Child Health Research Institute

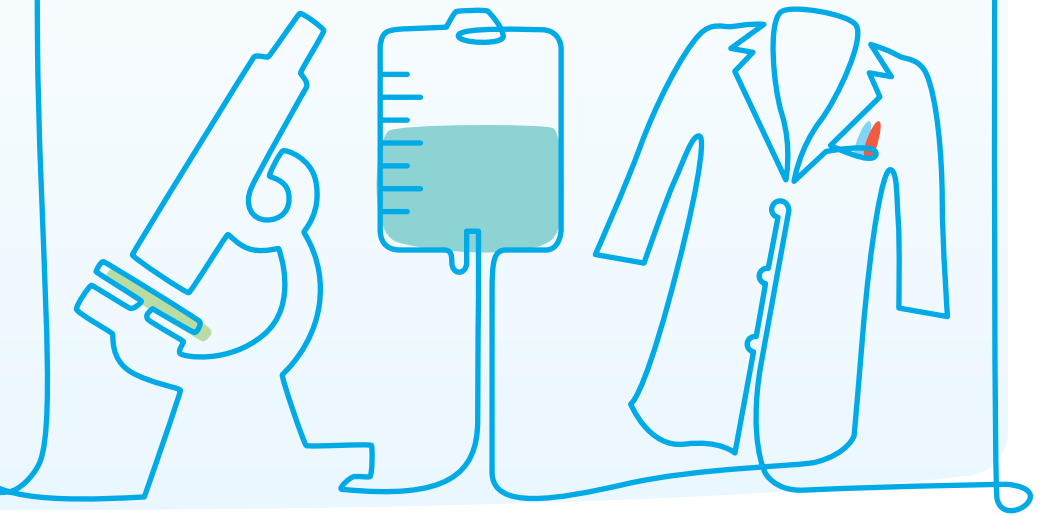
University of Nebraska Medical Center | Children's NEBRASKA

22nd ANNUAL

Pediatric Research Forum

May 9-10, 2024

Children's Nebraska



Welcome!

Welcome to the 22nd annual Child Health Research Institute's (CHRI) Pediatric Research Forum. A highlight of the academic year, the forum allows us to share our work and once again celebrate the scientific curiosity of CHRI child health investigators and our trainees and see what the future holds for innovations in the care of children everywhere.

Science is complicated, the route can be circuitous, and it can take years to complete projects and begin to answer important questions, yet, the scientific process, mentoring, research training, and career development are critical to the health and welfare of our children and our communities. This progress will not happen without each person here today. I am grateful for your attendance, interactions with our presenters, and your engagement with this great event.

The forum has been a staple of our celebration of academic work of trainees and faculty, from when it started within the department of pediatrics to now, in 2024, with the resources of CHRI supporting our research. Seeing trainees, faculty and staff present in both poster and oral formats provides evidence of how we work together to improve the health of the patients we all care for in our clinical work. The breadth and depth of research is awe-inspiring. We have research presented in multiple domains including clinical, translational, basic science, biomedical-informatics and public health. This is a great opportunity to showcase the diversity of CHRI investigators from across Children's Nebraska, UNMC, the greater University of Nebraska system and Creighton University. Working together in multi-disciplinary teams, we can impact child health with our research endeavors.

As you know, great events like this take a lot of expertise and planning, and I would like to recognize the CHRI team for organizing our event again this year and the volunteers for making everything happen today.

Please enjoy yourself today as we celebrate child health research at UNMC and Children's Nebraska, and I encourage you to pause and congratulate the presenters you interact with for completing such impressive work.

Wishing you productivity in your own research.

Ann L Anderson-Berry, MD, PhD, FAAP
Professor, Pediatrics
Executive Director, Child Health Research Institute
Vice-Chair, Research, Department of Pediatrics
Division Chief, Neonatology
University of Nebraska Medical Center
Vice President for Research, Children's Nebraska
Dr. John and Patti Sparks Chair of Pediatric Research

Agenda

Thursday, May 9

4:30 P.M. WELCOME (GLOW AUDITORIUM)

Ann L. Anderson-Berry, MD, PhD
Executive Director, CHRI
Professor, Department of Pediatrics, UNMC
Vice President for Research, Children's Nebraska

KEYNOTE PRESENTATIONS

Wings of Fire
Ram Kumar Subramanyan, MD, PhD, FACS
Chief, Division of Pediatric Cardiothoracic Surgery
Professor of Surgery, University of Nebraska Medical Center

5 P.M. AWARD CEREMONY

Trainee Awards

5:45-7 P.M. RECEPTION & POSTER SESSION (CHILDREN'S SOLARIUM)

Friday, May 10

8 A.M. GRAND ROUNDS (GLOW AUDITORIUM)

Paul Witt, MD
HO-II Pediatric Resident

8:30 A.M. MEDICAL STUDENT AWARD CEREMONY

Speaker Bios

Ram Kumar Subramanyan, MD, PhD, FACS

Ram Kumar Subramanyan, MD, PhD, FACS, is a pediatric cardiothoracic surgeon-scientist. After finishing medical school in India, he completed his General Surgery training at the University of Southern California ("USC") under Tom R. DeMeester, MD. He subsequently trained in Thoracic Surgery at USC and Congenital Cardiac Surgery at Children's Hospital Los Angeles, under Vaughn A. Starnes, MD. He also has a PhD from USC, studying membrane protein biology and cell-cell interaction.

Dr. Subramanyan is currently the chief of pediatric cardiothoracic surgery at Children's Nebraska, Omaha and professor of surgery at University of Nebraska Medical Center. In addition to practicing the full spectrum of pediatric cardiothoracic surgery, he runs an extramurally funded research lab that studies cardiac outflow track development and cardiomyocyte biology. He participates in robust translational research initiatives, including being the site lead on four regenerative therapy clinical trials for children with single right ventricle heart disease. Dr. Subramanyan has published more than 100 peer-reviewed publications, authored several textbook chapters, and has delivered many invited lectures and presentations. He is the editor of the congenital section of the Seminars in Thoracic and Cardiovascular Surgery and is on the editorial board of three other major surgical journals. He has served on the study sections of various funding agencies, including the NIH and American Heart Association and currently serves as Chair of the Society of Thoracic Surgeons Congenital Heart Surgery Database and the Vice-Chair of Workforce on National Databases. He is also a member of the executive council of the Western Thoracic Surgical Association and participates in several committees in national organizations.

Dr. Subramanyan is married to Charanya Ram Kumar, a software executive, and they have two wonderful children – Adrishya and Vivash. In addition to all manner of family escapades, Dr. Subramanyan's enjoys various forms of music and travel.

Paul Witt, MD

Paul grew up in Omaha, Nebraska. He graduated from Creighton Prep High School in 2014. He completed his undergraduate degree at Marquette University in Milwaukee, Wisconsin in 2018. He completed medical school at the University of Nebraska College of Medicine and graduated in 2022. He is currently a second-year pediatric resident at the UNMC/Creighton/Children's joint residency program and will be one of the co-chief residents from 2025/2026.

Table of Contents

14. Stressed Erythropoiesis in Liver of Neonatal Preclinical Murine Model of Phlebotomy induced Anemia
15. Investigation of Novel Combinatorial Strategies for Treatment of Neuroblastoma
16. Neuroblastoma Presenting as Opsoclonus Myoclonus Syndrome
17. Spondylolysis, Spondylolisthesis, and Associated Variables in Pediatric Patients with Osteogenesis Imperfecta: Follow-up from a 2011 Study
18. A Central Resource for Genetically Engineered Models useful for CHRI Researchers
19. Investigating the Pathogenesis of Hypertensive Disorders of Pregnancy: Role of Placental Inflammation and Mitochondria
20. Urban and Rural Maternal Postpartum Depression Scores in NICU Follow-up Visit
21. Who Chooses Water Births?
22. Predictors of Pediatric Cancer Survival in Iowa and Louisiana: A Multilevel Analysis of SEER Data
23. TCF12-Related Craniosynostosis with Recurrent Multi-suture Synostosis
24. **Does Routine Upper GI Series before Gastrostomy Tube Placement Add Value: A Retrospective Look Over a Decade?
25. Comparison of Clinically Relevant Factors Between Infants Born at 33 and 34 Weeks Gestation at CHI Bergan Mercy
26. Myeloid Specific Deletion of Triggered Myeloid Receptor-1 (trem1) Attenuates Murine Transfusion-Associated Necrotizing Enterocolitis Injury
27. Corticosteroids on Renal Function in Preterm Infants
28. Multi-Modal Ensemble Learning for Categorizing Pediatric Acute Myeloid Leukemia
29. Trends in Age at Diagnosis of Turner Syndrome in the United States
30. Synovial Sarcoma Presenting as a Chest Mass in a 16 Year Old Girl with Tuberculosis
31. A Case of Acute Ischemic Stroke in a 16-year-old

32. Addressing Social Determinants of Health Challenges in a Rural Migrant Population and the Unanticipated Benefits of a Local Research Team

33. Evaluation of Maternal COVID-19 Vaccination Status and Associated Demographic and Birth Outcomes

34. Behind the Curve: An Uncommon Cause of Malnutrition in a 7-Month-Old Male

35. Free Pediatric Healthcare Clinic: A Longitudinal Analysis of Challenges, Successes, and Demographic Outcomes of the 2019-2023 Back-to-School Clinic in Omaha, Nebraska

36. Needs Assessment to Support Continuing Education and Training Modalities for High-Consequence Pathogen Preparedness in Pediatric and Obstetric Populations

37. Validation of the Arabic Language Autism Diagnosis Inventory

38. Quality of Life Measures in the Study of Neurogenic Bowel Dysfunction among Individuals with Spinal Dysraphism

39. Congenital Chylothorax Resulting in Hydrops Fetalis in a Preterm Infant

40. **The Relationship Between Neonatal Anthropometric Measurements And Body Composition In Term Infants

41. **Predictive Modeling with Clinical and Laboratory Values in Neonates with Hypoxic-ischemic Encephalopathy

42. SAP30: A Novel Gene Governing Autophagy in Neuroblastoma Tumors

43. Data Collection Variability: A Global Profile of Neonatal Hypoxic-Ischemic Encephalopathy Registries

44. Posterior Urethral Valves and Ascites in a Male Neonate

45. Medical Record-Level Evaluation of Impact of Demographic and Socioeconomic Factors on Pediatric Neuro-Oncology Outcomes at Children's Hospital Colorado

46. Cold Truths Exposed: An Uncommon Culprit of Neonatal Hypothermia

47. Second Individual with Craniosynostosis and Microdeletion Including 14q22: Premature Fusion of Cranial Sutures and Copy Number Variation

48. Developing, Customizing, and Testing a Preventive Care Mobile Health Tool

49. A Rare Case of Acute Pancreatitis in a Pediatric Patient with Bifid Pancreatic Tail

50. Activated STAT3/P-TEFb Complex Functions in Medulloblastoma

51. **An Association between Declarative/relational Memory and Hippocampal Volume in Periadolescent Children: Preliminary Findings from the PRANK Study

52. TAB2-Related Disorder: A Review of the c.679C>T (p.Arg227*) Documented Cases and a Clinical Report

53. Oh, it's just RSV; when Bronchiolitis becomes Lethargy

54. Dual Diagnosis of DNMT3A- and KDM4B-Related Syndromes: An Epigenetic Combo

55. Neuropsychological Assessment in FIRES/NORSE Mouse Model

56. **Red Blood Cell Transfusion Causes Brain Inflammation in Murine Pups with Phlebotomy-Induced Anemia

57. Identification and Treatment Challenges of Disseminated Fungal Infection in Pediatric Patient with Pre-B ALL

58. Urbach-Wiethe Syndrome, a Rare Cause of Eyelid Margin Lesions

59. Social Health Programming is Not Associated with Reduced Stress Levels in Adolescent Girls

60. X-linked Opitz G/BBB Syndrome: A Case Report

61. **Platelet Indices are an Early Predictive Tool During Murine Transfusion-Associated Necrotizing Enterocolitis Injury

62. Identifying Medulloblastoma Subtypes by Leveraging Heterogenous Transcriptome Data with Batch Effects

63. Evaluating Physiologic Z-Score Changes and Subsequent Malnutrition Classifications in Extremely Low Birth Weight Infants Based on Birth Gestational Age

64. Should Infants Born at 35 Weeks Be Admitted into the NICU?

65. Transition to Adult-centered Care: Models for Successful Programs Serving Individuals living with Spina Bifida

66. CARM1 Arginine Methyltransferase as a Therapeutic Target for Medulloblastoma

67. Incorporation of Choice and Promotion of Autonomy for a Long-lasting Durable Treatment for Severe Challenging Behavior

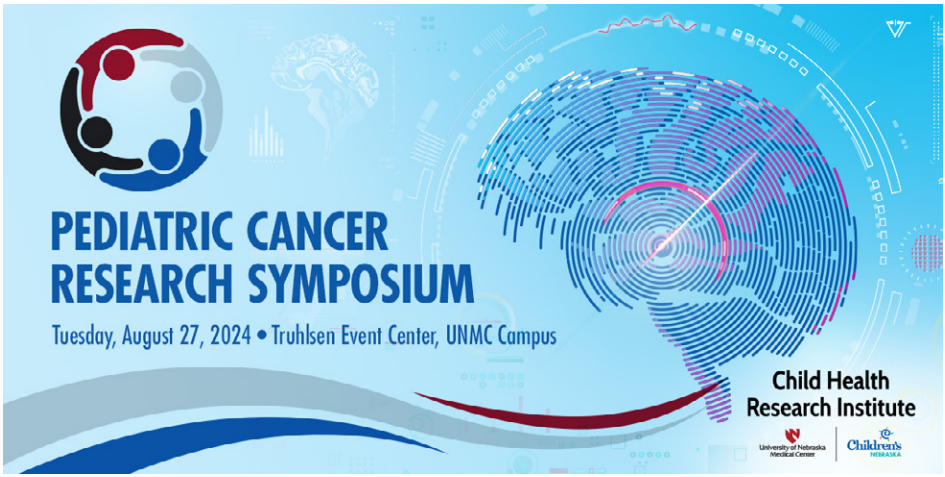
68. **Relationships Between Maternal Vascular Reactivity Index at 24-30 Weeks Gestation and Neonatal Birth Outcomes

69. Effects of the COVID-19 Pandemic on Maternal Mental Health

*** Notates abstracts awarded 1st, 2nd, or 3rd place in their designated category*

** Notates Pediatric Honors Program student*

Due to limited space, any references included may have been removed but are available by contacting the investigator.



Join CHRI today!

Scan the QR Code above to join CHRI. We have five tiers of membership: full, associate, affiliate, trainee and community. As a member you will have access to a collaborative network of researchers dedicated to improving child health outcomes, as well as a pool of professional resources to support research endeavors. Membership is also a great way to receive communications about upcoming available funding and research development opportunities, as well as our slate of sponsored events. Join us on November 8 for our flagship event, the CHRI Annual Scientific Conference.

2023-2024
Pediatrics Honors Program

The Pediatric Honors Program is an application-based program designed to foster the growth and development of UNMC students interested in pediatrics.

A key component of the program involves providing students with exposure to faculty in informal settings who will mentor students and share their own journeys within and outside of pediatric medicine. Many such interactions will come from monthly seminars (fireside chats) hosted by faculty. Fireside chats include faculty from diverse specialties, backgrounds, and experiences.

The program also aims to match faculty mentors with students to work in collaboration on a scholarly project, including research abstracts, manuscripts, case reports, or projects that have the potential to impact clinical care or the educational experience in pediatrics.

The underlying hope is that this program excites, energizes, and prepares them as they move toward their next step of residency and beyond.

We would like to recognize our senior medical students who have successfully participated in this year's Pediatric Honors Program:

Aly Freeman
Brian Smith
Caelyn Armshaw
Caleb Capellen
Drew Kortus
Eliza Fallick
Elizabeth Ramler
Jon Freese
Jordan Murman
Keaton Read
Morgan Klein
Nick Weaver
Nont Sricharoen
Olivia Paetz
Quinn Navarro
Sarah Sweeney
Sarah Tjards
Shaker Dukkipati
Stacie Schlange
Tazah Weinmaster
Trevor Lockard

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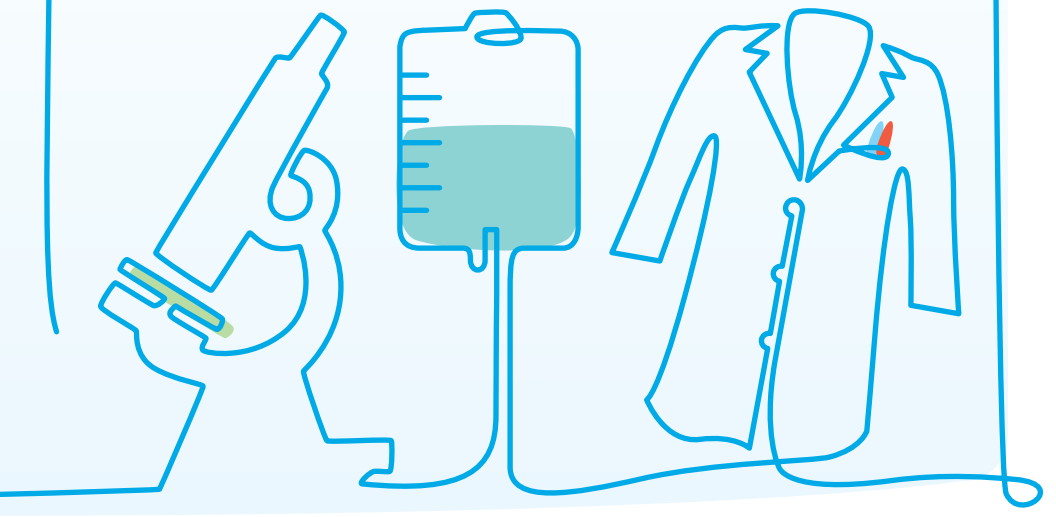
ABSTRACTS



Evaluating the Association Between Maternal Dietary Vitamin A Status and Fetal Kidney Development

Anum Akbar[1], Matthew VanOrmer[1], Rebecca Slotkowski[1], Taija Hahka[1], Rebekah Rapoza[1], Melissa Thoene[1], Corrine Hanson[2], Ann Anderson-Berry[1], Teri Mauch[1]

[1]Department of Pediatrics, University of Nebraska Medical Center, Omaha, NE 68198
[2]College of Allied Health Professions, University of Nebraska Medical Center, Omaha, NE 68198

Background: In vitro research suggests that kidney growth, as indicated by the total number of nephrons, may be influenced by vitamin A levels. Furthermore, limited human studies conducted in regions with prevalent vitamin A deficiency (VAD) have demonstrated that vitamin A affects renal parenchymal thickness and volume, which are proxies for the total number of nephrons in living humans. Our previous findings indicate that around 10% of pregnant women in Nebraska experience VAD. However, the impact of maternal dietary intake of vitamin A on fetal kidney development has not been explored in Nebraska women.

Significance: Suboptimal kidney growth and development can contribute to later renal dysfunction, hypertension, and cardiovascular issues. Therefore, identifying modifiable factors, such as vitamin A intake, is important.

Hypothesis: We hypothesize that maternal vitamin A intake affects fetal and infant kidney development.

Experimental Design: Following IRB approval, in our prospective cohort study, we recruited pregnant women at 18-22 weeks of gestation who planned to deliver at Nebraska Med. Women completed a food frequency questionnaire (DHQ III) to assess vitamin A intake between 24-28 weeks of gestation (n=72). Vitamin A intake, measured in retinol activity equivalents (RAE, mcg/day), encompassed food and supplemental sources. Bilateral kidney size and volume were measured between 16-23 weeks of gestation (n=69) and again 24-48 hours after birth (n=61). Kidney length and volume were correlated with maternal vitamin A intake using Spearman's R.

Results: A total of 72 maternal-infant dyads were included in this analysis, with a median maternal age of 32 years. The median daily RAE intake was 2099 mcg/day. Infant left kidney length (Rs=0.26; p=0.04) and volume (Rs=0.26; p=0.05) were positively correlated with continuous maternal vitamin A intake. After adjustment for total energy intake, a 1,000 mcg/day increase in maternal RAE intake predicted a 3 cm3 increase in infant left kidney volume (p<0.001). Similarly, a 1,000 mcg/day increase in maternal RAE intake predicted a 2.5x10-7 cm increase in infant left kidney length (p=0.01). There were no statistically significant associations between maternal vitamin A intake and the length or volume of the infant's right kidney.

Conclusion: None of our cohort mothers had VAD. We found only a positive correlation between maternal vitamin A intake and infants' left kidney length and volume. However, limitations include not measuring the association between serum vitamin A levels and kidney dimensions. Our future direction includes exploring these associations and investigating the link between maternal vitamin A status and renal parenchymal thickness.

Abstract 2

Bartonella henselae Hepatic Abscesses and Associated Osteomyelitis in a Pediatric Patient: A Case Report

Molly Antonson, BS[1], Lauren Klingemann, BS[1], Kari Neemann, MD[2]

[1]College of Medicine, University of Nebraska Medical Center, Omaha, NE
[2]Division of Pediatric Infectious Disease, University of Nebraska Medical Center, Omaha, NE

Background: Bartonella henselae is an aerobic, oxidase-negative intracellular gram-negative bacilli. B. henselae is transmitted to humans via cat saliva or scratch. Cat scratch disease, the typical clinical manifestation, presents in 85-90% of children as localized cutaneous or regional lymphadenopathy. The incidence of patients hospitalized with B. henselae is estimated to be 0.77-0.86 per 100,000 children less than five years old. Atypical presentations, generally reflecting bloodborne disseminated disease, can include hepatosplenic, cardiac, ocular, neurologic, or musculoskeletal involvement.

Case: A fully vaccinated 2-year-old male was admitted with 2.5 weeks of persistent fever and 1 day of right leg pain and limp. Prior to admission he had 7 medical encounters regarding the fevers without establishing a diagnosis or improvement. Laboratory findings on admission were notable for leukocytosis (WBC 14.4 109/L), anemia (10.1 g/dL), elevated inflammatory markers (ESR 80 mm/hr, CRP 3.2 mg/dL) and negative blood cultures. MRI of his right hip revealed an intraosseous abscess within the right ischium with surrounding myositis. Despite anti-staphylococcal coverage, fevers persisted, resulting in an abdominal MRI on Day 8 of hospitalization finding innumerable small hepatic ring enhancing lesions and abscess formation now in the pelvis. Despite negative pelvic abscess cultures, serology and broad-range PCR identified Bartonella henselae as the pathogen. The patient received a prolonged treatment course of azithromycin and rifampin with repeat imaging showing improvement in fluid collections at 6-weeks.

Discussion: Confirmed cases of B. henselae infection are rare secondary to their often-self-limiting nature. Blood and tissue cultures are often negative. Therefore, tests such as serology and PCR can be utilized in the diagnostic evaluation. This case represents an atypical, disseminated B. henselae infection with osteomyelitis and hepatosplenic involvement. Bartonella osteomyelitis most often occurs in the spine followed by the pelvic girdle. The differential diagnosis of the hepatosplenic radiologic findings could indicate numerous unique etiologies. Therefore, positive pathogen detection via PCR, culture, or serological titers is critical in the diagnosis.

Conclusion: Although osteomyelitis is a rare manifestation of B. henselae infection, it should be included in the differential diagnosis in pediatric patients presenting with fevers and musculoskeletal pain, especially in the setting of cat exposure. Hepatic involvement, another atypical manifestation, can cause significant morbidity. Therefore, abdominal imaging should be viewed as a critical step in the diagnostic workup of fever of unknown origin. While most cases of B. henselae resolve without treatment, in severe or disseminated cases, antibiotics such as azithromycin and rifampin should be utilized in treatment.

Effects of Transport Team Composition on Neonatal Intubation Success

Alyssa Averhoff, DO[1], Cori Kerr, APRN-NNP[2], Robyn Sawyer, BSN[2], Jodi Kozel, BS[2], Anna Perll, BSN[2], Junghyae Lee, PhD[1], Emily Mohs, APRN-NNP[2], Courtney McLean, MD, MS[1,2]

[1]Department of Pediatrics, University of Nebraska Medical Center
[2]Children's Nebraska

Background: Neonatal transport is necessary to move the smallest and sickest patients. Various team configurations exist for neonatal transport, yet little research has been done on optimal transport team compositions. One major concern with altering team composition is the ability to intubate neonates. Our institution transitioned from neonatal nurse practitioners (NNP) for neonatal transport to a critical care transport team (CCT) comprised of critical care nurses and paramedics.

Significance of the Problem: Understanding neonatal intubation success with variable transport team composition can help institutions form safe and effective transport teams.

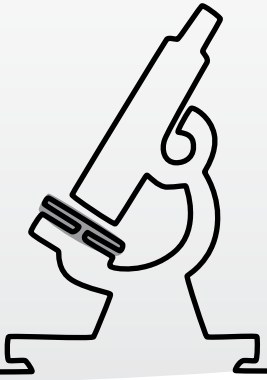
Hypothesis: We hypothesize no difference in intubation success when performed by NNP vs. CCT.

Experimental Design: We conducted a retrospective review of neonates <4 weeks of age intubated on transport from 2016-2023. Statistical analysis was completed using chi squared analysis and logistic regression to compare intubation success rates by NNP and CCT. Potential cofounding factors such as gestational age, birth weight, premedication, and videoscope use were also examined.

Results: We found 111 neonates required 119 transport member attempts for intubations. Infants were mean 34 weeks gestation (23-41 weeks) and birth weight of 2465 grams (500-4530g). Overall successful intubation occurred in 84% of the cases with no difference between NNP or CCT groups (p=0.68). When controlling for confounders, no statistical difference was found. (aOR: 0.197, CI:0.032-1.193). If our team members were not successful, the referral hospital provider intubated in 8 cases with 1 left extubated and 1 LMA placement.

First attempt success was higher in the CCT than NNP (51.8% vs. 30.6%: p=0.0324). With successful first attempt intubations, significantly more premedication (p=0.006) and videoscope (p=0.003) were used in the CCT group. When controlling for premedication and videoscope use, there was no difference in the first-time success of the two groups (p=0.9665).

Conclusion: Overall, neonatal intubation success was the same between NNP and CCT composition. This supports the use of varying levels of training on neonatal transports.



Abstract 4

Initial Temperatures and Prevalence of Hypothermia in Premature, Low Birth Weight Infants

Meghna Basavaraju, BS[1,2], Terence Zach, MD[1,2]

[1]Creighton University School of Medicine
[2]Creighton University Medical Center - Bergan Mercy, Omaha, NE

Background: Hypothermia has a significant impact on the outcomes of low-birth-weight infants. There are many causes of neonatal hypothermia, and the recorded temperature can be affected by the time the temperature was taken after birth, the birth weight, gestational age, etc. This study aimed to examine the relationships between these variables.

Hypothesis: We hypothesized that the warming protocols that have been implemented at CUMC Bergan Mercy have had a positive impact on health outcomes in premature, low birth weight infants.

Experimental Design: A retrospective study was performed to review 143 low birth weight infants born at Creighton University Medical Center- Bergan Mercy between January 2021 and May 2023. Data collected included birth time, admission time, gestational age, weight in grams at birth, and first/second/third recorded temperatures.

Results: The data showed that the average time after birth that the first temperature was taken was 39 minutes, the median was 19 minutes, and the distribution of temperatures were 68% normothermic, 20% mildly hypothermic, 8% moderately hypothermic, 1% severely hypothermic, and 3% hyperthermic. The average time to normal temperature for mild hypothermia was 82 minutes, 92 minutes for moderate hypothermia, and 134 minutes for severe hypothermia.

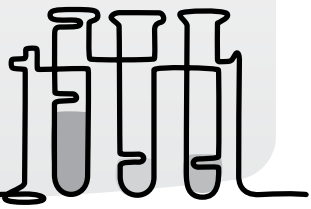
Conclusions: At CUMC-Bergan Mercy, infants born prematurely were treated with radiant heating, polyethylene bags, plastic lined hats, and heated and humidified gas. Numerous studies have shown that the use of heated and humidified resuscitation gas immediately after birth improves admission temperatures in preterm infants. The addition of heated and humidified resuscitation gas to the warming protocol may have a large impact on the prevalence of hypothermia in premature, low birth weight infants. The biggest limitations to this study were its length and sample size. The next goal of this study would be to compare the distribution of initial temperatures before and after the implementation of heated and humidified resuscitation gas in the initial treatment of infants in the NICU at CUMC in order to see the impact of this treatment.

Case Report of a Newborn with Chest Teratoma and Middle Cerebral Artery Infarct

Mustafa Beidas, BS[1], Eric Pederson, MD[1], Terence Zach, MD[2]

[1]Creighton University School of Medicine
[2]Department of Pediatrics, Creighton University School of Medicine
[3]CHI Health Creighton University Medical Center-Bergan Mercy

We report the clinical experience of a female infant born at 33 weeks gestation presenting with a chest teratoma who subsequently developed a stroke. Teratomas are tumors that are derived from the three germ cell layers, ectoderm, mesoderm, and endoderm. The incidence of teratomas is approximately 1 in 4000 live births. Mediastinal tumors originate from pluripotent embryonic cells. Mediastinal teratomas represent 10% of congenital teratomas. In our case, a premature infant developed respiratory distress after birth. Chest x-ray revealed a mediastinal mass. An echocardiogram on day 1 revealed a moderately dilated right ventricle with depressed function and bidirectional flow at the ductus arteriosus. On day 2, she developed seizures. A brain MRI revealed an acute large stroke in the distribution of the right middle cerebral artery. On day 11, she had a resection of the mediastinal mass which was determined to be an immature teratoma. Post-operatively she was a poor feeder with severe gastroesophageal reflux. On day 64, she had placement of a gastrostomy tube and was discharged on day 69. This case describes the unusual occurrence of a congenital immature teratoma of the mediastinum complicated by an acute stroke in the distribution of the middle cerebral artery.



Abstract 6

The Neuroblastoma Anti-Tumor Immune Response: Macrophage Modulation by Amyloid Precursor-Like Protein 2

Gabrielle L. Brumfield[1,2], Shelby M. Knoche[1,2], Alaina C. Larson[1,2], Kenadie R. Doty[1,2], Brittany Poelaert[1,2], Benjamin T. Goetz1,2, Poomy Pandey[1,2], Donald W. Coulter[2,3,4], Joyce C. Solheim[1,2]

[1]Eppley Institute, UNMC, Omaha, NE
[2]Fred & Pamela Buffett Cancer Center, UNMC, Omaha, NE
[3]Department of Pediatrics, UNMC, Omaha, NE
[4]Children's Nebraska, Omaha, NE

Background: Neuroblastoma (NB), a pediatric cancer of immature sympathetic nervous tissue, has a dismal five-year survival rate of only ~50% in high-risk patients. One contributor to meager survival rates for NB is insufficient immune-mediated tumor clearance due to the infiltration of pro-tumor, also called anti-inflammatory, macrophages. These anti-inflammatory macrophages augment angiogenesis, inhibit CD8+ T cell responses, and promote metastasis. Alternatively, macrophages with an anti-tumor, also referred to as pro-inflammatory, phenotype can aid the anti-NB immune response through release of inflammatory cytokines for additional immune cell recruitment, antigen presentation to T cells, and direct killing of tumor cells by phagocytosis. My findings associate anti-inflammatory macrophages with higher expression of amyloid precursor-like protein 2 (APLP2). In tumors, my laboratory has shown APLP2 expression enhances cancer cell migration and reduces surface level major histocompatibility complex (MHC) class I. These phenotypes (i.e., increased migration and lowered MHC expression) are also characteristic of anti-inflammatory macrophages, consistent with possible functional roles of APLP2 in this macrophage population.

Significance of Problem: Current treatment regimens for NB are largely insufficient in total disease elimination, as greater than half of high-risk patients have relapse after completion of standard therapy. In part, inadequate immune recognition of NB permits relapse. Therefore, there is clinical need to identify factors contributing to the anti-inflammatory macrophages that drive immune evasion and tumor survival, as well as therapeutic targets for enhanced production of their pro-inflammatory counterparts.

Hypothesis: The central hypothesis of this study is that APLP2 promotes an immunosuppressive phenotype in NB by suppressing inflammatory macrophage reactivity.

Experimental Design and Results: U937 monocyte-like cells and primary murine macrophages from wild type and APLP2-knock out (KO) mice were analyzed by flow cytometry and western blotting for APLP2 expression and phenotypic shifts post stimulus (NB cell-conditioned media, cytokines, PMA). Macrophage treatment with NB-conditioned media induced an anti-inflammatory phenotype. These anti-inflammatory macrophages had increased APLP2 expression compared to pro-inflammatory macrophages, and upregulated APLP2 expression was also observed in a model of monocyte-to-macrophage transition. Stimulation of APLP2 KO primary macrophages with pro- and anti-inflammatory stimuli resulted in increased Arginase-1+ anti-inflammatory macrophages at baseline and expanded mixed phenotype iNOS+Arginase-1+ cells with anti-inflammatory stimulation.

Conclusions: Increased APLP2 expression is associated with anti-inflammatory macrophages and suppression of inflammatory macrophage response. We anticipate identifying the influence of APLP2 in NB-reactive macrophages will contribute to future understanding of macrophage physiology and identification of potential therapeutic targets for this pediatric cancer.

Identifying Risk Factors for Significant Hyponatremia during Vasopressin Administration in Neonates

Hailey Cheek[1], Elizabeth Lyden[2,3], Eric S. Peeples[3,4,5]

[1]University of Nebraska-Lincoln
[2]Department of Biostatistics, University of Nebraska Medical Center
[3]Child Health Research Institute
[4]Department of Pediatrics, University of Nebraska Medical Center
[5]Children's Nebraska

Background: Although a growing body of literature has demonstrated that vasopressin is likely an effective method to raise blood pressure in neonates, limited literature exists detailing the safety of this medication in neonates. Specifically, local experience has raised concerns about the development of significant hyponatremia with vasopressin use; a concern not observed in the early small, published trials.

Significance: A better understanding of the risks and benefits of vasopressin administration in neonates could improve current clinical guidelines to help ensure the safe administration for blood pressure support in neonates.

Hypothesis: The development of significant hyponatremia during treatment with vasopressin for blood pressure support in neonates will be associated with specific risk factors.

Experimental Design: This was a retrospective case-control study of infants admitted to the UNMC or Children's Nebraska NICUs from Jan 2013 to April 2023 who developed significant hyponatremia during vasopressin treatment (cases) versus controls who had appropriate sodium concentrations throughout vasopressin treatment. Significant hyponatremia was defined as <130 mEq/L at any point during the first seven days of administration. Demographics, serum electrolyte, daily total fluid intake, and daily output values were abstracted from the medical record.

Results: A total of 47 infants met inclusion criteria: 22 developed significant hyponatremia. There were no significant differences in demographics (gestational age, sex, birth weight, Apgar scores, etc.) between groups. Those infants who developed hyponatremia started vasopressin with higher initial creatinine and initial daily total fluid administration. The hyponatremia group also demonstrated a longer vasopressin treatment duration. There were no differences in starting dose, peak dose, or the day of life vasopressin was initiated between groups.

Conclusions: These results suggest that infant who developed significant hyponatremia during vasopressin administration had lower serum sodium and serum creatinine and daily total fluid intake at the start of treatment. These findings can aid in the development of future clinical guidelines that stratify patients by risk to ensure safe and effective usage.

Abstract 8

Treatment of Rare Late Onset Sepsis in a Very Low Birth Weight Newborn

April Cooke, M3[1], Terence Zach, MD[1]

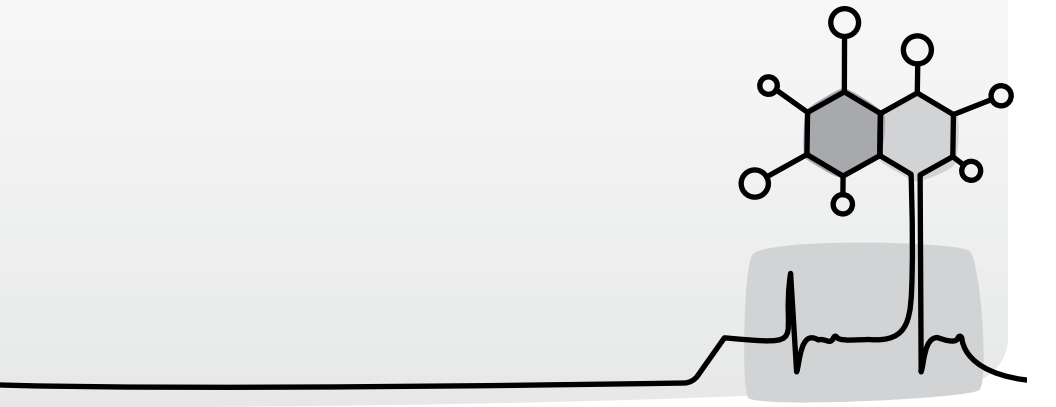
[1]Creighton School of Medicine

Neonatal sepsis is a major cause of mortality and morbidity in neonates that are preterm (<34 weeks) and of very low birth weight (VLBW). Late onset sepsis (LOS) as seen in this case report refers to sepsis occurring over 72 hours after birth. The risk of LOS increases with decreasing gestational age up to 32 percent for neonates born prior to 23 weeks. Risk of LOS also increases with decreasing birth weight up to 43% for neonates weighing less than 750 grams. LOS presents with a larger variety of pathogens compared to early onset sepsis, the most common being coagulase-negative staphylococci (CoNS). This can be acquired at birth or from environmental horizontal transmission. Neonatal sepsis with Enterobacter species is a rare event, and one that can be difficult to treat and is associated with high mortality. We report a case of Enterobacter cloacae sepsis in a very low birth weight 28-week neonate. This newborn weighed 990 grams at birth and was born to a 21-year-old G3P0020 woman with pregnancy complications consisting of obesity, oligohydramnios, intrauterine growth restriction, and preeclampsia. Due to non-reassuring biophysical profile of 2/8, an early cesarean section was performed. The membranes were ruptured at delivery revealing dark brown and red amniotic fluid. Almost immediately after both, the patient developed respiratory distress in delivery room and was intubated. Ampicillin and Gentamicin were started initially and stopped after negative blood cultures. Several days later following increased apnea alarms, blood cultures were drawn and grew Enterobacter Cloacae. This patient was treated successfully with two days of meropenem which was then switched to cefepime after a negative meningitis workup. Ultimately, after 14 days of treatment, this patient completed her antibiotics and had clear blood cultures. This case helps expand awareness of a rare cause of neonatal sepsis to increase the chance of early diagnosis and improve patient outcomes for an incredibly dangerous disease that causes up to 30% of infant deaths annually. Additionally, this case can help guide proper antibiotic usage and stewardship for future patients with similar presentations.

A Pre-health Program Designed to Boost Premed Applicants in Underrepresented Groups by Addressing Determinants of Academic Success Led by Medical Students as Near Peer Advisors

Sineah Donaldson, Nicole Bender, Hannah Im, Dr. Shirley Delair, Dr. Liliana Bronner

In the 2023 AAMC (Association of American Medical Colleges) report of the most recent medical school application cycle, Nebraska had only thirteen applicants out of 270 who identified as Black/African American or Hispanic. Of those thirteen applicants, only nine were accepted and matriculated into a medical school. These nine students represent three percent of the Nebraskan matriculants, yet those populations are almost 16% of Nebraska's total population. The report also shows the most recent class has a decrease in first generation matriculants; it has decreased the past 2 years. Research shows that increasing diversity of physicians improves healthcare access, outcomes, and patient satisfaction, but our medical school matriculation does not match our population. Long-term Enhanced Advising and Preparation (LEAP) aims to bridge the gap between under-resourced, under-advised, and underrepresented undergraduates whose goal is to become physicians which in turn increases the compositeness for medical schools. We recruit students from the Summer Health Professional Education Program (SHPEP) that are interested in becoming medical physicians. The program includes 1-on-1 advising for up to 5 years, near-peer advising with medical students, bimonthly group advising sessions, and access to resources and tools to improve their application competitiveness. We address social, economic, educational, and environmental determinants for academic success through personalized advising by using a custom intake survey. Having access to advice from people who have either been through the process of applying to medical school or have worked with admission committees can give undergraduate students more insight into how best to present themselves in their applications and interviews. These people consist of hired and volunteer medical students that create or help implement a curriculum for education of processes, one-on-one advising, and small group advising for undergraduate students. Our program has advised 133 scholars since 2021, with our first cohort applying this 2024-2025 cycle. The next step is to interpret the effect it has had on the students who have applied to medical school as well as the qualitative surveys on student preparedness as they complete each step of the process of applying to medical school.



Abstract 10

Comparison of Hospital Stay Duration and Clinical Features between Water Immersion and Conventional Births

Elizabeth Dort[1,2], Victoria Johnson[1,2], Terence Zach, MD[1,2]

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Background: Water immersion during delivery is a growing practice as a non-pharmacological method of pain relief during childbirth. The American Academy of Pediatrics (AAP) and the American College of Obstetrics and Gynecologists (ACOG) do not currently recommend water immersion over conventional births due to insufficient data. Prior to hospital discharge, the AAP recommends 16 criteria be met to identify problems in the newborn. Criteria completion takes around 48 hours, making any discharge before 48 hours "early," hence increasing the newborn's readmission risk. It is unclear if water immersion deliveries remain in the hospital long enough for criteria completion.

Significance of the Problem: There is a need to further investigate variations between water immersion and conventional deliveries due to the lack of data and possibility of increased newborn readmission risk.

Hypothesis: We aimed to determine if there is a difference in postnatal length of stay and other clinical features between water birth and conventional deliveries.

Experimental Design: In this retrospective cohort study, newborns were delivered via conventional birth at CHI-Immanuel Hospital or water immersion birth at the CHI Birth Center at Immanuel. 76 neonates born via water immersion and 69 neonates born via conventional birth were identified. All 145 newborns and mothers were included in the data analysis. The data set includes newborns born from May 2019-February 2022. Each water immersion newborn was matched to a conventionally delivered newborn delivered within seven days at the same hospital. Newborn and maternal charts were reviewed. Data collected included: times between hospital admission and delivery, membrane rupture and delivery, delivery and hospital discharge, as well as 1-minute and 5-minute Apgar scores, and gestational age at birth.

Results: There are significant differences in the length of stay and other clinical features between water immersion and conventional deliveries. Average admission to delivery time for water immersion births was 2.85 hours versus 13.23 hours for conventional births. 54% of water immersion births versus 12% of conventional births were born within two hours of admission. Average time between delivery and discharge for water immersion births was 16.90 hours versus 38.52 hours for conventional births. 78% of water births versus 1.45% of conventional births were discharged within 24 hours.

Conclusions: Patients who select the water immersion birth method have a shorter postnatal length of stay. These newborns have less time to fulfill the discharge criteria recommended by the AAP leading to higher health risks and chances of readmission.

Nortriptyline Triggers Apoptosis in Group 3 Medulloblastoma by Inducing Mitochondrial Dysfunction

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[2]University of Nebraska Medical Center, Department of Biochemistry and Molecular Biology, Omaha, NE
[3]Children's Hospital & Medical Center, Department of Pediatrics, Omaha, NE

Background: Medulloblastoma (MB), the most prevalent pediatric malignant brain tumor, is categorized into four groups, with Group 3 (G3MB) being the most aggressive and comprising 25% of cases. G3MB patients have significantly lower survival rates (<50% at 5 years) compared to other subgroups (70-95%). Current treatments involve surgery, irradiation, and chemotherapy, but these can lead to significant late effects or therapy limitation due to toxicity, particularly in G3MB.

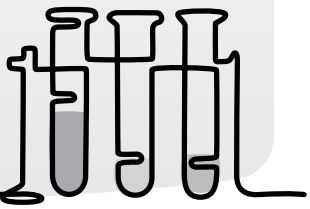
Significance: The dismal prognosis with G3MBs is driven by a) shortcomings of current chemotherapeutic regimens, as patients often cannot tolerate the high doses and b) lack of innovation in therapy stemming from poor understanding of mechanisms driving aggressiveness. As a result, recent advances in targeted therapies for other MB subgroups have not translated to G3MBs. Our work explores a unique drug discovery pipeline utilizing patient-derived RNA-sequencing data to find repositionable drugs for G3MB.

Hypothesis: We hypothesize that nortriptyline (NT), a tricyclic antidepressant, can be repurposed to treat G3MB by inducing apoptosis through mitochondrial dysfunction.

Methods: We conducted differential expression analysis on MB patient datasets (GSE148389, GSE164677) to generate a G3MB gene expression signature. This was analyzed against the LINCS database, yielding candidate antineoplastic compounds. Candidates were filtered for blood-brain barrier permeability and FDA approval. Functional assays evaluated drug effects on cytotoxicity, clonogenicity, wound healing, cell cycle, and apoptosis in G3MB cell lines (HDMB03 and D425). RNA sequencing of treated cells identified differentially regulated pathways to infer mechanism, followed by in vitro validation. Mitochondrial function, oxidative stress, and membrane potential were measured by Seahorse, MitoSOX and TMRM assays, respectively.

Results: Eighty-one candidates passed filtering. The leading drug class identified was antidepressants. Based on MTT assays, the top four candidates were nortriptyline, simvastatin, fluoxetine, and sertraline. Nortriptyline (NT) emerged as the lead compound, with IC50 of ~7uM (HDMB03) and ~11uM (D425). NT induced consistent anti-neoplastic effects on wound healing, colony formation, medullosphere generation, and apoptosis. Mechanistically, NT impaired oxidative phosphorylation without a compensatory increase in glycolysis, increased mitochondrial superoxide, and decreased mitochondrial membrane potential. SynergyFinder analysis revealed NT synergizes with cisplatin, a G3MB standard of care, in vitro.

Conclusions: Our integrated pipeline identified repurposable FDA-approved drugs with significant cytotoxic activity against G3MB cells. Nortriptyline's induction of mitochondrial stress and its potentiation of cisplatin present promising therapeutic avenues that will be further explored. This strategy could potentially offer more targeted, less toxic options for managing high-risk G3MBs, thus improving patient outcomes and quality of life.



Abstract 12

The Implementation of Guidelines for Skin Injury Among Spinal Neural Tube Defects: Is there Individualization of an Evidence-based Approach to Serve those Most at Risk?

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Background: Spina bifida (SB) is a neurodevelopmental disorder with neurocognitive deficits, restricted mobility, and decreased sensation. Given that many in this population have significant intellectual and executive function impairments, they are vulnerable to secondary conditions associated with the disorder, including skin breakdown and inadequate skin healing leading to chronic pressure injuries. Recent evidence-based guidelines to minimize skin-related issues in this population have been established, but it is unclear if they have been implemented and if novel treatment approaches for pressure injuries have been identified. The purpose of this systematic review was to examine and describe the literature on pressure injuries in children and adults with SB globally.

Methods: Utilizing the PRISMA guidelines for systematic reviews, relevant studies were identified in MEDLINE and EMBASE. The search strategy included terms and synonyms for "spina bifida" and "pressure ulcers". Studies written in English were included through March 2024. All included studies were focused on children and adults with SB. Review articles, validation studies, case reports, studies involving less than five subjects with SB, editorials, conference presentations, and animal studies were excluded.

Results: Eighty-six articles were identified from 1994-2024. Twenty-seven publications from studies conducted in eight countries met criteria for inclusion. Most (68.6%; 59/86) of the articles focused on factors associated with the prevalence of pressure injuries in children and adults with SB, which include male sex, lower socioeconomic status (SES), and older age. The prevalence of pressure injuries appears to be similar in both ambulatory individuals and individuals using a wheelchair. The location of pressure injuries was predominant in the feet and posterior pelvis. Less than one third (31.3%; 27/86) of the articles focused on either prevention strategies or treatment of injuries with the majority of these (n = 24) focusing on surgical approaches to mitigate injuries. Two studies addressed non-surgical treatments and only one examined prevention strategies.

Conclusions: Pressure injuries are a significant issue for many individuals with SB across the lifespan globally. Our findings suggest that redirecting guidelines to incorporate specific high-risk subgroups – specifically males, people of a lower socioeconomic status, and adults – is warranted. Given the prevalence and varying locations of pressure injuries in both ambulatory and wheelchair-using individuals, specific guidelines for these subgroups are also needed. In addition, it is critical that studies on prevention and non-surgical treatment options for pressure injuries include more individuals with SB.

Insights on Hypoxia Inducible Factors Trafficking Circulating Macrophages in Severely Anemic Murine Neonates

Megan Ferris[1], Balamurugan Ramatchandirin[1], Juanitaa George Raj[1], Arjun Subrramanya[1], Marie Amalie Balamurugan[1], Zainab D Lawal[1], Krishnan MohanKumar[1,2,3]

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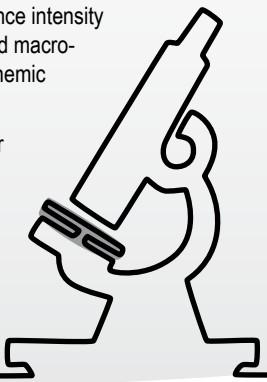
Background: Anemia is a physiologic phenomenon in all infants; however, it becomes pathologic in critically ill and premature infants who experience early, rapid declines in hemoglobin levels during concurrent illness. We have recently shown that the neonatal mouse model of phlebotomy-induced anemia causes chronic hypoxia in the intestine and is enriched with circulating inflammatory monocyte recruitment. Targeting this mechanism leads to the development of novel treatment strategies for anemia-related co-morbidities including red blood cell transfusion-associated necrotizing enterocolitis (TA-NEC).

Objective: To investigate the role of hypoxia-inducible factor-3 α (HIF-3α) in intestinally recruited monocytes and their functional activities in murine anemic neonates.

Methods: C57BL/6 mouse pups were studied in 2 groups (n=6 each): (1) naïve controls; (2) severely anemic. Pups were rendered severely anemic (hematocrit 27-32%) by facial vein phlebotomies on P2, 4, 6, 8, and 10. On P11, both groups were sacrificed, and the intestinal tissue was extracted and digested by collagenase to obtain a single-cell suspension. Ly6C+ monocytes were separated from the intestinal cell suspension by using Ly6C-biotin antibody and anti-biotin microbeads MACS method. Real-time qPCR was performed to analyze hypoxia-inducible factors (HIF-1α, HIF-2, and HIF-3) and key chemokine receptors (CXCR1 – CXCR6, CX3CR1). HIF-3α expression was confirmed by western blotting. Co-localization of Ly6C+ monocytes with HIF-3α was visualized by immunofluorescence staining of intestinal tissue sections from both groups and in human NEC tissue sections using CD14. A murine macrophage cell line overexpressing HIF-3a was used to investigate HIF-3a's role in CXCR2 expression via ELISA-based chemotaxis and phagocytosis assays.

Results: Severely anemic intestinal-derived Ly6C+ monocytes showed significantly higher expression of HIF-3α than control by qPCR (2.72±1.38) and immunoblotting, indicating that anemia-associated hypoxia was induced in intestinally recruited monocytes. Anemic monocytes also showed higher expression of the chemokine receptor, CXCR2 (5.82±1.24), than other migratory markers showing that hypoxia may induce gradual increased expression of CXCR2. Strong immunoreactivity for Ly6C+ monocytes with HIF-3α was noted only in anemic intestines but not in controls, confirming the hypoxic condition in monocytes. ELISA-based chemotaxis and phagocytosis assay showed a significant reduction of fluorescence intensity in HIF-3α-overexpressed macrophages than in scrambled-expressed macrophages, indicating that hypoxic monocytes are hyper-migratory to anemic intestine and defects in bacterial clearance, respectively.

Conclusion: This is the first study to describe the negative regulator of hypoxia-inducible factors such as HIF-3α directs circulating monocyte migration to the hypoxic intestine and these monocytes fail to perform bacterial clearance. These findings merit further evaluation of HIF-3a's role in causing and/or worsening NEC in severely anemic neonates.



Abstract 14

Stressed Erythropoiesis in Liver of Neonatal Preclinical Murine Model of Phlebotomy induced Anemia

Juanitaa George Raj[1], Balamurugan Ramatchandirin[1], Gopi Sundaramoorthy[1], Marie Amalie Balamurugan[1], Pramod Shrestha[2,3,4], Krishnan MohanKumar[1,2,3]

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Background: Anemia is a frequent diagnosis in premature and critically ill neonates, and its etiology is commonly subdivided into three major categories: phlebotomy/blood loss, decreased production, and increased destruction of erythrocytes that undergo accelerated postnatal turnover, triggering the levels of chronic hypoxia in mouse neonatal liver. Hypoxia is known to stimulate erythropoietin expression and regulate components of the hemoglobin synthesis pathway for promoting erythropoiesis by modulating erythroid maturation and proliferation. However, the role of phlebotomy-induced anemia (PIA) associated hypoxia on erythropoiesis in neonatal mouse developing liver is unclear. In this study, we are investigating the effects of PIA on hypoxia in the liver which is the hematopoietic organ in neonate.

Objective: Investigate the hypothesis that severe anemia in neonatal murine pups can cause chronic hypoxia and alter the erythropoietic niche in the liver.

Design/Methods: C57BL/6 mouse pups were studied in 2 groups (n=6 each) (1) naive controls, (2) severely anemic (hct 20-24%) Pups were rendered severely anemic by facial vein phlebotomies on P2 4,6,8 and 10. On P11, the liver tissue was extracted and used for single-cell RNA sequence analysis, mRNA analysis, protein analysis, and flow cytometry. For the scRNA seq experiments, liver tissues from control and severe anemic groups (n=6/each group) were processed through all steps to generate stable CDNA libraries (10x Genomics), sequenced on a NextSeq 500 (Illumina) and counts of nucleated RBC (NRBC) and their percentage measured by using Sysmex XN-1000 hematology analyser during each phlebotomy. Single-cell suspensions from the liver, bone marrow, and spleen were stained with antibodies against TER119 and CD71. Then, these cells were acquired by BD LSRII-flow cytometry followed by Flow Jo for gating the erythroid progenitors. Further mRNA expression and western immunoblotting for HIF genes (HIF-1α, HIF-2α, and HIF-3α) were performed for CD71 and TER119 cells isolated from the liver.

Results: The scRNA UMAP showed that PIA enriched the numbers of GYPA+ erythroid cell clusters with increased expression of DEGs of hemoglobin chains (HBB-61, HBB-62, HBA a1 HBA-a2) in severe anemic murine neonatal liver when compared to control liver. NRBC counts and their percentage was significantly increased during each phlebotomy compared to their respective age-matched controls. Consistent, flow cytometry analysis confirmed the higher frequencies (%) of CD71 erythroid cells were significantly increased in anemic liver, and flow gating with TER119 indicates the presence of immature erythrocytes and/or nucleated RBC than mature RBC showing that anemia-associated hypoxia skews the hematopoietic system toward stressed erythropoiesis with deficiency of maturation. Anemic liver-derived erythroid cells also showed increased expression of HIF3α. The erythroid-specific expression of HIF3α and its regulation on RBC maturation is currently under study.

Conclusion(s): Severe anemia-associated chronic hypoxia state in the liver-derived erythroid cells leads to increased expression of HIF-3α and alters the erythropoietic niche with increased production of erythroid cells with maturation deficits.

Investigation of Novel Combinatorial Strategies for Treatment of Neuroblastoma

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Background: High-risk neuroblastoma is a pediatric malignancy that employs immune evasion strategies: down regulation of MHC class I molecules on the tumor cells, infiltration of the tumor with regulatory T (Treg) cells, and release of immunosuppressive cytokines that impair dendritic cell (DC) antigen presentation, promote cytotoxic T cell exhaustion, and prevent effective CD4+ TH1 immunity. Successful immunotherapies for high-risk neuroblastoma must reverse this suppressive phenotype. In preclinical models of other cancers, chemokine CCL21 therapy has been shown to promote infiltration with CD8+ and CD4+ T cells and CD11c+ DCs, limiting tumor growth. Cyclophosphamide (CPX) is a standard chemotherapy for neuroblastoma, and our rationale behind combining CCL21 therapy with CPX is that immunomodulatory effects of CPX (observed in other cancers) include promoting DC antigen presentation and selectively depleting Tregs.

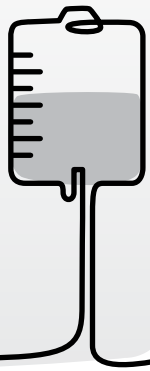
Significance of Problem: High-risk neuroblastoma has a poor prognosis, with the 5-year survival rate for high-risk neuroblastoma at a mere 46%, and so there is a clear and present need to develop superior treatment modalities for it.

Hypothesis: Our central hypothesis is that CCL21 will be an effective therapeutic approach for neuroblastoma in combination with low-dose, metronomic delivery of CPX.

Experimental Design: A prior study in our laboratory showed two-day therapy with nanoformulated CCL21, but not CCL21 alone, was effective against mouse neuroblastoma tumors. Because clinical implementation of CCL21 therapy will be facilitated if an effective CCL21 regimen can be established in combination with standard chemotherapy (such as CPX) and without a necessity for nanoformulation, we have begun testing CCL21 in alternative regimens along with low-dose, metronomic CPX.

Results: In a recent initial study, we have demonstrated a trend toward six-day, non-nanoformulated CCL21 therapy slowing tumor growth in a mouse model of neuroblastoma. Our current studies involve treating neuroblastoma tumor-bearing mice with both metronomic CPX and CCL21 therapy, comparing tumor growth rate and overall survival to CCL21, CPX, or vehicle alone. Furthermore, our in vitro studies have indicated that low-dose CPX chemotherapy increases cell-surface MHC class I expression on neuroblastoma cells, enhancing the antigenicity of the tumor cells.

Conclusions: Our results suggest CCL21 and CPX each have individual potential to facilitate immunological responses to neuroblastoma, and we will further assess their capabilities in tandem. In addition to testing CCL21 and CPX together in vivo, our future in vitro studies will interrogate the molecular mechanisms by which CPX treatment up-regulates MHC class I expression on neuroblastoma cells and facilitates tumor antigen presentation.



Abstract 16

Neuroblastoma Presenting as Opsoclonus Myoclonus Syndrome

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Background: Neuroblastoma is the most common extracranial solid tumor of childhood. It is an embryonic tumor of the sympathetic nervous system derived from neural crest cells. These tumors can arise anywhere throughout the sympathetic nervous system. The pathology of the tumor and malignant potential varies according to the degree of neural crest cell differentiation and stromal component. As these tumors can arise from different locations in the body and have varying malignant potential, there is a broad spectrum of clinical behavior and presentation.

Opsoclonus myoclonus syndrome is a rare presentation of neuroblastoma, reported in 1-3% of cases. The syndrome presents with rapid, dancing eye movements and rhythmic jerking of limbs and trunk. The myoclonus presentation of opsoclonus myoclonus syndrome is commonly mistaken for more common etiologies of cerebellar ataxia, particularly postinfectious acute cerebellar ataxia in children.

History/Presentation: A 3-year-old female presents with progressively worsening cerebellar ataxia and irritability, presumed to be postinfectious cerebellar ataxia, as work up including brain MRI and cerebrospinal fluid studies were unremarkable outside of mild sinusitis. She was started on IVIG and high-dose glucocorticoids and discharged to an inpatient rehabilitation facility. Two weeks later, she continued to have worsening ataxia and developed new, abnormal eye movements, concerning for opsoclonus myoclonus syndrome.

Physical Exam: Irritable, crying on exam. Extraocular movements intact, PERRLA. Dysmetria with intention, titubation and unsteady broad-based gait present. Motor strength and tone normal. Remainder of the physical exam unremarkable.

Diagnostic Evaluation: MRI brain, spine, chest, abdomen and pelvis remarkable only for a small nodule in the mediastinum. A MIBG scan and urine HVA/VMA within normal limits. Due to the severity and progression of her symptoms, despite a negative workup, the decision was made to biopsy the mediastinal nodule. Histology was positive for a ganglioneuroblastoma.

Diagnosis: Ganglioneuroblastoma; treated with surgical resection. Opsoclonus myoclonus paraneoplastic syndrome; treated with ACTH therapy and IVIG infusions

Discussion/Conclusion: Neuroblastomas can be difficult to diagnose due to their broad spectrum of clinical behavior and varying pathology of tumor subsets. Diagnostic testing may be negative, as urine catecholamines are only positive in 70-80% of cases and 10% of neuroblastomas are MIBG negative. If there is a high index of clinical suspicion, further evaluation is warranted. Opsoclonus-myoclonus is a rare but concerning presentation for neuroblastomas. Due to the rarity of this presentation, it may be misdiagnosed as postinfectious cerebellar ataxia in children on general hospital units and should remain on the differential diagnosis.

Spondylolysis, Spondylolisthesis, and Associated Variables in Pediatric Patients with Osteogenesis Imperfecta: Follow-up from a 2011 Study

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Background: Osteogenesis imperfecta (OI) is a rare genetic disorder that results in bone fragility and fractures, including spinal fractures and deformities. Our previous study from 2011 showed a prevalence of spondylolysis of 8.2% and spondylolisthesis of 10.9%. The average age of patients was 6.1 years at the time of study.

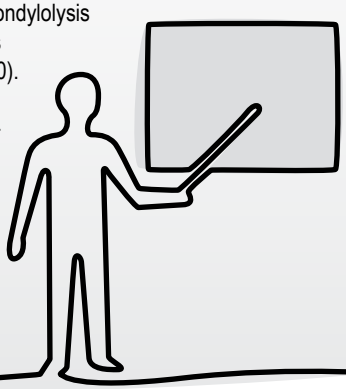
Significance: Spondylolysis and spondylolisthesis are common in patients with OI; however, these and other spinal deformities are not well understood in patients with OI nor well characterized in the literature, necessitating further exploration to guide clinical decision-making.

Purpose/Question: The purpose of this study was to evaluate these patients 10 years later to better understand the natural history of OI.

Experimental Design: An IRB-approved retrospective chart review was performed on the original 110 patients with OI enrolled in the prior study. Radiographic measurements in coronal and sagittal planes were performed with chart review to assess ambulatory status, OI type, and other relevant factors.

Results: 72 patients met the inclusion and exclusion criteria for this study. The average age of patients was 15.8 years, and 44% were Risser 4 or 5. In total, 33% (24/72) of the patients had radiographic evidence of either spondylolysis or spondylolisthesis. Spondylolysis was present in 15.3% of cases (11/72). Spondylolisthesis was present in 18.1% of the cases (13/72): 75% were isthmic and 25% were dysplastic. All spondylolistheses were grade 1. No surgeries were reported for spondylolysis or spondylolisthesis correction. All spondylolysis and spondylolisthesis were noted at L5-S1, other than one case of a concurrent L4-L5 and L5-S1 spondylolysis. Scoliosis was noted in 68% of patients (49/72). Comparing the current study to the 2011 study, there was no significant difference in ambulatory status ($p=0.17$). There was a higher incidence of spondylolysis ($p=0.01$), spondylolisthesis ($p=0.03$), and either condition combined ($p<0.01$) in the current study. Within the current study, comparisons were made between those who had spondylolysis or spondylolisthesis and those who did not. The presence of spondylolisthesis was correlated with higher angles of lumbar lordosis ($p=0.04$), but spondylolysis was not associated with lordosis ($p=0.43$). There was no correlation between spondylolysis and/or spondylolisthesis with the degree of thoracic kyphosis ($p=0.22$, $p=0.35$) or the presence of scoliosis ($p=0.58$, $p=0.60$). Ambulatory status correlated with the presence of isthmic spondylolisthesis only ($p=0.02$) and not with dysplastic spondylolisthesis or spondylolysis ($p=0.26$).

Conclusion: In our study, the incidence of spondylolysis and spondylolisthesis are notably higher than the 6-8% incidence rate which has been described in an otherwise healthy population.



Abstract 18

A Central Resource for Genetically Engineered Models Useful for CHRI Researchers

Channabasavaiah B. Gurumurthy[1]

[1]Mouse Genome Engineering Core Facility, UNMC

Background: Genetically engineered mouse (GEM) models are widely used for research involving every human disease. Over 70% of NIH-funded projects utilize mouse models.

Significance: In the past few years, several University of Nebraska Medical Center (UNMC)/Child Health Research Institute (CHRI) investigators have been interested in developing mouse models for their genes/diseases of interest, but some obstacles have prevented them from initiating their projects. For instance, generating disease models and breeding them takes at least two or more years. Also, such endeavors require larger resources (at least $100K or more) for personnel and operating costs, which are needed for testing a hypothesis or generate preliminary data for submitting an NIH R01 proposal.

Hypothesis: Mouse model projects are high-risk high-reward type and thus investigators require a lot of planning before venturing into such projects. We propose to solve this challenge through a central resource that would help projects of many pediatric researchers at much cheaper costs than it would be needed for CHRI to support several early-stage and/or established investigators wanting to utilize mouse models.

Experimental Design: The shared resource would develop some universal mouse models (for e.g., reporter models useful for lineage tracing experiments in an in vivo setting) and disease-specific mouse models including Cre-LoxP based gene expression systems. Unlike transgenic mouse cores elsewhere, UNMC mouse genome engineering core offers 'end-to-end services' in model designing. The core helps with all steps of mouse genetics including conceiving ideas of types of models useful for investigators' projects. For instance, whether transgenic or knockout and whether conditional or constitutive expressing type what type of CRISPR design and editing technology would be suitable for such model), and then the core designs and develops the models and custom breed them to establish the cohorts ready for experiments.

Results: This 'end-to-end service' offered at UNMC MGE core has eliminated many of the challenges investigators normally encounter when they begin their animal research projects. In addition, using the investigators projects as testbeds in the past, the core has developed technologies that are popular worldwide now, and the manuscripts on those technologies were published with numerous authors from the institution. One such example is Easi-CRISPR method, which has played a key role in earning numerous R01 awards and a few program projects to UNMC investigators. Because of such unique capabilities, and the worldwide recognition, UNMC MGE has attracted numerous investigators from outside seeking its services.

Conclusions: Through some minimal help from CHRI (with an average of $50K to $100K per year for next 1-2 years), the core can generate a few models, useful for investigators and concurrently develop new technologies, helping CHRI investigators to be part of the technology development publications and ultimately help them in securing extramural grants including NIH grants or equivalent awards in the coming years. Small investment on such a resource can have big impacts to many CHRI investigators in a long run.

Investigating the Pathogenesis of Hypertensive Disorders of Pregnancy: Role of Placental Inflammation and Mitochondria

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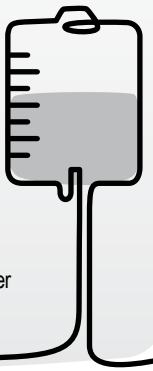
Background: Hypertensive Disorders of Pregnancy (HDP) contribute to 70,000 maternal and 500,000 fetal deaths annually worldwide. HDP is characterized by impaired placental trophoblast invasion and migration, triggering maternal inflammation. Elevated tumor necrosis factor alpha (TNFα) levels can disrupt mitochondrial function. Nuclear Factor Erythroid-2-Related-Factor-2 (NRF2) controls anti-inflammatory gene expression, including Mitochondrial Transcription Factor A (TFAM), which governs mitochondrial replication. NRF2-TFAM pathway dysregulation may lead to mitochondrial dysfunction in HDP. Resolvin D2 (RvD2), an omega-3 (n-3) fatty acid-derived specialized pro-resolving mediator (SPM), promotes anti-inflammatory and pro-repair processes. However, the precise mechanism by which SPMs regulate inflammation and mitochondrial function during HDP remains unclear.

Significance of the Problem: Limited knowledge persists regarding inflammatory signaling and metabolic dysregulation in HDP placenta, alongside the impact of TNFα and RvD2 on trophoblasts. This study bridges these gaps by revealing alterations in crucial mitochondrial and inflammatory genes within HDP placenta in vitro. Further, in vivo experiments demonstrate that RvD2 enhances placental cell migration without eliciting cytotoxic effects. RvD2 exerts protective effects on mitochondria by modulating anti-inflammatory genes, facilitating mitochondrial replication, and reducing oxygen consumption rates. These findings underscore the potential of SPMs as promising therapeutic targets for modulating inflammation and mitigating mitochondrial dysfunction.

Hypothesis: We hypothesize that Inflammatory associated signaling promotes metabolic imbalance and induces mitochondrial dysfunction that alters the fate trophoblasts.

Experimental Design: RNA-sequencing was performed on human placental cross-sections from HDP women, and the data were analyzed using Gene Set Enrichment Analysis with the hallmark gene sets from the human molecular signatures database. Human trophoblasts were subjected to TNFα (10-100 ng/mL) in vitro. RvD2 (10-100nM) was applied as a treatment strategy to mitigate inflammation and mitochondrial dysfunction. Migration assays were performed to measure trophoblast function. qPCR and immunoblots were used to measure NRF2 and TFAM mRNA and protein expression. Seahorse® was used to measure oxygen consumption rates (OCAR). LDH and CCK8 colorimetric assays were used to measure cytotoxicity and cell viability. One-way ANOVA or student t-test was performed.

Results: RNA-sequencing data identified notable changes in inflammatory and mitochondrial pathways in the human placenta, particularly showing elevated TNFα levels in HDP placenta in vivo. In vitro experiments demonstrated that RvD2 significantly enhanced trophoblast cell migration while TNFα inhibited it (RvD2: 42% vs. TNFα: 32%; p=0.019). TNFα exposure increased TFAM mRNA and protein levels in trophoblasts, which were mitigated by RvD2 treatment (TFAM relative expression to β-Actin: TNFα: 0.002 vs. TNFα+RvD2: 0.001; p=0.026). Nuclear NRF2 protein expression increased with the treatment of TNFα. Additionally, treatment of RvD2 modulated OCAR for maximal and basal respiratory rates and ATP production (ATP OCAR: RvD2: 119.7 vs. TNFα: 295 vs. RvD2+TNFa: 173; p=0.010; pmol/min/mg/mL). TNFα significantly decreased migration but did not affect cellular cytotoxicity or viability.



Conclusion: RNA-sequencing showed a change in mitochondrial and inflammatory pathways. RvD2 exhibits a protective role through modulation of the NRF2-TFAM pathway in the mitochondria of trophoblasts during TNFα-driven inflammatory insults and can functionally alter trophoblast migration.

Abstract 20

Urban and Rural Maternal Postpartum Depression Scores in NICU Follow-up Visit

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Background/significance/problem: Neonatal intensive care unit (NICU) hospitalization of newborns has been shown to have a negative impact on the mental health of postpartum women, with mothers of infants admitted to the NICU being 40% more likely to develop postpartum depression (PPD) than the general population. Nebraska statewide NICU follow-up program, Tracking Infant Progress Statewide (TIPS) serves families in both rural and urban areas and routinely conducts screening for PPD. To better understand caregiver's risks across geographical areas of the state, this study aims to assess the risk based on geographical residence for PPD in mothers of infants requiring a NICU hospitalization.

Methods: This is a retrospective review of the TIPS database, which includes demographic and medical information. An Edinburgh Postnatal Depression Scale (EPDS) was completed by mothers at the first TIPS follow-up visit at approximately 6-months corrected gestational age to screen for PPD. Based on the population of residence, infants were classified as living in an urban or rural area. An average EPDS score was calculated for both populations and compared via Mann-Whitney U test. Categorical data were analyzed using chi-square and binary logistic regression.

Results: For the 1,129 patients in the study, the average demographics were calculated: maternal age (30 years old), gestational age (32 weeks 3 days), birthweight (2.00kg), and length of NICU stay (49 days). Majority of infants were classified as living in an urban location (84.6%), Caucasian (76.5%), had private insurance (69.6%), and had married parents (78.9%). The average EPDS score for the urban population was significantly higher than the rural population (4.97 vs. 4.14, $p = 0.047$). There was also a significant association between high-risk EPDS scores (score >10) and living in an urban location ($X2(1) = 5.3$, $p = 0.021$). The logistic regression model showed that urban mothers have 2.117 times higher odds of being classified as high risk for PPD compared to mothers from rural areas and those with Medicaid have 1.903 times higher odds of being classified as high risk for PPD compared to individuals with private insurance.

Conclusion: NICU admission is a known maternal risk factor for the development of PPD, and this risk may be exacerbated for mothers living in urban settings. This is believed to be the first study to examine PPD regarding geographical differences, specifically in mothers of NICU graduates. We hope these findings will inform and integrate into new interventions and opportunities to promote optimal family development.

Who Chooses Water Births?

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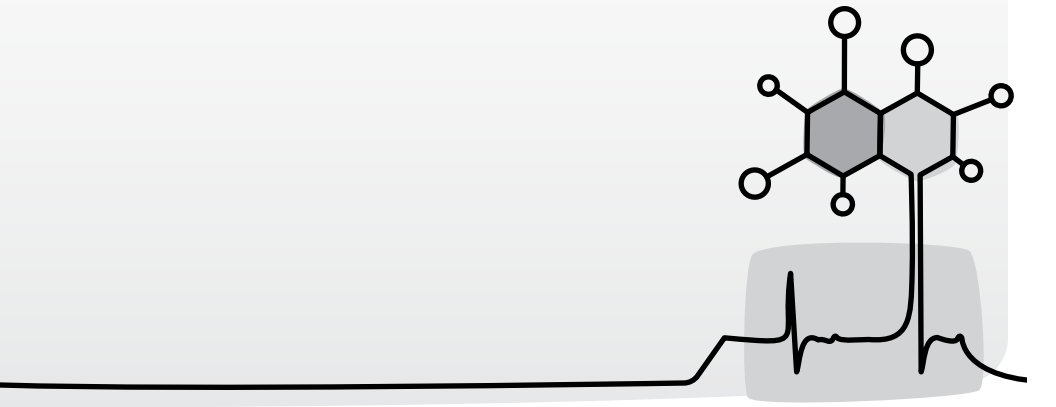
Introduction: Water immersion birth is the process of undergoing the second stage of labor and delivering an infant while submerged in a tub of warm water. This practice is becoming increasingly popular across the country. Potential benefits to water immersion during the second stage of labor include shorter labor duration and decreased use of spinal/epidural anesthesia, NICU admissions, and perineal lacerations. Previous demographic reviews reported that women who elect water births are primarily white, married, multiparous, college educated, and are English-speaking. The purpose of this study is to identify demographic factors of women who elect water births in Omaha, Nebraska and the surrounding area.

Methods: This case-control study identified patients who delivered via water birth at Immanuel Hospital between May 2019 and February 2022. Controls were randomly selected from a population of women who delivered vaginally within two days of each water birth. Age, marital status, gravidas, race/ethnicity, BMI, and preferred language were collected for each participant from the electronic medical record. Demographic data were analyzed and compared between groups.

Results: 70 patients were identified as having undergone water births and were matched to 70 controls. The average age of women in the water birth group was older than the control group (29.38 vs. 27.19 years, $p=0.010$). More women in the water birth group were married than in the control group (64.3% vs. 32.9%, $p<0.001$). 15.9% of women in the water birth group were primigravid as compared to 35.7% in the control group ($p<0.001$). Women in the water birth group were 83.8% white and 10.3% black, whereas women in the control groups were 39.7% white and 44.4% black ($p<0.001$). The average BMI in the water birth group was lower than in the control group (29.73 vs 30.97, $p=0.20$). All water birth patients were English-speaking compared to 87.1% of control participants ($p=0.11$).

Conclusion: Patients who elected water births at Immanuel Hospital were older on average than patients who underwent vaginal deliveries. Additionally, they were more likely to be married, multiparous, and white. No statistically significant differences existed regarding BMI and preferred language



Abstract 22

Predictors of Pediatric Cancer Survival in Iowa and Louisiana: A Multilevel Analysis of SEER Data

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Background and Significance: Cancer is the leading cause of death by disease among children under 15 in the US. While pediatric cancer survival rates have improved over time, they vary by age, sex, cancer type, race/ethnicity, and socioeconomic status. To our knowledge, no studies have comprehensively examined predictors of pediatric cancer survival in Iowa and Louisiana, two states with a large proportion of the population living in rural areas.

Question: What factors are associated with cancer survival among children in Iowa and Louisiana?

Methods: In this population-based longitudinal study, we used data from the Surveillance, Epidemiology, and End Results (SEER)-17 registries database. All primary cases of malignant cancer diagnosed among children aged 0-19 in Iowa and Louisiana from 2000 to 2020 were included. Cox regression models with shared frailty (modeling state as a random effect) were used to identify factors associated with pediatric cancer survival, including age, sex, race/ethnicity, cancer type, rurality, and median household income.

Results: We identified 7,174 cases of pediatric cancer in the two states (3,052 cases in Iowa and 4,122 in Louisiana). Iowa had a higher proportion of rural cases (41.64% vs. 19.63%), while Louisiana had a higher proportion of Non-Hispanic Black cases (30.96% vs. 4.39%). Overall, rurality was significantly associated with survival; compared to those living in urban areas of >1 million population, the risk of cancer death was higher among those in urban areas of <250,000 population (aHR: 1.278, 95% CI: 1.046-1.562). Although not statistically significant, the hazard of death was higher among those living in rural areas (both adjacent and not adjacent to urban areas). The risk of cancer death was lower for females compared to males (aHR=0.828, 95% CI: 0.732-0.937). Compared to Non-Hispanic Whites, the risk of cancer death was higher among Non-Hispanic Blacks (aHR=1.790, 95% CI: 1.546-2.074) and Non-Hispanic American Indians/Alaskan Natives (aHR=2.821, 95% CI: 1.337-5.951). Median household income was not associated with survival (p=0.1755).

Conclusions: Our results may help to identify individuals at a higher risk of death from pediatric cancer. The results can also help inform cancer care facilities to use social determinants of health more efficiently and identify special needs of patients.

TCF12-Related Craniosynostosis with Recurrent Multi-suture Synostosis

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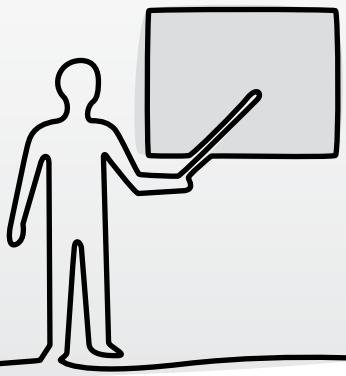
Introduction: Non-syndromic craniosynostosis affects approximately 1 in 2350 live births and is associated with a multitude of causative factors. Involvement of the sagittal suture remains the most common craniosynostosis, while coronal craniosynostosis has the strongest likelihood of molecular genetic diagnosis. TCF12 pathologic variants contribute to craniosynostosis, typically coronal and isolated, with most individuals having otherwise normal development. Herein, we expand the phenotype of TCF12-related craniosynostosis.

Clinical Report: We report a male who, at three months, due to abnormal cranial contour, was referred for a non-contrast computerized tomography (CT) that showed fusion of the right coronal suture and premature metopic suture fusion. The patient underwent anterior vault reconstruction and recovered well from the surgery at 6 months of age.

He was referred to genetics at age 9 months following his first procedure for unicoronal synostosis with metopic involvement. His head was asymmetric, with well-healing scars, translucent skin, and normal motor and social developmental features. We recommended a craniosynostosis next-generation sequencing study that revealed a likely pathologic variant in TCF12 c.1726dupT, p.Ser576Phefs*3.

At four years old, the patient had refusion of the sagittal suture, portions of the left coronal suture, and right lambdoid suture. Four months later, the patient's ophthalmologist identified papilledema on a scan, and the patient was referred to neurosurgery for an emergent cranial decompression for craniosynostosis and posterior vault expansion.

Discussion: Autosomal dominant craniosynostosis due to variants in TCF12 is becoming more well-established, with just over one hundred reports in the literature. However, to our knowledge, recurrent craniosynostosis associated with mutations in TCF12 requiring two, and possibly a third, surgical intervention has not been previously reported. This case report highlights the risk of recurrent craniosynostosis involving multiple sutures with rarely reported features in a patient with a pathogenic variant in TCF12. We suggest that TCF12 be included in genetic testing for individuals with craniosynostosis and to monitor for recurrent fusion of sutures with intracranial pressure monitoring and a low threshold for cranial imaging.



Abstract 24

Does Routine Upper GI Series before Gastrostomy Tube Placement Add Value: A Retrospective Look Over a Decade?

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[2]Children's Nebraska

Background: Upper gastrointestinal (UGI) fluoroscopy studies are often ordered before gastrostomy tube (G-tube) placement to evaluate anatomy. The evidence-based necessity of this preoperative test in patients without acute symptoms has been debated.

Significance of the Problem: The use of routine UGI studies prior to G-tube placement in pediatric patients is a common practice, adding radiation, cost, and logistical challenges to a patient's care.

Hypothesis, Problem, or Question: We hypothesize that UGI studies prior to G-tube placement are commonly normal and offer little value-added to the surgical care.

Experimental Design: An IRB-approved retrospective chart review was performed of 351 routine status upper GI studies prior to G-tube placement between 2007 and 2023. Midgut rotation was categorized according to published approaches. The presence of hiatal hernia or severe reflux was also cataloged. Patients with acute indications such as vomiting or obstruction were excluded.

Results/Data: Of 351 patients, 7 were found to have typical malrotation without volvulus, 3 of whom had a known history of left congenital diaphragmatic hernia and were therefore presumed to have an abnormal rotation before the study. One patient had atypical malrotation with a high cecum, warranting Ladd's procedure at the time of gastrostomy tube placement. An additional 6 patients were found to have an atypical malrotation with a normal cecum, which did not alter the surgical plan. Our overall incidence of surgical malrotation was (7/351), 2.0 %. However, the incidence of unanticipated malrotation warranting surgical treatment was only 1.1% (4/351). Severe gastroesophageal reflux was present in (32/351) 9.1% of the patients, and of these, only (1/32) 3.1% received a Nissen fundoplication at the time of G-tube placement. In our population, (6/351) 1.7% of patients had a hiatal hernia seen on the upper GI study. The average patient age in positive malrotation cases was 3.4 months.

Conclusion: The study found that the incidence of unanticipated but surgically relevant malrotation in patients without acute symptoms undergoing routine G-tube placement is very low, near 1%. The study suggests that upper GI studies in all patients prior to G-tube placement may not be necessary, and may be a potential area for cost and radiation reduction, as well as risk reduction for fragile infants by sparing them unnecessary transport to fluoroscopy. Clinicians should consider these findings when assessing the pretest probability of pre-operative upper GI studies in pediatric patients undergoing G-tube placement.

Comparison of Clinically Relevant Factors Between Infants Born at 33 and 34 Weeks Gestation at CHI Bergan Mercy

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Background: Infants born at 33 and 34 weeks gestation routinely get admitted to the Neonatal Intensive Care Unit (NICU), as they need respiratory and nutritional support. This study compares clinically relevant factors such as weight, APGAR scores, length of stay (LOS), and time between birth and admission between infants born at 33 and 34 weeks gestation at CHI Bergan Mercy.

Significance: The length of stay is important to families, providers, and hospital administrators. NICU admission may alter successful breastfeeding and comes with significant costs. LOS influences the occupancy and projected census of the NICU with resultant challenges for provider staffing. Time between birth and admission to NICU impacts clinical outcomes.

Hypothesis: We hypothesize that infants born at 33 weeks gestation will have a lower average 5 minute APGAR score, longer time between birth and admission, and longer LOS in the NICU than infants born at 34 weeks gestation.

Experimental Design: Newborn infants of 33 and 34 weeks gestation that were admitted to the NICU between January 2022 and May 2023 at CHI Bergan Mercy were included. The following data was collected: gestational age, date of birth, time of birth, time of admission to NICU, date of discharge, weight at birth, and APGAR score. Two-sample T tests were performed to determine statistical significance, and the p-value cutoff was set at 0.05.

Results: The study included 114 infants: 42 born at 33 weeks gestation and 72 born at 34 weeks gestation. The average corrected gestational age at discharge was 37 2/7 and 37 0/7 for the 33 and 34 week gestation infants, respectively. The average length of stay for newborns born at 33 weeks was 26.6 days compared to 18.2 days for newborns born at 34 weeks. ($P < 0.01$). The average time between birth and admission to the NICU was 22 minutes for the 33 week gestation infants compared to 23 minutes for the 34 week gestation infants. The average 5-minute APGAR score for both groups was 8. The average weight at birth was 2062 grams and 2273 grams for the 33 and 34 week gestation infants, respectively.

Conclusion: Infants that were born one week more-premature stayed in the NICU for only 8 days longer than the more mature infants, on average. These results suggest that infants develop the mechanisms necessary to feed independently and thus be discharged from the NICU around the corrected gestational age of 37 weeks.

Abstract 26

Myeloid Specific Deletion of Triggered Myeloid Receptor-1 (trem1) Attenuates Murine Transfusion-Associated Necrotizing Enterocolitis Injury

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Background: Necrotizing Enterocolitis (NEC) continues to be a leading cause of morbidity and mortality in premature neonates. We have recently described a pre-clinical model of anemia and RBC transfusion-associated NEC (TANEC), where severe anemia was associated with infiltration of inflammatory monocytes that are activated in situ by RBC transfusions. Based on preliminary studies, we hypothesized that activated monocytes expressing triggered myeloid receptor-1 (trem1) and lead to inflammatory response in TANEC injury.

Objective: Using murine RBC-transfusion associated NEC model, investigate whether monocyte-specific deletion of trem1 expression, thus reducing NEC-like injury in murine neonates.

Methods: The littermates of trem1-/-from Trem1flox crossed with Lyz2-cre were randomly studied in 4 groups (n=8 each): (1) naïve controls; (2) anemic (hct 20-24%); (3) transfusion control; and (4) anemic-transfused. Anemic group pups were rendered severely anemic by facial vein phlebotomies on postnatal days (P)2, 4, 6, 8, and 10. Transfusion controls received an intravenous FVB-donor-derived RBC transfusion (20 mL kg−1) into the retroorbital venous plexus, injected in two aliquots on each side) on P11. Naive controls were maintained without intervention. Flow cytometry and immunofluorescence staining were performed to confirm the deletion of trem1 on intestinal recruited monocytes in trem1-/- mice. Plasma levels of intestinal injury markers of iFABP2, CRP, CXCL2 and SAA were analyzed by ELISA. Histological analysis was performed to grade the gut injury. TANEC-associated inflammatory response were investigated by measuring the inflammatory cytokines in ileocecal tissue by qRT-PCR.

Results: Flow analysis of intestinal recruited monocytes showed no expression of trem1 and confirmed the deletion of trem1 gene by cre recombinase in trem1-/- mice. Consistently, anemic-transfused intestines from trem1-/- mice showed the no/minimal recruitment of monocytes with the absence of trem1 on a limited number of monocytes indicating that trem1 deletion inhibits the recruitment of monocytes to anemic intestines and few trem1 expressions on monocytes might be arise from intestinal resident macrophages. The plasma levels of intestinal injury markers in trem1-/- anemic-transfused mice were significantly reduced than Lyz2-cre mice indicating that monocyte-specific trem1 deletion significantly reduced the TANEC-associated intestinal injury and further confirmed by histology showed reduced injury grade in trem1-/- anemic transfusion. The mRNA fold change of key inflammatory genes (IL1β [3.5±0.2 vs 9.02±0.1], IFNγ [2.4±0.1 vs 5.26±0.1], TNFα [1.45±0.2 vs 4.42±0.2], IL6 [1.1±0.05 vs 5.62±0.2] data were represented as fold change in trem1-/- vs Lyz2cre) were reduced in trem1-/- anemic-transfused intestine, interestingly toll-like receptor-4 signaling mediators NF-kB1 and NF-kB2 both were also reduced when compared to Lyz2-cre mice confirming that trem1 might involve inflammatory activation in TANEC injury.

Conclusion: Myeloid-specific deletion of trem1 leads to inhibition of inflammatory response in the intestine, thus reducing the resulting intestinal injury.

Corticosteroids on Renal Function in Preterm Infants

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Background: Preterm birth can significantly impact an infant's development. One aspect of their immature physiology that exacerbates outcomes is relative adrenal insufficiency (RAI). Although there are many consequences of preterm birth, one of the significant effects is immature renal function. Recent studies have evaluated the potential benefits of administering prophylactic low-dose corticosteroids for RAI and prevention of lung disease but have not addressed their renal effects.

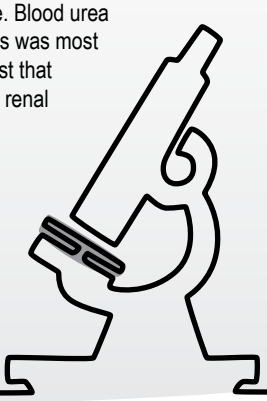
Significance of Problem: Steroids have been identified to hinder somatic growth, raising concerns about their impact on kidney development. However, the specific effects of using low doses of steroids on kidney outcomes remain uncertain. By understanding the systemic effects of corticosteroids on RAI, our results could lead to improved outcomes for preterm infants.

Hypothesis, Problem or Question: To establish the short-term effects of corticosteroids on acute kidney function in preterm infants.

Experimental Design: This retrospective study included preterm infants (gestational age of 24-28 weeks) admitted to Nebraska Medical Center or Children's Nebraska (Jan 1, 2013 to Jan 1, 2023). The experimental group consisted of infants that were administered hydrocortisone within the first two weeks of life, with controls that did not. Infants diagnosed with major congenital abnormalities, transferred in after 48 hours of life, or who received other glucocorticoids in the first two weeks were excluded. We collected pH, electrolytes, and blood pressure support for the first two weeks. We assessed blood pressure and creatinine levels at term equivalent age and/or prior to discharge. A linear mixed model with a random effect for patient and fixed effect for day and corticosteroid groups were used for lab value trends.

Results: The early hydrocortisone group had more death (20.8% vs. 3.7%, p=0.026) and increased vasopressor use (70.8% vs. 29.2%, p=0.013). There were no differences in electrolytes or nutritional content over the first two weeks except for blood urea nitrogen and total daily protein administration. At term equivalent age and discharge, there were no differences in creatinine, blood urea nitrogen or blood pressure between groups.

Conclusion: Our results showed no significant impact of early hydrocortisone on creatinine levels and blood pressure at term equivalent age. The lack of difference could have been affected by the high rate of steroid use in both groups after the first two weeks of life. Blood urea nitrogen levels were higher in the early hydrocortisone group, but this was most likely due to higher dietary protein administration. These data suggest that early hydrocortisone does not have a significant effect on short-term renal function.



Abstract 28

Multi-Modal Ensemble Learning for Categorizing Pediatric Acute Myeloid Leukemia

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As a rapidly progressing hematopoietic malignancy characterized by aberrant clonal expansion of abnormal myeloid progenitor cells, acute myeloid leukemia (AML) typically results in bone marrow failure and compromised hematopoiesis. Pediatric AML has been categorized into more than 20 molecular subtypes defined by genetic alterations, such as chromosomal alteration, fusion, mutations, or tandem duplications. Each subtype exhibits a specific response to treatment and prognoses, highlighting the critical need for precise subtype identification for effective clinical management and tailored therapeutic approaches. Conventional methods for AML subtype identification primarily depends on morphological analysis, cytogenetic analysis, immunophenotyping, or molecular profiling, which can be time-consuming, expensive, and technically demanding in clinical practice applications. Recent advancements have demonstrated the application of next generation sequencing (NGS) in the identification of AML subtypes, but they are limited to single omics data only. We hypothesize that by integrating multi-omics data, encompassing genomics, transcriptomics, and epigenetics data, we can capture the comprehensive and complementary across different omics, which could markedly enhance the discovery of biomarkers that are specific to AML subtypes and improve the precision of AML subtype classification. To overcome these challenges, we aim to establish a multi-modal ensemble learning framework to achieve precise identification of pediatric AML subtypes by integration of multi-omics (including genomics, transcriptomics, and epigenetics) data from several publicly available databases like NCI TARGET and St. Jude Cloud. Specifically, we implement two multi-modal ensemble learning frameworks, including multi-kernel learning and multi-modal deep learning, to synergistically consolidate omics-specific and cross-omics information of AML subtypes, thereby enhancing the accuracy of AML subtype classification. Our results indicated that the integration of multi-omics data using both models significantly outperforms those relying solely on single-omics data (gene expression or DNA methylation data alone), in the categorization of AML. We believe our multi-modal ensemble learning framework represents a significant advancement in pediatric AML subtype identification, offering a powerful tool and robust resource for clinicians and researchers. By integrating multiple diverse omics data and providing accurate, data-driven subtype predictions, this framework has the potential to refine risk stratification, optimize treatment strategies, and pave the way for personalized precision medicine. Additionally, we anticipate that the proposed framework can be tailored and expanded to facilitate the identification of subtypes for other pediatric, adolescent, and young adult (AYA) cancers.

Trends in Age at Diagnosis of Turner Syndrome in the United States

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Introduction: Turner syndrome (TS) is a chromosomal abnormality marked by complete or partial absence of an X chromosome. Recent data suggests that diagnosis before 12 years of age allows for improved long term natural history due to timely initiation of medical therapies.

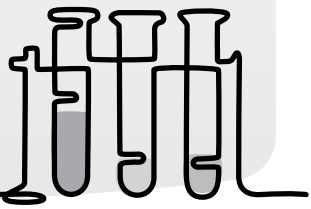
Significance of Problem: European studies have noted a median age at diagnosis of 15 years. There is little data on age of diagnosis in a contemporary US cohort.

Objective: We sought to assess a US cohort of patients with TS receiving clinical follow-up since 2000 to evaluate trends in the age of diagnosis over time.

Methods: A retrospective study of hospital records at 2 tertiary hospital networks covering a 5-state region was performed and included 601 patients with genetically confirmed TS. Clinical and karyotype data was collected. Patients were categorized into quartiles based on when they were diagnosed: Quartile 1: before 1999 (N = 122), Quartile 2: 1999-2003 (N=150), Quartile 3: 2004-2008 (N=160), Quartile 4: 2009-present (N=169). Statistical analyses were performed to explore the associations between age of diagnosis as a function of year of diagnosis. P value of <0.05 was considered statistically significant.

Results: There were significantly more prenatal diagnoses made in recent years: Q1 = 9.1%, Q2 = 8.1%, Q3 = 14.5%, Q4 = 21.4% ($p = 0.002$). For those patients born without a diagnosis (N=519), mean age increased over time at 6.3±6.3, 8.2±6.3, 7.1±5.9 and 10.8±8.9 years ($p<0.05$). In order to avoid the confounding of adult patients diagnosed in later quartiles, analyses were repeated excluding all adult diagnoses. Despite exclusion of these cases, there was a decrease in timely diagnoses over time with 80%, 67%, 69% and 64% diagnosed at < 12 years in the respective quartiles ($p<0.008$ Q1 vs Q4). When comparing karyotype data among quartiles, Q4 had significantly more patients with TS mosaicism than Q1 (52.0% vs 32.3%, $p = 0.01$).

Conclusion: Advances in prenatal testing have resulted in a significant improvement in the timely diagnosis of Turner syndrome. However, for those patients born undiagnosed, delays in diagnosis and thus initiation of medical surveillance and treatment remain commonplace. This may be explained by the increase in TS mosaicism over time in that these patients may have more subtle phenotypes. Efforts to mitigate diagnostic delays including routine newborn testing merit further discussion.



Abstract 30

Synovial Sarcoma Presenting as a Chest Mass in a 16 Year Old Girl with Tuberculosis

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In this case, a 16-year-old female returning from Mexico presented to the emergency room with an 8-month history of right sided back pain and a 4-month history of dyspnea. Imaging revealed a large 11.5 centimeter right lower lobe pleural-based mass with overlying atelectasis. Extensive infectious disease workup was conducted and yielded a positive Quantiferon-TB Gold Plus test, a negative PPD test, and three negative sputum samples. Given her potential exposure history and the threat of missing a tuberculosis diagnosis, the patient was started on Rifampin, Isoniazid, Pyrazinamide, and Ethambutol (RIPE) therapy. The patient's lung mass was surgically resected and subsequent histopathological examination demonstrated synovial sarcoma. This case posed numerous complexities due to the patient's age, travel history, and positive tuberculosis test that all suggested infectious etiologies for her lung mass. Synovial sarcoma is a rare soft tissue cancer typically found in the large joints of the arm and leg, with one third of patients diagnosed under the age of thirty. This cancer is primarily diagnosed using needle biopsy and pathology examination. Surgical resection is the first-line treatment for this cancer, but adjuvant radiation and chemotherapy may be required if complete resection is not possible. For this patient, PET CT was planned for staging, along with port placement, with a treatment plan for chemotherapy following ARST0332 arm C (ifosfamide and doxorubicin) plus pazopanib.

A Case of Acute Ischemic Stroke in a 16-year-old

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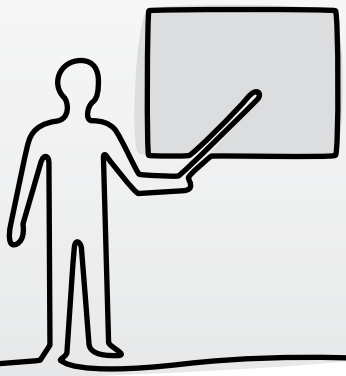
We present the case of a 16-year-old female who presented to the emergency department with sudden onset difficulty speaking and right-sided facial droop. Her physical examination showed right facial droop, expressive aphasia, and right upper extremity ataxia without other abnormality. She was evaluated with CT head without contrast and CT angiogram of the head and neck; both were negative for acute bleeding. MRI brain without contrast showed acute ischemic infarction of the left parietal lobe. MRA and MRV were unremarkable. Transthoracic echocardiogram was negative for patent foramen ovale. D Dimer was positive. Hypercoagulability studies including protein C & S, antithrombin, lipoprotein (a), factor VIII assay, prothrombin G20210A mutation, anti-phospholipid syndrome panel, and factor V Leiden mutation were all negative. Over the four-day hospitalization, the patient's speech and hand motion improved significantly, though she retained some dysarthria, short-term memory difficulty, difficulty masticating, and right-sided facial droop. She was discharged for follow-up including with neurology, hematology/oncology, and speech therapy.

Pediatric stroke is a rare diagnosis and can be a diagnostic challenge due to a wide range of risk factors and presentations. Commonly implicated risk factors include structural heart disease, head and neck trauma, infection, sickle cell disease, cancer, and hypercoagulable states. Even after workup, approximately one in three pediatric ischemic strokes are cryptogenic, as in our case. Pediatric stroke is a major cause of morbidity and mortality, with 20-40% of children dying after a stroke and 50-80% of survivors suffering permanent neurologic sequelae. Arterial ischemic stroke has a considerable risk of recurrence. Due to the rarity of pediatric stroke, management is not well-studied, but mainstays include neuroprotective measures. Children with ischemic stroke who present within 4.5 hours should receive tPA. Due to the heterogeneity of risk factors, presentation symptoms, and the potentially devastating consequences of acute ischemic stroke in children, clinicians who may see pediatric patients must keep acute ischemic stroke in their differential diagnosis and be prepared to order timely imaging and treatment. Timely administration of tPA greatly benefitted our patient, as she had a near complete return to baseline function except some speech difficulties when talking rapidly. She continues to follow with speech therapy. She also follows with neurology due to daily headaches and dizziness.



Abstract 32

Addressing Social Determinants of Health Challenges in a Rural Migrant Population and the Unanticipated Benefits of a Local Research Team

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Background: The National Institutes of Health (NIH) developed the Rapid Acceleration of Diagnostics Underserved Populations (RADx-UP) initiative to eliminate disparities in access to high-quality COVID-19 testing, including barriers imposed by social determinants of health (SDoH). In Nebraska (NE), the local RADx-UP-funded team developed the Mobile Health for Migrant Health (mHealth-4-Mhealth) program and mobile application (app) to improve access to at-home COVID-19 symptom and risk screening, rapid antigen testing, and health decision-making which was coupled with SDoH screening and linkages to community resources or aid.

Significance of the Problem: The COVID-19 pandemic disproportionately affected rural and minority populations.

Hypothesis, Problem OR Question: Does research teams being local complement the integration of SDoH screening into rural and migrant communities further enhancing healthcare access and quality?

Methods: Using descriptive data compiled from the mHealth app and interviews with research team members and a community partner, we draw special attention to the importance of the research team members being local to the participants they are enrolling. We also draw attention to the team's experience addressing the study participants' challenges and barriers to accessing healthcare or other resources.

Results: There has been ongoing enrollment of primarily (93%) Spanish speaking rural migrant populations. To date, there are 96 families enrolled (totaling 388 participants) who continue to perform at least biweekly SDoH challenges screening on the mHealth app with an average response rate of 83.6%. Dozens of challenges continue to be identified and addressed via the mHealth app.

Conclusion: The trust and rapport built by local research teams complemented by the integration of SDoH screening into digital health tools, presents a strategy for enhancing healthcare access and quality, particularly in rural and migrant communities.

Evaluation of Maternal COVID-19 Vaccination Status and Associated Demographic and Birth Outcomes

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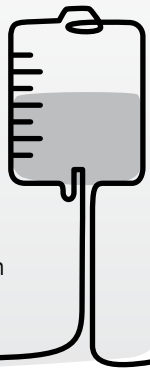
Background: On March 11, 2020, the World Health Organization declared COVID-19 a pandemic, and as of July 2022 the outbreak has claimed over six million lives worldwide. The COVID-19 pandemic has posed new risks and obstacles for pregnant women, especially since the original vaccination trials did not include pregnant women. Since their rollout, numerous studies have been completed evaluating vaccination during pregnancy and neonatal outcomes. These consistently demonstrate that vaccination during pregnancy does not lead to adverse outcomes in the perinatal period. Vaccinated women tend to be older women, with higher socioeconomic status. More data to support vaccine recommendations in pregnant women may be beneficial to both providers and patients.

Objective: The purpose of this study was to compare socioeconomic and demographic factors of vaccinated and unvaccinated women during pregnancy and health outcomes of neonates based on maternal vaccination status.

Experimental Design: An IRB-approved study enrolled 151 mother-infant pairs between December 2020 and July 2022 for collection of medical history and pregnancy outcomes at time of delivery. A Mann-Whitney U test was performed to compare continuous birth outcomes such as infant birth anthropometrics and maternal age between maternal COVID-19 vaccination status. Women were considered vaccinated if they were partially or fully vaccinated prior to or during pregnancy. A chi-squared test was used to associate COVID-19 vaccination status between the following categorical outcomes: preterm vs term, college graduate vs non-college graduate, owns a car vs any other mode of transportation, white vs non-white, and NICU admission vs non-NICU admission. A p-value of <0.05 was considered statistically significant.

Results: Of the women included in this study, 33.77% were vaccinated and 66.22% were unvaccinated at time of delivery. Vaccinated women were significantly older than unvaccinated women (32 vs 29, p=0.008). Vaccinated women had infants with significantly higher birth head circumference percentiles than those of unvaccinated women (80th percentile vs 60th percentile, p=0.017). Partial or full COVID-19 vaccination was associated with mothers who had at least a college degree vs those with no college degree ($\chi2=6.229$, p=0.013), with mothers who owned their own car for transportation ($\chi2=4.085$, p= 0.043), and with white vs non-white race ($\chi2= 4.169$, p=0.041). Partial or full vaccination against COVID-19 approached a significant association with term vs preterm birth (p=0.079).

Conclusions: This study found an association between maternal COVID-19 vaccination and increased birth head circumference percentile in the infants of vaccinated women. It is currently unknown if this is due to the protective effects of COVID-19 vaccination against COVID-19 infection, or demographic variables associated with vaccination status given this study also indicated demographic differences in pregnant women who are more likely to get vaccinated for COVID-19. All of the results associated higher socioeconomic status markers with increased likelihood of vaccination in pregnant women. This demonstrates the need for improvement in access and resources to underserved populations to improve the rates of vaccination during the vulnerable period of gestation. More research is needed to further evaluate maternal COVID-19 vaccination demographics and neonatal birth outcomes.



Abstract 34

Behind the Curve: An Uncommon Cause of Malnutrition in a 7-Month-Old Male

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Initial History/Presentation: A 7-month-old male was admitted to our hospital following one month of cough, post-tussive emesis and concerns for malnutrition. The family had recently immigrated to the United States (US) just prior to birth, and mom had regular obstetrics care leading up to delivery. Patient was otherwise up to date on vaccinations.

Physical Exam: He was afebrile with normal vitals. Weight was 7.82 kg on admission (27th percentile) Exam was notable for oral thrush as well as a cough with mild crackles noted throughout the lungs. Patient appeared to have oral aversion, presumed to be secondary to candidiasis. Patient was also noted to have multiple hypopigmented patches on skin and was started on Aquaphor. Exam was otherwise normal.

Diagnostic Evaluation: Patient was found to be positive for adenovirus on respiratory pathogen panel (RPP). Initial laboratory workup is summarized in Table 1, and was notable for mild AST elevation of 111 U/L. Complete blood count (CBC) notable for a slight lymphocyte predominance of 76%. Stool occult blood testing was negative.

Diagnosis: Nasogastric feeds were started while working with feeding therapy. Gentian violet, and eventually fluconazole, was started to treat his oral candidiasis. Prenatal records showed: negative sexually transmitted infection, HIV, rubella, hepatitis B/C testing two days prior to delivery. HIV testing was ultimately obtained given poor weight gain in the setting of oral thrush in a 7-month-old. Quantitative HIV by nucleic acid amplification testing was positive, with a viral load of >10,000,000 and CD4 count of 2745/cmm. Triple therapy with lamivudine, zidovudine and raltegravir was quickly initiated. Patient's family was offered HIV testing, and mom and dad were both found to be positive.

Discussion/Conclusion: Despite a negative maternal HIV test two days prior to delivery, HIV was possibly contracted in the period just before delivery or via breastmilk following birth. Unidentified HIV in infants in the US is quite rare, with an annual occurrence of ~25 cases per year (identified at age 6-11 months). Timing of HIV testing is imperative to identifying HIV in pregnant mothers and coordinating safe birth plans. Of infants born with HIV from maternal exposure, only 18% are born to mothers who were tested for HIV during pregnancy. Testing during pregnancy/after birth decreases the risk of unidentified HIV in infants, as HIV contraction in the mother can occur anytime leading up to birth. This case highlights the importance of considering HIV in patient with malnutrition and thrush, particularly outside of the newborn period.

Free Pediatric Healthcare Clinic: A Longitudinal Analysis of Challenges, Successes, and Demographic Outcomes of the 2019-2023 Back-to-School Clinic in Omaha, Nebraska

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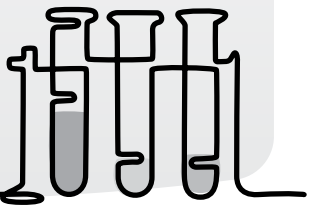
Magis is a student-run free healthcare clinic that hosts an annual pediatric event to provide children with the medical care they need to return to school. Since 2019, the clinic has offered free physical exams, hearing and vision screening, vaccinations, and school supplies for children in the Omaha metro area regardless of insurance status. This event ensures that students are eligible to attend school, based on the requirements of each school district.

The clinic's goals are to provide every child with the services they need to meet the requirements for attending school while learning more about barriers to care that families may face. At the beginning of the clinic, each family was given an optional survey inquiring about demographics, access to healthcare, and services provided that day. The collected data is used to better understand patients' social determinants of health and adjust services to better fit the needs of our community. This clinic is made possible through the efforts of Creighton University School of Medicine's Magis Clinic, Creighton family medicine residents and physical therapy faculty, and Catholic Health Initiative University Clinic staff.

The purpose of this study is to compile clinic data from 2019 to 2023 and assess trends in demographics, health insurance status, and the impact of advertisement. Post-pandemic, our Pediatric Back-to-School Clinic had a decrease in patients from 103 in 2020 to 41 in 2021. We attribute this change to the implementation of online schooling, but cannot say for sure what caused the downtrend in attendance. Over the last 5 years, we saw a change in the predominant race/ethnicity present at the clinic. In 2019, a majority of patients identified as Hispanic/Latino, while in 2023 most patients identified as Asian/Pacific Islander. Additionally, the number of patients seen at clinics without health insurance has declined. In 2019, 40% of patients lacked health insurance, compared to 13% of patients lacking health insurance in 2023. Lastly, we have shifted our outreach platforms as we started advertising primarily word-of-mouth to implementing social media platforms and advertising directly to schools in more recent years. This has led to an increase in online and school-based advertisement and greater outreach to various demographic groups within the community.

This data helps identify disparities in healthcare amongst different racial/ethnic groups and allows us to implement resources directed toward the needs of this community.



Abstract 36

Needs Assessment to Support Continuing Education and Training Modalities for High-Consequence Pathogen Preparedness in Pediatric and Obstetric Populations

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Background: High-consequence pathogens present complex challenges in United States (US) healthcare, with knowledge gaps existing in the provision of safe and effective treatment. The National Emerging Special Pathogens Training and Education Center (NETEC) aims to standardize guidance and care coordination across the healthcare continuum for suspected or confirmed infection with high-consequence pathogens through education, training, research, monitoring, evaluation, and funding. Information on the guidance and care coordination of pediatric and obstetric patients is lacking. The NETEC Special Populations Committee applies this mission to pediatric and obstetric care.

We conducted a needs assessment to optimize education and training opportunities for healthcare teams related to high-consequence pathogen preparedness for children and pregnant women.

Methods: Stakeholders received a needs assessment survey via email, social media, and NETEC website from 10/3/22-11/15/22. Questions targeted demographics, topics of interest for continuing education within the special populations: pathogen awareness, frontline care, infection prevention, and emergency preparedness, and learning modality preferences.

Results: Of the 20,600 impressions, the survey was completed by 145 persons (with 97 additional partial completions). The use of targeted emails had the highest engagement, with a 25% open rate (29% industry average) and click-through rate of 18% (5% industry average). Respondents were located across the U.S., mainly in academic healthcare settings (46%). Infection Preventionists (30%) represented the greatest proportion, but many institutional roles were reported. Responses to educational topics were widely distributed. Webinars (77%), in-person training (64%), and brief written summaries or updates (54%) were the most commonly preferred learning modalities.

Conclusions: Myriad healthcare team members are involved in the care of pediatric and obstetric patients with high-consequence pathogens. They represent an engaged group of NETEC stakeholders that, despite recent experience with the SARS-CoV-2 pandemic, express interest in continuing education on topics related to high-consequence pathogens across the care continuum via interactive, engaging, and collaborative learning modalities, led by subject matter experts.

Validation of the Arabic Language Autism Diagnostic Inventory

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Background: Autism is the most common neurodevelopmental disorder It affects 1-2% of the world's children and is the leading cause of disability in children under five years of age and contributes significantly to the global burden of disease.

80% of the world's children live in LIC or LMIC and have little to no access to autism services. Most information on the epidemiology, diagnosis and interventions for autism has originated in high income countries (HIC) and are validated on high income-and largely white populations. It is estimated that less than 10% of all research on autism comes from LICs or LMICs. This is problematic because it does not include relevant cultural perspectives or solutions that are workable in an LMIC context. In particular, the lack of diagnostic instruments validated in LMIC, and diverse populations is a major barrier for early diagnosis, intervention, and research. Research has demonstrated that culture significantly impacts symptom expression and conceptualization of autism in diverse cultures. This may lead to differences in clinical presentation, help seeking behavior and outcomes.

Aims: The aim of this study was to validate the Arabic Language Autism Diagnostic Inventory for the diagnostic evaluation of autism. This instrument was developed by the authors to create a DSM-5 based inventory adapted to the Arabic language and culture. Cultural and language adaptation was based on data obtained through qualitative research exploring presentations of autism in the local culture.

Methods: Case control study design was used to test the Arabic Language Autism Diagnostic Inventory for sensitivity and specificity in identifying a group of children with autism compared to a group of typically developing children.

Results: Parents of 48 children with autism and 152 neurotypical children recruited from the general pediatrics clinic at Jordan University Hospital in Amman, Jordan completed the Arabic Language Autism Diagnostic Inventory. Demographic information of the participants in each group is presented in table 1. A total score of 24 had 98% sensitivity and for autism 77% specificity for autism. ROC analysis indicated that the Area Under the Curve (AUC) is 0.976, (Figure 1) indicating very strong performance in identifying children with autism.

Discussion: The Arabic Language Autism Diagnostic Inventory is the first Arabic Language instrument created specifically for Arab populations and is informed by cultural and linguistic data of the target population. It has high diagnostic reliability for autism.

Conclusions: Culturally sensitive and informed instruments can improve the access to early diagnosis and interventions and enhance research in with the goal of improving diagnosis, care, and outcomes in global populations.

Abstract 38

Quality of Life Measures in the Study of Neurogenic Bowel Dysfunction among Individuals with Spinal Dysraphism

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Background: Neurogenic bowel dysfunction (NBD) has major impacts on individuals living with spinal dysraphism. There is a higher likelihood of bowel incontinence among individuals that are < 12 years of age, male, Hispanic or Black, and do not have private insurance. In adulthood, bowel incontinence is also significantly associated with decreased employment rates. Despite the measured impact of NBD, globally few studies have focused on the effect of NBD on quality of life (QOL). The purpose of this systematic review was to identify the approach and the utilized tools to assess the measure of the impact of NBD on QOL among individuals living with spinal dysraphism.

Methods: A literature review was conducted using the PRISMA guidelines. Relevant studies were identified in Embase and MEDLINE. The search strategy included search terms and synonyms for "spina bifida" and "neurogenic bowel". Studies written in English were included through January 2024. All included studies were focused on the population of interest - children and adolescents with spina bifida. Included studies utilized a formal process to measure the impact of neurogenic bowel on QOL. Review articles, validation studies, case reports, editorials, and animal studies were excluded.

Results: 1,759 articles were identified from 1955-2024. Twenty-eight studies met criteria for inclusion. Twenty-one distinct tools were identified in the assessment of NBD and QOL. Among the validated questionnaires used, the Neurogenic Bowel Dysfunction score (NBD) and the Pediatric Quality of Life Inventory (PedsQL) were both used in four of the 28 studies. Eighteen (64%) of the articles used a single questionnaire or tool, while the remaining 10 used more than one. Nine studies (32%) developed an ad hoc tool to assess QOL. Six studies were completed in the US and the remaining 22 studies were from Europe (13), Asia (7), Canada (1), and Australia (1).

Conclusions: Individuals with spinal dysraphism face many challenges, including developmental delay, paresis, and bowel and bladder dysfunction. As with other chronic conditions, one of the aims in their clinical management is to improve the associated health-related QOL. Along with lessons learned, this study describes the need for a standardized approach and of validated QOL tools in the study of bowel dysfunction in this population. Given the global prevalence of neural tube defects and the number of centers worldwide studying this issue a standardized and collaborative approach is needed to promote research equity for all people with spinal dysraphism.

Congenital Chylothorax Resulting in Hydrops Fetalis in a Preterm Infant

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Congenital chylothorax is a rare condition in which abnormal development of the lymphatic systemic or obstruction of lymphatic flow results in accumulation of chyle. Although rare, it is the most common etiology for neonatal pleural effusion and often detected during fetal life on antenatal ultrasound. Diagnosis is made by fluid analysis demonstrating a lymphocyte predominance and an elevated triglyceride level, although the level may be normal if the infant has not received enteral nutrition. Accumulation of chyle can present isolated to the thorax (chylothorax) or diffusely in the body (non-immune hydrops fetalis). At birth, infants can present with respiratory and cardiovascular failure due to compression on the lungs and heart from chyle accumulation. Management strategies include evacuation with thoracentesis and paracentesis while providing cardiorespiratory support, withholding enteral nutrition to reduce chyle production and lymphatic flow, parenteral nutrition, and eventual initiation of enteral feeds with low fat formula or skimmed breast milk. We report a case of an infant born at 34 weeks gestation with hydrops fetalis who subsequently was diagnosed with congenital chylothorax. Treatment included bilateral thoracentesis and chest tube placement, respiratory support and a modified diet consisting of skimmed maternal breast milk. The infant was discharged home on day of life 40.

Abstract 40

The Relationship between Neonatal Anthropometric Measurements and Body Composition in Term Infants

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Background: Infant body composition is an important tool to track growth quality and evaluate potential risk for malnutrition, obesity, or metabolic disorders. Air displacement plethysmography is the gold-standard for measuring body composition but is often cost-prohibitive. Mid-upper arm circumference, lower chest circumference, and mid-thigh circumference have been proposed as simple and cost-effective measurements of infant growth, but little is known about how well these anthropometric measurements correlate with infant body composition.

Significance: Identifying cost-effective measures of infant body composition could improve infant health through early identification and/or treatment of altered growth.

Hypothesis: Infant percent body fat will be positively correlated with anthropometric measurements.

Methods: An IRB-approved study enrolled 34 term (gestational age ≥37 weeks, 0 days) infants at the time of delivery. Birth weight, length, and head circumference percentiles were collected from infant medical records. Weight-for-length percentiles were calculated using the 2006 WHO growth standards. Mid-upper arm (n=24), lower chest (n=24), and mid-thigh (n=20) circumference were measured within the first week of life. Fat mass, fat-free mass, and percent body fat were measured by air displacement plethysmography (PEA POD). Spearman correlations were used to evaluate the relationship between anthropometric measurements and body composition.

Results: Median birth gestational age was 39.3 weeks (IQR 38.3-40.1) and 47.1% of infants were male. Percent body fat was positively correlated with birth weight percentile (rs=0.36, p=0.04) and weight-for-length percentile (rs=0.38, p=0.03). There was no correlation between percent fat and birth length (p=0.52) or head circumference (p=0.20) percentile. Similarly, there was no correlation between percent fat and mid-upper arm (p=0.40), lower chest (p=0.14), or mid-thigh circumference (p=0.08). However, fat mass and fat-free mass were both positively correlated with infant arm, chest, and thigh circumference.

Conclusion: Infant percent body fat was not correlated with mid-upper arm, lower chest, or mid-thigh circumference, suggesting that these anthropometric measurements are not an accurate measure of infant body composition. Additional research is needed in a larger cohort to identify other potential cost-effective measures of infant body composition.

Predictive Modeling with Clinical and Laboratory Values in Neonates with Hypoxic-ischemic Encephalopathy

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Background: Hypoxic-ischemic encephalopathy (HIE) can have lifelong detrimental effects. One of the most effective therapies is therapeutic hypothermia, which can reduce death or disabilities. The cooling must begin within the first 6 hours after injury. Diagnosis currently relies on clinical findings that are subtle, making it difficult to assess the need for treatment within the therapeutic window.

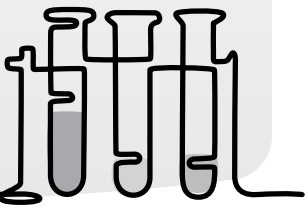
Significance of Problem: There are limitations in providing timely care for HIE. Many studies have sought to identify a single diagnostic biomarker with minimal success, but few have attempted to develop prognostic models that integrate both laboratory and clinical values that are typically obtained in the first 6 hours. An effective predictive model could allow for earlier treatment, potentially attenuating the adversities seen in neonates with HIE.

Hypothesis, Problem or Question: To develop models to predict brain injury on MRI after neonatal HIE, using a combination of laboratory and clinical values available either immediately upon admission or within 24 hours of admission.

Experimental Design: This is a retrospective study including data from infants born 2012-2022 with HIE and admitted to the UNMC or Children's Nebraska NICUs. Patient demographics, diagnostic variables (including lab values of nRBC, pH, base deficit, pCO2, bicarbonate, sodium, creatinine, and lactate), and clinical values (including encephalopathy severity, intensity of resuscitation, 5 minute Apgar, and 10 minute Apgar scores) were collected. The primary outcome of interest was the combined outcome of abnormal MRI or death. Multivariable logistic regression was used for variables that were significant on univariate analysis to determine predictive value. A backward selection method was used to obtain the best subset of variables. Model 1 included variables available on admission and Model 2 included variables that were available within the first 24 hours.

Results/Data: 139 infants met inclusion criteria. There were no differences between groups in demographics. Model 1 (AUC 0.711) resulted in three variables significantly associated with the combined outcome, including a 4x increased odds if chest compressions required in the delivery room. Model 2 (AUC 0.680) ultimately included two variables, including 5.5x increased odds if requiring chest compressions in the delivery room.

Conclusions: The two models provided moderate prognostication for identifying those at risk of death or abnormal MRI with a prominent association with the need for chest compressions in the delivery room. Model 1 performed as well or better than Model 2, suggesting that most of the predictive variables were present at initial admission.



Abstract 42

SAP30: A Novel Gene Governing Autophagy in Neuroblastoma Tumors

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Background and Significance of the Problem: Neuroblastoma (NB), a devastating pediatric cancer originating from neural crest cells crucial for nervous system development, poses a significant therapeutic challenge. Despite chemotherapy being the primary treatment, approximately 70% of high-risk NB cases develop resistance. Autophagy is a vital process involved in neuronal development, neuronal balance, and the differentiation of neural stem cells into mature neurons. Its role is especially significant in the advancement of NB, a cancer that emerges from immature nerve cells. However, the intricate mechanisms governing autophagy and the pivotal genes orchestrating its regulation in NB remain largely elusive.

Hypothesis: The small number of articles on Sin3A Associated Protein 30 (SAP30) to date have mainly focused on its association with HDAC complexes, primarily involved in transcriptional repression. We were the first to report the oncogenic role of SAP30 in NB. Here, we hypothesize that SAP30, identified as a novel autophagy regulatory gene in NB, plays a pivotal role in regulating autophagy crucial for NB development and chemoresistance.

Experimental Design: NB cell lines will be subjected to gene modulation via SAP30 knockdown and overexpression using siRNA and shRNA transfections and transductions, with subsequent evaluation through confocal microscopy, RT-PCR, Western blotting, and cell viability assays, in combination with treatment utilizing chemotherapeutic agents.

Results: In this study, we first identified SAP30 as a novel regulator of autophagy in NB. Silencing SAP30 inhibits autophagy and disrupts starvation-induced physiological autophagy in NB cells. Conversely, ectopic expression of SAP30 induces physiological autophagy in NB cells under starvation conditions. Mechanistically, SAP30 controls the transcription of STX17, an essential protein loaded onto autophagosomes during autophagy to facilitate their fusion with lysosomes. Reduction of SAP30 decreases STX17 expression, hindering its translocation to the autophagic membrane and inhibiting autophagosome-lysosome fusion. SAP30-mediated autophagy enhances cell growth and provides protection in NB cells treated with chemotherapy drugs such as cisplatin and doxorubicin. Notably, the suppression of SAP30 results in an increased accumulation of autophagy markers LC3B and P62, signaling autophagy inhibition, accompanied by a decrease in proliferation markers, both observed in vivo and in PDX tumors.

Conclusions: The role of SAP30 in autophagy and its regulation in NB remains unknown. Our study identified SAP30 as a novel autophagy regulatory gene that regulates autophagy in NB cells, granting them a growth advantage and enhanced survival under therapeutic stress. Therefore, SAP30 emerges as a potential target to enhance NB responsiveness to chemotherapy drugs.

Data Collection Variability: A Global Profile of Neonatal Hypoxic-Ischemic Encephalopathy Registries

Eric S. Peeples[1,2,3], Ulrike Mietzsch[4,5], Eleanor Molloy[6,7], Gabrielle deVeber[8,9], Khorshid Mohammad[10], Janet Soul[11,12], Danielle Guez-Barber[13], Betsy Pilon[14], Vann Chau[8,9], Sonia Bonifacio[15,16], Jehier Afifi[17], Alexa Craig[18], Pia Wintermark[19,20], on behalf of the Newborn Brain Society Guidelines and Publications Committee

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Background: Neonatal encephalopathy (NE) – including hypoxic-ischemic encephalopathy (HIE) – is prevalent worldwide and is associated with significant morbidity and mortality.

Significance: Data registries can provide hypothesis-generating and monitor trends in outcomes, but variability between registries significantly limits data pooling across registries for stronger analyses; analyses which could improve care delivery and outcomes for this high-risk population.

Hypothesis: We hypothesized that considerable variability exists in the data elements collected by existing worldwide NE/HIE data registries.

Design/Methods: Cross-sectional study collecting data elements from current or recent NE/HIE registry data forms. Registries were identified by literature search and email inquiries to investigators worldwide. Data were categorized by group consensus. Descriptive statistics summarized characteristics and variability in data elements between registries.

Results: 1100 total data elements were abstracted from 21 registries, representing 14 countries, including 3 middle-income countries. Registries had a median of 106 distinct data elements per registry (range 59-367). The most commonly collected data were related to pregnancy, hypothermia therapy, and short-term hospital outcomes. Least consistently collected data were non-acid/base status laboratory values. Only 4 of 1100 (0.4%) variables were consistently collected in every registry. Even when elements were collected by multiple registries, the format of the individual data element (numeric, categorical, free text, etc.) often differed across registries. 18 of 21 (85.7%) registries included at least one free text response element, with a median of 2 free text response elements (range 0-18) per registry. Only 3 of 21 (14.3%) registries included developmental follow-up fields and 2 others (9.5%) linked their data to a separate follow-up registry.

Conclusion(s): This study identified many ongoing NE/HIE registries around the world and demonstrated considerable variability in the number, type, and format of data collected. Future attempts to develop standard data elements to harmonize data collection will be crucial to facilitate collaboration between registries.

Abstract 44

Posterior Urethral Valves and Ascites in a Male Neonate

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Background: Posterior urethral valves (PUVs), first described by Young in 1919, are a malformation in which a membranous fold of the urogenital membrane obstructs urinary flow. Posterior valves, though rare, are the most common cause of urinary ascites and urinary tract obstruction in male neonates. Here we describe a unique case of PUVs resulting in in utero bladder rupture and development of late onset isolated fetal ascites.

Case Description: A preterm male infant was delivered via c-section at 32w4d gestation with diagnosis of fetal ascites. Maternal history was significant for gestational diabetes, with fetal ascites first noted on ultrasound at 31w4d after a previously normal 24-week anatomy scan. The infant was intubated in the delivery room for respiratory distress. Paracentesis with drain placement was performed shortly after arrival to the NICU. The initial creatine of the ascitic fluid was 1.1 mg/dl which increased to 3.9 mg/dl on day of life (DOL) 4 in the setting of anuria. A voiding cystourethrogram (VCUG) on DOL 6 demonstrated the presence of PUVs and bladder rupture with extravasation of contrast into the peritoneal cavity. A foley catheter was maintained and the study was repeated 1 week later demonstrating resolution of bladder rupture. The infant then underwent cystoscopy and ablation of the PUVs, with follow-up ultrasounds showing no evidence of hydronephrosis.

Discussion: Posterior valves can be detected on prenatal ultrasound (US) demonstrating a dilated bladder, bilateral hydronephrosis, and oligohydramnios. Post-natally, neonates can present with respiratory distress due to pulmonary hypoplasia from oligohydramnios. Other presenting symptoms include infection, renal/bladder dysfunction, and failure to thrive. Diagnosis is made on VCUG demonstrating a dilated and elongated urethra. Management in the initial neonatal period involves stabilization of the infant with respiratory support for pulmonary hypoplasia, placement of a urinary catheter to drain the bladder, and electrolyte correction. Once the infant is stabilized, definitive treatment occurs with valve ablation performed during cystoscopy. Long term complications include chronic kidney disease and bladder dysfunction.

Conclusion: Posterior urethral valves with subsequent bladder rupture should be included in the differential diagnosis of a newborn male infant with isolated ascites and oliguria.

Medical Record-Level Evaluation of Impact of Demographic and Socioeconomic Factors on Pediatric Neuro-Oncology Outcomes at Children's Hospital Colorado

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Background: Despite advances in the care of pediatric oncology patients, disparities exist in outcomes based on demographic and socioeconomic factors.

Significance of Problem: Previous studies have identified disparities affecting outcomes in pediatric CNS cancer population; however, they have not shown why on an individual level, given limitations of individual information available through cancer registries.

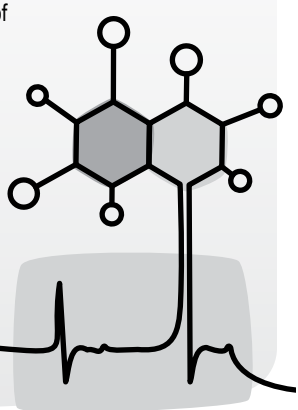
Hypothesis: We expected to observe similar disparities to those observed in registry studies and to find more specific factors explaining them.

Experimental Design: We reviewed 898 patients treated for CNS tumors at Children's Hospital Colorado (CHCO) from 1986-2020. Outcomes of interest were 5-year survival, timing of presentation to diagnosis, and type of treatment. Multivariable logistic and Cox regressions were used to identify covariates associated with outcomes of interest.

Results: Age, race, tumor, diagnosis year, and social concerns influenced type and timing of treatment. Time to presentation and treatment were significantly different between White and minority patients. American Indian/Alaska Native (AI/AN) and Black patients were less likely to receive chemotherapy than White patients. AI/AN patients were more likely to receive radiation than White patients. Asian/Pacific Islander (API) patients were less likely to be enrolled in a clinical trial than white patients. Black children were less likely than White to receive chemotherapy. Black children with low-grade tumors were more likely than White to receive care within 54 days of symptom onset, but less likely to receive a diagnosis within 5 days from first care. Children with low-grade tumors and 3+ social concerns were more likely than children with no/unknown social concerns to receive care within 54 days of symptom onset. Hispanic children were less likely than non-Hispanic with a high-grade tumor to receive care within 31 days of symptom onset.

Age, race, and rural vs. urban residence impacted survival outcomes. Patients with 3+ social concerns were more likely to survive after 5 years than children with no/unknown social concerns. With an adjusted hazards ratio, children with 2 social concerns were less likely to survive 5 years than children with no/unknown concerns. When adjusting for covariates of interest, we found that API patients had significantly worse survival than White patients.

Conclusions: Demographic and socioeconomic factors influence timing of care and survival outcomes in pediatric patients with CNS tumors. Minority status, age, social factors, rural, and urban patients experience differences in care. These findings emphasize the importance of considering these factors and addressing disparities to achieve equitable care.



Abstract 46

Cold Truths Exposed: An Uncommon Culprit of Neonatal Hypothermia

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Background: A 3-day-old term male born vaginally after induction due to FGR presented with hypothermia, poor feeding, 10% weight loss and decreased responsiveness. Mother was GBS negative with a history of genital HSV on suppressive therapy throughout pregnancy and with no visible lesions at delivery. His father had a recurrent vesicular rash on one finger, concerning for herpetic whitlow. Given patient's age and hypothermia, a neonatal sepsis workup was initiated; however, LP was unsuccessful on multiple attempts. Labs were significant for hypernatremia and elevated procalcitonin. Other electrolytes and LFTs were normal with mild hyperbilirubinemia. UA and RPP were unremarkable. Blood cultures, HSV serum and surface PCR swabs were negative. IV antimicrobials were initiated. Due to persistent somnolence, intermittent bradycardia and hypotension, brain MRI was obtained showing small IVH. Hospital days 2-4 he weaned to a crib and was feeding well with adequate weight gain. On day 5 the patient had recurrent hypothermia requiring return to the isolette and reevaluation of the diagnosis. Newborn screening was normal. On day 5 the infant had normal vitals except hypothermia to 35.4 C. Complete exam was normal.

The following morning, cortisol was low at 1.6µg/dL. ACTH stimulation test had inadequate response. ACTH was elevated at 65.6pg/mL. Sella MRI and renal US showed no abnormalities. Electrolytes remained within normal limits. Baby did well upon initiation of hydrocortisone with no further hypothermia.

Results: Hypocortisolism, elevated ACTH, and lack of response to exogenous ACTH indicated a diagnosis of primary adrenal insufficiency.

Discussion: The initial presentation demonstrates non-specific symptoms associated with AI, including poor feeding and neurologic changes. Despite the overall low prevalence of neonatal sepsis presenting as isolated hypothermia, risks of morbidity and mortality made it the primary suspected diagnosis (1). PAI in newborns is rare, occurring in 1:10,000-20,000 live births, with the newborn screen detecting 90% of cases in the most common form of CAH (2). High suspicion is needed to diagnose the 10% of PAI cases not initially diagnosed by newborn screening, as many are initially misdiagnosed as sepsis, metabolic disorders, or cardiovascular causes (3). Deterioration despite adequate treatment in patients with hypothermia, as this case shows, should prompt further examination of the suspected diagnosis, including assessment for adrenal insufficiency.

Second Individual with Craniosynostosis and Microdeletion Including 14q22: Premature Fusion of Cranial Sutures and Copy Number Variation

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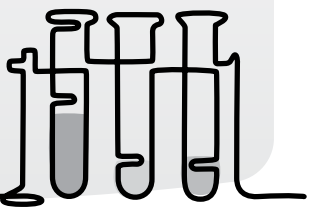
Background: Interstitial microdeletions within the long arm of chromosome 14 containing q22 are extremely rare. Most reported deletions span q22 and q23, a region of the genome containing several genes. While literature suggests that homozygous deletions in the q22-q23 region result in fetal demise, heterozygous deletions have previously been associated with bilateral anophthalmia, ear and pituitary anomalies, developmental delay, and craniofacial anomalies. One previous case report documented lambdoid craniosynostosis on skeletal x-ray and pituitary hypoplasia on brain MRI attributed to a deletion at 14q22.1q23.2. To identify a genetic diagnosis, patients with premature fusion of cranial sutures are often recommended next-generation sequencing panels including genes commonly associated with craniosynostosis. We describe the second documented patient with craniosynostosis and a deletion of 14q22.

Case Presentation: We report a 14-month-old girl with a 4.6 Mb heterozygous de novo deletion at 14q22.1q22.3 and a 724 kb duplication on chromosome 22q11.23, inherited from a healthy, neurotypical mother, detected by exome sequencing with confirmed parentage. She was born at 34 weeks gestation. To date, the patient's clinical features include craniofacial dysmorphia with craniosynostosis and ocular asymmetry, global developmental delay, poor growth, hypotonia, a history of patent ductus arteriosus, and mild unilateral pelviectasis. Similar features have previously been associated with heterozygous deletions in the 14q22q23 region. Our patient is the first reported case with confirmed multi-suture craniosynostosis.

Conclusions: This is the eighth reported case of a heterozygous microdeletion on chromosome 14 limited within the q22 region and the third ever documented case with a microdeletion at q22.1q22.3. While developmental delay and hypotonia were noted in all three patients with del 14q22.1q22.3, other clinical features varied. Interestingly, ours is the second report of craniosynostosis. The mechanism for this is not well elucidated but it may be related to the relative expression of bone morphogenetic protein 4 (BMP4), which maps to the 14q22 and is known to be involved in skeletal formation during embryonic development. As the second known case of craniosynostosis with copy number loss in this remarkably rare region, this report suggests that microdeletions – including 14q22.1q22.3 – should be considered in the differential diagnosis of craniosynostosis. Incorporating copy number variation (CNV) analysis in the testing algorithm is important as the literature body documenting CNV in patients who present with craniosynostosis is rapidly growing.



Abstract 48

Developing, Customizing, and Testing a Preventive Care Mobile Health Tool

Elizabeth Reisher, MS[1], Ellen Kerns, PhD, MPH, CPH[1,2], Martina Clarke, PhD[3]

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The delivery of childhood vaccinations using an established schedule has been a top public health achievement.1, 2 Among U.S. children born 1994-2013, it is estimated that vaccinations prevented 732,000 deaths and 21 million hospitalizations3. Currently, the Advisory Committee on Immunization Practices (ACIP) recommends children receive 11 vaccine series, each with 1-4 doses, to protect against 15 diseases before the 2nd birthday.4 However, among U.S. children born 2016-2017, only 70.5% had completed the combined 7-vaccine series by age 24 months.5

The time available to educate and discuss vaccinations is limited during clinic visits, causing caregivers to seek information about vaccines outside of clinic visits. This mHealth tool aims to promote vaccination confidence and uptake among caregivers of young children by addressing vaccine safety concerns, what to expect at each well-child visit, and information regarding vaccine availability if needed outside clinic hours.

Vaccine safety concerns, what to expect at each well-child visit, and information regarding vaccine availability can be addressed using an mHealth tool.

An alpha version of an mHealth tool using institutionally owned software was developed and sent out to members of two community advisory boards (CAB) (one rural, one urban). CAB members provided feedback on what adaptations are necessary before usability testing. Using the focus group results, a resulting beta version for usability testing will be translated into Spanish, and a Spanish-speaking CAB will assess for cultural compatibility and necessary linguistic modifications before usability testing in Spanish. Remaining content display decisions will undergo A/B testing. The caregivers will be asked to complete representative scenarios of expected caregiver work-flows. While completing these scenarios, caregivers will be asked questions on the content to determine how well they understood the information displayed. Finally, caregivers completed both the mHealth app usability questionnaire (MAUQ) survey6 and the Propensity to Trust assessment7 to determine their overall perception of usability and willingness to trust the information displayed. Caregivers will also be assessed for the perception of importance and hesitancy towards the preventive care measures before and after use of the app.

Themes, resources to be included, and content preferences from the focus groups included providing local resources for after-hours clinics, post-partum, food, housing, and when should I call the doctor.

Both community feedback and individual usability testing from representative users can be incorporated to customize preventive care content for parents in mHealth format leading to a usable and acceptable tool.

A Rare Case of Acute Pancreatitis in a Pediatric Patient with Bifid Pancreatic Tail

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Bifid pancreatic tail (also known as fishtail pancreas) is an anomaly of the pancreas thought to be caused by a branching abnormality during embryological development. Although anomalies of the pancreas are common, bifid pancreatic tail is extremely rare, with only a small number being reported in the literature. The clinical significance of bifid pancreatic tail is not clearly defined, however, there have been a few cases proposing bifid pancreatic tail as a cause of acute pancreatitis. In this case report, we expand upon this clinical finding by describing the case of an 18-year-old female presenting with abdominal pain, nausea, vomiting, and other symptoms consistent with acute pancreatitis. The patient reported a history of similar episodes of pain, although no previous CT was performed for diagnosis of acute pancreatitis. When we performed CT, a pancreatic pseudocyst and walled-off necrosis were found, indicating a previous episode of acute pancreatitis prior to this one. Magnetic resonance cholangiopancreatography (MCRP) showed a new finding of bifid pancreatic tail, suspicious as the cause of her recurrent pancreatitis. Patient underwent axios stent placement and drainage of the pseudocyst, followed by stent removal and necrosectomy. Patient is currently stable and a repeat MCRP is scheduled. This case reiterates bifid pancreatic tail as an etiological factor for acute pancreatitis, and further characterizes this rare anomaly as a cause of recurrent pancreatitis, particularly in the pediatric population.

Abstract 50

Activated STAT3/P-TEFb Complex Functions in Medulloblastoma

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Background: Medulloblastoma (MB) is one of the most common pediatric brain tumors. MB is composed of four molecular subtypes one being Group 3 which has the worst prognosis among the MB subtypes due to MYC-overexpression. STAT3 is constitutively activated in MB and is known to regulate MYC expression. Further, CDK9, a major component of P-TEFb, is also dysregulated in MB. P-TEFb activates RNA Pol II and transitions the paused RNA Pol II to a productive transcriptional elongation mode. STAT3 and CDK9 are overexpressed in human MB tumors and correlate with poor patient survival.

Significance of Problem: High-risk MYC-driven G3MB has a poor clinical outcome and many of the current treatments have adverse side effects. Therefore, there is a critical need to understand MYC-driven MB, to identify targeted drug candidates and improve patient treatment and survival.

Hypothesis: Our overarching hypothesis is that constitutively activated STAT3 recruits P-TEFb complex and promotes enhanced transcription of its oncogenic targets, leading to MB tumorigenesis.

Experimental Design: We utilized co-immunoprecipitation (Co-IP) and proximal ligation assay (PLA) to determine whether STAT3 and CDK9 interact in MB cell lines. Then we used a luminescence and colony formation assay (CFA) to determine the effects of targeting STAT3 and CDK9 alone and in combination in MB. Additionally, a western blot (WB) was used to determine if our treatments were cytostatic or cytotoxic. Finally, we have used a subcutaneous xenograft mouse model using a group 3 MYC amplified MB cell line to test efficacy of targeting STAT3 and CDK9 in vivo as well as its effects on tumor growth, by measuring tumor size, and immunohistochemistry (IHC).

Results: Our Co-IP and PLA showed endogenous STAT3 directly interacts with CDK9 in MB. Additionally, we showed targeting both STAT3 and CDK9 in combination caused significant down regulation in MB cell growth and viability by causing the cells to undergo apoptosis by our luminescence, CFA, and WB assay. The results of the mouse experiment showed a significant reduction in tumor size as well as decreased expression in MYC and proliferation as well as an increase in apoptosis in the tumors by IHC.

Conclusions: Our study demonstrates that endogenous STAT3 interacts with CDK9 to promote MB tumorigenesis. Furthermore, STAT3-CDK9 inhibition and concomitant downregulation of MYC have a significant regulatory effect on MB tumorigenesis. Thus, STAT3-CDK9 inhibitors can be used as potential adjuvant therapy to treat high-risk MB patients, eventually improving pediatric patients' quality of life.

An Association between Declarative/relational Memory and Hippocampal Volume in Periadolescent Children: Preliminary Findings from the PRANK Study

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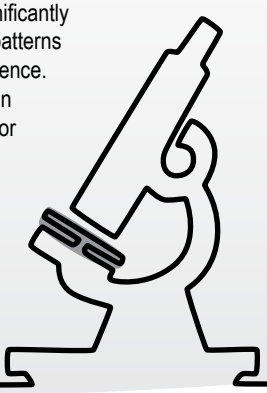
Introduction: Significant changes to brain structure/function and cognition occur during development. One brain structure that is critical for normal declarative/relational memory, the hippocampus, develops rapidly during the periadolescent period (ages 8-13 years). Changes in hippocampal structure may underlie developmental improvement in declarative/relational memory. An ongoing NIA-funded research study, Polygenic Risk of Alzheimer's disease in Nebraska Kids (R01AG064247), measures brain structure/function, cognition, and Alzheimer's polygenic risk in periadolescent children. Here, we provide preliminary analysis measuring the association between declarative/relational memory and hippocampal volume in this sample (N =133). We hypothesize that greater hippocampal volume will be associated with better memory performance.

Methods: Declarative/relational memory was assessed using The Child and Adolescent Memory Profile (ChAMP) including two subtasks ("objects delayed" and "places delayed"). Hippocampal volumes (HcV) were collected from structural MRI using protocols adapted from the Human Connectome Project. HcV was measured via FreeSurfer automated segmentation and corrected for total intracranial volume. We used partial correlations to measure the association between HcV (bilateral, left, and right) and declarative/relational memory performance on ChAMP whilecontrolling for age and sex.

Results: We found preliminary evidence consistent with associations between ChAMP memory performance and HcV. Performance on the objects subtask was significantly associated with HcV such that bilateral, left, and right HcV were directly associated with better memory performance, bilateral HcV: r(131) = .24, p = .005, left HcV: r(131) = .24, p = .006; right HcV: r(131) = .23, p= .01. No significant positive association between performance on the ChAMP places memory subtask and hippocampal volumes was observed, bilateral HcV: r(131) = .14, p = .11, left HcV: r(131) = r = .15, p = .09; right HcV: r(131) = r = .12, p = .16. Although this relationship was not statistically significant, the direction of the relationship (larger HcV associated with better ChAMP places delay performance) was consistent with directional expectations based on previous literature.

Conclusions: These preliminary results suggest an association between HcV and memory during periadolescence. Specifically, larger HcV was associated with better ChAMP object memory.Although ChAMP places memory performance was not significantly associated with HcV, future longitudinal data may elucidate unique patterns of hippocampal development within subjects throughout periadolescence. Measuring HcV and memory ability thus demonstrates an association between brain structure and cognitive ability, and lays a foundation for studies of how brain development may contribute to lifespan risk of neurological diseases that target the hippocampus, such as Alzheimer's disease



Abstract 52

TAB2-Related Disorder: A Review of the c.679C>T (p.Arg227*)

Documented Cases and a Clinical Report

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Deletions and loss-of-function variants in the gene TAB2 cause the autosomal dominant TAB2-related disorder, a condition that presents with congenital heart defects and other extracardiac features, namely facial dysmorphisms, short stature, and joint hypermobility. With only an estimated 110 reported cases in the medical literature as of 2024, TAB2-related disorder appears to be quite rare. Contributing to the difficulty in detecting TAB2-related disorder is the diverse clinical presentation and progression reported in the literature, which may be explained in part by genotype-phenotype correlations of different TAB2 variants. To better understand the clinical presentation and progression of TAB2-related disorder, comparative analysis of the same TAB2 variants is crucial. Notably, recent research by Hanson et al. identified a potential hotspot variant, c.679C>T (p.Arg227*), observed in two unrelated families. In this poster, we conduct a comprehensive literature review, compiling all documented cases of patients with the TAB2 c.679C>T (p.Arg227*) variant, and expand the clinical presentation of the TAB2 c.679C>T (p.Arg227*) variant by reporting an additional case of an unrelated female seen in the Children's Nebraska Cardiovascular Genetics clinic with the same variant. Our search yielded 18 studies from which we extracted three cases of the c.679C>T (p.Arg227*) TAB2 variant (n= 4, including our patient). All four patients were female, had variable congenital heart defects, and facial dysmorphisms. While not universally present, joint hypermobility, short stature, and musculoskeletal abnormalities were also common in this patient population. In conclusion, our study attempts to elucidate the varied clinical presentation of TAB2-related disorder by comparing cases with a recurrent pathogenic TAB2 variant, further developing our understanding of the phenotype of TAB2-related disorder

Oh, it's just RSV; When Bronchiolitis Becomes Lethargy

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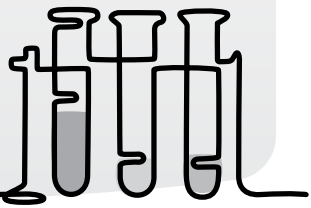
Initial History/Presentation: A term seven-month-old male presented to the emergency department (ED) with five days of cough, congestion, and worsening work of breathing. Mom noted decreased urine output, multiple episodes of non-bloody emesis, and non-bloody loose stools. Patient had been afebrile and was up to date on vaccinations. He was admitted and started on IV fluids with supportive cares, but continued to have frequent episodes of emesis, poor oral intake, and progressive lethargy necessitating further work-up.

Physical Exam: Initially, well appearing with no acute distress. By day two of admission, our patient had become irritable, less reactive to voice and physical touch, and not willing to eat or drink. He had cough, congestion, subcostal retractions, and mild crackles throughout lung fields. Cardiac unremarkable. Abdomen was soft, nontender, nondistended with normal bowel sounds. No focal neurologic deficits were present, though by day two of admission he was lethargic with poor muscle tone and responsiveness.

Diagnostic Evaluation: Initial evaluation pertinent for a RPP with RSV. Gastrointestinal pathogen panel and blood cultures were negative. CBC indicated thrombocytosis (578,000) and a BMP was unremarkable. Due to clinical decompensation, a septic work-up was initiated. A lumbar puncture and urinalysis were planned, but prior to collection, patient had a bloody bowel movement, which resulted in the completion of an abdominal US and x-ray.

Diagnosis: An abdominal US revealed our patient's course of RSV bronchiolitis was complicated by large bowel intussusception within the mid to left hemiabdomen and mild-moderate free fluid in the lower abdomen. X-ray did not indicate free air. A hydrostatic enema was attempted but incomplete reduction was achieved. Repeat US the next morning demonstrated persistent incomplete reduction. Complete reduction was achieved following a second enema.

Discussion/Conclusion: While intussusception is associated with episodic/cyclical abdominal pain, fussiness, and bloody/jelly-like stools, our patient did not have this presentation until the bloody bowel movement on day two of admission. Surprisingly, only 15% of patients have a classic presentation at time of diagnosis. On rarer instances, lethargy, specifically in infants, can be the initial presenting symptom, which can be confused with sepsis, seizures, or trauma. A delay in diagnosis and treatment can lead to bowel perforation or ischemia. This patient's case highlights the importance of intussusception being included on the differential for a lethargic infant.



Abstract 54

Dual Diagnosis of DNMT3A- and KDM4B-Related Syndromes: An Epigenetic Combo

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Epigenetic modifications, such as DNA methylation and histone modifications, are important transcriptional regulators that may alter gene expression without altering the order of nucleotides. Three active human DNA methyltransferases (DNMTs) accomplish this function: DNMT1, DNMT3A, and DNMT3B. DNMT1 is responsible for preserving maintenance methylation through mitotic cell division, while DNMT3A and DNMT3B are de novo methyltransferases required for processes such as gametogenesis, embryogenesis, and differentiation. KDM4B is an example of a lysine demethylase, which removes methyl groups from histone H3, allowing underlying chromatin to become activated and accessible for transcription.

Germline loss-of-function variants in DNMT3A are associated with DNMT3A Overgrowth syndrome, also known as Tatton-Brown-Rahman syndrome (TBRS). Clinical phenotypes of this syndrome include tall/large stature, macrocephaly, distinctive facial features, intellectual disability, and developmental delays with less frequent findings of cardiac defects, hernias, scoliosis, afebrile seizures, and malignancies. KDM4B is responsible for epigenetic histone methylation across the genome, and pathogenic variants are associated with global developmental delays, dysmorphic features, and variable neurological abnormalities.

This patient presented to genetics for workup regarding his tall stature and global developmental delays. Additional clinical features include joint hypermobility, left femoral head fracture (9 yo, normal DEXA), leg length discrepancy, mild intellectual disability, myopia, mild scoliosis and kyphosis, down slanting palpebral fissures, micrognathia, absent lower canines, pes planus, and bilateral hindfoot deformities. Imaging showed normal bone age, brain structure, and cardiac structure. He was diagnosed via exome platform sequencing. Two pathogenic variants were identified, one in DNMT3A and the other in KDM4B, both of which fit with his clinical phenotype.

This is the first report of DNMT3A- and KDM4B-related disorders in the same individual. Both genes are involved in epigenetic regulation and epigenetic signature evaluation was performed via EpiSign at Greenwood Genetic Center. Abnormal DNA methylation patterns consistent with both DNMT3A and KDM4B-related disorders were detected. Interestingly, while an epigenetic signature related to DNMT3A was detected with high confidence, a KDM4B methylation pattern was still detected but with likely interference. With both genes affecting methylation patterns across the genome, it is unclear how their methylation signatures would interact with each other. This clinical report may help expand the phenotypic variations found within this rare and still relatively newly described syndrome, illustrate findings regarding DNMT3A-related epigenetic signature for this patient, and present its potential interaction with other methylation-associated disorders on genome-wide epigenetic signatures.

Neuropsychological Assessment in FIRES/NORSE Mouse Model

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Background: Febrile Infection-Related Epilepsy Syndrome (FIRES), categorized under New Onset Refractory Status Epilepticus (NORSE), represents a severe epileptic condition triggered by febrile illnesses or infections. Managing FIRES poses significant challenges, often leading to refractory epilepsy and neuropsychological impairments. Recently, we established a novel FIRES/NORSE model using interleukin-1 receptor antagonist (IL-1RA) deficient mice, which faithfully recapitulates key clinical features observed in FIRES patients including the emergence of spontaneous recurrent seizures after status epilepticus without latent period and cell death accompanied by marked microglia and astrocyte activation in the hippocampus.

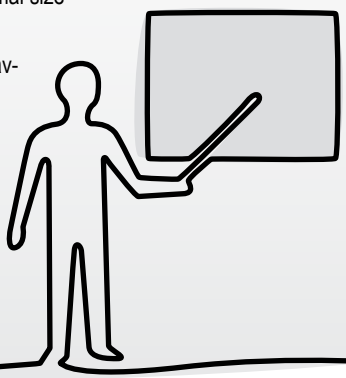
Significance of the Problem: Addressing the combined neuropsychological impairments in FIRES/NORSE is crucial but remains an unmet goal, partly due to the lack of a suitable animal model.

Hypothesis, Problem or Questions: This pilot research aims to explore the neuropsychological dimensions of our developed FIRES/NORSE model, with an ultimate goal of utilizing it as a platform for developing treatments targeting FIRES/NORSE.

Experimental Design: A total of 41 mice, comprising IL-1RA deficient and wildtype (WT) cohorts, were utilized. Cohort one underwent the FIRES model procedure (n=14), involving systemic lipopolysaccharide (LPS) injection + hyperthermia at P25 (as the first hit) followed by intrahippocampal kainic acid (IHKA) injection at P30 (as the second hit). Control mice (n=5) were not subjected to IHKA modeling. Cohort two mice underwent the NORSE model (n=12), receiving IHKA injection at P40, with n=10 sham control mice. Neuropsychological assessments were conducted between P47-P54 for FIRES mice and P70-P80 for NORSE mice, including open field, Y-maze, and Barnes maze tests. Mice behavior was monitored and analyzed in real-time using the ANY-maze system.

Result: The open field test was employed to evaluate both anxiety-like behavior and locomotor activity. (i) Locomotor function was determined by total distance traveled (TAT) and an increased TAT was shown in FIRSE/ NORSE mice vs. controls, suggesting hyperactive behavior in FIRSE/ NORSE mice. (ii) Anxiety-like behavior was evaluated by measuring time spent in peripheral vs. the central areas of open field. Data showed that FIRES mice spent longer time in peripheral zone vs controls, suggesting their higher anxiety levels. (iii) Y-maze test and Barnes maze were used to evaluate cognitive function, and data showed that FIRES mice had more errors in enter novel arm vs controls, which indicate an impaired cognitive function. However, the Barnes maze did not yield positive result with limited animal size numbers tested.

Conclusion: This pilot study demonstrated anxiety-like behavior and cognitive impairments in our mouse model of FIRES/ NORSE, warranting further investigation with larger sample sizes and expanded behavioral testing.



Abstract 56

Red Blood Cell Transfusion Causes Brain Inflammation in Murine Pups with Phlebotomy-Induced Anemia

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Background: Anemia is the common comorbidity in premature infants. RBC transfusion remains the treatment of severe anemia that improves oxygen carrying capacity and promotes growth in the premature infants. In contrast anemia, blood transfusion and brain inflammation have correlation in clinical and animal studies. Severe anemia has shown hippocampal injury in animal study, but the effects of RBC transfusion on brain inflammation after anemia has not yet been evaluated.

Objective: To identify the inflammatory changes in the neonatal mouse brain of phlebotomy-induced anemia and RBC transfusion.

Design/Methods: C57BL/6 pups were studied in 4 groups namely naïve control, RBC transfused, severe anemia and severe anemia with RBC transfusion. Severe anemia was induced by facial vein phlebotomy on postnatal day (P) 2, 4, 6, 8, and 10. RBC transfusion consisted of 20 ml/kg of leukoreduced and stored packed RBC from allogeneic adult FVB mice donors, administered intravenously into the retro-orbital plexus on P11. Whole brain tissue was extracted 24 hr post-transfusion, and total protein concentration was estimated by BCA Bradford assay. Milliplex Map Mouse cytokine/chemokine multiplex assay were used to quantify the cytokines and chemokines in brain tissue homogenate. Immunostaining was performed to localize the circulating monocyte recruitment and microglial activation by using antibodies for Ly6c and Iba-1. The recruitment of monocytes in anemic-transfused brain were investigated by flow cytometry.

Results: The inflammatory cytokines IL-1α, IL-1β, IL-6, TNF-α and IL-12p70 were significantly increased in the brain of anemic transfused mouse compared to transfused controls. There were no significant changes on Il4 and IL5 levels. The chemokines (C-C motif ligands) MCP1 [CCL2], MIP1-α [CCL3], MIP1-β [CCL4], RANTES [CCL5] and Eotoxin [CCL11] were significantly increased in anemic-transfused mouse pups. Immunostaining of anemic-transfused brain showed presence of increase n umber of Ly6C+ monocytes than transfusion control and confirmed that anemic-transfusion related brain inflammation was associated with increased number of Ly6C+ monocytes and activated microglia (Iba1+ with round amoeboid shape) in the brain. Flow cytometry also confirmed the presence of circulating monocyte phenotype with CD11b+CD45+Ly6C+ markers in anemic-transfused brain.

Conclusion(s): RBC transfusions increase the inflammatory cytokines and monocyte attractant chemokines in murine pups' brain with severe anemia. Circulating monocytes were recruited in the anemic-transfused brain that exacerbate anemia-induced inflammation.

Identification and Treatment Challenges of Disseminated Fungal Infection in Pediatric Patient with Pre-B ALL

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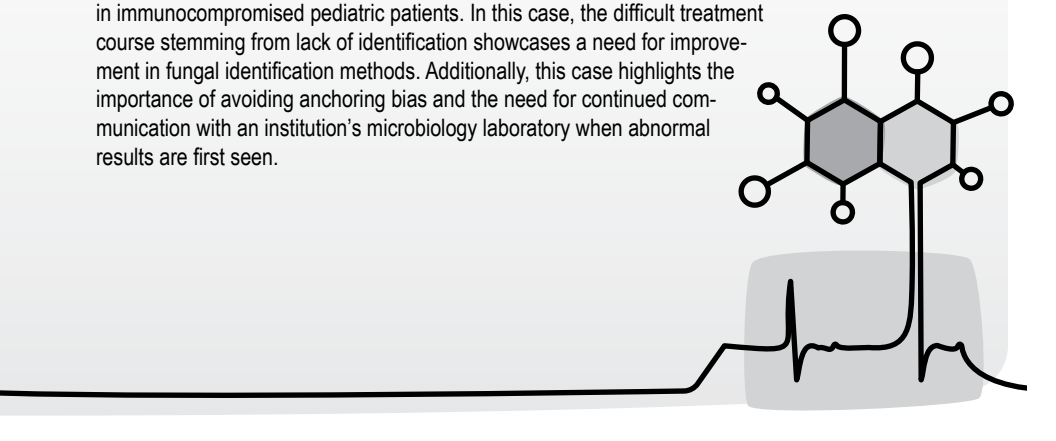
Background: Magnusiomyces clavutus, previously classified as Geotrichum clavatum and Saprochaete clavata, is an ascomycetous fungus commonly found in soil or water and as part of human normal flora. Few cases of disseminated disease have been reported, mostly described in immunocompromised patients with hematologic malignancies. This species has intrinsic resistance to many commonly used antifungal agents, making prompt identification viral for antifungal selection.

Case: A 2-year-old female with pre-B ALL undergoing consolidative chemotherapy, on antimicrobial prophylaxis, presented with febrile neutropenia. On admission, peripheral and port blood cultures (BC) were obtained, and cefepime initiated. Fevers persisted and on hospital day (HD) 4, BCs from HD#2 grew large gram-positive rods (GPR). Vancomycin was initiated but subsequent daily blood cultures continually grew GPRs that were unidentifiable, with the lab unable to rule out B. anthracis. On HD#5 she developed abdominal pain. CT demonstrated inflammatory or infectious involvement of multiple organs. During imaging, she developed hemodynamic collapse requiring ECMO and further supportive measures. Additional antibiotics and liposomal amphotericin B were started, and the isolate was sent to the Nebraska Public Health laboratory for further identification. On HD#6, after worsening neurological exam, a CT head revealed large, diffuse areas of ischemia. The isolate was reported negative for B. anthracisand sent to a commercial laboratory for identification. On HD#7 care was withdrawn. Nine days later, the isolate was identified as Magnusiomyces clavatus.

Discussion: Disseminated Magnusiomyces clavatus infection almost exclusively occurs in profound neutropenia patients, with other possible risk factors being contaminated catheters or previous antifungal therapy. There has previously been one documented case of M. clavutus infection in North America and 12 total pediatric cases. As demonstrated in this case, identifying M. clavatus is difficult with current methods, complicating antimicrobial selection. Anti-fungals are generally initiated after 72-96 hours of persistent fever in a neutropenic patient. However, there is no standardized treatment for M. clavatus due to disease rarity and lack of standardized anti-fungal breakpoints, but previous cases have reported mixed success with amphotericin B or voriconazole monotherapy, or some combination.

Conclusion: Magnusiomyces clavatus is a rare but emerging source of disseminated infection in immunocompromised pediatric patients. In this case, the difficult treatment course stemming from lack of identification showcases a need for improvement in fungal identification methods. Additionally, this case highlights the importance of avoiding anchoring bias and the need for continued communication with an institution's microbiology laboratory when abnormal results are first seen.



Abstract 58

Urbach-Wiethe Syndrome, a Rare Cause of Eyelid Margin Lesions

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Urbach-Wiethe syndrome is an extremely rare autosomal recessive multisystemic disorder caused by a mutation in the extracellular matrix protein-1 gene located on chromosome 1q21. Also known as lipoid proteinosis, it was first described in 1929 with approximately 300 reported cases since then. It is characterized by the deposition of collagenous material in the skin, mucosa, larynx, vocal cords, and as in this case, the eyelid margins. Patients typically present to otorhinolaryngologists with hoarseness of voice, or to neurologists due to seizures or cognitive abnormalities. Few may however present to ophthalmologists with lesions over the eyelid margins which could be misdiagnosed as blepharitis. It is therefore important for all ophthalmologists to be aware of the entity in order to adequately diagnose and manage the condition.

A 7-year-old boy was brought to the ophthalmology clinic at Children's Nebraska with a history of multiple bumps on his eyelids since childhood which were progressively increasing in number. He also had a history of chronic hoarseness of voice, recurrent oral ulcers, generalized eczema of the skin, and multiple soft tissue infections. On ophthalmic examination, his corrected visual acuity was 20/20 in both eyes and he was found to have multiple pearly beaded papules on the upper and lower eyelid margins of both eyes suggestive of moniliform blepharosis. The rest of the anterior and posterior segment examination was found to be within normal limits. He had been seen by ENT specialists in the past who had twice carried out Laryngoscopy and Bronchoscopy to determine the cause of his chronic hoarseness. The procedures were suggestive of posterior oropharyngeal cobble-stoning along with thick fibrinous tissue at the posterior glottis. A biopsy of the mucosa overlying the glottis showed non-specific inflammatory changes and he was being managed conservatively.

In the ophthalmology clinic, we obtained high-quality magnified images of the eyelid margin lesions. Based on his history and the pathognomonic clinical features, he was diagnosed with Urbach-Wiethe syndrome. Due to the known high recurrence rate of these lesions, the decision was made to forego lesion excision. An excision biopsy of an eczematous axillary lesion by the dermatologist confirmed the diagnosis. This case reinforces the importance of a thorough clinical examination along with good communication, between various subspecialists in helping reach a diagnosis and managing patients with rare diseases.

Social Health Programming is Not Associated with Reduced Stress Levels in Adolescent Girls

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Background: Cardiovascular disease is the leading cause of death in the United States. Weathering, which encompasses the cumulative effect of chronic psychological stressors, contributes to cardiovascular disease by elevating the biological stress response and disrupting multiple biological systems including the cardiovascular system. However, the severity of weathering may be reduced through resiliency training provided through social health programming (SHP).

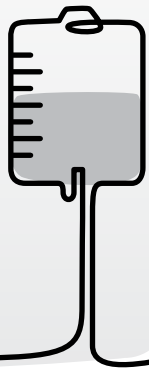
Significance: SHP has the potential to reduce cardiovascular morbidity and mortality by empowering participant's ability to cope with stressful experiences. However, little is known about how SHP impacts biological markers of stress, including hair cortisol concentrations.

Hypothesis: We hypothesize that participation in SHP provided by Girls Inc., Omaha will be associated with higher emotional resiliency and lower hair cortisol concentrations.

Experimental Design: Girls 12 to 18 years old who had either never participated in any SHP (control group; N=27) or participated in Girls Inc. (intervention group; N=23) were enrolled in this study. Participants completed the validated 6-question Brief Resilience Scale (BRS) to measure emotional resiliency. Possible scores from the BRS range from 1.0 to 5.0, with higher scores representing higher emotional resiliency. The CYW Adverse Childhood Experiences (ACEs) Questionnaire Teen Self-Report was used to measure exposure to traumatic experiences. A 3 cm hair sample was collected from the posterior vertex of the head (N=13 intervention and N=16 control) and cortisol concentrations were measured using enzyme-linked immunosorbent assays. Mann-Whitney U tests were performed to identify differences between groups.

Results: Girls Inc participants attended Girls Inc for a median of 5 years prior to study participation. Emotional resiliency was not significantly different between the intervention (median BRS score 3.2) and the control group (median BRS score 3.2; p=0.87). Similarly, there was no significant difference in median hair cortisol concentrations between the intervention (44.6 pg/mL) and control group (28.2 pg/mL; p=0.14). Additionally, there was no significant between-group difference in median adverse childhood experience (ACEs) exposure (invention: 5 ACEs vs control: 3 ACEs; p=0.19). However, there were demographic differences between the intervention and control groups, with the intervention group being more likely to identify as non-Hispanic Black than the control group (p=0.002).

Conclusion: Participation in SHP through Girls Inc. was not associated with changes in emotional resiliency or hair cortisol concentrations. However, demographic differences between the intervention and control group may have impacted these results. More research in a larger sample is needed to clarify the impact of SHP on biological markers of stress in adolescent girls.



Abstract 60

X-linked Opitz G/BBB Syndrome: A Case Report

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X-linked Opitz G/BBB Syndrome results from a mutation in the MID1 gene, responsible for producing midline-1 protein, which aids in protein recycling. This genetic disorder leads to congenital midline defects, including hypertelorism and hypospadias. Our patient, a term infant diagnosed with X-linked Opitz G/BBB Syndrome, was identified after the 20-week ultrasound detected anomalies, including cleft lip and palate, Dandy-Walker malformation, and 2-vessel umbilical cord with an intraabdominal umbilical vein varix. Amniocentesis with microarray analysis and High-Resolution Deletion/Duplication studies were subsequently performed, confirming the diagnosis. Following delivery, physical exam was significant for up-slanting palpebral fissures with wide-spaced eyes, bilateral cleft lip and palate, large anterior fontanelle, and bilateral microtia with prominent inner helices and minimal earlobes. He had mild respiratory distress that resolved shortly after birth. Chest radiographs demonstrated eventration of the diaphragm. An MRI revealed an absence of Foramen of Magendie. He was discharged on day 16 with a positive outlook. Clinical signs aid in diagnosis of X-linked Opitz G/BBB Syndrome, but genetic testing is needed for confirmation. This can be done via single-gene testing, a multigene panel, or exome testing. These patients require the attention of a multidisciplinary healthcare team. Surgery may be necessary to address major congenital anomalies, and regular monitoring is necessary to identify any further issues that may arise with age.

Platelet Indices are an Early Predictive Tool During Murine Transfusion-Associated Necrotizing Enterocolitis Injury

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Background: Necrotizing enterocolitis (NEC) including Transfusion-associated NEC (TA-NEC) is an idiopathic, inflammatory bowel necrosis of low-birth-weight premature infants born before 32 weeks gestation. The diagnosis of NEC currently depends on clinical symptoms and radiological findings, which appear late and leave limited time for therapeutic interventions.

Objective: To investigate whether platelet indices can be a predictive early diagnostic index for NEC, we studied time-kinetic NEC disease progression and possible underlying factors in preclinical models of anemia and RBC transfusion-associated NEC-like injury.

Methods: C57BL/6 mouse pups were randomly studied in 4 groups (n=15 each): (1) naïve controls; (2) anemic (hct 20-24%); (3) transfusion control; and (4) anemic-transfused. Anemic group pups were rendered severely anemic by facial vein phlebotomies on postnatal days (P)2, 4, 6, 8, and 10. Transfusion controls received an intravenous FVB-donor-derived RBC transfusion (20 mL kg−1) into the retroorbital venous plexus, injected in two aliquots on each side) on P11. Naive controls were maintained without intervention. Time-kinetic measurements included platelet numbers (PLT), mean platelet volume (MPV), platelet-large cell ratio (P-LCR), and immature platelet fraction numbers (IPF) were analyzed during each phlebotomy and 3h, 6h, and 9h, 12h and 24h after RBC-transfusion. Bone marrow megakaryocyte ploidy was analyzed by flow cytometry, and plasma PF4/CXCL4 was measured by ELISA. Primarily isolated megakaryocytes were used to study platelet release in vitro.

Results: Time-kinetic measurement showed a progressive increase in IPF, P-LCR, and MPV at 3h after RBC-transfusion, indicating early immature platelet release and developed thrombocytopenia by decreased platelet numbers. Megakaryocyte ploidy and early (3h) elevation in plasma PF4/CXCL4 concentrations further supported possible activation and resulted in early platelet release from the bone marrow. In vitro, bone marrow-derived megakaryocytes treated with anemic-transfused NEC plasma also showed early immature platelet release. In support of these findings, pharmacological inhibition of PF4/CXCL4 in plasma samples obtained at 3h (and later) after initiation of TA-NEC injury also blocked platelet release ex vivo.

Conclusion: Time-kinetic measurement showed an early rise and progressive increase in IPF, P-LCR, and MPV during TA-NEC injury indicating these indices as potentially valuable in early diagnosis of NEC. These findings merit further clinical validation and may also have translational relevance in understanding the pathophysiological progression of human NEC.

Abstract 62

Identifying Medulloblastoma Subtypes by Leveraging Heterogenous Transcriptome Data with Batch Effects

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As a malignant pediatric brain cancer, medulloblastoma (MB) accounts for around 20% of all pediatric central nervous system (CNS) neoplasms. MB has notable heterogeneity in its tumor, resulting in a complex array of distinct molecular subtypes characterized by morphological, molecular, and genetic alterations, mainly including SHH, WNT, Group 3 and Group 4. Although the overall cure rates for MB are around 70%, the survival rate varies significantly across different molecular subtypes. Conventional experimental methods for identifying MB subtypes are usually costly, time-consuming, and labor-intensive. Accurate identification of MB subtypes enables improved downstream risk stratification and tailored therapeutic treatment design. Previous studies indicate that identifying MB subtypes based on transcriptome data is an efficient and feasible way. However, their performance may be poor due to limited cohorts and severe batch effects if combining data in different sequencing platforms and various data sources. To address these concerns, we propose a machine learning approach to effectively integrate heterogeneous transcriptomic data with batch effects for accurate identification of MB subtypes. Specifically, for a baseline RNA-seq or microarray data, we performed pairwise analysis of gene expression based on subtype-specific differential gene expression analysis. By comparing gene pairs within cohorts rather than across cohorts, we could avoid batch effects and successfully identify those gene pairs that significantly contribute to the identification of MB subtypes. Then, to enhance the MB subtyping performance, we integrated different transcriptomic data in different sequencing platforms (e.g., either RNA-seq or microarray) by identifying overlapping gene pairs in different cohorts. In case too many gene pairs were identified, we leveraged ensemble random projection to reduce dimensions of gene pair expressions. Subsequently, the transformed low-dimensional feature vectors were classified by an ensemble of support vector machine (SVM) classifiers to identify MB subtypes. Results suggested that our approach outperformed state-of-the-art MB subtyping approaches in terms of different performance metrics including accuracy, MCC and F1-score. In addition, our approach could effectively deal with heterogeneous transcriptomic data with severe batch effects across different sequencing platforms and cohorts. We believe that our proposed approach has direct positive impacts on downstream MB risk stratification and tailored treatment design. We also expect that our proposed approach has great potential to address many biomedical problems with batch effects for various types of pediatric, adolescent, and young adult (AYA) cancers.

Evaluating Physiologic Z-Score Changes and Subsequent Malnutrition Classifications in Extremely Low Birth Weight Infants Based on Birth Gestational Age

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Background: Extremely low birth weight (ELBW, <1000 grams) infants are at high risk for inadequate growth resulting from inadequate nutrition provision. Current suggested indicators for identifying neonatal malnutrition include evaluating changes in weight z-score over time with normal physiologic decline after postnatal diuresis suggested to be no greater than 0.80.

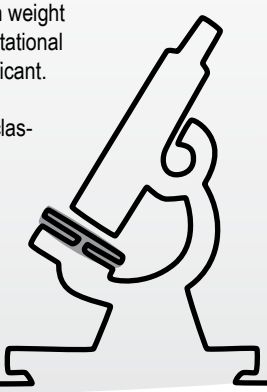
Significance of the Problem: ELBW infants—especially those born at decreasing gestational ages—may be observed to demonstrate z-score declines from birth by >0.80 with normal postnatal diuresis, so current suggested indicators for neonatal malnutrition may incorrectly suggest malnutrition at varying time points.

Objective & Hypothesis: The objective of this study was to evaluate changes in weight z-score between birth to discharge in ELBW infants across varying birth gestational ages and resulting malnutrition classifications. We hypothesize observing larger declines in weight z-score following postnatal diuresis in ELBW infants of younger gestational ages.

Experimental Design: IRB-approved study retrospectively evaluated 37 ELBW infants between 2016-2020, admitted to a level III neonatal intensive care unit (NICU) at a Midwestern academic medical center (Omaha, NE, USA), and surviving at >28 days. Weight z-scores were collected from the 2013 Fenton growth chart at birth, the nadir of peak weight loss from postnatal diuresis, and discharge. Changes in z-scores were calculated and compared with current suggested classifications for identifying neonatal malnutrition: <0.8 = no malnutrition, >0.80 malnutrition. Non-parametric statistics were used and p-value <0.05 was considered significant.

Results: There was no statistical difference in weight z-score change from birth to postnatal diuresis nadir (p=0.169), birth to discharge (p=0.647), or postnatal diuresis nadir to discharge (p=0.191) across groups of birth gestational age. However, clinical observations demonstrated greater decreases in weight z-score at 22-23 (median -0.99) and 24-25 weeks (-0.55) compared to 26-27 (-0.40) or 28-30 weeks (-0.38). Likewise, there was no difference in suggested malnutrition classifications across birth gestational age. However clinically, more infants met malnutrition criteria when comparing birth to discharge z-score change vs. postnatal diuresis nadir to discharge (25 vs 0%, 40 vs. 0%, 42 vs. 17%, and 0 vs. 0% at 22-23, 24-25, 26-27, and 28-30 weeks respectively).

Conclusion: No statistically significant differences were observed in weight z-score change during NICU hospitalization across varying birth gestational ages of ELBW infants, however observations may be clinically significant. Furthermore, current suggested indicators for identifying neonatal malnutrition based on weight z-score change require validation, as classifications may incorrectly identify malnutrition at varying time points of evaluation.



Abstract 64

Should Infants Born at 35 Weeks Be Admitted into the NICU?

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Introduction: While certain hospitals, including CUMC Bergan, admit infants born at 35 weeks' gestation into the NICU, other institutions administer care in a mother/baby unit. Late preterm infants are at a high risk for complications including respiratory distress, hypoglycemia, and feeding difficulties that may require intensive treatment including ventilation, intravenous glucose, and nasogastric feedings, respectively. Such treatment modalities are infrequently provided in a mother/baby unit. The goal of this study was to review the rate of complications associated with infants born at 35 weeks' gestation to provide insight that can shape admission policies for this high-risk population.

Methods: This was a retrospective chart review of 123 infants born at 350/7 to 356/7 weeks' gestation at CUMC Bergan Mercy initially admitted into the Neonatal Intensive Care Unit between January 1, 2022, and June 1, 2023. Descriptive statistics and figures were analyzed using Microsoft Excel and SPSS.

Results: In this study, 91.9% of infants received one or more of the following treatments: intravenous therapy, respiratory support, or nasogastric feedings. Overall, 67.5% of neonates born at 35 weeks' gestation required intravenous therapy. 60.2% of neonates demonstrated hypoglycemia. Additionally, 30.9% of infants received respiratory support. 82.1% of neonates required a nasogastric tube and infants received gavage feeds for 10.2 ± 7.2 days. PO feeds were initiated on an average of 1.4 days after birth.

Conclusion: Our data supports NICU admission of newborns born at 35 weeks' gestation because of their high incidence of problems best managed in specialized settings.

Transition to Adult-centered Care: Models for Successful Programs Serving Individuals living with Spina Bifida

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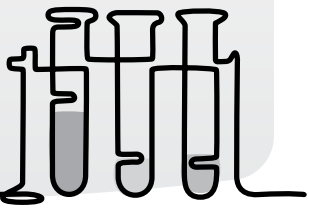
Background: Children and adolescents with spina bifida face a unique set of challenges as they transition to adult medical care. For this reason, several medical centers have sought to create multidisciplinary transitional care clinics with a sizeable focus in urologic care. The multidisciplinary care model is the standard of care in a pediatric setting for those with spina bifida, but not in adult care, making transitional programs essential for the success of these patients. The purpose of this study was to review current literature on transition programs for children and adolescents with spina bifida, particularly looking at urological care, with an aim to guide future providers on building their own successful transition programs.

Methods: A comprehensive literature review was conducted in PubMed using search terms “spina bifida” and “transition”, with no date restriction. Inclusion criteria included established programs and processes for transitioning to adult care, and ages >10 years old. Exclusion criteria included pilot programs, multiple non-spina bifida diagnoses, and lack of description of the specific transition program.

Results: This review identified four programs with successful multidisciplinary transitional care clinics. Each program had a different service model, varying ages served, and unique transition goals, but all similarly emphasized the importance of longitudinal urologic care. Obtaining resources to manage spina bifida clinics requires considerable effort and the involvement of many specialists and staff, with a large focus on social workers. Only one program (25%), to date, has published data on the success of their model.

Conclusion: Several programs have described a successful approach to transitional care clinics for children and adolescents with spina bifida. Outlining these models can provide a framework for future providers aiming to create similar programs to enhance the health and quality of life into adulthood for individuals with spina bifida.



Abstract 66

CARM1 Arginine Methyltransferase as a Therapeutic Target for Medulloblastoma

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Background: Medulloblastoma (MB) is the most common primary malignant brain tumor in children and is the leading cause of cancer-related death among children and adolescents. Based on genomic profiling, MB is classified into four subgroups Wingless (WNT), Sonic Hedgehog (SHH), Group 3 and 4. Activated signal transducers and activators of transcription-3 (STAT3) is aberrantly activated and promotes the transcription of the MYC oncogene in MB. Additionally, many epigenetic modulators are altered in MB suggesting epigenetic deregulation is key in mediating MB tumorigenesis. We aim to characterize and investigate the therapeutic potential of an epigenetic modifier, Coactivator Associated Arginine Methyltransferase 1 (CARM1) alone or in combination with STAT3 in high-risk MB.

Significance of Problem: G3MB tumors are highly metastatic, have high rates of recurrence, and have very low survival rates compared to other MB subgroups. CARM1 is often overexpressed in many cancers and is an important coactivator that asymmetrically dimethylates (ASDM) arginine residues on many different cancer-associated transcription factors thereby modulating functional activities and promoting tumor initiation. However, there is no previous research eluding the role of CARM1 in MB.

Hypothesis: We hypothesize that CARM1 triggers hypermethylation of its substrates including STAT3, thereby activating STAT3 and accelerating the process of MB tumorigenesis.

Experimental Design: This study aims to determine the functional role of the CARM1-STAT3 axis in MB and the efficacy of a CARM1 inhibitor alone and in combination with a STAT3 inhibitor in G3MB. We will utilize co-immunoprecipitation, proximity ligation assay, cell viability assay, and Western blot to achieve our goals.

Results/Data: Screening an epigenetic drug library of 462 inhibitors that modulate the activity of a variety of epigenetic modulator proteins revealed a CARM1 inhibitor (CARM-1-IN) as the most promising modulator that consistently synergizes with the STAT3 inhibitor WP1066. Cell viability assay by luminescence revealed that treatment with CARM-1-IN alone showed cytotoxic effects while the combination of CARM-1-IN and WP1066 showed a synergistic effect in multiple MB cell lines. Immunoprecipitation/immunoblot assay revealed that STAT3 is ASDM in MB. Furthermore, co-immunoprecipitation and proximity ligation assay showed that CARM1 directly interacts with STAT3 in a G3MB cell line.

Conclusion: We conclude that endogenous CARM1 directly interacts with STAT3 and inhibition of CARM1 alone regulates a subset of STAT3 target gene transcription. These early results suggest that STAT3 may be a direct target of CARM1-mediated ASDM and CARM1-mediated ASDM of STAT3 might affect its activation and subsequent transcription of its target genes.

Incorporation of Choice and Promotion of Autonomy for a Long-lasting Durable Treatment for Severe Challenging Behavior

Brittany H. Loder, MS, BCBA, Amanda N. Zangrillo, PsyD, BCBA-D, Cynthia P. Livingston, PhD, BCBA-D, Jessica P. Tran, MA, BCBA, Alexandra M. Cicero, MA, BCBA, Leslie J. Van Winkle, MA, CCC-SLP, BCBA

Background: Challenging behavior often serves to communicate wants and needs and thus teaching functional communication is an essential first step for clinicians who provide treatment to suppress severe challenging behaviors. One effective treatment method for reducing challenging behavior while promoting the use of communication is functional communication training. Once the function (i.e., cause) of the challenging behavior is identified, functional communication training involves no longer arranging reinforcement for the challenging behavior (i.e., extinction), and instead, teaching the individual an appropriate alternative communication response to gain access to the same reinforcer. Translational research within the field of behavior analysis has suggested that teaching multiple alternative communication responses (e.g., teaching a button press, gesture, and speech-generated response) can mitigate the reoccurrence of severe challenging behavior.

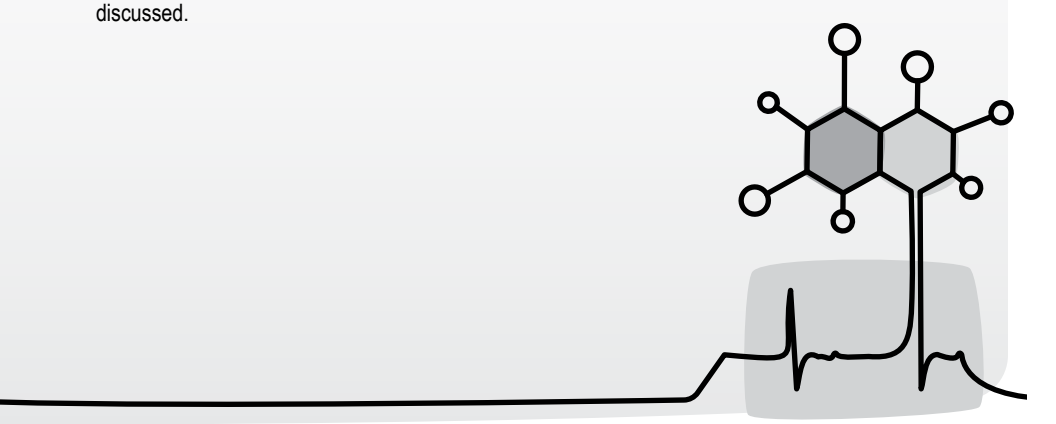
Significance of the Problem: The implications of this study are incredibly important as they could increase the effectiveness of functional communication training, decrease the risk of relapse, and in turn, decrease the re-admit rate for services. As behavioral health services are not meeting the current demand and individuals are being placed on waitlists, decreasing the risk of re-admittance will greatly impact waitlists and access to services.

Hypothesis: We hypothesize that teaching multiple modes of communication will lead toward a more durable and long-lasting treatment, and preference for a specific mode of communication will shift after contact with treatment challenges.

Experimental Design: We used a within participant single subject design and the standard three-phase resurgence preparation consisting of a baseline, acquisition, and resurgence test phase.

Results: This representative data set thus far demonstrates that individuals demonstrate a preference for communication modalities and preference does not shift following contact with treatment challenges. Additionally, we hypothesize that when compared to a single modality, teaching multiple modalities will decrease relapse in challenging behavior and lead to more increased communication when treatment challenges are encountered.

Conclusions: These data will inform advancements in communication training by promoting the incorporation of teaching multiple communication modalities to increase the durability in treatment effects, along with independence and autonomy through development of more robust communication repertoires. This poster displays a representative data set and prospective results will be discussed.



Abstract 68

Relationships Between Maternal Vascular Reactivity Index at 24-30 Weeks Gestation and Neonatal Birth Outcomes

Allison Zetterman[1], Matthew VanOrmer[1], Anum Akbar[1], Rebecca Slotkowski[1], Rebekah Rapoza[1], Taija Hahka[1], Anita Zhou[1], Megan Ott[1], Colman Freel[1], Kayla Adams[1], Andrea Rodriguez-Dasta[1], Aly Freeman[1], Sarah Sweeney[1], Melissa Thoene[1], Teri Mauch[1], Corrine Hanson[2], Ann Anderson-Berry[1]

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Background: Hypertensive disorders of pregnancy (HDP) affect one in seven US pregnancies and can lead to adverse neonatal outcomes, including increased risks of fetal growth restriction and preterm birth. Maternal endothelial dysfunction is implicated in the pathogenesis of HDP. Vascular reactivity index (VRI) is a validated, non-invasive measure of endothelial function. Previous studies have shown that VRI is positively associated with well-regarded cardiovascular health indices. Currently, a non-invasive and cost-effective method preemptively assessing the risk of HDP development during gestation does not exist. This study aimed to evaluate the relationship between maternal VRI between 24-30 weeks' gestation and neonatal birth outcomes.

Hypothesis: As previous studies show a higher VRI is associated with improved cardiovascular health, which extends to placental nutrient transfer and pregnancy maintenance, we hypothesize that maternal VRI will directly correlate with gestational age, birthweight percentile, birth head circumference percentile, and birth length percentile.

Experimental Design: An IRB-approved study enrolled 57 pregnant women receiving prenatal care at Nebraska Medicine. VRI was measured between 24-30 weeks' gestation using the Endothelix VENDYS machine per manufacturer protocol. In non-pregnant populations, a VRI below 1.4 is considered low reactivity, between 1.4-1.6 is average reactivity and above 1.6 is high reactivity. Birth outcome data was collected from the electronic medical record. Spearman's R assessed the relationship between continuous neonatal birth outcomes and VRI. A linear regression was performed to adjust for relevant confounders: smoking, maternal age, and hypertensive status. A p-value < 0.05 was considered statistically significant.

Results: Median gestational age at birth was 39.3 weeks, with 50.8% female neonates and 49.2% male. Median maternal age was 32 years old, and 42.4% of women had HDP. Median maternal VRI at 24-30 weeks gestation was 1.93 (IQR: 1.69-2.20). Gestational VRI was inversely correlated with birthweight percentile ($r_s = -0.437$ $p=<0.001$). After adjustment, a 1 unit increase in VRI predicted an 18.92% decrease in birth weight percentile (95% CI -32.90 to -4.93, $p = 0.01$). Birth head circumference percentile ($r_s = -0.024$, $p = 0.86$), birth length percentile ($r_s = -.080$, $p = 0.55$), and gestational age ($r_s = -0.227$, $p = 0.08$) were not significantly correlated with maternal VRI.

Conclusion: To our knowledge, our study is the first to assess maternal gestational VRI in relation to neonatal birth outcomes. Contrary to our hypothesis, VRI appears to be inversely related to birthweight percentile. Further studies with larger sample sizes are needed to explore this trend.

Effects of the COVID-19 Pandemic on Maternal Mental Health

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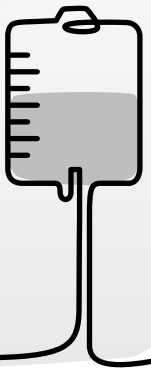
Background: March of 2020 marked the start of the coronavirus-19 (COVID-19) pandemic, resulting in more than 6.9 million deaths worldwide, significant job losses, and societal lockdowns due to the spread of severe respiratory syndrome coronavirus 2 (SARS-CoV-2). Though the pandemic's toll was universal, women experienced greater effects on their mental health than their male counterparts. Pregnancy marks a turbulent period of physiologic change, during which women are at risk of developing psychiatric disorders. Psychiatric conditions during pregnancy increase risk of delivery complications and preterm birth; children of mothers with psychiatric conditions are at risk of outcomes including failure to thrive and altered cognitive and language development.

Significance of Problem: Research suggests that stressors exacerbated by the pandemic such as financial security and health heightened strains on maternal mental health. Poor maternal mental health contributes to poor infant outcomes including preterm birth and altered infant development. However, additional data is needed to fully elucidate the pandemic's impact on pregnant women and their mental health.

Problem: How did the COVID-19 pandemic affect maternal mental health during and after pregnancy?

Experimental Design: A retrospective chart review of 709 mothers was conducted between 2015-2023 with mothers divided into pre- (06/01/15 to 02/29/20), during- (03/01/20 to 12/31/21), and post-COVID-19 (01/01/22 to 08/31/23) groups based on time of enrollment in an observational cohort. Clinical variables including anxiety, depression, history of post-partum depression (PPD), and medication use were collected from the electronic medical record (EMR). Socioeconomic variables such as employment status and insurance type were collected from the EMR and surveys. Fisher's exact tests, Chi-squared analyses, and analyses of variance (ANOVAs) were conducted using Tukey's method to adjust for multiple comparisons.

Results: Our study population had 525 (74.0%), 107 (15.1%), and 77 (10.9%) mothers in pre-, during-, and post-COVID groups. The mean maternal age was 29 years (standard deviation=5.50 years). 458 mothers (64.7%) were white and 250 mothers (35.3%) were non-white. We observed significant increases in the incidence of anxiety ($p<0.0001$), anxiety medication use ($p<0.0001$), depression ($p=0.0007$), depression medication use ($p=0.0003$), and history of PPD ($p<0.0001$) during COVID-19 that remained elevated post-COVID-19. Income>150% of poverty level ($p=0.0385$), food security level ($p<0.0001$), and private insurance type ($p<0.0001$) significantly increased during- compared to pre-COVID-19.



Conclusions: This study supports other work elucidating the COVID-19 pandemic's worsening of mental health among pregnant women. Future directions include stratifying pandemic stressors on maternal mental health by race and ethnicity and determining guidelines that support the mental health of pregnant women.

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