary analysis of data from a randomized controlled trial that evaluated the effect of animal-assisted interactions on anxiety and quality of life in patients with advanced (relapsed or refractory) pediatric cancers and their caregivers. Twenty-nine children and their caregivers were included in analysis. Family income was determined from parent-reported demographics forms completed at study enrollment. Patient and caregiver baseline STAI Trait (STAI-T) and State (STAI-S) sub-scores as well as PedsQL scores were also obtained for analysis.

Results: Of 29 families included in this analysis, child participants were 3-17 years old, with a mean age of 9.0 years (SD 3.9). There were slightly more male children (51.7%) than female children (48.3%). Among child participants, 15 patients (51.7%) were diagnosed with a solid tumor, 8 patients (27.6%) had a hematologic malignancy, and 6 patients (20.7%) had a CNS tumor. Family income was reported in ranges, with most families reporting an annual income of greater than 25,000 dollars (75.9%). The remaining 24.1% of families reported annual income of less than 25,000 dollars, which is below the 2022 federal poverty level (FPL) for a family of four (26,500 dollars). Associations of income with anxiety, and quality of life for both child and adult participants will be presented.

Conclusions: Among families included in this secondary analysis, nearly 1 in 4 reported annual income of less than 25,000 dollars, indicative of substantial financial hardship. Determining the impact financial status has on pediatric patients with advanced cancer will allow us to better address who may benefit from additional supportive care and resources.

Mentor: Mary Jo Gilmer, PhD, MBA, FAAN (maryjo.gilmer@vanderbilt.edu)

UTILIZATION OF POINT-OF-CARE ULTRASOUND FOR CONFIRMATION OF GASTRIC AND POST-PYLORIC ENTERAL FEEDING TUBE PLACEMENT IN A PEDIATRIC INTENSIVE CARE UNIT: A RESEARCH PROPOSAL

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Objective: Enteral feeding is associated with lower mortality in critically ill patients. Critically ill patients, however, often cannot be fed orally due to their illness. Enteral feeding tubes allow medical teams to provide nutrition and medications to these patients. The study aims are to assess the accuracy, feasibility, and safety of Point-of-care ultrasound (POCUS) as an alternative imaging modality for the confirmation of placement of gastric and post-pyloric enteral feeding tubes in patients admitted to the pediatric intensive care unit (PICU). Results will be compared to abdominal radiographs, the current standard of care.

Study Design: We plan to conduct a prospective descriptive study performed at a tertiary care children's hospital. Patients less than 18 years of age admitted to the PICU at Monroe Carell Jr. Children's Hospital at Vanderbilt who require placement of an enteral feeding tube to be placed will be eligible for enrolment. Patients will be recruited during the hours 0800-1700 Monday through Friday while the study physician is present. Bedside ultrasound examination of the epigastric region will be performed to examine the stomach and the pyloric/post-pyloric region. Ultrasound of the neck will be performed on patients when the enteral feeding tube cannot be visualized in the abdominal examination. The study physician will determine the location of the enteral feeding tube based on the POCUS exam. The time spent performing these examinations will be recorded. Images and videos of these areas will also be taken and will later be independently interpreted by an expert Pediatric radiologist. The study physician's interpretation of the POCUS examination will be compared with the pediatric radiologist's interpretation of the POCUS images obtained and with the official interpretation of the abdominal radiograph. The primary outcome will be the sensitivity and specificity of POCUS for the confirmation of placement and location of enteral feeding tubes when compared to abdominal radiographs.

Results: This study proposal is awaiting approval by the institutional review board at the Vanderbilt University Medical Center. All data collection will begin once approved. The sensitivity and specificity of POCUS for determining enteral tube location will be ascertained. Additionally, the sensitivity and specificity will be computed in subgroups for intended gastric enteral feeding tubes and intended post-pyloric feeding tubes, respectively. Additional outcome measures will include the average duration of the POCUS exam to demonstrate the feasibility of POCUS as an alternate imaging modality for this indication.

Conclusion: This study seeks to contribute to the growing body of evidence supporting utility of POCUS to confirm the placement of enteral feeding tubes in pediatric patients and demonstrate the feasibility of implementing this technique at our institution. Our findings may lead to larger multi-center studies to assess whether POCUS is an objectively accurate, safe, and feasible imaging modality for confirming the placement and location of enteral feeding tubes in patients admitted to the PICU. This could help lead to a reduction in the number of radiographs and ionizing radiation to which these vulnerable patients are exposed during their PICU course.

Mentor: Michael S. Wolf, MD (michael.wolf@vumc.org)

GUT MICROBIOME DIFFERENCES IN PREMATURE INFANTS FED RETORT VERSUS HOLDER PASTEURIZED DONOR BREAST MILK

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[2]Monroe Carell Jr. Children's Hospital at Vanderbilt

Introduction: The use of donor breast milk for preterm infants when mother's own milk is insufficient or not available is widely implemented across Neonatal Intensive Care Units (NICUs). There are three main methods of pasteurization used by commercial milk banks to pasteurize donor breast milk: Holder, Retort and Vat. While there have been a few published studies in the last 5 years comparing the nutritional profile of such pasteurized donor breastmilk versus mother's own milk, there is lack of research looking at the differences in pasteurization and impact on the gut microbiome of these infants.

Objective: To compare the gut microbiota of infants admitted to the Vanderbilt NICU who received Holder pasteurized donor breast milk to those who were fed donor breast milk that underwent Retort pasteurization. Secondary outcomes of interest include incidence of Necrotizing Enterocolitis (NEC), Intraventricular Hemorrhage (IVH), death, Bronchopulmonary Dysplasia (BPD), malnutrition and length of hospital stay in each cohort.

Study Design: This is a retrospective/prospective study of stool samples collected weekly from infants born at less than 34 weeks gestation and/or less than 1,500 g. Samples were collected from July 2021 to December 2022. Infants will be chosen for analysis if on exclusive DBM diet. Following DNA extraction, metagenomics and metatranscriptomics will be used for microbiome composition analysis and alpha diversity.

Results: Preliminary analysis comparing four Holder pasteurized DBM and five Retort pasteurized DBM samples showed that the microbiome abundance is starkly different between them. A total of 120 samples (60 from each group) will be sequenced pending institutional grant approval.

Conclusions: Given the small sample size of each group (2 in Holder period and 4 in Retort period), a larger sample size is needed to interpret the results. The antibiotic exposure in both groups was also different, with a higher exposure to broad spectrum antibiotics in these infants fed Holder DBM.

Mentor: Hendrik Weitkamp, MD (hendrik.weitkamp@vumc.org)

MAPPING ALLERGY AND IMMUNOLOGY UNDERGRADUATE MEDICAL EDUCATION: USING A DIGITAL CURRICULUM MAP AS A TARGETED NEEDS ASSESSMENT

Jessica Plager, MD

Objective: Approximately 10% of patients report a history of reacting to penicillin, however when evaluated for a penicillin allergy, over 90% or more of these individuals tolerate penicillin. This penicillin mislabel is not benign and is associated with numerous negative individual and public health consequences. In order to combat this threat, we must improve drug allergy undergraduate medical education, specifically in regard to penicillin allergy. Applying Kern's 6-step model for Curriculum Development, we utilized the digital curriculum map to perform a targeted needs assessment of drug allergy education at Vanderbilt School of Medicine (VSM)

Study Design: In collaboration with the Vanderbilt Educational Design and Informatics team, we searched VSM's Ilios© digital curriculum map (available from 2017 onwards) with the MeSH terms "Drug related side effects and adverse reactions" and "Drug hypersensitivity."

Results: Utilizing PRISMA analysis, we identified 92 total records. After screening, a total of 10 records were selected for review. While 3 sessions in total discussed drug hypersensitivity, it was not the primary focus of any session; 1 session covered cross-reactivity among local anesthetics, 1 session reviewed the Gell-Coombs classification of hypersensitivity reactions, and 1 session provided examples of immunologically-mediated adverse drug reactions.

Conclusions: Even though nearly all physicians will take a drug allergy history, and despite the prevalence of penicillin allergy affecting 10% of the U.S. population, our targeted needs assessment identified major gaps in drug allergy education at the UME level.

Mentor: William B. Cutrer, MD Med (bill.cutrer@vumc.org)

USING A QR CODE TO CONNECT FAMILIES TO FOOD RESOURCES – A NOVEL TOOL FOR ADDRESSING FOOD INSECURITY IN THE PEDIATRIC EMERGENCY DEPARTMENT

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Objective: During the Covid-19 pandemic, food insecurity (FI) tripled in households with children. FI has been linked to poor health outcomes such as obesity, asthma, and depression, and increased rates of pediatric emergency department (PED) use. While connection to food resources can improve health outcomes, answering FI screening questions may invoke stigma among families who prefer anonymity. Additionally, the implementation of routine FI screening in the PED is challenging due to time constraints. Yet, the frequency that families will utilize anonymous, universal resources is unknown. The aim of this study was to pilot and assess the use of universal resource provision in the PED through a poster with an anonymous and independently accessed Quick Response (QR) code.

Study Design: Using https://www.qr-code-generator.com, a QR code was created to allow any user with a smartphone camera to access the website: ineedfoodnow.org. Created and trademarked by affiliates of Vanderbilt University, the website contains downloadable food resource packets in multiple languages, healthy food tips and videos, and additional website links to Aunt Bertha, Supplemental Nutritional Assistance Program (SNAP), and Women, Infants, and Children (WIC). The QR code was placed on food resource posters with information in English, Spanish, and Arabic. On December 28, 2021, fifty posters were displayed in triage, patient rooms, and shared bathrooms throughout the PED, which has an annual volume of approximately 50,000 visits. From January 1, 2022, to December 14, 2022, the number of unique scans per day and time of unique scans were tracked. Daily PED volumes were also recorded. We used descriptive statistics to characterize included variables.

Results: During the data collection period, there were 447 unique scans, with 0.84 scans per 100 patient encounters. The median number of scans per day was 1.0 (range 0-7 scans). Most scans occurred during midday (1601-2200, n=142) and evening (2201-0400, n=168).

Conclusions: This pilot demonstrates that the novel approach of universal resource provision through a poster containing an anonymous and independently accessed QR code is a viable method for providing food resources to families. Future focus groups with families with FI will provide insight into acceptability of this approach as well as family's preferred method(s) of receiving food resource information in the PED.

Mentor: Cristin Fritz, MD, MPH (cristin.fritz@vumc.org)

FINANCIAL TOXICITY ASSOCIATED WITH SARCOMAS IN PEDIATRICS THROUGH YOUNG ADULTHOOD: A SINGLE INSTITUTION RETROSPECTIVE-PROSPECTIVE STUDY

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Objective: Sarcomas are a rare heterogeneous group of malignancies, with varied but often intensive treatment, including surgery, radiation, and systemic therapy. Such therapy is intended to improve survival but may also lead to adverse social outcomes, including financial toxicity, which may be associated with decreased quality of life and outcomes. Previous studies performed in countries with universal healthcare have demonstrated higher levels of financial distress in patients with sarcoma, compared to both age and sex matched general population. In a cohort of sarcoma patients treated at Vanderbilt University Medical Center with contemporary therapy, we evaluated self-reported measures of patient or parental financial toxicity.

Study Design: The “Cohort to Augment the Understanding of Sarcoma Survivorship Across the Lifespan” (CAUSAL), is an ongoing retrospective-prospective cohort of sarcoma patients, designed to assess the impact of sarcoma and its treatment on health and psychosocial outcomes. A total of 99 sarcoma patients up to age 30 years, treated at Vanderbilt University Medical Center from 2012-present have been recruited to the study to date. Self-reported measures of financial toxicity were assessed via the Comprehensive Score for Financial Toxicity (COST), a validated questionnaire, at the time of enrollment. The COST score is inversely associated with financial toxicity. Sarcoma and treatment data were abstracted from the electronic medical record.

Results: 63 of the 99 participants completed a COST questionnaire and were included in this analysis. There was a slight female predominance (54%), and the median age was 19 (range 3-30). 52 participants identified as “White” and 5 as “Black or African American.” The most common diagnoses included osteosarcoma (16), Ewing sarcoma (10), and rhabdomyosarcoma (14). 26 participants (41%) were actively receiving therapy for their sarcoma at the time of survey completion. 22 participants reported having a household income of <$45,000, 25 between $45,000-$90,000, and 16 >$90,000. The median number of household members was 3 (range 1-6). Multivariable linear regression was applied in the analysis to assess the association of age, sex, race, education level, household income, and patient treatment status with financial toxicity. We found that female gender and income level >$90,000 were significantly associated with higher COST scores, i.e., lower financial toxicity, with β (95% confidence interval) of 6.0 (0.64, 11.0; p= 0.033) and 7.4 (0.82, 14.0; p = 0.032 and p_{trend} = 0.022), respectively. Current treatment status, however, was unrelated to the financial toxicity.

Conclusions: Lower levels of financial toxicity were significantly associated with females and a higher income level. Future analyses of the still-enrolling CAUSAL cohort will continuously expound these preliminary observations and examine the association of financial toxicity with other patient characteristics as well as their impact on quality of life and sarcoma outcomes. Further research will help develop personalized supportive care strategies, by better identifying patients who are at risk for financial toxicity and connecting them with helpful resources to reduce the financial burden, stress, and hardships associated with diagnosis and treatment.

Mentors: Debra Friedman, MD, MS (debra.l.friedman@vumc.org) and Xiao-ou Shu, MD, PhD (xia-ou.shu@vumc.org)

DEVELOPING ELECTRONIC HEALTH RECORD ALGORITHMS THAT ACCURATELY IDENTIFY PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA

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Objective: Accurately identifying patients with Chronic Spontaneous Urticaria (CSU) is crucial for utilizing electronic health records (EHRs) and administrative databases to study the condition. However, there is currently no verified EHR algorithm available for identification of this condition. Through this study we aimed to create a new EHR algorithm using International Classification of Diseases, Ninth and Tenth Revision (ICD-9/10) billing codes to accurately identify patients with CSU.

Study Design: The Synthetic Derivative (SD), Vanderbilt University's research electronic database with de-identified clinical data from the EHR was utilized in this study. Potential CSU cases were identified in the SD if they had at least one ICD-9/10 code. Out of the potential cases, 200 subjects were chosen randomly as a training set for chart review in order to confirm the true cases. To be considered a case, a subject had to be diagnosed with CSU by an allergist or dermatologist or exhibit recurrent urticaria with or without angioedema for a period of six weeks or more without any definite eliciting factor. The study calculated positive predictive values (PPVs) and sensitivity for various combinations of ICD-9/10 code counts.

Results: The study identified 32,685 potential cases of CSU with at least one ICD-9/10 code, with a median age of 32 ± 19 years. Out of these potential cases, 67% were female and 68% were white. The total follow-up duration in the EHR was 11 ± 8 years. The study identified the algorithms with the highest PPVs, which are listed in Table 1. The algorithm with the best PPV, at 95.1%, was found to be a combination of at least 4 CSU codes or 1 allergist code or 1 dermatologist code.

Conclusions: We have developed a new algorithm that utilizes ICD counts to accurately identify patients with CSU with a PPV of 95%. This algorithm is a valuable tool for clinical and translational researchers to efficiently and accurately identify and study CSU patients. This approach can also be extended to identify and gather data on other allergic diseases or outcomes in the EHR. Ongoing study is being conducted to validate the algorithm within Vanderbilt's HER.

Algorithm	Sensitivity	PPV	F score
>= 4 CSU codes OR 1 Allergist code OR 1 Dermatologist code	81.3%	95.1%	0.88
>= 4 CSU codes OR Angioedema codes OR 1 Allergist code OR 1 Dermatologist code	81.3%	90.7%	0.86
>= 4 CSU codes OR 1 Allergist code	77.1%	94.9%	0.85

Table 1. Positive Predictive Values of Electronic Health Record Algorithms to identify CSU cases in the training set.

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DURATION OF INTRAVENOUS ANTIBIOTICS IN HOSPITALIZED CHILDREN WITH HIGH-INTENSITY NEUROLOGIC IMPAIRMENT AND URINARY TRACT INFECTIONS

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Objective: Children with high-intensity neurologic impairment (HINI) commonly have neurogenic bladder (NB), increasing their risk of urinary tract infection (UTI). Complexities in this population often lead to selecting intravenous (IV) antibiotics for both empiric and treatment therapy. Prolonged IV courses can cause unanticipated outcomes and resistance. Our objective was to determine the association between short (≤3 days) and long (>3 days) IV antibiotic course and UTI treatment failure in children with HINI in the inpatient setting.

Study Design: We performed a retrospective cohort study examining primary UTI hospitalizations at 49 hospitals in the Pediatric Health Information System from 2016-2021 for children (1-18 years) with a diagnosis of HINI. The primary outcome was defined as readmission for UTI within 30 days. Secondary outcomes included 30-day all-cause readmission and hospital-level treatment variation. Readmission rates were compared between short and long courses of IV antibiotics after adjusting for age, sex, payor, patient home location, bacteremia, sepsis, calculus, NB, genitourinary (GU) abnormality, surgically-diverted GU system, drainage procedure, intensive care unit (ICU) stay, illness severity, antibiotic resistance, and number of non-neurologic complex chronic conditions (CCCs).

Results: The cohort included 5612 hospitalizations, of which 3840 (68.4%) were short IV antibiotic courses and 1772 (31.6%) were long courses. Long courses were associated with bacteremia, sepsis, calculus, NB, GU abnormality, surgically-diverted GU system, resistance, drainage procedure, requirement of ICU care, higher illness severity, more non-neurologic CCCs, and longer stays. In models adjusting for baseline differences, patients with short IV courses were less likely to have 30-day UTI (4.1% vs. 6.2%; $p<0.001$) and all-cause readmissions (18.5% vs. 24.2%; $p<0.001$). Despite marked variation in the percentage of short course use across institutions, there was no difference in readmission rates.

Conclusions: Children with HINI hospitalized with UTI who received long courses of IV antibiotics were more likely to experience UTI and all-cause readmission compared to those receiving short IV courses. We also noted treatment variation across hospitals. Long IV courses are associated with risks and may not confer benefit in this population. Further work will explore whether urinary isolate resistance patterns modify observed associations.

Mentor: Katherine Freundlich, MD (katie.freundlich@vumc.org)

GLYCEMIA AND CARDIAC INVOLVEMENT IN FRIEDREICH'S ATAXIA

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Objective: Friedreich's Ataxia (FRDA) is a recessively inherited, progressive neurologic disorder primarily arising from GAA triplet repeat expansions of both *frataxin* alleles. FRDA is commonly complicated by cardiomyopathy (CM) and diabetes (DM) or impaired glucose tolerance (IGT). FRDA-related CM is a common cause of death in FRDA. In individuals without FRDA, DM and IGT are associated with non-ischemic CM. However, the relationship between DM and CM in FRDA is unknown. The objectives of this study were to test the hypotheses that i) remote glucose monitoring, using continuous glucose monitors (CGMs) in the research setting is feasible and ii) that greater glycemic excursion, as assessed by remote CGM, will be associated with more extensive CM.

Study Design: Participants were from two ongoing studies: i) an observational study (F32DK128970) using remotely placed CGMs (FreeStyle Libre Pro, Abbott Laboratories, Abbott Park, IL) for 14 days in children and young adults with FRDA and a recent echocardiogram and ii) a clinical trial (NCT04192136; R01HL149722) in children and young adults with FRDA who had baseline CGMs for 14 days and recent echocardiograms.

Results: Forty-four individuals have had CGMs reviewed; 43 wore the CGM for at least 1 day and were included. Median age was 19y (IQR 15-26). Eighteen of 43 (42%) were female and 3 of 43 (7%) had DM. By age-appropriate BMI criteria, individuals were underweight (3), normal weight (27), overweight (11), and obese (2). Eleven CGMs were placed remotely by the participant or a family member, most of whom had never used a CGM previously. Remote CGM placement was feasible and well-tolerated. Participants wore the CGM for a median of 13 days (IQR 6-14). Those without DM had an average glucose of 84mg/dL (IQR 80, 95 and range 70-113) and percent hyperglycemia, based on number of glucoses >140mg/dL, of 0.7 (IQR 0,1.5). Thus far, 24/43 (56%) have had echocardiograms centrally reviewed. Over half have evidence of hypertrophy, with interventricular septal thickness (IVSd) and/or posterior wall thickness (LVPWd) z-score ≥2. In this preliminary analysis, there is a positive association between mean glucose via CGM and IVSd z-score that is attenuated if those with DM are excluded.

Conclusions: Remote placement of CGMs in individuals with FRDA is a viable way of collecting real world data about glycemic excursion. Individuals with FRDA without DM did not experience significant hyperglycemia. The relationship between glycemia and cardiac hypertrophy deserves additional investigation. Ongoing studies will make more detailed evaluation of glucose and insulin metabolism and FRDA-related CM.

PERIPHERAL VS. CENTRAL CANNULATION IN VA ECMO PEDIATRIC PATIENTS WITH SEPTIC SHOCK

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Objective: Using the Extracorporeal Life Support Organization (ELSO) database, we will determine the rate of complications and survival in pediatric septic shock patients on VA ECMO flowing at ≥150 ml/kg/min versus <150 ml/kg/min (standard flow) as well as the rate of complications and survival between central and peripheral VA cannulation amongst patients flowing at ≥150 ml/kg/min.

Study Design: We queried ELSO for patients with an ICD-9 or ICD-10 diagnosis code of sepsis, septicemia, or septic shock requiring VA ECMO from Jan 1, 2000-Dec 31, 2021. We removed patients who had multiple ECMO runs, peripheral to central conversions, and conversion from VA ECMO to another mode. We compared survival to hospital discharge, survival to ECMO decannulation, hours on ECMO, length of stay, complications, other support modalities, and frequency of patients with a congenital heart disease diagnosis between patients flowing at high versus standard flows and between centrally versus peripherally cannulated patients on high flow VA ECMO. We also compared these variables between patients from 2000-2016 (early) and 2017-2021 (late). We then performed a subgroup analysis of patients with a primary diagnosis of sepsis, septic shock, or septicemia while excluding all patients with an ICD-9 or ICD-10 congenital heart disease diagnosis. For univariate analysis we performed chi square for categorical variables and Wilcoxon rank sum test for continuous variables. Finally, we performed multivariate logistical regression analysis to determine which variables had an association with survival to hospital discharge.

Results: A total of 6,154 VA ECMO runs were included in our dataset. At four and twenty-four hours, 5,779 and 5,387 were included in the flow analysis, respectively. At four hours and twenty-four hours, 708 and 775 patients were included in the central vs peripheral on high flow analysis, respectively. All patients were included in the early versus late analysis. Survival to hospital discharge was higher in standard flow than high flow at four and twenty-four hours (49% vs 42% and 53% vs 41% respectively; p<0.001). Survival to hospital discharge was higher in peripherally cannulated patients flowing ≥ 150 ml/kg/min than in centrally cannulated patients flowing ≥ 150 ml/kg/min at four and twenty-four hours but was insignificant in the former (44% vs. 37%; p=0.08 and 45% vs. 32%; p<0.001). The incidence of mediastinal cannulation bleeding was higher in centrally cannulated patients (8.1%) than the incidence of bleeding in peripherally cannulated patients (1.9%). Cannula problems and CNS infarction were more frequent in the peripherally cannulated patients compared to the centrally cannulated patients (10.4% vs 6.3% and 7.0% vs. 4.9%; p<0.001). Patients treated during later years had a higher survival to hospital discharge compared to early years (52% vs. 46%; p<0.001). There were 1,235 patients with a primary diagnosis of sepsis, septic shock, or septicemia without a cardiac diagnosis. There was no significant difference in survival to hospital discharge between high and standard flow at four hours. At twenty-four hours, survival to hospital discharge was significantly higher in standard flow compared to high flow (54% vs. 41%, p=0.002). Peripherally cannulated patients had a lower survival to hospital discharge compared to centrally cannulated patients within this subgroup (44% vs. 56%; p=0.013). In the multivariate analysis of this subgroup, peripheral cannulation, lower flow at 4 hours, lower pH, pre-ECLS arrest, younger age, higher pre-ECLS lactate, and CNS infarction were associated with a decreased survival to hospital discharge.

Conclusion: In a pediatric ECMO patients with a sepsis diagnosis, peripheral cannulation and standard flow VA ECMO are associated with an increased survival to hospital discharge for refractory septic shock than central cannulation and high flow. In children with a primary diagnosis of sepsis, septic shock, or septicemia and without congenital heart disease, peripherally cannulation was associated with a decreased survival to hospital discharge.

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AUTOIMMUNE ENCEPHALITIS CLINICAL PRACTICE GUIDELINE: IMPROVING TIME TO DIAGNOSIS AND TREATMENT AND DECREASING HOSPITAL LENGTH OF STAY

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Objective: Anti-N-methyl-D-aspartate receptor (NMDAR) antibody mediated encephalitis is a common type of autoimmune encephalitis (AE), accounting for up to 86% of AE in patients less than 18 years old. Studies have demonstrated improvement in outcomes with prompt and appropriate workup and treatment. A clinical practice guideline (CPG) was created at our institution for patients suspected to have anti-NMDAR autoimmune encephalitis to standardize and promote appropriate initial workup, including early consultations with specialists to assist with additional workup and management as indicated. This study evaluates the impact of the CPG in terms of time to diagnosis and treatment and hospital length of stay.

Study Design: Patients with an inpatient consult order placed to pediatric rheumatology for a three-year period after publication of the CPG were extracted from the electronic medical record using Epic reports. Charts were manually reviewed. Consults placed for AE were included while the remainder were excluded. Data were manually extracted from each chart including final diagnosis, time to treatment and length of hospital stay. IRB approval was obtained. This information was compared to previously published data at the same institution, during a four-year period prior to publication of the CPG.

Results: During the four-year period prior to use of the CPG, 34 patients received testing for AE. Nine were diagnosed with anti-NMDAR autoimmune encephalitis, four with antibody negative autoimmune encephalitis and 21 with non-autoimmune encephalitis/other diagnosis. In the three-year period after the CPG inception, pediatric rheumatology was consulted on 63 patients with concern for AE. Seven were diagnosed with anti-NMDAR autoimmune encephalitis, two with Hashimoto's thyroiditis, four with antibody negative autoimmune encephalitis and 50 with non-autoimmune encephalitis/other diagnosis. Average time from admission to treatment of confirmed AE diagnosis was reduced from 5.8 to 3.8 days. Additionally, length of hospitalization decreased from 49.8 to 33 days.

Conclusions: Creation of a CPG for patients with suspected AE has led to improved time to workup, diagnosis, and initiation of treatment. Additionally, it has led to decreased hospital length of stay. Since publication of the CPG, more patients have undergone workups for AE in a shorter period, which includes sedated brain magnetic resonance imaging and lumbar punctures, though the number of AE diagnoses has remained the same. Next steps should include assessment of clinical information on patients that were negative for AE to confirm consistent application of the Graus criteria in decision making regarding workup for AE. That information will help to identify potential for risk of unnecessary invasive procedures on patients.

Mentor: T. Brent Graham, MD, MS (brent.graham@vumc.org)

ASSOCIATION OF HYPEROXIA ON BYPASS TO POSTOPERATIVE DELIRIUM IN THE PEDIATRIC CARDIAC POPULATION: IS OXYGEN A MODIFIABLE RISK FACTOR?

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Objective: Nearly half of children with congenital heart disease who undergo cardiopulmonary bypass (CPB) develop delirium during their ICU stay. Delirium has been linked to increased mortality and increased hospital length of stay (LOS). Recent adult literature has suggested a link between hyperoxia on CPB and post-operative delirium but is yet to be studied in pediatrics. The accepted definition of hyperoxia and toxic oxygen exposure remains highly variable. We sought to investigate the association of hyperoxia on bypass and post-operative delirium in pediatrics via an exploratory analysis.

Study Design: Retrospective analysis of a prospectively collected cohort. All patients (age 0d to 18yr) who were admitted to the Pediatric Cardiac ICU post-operatively with documented Pediatric Confusion Assessment Method (pCAM/psCAM) scores and who were also enrolled in the Precision Medicine in Pediatric Cardiology (PMPC) Cohort from Feb 2021-Nov 2021 were included. We assessed for the primary outcome of delirium within the first 72 hours of post-operative admission with pCAM/psCAM documentation within the EHR. Exclusion criteria included patients both intubated and on sedation drips within 24h prior to surgery, pre-operative delirium, repeat CPB runs within the same hospitalization, absence of documentation of pCAM/psCAM within the first 72h of post-operative ICU admission, and mortality within the first 72h of post-operative admission. Differences in baseline characteristics and exposures in patients who were delirious vs not delirious were assessed for statistical significance. We calculated the mean and SD for continuous normal variables, median and IQR values for continuous non-normal variables, and counts and proportions for categorical variables. We evaluated the association between hyperoxia during bypass and postoperative delirium using a logistic regression framework to predict presence or absence of delirium within 72 hours of admission. Our descriptions of hyperoxia include maximum paO2, median paO2, SD of paO2, hyperoxic AUC quartiles above 5 pre-determined paO2 levels (150, 175, 200, 250, 300), hyperoxic AUC quartiles standardized by CPB time at the same paO2 levels, and hyperoxic AUC as a continuous measure.

Results: 148 total patients met inclusion criteria, and 35 had delirium within the first 72h (24%). There was no statistically significant difference between the delirium positive and negative groups in age, gender, mechanical ventilation days, PIM3 score, STAT score, days on benzodiazepines, opioids, or dexmedetomidine. There was a significant difference in the z-score for weight between the two groups ($p<0.05$). For all definitions of hyperoxia as listed above, there was no association with post-operative delirium within 72h.

Conclusions: We did not find an association between hyperoxia on CPB and delirium within the first 72h after CPB. However, nearly all patients were hyperoxic for the entirety of their time on bypass, which may have confounded the results. Lower z-score for weight was associated with an increased risk of delirium, and as such nutritional status could be a potentially modifiable risk factor for the prevention of delirium. Future work will focus on all patients who experienced delirium at any point during their hospitalization. Additional interventional studies could control for hyperoxia vs normoxia on bypass given the lack of patients without hyperoxia within the cohort.

Mentor: Kristina Betters, MD (kristina.betters@vumc.org)

THAT DE-ESCALATED QUICKLY: A SIMULATION-BASED DE-ESCALATION CURRICULUM FOR PEDIATRIC TRAINEES

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Objective: To create a novel de-escalation curriculum and improve trainee knowledge, confidence, and skill surrounding de-escalation of agitated/aggressive pediatric mental health patients.

Background: Children's hospitals serve as a safety net for children who present to the emergency department in a mental health crisis. Patients admitted to board while awaiting inpatient psychiatric beds may exhibit acute agitation/aggression requiring de-escalation by staff.[1,2] As a result, pediatric residents are often first line providers for de-escalation. An internal needs assessment of pediatric residents found that 84% of residents reported responding to an agitated or aggressive pediatric behavioral health patient at least once per shift, while 86% of residents had "none" or "a small amount" of training on verbal de-escalation. To date, there are no studies measuring the effectiveness of a resident de-escalation curriculum in children's hospitals.

Study Design: The curriculum was devised using Kern's 6 steps and Kolb's theory of experiential learning. A 90-minute workshop occurred monthly for 2 pediatric interns at a time (7/2022-ongoing). It consisted of an interactive online module, two simulation scenarios with agitated/aggressive standardized patients, and debriefs. A retrospective pre/post survey assessed trainee knowledge (0-100), confidence (1-5), and skill (1-5) surrounding de-escalation of agitated/aggressive pediatric mental health patients. Wilcoxon signed-rank test was performed to assess for differences between pre/post data.

Results: A total of 18 trainees completed the curriculum so far. After participation, trainee de-escalation knowledge, confidence, and skill increased from 25 to 75 (p=0.01), 2.5 to 3.75 (p=0.01), and 2 to 3 (p=0.01), respectively.

Conclusions: Our study is limited by challenges in measuring translation to clinical practice and small sample size. Preliminary data shows a de-escalation curriculum is an effective intervention. This curriculum could be incorporated into resident and interdisciplinary education. Role play could be used if a simulation center is not available.

Mentor: Jennifer King, MD (jennifer.c.king@vumc.org)

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Resident Poster Abstracts

Student and Resident Poster Abstracts

RP – 1	Laura Armstrong
RP – 2	Natasha Belsky
RP – 3	Sarah Bowlby
RP – 4	Richard Carozza
RP – 5	Lauren Chan
RP – 6	Yutaka Furuta
RP – 7	Jessica Hayes
RP – 8	Anna Hughes
RP – 9	Alexa Love
RP – 10	James Maiarana
RP – 11	Cara Miller
RP – 12	Charles Oertli
RP – 13	Jennifer Overfield
RP – 14	Lindsay Podraza
RP – 15	Maria Strobel
RP – 16	Ryan Sutyla
RP – 17	Rory Tinker
RP – 18	Alexandra Williams
RP – 19	MacKenzie Wyatt

RELATIONSHIP BETWEEN PERINATALLY IDENTIFIED CONGENITAL BRAIN MALFORMATIONS AND SEIZURE INCIDENCE, EEG FINDINGS, AND DEVELOPMENTAL OUTCOMES

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Objective: With improvements in pre- and post-natal imaging, congenital brain malformations are increasingly found prior to onset of symptoms. Effectively counseling families requires knowledge of expected outcomes but there is limited literature to provide accurate prognostication in terms of epilepsy and developmental outcomes. Although guidelines recommend EEG monitoring for these infants, data is lacking regarding the incidence and timing of seizures.

Study Design: In this retrospective study, we identified neonates with congenital brain malformations who received a Neurology consult in the newborn nursery or the NICU. We collected data via chart review on EEG characteristics, seizure incidence, and developmental outcomes.

Results: We identified 46 patients that met inclusion/exclusion criteria and divided them into groups as follows: disorders of neuronal migration/organization (polymicrogyria, lissencephaly, pachygyria, simplified gyral pattern, heterotopias, schizencephaly, hemimegencephaly), disorders of early prosencephalic development (absent septum pellucidum, holoprosencephaly), complex malformations (abnormalities in both migration and early prosencephalic development), and isolated corpus callosum dysgenesis/agenesis. Twenty patients (43%) had evaluation with EEG during the initial hospitalization. In our study, disorders of early prosencephalic development conferred the highest risk of seizures during the initial admission (43% 3/7), followed by complex malformations (25% 1/4), disorders of neuronal migration (14% 3/21), and isolated corpus callosum dysgenesis/agenesis (8% 1/13). Of the 7 patients with EEG confirmed seizures, 2 were electrographic only. After discharge, 5 patients (15% of those discharged from the hospital without seizures) later developed seizures and were started on anti-seizure medications. Of the patients surviving to discharge 44% had developmental delay noted at follow-up, 21% had normal development, and 36% had no clinic follow-up.

Conclusions: Our data highlights the significant morbidity and mortality associated with congenital brain malformations. We found that disorders of early prosencepahlic development were associated with the highest incidence of seizures during the initial admission, while corpus callosum dysgenesis had the lowest incidence of seizures. However, only 43% of patients underwent EEG monitoring during the initial admission and future studies using more systematic screening are needed to better stratify the risk of seizures, the timing of seizure onset, and the benefits of early identification/intervention. We identified a population of patients who developed seizures post-discharge and who could potentially benefit from early identification and intervention. Patients with congenital brain malformations are at risk for developmental delay, but inconsistent follow-up limited analysis by malformation category. Future studies with evaluation using more precise developmental scales would allow for more effective counseling regarding prognosis of patients with congenital brain malformations.

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RISK FOR TYPE 2 DIABETES PROGRESSION IN A PEDIATRIC PREDIABETES CLINIC POPULATION

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Objective: The incidence and prevalence of Type 2 Diabetes (T2D) in children has dramatically increased over the past twenty years. Despite this rise, the pathophysiology and disease progression in children is less understood than in adults, and pediatric prediabetes diagnostic criteria are derived from the adult definition. It is unclear what definition of pediatric prediabetes predicts progression to T2D or long-term morbidity. Strategies are needed to better identify at risk children who could benefit from closer follow up and early intervention. In this study, we utilized the Vanderbilt Pediatric Prediabetes Clinic to assess what factors may be associated with increased risk of progression to T2D in children over time.

Study Design: We conducted a retrospective chart review of the initial visit for all children referred to the Vanderbilt Pediatric Prediabetes Clinic over 7 years. To be included, children had to have a hemoglobin A1c and at least one glucose result from an oral glucose tolerance test. Children diagnosed with type 1 diabetes, maturity onset diabetes of the young, or T2D on initial visit were excluded from analysis. Patients were assigned to either the T2D progression or non-progression group for further analysis based on the 2022 ADA criteria. For patients that progressed to T2D, relevant additional information was manually charted for each visit at the center from initial presentation through diagnosis.

Results: Of the 552 patients included, 6.5% (n= 36) progressed to T2D over an average of 2.4 $\pm$ 1.5 years. At the initial visit, T2D progressors had a higher BMI (mean difference 4.4 kg/m^2, $p = 0.002$) and weight (mean difference 14.2 kg, $p = 0.004$). Initial visit HbA1c (5.7 vs. 6.0%, $p < 0.001$), 2h glucose (141 vs. 114 mg/dL, $p < 0.001$) and fasting c-peptide (4.8 vs. 3.6 ng/mL, $p = 0.001$) were also higher in the T2D progression group. On a fasting lipid panel, triglyceride levels (138 vs. 109 mg/dL, $p = 0.015$) were higher and HDL was lower (38 vs. 41 mg/dL, $p = 0.003$) in the T2D progression group. Fasting plasma glucose was not significantly different between the groups. For patients who progressed, age at T2D diagnosis was on average 14.9 years old, with ages ranging from 9.9 – 18.3 years. In a multivariable model, male sex (HR 2.4, $p = 0.012$), initial visit HbA1c (HR 1.3, $p < 0.001$), and 2-hour glucose level (HR 1.2, $p = 0.014$) were all predictive of increased likelihood of progression over time, while age did not reach significance (HR 0.9, $p = 0.05$). On average, patients who progressed to T2D had an increase in BMI of 4.2 kg/m^2 from initial visit to time of T2D diagnosis.

Conclusions: Overall, few patients with prediabetes developed T2D over the 7-year period, highlighting the importance of identifying which patients should receive early intervention and close follow-up. Initial visit laboratory values and clinical characteristics may allow for risk stratification. Male sex and baseline BMI, hemoglobin A1c, c-peptide, and impaired glucose tolerance may be more predictive of T2D risk than fasting plasma glucose. Preventing further worsening of obesity could be an important intervention for diabetes prevention in children.

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ELEVATED HEMATOCRIT LEVELS IN PEDIATRIC PATIENTS WITH ACHONDROPLASIA

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Introduction: Baseline hematologic data from a clinical trial using Vosoritide, as a study drug (SD), to increase growth in pediatric patients with achondroplasia documented to have *FGFR3* gain of function mutations was studied. Interestingly, almost all subjects had unexpected, elevated hematocrit levels. We hypothesize that the *FGFR3* gain of function mutation that causes achondroplasia may result in a cascading effect on JAK2 protein expression which could result in erythrocytosis and elevated hematocrits.

Objective: To investigate the relationship between achondroplasia and elevated hematocrit levels.

Study Design: Seven subjects with achondroplasia who were 5-18 years old were enrolled in a longitudinal study in a clinical trial sponsored by BioMarin Pharmaceutical Inc. at Vanderbilt University Medical Center (VUMC) Baseline and subsequent data from our seven subjects (VUMC Cohort) was analyzed. Additionally, hematologic data from the entire BioMarin Cohort of 60 subjects receiving the SD and 61 subjects receiving placebo was also analyzed. All subjects in the VUMC and BioMarin cohorts were genetically confirmed to have the same *FGFR3* gain of function mutation that causes achondroplasia. Polysomnography done on the VUMC Cohort to detect apnea and hypoxemia. Hematologic data from both cohorts was evaluated to determine how often elevated hematocrits were found in subjects with achondroplasia.

Results: We found that 6/7 (86%) of the VUMC Cohort had elevated hematocrit levels at baseline. Their polysomnographic studies showed that 6/7 (86%) had no significant sleep or central apnea or hypoxemia. The 1/7 (14%) of subjects in this cohort who had significant sleep apnea did not have an elevated hematocrit. The BioMarin cohort data showed that106/121 (88%?) of subjects had an elevated versus 9/121 (7%) a low hematocrit as their most irregular hematologic lab result. Further investigation via STRING (https://string-db.org/) analysis was done to determine, if possible, relationships existed between *FGFR3, and* JAK2 or other proteins that might be linked to erythrocytosis. The STRING analysis results suggest a possible functional relationship between *FGFR3* and *JAK2* (whose gain of function mutations are known to cause erythrocytosis). A relationship between FGFR3 and JAK2was reported by Kawahara et. al. (31369573) in their physiological pathway studies of bladder cancer.

Conclusions: 1) Data from the VUMC and BioMarin cohorts suggests that elevated hematocrits occur in many more subjects with achondroplasia than was expected. 2) Normal polysomnographic studies in our 6/7 (86%) of VUMC subjects with elevated hematocrits suggest that hypoxemia that results in erythropoietin induced erythrocytosis is unlikely. Furthermore our 1/7 (14%) of subjects with hypoxemia did not have elevated hematocrits. 3) Results from our STRING analyses suggest that possible interactions between FGFR3 and JAK2 may increase JAK2 expression that results in erythrocytosis.

Future directions: To test our hypothesis, further collaborative research is planned with Dr. Joseph Prchal, who is an expert in the molecular basis of erythrocytosis. This will involve functional studies of cells derived from our achondroplasia subjects with increased versus normal hematocrits along with erythropoietin levels.

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PAROXYSMAL SYMPATHETIC HYPERACTIVITY: DEVELOPMENT OF A CLINICAL PRACTICE GUIDELINE

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Objective: Paroxysmal sympathetic hyperactivity (PSH) is a syndrome associated with antecedent brain injury, characterized by episodes of sympathetic overdrive, manifested by vital sign instability and increased neuromuscular tone. PSH is independently associated with adverse neurological outcomes, including rehabilitation, ICU, and hospital length of stay. Despite a myriad of pharmacotherapeutic options, high-value clinical evidence and broad consensus on the evaluation and management of PSH is limited. The 2014 consensus statement by Baguley, et al., does not stipulate guidelines for the pediatric population. We aim to streamline evaluation and treatment of PSH in children.

Study Design: We performed a literature search using "paroxysmal sympathetic hyperactivity" or other historic synonyms, and identified thirty-six studies including twenty case reports, ten case series, three retrospective case control studies, two prospective observational studies, and one retrospective cohort study. Agents analyzed included α_2-adrenergic agonists, anti-seizure medications, benzodiazepines, β-adrenergic antagonists, barbiturates, dopamine agonists, $GABA_B$ receptor agonists, gabapentinoids, opiates, ryanodine receptor antagonists.

Results: We engaged in a multidisciplinary effort including the divisions of pediatric neurology, critical care, physical medicine and rehabilitation, hospital medicine, emergency medicine, complex care, palliative care, and pharmacy. A modified form of the clinical feature scale from the 2014 consensus guidelines was adapted to the pediatric population. Nursing staff was instructed to obtain CFS subtotal once per 12-hour shift with PSH-AM > 8, and to prioritize non-pharmacologic measures, followed targeted pharmacotherapy based on primary symptomatology including neuromotor tone (baclofen, benzodiazepines), vital sign abnormalities (clonidine, propranolol), and pain (gabapentin, opiates). Dosing guidelines were also stipulated.

Conclusions: Our group created an evidence-based, novel framework to optimize care and improve outcomes in children with PSH, which we believe is transferrable to other institutions as well. Following implementation, we are studying its effect on total hospital and ICU length of stay, effect on short- and long-term morbidity and mortality, and any relative superiority of treatments in the pediatric population.

Mentor: Lindsay Pagano, MD (lindsay.m.pagano@vumc.org)

FAMILY CENTERED ROUNDING FROM PEDIATRIC RESIDENT AND ATTENDING PERSPECTIVE

Lauren Chan, Abhinaya Ganesh, Alison Herndon

Objective: Since the American Academy of Pediatrics 2003 guidelines to implement family centered rounding (FCR), FCR has been the standard for providing inpatient pediatric care. However, there continues to be varying definitions and implementation of FCR that makes it difficult to assess its effectiveness in providing patient care, ability to build resident autonomy, and improve resident education. The purpose of these surveys was to identify resident and attending attitudes, perceived benefits, challenges, and areas of improvement in FCR in a pediatric inpatient setting.

Methods: Survey collection took place at a single site, academic teaching hospital. All 23 pediatric hospital medicine attendings and 97 pediatric residents were emailed a REDCap survey of 13 and 16 questions, respectively.

Results: A total of 46 residents (47%) and 11 attendings (48%) completed the survey.
Both residents and attendings agreed or strongly agreed that patients and their families are engaged during FCR, feel comfortable asking questions, had a role in medical decision making, and understood the diagnosis or plan by the end of rounds. Residents felt that FCR improved their relationship with families, interdisciplinary communication, and role modeling opportunities. However, FCR did not improve clinical decision making, physical exam skills, or didactic learning. Most were unable to attend daily noon conference for didactic learning.
Despite the benefits of FCR and attending preference for full bedside rounding, most residents (91%) preferred alternative forms of rounding. Residents identified duration of rounds, large team size, and repetition during rounds as the greatest barriers to FCR, which was statistically different from attendings who did not see those as barriers. Almost half of residents did not feel comfortable asking clarifying questions in front of families during FCR. Top barriers to FCR for attendings included language and cultural barriers and resident fear during rounds.

Discussion/Conclusion: Although residents and attendings agreed that family engagement is central to FCR, resident preference for non-bedside rounding highlights the need for improvement. FCR should be optimized to provide high quality patient care and help build resident autonomy. While factors like team size cannot be controlled for, strategies to standardize rounds, minimize redundancy, and empower residents can improve FCR. Further education for residents and attendings to build cultural competency and skills to navigate socially sensitive situations can improve patient care.

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CHARCOT-MARIE-TOOTH DISEASE TYPE 2 DIAGNOSED WITH BIALLELLIC MUTATIONS IN *SORD* GENE CAUSING SORBITOL DEHYDROGENASE DEFICIENCY IN A 72-YEAR-OLD MAN

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Introduction: Sorbitol dehydrogenase (SORD) deficiency is characterized by a progressive neuropathy that results in limb weakness and difficulty walking. Previously, SORD deficiency was diagnosed symptomatically as Charcot-Marie-Tooth disease Type 2 (CMT2) or distal hereditary motor neuropathy (dHMN) since the genetic cause of the SORD deficiency was unclear. However, a recent study discovered biallelic mutations in the *SORD* gene accounted for up to 10% of patients with CMT2 and dHMN. Currently, an investigational drug is being studied in patients with SORD deficiency, which could potentially enable the development of treatments of affected individuals for neuropathy caused by SORD deficiency.

Methods: This report describes a 72-year-old man who was referred to the Undiagnosed Diseases Network (UDN) suffering from gradual progressive weakness in both lower extremities since the age of 27. The subject was initially diagnosed as having CMT2 without a defined genetic cause.

Results: SORD deficiency was suspected and the sorbitol level in urine samples was found to be significantly elevated to greater than 1,000 μM (normally hardly detectable in healthy individuals), which diagnosed him as having SORD deficiency. The subject was formally diagnosed by the Vanderbilt UDN clinical site as having SORD deficiency due to homozygous *SORD* frameshift mutation (c.757delG:p.A253Qfs*27) found through UDN Genome Sequencing.

Conclusions: 1) The subject's medical odyssey was solved by next generation sequencing and detection of pathogenic levels of sorbitol. 2) His diagnosis provided him the opportunity to receive potential treatment with an investigational drug in a clinical trial. 3) We suggest that similar studies be considered in other individuals thought to possibly have CMT2 or dHMN if clinically indicated.

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IMPROVING TIME TO ANALGESIA IN PATIENTS WITH LONG BONE FRACTURES IN A PEDIATRIC ED

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Objective: Long bone fractures are the most common injury in the pediatric population. Analgesia is often delayed due to inefficient triage processes and attempts at IV placement prior to giving analgesics. The aim was to decrease the average time from ED arrival to administration of analgesics for patients presenting to our Pediatric ED with moderate-severe pain in the setting of long bone fracture from 1 hour 22 minutes to <41 minutes by June 2023.

Study Design: A multidisciplinary team developed a key driver diagram (Figure 1). Retrospective baseline data were obtained from 7/1/21-4/30/22, after which data were followed prospectively. The population included children ages 0-18 who presented to the ED with moderate-severe pain, as measured by a validated numeric pain score, and had a final diagnosis of long bone fracture. The primary outcome was average time from ED arrival to analgesic administration. Statistical process control charts were used to analyze data. Nelson rules were utilized to detect special cause variation. Process measures included percent of patients with IV placement prior to analgesics and who received IN fentanyl on arrival. Balancing measures included percent of patients receiving non-opioids on arrival.

Results: Of 295 total encounters, baseline data represented 165 encounters with an average time to pain medication administration of 1 hour 22 minutes. Following multidisciplinary education as well as clinical practice guideline and order set implementation, special cause variation was detected with a centerline shift to a new sustained average time of 46 minutes (Figure 2), which was sustained for 7 months. The percent of encounters in which IVs were placed prior to analgesic administration decreased from 18% to 5%. Percent of patients in moderate-severe pain who received IN fentanyl on arrival increased from 22% to 30% and who received a non-opioid on arrival increased from 59% to 65%.

Conclusions: We reduced the time from ED arrival to analgesic administration from 1 hour 22 minutes to 46 minutes, sustained over 7 months. While a greater percentage of patients in significant pain initially received non-opioids, there was a shift away from IV placement before analgesia was achieved. Ongoing efforts are focused on best practice advisory alerts and multidisciplinary reviews of performance with focused feedback to clinicians.

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DISCONTINUING UNNECESSARY PROTON-PUMP INHIBITORS IN A PEDIATRIC CYSTIC FIBROSIS CLINIC: A QUALITY IMPROVEMENT INITIATIVE

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Objective: Gastroesophageal reflux disease (GERD) is common in people with cystic fibrosis (PwCF) and frequently treated with proton pump inhibitors (PPI) and histamine blockers. Long-term PPI use may be associated with negative health consequences such as increased risk of bacterial pneumonia or C. difficile infection, bone health concerns, and potential drug-drug interactions with CFTR modulators. Given the long-term health consequences of PPI use, the ongoing need for PPI use must be monitored. At baseline, the Vanderbilt Pediatric CF program prescribed more PPI and histamine blockers compared to the majority of CF programs. As such, we aimed to have 90% of eligible pediatric patients in the Vanderbilt Pediatric CF clinic complete the PPI discontinuation algorithm at least once from 6/1/2022 to 12/31/2022 to decrease PPI use in appropriate patients.

Study Design: A team of physicians and a clinical pharmacist developed a key driver diagram. Baseline data were obtained from the electronic medical record and an institutional patient registry. Patients were eligible for the algorithm if they were at least 12 years old, filled a PPI consistently, and were asymptomatic from a gastrointestinal standpoint. The primary outcome was the percentage of eligible patients who completed the algorithm and the number of patients who stopped a PPI was the secondary outcome. The process measure was the number of patients who completed the algorithm. The balancing measure was the number of patients who had to re-start a PPI due to symptom recurrence. Data were analyzed using P-charts.

Results: Prior to the intervention, 56.6% of patients were on a PPI. 89.7% of eligible patients completed the PPI discontinuation algorithm during the first 6 months of the intervention. PPI use decreased by 23% with the intervention. Two patients had to restart a PPI due to recurrence of gastrointestinal symptoms after the medication was discontinued with the algorithm.

Conclusion: We demonstrate that a standardized algorithm to monitor PPI use in a pediatric CF clinic can effectively decrease PPI use in appropriate patients. This framework provides a systematic approach to guide PPI use in PwCF, which may decrease treatment burden and minimize side effects from unnecessary long-term PPI use.

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A NOVEL INTERPROFESSIONAL APPROACH TO PEDIATRIC RESIDENT MENTAL AND BEHAVIORAL HEALTH EDUCATION

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Objective: Due to an increasing number of children with mental health diagnoses without a corresponding increase in resources, it is imperative that pediatricians be adequately trained to "provide behavioral and mental health care across all clinical settings," per the American College of Graduate Medical Education. Many pediatric hospitals have seen a rise in mental health visits, which has been exacerbated by the COVID-19 pandemic, and many trainees report feeling unprepared to care for this population. Our objective was to create a novel Mental and Behavioral Health (MBH) rotation and curriculum and assess whether these improved resident knowledge and comfort in caring for these patients.

Study Design: Thirty-six interns will rotate on the MBH team for five days. The MBH team is comprised of advanced practitioners, pediatric hospitalists, pediatric psychologists, social workers, case managers, and consult psychiatrists. Interns work with pediatric psychologists and social workers to learn interviewing and de-escalation techniques. They also complete learning modules, including lethal means counseling, safe firearm storage, pharmacology, and trauma informed care. To study curriculum effectiveness, interns complete REDCap surveys at the beginning and end of their week. The survey includes 10 subjective questions to assess comfort in caring for MBH patients on a Likert scale (1=Not at all true to 4=Very true), and 10 questions to assess knowledge of topics covered during the week. Descriptive statistics were used for analysis.

Results: To date, 23/36 interns have completed the MBH rotation. Twenty-one have completed the pre-rotation survey, and ten have completed the post survey. Mean knowledge scores increased from 51.9% to 61.0%. Mean comfort increased for all scenarios (e.g., "I am comfortable with providing lethal means counseling" increased 2.0 to 3.5).

Conclusions: The purpose of this study was to create a novel MBH rotation and curriculum and to determine whether these improved resident knowledge and confidence in caring for these patients. This rotation and curriculum have been successfully implemented. Scores for knowledge and all subjective measures were higher after the rotation. One limitation of this study is the variability in patient volumes and acuity, which may impact the resident experience. Another limitation is the low number of survey responses; this study is ongoing, and we continue to collect data. This is the first phase of our MBH curriculum; going forward, we plan to expand into the outpatient setting.

Mentors: Alison Herndon, MD (alison.herndon@vumc.org) and Whitney Browning, MD (whitney.browning@vumc.org)

DEEP IMMUNOPHENOTYPING SHOWS ALTERED IMMUNE CELL SUBSETS IN CTLA-4 HAPLOINSUFFICIENCY

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Background/Objective: Cytotoxic T lymphocyte antigen-4 (CTLA-4) is a transmembrane protein found on most activated T cells and constitutively expressed by regulatory T cells. CTLA-4 opposes the interaction of costimulatory CD28:CD80/CD86 signaling through various cell extrinsic and intrinsic mechanisms [1]. In mice, homozygous deletion of *Ctla4* causes fatal multiorgan tissue destruction due to excessive lymphoproliferation and expansion of $CD4^+$ T cells, while heterozygous mice are unaffected [2]. Human heterozygous germline mutations in *CTLA4* can cause a monogenic inborn error of immunity (IEI) with hypogammaglobulinemia, variable autoimmune manifestations and incomplete clinical penetrance [3,4]. Over 200 patients with this IEI have been reported, yet we do not completely understand the cellular drivers of disease [5]. To better understand the cellular basis of autoimmune disease in CTLA-4 haploinsufficiency, we used time-of-flight mass cytometry to study samples from a large pedigree with a novel heterozygous *CTLA4* mutation (D159Y).

Results: The index patient (Figure 1A, IV-4) presented as a 6-year-old male with enteropathy, a history of recurrent non-infectious diarrhea since infancy, and hypogammaglobulinemia. The patient also had upper respiratory infections and pneumonia (ages 7-8) and a gut biopsy showed follicular lymphoid hyperplasia. Family history revealed numerous other members with autoimmune features. Clinical genetic analysis revealed a novel heterozygous variant (c.475T>G; D159Y) in *CTLA4*, which was confirmed by Sanger sequencing. Sanger sequencing in additional members of this family identified 6 additional individuals with the c.475T>G mutation. Four of the 7 genetically affected individuals (57%) had clinical symptoms consistent with CTLA-4 haploinsufficiency. Next, $CD4^+$ T cells from patient IV-4 were obtained and showed normal frequencies of CTLA-4^+ $CD4^+$ T cells but diminished CTLA-4 protein expression after 5 hours of Phorbol myristate (PMA) and Ionomycin stimulation compared to healthy controls. Additionally, CHO cells transfected with mutant D159Y *CTLA4* plasmid showed significantly decreased CTLA-4 protein expression as measured by mean fluorescence intensity (MFI) compared to CHO cells transfected with wild type (WT) *CTLA4*. To assess the functional consequence of this mutation, a transendocytosis assay was conducted [6]. CHO cells expressing mutant D159Y CTLA-4 protein showed significantly reduced transendocytosis of $CD80^{GFP}$ compared to CHO cells expressing wild type (WT) CTLA-4, thus the D159Y mutation impairs CTLA-4 function.

To uncover cellular phenotypes in individuals with the *CTLA4* D159Y mutation, we analyzed peripheral blood mononuclear cells (PBMCs) from 5 mutation carriers and 4 healthy controls by mass cytometry. Interestingly, immunophenotyping revealed marked differences in $CD4^+$ T cell subset frequencies in individuals with the CTLA4 D159Y mutation. Gating on CXCR3 vs CCR6 can identify 4 different $CD4^+$ helper T cell subsets: $CCR6^+CXCR3^-$ Th17, $CCR6^+CXCR3^+$ Th1, $CCR6^-CXCR3^+$ Th1, and $CCR6^-CXCR3^-$ Th2 [7]. Patients with the D159Y mutation had decreased frequencies of $CCR6^+CXCR3^+$ Th1 (15.9% vs 45.6%, $p<0.05$) and significant increases in $CCR6^-CXCR3^-$ Th2 (36.1% vs 13.0%, $p<0.05$) compared to healthy controls without changes in Th17 or $CCR6^-CXCR3^+$ Th1 subsets. Given these differences, we sought to identify changes in other helper T cell subsets and interrogated circulating $CXCR5^+$ $CD4^+$ follicular helper T cells (Tfh). Patients with the D159Y mutation had ~3-fold decrease in circulating Tfh (4.2% vs. 12.5%, $p<0.05$) and significant reduction in the MFI of CXCR5 on all $CD4^+$ T cells (1.3 vs 4.8, $p<0.05$). Given the role of Tfh cells in B cell homeostasis, we next interrogated the B cell compartment. We observed a significant reduction in $CXCR5^+$ $CD19^+$ circulating B cells amongst individuals with the CTLA4 D159Y mutation, compared with healthy controls (17.2% vs 86.1%, $p<0.05$). These data suggest that the CTLA4 D159Y mutation alters CXCR5 expression, which could lead to dysregulated migration of Tfh and B cells.

Conclusions: In this study, we identified a novel D159Y mutation leading to clinical CTLA-4 haploinsufficiency and performed mass cytometry on 5 members of a family harboring this autosomal dominant mutation. Analysis revealed increased frequencies of Th2 cells and reductions in $CXCR5^+$ Tfh cells and $CXCR5^+$ B cells. Information from this deep immunophenotyping could help explain the development of hypogammaglobulinemia and provide human evidence of Th2 skewing in patients with CTLA-4 Haploinsufficiency.

Mentor: Janet Markle, PhD (janet.markle@vumc.org)

UTILIZING THE EHR TO IMPROVE THE STANDARD OF CARE AT FOLLOW-UP APPOINTMENTS FOR CHILDREN WITH NEWLY DIAGNOSED AUTISM SPECTRUM DISORDER: A QUALITY IMPROVEMENT INITIATIVE

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Objective: Parents of children with newly diagnosed autism spectrum disorder (ASD) report inadequate guidance regarding the complexities that often accompany ASD. Primary care providers (PCPs) play an important role in this, however, report insufficient training in discussing diagnosis or providing follow-up care for children with ASD. Using best practice guidelines, we created a standardized template for ASD-specific follow-up appointments within primary care that could help alleviate some of these concerns. Our aims were to increase the use of a standardized EHR template at follow-up appointments for children (aged 0-48 months) with newly diagnosed ASD to 75% and to promote the standard of care for these patients by offering and discussing genetic testing per the AAP Guidelines at 75% of these appointments.

Study Design: Our study population consisted of children aged 0–48 months who are patients of the Vanderbilt Primary Care Clinic (PCC) and received a new diagnosis of ASD. All providers were trained in the use of a novel clinic note template that integrated best practices, including genetic testing and co-occurring medical concerns. Patients were scheduled for a follow-up appointment with a PCC provider. Baseline data were obtained for 12 months and were followed prospectively using statistical process control charts while the team tested changes using Plan-Do-Study-Act (PDSA) Cycles monthly.

Results: At baseline, only 21% of children diagnosed had an ASD-specific follow-up at some point. Of the patients who had an ASD-specific follow-up appointment prior to project initiation and development of the EHR note template, genetic testing was discussed at 23% of the appointments.

In the 12 months post-project initiation, we have had 70 ASD-specific follow-up appointments for 73% of patients. Our EHR note template usage is 83% at ASD specific follow-up appointments. Additionally, genetic testing has been discussed at 78% of ASD-specific follow-up appointments in the 12 months post-intervention. An additional 2 patients with ASD-specific follow-up appointments already had genetic testing obtained elsewhere.

Conclusion: Our data has exceeded our QI goals since project initiation. It is likely that both the use of the note template in the EHR as well as the education of our providers throughout the administration of this project has supported our goals of better standardized care of patients with newly diagnosed ASD based on AAP guidelines. With additional PDSA cycles including further provider education, expansion of telehealth within the clinic, as well as provider surveys on the use of our note template we hope to sustain our goal and improve the consistent evidence-based management for children with newly diagnosed ASD. Our next steps include surveying families for feedback in regard to the follow-up appointments to address the satisfaction of our families and further improve this process.

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CONGRUENCE BETWEEN ICD-10 CODE AND WRITTEN DOCUMENTATION FOR OUTPATIENT ENCOUNTERS WITH ANTIBIOTIC PRESCRIPTIONS

Charles Oertli, Milner Staub, and Sophie Katz

Objective: Antimicrobial stewardship programs (ASPs) often rely on *International Classification of Diseases, Tenth Revision* (ICD-10) codes to assess antibiotic appropriateness for provider feedback. Concordance between encounter ICD-10 codes and documented indication for antibiotics based on manual chart review varies greatly (74-95%) in the inpatient setting. Data on concordance between documented indication and ICD-10 code in the outpatient setting are scarce.

Study Design: Retrospective cohort study of 650 randomly selected outpatient encounters with antibiotic prescriptions from walk-in and retail clinics between July 15 to September 15, 2021, at Vanderbilt University Medical Center. We performed chart review to compare documented antibiotic indication to the top three encounter-associated ICD-10 codes. Twelve encounters were excluded due to insufficient available written documentation. The 95% confidence interval (CI) for proportion of encounters with concordant antibiotic indications was calculated using Stata version 15.1.

Results: Of the 638 antibiotic prescriptions with written documentation available for chart review, 204 (32%) were for amoxicillin, 102 (16%) amoxicillin/clavulanate, 61 (10%) cefdinir, and 56 (9%) azithromycin. We found that 84.6% (540/638; 95% CI 81.6% to 87.4%)) of encounters had concordant antibiotic indication based on documentation in the note and associated ICD-10 for the encounter. Of the encounters with concordant ICD-10 and documented indications, 64% (348/540), 24% (130/540), and 6% (35/540) were listed as the first, second, and third ICD-10 code, respectively. An additional 5% (27/540) had a concordant ICD-10 code listed beyond the third position. A total of 125/638 (19.6%) encounters did not have the intended antibiotic indication as documented in the note in the top 3 associated encounter ICD-10 codes (whether a lower position or incongruent ICD-10 code with documentation). Of those encounters, 42/125 (34%) had a documented diagnosis of strep pharyngitis, 16/125 (13%) skin or soft tissue infection, 11/125 (9%) urinary tract infection, and 11/125 (9%) acute otitis media.

Conclusions: Our data suggest that outpatient antimicrobial prescriptions correlate relatively well with encounter ICD-10 codes. However, most ASP prescribing goals aim to reduce inappropriate prescribing to 10% or less of prescriptions based on indication. Therefore, providers may not trust individual prescribing feedback that is based on data that is only correct 85% of the time. For ASPs to accurately assess prescribing and provide trusted, meaningful recommendations and specific feedback to individual prescribers, more reliable and valid data are needed. We intend to evaluate whether requiring outpatient antibiotic indications on prescriptions increases data reliability and validity.

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AVOID THE RADIATION: OPTIMIZING UTILIZATION OF COMPUTED TOMOGRAPHY IMAGING FOR PEDIATRIC APPENDICITIS

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Objective: Appendicitis is a common pediatric surgical emergency, and computed tomography (CT) is overused in diagnosing pediatric appendicitis. Our institutional rates of CT utilization for suspected appendicitis are higher than peer participants in the NSQIP-P Pediatric Surgery Quality Collaborative. We aimed to reduce CT utilization in the diagnostic evaluation of pediatric appendicitis from 32% to the NSQIP-P benchmark of 15% by 6/2022.

Study Design: Retrospective chart review was done for baseline data from 1/2021- 8/2021 and followed prospectively. Patients in the pediatric emergency department (ED) were identified based on ICD-10 codes for abdominal pain and acute appendicitis. A multidisciplinary team formed in 6/2021 and developed a key driver diagram (Figure 1). A clinical practice guideline (CPG) utilizing the Pediatric Appendicitis Score was developed in 9/2021 and trialed in the clinical setting. The CPG was institutionally published in 12/2021 with accompanying education and a complaint-based order set embedded in the electronic medical record for clinical decision support. The primary outcome was percent of patients with CT scan. Timing of surgical consultation and radiology template use were process measures. Balancing measures were negative-pathology appendectomies (NPA) and ED return visits within 72 hours with subsequent appendicitis diagnosis. Data were analyzed using statistical process control charts and Nelson rules to detect special cause variation.

Results: The cohort included 2010 total encounters, 624 of which represented the baseline with a CT rate of 31.3%. Following multiple PDSA cycles to develop and test the CPG, special cause variation was detected in CT use to 22.5%. Order set launch was also associated with special cause variation resulting in a centerline shift to 12.1% that has been sustained for 10 months (Figure 2). Rate of surgical consultation prior to CT imaging increased from 69.4% to 94.6% (Figure 3a) and radiology template use increased from 24.6% to 83.3% (3b). There was one ED return visit within 72 hours. Special cause variation in NPA was appreciated in 10/2022, with a decreasing frequency of NPA, indicating more cases between these rare events (3c).

Conclusions: CT imaging was safely reduced in the workup of pediatric appendicitis. Workflow standardization with the use of a CPG and order set, along with earlier involvement of the surgical team, facilitated the reduction in CT utilization. Ongoing efforts include standardizing surgical serial exams and continuous performance review.

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"SAY AH": A NEAR-PEER PHYSICAL DIAGNOSIS CURRICULUM ON STREP PHARYNGITIS WITHIN THE PEDIATRICS CLERKSHIP

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Objective: With increasing clinical demands for faculty physicians, time spent teaching physical diagnosis skills to medical students during hospital medicine rounds can be limited. Near-peer teaching sessions by residents offer additional opportunities for students to master clinical skills. A needs assessment identified the throat swab as the most commonly missed pediatric clerkship skill at our institution. The objective of this project is to develop and assess the effectiveness of a resident-led, evidence-based physical diagnosis curriculum on improving medical student confidence, knowledge, and procedural skills related to the diagnosis of streptococcal pharyngitis in children.

Study Design: Kern's six-step approach for curriculum design was used. Residents gave a didactic and demonstration on approaching a patient with sore throat based on JAMA's *Rational Clinical Examination,* and throughout the clerkship, led brief head-ears-eyes-nose-throat-focused physical diagnosis rounds. Students were assessed at the beginning and end of clerkship on outcomes mapped to Kirkpatrick's first three levels (reaction, learning, behavior). This included five-point Likert scale surveys on confidence (1= "Not at all confident," 5= "Extremely confident"), multiple choice questions on knowledge, and clinical skills evaluation using a rubric based on the JAMA article and an Elsevier Clinical Skills checklist. Students provided both quantitative and qualitative feedback of their perceived benefit from the curriculum. A control group received the survey at the end of their clerkship without experiencing the curriculum. T-tests compared end-of-clerkship results of the intervention group to their results at the beginning of the clerkship and to the control group.

Results: Of 19 intervention group students, 12 (63%) completed surveys and 8 (42%) completed clinical skills assessments at the start and end of clerkship. Post-intervention, students had significantly higher average scores on confidence (4.1 vs 1.6, $p<0.001$), knowledge (74 vs 42% correct, $p=0.002$), and skills (mean satisfactorily-performed items 6.8 vs 5.1, $p=0.009$) compared to pre-intervention scores. They also scored higher on confidence (4.1 vs 3.0, $p=0.001$) and knowledge (74 vs 50% correct, $p=0.008$) compared to the control. 100% of students felt that they benefited from the curriculum.

Conclusions: A resident-led physical diagnosis curriculum improved clerkship students' knowledge, confidence, and skills related to strep pharyngitis diagnosis. This type of activity can be useful in systematically achieving total compliance for required clerkship skills.

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CASES OF ADRENAL INSUFFICIENCY WITH COMBINED INHALED CORTICOSTEROID/LABA

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Objective: To review three cases of growth failure and adrenal insufficiency in pediatric patients who were prescribed inhaled mometasone furoate/formoterol fumarate.

Study Design: An IRB was submitted and approved prior to initiation of this study. All research information was retrieved using the Research Derivative which is a database of clinical and related data derived from the Vanderbilt University Medical Center's clinical systems and restructured for research. We used inclusion and exclusion criteria to identify three patients via the Research Derivative. Inclusion Criteria: Any pediatric patient (age <18 years old prescribed mometasone furoate/formoterol fumarate who had a diagnosis of asthma AND a diagnosis of adrenal insufficiency. Exclusion Criteria: Any pediatric patient who had concurrent use of an oral corticosteroid while on mometasone furoate/formoterol fumarate were excluded. We used a data collection sheet to identify key information from each patient's chart review and then summarized each patient's case.

Results: Prolonged inhaled corticosteroid use can lead to clinically significant adrenal suppression and growth failure. Two of the patients required daily physiologic steroids and stress dose steroids. One patient required only stress dose steroids when weaning off mometasone furoate/formoterol fumarate to a different inhaler. Two patients required growth hormone injections and one patient had improvement of his linear growth after changing to a different inhaled corticosteroid/LABA. All three of these pediatric patients were prescribed mometasone furoate/formoterol fumarate prior to its approval for pediatric patients in their age group (5-11) and therefore, received a higher dose than that approved in 2019 for their age.

Conclusion: Pediatric patients presenting for short stature evaluation should have a thorough history and physical with medication review. Prolonged inhaled corticosteroid use increases risk of adrenal suppression; symptoms include nausea, vomiting, or hypoglycemia. Performing an ACTH stimulation testing may be needed to evaluate for iatrogenic adrenal insufficiency. Collaboration with pulmonology is necessary to achieve appropriate asthma control while minimizing side effects. When switching inhalers, it is also important to educate patients on the symptoms of adrenal insufficiency – abdominal pain, vomiting, fatigue, weight loss. In conclusion, inhaled corticosteroid can be systemically absorbed, resulting in significant endocrinopathies and prescribing physicians should carefully monitor pediatric patients for these side effects.

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EFFECTIVENESS OF A TRAINEE-LED ETHICS CURRICULUM FOR PEDIATRIC RESIDENTS

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Background: Biomedical ethics is pertinent to a wide range of clinical settings in pediatric residency training. The AAP recognizes that all pediatric residents should have a foundation in the core competencies of bioethics and pediatric specific domains. However, many residents are not exposed to a formal curriculum that addresses these topics.

Objective: Our primary objective was to determine the effectiveness of a trainee-led structured ethics curriculum for pediatric residents.

Study Design: Pediatric residents at a single institution participated in five bioethics lectures over the course of an academic year. Each lecture was provided by a pediatric resident or fellow and developed with faculty mentorship. Topics covered were related to pediatric ethics and chosen by the presenter; the topics represented in the AAP Bioethics Case Based Teaching Guide for Resident Training were provided as examples. Residents completed anonymous pre- and post-lecture board style questions related to the topic of the lecture. Residents also completed a retrospective pre-post survey at the completion of the lecture to assess their perceived change in knowledge and comfort with the ethics topic. Descriptive statistics and statistical hypothesis testing were used to analyze differences in knowledge and comfort.

Results: The five lecture topics chosen by presenters were adolescent decision making, uncertain prognosis, religious and cultural considerations in care, the critically ill newborn, and unilateral DNR. Following each lecture, an average of 8 residents completed the retrospective pre-post survey (range = 5-14). Using a Likert scale from 1 (very poor) to 5 (excellent), residents reported that their average knowledge about the ethics topic, as well as comfort in managing a clinical scenario involving the ethics topic, improved after having listened to the lecture. These trends were significant ($p < 0.05$) in two of the five lectures (adolescent decision making and unilateral DNR). There was no significant difference in the residents' performance between the pre- and post- lecture objective questions.

Conclusion: A trainee-led ethics curriculum can be effective in improving residents' reported knowledge about pediatric ethics topics and comfort in managing clinical scenarios involving these ethics concepts. This study relied on survey data and was limited by a low number of respondents. Further work is needed to determine how a curriculum can lead to observable changes in residents' clinical knowledge and practice involving biomedical ethics.

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DIAGNOSTIC CONVERGENCE: A NOVEL PHENOMENON IN THE DIAGNOSTIC PROCESS OF MENDELIAN GENETIC DISORDERS

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Objective: To investigate the phenotypic presentation of Mendelian disease across the diagnostic trajectory in the electronic health record (EHR).

Study Design: We applied a conceptual model to delineate the diagnostic trajectory of Mendelian disease to the EHRs of patients affected by one of nine Mendelian diseases. We assessed data availability and phenotype ascertainment across the diagnostic trajectory using phenotype risk scores (PheRS) and validated our findings via chart review of patients with hereditary connective tissue disorders.

Results: We identified 896 individuals with genetically confirmed diagnoses, 216 (24%) of whom had fully ascertained diagnostic trajectories. PheRS increased following clinical suspicion and diagnosis ($p<1x10-4$, Wilcoxon rank sum test). We found that of all ICD-based phenotypes in the EHR, 66% were recorded after clinical suspicion, and manual chart review yielded consistent results.

Conclusion: Using a novel conceptual model to study the diagnostic trajectory of genetic disease in the EHR, we demonstrated that phenotype ascertainment is, in large part, driven by the clinical exams and studies prompted by clinical suspicion of a genetic disease, a process we term diagnostic convergence. Algorithms designed to detect undiagnosed genetic disease should consider censoring EHR data at the first date of clinical suspicion to avoid data leakage.

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IDENTIFYING AND EVALUATING THE ROLE OF POTENTIALLY DISEASE-CAUSING CARDIAC INDELS IN SUDDEN UNEXPLAINED INFANT DEATH (SUID)

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Objective: Sudden unexplained infant death (SUID) is a leading cause of death in the first year of life. About 10% of SUID cases harbor variants in cardiac channelopathy or cardiomyopathy genes, however insertion/deletions (indels) in these genes remain underexplored and population frequency data is often lacking. We hypothesized that indels in channelopathy and cardiomyopathy genes are overrepresented in SUID cases vs controls (explained deaths).

Study Design: We extracted DNA from left ventricular tissue collected at autopsy and performed whole exome sequencing on 243 unexplained SUID case samples and 80 controls, all < 1 year of age. Indels were called with GATK best practice pipelines for germline variant calling and filtered using a list of 174 channelopathy and cardiomyopathy candidate genes. Indels were manually reviewed and classified based on ACGME criteria using the Genoox Franklin online platform, with likely pathogenic (LP), Pathogenic (P), or variant of uncertain significance (VUS) included in the final results. Indels were considered novel if they were not previously reported in ClinVar or gnomAD.

Results: We identified 97 (4 P, 54 LP, 39 VUS) potentially disease-causing indels across all samples. The SUID group had 68 total indels, 29 of which were in genes unique to the SUID group. In decedents with known cause of death, there were 29 total indels, 9 of which were in genes unique to this control group. 59 total indels were spread across 11 genes that were shared between the two groups. There was no significant difference in number of samples with VUS, LP, or P indels between unexplained (12%) and explained groups (17.5%, p=0.205). There was also no significant difference in the number of samples containing one indel versus multiple indels in unexplained (4%) versus explained groups (6.25%, p=0.939). All observed LP and VUS indels were novel, while 2 out of 4 observed P indels had been previously reported.

Conclusions: We observed indels in channelopathy/cardiomyopathy genes in 12% of SUID cases, with no significant difference in indel burden between SUID cases and controls. With a paucity of valid in silico models and population frequency data, evaluating pathogenicity of indels is limited. Improved in silico methods and larger databases for indels will be helpful as next generation sequencing data becomes widely available.

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TEACHING PEDIATRIC RESIDENTS STRUCTURAL COMPETENCY THROUGH EXPERIENTIAL, SELF-GUIDED COMMUNITY TOUR: NORTH NASHVILLE BLACK HISTORY TOUR

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Objective: Structural competency is the concept that social determinants of health and health systems affect patients' health and disease. This differs from cultural competency and humility which focuses primarily on individual biases. To address the knowledge gap of structural competency in pediatric residents, we developed a tour of North Nashville, which is a historically Black community to show policies and social determinants of health that impact these patients. Multimodal and experiential learning is shown to be a model for teaching social determinants of health.

North Nashville was a thriving Black community, but faced gentrification, redlining, and food resources. Now, the zip code is one of the highest incarcerated populations in the U.S. Despite this, the community has been resilient and initiated the Civil Rights Movement with the Nashville sit-ins. We created a tour that takes residents to different locations in the community to demonstrate social determinants of health such as food and medical deserts, adverse childhood experiences, and adultification leading to the school-to-prison pipeline. The policies that affected the community such as the Federal Highway Act of 1956 are shown with the interstate and how it intersected and disrupted the thriving community. Pediatric residents are encouraged to take the tour in small groups during their advocacy course rotation or elective time. A pre-set google map is given to them and they read along to a slideshow that teaches them about each location they go to.

Study Design: Residents take a pre-tour Redcap survey and post-tour survey where they answered a series of questions to assess their biases, knowledge of structural competency, and social determinants of health in the area. Residents created their own unique identifiers to blind the study. For continuous variables, t-test was performed. Qualitative answers will be coded thematically.

Results: On the pre-test survey, only 4/18 residents had heard of structural competency, and on the post-survey 14/15 were able to define the term. Residents had heard an average of 1.39 (+/- 1.55) policies on pre-tour survey compared to 3.47 (+/- 0.84) on post-tour survey (p-value<0.01). Residents had heard an average of 3.78 (+/- 1.83) concepts on pre-tour survey compared to 5.67 (+/- 0.52) on post-tour survey (p-value<0.01). Residents were asked to define the policies and concepts and had increased length of answers and higher percentage correct on pre vs post survey. Both of these demonstrated an absolute increase in knowledge. Residents were asked to reflect on their medical changes, and qualitative answers reflected themes of increased awareness, improving trauma-informed care, and offering increased resources to combat the lack of access in the North Nashville community. Further analysis will be coding the themes for the qualitative answers.

Conclusions: We created a novel method of teaching structural competency through a community tour that has increased knowledge of policies and concepts to pediatric residents. Further investigation will analyze how pediatric residents will change their medical practice based on this knowledge.

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