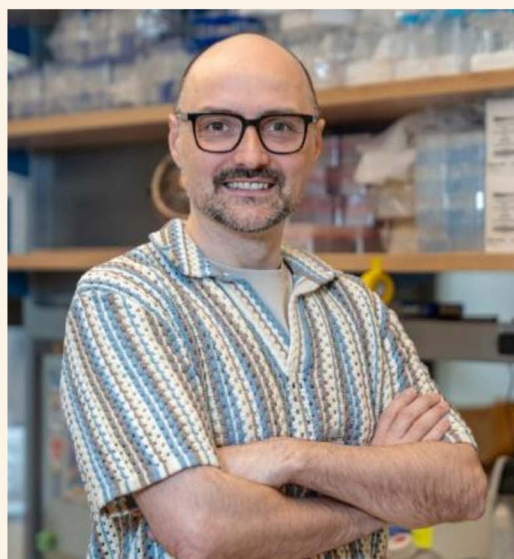


WEILL CORNELL MEDICINE DEPARTMENT OF PEDIATRICS
GALE AND IRA DRUKIER INSTITUTE FOR CHILDREN'S HEALTH
PRESENT

THE FOURTH ANNUAL PEDIATRICS RESEARCH DAY

Highlighting basic and clinical research in children's health by Weill Cornell Medicine/ NewYork-Presbyterian faculty, fellows, residents, medical students, and staff.

KEYNOTE ADDRESS BY:



Dusan Bogunovic, PhD

Professor of Pediatric Immunology
Vice Chair of Basic Research in Pediatrics
Director - Center for
Genetic Errors of Immunity
Columbia University
Department of Pediatrics

EVENT DETAILS:

THURSDAY JUNE 3, 2025
BELFER RESEARCH BUILDING
2ND AND 3RD FLOOR
CONFERENCE ROOMS

REGISTER HERE:



4th Annual Pediatric Research Day
June 3, 2025

8:00 – 8:30 am

Registration

8:30 – 9:30 am

Basic Sci/Translational Oral Presentations (2nd floor)

Moderator: Dr. David Lyden (4 orals)

9:30 – 9:40 pm Break

9:40 – 10:40 am

Translational/Clinical Oral Presentations (2nd floor)

Moderator: Dr. Lisa Roth (4 orals-1 Resident)

10:40 – 12:00 pm

Poster Session 1 (3rd Floor)

12:00 p– 12:30 pm

Lunch & Networking (2nd floor)

12:30 – 12:40 pm

Welcome Address from Drs. Virginia Pascual and Sallie Permar (2nd floor)

Dr. Cami Martin to introduce Dr. Zach Grinspan

12:40 - 1:00 PM

Data Science and AI to advance Pediatric Health

Zach Grinspan, MD

1:00 – 1:45 pm

Keynote Address w/ intro by Cami Martin (2nd floor)

Dusan Bogunovic, PhD

Professor of Pediatric Immunology, Columbia University Department of Pediatrics

1:45 – 1:55 pm Break

2:00 – 3:15 pm

Poster Session 2 (3rd Floor)

3:15 – 4:15pm

Clinical & EQ/Health Services Oral presentations (4 orals) (2nd floor)

Moderator: Dr. Bernhard Kuhn

4:15 – 4:25 pm Break (Poster Judging/Results)

4:25 – 5:25 pm

Translational and basic science oral presentations (2nd floor)

Moderator: Dr. David Lyden

5:25 – 6:00 pm

Reception and Awards announced at 5:30 (2nd floor)

The Weill Cornell Medicine Department of Pediatrics and the Drukier Institute for Children's Health is hosting the fourth annual Pediatric Research Day to highlight research conducted by faculty, fellows, residents, graduate students, postdocs, medical students, and other researchers working in the Department of Pediatrics or collaborating departments and institutions. All fellows and senior residents are present their scholarly work during this event.

This event celebrates the depth and breadth of the research performed in the Department and Institute, fosters collaborations across research teams and between faculty and trainees, and is a wonderful demonstration that research contributes personally and collectively towards the goal of advancing care for children. Additionally, the event aims to foster mentoring and networking relationships across career levels and between the College and affiliated institutions.

The day will consist of four sessions throughout the day. Posters categories are divided into (1) basic science, (2) translational research, (3) clinical research, and (4) education, health services, healthcare policy, quality improvement, and others. Posters will be judged by a panel of experts in their respective fields, and an award for outstanding poster will be presented for each category.

A plenary talk will be provided by our invited keynote speaker, Dr. Dusan Bogunovic, Professor and Principal Investigator, of the Bogunovic Lab at Icahn school of Medicine at Mount Sinai.

Sallie Permar, MD, PHD

Chair, Department of Pediatrics, Nancy C. Paduano Professor in Pediatrics

Virginia Pascual, MD

Director, Drukier Institute for Children's Health, Ronay Menschel Professor of Pediatrics

Research Day Director

Camilia R. Martin, MD, MS, Professor of Pediatrics, Chief of Neonatology, Vice Chair of Pediatric Research

Co-Director

Marianne Nellis, MD, MS, Associate Professor of Pediatrics, Director of Fellowship Research

Planning Committee Member(s):

Marianne Sharko, MD, Assistant Professor, Department of Pediatrics, Clinical Population Health Sciences

Veronika Hostiuk, Administrative Director, Research and Administration, Department of Pediatrics

Chani Traube, MD, Gerald M. Loughlin, MD Professor of Pediatrics

Virginia Pascual, MD, Director, Drukier Institute for Children's Health, Ronay Menschel Professor of Pediatrics

Genevieve Fouda, MD PHD, Professor, Department of Pediatrics, Professor of Microbiology and Immunology

Coordinator(s):

Carlene Bryan, MA, Fellowship Program Manager

Dakota Koop, Program Assistant II

Kadiatou Diallo, MPH, Program Coordinator

DISCLOSURE OF RELATIONSHIPS/CONTENT VALIDITY

The following presenters have the following disclosures:

- Has no relevant financial relationship with ineligible companies to disclose
- Will not be discussing the off-label or investigational use of products or services

Ioanna Pahountis, BS

Isabella Kong, PhD

Masuda Begum

Zurong Wan, Ph.D

Jacqueline Cho, BS

Nuran Golbasi, BS

David Gragirenes-Delgado, B.S.

Salar Bani Hani, MD

Asmita Mittal, BS in progress

Alexandra Huttie, MD MSc

Dariana Argueta-Zamora, B.S., Lamisa

Nubayaat, B.A., Jhoanny Revilla, M.D.

Chelsea M. Crooks, PhD

Zeynep Bahadir, MD

Kelly Banks, MD

Dianna Meija, MD

Robert Schwartz, MD/PhD

Chani Traube, MD

Marianne Sharko, MD

Genevieve Fouda, MD PHD

Sallie Permar, MD, PHD

Consultant: Merck, Moderna, Dynavax, Pfizer

Will not be discussing the off-label or investigational use of products or services.

All of the relevant financial relationships listed for this individual have been mitigated.

Virginia Pascual, MD

Consultant: GlaxoSmithKline and Regeneron

Advisor: Moderna

Royalties: Novartis

Research Grant: Sanofi

Will not be discussing the off-label or investigational use of products or services.

All of the relevant financial relationships listed for this individual have been mitigated.

Camilia Martin, MD, MS

Consultant: Baxter, Infant Bacterial Therapeutics

Scientific Advisory Board: Evive, Plakous, Lactalogics, Vitara

Research Grant: Mead Johnson

Expert Testimony: Winston & Strawn/Abbott Nutrition

Will not be discussing the off-label or investigational use of products or services.

All of the relevant financial relationships listed for this individual have been mitigated.

Marianne Nellis, MD, MS

Will not be discussing the off-label or investigational use of products or services.

All of the relevant financial relationships listed for this individual have been mitigated.

Keynote Speaker

DUSAN BOGUNOVIC, PHD

Professor of Pediatric Immunology
Columbia University Department of Pediatrics



Dr. Dusan Bogunovic is Professor of Pediatrics at Columbia University in New York, NY, USA. He finished his undergrad studies at University of Bridgeport, CT, later did his PhD training at NYU and a postdoc at Rockefeller university in the lab of Jean Laurent Casanova. After his postdoctoral training in 2014 he established his lab at Icahn School of medicine at Mount Sinai and after 10 years there, he moved to Columbia University Irving Medical Center **in March 2024**.

His lab focuses on the study of human immunogenetics. His group aims to improve understanding of the human immune system by studying 1) individuals with rare auto-inflammatory syndromes 2) individuals with severe clinical presentations of infections usually causing mild or no clinical disease 3) individuals with Down Syndrome and 4) transcriptional regulation of monoallelic expression. To dissect these phenotypes they use genomic, genetic, molecular biology, cellular biology, immunology and clinical tools.

Dusan Bogunovic, PHD

Lab 11 Therapeutics Inc, Owner/ CEO

will not be discussing the off-label or investigational use of products or services. All of the relevant financial relationships listed for this individual have been mitigated.

Research Tools and Resources

Institutional Information

Institutional information useful when applying for grants.

Funding Opportunities

WCM offers a variety of external and internal funding opportunities, including open and limited submission grants, compiled in a database for use by faculty and staff.

Award Opportunities

WCM offers a variety of award opportunities and distinguished honors to which faculty members and researchers can be nominated.

Weill Research Gateway

The Weill Research Gateway (WRG) streamlines the research administration process by replacing multiple legacy systems with one consolidated online portal.

Writing & Submitting a Grant Proposal

Writing resources are available at WCM for information and assistance in writing and submitting grant proposals to funding agencies.

Research Awards and Grant Writing Resources

Visit the Research Awards and Grant Writing Resources page for CV templates, grant writing templates, and library resources.

Office of Sponsored Research Administration (OSRA)

Visit WCM's Sponsored Research Office's landing page for more information on grant submissions and contract management.

Grants Management

For assistance with your research related applications and post-award financial management, please contact our Grants Management Unit:

Sharon Amos, ssa4010@med.cornell.edu

Research Concierge

The Research Concierge provides information on establishing websites, maintaining VIVO, and other information regarding research laboratory management.

Professional Development & Mentoring

WCM is proud to provide a variety of resources for faculty and staff to enhance their professional experience and gain insights into career development.

The Department of Pediatrics Faculty Mentoring Program is a comprehensive initiative aimed at nurturing the growth and success of junior faculty members and postdoc research associates within the department. Mentors play a crucial role in assisting mentees in developing their research programs and academic careers, offering guidance, facilitating professional development, and participating in ongoing group meetings. The program is structured to address various aspects of professional development, including professional career growth, academic success, networking, promotion, and faculty retention.

For more information, please contact PedsResearchAdmin@med.cornell.edu.

Clinical Research

WCM offers a wide variety of clinical research opportunities.

Research Data Management, Retention, and Sharing

Guidance and resources for managing research data and adhering to policies.

Samuel J. Wood Library

Here you will find information about accessing resources, requesting help with searches, and managing your scholarly output

For more information and resources, please visit:

<https://research.weill.cornell.edu/>

2025 ORAL PRESENTATIONS SCHEDULE

8:30 – 9:30 am

Basic Sci/Translational Oral Presentations (2nd floor)

Moderator: Dr. David Lyden (4 orals)

- Zeynip Bahadir, MD (post doc)- Development of polyfunctional antibody responses in children living with HIV
- Kelly Banks, MD (resident) – Sex Differences and Microbial Regulation of Neonatal Gut Development
- Masuda Begum (medical student) - Identifying the nucleosome-binding domain of MeCP2
- Zurong Wan, PhD (post doc) - Unlocking Insights into Juvenile Dermatomyositis (JDM): A Deep Dive into Muscle

9:40 – 10:40 am

Translational/Clinical Oral Presentations (2nd floor)

Moderator: Dr. Lisa Roth (4 orals-1 Resident)

- Asmita Mittal (undergrad) - Reproductive and Bone Health Counseling for Adolescent Females with Epilepsy
- David Gragirenes-Delgado, B.S (post-bac) - Characterizing novel vulnerabilities associated with acquired mTOR-inhibitor resistance in breast cancer
- Diana Mejia, MD (resident) - Pediatric Hospitalization and the Parent-Child Relationship
- Dariana Argueta-Zamora, BS (research tech) - Impact of Socio-Demographic Factors on Survey Completion Rates

3:15 – 4:15pm

Clinical & EQ/Health Services Oral presentations (4 orals) (2nd floor)

Moderator: Dr. Bernhard Kuhn

- Salar Bani Hani (Methodist resident) - Inpatient and outpatient management of anemia in infants with CKD during the 1st year of life
- Jacqueline Cho, BA (research fellow) - Risk Factors for Postoperative Coagulopathy in PICU Patients
- Alexandra Huttie (faculty) - Differences in Reporting Suicide Ideation and Attempt: Implications for Suicide
- Nuran Golbasi, BS (medical student) - Evaluating AI-Generated Clinical Summaries for Pediatric Epilepsy Transitions of Care

4:25 – 5:25 pm

Translational and basic science oral presentations (2nd floor)

Moderator: Dr. David Lyden

- Chelsea Crooks, PhD (post doc) - HCMV-specific binding antibody responses are associated with transmission odds
- Robert Schwartz, MD, PhD (faculty) - Leveraging mouse genetics, human single cell and spatial transcriptomics to reveal the defects in Alagille syndrome hepatocyte to cholangiocyte reprogramming
- Ioanna Pahoutis, BS (research tech) - Utilization of an HIV envelope trimeric protein BAMA for assessment
- Isabella Kong, PhD (post doc) - Dual Targeting of DNMT1 and EZH2 in EBV+ Lymphomas Enhances Immunogenic Viral Antigen

ORAL PRESENTATION ABSTRACTS

Development of Polyfunctional Antibody Responses in Children Living With HIV

Presenting Author: Zeynep Bahadir, MD (Postdoc)

Authors: Zeynep Bahadir¹, Kenneth Vuong¹, Maria Dennis¹, Ashley Nelson¹, Genevieve G. Fouda¹

¹ Department of Pediatrics, Division of Infectious Diseases, Weill Cornell Medicine, NYC, NY, US

Background: Understanding immune responses in children living with HIV (CLWH) can provide important insights for the development of immune based interventions to reduce the >100,000 new pediatric infections occurring every year. In a previous study, we reported that 1–3-year-old ART naïve CLWH develop neutralization breadth earlier than adults with chronic HIV-1. Yet the ability of CLWH to develop non-neutralizing antiviral functions such as antibody-dependent cellular phagocytosis (ADCP) and antibody-dependent cellular cytotoxicity (ADCC) has not been studied.

Objective: Investigate the development of non-neutralizing antibodies in CLWH and their association between neutralizing antibody responses.

Methods: Plasma neutralization was assessed in 33 ART naïve CLWH (age 4-5) against 10 viruses from a global HIV-1 panel representing various clades using a two-phase screening approach. Samples neutralizing ≥ 5 of 10 viruses in the panel were defined as having neutralization breadth. Plasma ADCP activity was measured using beads coated with the native-like HIV envelope trimeric protein TRO.11 (clade B antigen) and the monocytic cell line THP1. Phagocytosis scores were calculated by multiplying mean fluorescence intensity (MFI) and frequency of positive cells, divided by the negative control's MFI and frequency.

Results: Most children (4 year: 12/13; 5 years: 14/20) neutralized ≥ 3 of 5 viruses in the first phase of the neutralization screening. Overall, 77% of children at 4 years (n=10 of 13) and 60% at 5 years (n=12 of 20) neutralized ≥ 5 of 10 viruses, with a combined frequency of 67%. The neutralization potency in 4 and 5-year-old children were comparable (ID50: 112 vs 127). Of 32 samples tested, 6 exhibited plasma ADCP activity against TRO.11 (Median plasma ADCP score 1.28 (range 0.54-21.53). Interestingly five of six samples that demonstrated ADCP also demonstrate broad plasma neutralization, although higher plasma ADCP scores were not associated with increased plasma neutralization breadth or potency.

Conclusion: Our findings suggest that CLWH may generate polyfunctional antibodies against HIV-1, offering new insights into immune responses that could inform future therapeutic strategies. Future work will focus on characterizing ADCP activity against other virus strains from the global and investigating other non-neutralizing antibody functions.

Sex Differences and Microbial Regulation of Neonatal Gut Development

Presenting author: Kelly Banks, MD (Fellow)

Authors: Banks Kelly M., Rager Stephanie L., Jin Jenny L., Sanidad Katherine Z., Ahmad Mehrose, Ananthanarayanan Aparna, Perlman Jeffrey, Zeng Melody

Background: Preterm infants are exceptionally vulnerable to infection and inflammation. Female premature neonates show reduced morbidity and mortality compared to males through poorly understood mechanisms. Gut barrier formation and bacterial colonization are key to preventing infection and the development of the immune system. During the neonatal period, transient activation of the hypothalamic-pituitary axis triggers sex hormone production. Estrogen stimulates the immune system, supports gut homeostasis and recovery, and can be recycled by the microbiome via GUS enzymes.

Objective: This work aims to define sex differences in neonatal intestinal stem cell (ISC) function and the microbiome.

Methods: We studied gut microbiota in preterm infants using metagenomic sequencing, LCMS and in vitro enzymatic assays. We also used murine intestinal organoids, fecal transplants into germ-free colitis mice, RNA sequencing, and histology.

Results: Using a neonatal murine intestinal organoid model, we demonstrate that female ISCs have greater organoid-forming potential and elevated estrogen signaling gene expression (Fig1A-D). Fecal transplantation from premature infants into germ-free mice reveals that female-derived microbes are protective against inflammation and induce colonic estrogen signaling in both sexes (Fig2A-D). In vivo GUS enzymatic assays show enhanced estrogen recycling in female stool samples (Fig2E). Finally, we show that microbial GUS enzymes confer protection against colitis, particularly in male mice (Fig2F-H).

Conclusions: We conclude that estrogen derived from the transient neonatal HPA activation in female neonates is driving increased proliferation of ISCs and is being amplified by gut microbes enriched in the female microbiome, which may contribute to better health outcomes in premature female neonates.

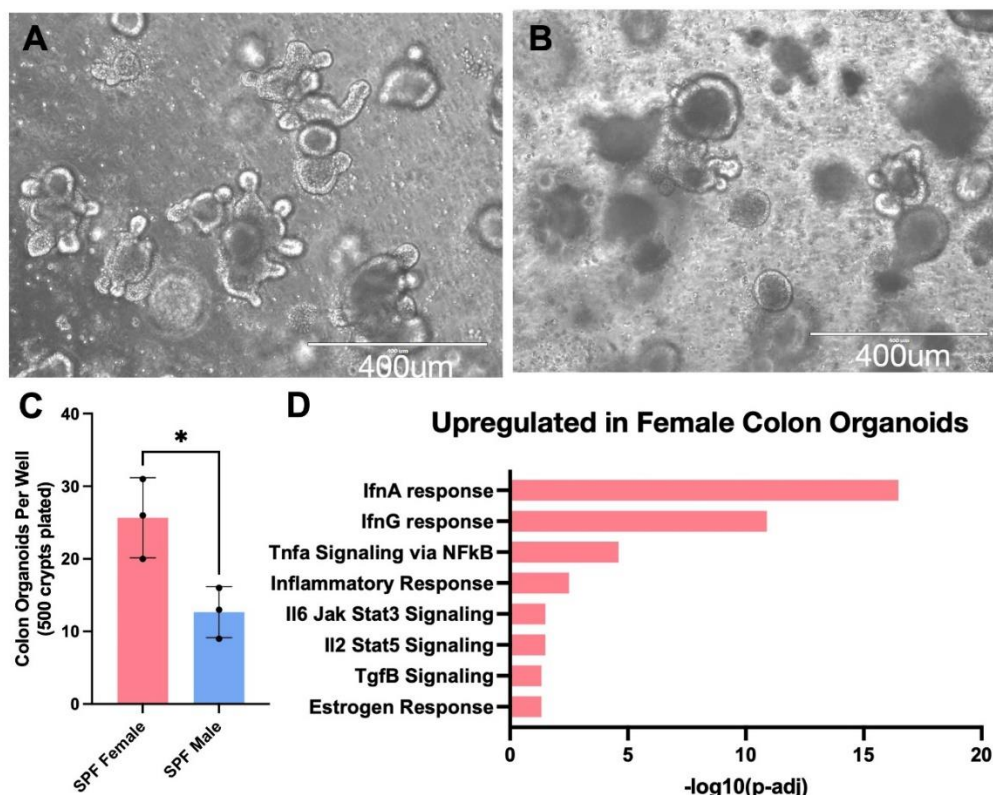


Figure 1. Sex differences in murine neonatal organoids. Brightfield microscopy of small intestine organoids from (A) female and (B) male P14 mouse pups on passage 2, day 5 showing more crypt formation and therefore more maturity of female neonatal organoids. (C) Bar plot showing increased count of organoids formed per well after plating 500 crypts in female compared to male neonatal colon samples, * represents $p < 0.05$ by un-paired t-test. (D) Barplot of adjusted p values for gene sets enriched in female organoid samples via gene set enrichment analysis of female vs male neonatal colon organoid bulk RNA sequencing data.

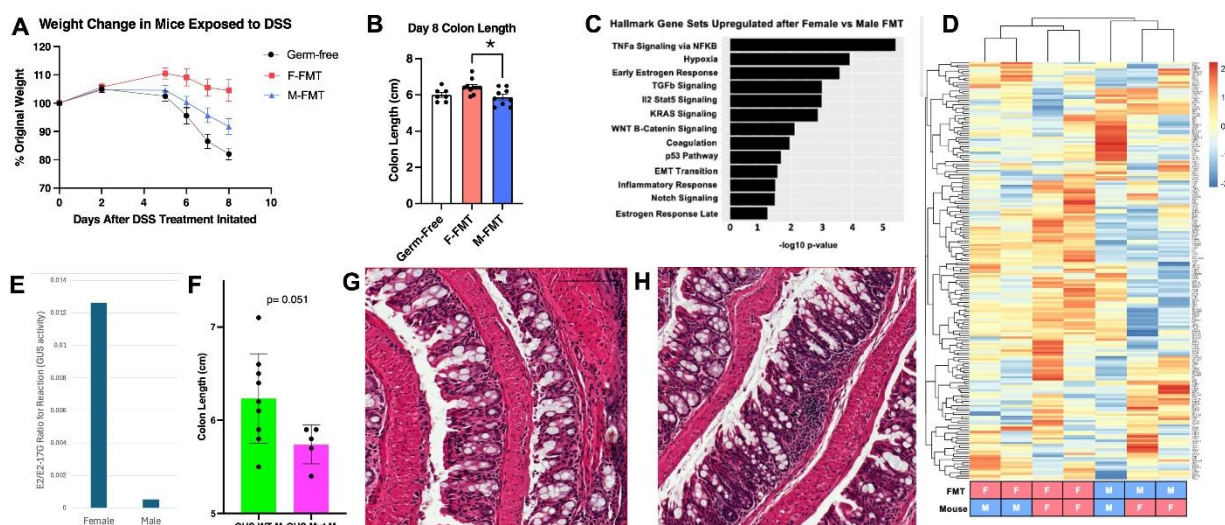


Figure 2. Sex differences in protective effects of neonatal microbiome may be mediated by increase in Estrogen signaling via microbe-derived GUS enzymes. (A) Fecal transplant of slurry of female vs male late pre-term stool into germ-free mice at 8 weeks showed increased protection against DSS-induced colitis by female microbial samples via weight loss (A) and colonic length at day 8, with shorter colons indicating more inflammation. (C) Hallmark gene sets enriched in the transcriptome of mouse colons after receiving female compared to male fecal transplant (FMT) from bulk RNA sequencing showing similar gene expression patterns to neonatal murine female organoids. (D) Heat map of estrogen signaling gene set broken down by gender of FMT and mouse for RNA sequencing showing similar gene expression patterns to neonatal murine female organoids. (E) Pilot experiment showing increased GUS activity in female samples. (F) Colon length after FMT into germ-free mice with E coli containing WT GUS enzyme capable of recycling estrogen and mutant enzyme followed by DSS colitis model, $p = 0.051$ by unpaired t-test. H&E staining of colon from (A) FMT with GUS WT and (B) FMT with GUS mutant followed by DSS colitis showing increased infiltration of leukocytes into tissue in GUS mutant sample.

Identifying The Nucleosome-Binding Domain Of MeCP2

Presenting Author: Masuda Begum (Medical Student)

Authors: Masuda Begum, Gabriella N. L. Chua, and Shixin Liu

Weill Cornell Medical School

Methyl-CpG-binding protein 2 (MeCP2) is a highly abundant chromatin-binding protein in mature neurons and is generally thought of as a DNA methylation-dependent transcriptional repressor. Mutations in the X-linked MeCP2 gene cause Rett syndrome (RTT), a severe neurological disorder that occurs 1 in 10,000-15,000 live female births, constituting one of the most frequent causes of monogenic intellectual disabilities in young girls. Currently, there is no cure for RTT, in part due to the heterogeneous and complex molecular functions of MeCP2 on chromatin that remain poorly understood beyond its known affinity for methylated DNA. In a recent study, we made the unexpected finding that MeCP2 preferentially and stably binds nucleosomes irrespective of the DNA methylation status, suggesting that nucleosomes may serve to regulate the availability of MeCP2 for canonical methyl-CpG recognition. In light of this finding, we sought to further understand the nucleosome-binding activity of MeCP2 and map the amino acid sequence responsible for nucleosome interaction. By purifying and fluorescently labeling a series of MeCP2 truncations and testing them in our single-molecule platform, we showed that the nucleosome-binding capacity of MeCP2 is located between amino acid residues R255 and G269. These results suggest the existence of a specific domain dedicated to nucleosome binding that is separate from its well-characterized methyl-binding domain (MBD). Our results suggest a separation-of-function domain in MeCP2 dedicated to nucleosome interaction and refine our understanding of MeCP2's chromatin-binding activities, which may help inform the pathological mechanisms of Rett syndrome truncations occurring within this region

Unlocking Insights Into Juvenile Dermatomyositis (JDM): A Deep Dive Into Muscle

Presenting Author: Zurong Wan, Ph.D (Postdoc)

Authors: Wan Zurong, Gu Jinghua, Balaji Uthra, Smitherman Cynthia, Baisch Jeanine, Walters Lynnette, Cai Chunyu, Pascual Virginia

Drukier Institute

Background: Juvenile dermatomyositis (JDM) is a systemic, childhood onset autoimmune disease characterized by skin rash and proximal muscle weakness. Current therapies rely heavily on prolonged glucocorticoids and broad immunosuppression, which carry substantial toxicity. Myositis specific autoantibodies (MSAs) occur in 50–70% of JDM patients and delineate clinically and prognostically distinct subgroups. Previous histopathology hints at MSA dependent patterns of muscle injury, but the underlying cellular and molecular drivers remain poorly defined.

Methods & Results: We leveraged cutting edge spatial transcriptomics to chart immune cell subsets and their transcriptional programs in JDM muscle at single cell resolution. Biopsies from patients with anti-TIF1γ, anti-NXP2, or anti-Mi2 autoantibodies revealed striking differences:

- Anti-TIF1γ & Anti-NXP2: Immune infiltrates were largely restricted to perivascular regions, with minimal penetration into muscle fibers.
- Anti-Mi2: In contrast, Mi2 positive muscles showed extensive endomysial infiltration between individual myofibers. These samples also harbored ectopic lymphoid like structures, around which we detected in situ B cell class switch recombination and plasma cell differentiation.

Conclusions: Our data uncover marked heterogeneity in immune cell localization and local humoral responses across JDM subgroups. By linking MSA status to distinct spatial immune niches and transcriptional signatures, this work may illuminate new pathogenic pathways and highlights opportunities for targeted therapies in JDM.

Reproductive And Bone Health Counseling For Adolescent Females With Epilepsy

**Presenting Author: Asmita Mittal, BS in progress (Third-year Student at Cornell University -
Joined Weill Through Dept Of Pediatrics Summer Internship)**

Authors: Mittal A, Harpel L, Kirkpatrick L, Chang J, Lin-Su K, Grinspan Z

Department of Pediatrics

Background: Adolescent females with epilepsy (AFWE) taking anti-seizure medications are at risk for decreased bone density, reduced contraceptive efficacy, and adverse pregnancy outcomes, yet rarely receive adequate counseling (PMID: 35247834). Barriers to discussions include limited time and patient privacy (PMID: 33545192).

Objective: Develop educational materials for AFWE on reproductive and bone health to encourage health literacy and clinical engagement.

Methods: We conducted a literature review to identify reproductive and bone health challenges faced by AFWE and to explore recommendations for medical communication. We designed educational materials that were vetted by experts in pediatric epilepsy (ZG, LK), adolescent medicine (JC), and pediatric endocrinology (KLS). We assessed readability using the Flesch-Kincaid Reading Level Calculator.

Result: This pamphlet explores three topics: bone health, menstruation, and contraception. Information is provided according to recommendations from the Center for Disease Control that messaging is focused and relevant. The content is presented with icons and bullet points to dissect complex concepts into digestible pieces, medical jargon is limited, and a legend is included to define terms like “hormones” and “puberty.” The Flesch-Kincaid reading level is 7th grade [range 5th to 11th grade, averaged across 19 sections], aligned with recommendations from the American Medical Association (6th grade) and National Institute of Health (8th grade) (PMID: 34179407).

Conclusion: We developed a pamphlet that meets recommendations for health education to encourage and guide conversations about reproductive and bone health between AFWE and their physicians. In ongoing work, we are exploring the real-world effectiveness of providing AFWE with these materials.

Characterizing Novel Vulnerabilities Associated With Acquired mTOR-inhibitor Resistance in Breast Cancer

Presenting Author: Gragirenes-Delgado, David, B.S. (Post-Baccalaureate Student)

Authors: Gragirenes-Delgado, David A, Koundouros Nikolaos, Blenis John

Weill Cornell Medical School

Introduction/Background: The mechanistic target of rapamycin (mTOR), a serine/threonine kinase and the catalytic subunit of the protein complexes mTORC1 and mTORC2, is a central regulator of anabolic metabolism and cell growth, with critical roles in modulating protein translation, ribosome biogenesis, de novo lipid synthesis, and autophagy. To help tumor cells meet their energy needs and proliferate, mTOR signaling is often dysregulated in human cancers, with hyperactivation in about 50% of breast cancers. The growing interest in mTOR as a therapeutic target over the last few years has led to the development of three major classes of mTOR inhibitors: (1) rapamycin and its rapalog derivatives (allosteric inhibitors), (2) ATP-competitive inhibitors, and (3) Rapalink-1 (a bivalent agent formed by crosslinking the other two types). While these drugs have some promising antineoplastic properties, their clinical utility remains limited due to resistance acquired by cells after prolonged treatment. Therefore, gaining phenotypic and mechanistic insights associated with drug response and acquired resistance is pivotal to optimizing the efficacy of these inhibitors or developing combinatorial strategies for anticancer therapy. We have generated a panel of Rapamycin, Torin and Rapalink-resistant MCF7 cell lines – a model for PIK3CA mutant, estrogen receptor positive breast cancer – thereby allowing us to compare resistance mechanisms within and between different inhibitor classes. Notably, the acquirement of resistance is associated with profound morphological changes in 3D spheroid cultures, along with increased stemness phenotypes. These fundamental observations provide opportunities to interrogate the metabolic, nutrient acquisition and signaling pathways that drive mTOR inhibitor resistance.

Pediatric Hospitalization and the Parent-Child Relationship

Presenting author: Dianna Mejia, MD (Resident)

Authors: Mejia Dianna L, Smith Morgan, Bruno Samantha, Andy Caroline, Gerber Linda, Berardi-Bloomfield Alexandra, Habermann Lauren, Smalls Keisha, Traube, Chani

Department of Pediatrics

Background: A child's hospitalization is disruptive for the entire family and effects can persist after discharge home. There is limited research as to how a child's hospitalization may impact parenting and the parent-child relationship.

Objective: Primary objective is to measure parenting self-efficacy (PSE) in parents of recently hospitalized children. PSE refers to a parent's confidence in ability to effectively manage parenting tasks (e.g. attachment, communication, discipline, involvement, and overall parent-child relationship). A secondary objective is to identify family factors associated with PSE after discharge.

Design/Methods: In this prospective cohort study, participants include parents of patients 2-18 years old who were admitted to the hospital for >2 nights. Two weeks after discharge, parents received a computerized link to complete the BASC-3 Parenting Relationship Questionnaire (PRQ). Parental scores on each domain were compared to the national average. Kruskal-Wallis rank sum tests assessed domain-specific parenting scores by family characteristics (e.g. religiosity, siblings, prior hospitalization, parent history of mental illness).

Results: 1268 parents were contacted; 214 (17%) responded; 182 (85%) completed the PRQ. Compared to the national average, the overall cohort reports less confidence in their ability to discipline their child (PSE score 20 vs. 50, $p < 0.001$) and more involvement in their child's lives (63 vs. 50, $p < 0.001$) (Fig 1). Families who describe themselves as religious score higher on communication (65 vs. 32, $p = 0.018$), and lower on discipline (16 vs. 7, $p = 0.007$). Parents with only one child have higher overall attachment (65 vs. 51, $p = 0.026$) and involvement (89 vs. 62, $p = 0.004$), and less frustration (37 vs. 51, $p = 0.04$), than families with siblings. Parents with a history of mental health issues report lower scores on attachment (40 vs. 58, $p = 0.009$) and overall parenting confidence (31 vs. 54, $p = 0.033$). There is no difference in PSE domain scores from the national average among families where the child had a previous admission. Exploratory factor analysis (EFA) identifies the underlying structure in the parenting domains, with 72% of variance explained by 2 factors (Fig 2).

Conclusion: Parents report lower efficacy in parenting after a child's first hospitalization, with marked effects on discipline practices when compared to national norms. Parents with a prior mental health diagnosis, more than one child, and without religious affiliation may benefit most from interventions designed to increase PSE after hospital discharge.

Figure 1. Average Parenting Relationship Questionnaire Scores by Domain: Sample vs. National Data

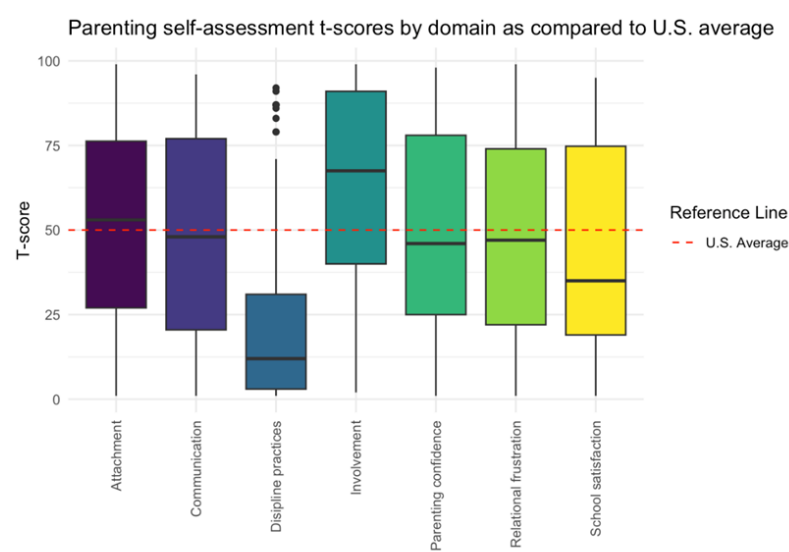
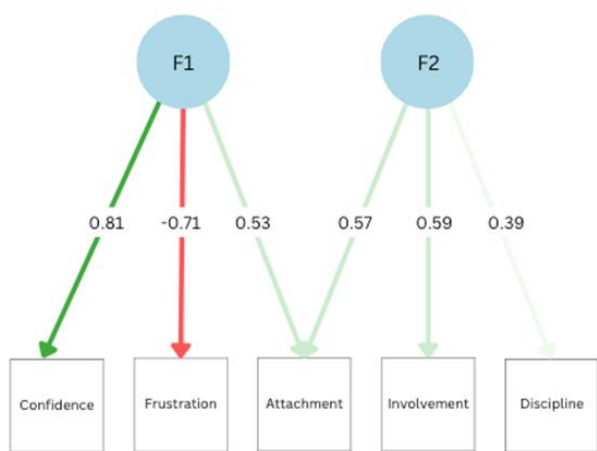


Figure 2: Exploratory Factor Analysis and Underlying Structure in Parenting Domains



Inpatient And Outpatient Management of Anemia In Infants With CKD During The 1st Year Of Life

Presenting Author: Salar Bani Hani, MD (Resident)

Authors: Salar Bani Hani, Abhinav Parikh, Ali Nadroo, Camilia Martin, Juhong Lee, Oleh Akchurin

Department of Pediatrics

Background: Anemia and kidney dysfunction are common in NICU-managed neonates. While prolonged kidney dysfunction impairs erythropoiesis in older children, its impact on anemia management in NICUs is unclear. The transition of anemia management from NICU to outpatient nephrology clinics in infants with significant kidney disease is crucial but uninvestigated.

Objective: To define inpatient and outpatient anemia management patterns in NICU patients diagnosed with CKD within the first year of life.

Design/Methods: This retrospective cohort study included infants referred to pediatric nephrology within a large urban healthcare network from 2014 to 2022, diagnosed with CKD within the first 12 months, who received NICU care, and had relevant variables available. Eligible patients were identified through electronic medical records.

Results: We identified 37 patients, 30 with sufficient inpatient, and 24 with follow-up outpatient data. 73% were male, 40% born prematurely. At 12 months, 29% had stage 1 CKD, 12.5% stage 2, 33% stage 3, 12.5% stage 4, and 12.5% stage 5 (all on dialysis). CKD was caused by CAKUT in 88%, with PUV being the most common anomaly (33%). 76% did not receive antibiotics beyond the first 48 hours. The hemoglobin nadir in the NICU was 11.2 ± 3.3 mg/dL, with 37% having hemoglobin ≤ 10.0 . During the NICU stay, 58% received iron supplementation, 37.5% received ESAs, and 21% received blood transfusions. There was a significant correlation ($p=0.006$) between hemoglobin nadir in the NICU and eGFR at 12 months ($r=0.6$). At 12 months, 21% had anemia (KDIGO definition); 37% were receiving iron therapy, and 25% were receiving ESAs. Of the 8 patients not requiring iron in the NICU, only one started iron by 12 months. Of the 14 treated with iron in the NICU, 10 remained on iron at 12 months. Iron status was assessed in 21% during NICU stay and 33% post-discharge, with 50% being iron-deficient ($TSAT \leq 20\%$).

Conclusion: In NICU patients developing CKD within the first year, anemia severity during NICU stay correlates with CKD severity at 12 months, indicating early kidney disease impacts anemia development. Most CKD patients starting iron in the NICU continued it post-discharge. Our ongoing analyses include comparison of findings with a matching group of NICU graduates without CKD.

Differences In Reporting Suicide Ideation and Attempt: Implications For Suicide Risk Screening In Pediatric Primary Care

Presenting author: Alexandra Huttle, MD MSc (Fellow)

Authors: Huttle A, Rombola C, Ortin-Peralta A, Abramson EL, Waseem M, Miranda R. Differences in Reporting Suicide Ideation and Attempt: Implications for Suicide Risk Screening in Pediatric Primary Care. Acad Pediatr. Published online February 7, 2025. doi:10.1016/j.acap.2025.102795

General Internal Medicine and Pediatrics

Background: Pediatricians are uniquely positioned to identify suicide-related risk, yet clinical practices as to when, how, and who gets screened may vary due to differences in policy statements on youth suicide risk screening in primary care.

Objective: We examined agreement between reports of past suicide ideation (SI) and suicide attempt (SA) across multiple assessment methods and over time. We further explored associations across sociodemographic factors and severity of mental health symptoms on reporting patterns on these methods for adolescents at elevated risk.

Methods: Adolescents (N = 162) with SI and/or SA were recruited from multiple clinical sites in and around New York City. Adolescents completed interviews and self-report measures validated to assess suicide-related risk, depressive symptoms, and anxiety symptoms.

Results: Agreement between questions on verbal interviews over time was fair ($\kappa = 0.38$), with adolescents under-reporting lifetime SI as time from a crisis went by. Agreement between questions on self-report measures was moderate ($\kappa = 0.51$), with adolescents under-reporting past-month SI on a depression screen compared to a suicide-specific screen. Participants with less severe mental health-related symptoms were significantly less likely to report past-month SI consistently.

Conclusion: This study highlights important trends in suicide related reporting patterns among adolescents at elevated risk for suicide and may have important implications for clinical practice guidelines. To capture more adolescents at risk for suicide, results not only support a universal screening approach using suicide-specific tools but may suggest the need to increase screening frequency in pediatric primary care.

Impact of Socio-Demographic Factors on Survey Completion Rates In an Observational Study Of Preterm Infants

Presenting Authors: Dariana Argueta-Zamora, B.S., Lamisa Nubayaat, B.A., Jhoanny Revilla, M.D. (Faculty)

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Department of Pediatrics

Introduction: Surveys are a valuable research tool in longitudinal studies on preterm infants, detailing how early life circumstances affect health outcomes. However, variable response rates among different socio-demographic groups may lead to potential biases that compromise the generalizability and accuracy of the findings. Factors such as education and employment status may offer insight into patterns of parental survey participation.

Objective: To evaluate the impact of parental socio-demographic factors on REDCap e-survey completion rates in a nutrition and growth study of preterm infants in the Neonatal Intensive Care Unit (NICU) at Weill Cornell Medicine.

Methods: This study conducted a secondary data analysis of survey completion rates among sixty-eight mothers of preterm infants enrolled in an observational study. Categorical predictors such as race, ethnicity, education, employment status, and age were extracted from EPIC. Survey completion frequencies were summarized at four time points during the infant's NICU admission, and Chi-square tests assessed group differences.

Results: Survey respondents employed at the time of survey completion had higher survey completion rates than those not working or on maternity leave (Figure 1). Respondents who identified as white generally had a higher completion rate than respondents identifying as Asian, Black or African American, or Other (Figure 2).

Conclusion: Demographic distributions remained largely stable across time points, with no statistically significant changes in maternal age or education status, and only modest shifts in race and employment status. This suggests minimal attrition bias and supports the representativeness of the cohort over time. Future goals aim to reduce survey participation barriers and enhance distribution methods for future research.

Risk Factors for Postoperative Coagulopathy in PICU Patients Following Major Tumor Resections for Neuroblastoma

Presenting Author: Jacqueline Cho, BS (Research Fellow)

Authors: Cho Jacqueline S, Michael Samir, Drill Esther, Danzer Enrico, La Quaglia Michael, Gerstle Justin T, Pon Steven, Honeyman Joshua

Department of Pediatrics

Objective: To identify risk factors associated with postoperative coagulopathy in pediatric intensive care unit (PICU) patients following major tumor resections for neuroblastoma.

Background: Pediatric oncology patients are at a high risk of developing coagulopathy due to their disease and treatment. For those requiring major surgical resections, coagulopathy can lead to an increased risk of complications. The incidence and risk factors of postoperative coagulopathy in patients with neuroblastoma are poorly characterized.

Methods: We retrospectively analyzed data from 179 PICU patients (0-18 years) with neuroblastoma who underwent major tumor resection in the chest, abdomen, or pelvis between January 2019 and December 2023. Patients with a history of coagulopathy were excluded. Postoperative coagulopathy was defined as one or more of the following events: INR > 1.5, PT > 15 seconds, aPTT > 55 seconds, or platelet count < $100 \times 10^9/L$.

Results: Of the 179 patients, 126 (70.4%) met one or more criteria for postoperative coagulopathy. The median age at surgery was 37 months (IQR: 22-64 months), with 82% presenting with high-risk neuroblastoma. Multivariate logistic regression analysis identified younger age (OR = 0.98, 95% CI: 0.96-0.99), preoperative INR (OR = 1.11, 95% CI: 1.04-1.19), greater intraoperative blood loss (OR = 1.04, 95% CI: 1.01-1.08), and receipt of colloids (OR = 3.38, 95% CI: 1.50-7.85) as independent predictors of postoperative coagulopathy.

Conclusion: Postoperative coagulopathy is highly prevalent among pediatric neuroblastoma patients undergoing major tumor resections. The identified risk factors may help clinicians to better anticipate and prepare for potential postoperative coagulopathies in this population.

Evaluating AI-Generated Clinical Summaries for Pediatric Epilepsy Transitions of Care

Presenting Author: Nuran Golbasi, BS (Medical Student)

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Weill Cornell Medical School

Introduction: Transitions of care in pediatric epilepsy require synthesizing years of clinical data into coherent summaries. For patients with developmental and epileptic encephalopathies (DEEs), this process is especially challenging due to care fragmentation across specialties and systems.

Objective: To assess whether a large language model (LLM) can generate structured, clinically relevant epilepsy transition summaries, and to evaluate those summaries using a rubric-based framework.

Background: Patients with DEEs often receive care from multiple subspecialists across different settings, leading to fragmented documentation and difficult care transitions. Large language models (LLMs) may offer a scalable way to synthesize scattered information into coherent summaries. However, their ability to generate accurate, clinically useful overviews across longitudinal records remains underexplored—particularly in complex, chronic conditions like DEEs.

Methods: Using Gemini 1.5 Pro, structured summaries were generated for a small cohort of pediatric epilepsy patients based on up to 1.6 million characters of OMOP-formatted clinical notes per patient. Prompts followed a standardized format across seven domains (e.g., seizure history, diagnostics, medications). Summaries were evaluated using a five-domain rubric (accuracy, completeness, clarity, conciseness, clinical relevance), standard readability metrics (Flesch, FK Grade, Gunning Fog, SMOG), and cross-referenced against full source notes.

Results: Summaries scored highly for accuracy (mean 4.8/5), clarity (5.0), and clinical relevance (4.4). Readability was consistent with clinician-authored documentation (mean FK Grade: 11.9).

Conclusion: LLMs show potential to generate useful summaries for pediatric epilepsy transitions when grounded in full patient context. Further validation is ongoing.

Table: Rubric Evaluation of AI-Generated Summaries

Domain Mean Score (out of 5)

Accuracy 4.8

Completeness 4.0

Clarity 5.0

Conciseness 4.4

Clinical Relevance 4.4

Scored by LLM-assisted rubric with cross-verification from source notes.

HCMV-Specific Binding Antibody Responses Are Associated with Transmission Odds in Primary, Acute HCMV Infection During Pregnancy

Presenting Author: Chelsea M. Crooks, PhD (Postdoc)

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Department of Pediatrics

Background: Human cytomegalovirus (HCMV) is a leading infectious cause of congenital defects. Despite high prevalence and morbidity, there are no effective vaccines to prevent congenital CMV (cCMV) because correlates of protection remain poorly understood.

Objective. Here, we characterized the humoral immune response to primary HCMV infection in early pregnancy to determine the response associated with protection against placental transmission.

Methods: Samples were collected from 399 participants in a clinical trial who were diagnosed with acute HCMV, among whom 78 transmitted cCMV. We measured plasma IgG, IgM, and IgA binding to 17 HCMV antigens, IgG binding and avidity to HCMV virions and gB on the cell surface. We also measured neutralization, antibody-dependent cellular cytotoxicity (ADCC), and antibody-dependent cellular phagocytosis (ADCP).

Results: Whole-virion binding data revealed higher IgG avidity, but not magnitude, was associated with protection against cCMV. Higher binding to entry glycoproteins was associated with increased odds of cCMV for IgM, but not IgG. However, higher IgG binding to UL16, the prefusion conformation of gB, gB antigenic domain (AD) 4+5, gB AD-5, and gH/gL was associated with protection, while binding to gB AD-1 and gB on the cell surface was associated with increased odds of cCMV. Preliminary analysis suggests no association between ADCP or neutralization and cCMV.

Conclusions: These data suggest the quality and specificity of the IgG response impact cCMV odds more than the magnitude. Characterizing the protective immune response to acute HCMV in pregnancy will aid in the rational design of HCMV vaccines to speed the elimination of cCMV.

Leveraging Mouse Genetics, Human Single Cell And Spatial Transcriptomics To Reveal The Defects In Alagille Syndrome Hepatocyte To Cholangiocyte Reprogramming

Presenting Author: Robert Schwartz, MD/PhD (Faculty)

Authors: Andre F. Rendeiro, Sanjay Subramanian, Kari Huppert, Ashley Cast, Jennifer Burwinkel, Anna L. Peters, Stacey Huppert, Nathan Salomonis, Oliver Elemento, Robert E. Schwartz

Weill Cornell Medical School

Background: Alagille syndrome (ALGS) is a multisystem developmental disorder caused by autosomal dominant mutations in JAGGED1 (95%) or NOTCH2 (1-2%). We demonstrated in a mouse model that the process of hepatocyte to cholangiocyte reprogramming even in the absence of hepatic epithelial Notch activity can build the intrahepatic bile duct system that failed to form during development. The hepatocyte-derived biliary system enables resolution of cholestasis and reversal of fibrosis. Unfortunately, the process of hepatocyte to cholangiocyte reprogramming to repair bile duct paucity is impaired in most patients with ALGS resulting in liver transplantation. Our aim is to define the defects in ALGS hepatocyte to cholangiocyte reprogramming.

Methods: We used both Jagged haploinsufficient experimental mouse models of ALGS and liver samples from patients with ALGS. Cell lineage specific sufficiency of Jagged1 to alleviate Jagged1 haploinsufficient bile duct paucity was investigated. Single cell transcriptomics and Resolve spatial transcriptomic platform was used to assess cell states and spatial association in the liver of both the Jagged1 haploinsufficiency mouse and human patients with ALGS.

Results: Our transcriptomic data reveals that hepatocytes partially enter the cholangiocyte transcriptional program but are unable to fully implement the cholangiocyte transcriptional program in Jagged1 haploinsufficiency. We hypothesize that this failure is due to a defect in the peribiliary mesenchymal cell niche for intrahepatic bile duct development and reprogramming. We demonstrate that re-expression of human Jagged1 specifically in the peribiliary mesenchyme, but not the hepatic epithelium, can rescue the bile duct paucity of Jagged1 haploinsufficient mice.

Conclusion: We conclude that the peribiliary mesenchyme is defective in ALGS and if corrected can alleviate bile duct paucity. Further refining the subpopulations of cells comprising the peribiliary mesenchymal niche for intrahepatic bile duct development, bile duct homeostasis, and repair will potentially identify biomarkers, genetic modifiers, and/or novel therapeutic targets.

Utilization of an HIV Envelope Trimeric Protein BAMA for Assessment of Binding Breadth in ART-naïve Children Living with HIV

Presenting Author: Ioanna Pahountis, BS (Research Tech)

Authors: Ioanna Pahountis, Saad Memon, Caroline Phan, Devidas Chaturbhujb, P.J. Klasseb, Genevieve Fouda, Ashley Nelson

Department of Pediatrics

Background: A protective HIV vaccine will need to elicit broadly neutralizing antibodies, but inducing this type of response through vaccination has proven challenging. A better understanding of the pathways leading to HIV neutralization breadth during natural infection may provide important insights for informing vaccine development. In this study, we optimized a multiplex assay to measure antibodies against a cross-clade panel of Env trimers. This assay was applied to measure Env-specific antibodies in longitudinal samples from children living with HIV and examine if binding breadth is a predictor of neutralization breadth.

Objective: Develop a multiplex assay to assess antibody binding breadth across various HIV trimers

Methods: A multiplex antibody binding assay (BAMA) was developed to measure antibodies against 6 native-like HIV envelope trimeric proteins (TRO11, 246 F3, BJOX2000, CH119, CNE55,25710) representative of strains included in the global neutralization panel. This assay was used to measure binding responses in longitudinal plasma samples of children living with HIV (n=113). The binding breadth was compared to the neutralization breadth using previously generated neutralization data against the same virus strains.

Results: Binding to the HIV env trimeric proteins were observed as early as 1 year of age, with the magnitude and frequency of the binding response increasing with age. Out of 34 one year-old infants at , 22 demonstrated plasma antibody binding to all 6 trimeric envelope proteins with the remaining 12 showing binding to only 1 or 2 trimeric env proteins. At 3 years of age, 39 out of 41 tested plasma samples demonstrated binding to at least 50% ($n \geq 3$) of trimeric env proteins in the panel; whereas at 1 and 2 years of age respectively, 82.4% ($n=28$ out of 34) and 94.3% ($n=33$ out of 35) of the plasma samples demonstrated binding to $\geq 50\%$ of the Envs. In contrast 94% ($n=31$ out of 33) of children at 1 year of age, ($n=17$ out of 17) 100% at 2 years and 100% (at 3 years of age demonstrated $>50\%$ neutralization of these 6 virus strains. There was no statistically significant correlation between ID50s and MFIs against each virus/antigen.

Conclusion: Children living with HIV rapidly develop antibodies capable of binding diverse Env trimers. But surprisingly, these responses were not correlated with contemporaneous neutralization breadth. Further analysis will be conducted to determine if binding breadth can predict neutralization breadth at future timepoints.

Dual Targeting of DNMT1 And EZH2 in EBV+ Lymphomas Enhances Immunogenic Viral Antigen Expression and T Cell-Mediated Killing

Presenting Author: Isabella Kong, PhD (Postdoc)

Authors: Kong Isabella Y, Clark Sarah E, van Besien Herman, Sun Suhong, Alonso Vicenta Trujillo, Cesarman Ethel, Giulino-Roth Lisa

Department of Pediatrics

Introduction: Epstein-Barr virus (EBV) is associated with lymphomas like Burkitt lymphoma (BL) and diffuse large B-cell lymphoma (DLBCL), commonly seen in children. In EBV+ lymphomas, the virus exists in latent states: latency I (only EBNA1) and latency II/III (expressing immunogenic proteins such as LMP1/2 and EBNA2/3, which can be targeted by cytotoxic T cells). Understanding the regulation of these proteins is critical for EBV-specific T cell therapy.

We previously reported that DNA methyltransferase 1 (DNMT1) regulates EBV latency and that decitabine (DCB), a DNMT1 inhibitor, induces latency II/III antigen expression in BL, sensitizing tumors to EBV-CTLs. This effect is also seen in DLBCL, where DCB treatment increases EBNA2+ (1.19% to 15.3%; $p < 0.0001$) and LMP1+ (3.93% to 15.1%; $p < 0.0001$) cells.

However, DCB induces latency II/III protein expression in only a subset of cells. To investigate resistance mechanisms, we examined the epigenetic machinery involved using ChIP-qPCR. Resistant BL cells showed increased H3K27me3, a repressive mark, at both Cp (2-fold) and LMP1p (2.45-fold) loci. We tested tazemetostat (Taz), an EZH2 inhibitor, in combination with DCB, and found that this combination significantly increased EBNA2+ LMP1+ BL cells (DCB: 31.1%, TAZ: 3.07%, Combo: 45.9%; $p = 0.0001$). Additionally, T cells co-cultured with BL pre-treated with the combination showed a 1.46-fold increase in proportion of IFN γ + CD8+ T cells compared to those co-cultured with DCB alone ($p = 0.0032$).

Our findings suggest targeting H3K27me3 and DNMT1 can improve EBV-directed immunotherapy for immune-refractory EBV+ latency I lymphoma.

BASIC SCIENCES ABSTRACTS

BS-01

Plasma IgG, IgM, IgA binding responses and congenital transmission status following primary, acute human cytomegalovirus during pregnancy

Presenting Author: Adelaide Fuller, BS (Research Tech)

Authors: Fuller Adelaide S, Crooks Chelsea S, Ananyev Sergey, Barfield Richard T, Permar Sallie R

Department of Pediatrics

Background: Human Cytomegalovirus (HCMV) is the leading viral cause of congenital defects globally. Currently, no vaccine exists for cCMV. Undefined correlates of protection pose challenges to vaccine development. This study aims to understand the relationship between IgG, IgM and IgA binding and transmission status in pregnant women with acute HCMV infections.

Methods: 399 pregnant women with primary, acute CMV were identified from a clinical trial screening, 78 of whom transmitted CMV to their infant. Participants were 1:2 matched based on transmission status. A Luminex-based binding antibody multiplex assay (BAMA) was used to measure IgM, IgG and IgA antibody binding to 15 CMV antigens in the 185-participant matched cohort. The panels included entry glycoproteins, tegument proteins, immune evasins, and gB antigenic domains (AD).

Results: A significant increase in IgG binding responses in non-transmitters was observed against the immune evasin UL16, and gB ADs 4+5 and 5 ($p < 0.01$). Binding to prefusion gB was significantly lower in transmitters ($p < 0.05$). Binding to pp150 and gB AD-1 was higher in transmitters ($p < 0.01$). IgM responses to entry glycoproteins (gB ectodomain, full-length post-fusion gB, gH/gL/gO and pentameric complex ($p < 0.05$)), as well as some immune evasins (UL16, pp150, pp71 ($p < 0.05$)) were all higher in transmitters.

Conclusions: These data suggest that entry glycoproteins are not the only important targets of IgG binding responses that could reduce cCMV transmission risk, and immunogens like UL16 could be used as vaccine antigens. Moreover, specific epitopes of gB are critical to protection against cCMV risk, suggesting gB conformation is critical to vaccine development.

Spatial Transcriptomics for the Investigation of the Tumor Microenvironment**Presenting Author: Akua Agyemang, BS (ASPiRE Scholar)****Authors:** Agyemang, Akua A., Park, Jiwoon, Mason, Christopher E., Howell, Joy D.

Weill Cornell Medical School

In recent years, liver cirrhosis has become the major cause of liver-related morbidity and mortality. The most common cause, non-alcoholic fatty liver disease (NAFLD) can go undiagnosed for years and is estimated to affect more than a quarter of the adult population worldwide. Hepatic stellate cells (HSC) — located within the liver's stroma and primarily involved in the storage of vitamin A— are a minor cell population in the human liver yet have been identified as the main fibrogenic cell type. It is estimated that 82-96% of fibroblasts in various chronic liver diseases originate from HSCs. Researchers seek to better understand how HSCs, parenchymal and immune cells communicate and mount a response against infection or stenosis, observed to be more robust and aggressive in the event of repeat assault. Continued research is necessary to understand this trend, as well as to develop therapies to attenuate it, however, it is not feasible to obtain longitudinal samples from these patients due to the invasive nature of biopsies. In lieu of such samples, this project utilizes cancer samples from patients with a viral infection background and biologically matched controls. Leveraging the high-resolution spatial transcriptomic techniques such as Stereo-seq, a workflow which combines mRNA capture within tissue with spatial location tracking, the Mason lab investigates how gene expression as well as cell morphology and local environment varies from healthy to diseased tissue. Preliminary data from mouse models mapping spatiotemporal changes across timepoints will be used to map molecular signatures in human samples. Additionally, spatial multiomic data have been collected using nanoString CosMx/SMI imaging platform, capturing the in situ spatial location of proteins and transcripts at subcellular resolution via imaging of barcoded probes hybridized to their respective target. Identification of deviations from transcriptomic landscape observed in healthy tissue for cancer and liver cirrhosis alike will aid in understanding disease progression, as well as circumventing the limitations which persist for the employment of pre-existing therapies to enable researchers in developing new therapies attuned to the heterogeneous microenvironment.

The Role Of Maternal Antibodies In Vaccination: Understanding Influence On Pup mRNA Lipid Nano Particle Vaccine Responses

Presenting Author: Brittany Plummer, Dual Masters Degree (Research Tech)

Authors: Plummer B, Ramos J, Binuya C, Permar SR, Williams CA.

Department of Pediatrics

Background: Maternal antibodies provide crucial passive immunity to neonates, but their presence can hinder infant vaccine responses. We hypothesized that an mRNA-LNP vaccine platform could overcome maternal antibody interference and elicit de novo IgG responses using severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) as a model pathogen.

Methods: BALB/c female mice were immunized with 5 µg of Moderna mRNA-1273 or PBS. Following immunization, females were mated with C57Bl/6 males. All pups, regardless of maternal immunization status, received 5 µg of Moderna mRNA-1273. Pup serum samples were collected at days 0, 7, and 21 post immunization. Anti-Spike serum IgG levels were determined using ELISA, and the half-maximal dose (ED50) was calculated for comparative analyses.

Results: Pups from mRNA-1273-immunized mothers had detectable Spike-specific IgG at Day 0 (median ED50: 5184.5). By Day 7, pups from PBS-immunized mothers showed a trend towards higher Spike-specific IgG ED50 (median: 2185.2 vs. 1567.7). This difference was more pronounced at Day 21 (median: 4391.8 vs. 377.7), suggesting a potentially stronger and more sustained response without maternal antibodies.

Conclusion: This murine model allows for a detailed analysis of vaccine responses in early life, addressing critical gaps in understanding maternal antibody interference with infant SARS-CoV-2 mRNA-LNP immunization. Our study demonstrates that while maternal antibodies initially provide elevated levels of passive humoral immunity, they may also interfere with the development of de novo vaccine-specific IgG in pups. Antigen specific IgG subclass analysis is underway to determine the extent of maternal antibody inhibition of mRNA-LNP vaccines.

The Role Of Myeloid Ferritin Heavy Chain In The Pathogenesis Of Anemia In Chronic Kidney Disease

Presenting Author: Chantalle Campbell, BS (Research Tech)

Authors: Campbell Chantalle, Matthews-Balcombe Jade, Patino Edwin, Federman Hannah, Elsayed Heba, Freund Avery, Baqai Kanza, Voss Henning, Bhatia Divya, Choi Mary, Vinchi Francesca, Akchurin Oleh

Department of Pediatrics

Background: Anemia is a common complication of chronic kidney disease (CKD), with iron supplementation being the recommended first-line therapy. Ferritin is a classical marker of iron stores, but the mechanistic role of ferritin – especially ferritin heavy chain (Fth1), which has enzymatic ferroxidase activity that converts soluble ferrous iron to insoluble ferric iron for storage – remains unclear in the context of anemia in CKD.

Objectives: Elucidate the role of Fth1 in myeloid cells (which are responsible for iron storage) in the development of renal anemia.

Methods: A high-adenine diet (40 ppm iron) was used for two months to induce CKD in wild-type (WT) and myeloid-specific (LysM-Cre) Fth1-knockout (KO) mice. For iron supplementation studies, mice received 0.5% ferrous sulfate or 0.5% carbonyl iron-enriched diets. A low-iron diet (4 ppm) was used to induce absolute iron deficiency. Tissue iron content was assessed in bone marrow, spleen, and liver using chemical assays, histology, and MRI.

Results: Untreated WT CKD mice developed anemia and hypoferrremia, accompanied by higher serum ferritin and markedly increased iron deposition in the bone marrow, spleen, and liver compared to healthy controls. Interestingly, serum ferritin was reduced in CKD mice with absolute iron deficiency (low-iron diet) compared to CKD mice with functional iron deficiency (normal-iron diet) despite similar elevations in serum IL-6. Both iron supplementation regimens improved anemia and hypoferrremia but also exacerbated tissue iron loading, as reflected by elevated serum ferritin levels. Myeloid-specific Fth1-KO CKD mice exhibited improved hematologic parameters (anemia and hypoferrremia), reaching levels comparable to those achieved with iron supplementation. This improvement was likely due to a marked reduction in tissue iron accumulation observed in KO mice compared to WT littermates with CKD. Notably, deletion of myeloid Fth1 also led to reduced systemic inflammation, as indicated by lower serum IL-6 levels. No statistically significant differences in serum hepcidin were observed between WT and Fth1-KO CKD mice.

Conclusions: Myeloid ferritin heavy chain is essential for iron sequestration during CKD and contributes to the development of renal anemia independently of systemic hepcidin. Targeting ferritin heavy chain in myeloid cells may represent a novel therapeutic strategy for treating anemia in patients with CKD.

The Role of Plasma Broadly Neutralizing Antibodies In the Perinatal Transmission Of HIV.

Presenting Author: Christian Binuya (Research Tech)

Authors: Binuya Christian, Karthigeyan Krithika, Mielke Dieter, Goswami Ria, Omonije Olusola, Giorgi Elena, Pollara Justin, Isaac John, Eudailey Joshua, Connors Megan, Weinbaum Carolyn, Permar Sallie

Department of Pediatrics

Background: In 2023, 1.4 million children were living with HIV. Broadly neutralizing antibodies (bNAbs) target essential epitopes for viral entry but fail against variants with neutralization-resistant mutations. We hypothesize that maternal bNAbs targeting single HIV-envelope epitopes can drive the selection of perinatally transmitted transmitter/founder (T/F) variants.

Objective: Characterize the role of maternal plasma bNAbs in perinatal HIV transmission to guide intervention development.

Methods: Plasma from 21 transmitting and 70 non-transmitting mothers with HIV from the Mother-Infant Cohort Study (MICS) and NICHD International Site Development Initiative (NISDI) Perinatal Study were screened for neutralization breadth, magnitude, and epitope specificity, and antibody-dependent cellular cytotoxicity (ADCC). Viral infant sequences were obtained via single genome amplification to evaluate genetic motifs.

Results: Transmitting mothers showed higher broad neutralization frequency (38%) compared to non-transmitting mothers (27%, $p = 0.0002$, two-sided Fisher's test). A higher proportion of transmitters had mappable epitope-specific plasma-bNAb activity ($p = 0.02$, two-sided Fisher's test) with no significant difference in ADCC responses ($p = 0.02$, Wilcoxon test). Additionally, 38% of transmitters concurrently mapped to CD4bs and FP regions. Lastly, 4/5 infants gained a novel mutation of D325N in the conserved 324GDIR327 peptide stretch.

Conclusions: Contrary to the protective role conventionally associated with HIV-bNAbs, this study suggests that maternal plasma CD4bs and FP-specific broad neutralization may drive viral escape. Additionally, higher epitope specificity of plasma neutralization in transmitters demonstrate that potential epitope-specific mutations of maternal variants might contribute to perinatal HIV transmission risk. Hence, immunologic interventions to reduce perinatal transmission should target multiple viral epitopes.

Assessment of Cellular Immune Responses to Acute Cytomegalovirus Infection During Pregnancy

Presenting Author: Erica Garcia, PhD (Postdoc)

Authors: Garcia Erica C, Crooks Chelsea M, Omonije Olusola, Fuller Adelaide, Lee Esther, Beeton Komal, Permar Sallie R

Department of Pediatrics

Introduction/Background: Cytomegalovirus (CMV) is the most commonly transmitted congenital infection globally and can lead to lifelong health issues. The risk of vertical transmission is about 40% for women experiencing primary infection during pregnancy, compared to 1-2% for women with previous CMV infection, suggesting that maternal immunity plays a significant role in protection from vertical transmission. However, the contributions of individual immune cell populations in protection from transmission during pregnancy have not been defined.

Objective: Our goal is to uncover cellular immune correlates of protection to aid in vaccine design.

Methods: To understand which immune cells protect against transmission, we will utilize peripheral blood mononuclear cells (PBMC) from a cohort of women who experienced primary CMV infection during pregnancy. Of this group, 74 women vertically transmitted CMV, and 111 women did not. A panel of 27 markers is used to reveal the phenotype and proportions of PBMCs from each participant. To identify protective CMV antigen-specific T cell populations between transmitting and non-transmitting groups, T cells are treated with CMV peptides and assessed for activation. Similarly, participant NK cells are assessed for cytotoxicity following isolation from PBMCs and coculture with K562 cells.

Results: Preliminary data shows that non-transmitters tended to have higher proportions of NK cells and $\gamma\delta$ T cells compared to transmitters, suggesting that these populations are protective.

Conclusions: We find that our panel and functional assays are a useful tool for defining maternal immune responses correlated with protection from vertical transmission. Ultimately, our study aims to inform vaccine design strategies.

**Behavioral Modeling Of Synaptobrevin-2's Role In Alpha-Synuclein Aggregation And
Pathology In Parkinson's Disease**

Presenting Author: Eseosa Uwaifo, Sc.B. (Research Tech)

Authors: Uwaifo E, Black LS, Briano JA, Ahmad S, Haller JE, Chiang V, Gao V, Chlebowicz J, Gaskin K, Sharma M, Burré J.

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Introduction: α -Synuclein (α -Syn) is an intrinsically disordered protein prevalent at presynaptic terminals, that clusters synaptic vesicles and chaperones SNARE-complex assembly via binding to the SNARE protein vesicle-associated membrane protein 2 (VAMP2) and phospholipids on synaptic vesicles(SVs), to maintain neuronal communication. α -Syn aggregation in Lewy bodies is a molecular hallmark of Parkinson's disease (PD) and Lewy body dementia, with missense mutations, duplications, and triplications of the α -Syn gene linked to early onset PD. We have previously found decreased VAMP2 levels in synuclein null mice, and reduced synaptic localization of α Syn with VAMP2 deficiencies. Pathologically, levels of VAMP2 and functional monomeric α Syn simultaneously decrease with progression of dementia, implying a functional link between the two. Yet, the consequences of this interaction loss and PD-linked mutations remain unknown.

We hypothesize that VAMP2 stabilizes α -Syn in its functional conformation on SVs, mediating vesicle clustering and SNARE-complex assembly, and preventing pathological aggregation. We tested this hypothesis by examining the effect of decreased VAMP2 expression in wild-type and VAMP2 heterozygous mice on onset and progression of pathology in two transgenic mouse models expressing human alpha-synuclein: α -Syn A53T mice where human A53T α -Syn is driven by the thy-promoter causing ~10x expression of α -Syn, and α -Syn BAC mice where expression of WT α -Syn is driven by all human regulatory elements without mouse α -Syn, causing 1.5-2x expression of α -Syn.

For the first cohort, heterozygous VAMP2 mice were crossed with transgenic α -Syn A53T mice, to obtain four test groups: WT mice, transgenic mice with the A53T mutation (α -Syn+/A53T), VAMP2+/- mice, and VAMP2+/-: α -Syn+/A53T mice. For the second cohort, heterozygous VAMP2 mice were crossed with transgenic α -Syn BAC mice, to obtain four test groups: α -Syn+/- mice, α -Syn+/-:VAMP2+/- mice, α -SynBAC/- mice, and α SynBAC/-:VAMP2+/- mice. Mice are undergoing monthly weight checks and behavioral testing from 4 weeks to 52 weeks of age in assays assessing motor impairment (rotarod, grid hang, grip strength, open field). So far, we found that WT and VAMP2+/- mice perform better than α Syn+/A53T and α -Syn+/A53T:VAMP2+/- in the grid hang and grip strength assays starting from 8 weeks of age. However, α -Syn+/A53T and α -Syn+/A53T:VAMP2+/- mice performed similarly on all behavioral assays throughout the testing period, contrasting our original hypothesis of decreased VAMP2 expression causing increased α -Syn pathology in PD. We hypothesized that the massive overexpression of α -Syn in the A53T mice may mask differences between WT and VAMP2+/- genotypes, and are therefore now concurrently focusing on the VAMP2: α -SynBAC cross.

Dissecting The Tumor Microenvironment In EBV-Positive B Cell Lymphomas

Presenting Author: Hang Yin, MS (Graduate Student)

Authors: Yin H, Kong I, Ravichandran H, Elemento O, Roth LG

Weill Cornell Medical School

Introduction: Epstein-Barr virus (EBV) drives several B cell lymphomas through latent infection, with tumor cells adopting latency I, II, or III programs, each defined by distinct viral gene expression. Latency III expresses immunogenic proteins (EBNA2, LMP1/2), while latency I expresses only EBNA1. These programs likely influence B cell phenotype and the tumor microenvironment (TME), but their impact is not well understood. To address this, we used imaging mass cytometry (IMC) to spatially profile protein expression across a tissue microarray of EBV-positive B cell lymphomas, including primary effusion lymphoma (n=10), Burkitt lymphoma (n=15), diffuse large B cell lymphoma (n=18), Hodgkin lymphoma (n=2), polymorphic lymphoproliferative disorder (n=2), and plasmablastic lymphoma (n=6).

We asked whether latency programs alter B cell phenotype/function and shape the TME. Spatial analysis showed EBNA2 expression correlates with IL10, IL4, IL6, and CXCL13, while LMP1 correlates with IL10 and CXCL13. EBNA2-high cells also expressed more CD27 and CD28. In vitro, latency III cells (Kem3, Mutu3) were enriched for cytokine signaling pathways (e.g., TNF α /NF κ B, IL6/JAK/STAT3, IL2/STAT5, interferon responses), confirmed by GSEA and flow cytometry. Latency III cells also showed reduced CD20 and increased CD27 and CD38 versus latency I (Kem I, Mutu1).

For the TME, spatial neighborhood analysis of LMP1-high tumors revealed increased CD8⁺ T cells and macrophages, and fewer CD4⁺ T cells, dendritic cells, and EBNA2⁺ cells. These findings suggest EBV latency shapes both B cell behavior and immune architecture. Our spatial profiling framework offers a path to dissect and therapeutically target latency-specific immune contexts in EBV⁺ B cell lymphomas.

M-Phase Entry Induces Dedifferentiation Of Calcium Signaling In Cardiomyocytes

Presenting Author: Honghai Liu, PhD (Faculty)

Authors: Liu H, Ammanamanchi N, Mich-Basso JD, Panama BK, Li Y, Huang W, Almeida D, Lewarchik CM, Wu Y, Gotthardt M, Kotlikoff MJ, Baehr W, Rasmusson R, Salama G, Kühn B

Department of Pediatrics

Background and Introduction: Patients with congenital heart disease often exhibit defective cardiomyocyte function and proliferation. Cardiomyocyte proliferation is crucial for myocardial development and regeneration. Cardiomyocyte contractions are driven by calcium release from the sarcoplasmic reticulum (SR), but it is unclear how cardiomyocytes adjust calcium handling during cell division.

Objective: Determine how proliferating cardiomyocytes alter their calcium signaling, particularly calcium transients (CaTs), that drive contractions and the underlying molecular mechanisms.

Methods: We utilized live-cell and immunofluorescence microscopy to investigate CaTs and the structural remodeling of the SR in proliferating cardiomyocytes within intact mouse hearts, as well as in cultured human fetal and iPSC-derived cardiomyocytes, rat (neonatal, adult), and mouse (neonatal) cardiomyocytes during different sub-phases of the cell cycle, particularly in M-phase.

Results: Cardiomyocytes lose their striated SR distribution in prometaphase and reorganize the striations during cytokinesis. This SR remodeling was accompanied by a reversible decrease in CaTs and contractions, indicating dedifferentiation in M-phase cardiomyocytes. The decrease in CaTs was regulated by SR remodeling, driven by dynein 1, and under the direction of spindle microtubules. This dedifferentiation was blocked by SERCA2a blocker thapsigargin or by knocking out the cytoplasmic dynein 1 heavy chain (Dync1h1) gene. Both methods reduced M-phase cardiomyocytes. We show that the dedifferentiation of cardiomyocytes is a reversible M-phase event mediated by active Cdk1. These results are consistent across multiple mammalian species, suggesting a conserved mechanism of cardiomyocyte dedifferentiation.

Conclusions: This research underscores the transient and reversible nature of dedifferentiation during cardiomyocyte proliferation, ensuring that overall heart function remains uncompromised.

Immune Signatures of Pediatric Patients with Immune Thrombocytopenia Differs by Chronicity, Age, and Sex

Presenting author: Jennifer Schloss, MD, PhD (Fellow)

Authors: Schloss, Jennifer M; Miller, Thomas; Bussel, James B; Pascual, Virginia I; Kaicker, Shipra

Department of Pediatrics

Background: Immune thrombocytopenia (ITP) incidence is increased in adolescent females over males, consistent with their increased autoimmune susceptibility. Therefore, they may have different immune contributions to ITP pathogenesis, impacting biomarker and therapy development.

Objective: Identify altered immune populations in adolescent males and females with chronic ITP via longitudinal immunologic analysis on peripheral blood monocyctic cells (PBMCs).

Methods: We collected PBMCs from 6 female and 3 male patients ≥ 9 years with chronic ITP at 0, 3 and 12 months, and from healthy age- and sex-matched controls. Samples were stained with a 26-color antibody panel followed by flow cytometric analysis. Statistical analysis was performed using GraphPad Prism.

Results: T cell changes were almost exclusive to females, with decreased naïve CD4 and increased Th17 cells vs. controls and decreased regulatory T cells vs. males. In females only, naïve CD4 and Th1 cells negatively correlated and follicular helper 2 cells positively correlated with platelet count. Contrastingly, all had decreased NK cells and non-classical monocytes; in males, classical monocytes and plasma cells were decreased, while in females these positively correlated with platelet count.

Conclusion: We found substantial changes in the T cell compartment primarily in females, as found in other autoimmune conditions. Contrastingly, innate and B cell changes were largely shared between the groups. This suggests that while the impact of the latter on ITP pathogenesis is common among all patients, addressing T cell dysregulation in females may be essential. Single cell RNA sequencing studies are ongoing to interrogate the function of these immune subsets.

Maternal Antibody Inhibition Of Infant SARS-CoV-2 mRNA-LNP Vaccines

Presenting Author: John Ramos, B.S (Research Tech)

Authors: Ramos, John M., Plummer, Brittany, Binuya, Christian, Gross, Mackensie, Fuller, Adelaide, Karthigeyan, Krithika, Permar, Sallie R. and Williams, Caitlin A.

Department of Pediatrics

Introduction: In this study, we sought to determine the effects of maternal antibody on infant vaccine responses to SARS-CoV-2 mRNA-LNP immunization, as an early life vaccine strategy to improve outcomes for infants aged <6 months, who have the highest COVID-19 hospitalization rates among the pediatric population. It has been established that human infants <6 months will develop robust vaccine responses post-immunization. We hypothesize that mRNA-LNP vaccination of infants will not be inhibited by maternal antibodies.

Methods: Balb/c mice were injected intramuscularly with PBS or with 5 µg of SARS-CoV-2 Spike mRNA-LNP vaccine. Groups included: 1) unvaccinated pups from vaccinated dam, 2) vaccinated pups from vaccinated dams, and 3) vaccinated pups from unvaccinated dams. Pups were vaccinated at weaning (day 21) and blood was collected via tail bleed on days 21-35 post-vaccination.

Results: Vaccine-elicited antibody levels transferred to the pup in the maternal vaccine only group waned by day 28 post-immunization when serum Spike-specific IgG levels were compared to pups of unvaccinated dams. Notably, by day 21, vaccinated pups born to vaccinated dams had plasma vaccine-elicited IgG in levels that appear below that of the pup vaccine only group and remain lower through day 35.

Conclusion: Our data suggests that maternal SARS-CoV-2 Spike protein antibodies may result in inhibition of pup antibody responses and lead to lower IgG responses when compared to pups unexposed to maternal antibodies. Future work will assess B-cell responses through splenocyte phenotyping via flow cytometry to compare antigen specific B-cell levels in vaccinated pups exposed or unexposed to SARS-CoV-2-specific maternal antibody.

The Role of Maternal Broadly Neutralizing Antibody Activity in Perinatal Transmission of HIV-1

Presenting Author: Krithika Karthigeyan, PhD (Postdoc)

Authors: Krithika P Karthigeyan¹, Dieter Mielke³, Christian Binuya¹, Ria Goswami¹, Olusola Omonije¹, Elena E. Giorgi², Justin Pollara³, John Isaac¹, Joshua Eudailey¹, Megan Connors¹, Carolyn Weinbaum¹, Sallie R Permar¹

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Background: Despite increased availability to antiretroviral therapy (ART), up to 5% of women living with HIV (WLH) still transmit HIV-1 to the infant. Broadly neutralizing antibodies are the immunologic goal of HIV-1 vaccine candidates; however, in postnatal cohorts, we have reported the presence of bNAbs targeting a single epitope, which contributes to viral escape. We hypothesize that WLH with bNAbs against single epitopes of the HIV envelope are at higher risk of perinatal transmission due to viral escape, while Mult specific bNAbs could reduce transmission.

Methods: Plasma was acquired around delivery from 21 perinatal transmitters and 1:3 matched non-transmitters with HIV (n = 70) from the Mother-Infant Cohort Study (MICS) and the NISDI Perinatal study. Plasma was screened for neutralization breadth against a 10-virus HIV-1 panel. For participants with breadth, plasma was screened against viruses with epitope mutations in CD4 binding site, V2 and V3 Glycan, and the membrane proximal external region of HIV-1 Env. Antibody dependent cellular cytotoxicity (ADCC) was assessed against cells infected with a transmitted/founder subtype B virus (WITO).

Results: Transmitters had higher breadth and potency of neutralization compared to non-transmitters (p = 0.0002, two-sided Fisher's test). bNAb activity in 6 out of 7 transmitters (87%) were mappable, with 5 out of 7 mapping to the CD4 binding site (71%) and one transmitter mapping to two epitopes. In comparison, 4 out of 14 non-transmitters mapped to a single epitope (29%), while the majority remain unmapped. Overall, a higher proportion of transmitters had epitope-mappable plasma-bNAb activity (p = 0.02, two-sided Fisher's test). Additionally, regression analysis on pooled data suggests that when adjusted for cohort, transmitters have significantly higher ADCC against subtype B WITO compared to non-transmitters (p = 0.02, Wilcoxin test).

Conclusions: Our findings suggest the existence of increased bNAb activity in transmitters that is primarily specific to a single epitope, which could lead to emergence of bNAb-resistant viral variants that can be transmitted perinatally. While ADCC has been implicated in protection against transmission, our analyses indicates that transmitters have higher ADCC against a subtype B virus, though ADCC breadth analysis could reveal additional details. In conclusion, bNAb-based pediatric HIV prevention and treatments that are synergistic with ART will likely need to be multi-specific to effectively eliminate pediatric HIV.

BS-17

Interrogating Mucosal Immunity In Down Syndrome

Presenting Author: Lexi Tempera, B.S (Research Tech)

Authors: Tempera, Lexi; Qu, Sophia; Sonnenberg, Gregory F.

Department of Pediatrics

Down syndrome (DS) impacts approximately 1 in 1000 live births worldwide and is responsible for a wide range of medical challenges. Due to the triplication of chromosome 21, which encodes multiple genes crucial for immune function, individuals with DS experience increased susceptibility to infectious, autoimmune and inflammatory conditions. While some aspects of immune dysregulation in DS are characterized, little information is known on how mucosal immunity is impacted in the gastrointestinal tract, which contains most of the total immune system and is a frequent site of DS associated co-morbidities. Here, we investigate the gut immune phenotype in a mouse model of DS and identify a significant increase in peripherally-induced regulatory T cells. Consistent with this, using a dextran sulfate sodium (DSS)-induced intestinal inflammation, we found that DS mice exhibit enhanced protection compared to littermate controls. Ongoing studies are exploring the consequences of these changes in mucosal immunity to enteric infections, as well as exploring the mechanisms driving this enhanced regulatory T cell response in the intestine of DS mice, including the generation of mixed bone marrow chimeric mice to distinguish between cell-intrinsic and extrinsic contributions in triplication of chromosome 21. It is expected that this research will advance our understanding of the mechanisms underlying gastrointestinal co-morbidities in DS and could provoke novel concepts in immune regulation

Binding And Functional Humoral Immune Responses Induced By The VBI-1501A HCMV eVLP gB Vaccine Compared To The gB/MF59 Vaccine**Presenting Author: Megan Connors (Research Tech)****Authors:** Megan R Connors, Krithika P Karthigeyan, Adelaide Fuller, Libby Mitchell, Sergey Ananyev, Richard Stanton, David E Anderson, Sallie R Permar

Department of Pediatrics

Human Cytomegalovirus (HCMV) is a ubiquitous herpes virus that is the leading infectious cause of birth defects globally with no licensed vaccine. The most promising HCMV vaccine clinically tested to date is the MF59-adjuvanted gB subunit (gB/MF59) vaccine which yielded a 50% efficacy rate in prevention of HCMV acquisition in multiple phase II clinical trials. Though gB-based vaccines have typically elicited limited virus neutralization, enveloped virus-like particle (eVLP) expression of gB induced robust CMV-neutralizing antibodies in a phase I clinical trial in healthy, CMV-seronegative participants. In this study, we further characterized the binding and functional antibody responses induced by the VBI1501A gB eVLP vaccine and compared these responses to those induced by the gB/MF59 vaccine. We found that VBI1501A vaccination induced high IgG binding to known targets of neutralizing antibodies, AD-4 and AD-4+5, but did not induce binding to AD-2, which is a target of the most potently neutralizing antibodies against gB. VBI1501A vaccinees elicited minimal binding to AD-6, a domain associated with IgG blocking of viral cell-associated spread. VBI1501A vaccination also did not elicit detectable IgG binding to whole virion from the clade-matched strain, Towne, nor ADCC responses to infected cells. VBI1501A immunization elicited higher magnitude plasma IgG binding to cell associated CMV gB and ADCP responses compared to the gB/MF59 vaccine, responses associated with protection in the gB/MF59 vaccine trial and against fetal transmission, respectively. The results of this study offer insight into strategies to improve CMV vaccine design and can aid further gB-based CMV vaccine development.

Gut Bacteria-Derived GABA Regulates Immune Response In The Neonatal Gut.

Presenting Author: Purnima Ravisankar (Graduate Student)

Authors: Ravisankar P, Sanidad KZ, Li T, Guo CJ, Inohara N, Zeng MY

Drukier Institute

Background: Our recent study revealed that the neurotransmitter gamma-aminobutyric acid (GABA) is distinctly enriched in the neonatal gut. This increase in GABA coincides with the critical “window of opportunity” for crucial development of intestinal immune responses. However, the regulation and immunomodulatory function of GABA in the neonatal gut remains unknown.

Objective: My proposal aims to elucidate the role of GABA in regulating intestinal immune under homeostasis and in response to microbial colonization in the neonatal gut.

Results: My preliminary findings indicate that enrichment of GABA in the SI of mouse neonates is gut microbiome dependent, as detected by mass spectrometry measurement of GABA in SI luminal contents, and quantitative gene expression of host GABA-catalyzing enzyme gene Gad1 in germ-free (GF) and pathogen-free (SPF) neonates and adults (Fig. 1). SPF neonates orally gavaged with GABA showed increased numbers of T cells producing inflammatory cytokines IFN γ and IL-17A, compared to vehicle (PBS) treated neonates. Furthermore, in vehicle or GABA-gavaged GF neonatal littermates conventionalized via vertical transmission of maternal microbiota, I observed significant increases in antigen-presenting cells, neutrophils, and effector CD4 $^{+}$ T helper 17 (TH17) in the colon of GABA-treated neonates (Fig. 2). Finally, using a mouse strain with a CD4 $^{+}$ T cell-specific deficiency in the GABAA receptor, I observed a significant increase in TH17 cells in the SI of these mice, compared to littermate wild-type controls. Collectively, my findings support a role for GABA signaling in the regulation of CD4 $^{+}$ T-cell responses critical for neonatal gut homeostasis.

Conclusion: My results suggest that GABA signaling to T cells in the neonatal gut promotes differentiation of TH17 cells to microbial colonization during postnatal development.

Exosomal Basigin (CD147) mediates the tumor immune response in fibrosarcoma

Presenting Author: Richard Piszczatowski MD, PhD (Resident)

Authors: Piszczatowski Richard T, Patras Laura M, Bailey Kayleen, Hatano Miho, Frietas Daniela, Reis Celso, Matei Irina, Lyden David

Department of Pediatrics

Background: Immune-mediated spontaneous tumor regression has been well documented in pediatric malignancies including fibrosarcoma. However, mechanisms mediating this phenomenon remain unclear. Here, we identify Basigin (CD147), a transmembrane glycoprotein presents on tumor-derived exosomes, as a mediator of the tumor immune response in orthotopic models of fibrosarcoma.

Methods: Using cell lines modeling tumor progression and regression, we investigated the immune response to tumor exosome education in a xenograft transplant model. We identified CD147 from mass spectrometry data as a candidate protein mediating immune response. Through functional testing and immunohistochemistry, we identified a potentially differential role for exosomal CD147 in tumor progressor and regressor models.

Results: We show that exosomal CD147 mediates immune response and subsequent tumor regression in a fibrosarcoma model. Exosomal CD147 from progressor cell lines suppresses immune activation while exosomal CD147 from regressor cell lines facilitate immune infiltration and anti-tumor response. Differential modification of CD147, possibly through glycosylation changes, may play a role in immune-mediated tumor response.

The Role of SOCS1 And TNFAIP3 In Hodgkin Lymphoma

Presenting Author: Suhong Sun PhD (Postdoc)

Authors: Suhong Sun, Isabella Kong, Vicenta Trujillo-Alonso, Trisha Vinay, Sarah Clark, Michail Roshal, Seung Nam, Ethel Cesarman, Ari Melnick, Lisa Giulino-Roth

Department of Pediatrics

Hodgkin lymphoma (HL) is an aggressive lymphoma arising from germinal center B-cells (GCBs). The rarity of malignant Hodgkin and Reed-Sternberg (HRS) cells in HL and their dependence on the tumor microenvironment (TME) has resulted in a limited understanding of HL genomics and few preclinical models including no mouse model. We have identified genetic alterations in HRS cells, including in SOCS1 and TNFAIP3, and found that this combination is distinct to HL. In the current work we sought to: 1) to investigate the role of dual alterations in SOCS1 and TNFAIP3 in the development of HL, and 2) to establish the first mouse model.

To accomplish this, we knocked out SOCS1 and/or TNFAIP3 in murine GCBs using the Cre/LoxP system with Cg1Cre mice which express cre exclusively in GCBs. Mice with the following genotypes were immunized with sheep red blood cells to induce the GC reaction: Cg1Cre/wt, Cg1Cre/wt SOCS flox/flox; Cg1Cre/wt A20flox/flox; Cg1Cre/wt SOCS1flox/flox A20flox/flox (double knock out, DKO). Nine days after immunization, spleens were harvested. We observed increased spleen weight in DKO mice. In addition the splenocytes of DKO mice had features of HL including a decrease in B220+ cells, and an increase in CD30+ cells. They also harbored features of the HL TME including increased CD8+ cells and Foxp3+CD4+ T regulatory(Treg) cells. The cytokine profile of DKO mice also reflected HL including increased TNF-a, CXCL9, and IL10. In conclusion, we have successfully knocked out SOCS1 and TNFAIP3 in GCB cells, leading to an HL-like phenotype in a mouse model.

Immunogenicity of HIV BG505 germline-targeting GT1.1 SOSIP Envelope trimer immunization In Infant And Juvenile Rhesus Macaques.

Presenting Author: Yasmine Issah, ScM (Graduate Student)

Authors: Yasmine Issah , Ashley N. Nelson, Xintao Hu, John Isaac, Xiaoying Shen, Gabriel Ozorowski, Leigh M. Sewall, Shiyu Zhang, Andrew B. Ward, David C. Montefiori, Rogier W. Sanders, John P. Moore, Koen K.A. Van Rompay, Kristina De Paris, and Sallie R. Permar

Weill Cornell Medical School

Developing a vaccine that induces broadly-neutralizing antibodies (bnAbs) before sexual debut is critical to preventing the ~400,000 new HIV -1 infections annually among adolescents. Recent work found that children living with HIV develop bnAbs earlier and at a higher frequency than adults. This study compares the ability of a germline-targeting SOSIP trimer immunization to induce precursor bnAbs in infant and juvenile rhesus macaques (RMs).

Infant (n=5) and juvenile (n=4) RMs received three doses of the germline-targeting BG505 GT1.1 SOSIP trimer with 3M-052-SE adjuvant at six-week intervals, followed by three boosts of BG505.664 WT SOSIP trimer over 18 months and two late boosts with a mosaic Clade B Env trimer nanoparticle. Vaccine-elicited antibody responses were monitored through 2.5 years after the 1st vaccination.

B505 GT1.1 SOSIP immunization consistently induced higher magnitude vaccine-specific IgG binding in infants compared to juvenile RMs yet, autologous tier 1 and 2 neutralization responses were similar. 3 of 5 GT1.1 SOSIP-immunized infants exhibited a sera neutralization signature indicating CD4bs bnAb precursor development, compared to only 1 of 4 juvenile RMs. Following the nanoparticle boost, an additional infant developed the CD4bs precursor bnAb signature (4 of 5), while this response was not maintained in the one juvenile (0 of 4). Nanoparticle boosting also improved the breadth of the low-level heterologous virus neutralization in 4 of 5 infants and 2 of 4 juveniles.

Our findings suggest that sequential germline-targeting immunization may more effectively elicit CD4bs-specific bnAb precursors in infants, supporting early-life HIV vaccination strategies and informing future pediatric trials.

CLINICAL RESEARCH

Trajectory Of Neurocognitive Functioning In Children Treated For Acute Lymphoblastic Leukemia (ALL): Dana Farber Cancer Institute ALL Consortium Study 16-001

Presenting Author: Alexandra Thrope, MD (Fellow)

Authors: Alexandra Thrope, Ramjan Sameera, White Charlie, Mauguen Audrey, Silverman Lewis, Welch Jennifer JG, Kahn Justine, Kelly Kara M, Tran Thai-Hoa, Michon Bruno, Gennarini Lisa, Bona Kira, Park Yongkyu, Cole Peter D, Sands Stephen A

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Background: Children treated for acute lymphoblastic leukemia (ALL) are at risk for deficits in neurocognitive domains, including attention-concentration, working memory, executive function, psychomotor function.

Objectives: This study evaluated longitudinal trajectories as well as medical and demographic associations with neurocognitive outcomes during treatment of ALL.

Methods: Patients ages 3-18 treated on DFCI 16-001 (NCT03020030) across 8 North American sites (2017-2022) were evaluated using Cogstate across four timepoints from diagnosis through the Continuation phase of therapy. Linear mixed models were used to estimate trajectories and interactions with clinical factors over time, incorporating random effects for patient and site.

Results: Performance for 298 patients (median age 7.9 years, 53% male) revealed significant change over time in varying directions for executive functioning, attention, visual learning, and working memory-accuracy (all $p < 0.001$). Older age was significantly associated with worse performance on psychomotor function ($\beta = -0.06$, [-0.09, -0.03]), working memory-accuracy ($\beta = -0.19$ [-0.24, -0.13]), working memory-speed ($\beta = -0.07$ [-0.12, -0.02]), and attention ($\beta = -0.07$ [-0.1, -0.04]). Female sex was associated with worse performance on psychomotor function ($\beta = -0.37$ [-0.65, -0.09]) and working memory-accuracy ($\beta = -0.74$ [-1.2, -0.33]), while females performed better on visual learning ($\beta = 0.53$ [0.11, 0.96]). A greater-than-expected proportion of participants performed below -1.5 SD from the mean on tests of attention, executive functioning, and psychomotor functioning at all 4 time points.

Conclusions: While most patients demonstrated normal functioning in neurocognition, including variable trajectories, a subgroup performed poorly on attention, executive functioning, and psychomotor functioning. Risk factors include older age at diagnosis and female sex, which may provide insight into groups warranting early intervention.

Phenylbutyrate For GABA-A Related Developmental And Epileptic Encephalopathy

Presenting Author: Amelia Stone, BA (Clinical Research Supervisor)

Authors: Stone, Amelia, Demarest, Scott MD PhD , Cross, Jennifer MD , Jones, Dara MD, Lim, Jaehyung MD, Basma, Natasha MPH, Miele, Andrea PhD, Abila, Maria, Cobos-Hernandez, Carla, Grinspan, Zachary MS MD

Weill Cornell Medical School

Background: Children with monogenetic developmental and epileptic encephalopathies often have seizures that are refractory to common antiseizure medications. Preclinical data and unpublished data suggest treatment with 4-phenylbutyrate would improve protein function in SLC6A1- and STXBP1-related disorders and reduce seizure burden. By conceptualizing SLC6A1- and STXBP1- related disorders as “synaptopathies”, we hypothesized that 4-phenylbutyrate would also improve clinical outcomes in children with mutations in GABA-A epileptic encephalopathy.

Objectives: To evaluate the safety and preliminary efficacy of glycerol phenylbutyrate in reducing seizure frequency in children with GABA-A epileptic encephalopathy.

Methods: Five children with GABA-A, four female, aged 9 months to 7 years were enrolled. Each was admitted for a 48-hour video EEG, accompanied by a developmental evaluation (the Bayley-IV and the Vineland Adaptive Behavior Scales). Each child received an initial dose of glycerol phenylbutyrate, then titrated up to the goal dose of 11.2 mL/m²/day. After 12-weeks (about 3 months) on glycerol phenylbutyrate, each child returned for a 24-hour video EEG and a repeat developmental evaluation.

Results: Two participants had dramatic reductions in seizures (>90%). Another participant had a substantial decrease in seizures (>50%). Two participants had an indeterminate response or no response.

Conclusions: Glycerol phenylbutyrate is a promising new therapy for seizures in children with monogenetic epilepsy and merits additional study. In ongoing work, we are enrolling additional children with GABA-A and other monogenetic developmental and epileptic encephalopathies.

Relationship Of Strain Pattern on Electrocardiogram and Severity of Disease in Pediatric Patients with Left Ventricular Outflow Tract Obstruction

Presenting Author: Amir Jahanshad, MD (fellow)

Authors: Jahanshad, Amir; Liberman, Leonardo

Department of Pediatrics

Background and Objectives: In the pediatric population, the clinical implications of LV strain pattern on ECG are not as well understood as they are in the adult population. However, recent data has shown that strain pattern on ECG was associated with both systolic and diastolic dysfunction in children with LVH on echocardiogram.

We aim to determine if there is an association between LV strain pattern on ECG in pediatric patients with left ventricular outflow tract obstruction (LVOTO) and severity of disease. These results could provide prognostic implications that could potentially be used by clinicians to better risk stratify their patients with LVOTO and to help provide data supported evidence for decision-making within this population.

Methods: This is a single-center, retrospective study analyzing all pediatric patients 0-18 years of age from Children's Hospital of New York who were diagnosed with congenital valvar aortic stenosis, subaortic stenosis, supraaortic stenosis, or mixed disease. LV Strain pattern on ECG was defined as down-sloping convex ST-segment depression, with an inverted asymmetrical T-wave opposite to the QRS axis in leads V5 and V6. To correlate with progression of disease, both ECG and echocardiogram data used in this study were from the last documented ECG and echocardiogram in the patient's chart.

Results and Conclusions: Results are pending

Evaluating The Need for Routine Ophthalmic Screening in Infants Who Screen Positive for Congenital Cytomegalovirus During the Neonatal Period

Presenting Author: Ana Garcia, BA (Medical Student)

Authors: Garcia, Ana P., Wole, Bethlehem, Sun, Grace

Weill Cornell Medical School

Background: Congenital cytomegalovirus (cCMV) affects 1 in 150 live births. While most infected infants are asymptomatic at birth, long-term sequelae like hearing loss and neurologic impairment are common. Ocular manifestations occur in a minority of cases. In 2023, New York launched a pilot program to screen all newborns for cCMV. At New York Presbyterian/Weill Cornell, all infants who tested positive underwent an ophthalmic evaluation, regardless of clinical presentation.

However, there is no consensus on the timing or frequency of eye screening in cCMV-positive infants. This study evaluates whether universal ophthalmic screening contributed to the detection of CMV-related eye disease.

Objectives: To determine the prevalence of ocular manifestations in cCMV-positive infants who underwent a comprehensive ophthalmic evaluation.

Methods: A retrospective chart review was conducted of all infants who tested positive for cCMV during the statewide pilot program (October 2023-September 2024) and underwent a dilated eye exam (n=21). Data collected included demographics, ophthalmic findings, and results from additional workup.

Results: All 21 cCMV-positive infants had at least one related systemic abnormality, including elevated GGT (86%), abnormal brain imaging (ultrasound: 67%, MRI, 62%), neutropenia (29%), and sensorineural hearing loss (14%). None exhibited CMV-related ocular disease on exam. One patient had isolated retinal hemorrhages attributed to birth trauma. The mean age at eye exam was 35 days.

Conclusion: Early, universal ophthalmic screening in cCMV-positive infants did not identify any cases of CMV ocular disease in this cohort, supporting consideration of a more targeted, risk-based approach. Further studies with long-term follow-up are needed to refine current screening guidelines

Assessment Of Growth Trajectories and Its Relationship with The Neurodevelopment Status Of Preterm Infants With Growth Faltering

Presenting Author: Witte-Castro, Ariadna (PhD student)

Authors: Witte-Castro, Ariadna; Díaz González, Celia; Ares Segura, Susana; Sáenz de Pipaón, Miguel

Background and Aims: Growth faltering (GF) is common in preterm infants and involves poor postnatal weight and linear growth. Promoting adequate catch-up in both weight and length is critical to reduce the risk of long-term metabolic, cardiovascular, and neurodevelopmental impairments. This study aims to assess postnatal growth trajectories in growth-faltering preterm infants and evaluate the association between impaired growth and neurodevelopmental outcomes.

Methods: included infants with a gestational age (GA) ≤ 32 weeks and/or a birthweight ≤ 1500 grams, that completed the follow-up at the neonatology outpatient clinic. We divided the sample into two groups according to growth evolution during the hospital stay: infants who suffered from growth faltering (GF, n=102) and infants who did not suffer from growth faltering (Non Growth Faltering, NGF, n=66), according to the World Health Organization definition.

Results: In the Parent Report of Children's Abilities-Revised (PARCA) questionnaire, NGF infants had a higher score in language development scale at 2 years (88.5 [78.5; 96.5] vs. 84.5 [69.5; 91.5], $p = 0.037$). In the Bayley-III, we found a significant difference in motor development scale, with a higher score in the NGF group (94 [88; 100] vs. 85 [79; 91], $p = 0.033$). Infants with a higher difference in z-score from birth to discharge obtained worst results in both PARCA scales at 2 years (language scale $\rho = -0.26$, $p = 0.0064$; non-verbal cognition scale $\rho = -0.19$, $p = 0.039$).

Conclusions: In this cohort study, we identified GF of very preterm infants associated with a higher risk of adverse neurodevelopmental outcome at 2 years corrected age (CA).

Table 1. Regression models between groups, timepoints, and the z- score of weight, length and HC.

Data shows estimated beta (β) coefficients \pm standard error (SE) and p-Value. Birthweight, birth length and birth HC Z-score were considered the reference. Models were adjusted by sex, sepsis and bronchopulmonary dysplasia during hospital stay and gestational age. CA = Corrected age; HC = Head Circumference; GF = Growth faltering; NGF = No growth faltering.

Table 5 (a and b). Differences in neurodevelopment scales between groups.

Values expressed as 50th percentile and quartiles (Q1; Q3). Data was analyzed using U-Mann Whitney test for non-parametric data. CA = Corrected age; HC = Head Circumference; GF = Growth faltering; NGF = No growth faltering.

Near Final Height In Males treated with Aromatase Inhibitors

Presenting Author: Athanasia Bouliari, MD (Fellow)

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Department of Pediatrics

Background: Aromatase inhibitors have been used off label in males with short stature to delay epiphyseal fusion, extending the period of linear growth and potentially increasing adult height. There is limited data on patients treated with aromatase inhibitors who have attained final or near-final adult height (FNFH). This study aims to evaluate whether anastrozole therapy improves FNFH of males with advanced or rapidly advancing bone age (ABA) and compromised predicted adult height.

Methods: Data of male patients treated with aromatase inhibitors were collected through retrospective chart review. Descriptive statistics were used to characterize the study cohort while Fisher's exact test and Wilcoxon rank-sum test were used to compare outcomes between anastrozole and letrozole treatment.

Results: A total of 72 patients treated with aromatase inhibitors were reviewed; 59 (82%) patients received anastrozole only, 11 (15%) received letrozole only, and 2 (2.8%) switched from anastrozole to letrozole. Most patients identified as white (62%) and were privately insured (94%). The median duration of treatment was 25 months (IQR: 18, 32), with a median chronological age of 13.33 years (IQR: 12.25, 14.17) and median bone age of 14 years (IQR: 13, 14.25) at treatment initiation. Diagnoses included growth hormone deficiency (31%), early or rapid progression of puberty and premature adrenarche (18%), idiopathic short stature (15%), overweight/obesity (14%), short stature (13%), small for gestational age (9.9%), ABA only (9.9%), congenital adrenal hyperplasia (4.2%) and other conditions (14%). Concurrent treatment with growth hormone was used in 66% of the patients. The overall median gain in height (FNFH minus initial predicted height) was 1.2 cm (IQR: -1.9-4.2), while the median gain in predicted height was 3 cm (IQR 0, 6). Adverse effects included acne (30%), elevated liver function tests (28%), mental health concerns (8.5%), and hair loss (2.9%). Letrozole-treated patients showed a greater median height gain (4.2 cm, IQR: 0.6 to 13) compared to the anastrozole group (0.8 cm, IQR: -2.6 to 3.5; p:0.013) and reached a FNFH closer to mid-parental target height (MPTH) (p:0.031).

Conclusion: Our findings suggest that letrozole results in greater gain in height and a higher likelihood of achieving a FNFH closer to MPTH compared to anastrozole in males with advanced bone age, though adult heights may have been underestimated in the anastrozole group.

Lessons Learned from Integrating Clinics Serving Publicly And Privately Insured Pediatric Patients At An Urban Academic Hospital In New York City

Presenting Author: Beemnet Neway, MD (Resident)

Authors: Beemnet Neway, MD, Marianne Sharko, MD, MS, Erika Abramson, MD MSc

Department of Pediatrics

Background: Healthcare disparities by race, ethnicity, and socioeconomic status have been well documented. At Weill Cornell Medicine, pediatric clinics were historically divided by insurance type, resulting in differences in socioeconomic status. In 2020, a Health Equity Taskforce recommended integrating care, leading to the merger of clinics serving publicly and privately insured patients in January 2022.

Objective: To explore the experiences of families and providers following the merger of clinics serving publicly and privately insured patients. We hypothesize that while the merger will reduce inequities in care, the transition process poses unique challenges.

Methods: This is a qualitative interview study of pediatric patients and providers who experienced care before and after the merger. Using a semi-structured interview guide, we explore topics such as visit scheduling, wait times, visit experience, support and resident teaching. After transcribing the interviews, we are using inductive thematic analysis to identify recurring themes.

Results: To date, we've completed four guardian and five provider interviews, aiming for 15 each or until thematic saturation. Guardians noted easier scheduling, shorter wait times, improved clinic space, and challenges with timely arrival (Table 1). Providers reported increased access to subspecialty care, improved coordination, and also challenges related to clinic space and teaching time constraints (Table 2).

Conclusions: Merging care for pediatric patients with private and public insurance reduces inequities of care and improves many aspects of the patient visit experience. However, we have also identified challenges in this process that would be beneficial to address for a successful merging process.

Table 1. Emerging themes from guardian interviews		
Theme	Summary	Representative quotes
Ease of scheduling	Although respondents did not identify general challenges in scheduling visits, there was some increased ease in scheduling reported in at least one subspecialty clinic after the merger.	'I've never had a problem making appointments.' 'All of my son's doctors communicate with each other.' 'Have noticed a change only in (redacted) clinic - we used to have trouble scheduling an appointment there.'

Differing acceptance of challenges in arriving to appointments.	Participants have reported that less acceptance of being late for appointments has impacted patient care for patients with increased medical or social challenges.	<p>'They don't understand people being late – for children who have seizures – I can't not pull over on the side of the road and not give you a seizure medicine because then I'll be more than 15 minutes late for an appointment. And that has happened...I get there and turn around, and they aren't going to see him.'</p> <p>'If I had waited for the ambulance to get there, I would have been 15 minutes late and I would have had to turn around.'</p> <p>'After the 20 minutes late time, the appointment disappears in the system, and you can't sign in.'</p> <p>'</p>
Physical space of clinic has improved.	New clinic space is perceived as being nicer, with larger clinic rooms.	<p>'The space is much bigger.'</p> <p>'It's nicer, it's not as congested.'</p> <p>'The waiting area is larger.'</p> <p>'I like the third floor -I think it's a little prettier. Space is better.'</p>
Wait times have decreased.	The improved workflow has resulted in less wait time to see the provider.	'Much faster on the third floor.'
Visit itself remains the same.	The visits themselves have not changed.	'It's the same doctors.'

Table 2. Emerging themes from provider interviews		
Theme	Summary	Representative quotes
The opportunity to provide equitable care.	The merger provides the possibility of providing equitable care independent of insurance type.	"I do precepting for residents and I don't pay any attention when residents are coming which insurance anyone had that led them to come to our clinic, which is ideally the way you want it to be from the provider giving side."
Increased access to appointments for subspecialty care	The merger provided increased access to subspecialty care by providing increased appointment scheduling availability.	<p>"Before you were very restricted with the patient times that were available. For some families, the one day a week may not work based on their work or school schedules. The availability has been a really nice change for our families."</p> <p>"The availability to get families into (subspecialty) appointments makes it easier to care for them due to the shorter wait time to see subspecialists."</p> <p>"I'd summarize it as a world of difference just in terms of access. But it's not just access. Like, you call, and you have an appointment availability."</p> <p>"Wait times were also very, very long because we only used to have one clinic a week for most subspecialty sessions, and now they can be seen by</p>

		<p>anyone, anywhere. And so families don't have to just line up for a Tuesday morning and they can actually get in and be seen.”</p>
<p>Differing acceptance of care provided by junior care providers and its impact on continuity of care.</p>	<p>-Commercially insured patients may have lower tolerance for being seen by junior care providers instead of attendings.</p> <p>-This impacts continuity and may be more pronounced for patients with previous relationship with an attending.</p> <p>-Tolerance may vary for higher acuity of care.</p> <p>-Explanations on the process may add time to the visits.</p>	<p>“On two levels – One, knowing I may have a junior provider will be a barrier for some families, more so with commercial insurance, and this idea that I’m not going to have the same person all of the time.”</p> <p>“Being clear about the way the clinic operates, and we can’t change the model for individual patients. We have to have patients that are willing to accept the model.”</p>
<p>Competition for clinic space</p>	<p>With more patients being seen in the same space, there may be competition for the available space for clinic care which may impact patient care and trainee teaching.</p>	<p>“Now everybody's on the third floor. It's very, very crowded. It's difficult to get a room sometimes. It can often be difficult to find the space.”</p>
<p>The opportunity to provide equitable care.</p>	<p>The merger provides the possibility of providing equitable care independent of insurance type.</p>	<p>“I do precepting for residents and I don't pay any attention when residents are coming which insurance anyone had that led them to come to our clinic, which is ideally the way you want it to be from the provider giving side.”</p>
<p>Improved coordinated care.</p>	<p>The merger has improved the ability to provide integrated care among subspecialties that can communicate care more effectively and efficiently.</p>	<p>“We can group blood work together. So maybe I'll hold off my blood work because I know allergy is going to put some blood work in as well.”</p>
<p>Themes relevant to privately insured general pediatrics care now provided on HT5</p>		
<p>Differing resource expectations</p>	<p>-Private patients may expect more resources than what is available in public clinic areas, such as nursing support and physical equipment.</p> <p>-Conversely, there may also be increased access to support generally provided to publicly insured patients,</p>	<p>“There are very different expectations in private practices – scales in every room, getting gowned and undressed. The culture has not always been the way you ideally want to see things run in a Medicaid practice”P1</p>

	such as increased social work support or Healthy Steps care.	
Themes relevant to subspecialty pediatric care now provided on HT3		
Lower financial reimbursement for public patient visits	Private clinics may need to adapt to lower visit reimbursement provided by publicly insured patients.	"We have a higher percentage of total practice families who have Medicaid managed care insurance compared to private insurance. I think it was something like 80, 20 before and now we're somewhere close to 60, 40...it does bring some financial pressure to the department. I've never been told because of the merger you need to see more families. But we overall as a group do need to see more families and more visits."
Differing appreciation of patient social challenges.	Private clinics staffing may not have an appreciation of the challenges posed by social determinants of health for patients when accessing healthcare. -This may result in different tolerance levels to lateness or missed appointments in the merged clinic.	"I'm more tolerant about lateness, etc, for the families that I'm familiar with their challenges" "There are also challenges for families, getting there and getting them on time. We try to be very accommodating, but when you have a mixture of patients, that's not always possible." "Medicaid may still exacerbate challenges – jobs that require them to be in person that don't necessarily allow them to take time off – that's a larger societal problem. When your scheduling is restrictive and your competing with lots of other families, the ramifications may be larger in terms of job insecurity."
Improved patient experience.	Improved space and consistency among subspecialists	"If I say to them, you'll be seeing the subspecialist, and they say, where? And I say, right here. Like, it'll be one of these rooms, you know, but it'll be a different doctor. I think to them it's familiar. They know they can come back here." "It's an easier flow and they're happy when I say to them that they'll be able to be seen there."

Metabolomic Dysregulations In Severe Obesity-Related Asthma: Insights from a New York City Pediatric Urban Cohort

Presenting Author: Catalina Acosta, MD (Fellow)

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Rationale: The obesity-related asthma phenotype in children is often severe and difficult to control, in part due to a lack of understanding of its underlying pathophysiology. Given the distinct presentation of obese individuals with severe persistent asthma, we hypothesize that these patients have a unique dysregulated metabolomic profile compared to those with obesity or asthma alone. Identifying this profile may provide further insights into the mechanisms underlying this phenotype.

Method: Data from the prospective observational NewYork-Presbyterian Pediatric Asthma Cohort Study of 73 participants, aged 7-21 years with physician-diagnosed severe persistent asthma and without asthma were analyzed. Mass spectrometry-based untargeted metabolomic profiling was performed on plasma samples. Participants had baseline determination of body mass index (BMI) percentile. A comprehensive survey was administered. Metabolites with less than 25% missing data were included; data were normalized and imputed. Linear regression was used to identify altered metabolomic pathways and metabolites, in obese participants with severe asthma, adjusting for age, sex, race/ethnicity, and atopic conditions. Significance was set at $q < 0.2$ to account for the high dimensionality of metabolomic data.

Results: Of 73 participants included in analyses: 62 were non-asthmatics (64% Hispanic, 16.1% Caucasian, 12.9% Black), 11 had severe persistent asthma (45% Hispanic, 36.4% Black, 9.1% Caucasian). Among severe asthmatics, 72.7% were obese and 27.3% healthy weight, and in non-asthmatic individuals, 62.9% were healthy weight and 37.1% obese. In asthmatics, 45.5% had eczema, 54.5% rhinitis, and 54.5% food allergies.

Twenty-nine metabolites from 15 sub-metabolic pathways were altered; 10 involved upregulated lipid pathways. The most impacted were branched fatty acid (75% of identified metabolites), followed by long-chain saturated (57%), long-chain polysaturated (n3 and n6) (29%), long-chain monosaturated (29%), medium-chain fatty acids (29%), phosphatidylethanolamines (18%). Additional fatty acids identified included 7% of the monohydroxy subpathway and 6% of the dicarboxylate subpathway. These findings showcase the predominant dysregulation in fatty acid metabolism, particularly in long-chain and branched fatty acids. Other sub-pathways impacted included Alanine metabolism (11%), amino sugar metabolism (20%), uracil containing Pyrimidine Metabolism, (9%).

Discussion: Findings reveal a high prevalence of obesity in severe asthmatics, suggesting a potential interaction between obesity and asthma severity, and a complex interplay of lipid metabolism. Children/adolescents with severe asthma and obesity demonstrated dysregulation in multiple metabolic lipid pathways, with a particular increase in those related to long-chain fatty acids. Some of these metabolites have been shown simultaneously to exhibit anti-inflammatory properties and contribute to airway remodeling and contraction. Additionally, a significant number of obese asthmatics were atopic. Further mechanistic studies are needed to understand whether Th2 and lipid pathways are linked.

Assessing Needs of Critically Ill Children with Non-Cancer Diagnoses: An Innovative Qualitative Study

Presenting author: Christina Tempesta, MD (Fellow)

Authors: Tempesta, Christina, Abramson, Erika, Salant, Jennifer

Department of Pediatrics

Background: Families of children with complex illnesses face unique challenges including social isolation, sibling stress, and physical/mental health issues. These challenges have been explored in pediatric oncology populations but are less studied in patients with other diagnoses. Studies have identified that families of patients with non-cancer diagnoses have higher unmet needs compared to counterparts with cancer diagnoses but did not explore in depth the details of those unmet needs. This is despite the fact that among the majority of PICU admissions nationally from 2001-2019, patients with oncologic diagnoses accounted for only 2.4-4.7% of admissions.

Objectives: To identify/explore the needs of families of critically-ill pediatric patients with non-cancer diagnoses for the development of mitigation strategies/interventions.

Methods: We conducted one-on-one interviews with parents of critically-ill pediatric patients with non-cancer diagnoses admitted to a large urban PICU. We used a constant comparison analytic approach to derive themes.

Results: We have conducted 10 interviews and identified three themes. First, families feel an obligation to be present at the bedside, making it difficult to address their own needs. Second, families often feel immense fear and loneliness while admitted, which can persist after discharge. Third, families shared that the physical environment of the PICU can provide challenges that hinder their ability to care for themselves and their children.

Conclusions: From these identified needs, PICUs can develop procedures/interventions to mitigate the psychosocial effects associated with a complex admission and create a more balanced support system for all children in the PICU.

Using The CBC As a Prognostic Factor in Pediatric Solid Tumors

Presenting Author: Christopher Mazzeo, MD (Fellow)

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Background: The immune system plays a key role in inhibiting cancer growth and mediating inflammation. A complete blood count (CBC) reveals various components of the immune system. Previous studies have shown mixed results regarding if lymphocyte, neutrophil (ANC), and monocyte (AMC) counts obtained from a CBC can be used as prognostic factors in pediatric solid tumors. Using a CBC would be a quick and inexpensive way to stratify patients in resource-limited settings.

Objectives: To determine if a CBC can be used as a prognostic factor in pediatric patients with Ewing sarcoma, osteosarcoma, and rhabdomyosarcoma.

Methods: CBC results at diagnosis were collected via retrospective chart review. Survival analysis was performed using Kaplan-Meier method and optimal cutoffs were determined using the maximal standardized log-rank statistic. Significance of potential prognostic factors were determined via univariate cox regression analysis.

Results: An ANC greater than 4300 was associated with a worse progression-free survival (PFS) in patients with Ewing sarcoma and overall survival (OS) in patients with osteosarcoma.

A lymphocyte percentage greater than 30.6% was associated with a favorable PFS in patients with Ewing Sarcoma and osteosarcoma and a favorable OS in osteosarcoma.

An AMC greater than 800 was associated with worse PFS and OS in patients with osteosarcoma.

A monocyte/lymphocyte ratio greater than 0.3 was associated with a worse OS for patients with osteosarcoma and rhabdomyosarcoma.

Conclusions: The ANC, lymphocyte count, and AMC at time of diagnosis are potential prognostic factors for pediatric patients with Ewing sarcoma, osteosarcoma, and rhabdomyosarcoma.

Outcomes of Autism Screening in an Urban Pediatric Clinic

Presenting Author: Cindy Do, MD (Resident)

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Department of Pediatrics

Background: The prevalence of Autism Spectrum Disorder (ASD) has risen dramatically. Literature indicates that appropriate interventions before the age of 36 months are associated with improved outcomes. Despite the use of validated tools for ASD screening at 18 and 24 months, the average age of diagnosis in the U.S. is still 4.5 years. Prior studies have examined strategies to increase screening and factors associated with screening for ASD. It remains unclear which factors are related to appropriate referrals and completed evaluations.

Objectives: To define factors associated with appropriate referral for evaluation and services in children who screen positive on the M-CHAT-R at an urban pediatric outpatient practice.

Methods and Results: A retrospective chart review was conducted with IRB approval. Subjects were identified from an existing research database repository. A total of 174 patients screened positive on the MCHAT. Of these, 81% were referred to EI, 40% were referred to Child Development, 62% were referred to audiology. Of those referred, 86% were evaluated by EI, 29% were evaluated by Child Development, and 66% were evaluated by audiology. Earlier age of first positive MCHAT was associated with increased likelihood EI evaluation ($p = 0.042$). English language ($p = 0.001$) and speech delay ($p < 0.001$) were statistically associated with EI referral.

Conclusions: Although the clinic has a standardized protocol in place to screen patients for autism, there is still a disparity in referring patients to the appropriate services and ensuring that patients receive the evaluations and services they need.

Thrombolytic Use and Outcomes in Pediatric Congenital and Acquired Heart Disease

Presenting Author: Devika Richmann, M.D. (Fellow)

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Department of Pediatrics

Background: Patients with congenital heart disease have a unique risk of thrombosis as they often have external hardware and altered cardiac physiology. While the use of tissue plasminogen activator (tPA)'s fibrinolytic activity has been demonstrated to be effective in other adult and pediatric settings including stroke and pulmonary embolism, its use in pediatric patients with congenital heart disease has not been well reported.

Methods: This is a single center retrospective case series. All pediatric patients (age 0-18 years) who received tPA between 2008 - 2024 and had acquired or congenital heart disease were identified. Chart review was conducted to collect patient data. Thrombus response and adverse events related to tPA use were evaluated. Descriptive statistics were performed.

Results: There were a total of 44 instances of tPA administration (57% of patients male, median age 5y, median weight 18kg). 45% of patients had a history of thrombosis or hematologic diagnosis predisposing them to thrombosis; 68% of patients had single ventricle CHD. Diagnosis was most frequently made by echocardiogram (68%) with other diagnostic modalities including ultrasound, CT, and catheterization. Venous thrombi were the most frequent type of thrombosis seen with cavopulmonary circulation being the most frequent location of thrombus. Patients with thrombus resolution had lower mortality (20% vs 63%, $p=0.009$). Thrombus resolution was associated with older age and higher weight. All 5 patients with major bleed did not survive; 80% of these patients had fibrinogen levels at some point less than 100mg/dL. Duration and doses of tPA therapy and D-dimer levels did not differ between outcomes.

Precision Treatment in Pediatric Inflammatory Bowel Disease: Utilizing Alternative Dosing Strategies for Optimal Therapeutic Outcomes

Presenting Author: Elliott Gordon, MD, MSc, FAAP (Faculty)

Authors: Gordon, Elliott S., Lentine, J., Thomas, C., Sockolow, R., Gerber, L.

Department of Pediatrics

Introduction/Background: Inflammatory bowel disease (IBD) in pediatric patients presents complex treatment challenges, particularly in optimizing anti-TNF therapy with infliximab (IFX). Despite growing evidence of treatment variability, comprehensive understanding of dosing strategies remains limited. This study investigates the relationship between infliximab dosing, therapeutic drug monitoring (TDM), and clinical outcomes in pediatric IBD patients.

Methods: We conducted a single-center retrospective chart review of patients aged 3-26 years diagnosed with Crohn's disease or ulcerative colitis, receiving infliximab therapy. The study examined multiple factors influencing drug pharmacokinetics, including age, weight, disease severity, and trough levels. Comprehensive medical record analysis captured demographic information, disease characteristics, treatment details, and clinical response metrics.

Results: results revealed significant variability in infliximab pharmacokinetics across the pediatric population. Younger patients (< 10 years) demonstrated notably different drug disposition, with 25-40% lower drug exposure compared to older pediatric and adult patients. Dose escalation to 2-3 mg/kg/week was associated with higher therapeutic drug levels and improved disease maintenance. Weight emerged as a critical factor, with a nonlinear correlation between body weight and drug clearance.

Multivariate analysis identified key covariates affecting infliximab clearance, including serum albumin levels, inflammatory markers, and the presence of antidrug antibodies. Patients with lower body weight and younger age required more intensive treatment regimens, with a higher likelihood of developing antibodies to infliximab.

These findings have critical implications for personalized treatment strategies in pediatric IBD. The study underscores the importance of individualized dosing approaches, emphasizing that a one-size-fits-all strategy is inadequate. Proactive therapeutic drug monitoring, targeting exposure concentrations above 5 µg/mL, demonstrates potential for improving disease remission and treatment durability.

Conclusion: Our research provides empirical evidence supporting more nuanced, patient-specific approaches to infliximab therapy in pediatric inflammatory bowel disease, challenging existing paradigms of uniform dosing strategies.

Pediatric Patient Preferences For Testosterone Therapy: A Qualitative Study

Presenting Author: Frances Bullard, MD (Fellow)

Authors: Bullard FB, Scharf E, Abramson E, Lekarev O, Su KL

Department of Pediatrics

Objective: Testosterone is used to treat hypogonadism in cisgender males and for gender-affirming therapy in transgender males. Therapy is long-term, with options including intramuscular injections, subcutaneous injections, or topical gel. This study aims to understand the experience of adolescent patients on long-term testosterone therapy and explore factors most important to patients in choosing a specific formulation.

Methods: In this qualitative descriptive study, we conducted virtual semi-structured interviews with cisgender and transgender male patients, and one non-binary patient, who are currently or were previously on testosterone therapy. Patients ages 12-25 years old were included, as well as parents of patients <18 years old. Interviews were transcribed and analyzed using a thematic analysis method. Data collection proceeded until multiple transcripts produced no additional codes, indicating that thematic saturation had been achieved.

Results: Ten participants were interviewed (ages 15-22, 5 cisgender, 4 transgender, and 1 non-binary) and 7 parents/caregivers. Qualitative analysis identified 5 themes based on patient experiences with testosterone therapy: (1) overall satisfaction with treatment, (2) skepticism towards using gel, (3) online resources often used prior to starting testosterone therapy, particularly in the transgender population, (4) different formulation options were not always offered, and (5) patients experienced minimal side effects regardless of formulation.

Conclusion: Adolescent patients on testosterone therapy report overall satisfaction with treatment, regardless of formulation. However, patients who do not use a gel formulation tend to have a negative perception of this type. Patients also experience minimal side effects regardless of the formulation. There are some differences between cisgender and transgender patients in their approach to starting testosterone, particularly with use of online resources. By understanding patient experiences on testosterone therapy, providers can better counsel patients on which testosterone formulation is best for them.

Effect Of Acupuncture Versus Massage on Pain in Adolescent and Young Adult Patients with Advanced Cancer: Subgroup Analysis of a Randomized Clinical Trial

Presenting Author: Han-Wei Wu, MD (Fellow)

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Department of Pediatrics

Background/Objectives: Pain management remains challenging for adolescent and young adult (AYA) cancer patients. Acupuncture and massage have been recommended for cancer-related pain management, but no prospective trials have been conducted in AYA patients. We explored the effects of acupuncture and massage on pain in AYAs.

Methods: This subgroup analysis focused on AYA-aged patients (18-39 years) enrolled in a randomized control trial comparing acupuncture or massage for pain in advanced cancer patients. Interventions were delivered weekly for 10 weeks with monthly booster treatments up to 26 weeks to consolidate initial treatment effects. The primary outcome was the Brief Pain Inventory's worst pain score. A linear mixed model was used for analyses.

Results: Thirty participants (13 received acupuncture; 17 received massage) met eligibility criteria (mean [SD] age, 33.7[4.9] years; 17[57%] were female; 20[67%] were White; 16[53%] had solid tumors). Patients who received acupuncture or massage experienced reduced pain over time. Relative to baseline, patients receiving acupuncture had a mean change of -1.26 points (95% CI, -2.54 to 0.01) at 10 weeks and a mean change of -1.46 points (95% CI, -2.78 to -0.14) at 26 weeks. Patients receiving massage experienced a mean change of -2.81 points (95% CI, -3.92 to -1.70) at week 10, and a mean change of -3.79 points (95% CI, -4.85 to -2.73) at week 26.

Conclusion: AYA patients with advanced cancer receiving either acupuncture or massage experienced clinically meaningful and persistent pain reduction. Our findings provide a promising foundation for future trials to evaluate integrative pain management in AYAs.

Data Tables**Table 1: Baseline characteristics of adolescent and young adult-aged participants, 18 to 39 years old (n=30)**

Characteristic	Total (n=30)		Acupuncture (n=13)		Massage (n=17)	
Age, mean (SD), y	31.1	(5.8)	27.8	(5.4)	33.7	(4.9)
Sex, n (%)						
Female	17	(56.7)	7	(53.8)	10	(58.8)
Male	13	(43.3)	6	(46.2)	7	(41.2)
Race, n (%)						
White	20	(66.7)	8	(61.5)	12	(70.6)
Non-White	10	(33.3)	5	(38.5)	5	(29.4)
Ethnicity, n (%)						
Hispanic	11	(36.7)	5	(38.5)	6	(35.3)
Non-Hispanic	19	(63.3)	8	(61.5)	11	(64.7)
Cancer type, n (%)						
Hematologic	14	(46.7)	7	(53.8)	7	(41.2)
Breast	7	(23.3)	2	(15.4)	5	(29.4)
Testicular	4	(13.3)	1	(7.7)	3	(17.6)
Other*	5	(16.7)	3	(23.1)	2	(11.8)
Cancer Treatment, n (%)						
Surgery	19	(63.3)	8	(61.5)	11	(64.7)
Chemotherapy	29	(96.7)	13	(100)	18	(94.1)
Radiotherapy	18	(60.0)	6	(46.2)	12	(70.6)
Immunotherapy/biological therapy	7	(23.3)	1	(7.7)	6	(35.3)
Hormonal	5	(16.7)	1	(7.7)	4	(23.5)
Years since cancer diagnosis, mean (SD), y	5.7	(5.5)	4.1	(4.8)	7.0	(5.9)
Duration of pain symptom, mean (SD), y	1.7	(2.7)	0.8	(0.6)	2.4	(3.4)
Baseline measures						
Brief Pain Inventory severity, mean (SD)	4.8	(1.4)	5.3	(1.4)	4.3	(1.2)
Worst pain item	6.9	(1.6)	7.4	(1.9)	6.5	(1.3)
Average pain item	5.0	(1.4)	5.0	(1.8)	4.9	(1.0)
Brief Pain Inventory interference, mean (SD)	4.6	(2.2)	5.1	(1.6)	4.3	(2.6)
Opioid use, n (%)	12	(40.0)	5	(38.5)	7	(41.2)

*Other includes endocrine, gastrointestinal, gynecological, head and neck, and lung cancers

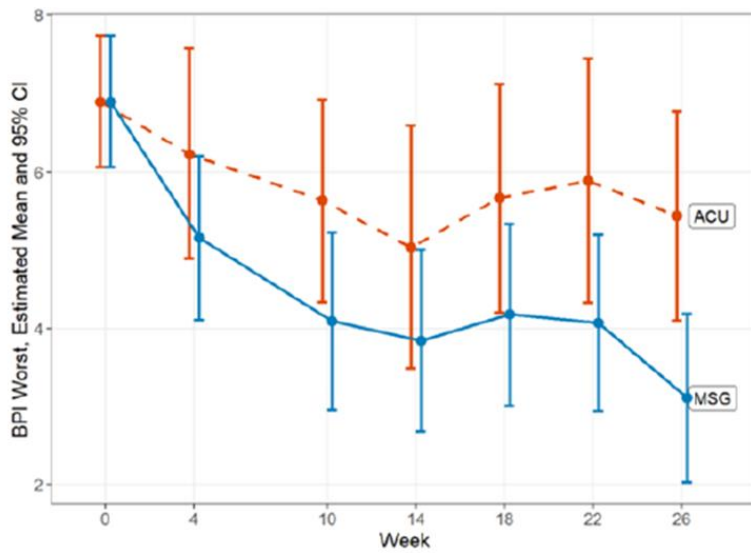
Table 2: Estimates of within-arm and between-arm differences for primary and secondary pain outcomes in adolescent and young adult-aged participants, 18 to 39 years old (n=30)*

Outcome measure	Acupuncture		Massage		Between-arm differences, mean (95% CI)	p value ^b (between arms over time)
	Mean (95% CI)	Change from baseline, mean (95% CI)	Mean (95% CI)	Change from baseline, mean (95% CI)		
BPI worst pain item						
At baseline	6.90 (6.07 to 7.73)	NA	6.90 (6.07 to 7.73)	NA	NA	0.11
At 10 weeks	5.64 (4.34 to 6.93)	-1.26 (-2.54 to 0.01)	4.09 (2.96 to 5.23)	-2.81 (-3.92 to -1.70)	-1.54 (-3.14 to 0.06)	
At 26 weeks	5.44 (4.10 to 6.78)	-1.46 (-2.78 to -0.14)	3.11 (2.03 to 4.19)	-3.79 (-4.85 to -2.73)	-2.33 (-3.93 to -0.73)	
BPI average pain item						
At baseline	4.97 (4.23 to 5.70)	NA	4.97 (4.23 to 5.70)	NA	NA	<0.01
At 10 weeks	4.81 (3.76 to 5.86)	-0.16 (-1.12 to 0.81)	3.36 (2.42 to 4.29)	-1.61 (-2.44 to -0.77)	-1.45 (-2.68 to -0.22)	
At 26 weeks	4.76 (3.67 to 5.84)	-0.21 (-1.21 to 0.79)	2.22 (1.32 to 3.12)	-2.74 (-3.54 to -1.95)	-2.54 (-3.77 to -1.31)	
BPI pain severity score						
At baseline	4.73 (4.00 to 5.46)	NA	4.73 (4.00 to 5.46)	NA	NA	0.06
At 10 weeks	4.07 (3.02 to 5.12)	-0.66 (-1.62 to 0.30)	3.09 (2.16 to 4.02)	-1.64 (-2.47 to -0.81)	-0.98 (-2.21 to 0.24)	
At 26 weeks	4.11 (3.03 to 5.19)	-0.63 (-1.62 to 0.37)	2.27 (1.37 to 3.17)	-2.46 (-3.26 to -1.67)	-1.84 (-3.06 to -0.61)	
BPI interference						
At baseline	4.63 (3.77 to 5.50)	NA	4.63 (3.77 to 5.50)	NA	NA	0.41
At 10 weeks	4.14 (2.95 to 5.34)	-0.49 (-1.55 to 0.57)	3.60 (2.52 to 4.67)	-1.04 (-1.95 to -0.13)	-0.55 (-1.90 to 0.81)	
At 26 weeks	3.33 (2.10 to 4.56)	-1.30 (-2.40 to -0.21)	2.32 (1.28 to 3.35)	-2.32 (-3.18 to -1.45)	-1.01 (-2.37 to 0.34)	

*For each outcome, estimates are derived from a linear mixed model with baseline means constrained to be equal across study arms. The dependent variable vector included the pre-randomization baseline (week 0) assessment, as well as all post-randomization assessments at weeks 4, 10, 14, 18, 22, and 24. The independent variables were treatment arm, week (categorical), and the arm-by-week interaction. A patient-level random intercept was included in the model to account for the repeated outcome measurements within patients.

^bThese p-values represent the overall difference between arms over time, derived from multivariate Wald tests of the arm-by-time interaction coefficients across all time points (i.e., weeks 0, 4, 10, 14, 18, 22, and 24).

Figure 2: Estimated Brief Pain (BPI) Worst Pain Means by Week and Arm^a



^aBrief Pain Inventory (BPI) worst pain scores range from 0 to 10, with higher scores indicating worse pain. Data points represent the model-estimated BPI worst pain means and 95% CI (indicated by the I bars) from a linear mixed model with baseline means constrained to be equal across study arms. The dependent variable vector included the pre-randomization baseline (week 0) assessment, as well as all post-randomization assessments at weeks 4, 10, 14, 18, 22, and 26. The independent variables were treatment arm, week (categorical), and the arm-by-week interaction. A patient-level random intercept was included in the model to account for the repeated outcome measurements within patients. Abbreviations: BPI, Brief Pain Inventory; CI, Confidence Interval; ACU, acupuncture; MSG, massage.

The Impact of Respiratory Pathogen Panel Testing on Pediatric Emergency Department Return Visits and Management

Presenting Author: Jaime Y. Perez Lizardi, MD (Resident)

Authors: Jaime Y. Perez Lizard, Stephan, Alexander M; Stern, Lana M; Jonas, Jennifer; Thomas, Charlene; Gerber, Nicole; Acker, Karen; Levine, Deborah

Department of Pediatrics

Background: In 2022, the AAP's Choosing Wisely initiative advised against routine comprehensive respiratory pathogen panel (RPP) testing in children with clinically diagnosed viral illness, citing minimal impact on outcomes. However, these recommendations pre-date the COVID-19 pandemic, necessitating updated analysis.

Objective: To assess whether the type of RPP testing (limited vs comprehensive) affects 1) 7-day return visits to the pediatric emergency department (PED) and 2) subsequent patient management.

Methods: We conducted a retrospective chart review of children aged 61 days to 18 years discharged from NYP-Weill Cornell PED between June–August 2023 and December–February 2024 after RPP testing for a clinically diagnosed viral illness. Patients were grouped by RPP type: limited (COVID-19, influenza A/B, RSV) vs comprehensive (21 pathogens). Data included demographics, Emergency Severity Index (ESI), 7-day return visits, and interventions at return. Analyses included univariate tests and multivariable logistic regression.

Results: Among 2,346 patients (1,417 limited RPP; 929 comprehensive), no significant difference in 7-day return rates was found between groups, even after adjusting for covariates (OR 0.96, 95% CI 0.67–1.37). On return visits, those initially receiving limited RPP testing were more likely to undergo urine studies ($p = 0.045$); no other differences in additional testing, treatment, or disposition were observed.

Conclusion: Comprehensive RPP testing does not reduce 7-day PED return visits or significantly alter follow-up care. Limited RPP testing appears sufficient for managing clinically diagnosed viral illnesses in pediatric ED settings.

Prevalence Of Anxiety and Depression Diagnoses Over Time in Resident Run Pediatric Continuity Clinic

Presenting Author: Jeffrey Maniko, MD (Resident)

Authors: Maniko, Jeffrey A, Rajan ,Mangala

Department of Pediatrics

Background: The prevalence of mental health disorders in the pediatric population have been increasing over the past decade.

Objective: The purpose of this study was to determine the prevalence of anxiety and depression diagnoses over time among the pediatric population in an urban academic practice.

Methods: This was a retrospective cohort study. Children ages 3 to 17 who were seen in the HT5 Pediatrics Primary Care Clinic were eligible for participation. A diagnosis of depression and/or anxiety was made for a patient with two codes coding for depression or anxiety (utilizing the CAHMD Classification System for diagnosis codes) at visits within a period of 24 months.

Results: The prevalence of depression in the clinic increased from 1.7% in 2016 to 2.1% in 2024. The prevalence of anxiety increased from 5.1% in 2016 to 7.1% in 2024. These rates are consistent with national trends, and subgroup analysis demonstrated that both depression and anxiety were more common in the older age cohort (age 12-18) then in younger age cohort (ag 3-11).

Conclusions/Next steps: Overall, the findings support that mental health disorders are increasing in our clinic population consistent with national trends over time. Whether this observed increase is secondary to increased screening or is consistent with a true increase in the prevalence of the disorders is difficult to determine. Next steps include regression models to assess whether there were specific patient populations that had higher odds of having increased diagnoses of anxiety and/or depression

Disparities In RSV Protection with Nirsevimab And Maternal RSV Vaccine In 2023-2024 & 2024-2025 RSV Seasons

Presenting Author: Jessica DeAngelis, MD (Resident)

Authors: Acker Karen P, Strobino Kevin, DeAngelis Jessica M, Staniczenko Anna P, Son Moeun, Riley Laura E, Han Jin-Young, Abramson Erika L, Levine Deborah A

Department of Pediatrics

Introduction/Background: Respiratory syncytial virus (RSV) is the leading cause of infant hospitalization. In 2023, two preventive options became available: maternal RSV vaccine and Nirsevimab, an RSV monoclonal antibody. Both faced supply shortages during the 2023-2024 season. Demographic factors influencing uptake remain unclear.

Objectives: To describe maternal RSV vaccine and Nirsevimab uptake during the 2023-2024 and 2024-2025 RSV seasons and identify sociodemographic factors associated with infant RSV protection.

Methods: This retrospective single center cohort study included infants < 8 months old with documented vaccine history who were seen at an urban quaternary medical center in New York City from October 1 to March 31 during both seasons. The primary outcomes were receipt of maternal RSV vaccine, Nirsevimab, or no RSV protection. Infant characteristics were collected. Multinomial logistic regression identified factors associated with RSV protection.

Results: Among 13,195 infants, 3832 (29%) received appropriate maternal RSV vaccination and 4998 (38%) received Nirsevimab. Most were newborns, non-Hispanic white, term, without chronic conditions and born at the study site (Table 1). Between seasons, maternal RSV vaccination rose from 21% to 36%, and Nirsevimab from 37% to 39%. Nirsevimab delivery shifted from nursery (56%) to outpatient settings (57%). Publicly insured infants had lower odds of maternal RSV protection (OR 0.18, 95% CI, 0.15-0.22) and Nirsevimab (OR 0.80, 95% CI 0.70-0.89).

Conclusions: RSV protection improved in 2024-2025 RSV season. Nirsevimab delivery shifted from nursery to outpatient settings. The largest disparities for RSV protection were in publicly insured infants, with more pronounced disparities in maternal RSV vaccination than Nirsevimab.

Oxygen Saturation and the Risk of Necrotizing Enterocolitis in Infants with Single Ventricle Physiology Following Stage I Palliation

Presenting Author: Jillian Wen, MD (Fellow)

Authors: Wen, Jillian, Goldshtrom, Nimrod, Liberman, Leo, Vargas, Diana

Department of Pediatrics

Background: Necrotizing enterocolitis (NEC) is a serious complication in neonates that can lead to intestinal perforation, sepsis, and death. Neonates with single ventricle disease (SVD) are at increased risk of NEC due to altered cardiac physiology. Following stage I palliation, these patients require careful management to balance their systemic and pulmonary blood flow. Pulse oximeter measurements are one of the tools used to assess the balance of these two circulations.

Objective: We aim to examine the relationship between SpO₂ and the development of NEC in infants with SVD following stage I palliation. We hypothesize that higher a post-operative SpO₂ suggests a higher ratio of pulmonary to systemic blood flow, and thus an increased risk for NEC.

Design/Methods: This is a single-center retrospective study including infants with SVD admitted to the neonatal cardiac intensive care unit at Columbia University Medical Center who required cardiac surgery between 1/1/2010 and 12/31/2023. We evaluated the average SpO₂ on day of life two, pre-operatively, 48-hours post-operatively, 24-hours prior to NEC (cases), and 72-hours prior to discharge (controls). Univariate analysis and logistic regression were used.

Results: Ten post-operative NEC cases and 17 matched controls were identified. There was no significant difference in SpO₂ trends in cases versus controls, although NEC cases had a lower 25th quartile of SpO₂ on the day prior to NEC than controls at time of discharge (78.7% vs 83.76%, $p = 0.04$). NEC cases had a lower SpO₂ on day of life two compared to controls (median 86.5% vs 93.2%, $p = 0.01$).

Conclusions: Our study found that a higher post-operative SpO₂ was not associated with an increased risk of NEC. NEC cases had significantly lower SpO₂ on day of life 2, indicating a possible preoperative predisposition to development of NEC. Our study was limited by a small cohort size, future studies involving multiple centers may be helpful to further delineate the relationship between SpO₂ and NEC following stage I repair in infants with single ventricle disease.

Sleep And Breathing: Postsurgical Outcomes In Children With Achondroplasia

Presenting Author: Joanna Lee, MD (Resident)

Authors: Graw-Panzer Katharina, Lee Joanna G

Department of Pediatrics

Introduction: Achondroplasia is the most common bone dysplasia in humans, occurring in 1/20,000 live births. Most patients with achondroplasia have concomitant sleep apnea and foramen magnum stenosis. This study examines the characteristics of sleep-disordered breathing in children with achondroplasia and determines how adenotonsillectomy and foramen magnum decompression surgery affect clinical outcomes.

Methods: A retrospective chart review of patients seen at New-York-Presbyterian Hospital/Weill Cornell Medical Center between January 2013 and October 2024 who had polysomnography performed. Demographic information, BMI, comorbidities, polysomnography data, and surgical outcomes were collected. The severity of obstructive sleep apnea (OSA) was defined based on obstructive apnea-hypopnea index (OAHI): 1-4.9 mild, 5-9.9 moderate, 10 and above severe. Results are presented as Median (Q1, Q3). Analysis of variables between pre- and post-operative polysomnography was performed using the Wilcoxon test.

Results: 22 individual patients underwent polysomnography. 55% were female. 19% White/Caucasian, 19% Latino/Hispanic, 14% Black/African American, 14% Asian American. 91% had foramen magnum stenosis, and 55% had symptoms of sleep disordered breathing. Median number of polysomnography performed per patient was 2 (1, 5). 33% had undergone decompression surgery prior to the sleep study. Age at first study was 14 months (4.8, 41.3). The study showed no OSA in 18%, mild OSA in 27%, moderate OSA in 14% and severe OSA in 41% of patients. OAHI was 5.4 (1.6, 15.2) and central apnea index 0.7 (0.4, 1.5). 8 patients had polysomnography done pre- and post-adenotonsillectomy. All had foramen magnum stenosis and 4 had prior decompression surgery. Adenoidectomy and/or tonsillectomy was done at the discretion of the surgeon. All 8 patients had severe OSA before surgery and 6 had severe and 2 moderate OSA after surgery (OAHI pre 47.0 (20.1, 77.4), post 14.2 (7.55, 77.35), p-value 0.8). Decompression status resulted in no significant differences. Postoperatively all patients received positive airway pressure (PAP) for sleep, 1 tracheostomy and 4 revision surgery.

Conclusion: Children with achondroplasia present with a very high rate of obstructive sleep apnea. Despite adenotonsillectomy and decompression surgery there is residual moderate-severe OSA requiring PAP as well as further surgeries. We are hopeful that new therapies for achondroplasia will change that outcome.

Electrocardiogram Normal Values in Hispanic Children: A Re-examination of the Pediatric Heart Network ECG Normal Data

Presenting author: Joshua M. Fisher, MD (Fellow)

Authors: Fisher, Joshua M. Liberman, Leonardo. Anderson, Brett R.

Background: Pediatric electrocardiogram (ECG) is an important tool to screen for congenital heart disease or causes of sudden cardiac death. While it is known that ECG values are affected by age, sex and race, there are limited data on the effects of ethnicity. Common standards in pediatric patients were derived from homogenous patient populations and might not be applicable in diverse populations. The Pediatric Heart Network (PHN) 2018 Echo Z-Score and Normal Electrocardiogram studies described normal measurements but did not examine the effects of ethnicity.

Methods: Using the PHN Normal ECG datasets, ECG parameters were analyzed for children ≤ 18 years old with normal echocardiograms at 19 PHN centers, stratified by age and sex.

Results: Of 2400 patient ECGs, 2287 had documented ethnicity. Of these, 596 (26%) were Hispanic/Latino/a, 841 (37%) were non-Hispanic White (NH-White), and 691 (30%) were NH-Black. Most Hispanic patients (36%) were recruited from two institutions with predominantly Dominican and Mexican patient populations. The R wave amplitude in V6 was smaller for Hispanic adolescent females (>12 years-old) compared to both NH-White and NH-Black adolescent females. The R wave in V6 was smaller for Hispanic adolescent males compared to both NH-White and NH-Black adolescent males, although the former did not reach statistical significance. The QTC interval in lead II was shorter for Hispanic adolescent females compared to NH-White adolescent females, but there was no difference compared to NH-Black adolescent females. There was no significant difference in QTC interval length between adolescent males by ethnicity.

Conclusion: In a large multicenter dataset of pediatric patients with normal echocardiograms, ECG parameters used to screen for left ventricular hypertrophy and long QT syndrome differed by ethnicity for adolescents. Using ethnicity specific norms might influence follow-up testing for Hispanic-Latino/a patients undergoing screening ECGs.

Urinary metabolites associated with growth failure in the preterm infant

Presenting Author: Kathleen Fan, MD (Resident)

Authors: Fan Kathleen, Nair Jayasree, Mandalaywala Divya, Andrews Chloe, Sen Sarbattama, Martin Camilia

Department of Pediatrics

Background and Objectives: Postnatal growth failure (GF) in preterm infants is linked to higher morbidities and poor neurodevelopmental outcomes. The study aims to identify urinary biomarkers in infants with GF.

Methods: 54 infants < 32 weeks' gestation were selected from a data biorepository at the NICU, Beth Israel Deaconess Medical Center in Boston, MA from October 2009 to October 2012 (IRB approved at BIDMC). Infants were included if urine samples were available for at least two of the study timepoints.

Maternal and infant data were collected from electronic medical records. Growth was assessed from birth to discharge defined as change in z-scores (weight) over time. Infants were divided into growth tertiles and designated as adequate growth (AG), moderate growth failure (MGF), or high growth failure (HGF). Urine samples were collected at postnatal ages of 2, 3, and 6 weeks. Samples were analyzed by Metabolon (Durham, NC). Differential metabolites as a function of growth status were determined using ANOVA followed by post-hoc analysis. Statistical significance was defined as $p < 0.05$ and corrected for multiple comparisons.

Results: At 2 weeks, compared to infants with AG, infants with HGF showed decreased urinary secondary bile-salt lipid metabolites, namely 12-dehydrocholate, 3-dehydrocholate, 7-ketodeoxycholate ($p = 0.008$, 0.03 , 0.03 , respectively). In contrast at 6 weeks, primary bile-salt lipid metabolites were increased in HGF versus AG, suggesting delayed lipid metabolism in the early postnatal period may correlate with early high growth failure. Importantly, these differences were independent of maternal and infant clinical data and nutritional intake as these variables were not different between groups ($p \geq 0.05$).

Conclusions: Urinary metabolomic profiles distinguish postnatal growth patterns in preterm infants. Lack of differences in maternal, clinical, and nutritional profiles support that endogenous drivers of metabolism determine nutrient utilization and overall growth. Gut microbiota, which convert primary to secondary bile acids, may influence these metabolic patterns and thus postnatal growth.

Pediatric Inflammatory Bowel Disease Epidemiology Pre and Post COVID-19 Pandemic

Presenting Author: Michelle Ramos, MD (Fellow)

Authors: Ramos, Michelle A; Lentine, Jennifer; Gerber, Linda; Thomas, Charlene; Abramson, Erika; Grinspan, Zachary; Rose, Melissa

Department of Pediatrics

Background: This study aims to examine pediatric inflammatory bowel disease (IBD) prevalence before, during, and after the COVID-19 pandemic. While pediatric IBD diagnoses has been rising globally, the pandemic introduced new variables—namely, COVID-19's gastrointestinal manifestations and potential links to autoimmune conditions such as type 1 diabetes. Given observed increases in very early onset IBD (VEO-IBD) at our institution, we investigated trends stratified by age groups with a particular focus on VEO-IBD.

Methods: We conducted a retrospective review using data from the INSIGHT Clinical Research Network, which aggregates electronic health records from six New York City health systems (15.1 million patients). Children aged 0–17 diagnosed with IBD between 2017 and 2023 were identified using ICD-10 codes and medication records. A validation cohort from our institution ensured accurate case identification.

Results & Conclusion: Preliminary analysis revealed that IBD prevalence increased across the study periods: 0.141% pre-COVID, 0.151% during, and 0.158% post-pandemic. Out of all children with IBD the rate of VEO-IBD also rose from 3.2% to 3.9%. The odds of an IBD diagnosis were significantly higher during (OR 1.23, 95% CI: 1.19–1.26) and after the pandemic (OR 1.46, 95% CI: 1.40–1.52) compared to the pre-COVID period. Similar trends were observed for both VEO-IBD and pediatric IBD (ages 6–17). Trends on healthcare utilization and medical management were also analyzed as secondary aims and have revealed a decrease in ED visits and inpatient hospital admissions during the COVID19 pandemic and an increase in telehealth visits. Interestingly an increase in Solumedrol was seen during the COVID19 years.

Subsequent Neoplasms in Survivors of Neuroblastoma

Presenting Author: Priya H Marathe, MD (Fellow)

Authors: DeRosa Amelia, Antal Zoltan, Wolden Suzanne, LaQuaglia Michael P, Basu Ellen M, Iglesias Cardenas Fiorella, Kramer Kim, Kushner Brian H, Cheung Nai-Kong V, Modak Shakeel, Friedman Danielle N

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Background: Data on subsequent neoplasms (SN) and subsequent malignant neoplasms (SMN) in neuroblastoma (NB) survivors treated with multimodal therapy are limited. We sought to characterize SN and SMN in a cohort of NB survivors.

Methods: Retrospective review of NB survivors diagnosed 1980—2018 with ≥ 5 years of follow-up at a tertiary cancer center. SN included subsequent benign tumors and basal cell carcinomas; SMN included new primary malignancies occurring ≥ 5 years from NB diagnosis.

Results: Of 372 NB survivors, 36 (9.7%) were diagnosed with ≥ 1 SN or SMN. Median age of first SN/SMN diagnosis was 14.9 years, a median of 9.6 years from primary NB diagnosis. Median follow-up from diagnosis was 18.6 years. Most (89%) had stage 4 neuroblastoma and received multiagent chemotherapy and RT; 50% also had autologous stem cell transplantation (Table 1). 89% received anti-GD2 directed antibody therapy and 11% received metaiodobenzylguanidine (MIBG) therapy.

These 36 patients had 50 SN and SMN diagnoses: 25 (50%) benign and 25 (50%) malignant. 18 SN and 5 SMN were in the radiation field or following MIBG. The most common SN diagnoses were non-melanomatous skin cancer and meningioma. The most common SMN diagnoses were hematologic malignancies, papillary thyroid carcinoma, and osteosarcoma (OS). Two thyroid cancers and two OS diagnoses occurred outside of RT fields in patients who also did not receive MIBG.

At time of last follow-up, 8/36 patients with SN/SMN were deceased, two from relapsed/recurrent NB and six from complications related to their SN/SMN. Median time from NB diagnosis to death was 17.9 years (range 9.8-38.8 years).

Conclusion: NB survivors treated with multimodal therapy are at risk for a variety of SN/SMN. Longer follow-up by risk/treatment exposures will allow for more detailed analysis of SN/SMN development.

Exploring Patterns and Trends of Pediatric Status Epilepticus: Insights from the National Inpatient Sample

Presenting Author: Ryan Jarrah, BS (Medical Student)

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Background: Status epilepticus (SE) is a neurological emergency defined as a seizure lasting over five minutes. Current SE management lacks large-scale, multifactorial outcome analysis in pediatric populations. The National Inpatient Sample (NIS), a national database, provides key insights into SE presentations based on clinical and demographic factors. This study leverages NIS data to establish benchmarks on recent trends and guide future research on improving pediatric SE surveillance.

Objective: This study aims to analyze pediatric SE trends using a national database. By identifying these patterns, we hope to lay the groundwork for data-driven SE prediction models and future research development.

Methods: The Healthcare Cost Utilization Project - Nationwide Inpatient Sample (HCUP-NIS) was queried for pediatric SE hospitalizations from 2016 to 2019. Trends in admissions, age groups, and pediatric mortality were examined.

Results: Among 13,140 pediatric SE admissions, 45.9% were female. There were 273 deaths, with 60% of those deceased from lower-income households and government insurance. Nearly 48% of admissions occurred in children under six, and 55% of deaths were in patients under three. Nonroutine discharges totaled 1,707, while 30% had extended hospital stays beyond five days.

Conclusion: These findings emphasize the need for early SE management and ongoing pediatric SE surveillance to improve outcomes. Additionally, this study supports the development of AI-driven models to aid in SE diagnosis, management, and outcome prediction in pediatric patients.

Congenital CMV: Does “Asymptomatic” Always Mean “Asymptomatic”?

Presenting Author: Stephanie Trimboli, MD (Resident)

Authors: Trimboli, Stephanie, Acker, Karen, Dubois, Melanie, Han, Jin-Young, Salvatore, Christine M

Department of Pediatrics

Introduction: This is a retrospective chart review of infants diagnosed with congenital cytomegalovirus (cCMV). It includes infants who were diagnosed through a universal screening program and infants who were diagnosed through a traditional targeted screening program.

Objective: The objective of this study is to evaluate if infants who appear asymptomatic at birth are truly asymptomatic after a comprehensive workup.

Background: cCMV is the most common congenital infection, affecting an estimated 0.5 to 1% of all live births. Clinical manifestations vary; while an estimated 90% of patients appear asymptomatic at birth, 20% go on to develop permanent long-term sequelae including sensorineural hearing loss and cognitive impairment. Given this morbidity some experts advocate for universal screening programs.

Methods: Medical records of all pediatric patients (≤ 21 years of age) diagnosed with cCMV and referred to NewYork- Presbyterian Weill Cornell starting from January 1, 2014 were retrospectively reviewed.

Results: 84 total patient charts were reviewed. 27 patients were diagnosed through targeted screening and 57 through universal screening. 43/57 (75%) diagnosed through universal screening completed a comprehensive workup. 22 patients in each group had symptomatic cCMV. Importantly, 37/43 (86%) of patients diagnosed through universal screening would not have been diagnosed based on targeted screening, and 16/37 (43%) were found to have symptomatic cCMV.

Conclusions: Not all symptoms of cCMV are clinically evident at birth, and many infants who have symptomatic cCMV after a comprehensive workup would not have been diagnosed without universal screening.

Early Nutritional Intake and Postnatal Brain Growth in Very Preterm Infants

Presenting Author: Yurhee Lee, MD (Fellow)

Authors: Lee Y., Quintana L., Cohen S., Mandalaywala D., Martin C.

Department of Pediatrics

Background: Very preterm infants are vulnerable to deficits in postnatal brain growth, which impact neurodevelopmental outcomes. The optimal early nutritional interventions to improve brain development have not been identified.

Objective: To identify early nutritional practices in the first two postnatal weeks associated with brain growth on head ultrasound (HUS) at one month of age in very preterm infants.

Methods: We conducted a retrospective cohort study of infants born ≤ 32 weeks gestational age (GA). Daily caloric, protein, and lipid intake from day of life (DOL) 0 to 14 were collected. Brain structures were measured on HUS at one week and one month of age. The relationship between nutritional intake and growth velocity of brain structures was analyzed using linear regression.

Results: We included 57 patients, with mean GA 29.2 weeks (SD 2.1) and birthweight 1223g (SD 325). There was a positive correlation between enteral caloric intake and growth of biparietal diameter (BPD) ($r = 0.155$) and corpus callosum (CC) length ($r = 0.200$), with a contrasting negative correlation between parenteral caloric intake and BPD ($r = -0.116$) and CC length ($r = -0.271$, $p < 0.05$). Growth of BPD, CC length, and vermis height was positively correlated to enteral protein intake ($r = 0.193$, $r = 0.155$, $r = 0.066$, respectively) and negatively correlated to parenteral protein intake ($r = -0.127$, $r = -0.178$, $r = -0.181$). Growth of BPD, CC length, and vermis height was positively related to enteral lipid intake ($r = 0.107$, $r = 0.253$, $r = 0.098$) and negatively related to parenteral lipid intake ($r = -0.081$, $r = -0.210$, $r = -0.144$). Greater enteral nutrition was associated with increased HC, length, and weight gain. Results were not significantly altered when adjusted for GA, sex, and SGA status.

Conclusions: In very preterm infants, greater early enteral caloric, protein, and lipid intake is related to brain growth. Conversely, higher macronutrient intake from parenteral nutrition may have an opposing impact, suggesting the preferential importance of early enteral nutrition on brain development.

Impact of Genetic Syndromes On Outcomes in Neonates with Symptomatic Tetralogy of Fallot

Presenting Author: Joanna Nelson, MD (Fellow)

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BACKGROUND: Neonates with symptomatic tetralogy of Fallot (sTOF) frequently have genetic abnormalities that may influence outcomes.

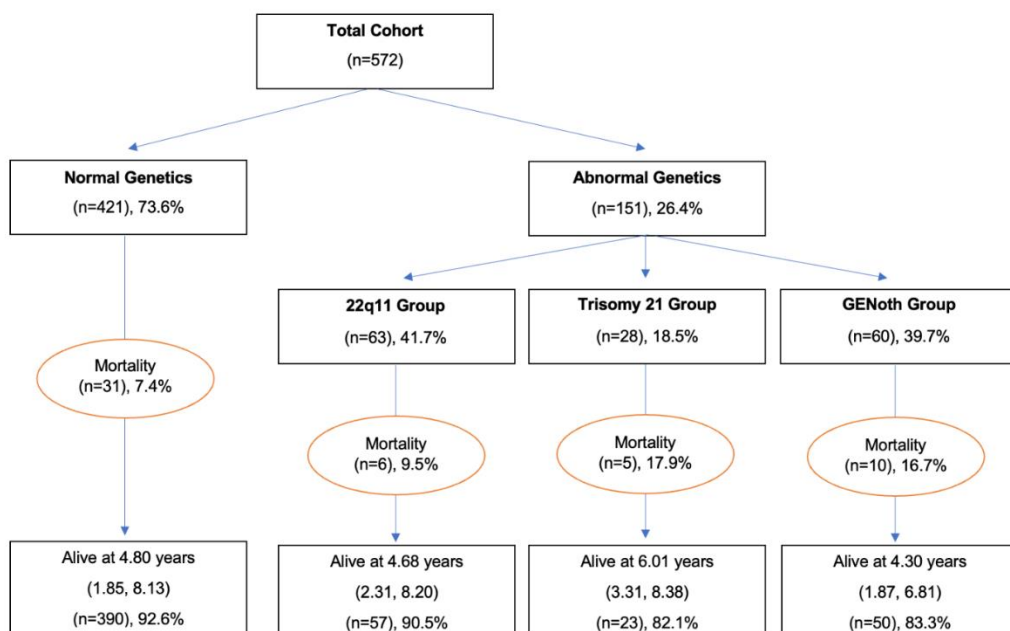
METHODS: We conducted a secondary analysis of a prior multicenter retrospective cohort study of sTOF patients from 2005–2017 at the 9 centers of the Congenital Cardiac Research Collaborative. All patients had an index procedure within 30 days of life. Patients were categorized as having normal genetics, 22q11 deletion syndrome, trisomy 21 or other genetic diagnoses. Patients without a specific genetic diagnosis or available testing were considered to have normal genetics. The primary outcome was transplant-free survival at latest follow-up.

RESULTS: Among 572 neonates with sTOF, 151 (26.4%) had an identifiable genetic syndrome, including 22q11 deletion (n=63, 41.7%), trisomy 21 (n=28, 18.5%) and other genetic diagnoses (n=60, 39.7%)(Figure 1). Patients with 22q11 deletion more frequently

underwent a staged repair strategy. Unadjusted analysis at a median follow-up of 4.9 years demonstrated a survival advantage in patients without identified genetic abnormalities ($P=0.025$)(Figure 2). After adjustment, this advantage was not significant ($P=0.070$). Patients with abnormal genetics had longer admission times and were more likely to be discharged with feeding tubes.

CONCLUSIONS: We found that neonates with sTOF with abnormal genetics had survival that may be inferior to those with normal genetics, as well as higher risks for other hospital morbidities including longer admissions and the need for feeding tubes. Genetic testing in this population can inform clinicians and families regarding these important considerations within this congenital heart disease population prompting the need for early interdisciplinary involvement.

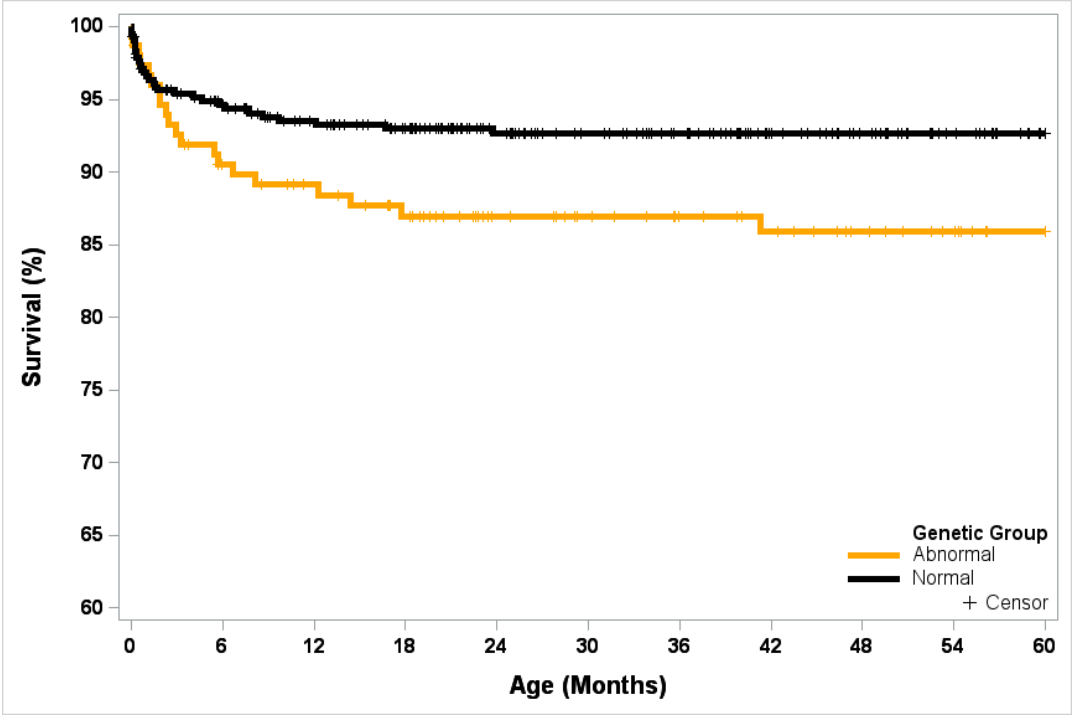
Figure 1. Cohort Flow Diagram and Follow-up Duration



Variable	Normal genetics	Abnormal genetics	Abnormal genetic subgroups			P value
			22q11 deletion	Trisomy 21	Other Genetic Diagnoses	
	N=421	N=151	N=63	N=28	N=60	
Follow-up duration	4.37 (1.61, 7.82)	4.12 (1.53, 7.47)	4.12 (1.58, 7.90)	5.33 (1.70, 7.64)	3.28 (1.41, 6.62)	0.641

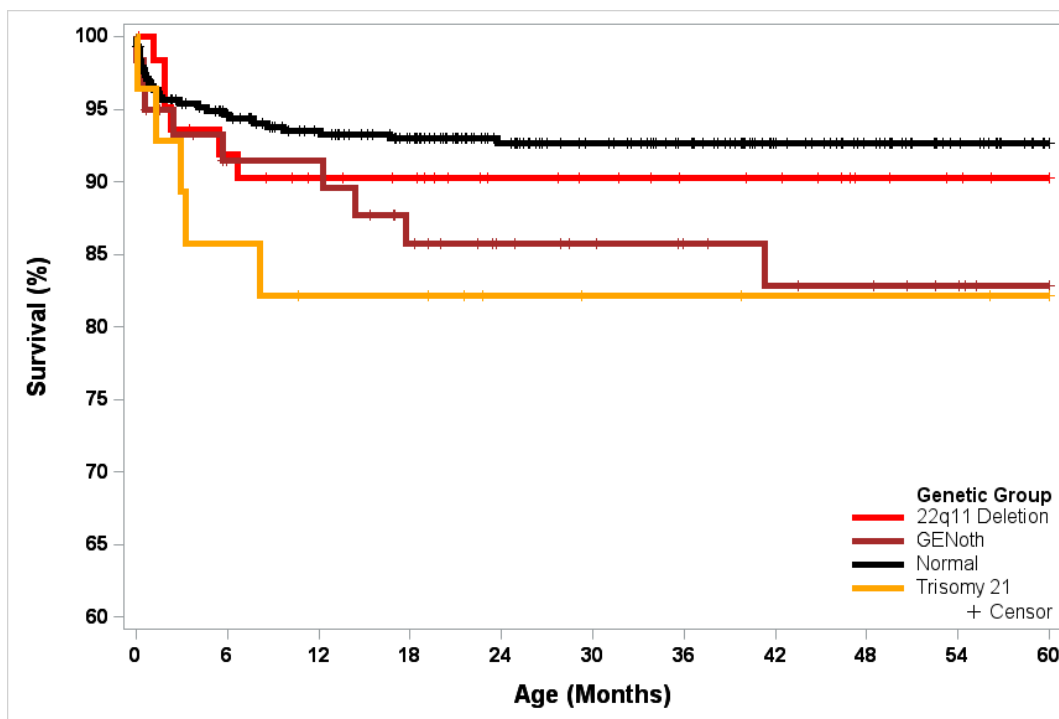
Figure 1. Cohort flow diagram and follow-up duration.

In the flow chart, the percentage of each genetic subgroup is included as the percentage of subjects from the entire cohort. Mortality and alive percentages refer to the percentage of subjects who suffered mortality or survived within each genetic subgroup, respectively. In the table, median follow-up duration is expressed in years (95% CI) as evaluated by a Kruskal-Wallis test. CI indicates confidence interval; and GENoth, other genetic diagnoses.



a. Number at Risk by Genetic Group in Survival Analysis

Age (Months)	0	6	12	18	24	30	36	42	48	54	60
Normal	421	366	343	324	287	270	255	235	222	207	192
Abnormal	151	129	123	115	99	93	87	83	77	72	66



(b) Number at Risk by Genetic Subgroup in Survival Analysis

Age (Months)	0	6	12	18	24	30	36	42	48	54	60
Normal	421	366	343	324	287	270	255	235	222	207	192
22q11 Deletion	63	56	52	50	43	41	38	37	32	30	28
Trisomy 21	28	24	22	22	19	18	18	17	17	17	16
GENoth	60	49	49	43	37	34	31	29	28	25	22

Genetic group	Unadjusted		Adjusted	
	HR	P value	HR	P value
Total abnormal	1.88 (1.08, 3.27)	0.025	1.71 (0.96, 3.07)	0.070
22q11 deletion	1.26 (0.52, 3.01)	0.610	1.17 (0.48, 2.85)	0.737
Trisomy 21	2.41 (0.94, 6.20)	0.068	2.41 (0.91, 6.38)	0.076
GENoth	2.32 (1.14, 4.73)	0.021	2.00 (0.94, 4.28)	0.073

Figure 2. Survival analysis among normal and abnormal genetic groups.

Kaplan-Meier survival curve (a) demonstrates freedom from death (primary outcome) on the basis of normal vs. abnormal genetics. A second Kaplan-Meier survival curve (b) demonstrates freedom from death on the basis of normal vs. abnormal genetic subgroups. Cox proportional hazards models were employed. Results were adjusted for variables including center, presence of antegrade pulmonary blood flow, repair strategy (staged vs. primary repair), prematurity and invasive ventilation before intervention. GENoth indicates other genetics diagnoses; and HR indicates hazard ratio.

TR-01

Comparison of Antibody Responses Elicited by Germline-Targeting HIV Env SOSIP Trimer Immunization In SHIV-Infected and Uninfected Infant Rhesus Macaques.

Presenting Author: Aiquan Chang, 2nd-year PhD student at Weill Cornell (Graduate Student)

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Background: Currently, 1.4 million children are living with HIV and require daily antiretroviral therapy (ART). To avoid long-term ART-related complications, strategies to achieve drug-free viral control are needed. Broadly neutralizing antibodies (bNAbs) can potentially control HIV, yet spontaneous generation of bNAbs is extremely rare. Our group showed that a germline-targeting (GT) HIV envelope SOSIP trimer can elicit bNAb precursor responses in uninfected infant rhesus macaques (RMs). We hypothesize that prior HIV infection will drive B cell maturation and enhance HIV-specific immunity.

Objective: To evaluate the immunogenicity of a GT HIV envelope SOSIP trimer in uninfected vs. simian HIV (SHIV)-infected infant RMs.

Method: 10 infant RMs were recruited for the study, of which 5 remained uninfected and 5 were orally infected with SHIV SF162P3 and treated with ART one-week post-infection. Both uninfected and infected RMs were immunized at regular intervals with BG505 GT1.1 SOSIP trimer and adjuvant 3M052-SE. Total plasma or purified IgG was used to assess HIV-specific neutralizing and non-neutralizing antibodies and development of bNAb precursor responses.

Results: Compared to uninfected RMs, infected RMs elicited a lower GT1.1-specific antibody response after 2nd (median: 10.27-fold) and 3rd (median: 4.8-fold) immunizations. While 3/5 uninfected RMs developed VRC01-like bNAb precursor response, only 1/5 infected RM developed this response. Finally, both uninfected and infected animals showed comparable non-neutralizing antibody responses.

Conclusions: GT native-like HIV SOSIP immunization elicited higher antibody responses in uninfected RMs compared to SHIV-infected RMs. The mechanisms contributing to this improved response in uninfected macaques are currently underway.

Development of a Lactotherapeutic for The Prevention of Rotavirus Diarrheal Disease in Infancy

Presenting Author: Caitlin Williams, PhD (Postdoc)

Authors: Caitlin A. Williams, Brittany Plummer, Christian Binuya, John Ramos, Stephanie Langel, Maria Blasi, Sallie R. Permar

Department of Pediatrics

Introduction: Naturally occurring breastmilk antibodies are associated with the prevention of severe disease in infancy such as Rotavirus (RV) which is a leading cause of mortality in children under the age of 5. Given the ubiquitous nature of viral diarrheal disease, it is crucial to develop lactotherapeutics to address this gap in research and existing health disparity.

Objectives: Our overarching goal is to develop an mRNA-LNP based approach to deliver potentially neutralizing anti-RV Antibody during lactation to facilitate protection from Rotavirus diarrheal disease.

Methods: We conducted a dose escalation study to determine optimal dosing and timing of viral challenge by infusing dams with 3,5, or 10mg/kg either of mRNA-LNP encoding mAb41, and anti-RV dIgA. For viral challenge studies. dams were given 5mg/kg of mAb41 dIgA mRNA-LNP or control mRNA-LNP by followed by viral challenge of suckling pups 48 hours post infusion. We collected daily maternal and pup samples to assess mAb41 levels.

Results: IV infusion with 5mg/kg yielded mAb41 levels above the therapeutic threshold. In challenge studies, pups suckling from dams given mAb41 anti-RV dIgA therapy developed diarrhea at similar rates as control pups. We detected mAb41 dIgA in the stomach and intestines of the treatment group pre- and post-viral challenge. These findings indicate that while 5mg/kg intravenous infusion yielded mAb41 levels above the monomeric and dimeric mAb41 IC50, this was not indeed protective in vivo viral challenge. Further optimization of mAb41 dIgA dosing and viral challenge timing is warranted.

Cytomegalovirus Viral Fc Gamma Receptors as Vaccine Antigens to Enhance Anti-Viral Fc-Mediated Effector Antibody Functions

Presenting Author: Claire Otero, PhD (Postdoc)

Authors: Otero Claire E, Mitchell Libby, Oschwald Ricarda, Gross Mackensie R, Herbek Savannah L, Connors Megan R, Kolb Philipp, Permar Sallie

Department of Pediatrics

Background: Cytomegalovirus (CMV) is the most common congenital infection and infectious cause of neurologic birth defects, yet a licensed CMV vaccine remains elusive. Fc-mediated antibody effector functions, such as antibody dependent cellular phagocytosis (ADCP) and cytotoxicity (ADCC), are associated with protection from placental CMV transmission. Intriguingly, human CMV encodes three viral Fc gamma receptors (vFcγRs) to evade Fc-mediated immune responses, which could be leveraged as vaccine antigens.

Objective: We investigated the effect of adding CMV vFcγRs to a glycoprotein B (gB) subunit vaccine on elicited Fc-mediated effector functions.

Methods: We immunized rabbits (n=4 per group) at Weeks 0, 4, and 8 with 20μg gB alone or with 20μg or 40μg of one vFcγR (gp34, gp68, or gp95), all as protein subunits lacking transmembrane domain and adjuvanted with squalene emulsion. Plasma from immunized rabbits was analyzed for antigen-specific IgG binding and Fc-effector functions.

Results: Each vFcγR demonstrated immunogenicity in terms of plasma IgG binding, with higher titers observed in 40μg dose groups. Preliminary results comparing groups at Week 10 demonstrate broad improvement in FcR activation in vitro by IgG targeting infected cells from groups immunized with gB with individual vFcγRs compared to gB alone. Interestingly, while ADCC responses were undetectable in animals immunized with gB alone, those receiving gB with 40μg gp34 or gp95 demonstrated detectable ADCC. However, measured ADCP responses were comparable among all vaccine groups.

Conclusions: A CMV vaccine including vFcγRs can improve potentially-protective vaccine-elicited Fc-effector responses, a promising step toward reducing the global burden of congenital CMV.

Decipher Complex Cellular Changes and Interactions from Spatial Transcriptome Data Using Slidescope

Presenting Author: Jinghua Gu, PhD (Faculty)

Authors: Gu J, Balaji U, Rodríguez-Alcázar J, Smitherman C, Baisch J, Pascual V

Drukier Institute

Background: Advances in spatial transcriptomics (ST) has provided powerful means for in-depth investigation of tissue heterogeneity and cellular crosstalk. The massive growth of ST data calls for efficient and scalable analysis tools.

Objectives: To develop new computational tools for comprehensive analysis of ST data and illustrate its efficacy in biomedical applications.

Methods: Developed software Slidescope for automated cell type deconvolution, graph-based spatial modeling and correlation analysis, and spatial differential gene expression analysis.

Results: Three ST datasets were analyzed to demonstrate the utility of Slidescope.

Mouse brain: Slidescope deconvoluted hippocampus ST data from mice w/wo spatial object recognition (SOR) into CA1, CA2, CA3 and DG subregions, which was consistent with anatomical structures from H&E staining images. Spatial differential analysis identified 192 over-expressed genes in SOR mice compared control mice in hippocampus.

Psoriatic skin: Data from human lesional, non-lesional psoriatic and healthy skins were deconvoluted. Spatial correlation analysis revealed that while T cells from healthy skins were spread across pilosebaceous areas, suggesting a perifollicular immune niche, they were mostly enriched in dermal peri-basement membrane regions in lesional skin. Further ligand-receptor analysis showed lesional psoriatic skin were characterized by proinflammatory processes driven by S100A8/9/12-CD36 interactions in keratinocytes and CX3CL1-mediated immunity in T cell regions.

Pediatric lupus nephritis kidney: A graph-based pseudo-distance metric automatically grouped and annotated Visium HD ST data into glomerular regions and visualized spatial transcriptome changes across nephritis classes.

Conclusion: Slidescope is an effective, robust, and scalable computational tool to investigate complex cellular changes and interactions from spatial transcriptome data.

Spatial Molecular Profiling of the Kidney of Children with Lupus Nephritis

Presenting Author: Juan Rodriguez-Alcazar, PhD (Postdoc)

Authors: Rodriguez-Alcazar Juan, Balaji Uthra, Troncoso Leanna, Reid Amanda, Hamon Pauline, Houghton Sean, Walters Lynnette, Smitherman Cynthia, Baisch Jeanine, Santos Marina, Larosiliere Owen, Robinson Lauren, Wright Tracey, Caielli Simone, Merad Miriam, Gu Jingh

Drukier Institute

Background: Childhood-onset lupus nephritis (cLN) affects most systemic lupus erythematosus pediatric patients with diverse prognosis. The current renal histological classification does not provide effective guide for treatment choices. Understanding the molecular landscape of cLN kidneys could provide a more informative patient classification and guidance for precise therapies.

Objectives: To find cellular and molecular features that segregate cLN patients into renal molecular endotypes. Molecular classification will increase LN clinical trials' success with targeted therapies, paving the way for precision medicine in autoimmune disorders.

Methods: We employ high-dimensional spatial transcriptomics and proteomics techniques to profile kidney biopsies of cLN patients. We use bioinformatic analysis tools to define the spatial and molecular features of the immune compartment of cLN kidney biopsies.

Results: Myeloid cells with phagocytic and inflammatory transcriptional programs infiltrate glomeruli of proliferative cLN. A subset of proliferative glomeruli presents myeloid cells expressing IL-1 β . Lipid-associated macrophages are present in the glomeruli of a subset of proliferative and membranous patients. Periglomerular lymphoid hubs expand in a subgroup of membranous and mixed cLN. Lymphoid immune hubs contain T and B cells with antigen presentation signatures or plasma cells with different isotype specificity.

Conclusions: Distinct spatial organization of the renal immune compartment defines cLN patients. Targeting specific subpopulations of myeloid and lymphoid cells, which differentially localize within distinct kidney regions, offers a strategy for developing precise therapies. The prognostic significance of these findings and their potential for therapeutic targeting are currently under investigation

Antibody Profiling of Cytomegalovirus Proteins

Presenting Author: Judy Jiang (Volunteer)

Authors: Jiang Judy, Otero Claire E, Permar Sallie R

Department of Pediatrics

Cytomegalovirus (CMV) is the leading intrauterine viral infection, causing complications such as sensorineural hearing loss and neurodevelopmental disabilities in affected infants. Diagnosing CMV infection remains a challenge as a majority of immunocompetent adults are asymptomatic with infection. The risk of vertical transmission increases with advancing gestation, while disease severity in congenital CMV infections is greater if infection occurs in earlier trimesters. Thus, it is critical to identify the time of maternal infection; however, current serological testing can only distinguish acute from chronic CMV infections. To refine the time of infection in maternal CMV infections, we aim to characterize the antibody profile of proteins expressed across the viral replication cycle using longitudinal samples from the rhesus macaque model in which we experimentally infected pregnant animals. We expect the kinetics of IgM and IgG to fluctuate, allowing differentiation of acute infection stages. We are currently producing envelope, tegument, and assembly proteins that play key roles in viral replication, regulation, and virion assembly. We will then assess antibody kinetics using a multiplex assay. We have characterized the kinetics of antibody responses against highly immunodominant glycoproteins, glycoprotein B (gB) and the pentameric complex (PC). Both appear about 2 weeks post-infection, with IgG responses to gB peaking about 4 weeks before PC. However, there were high IgG levels against both glycoproteins maintained 12 weeks post-infection. Measuring the antibody levels against CMV proteins can allude to better diagnostic testing and identification of transmission and severity risk in congenital CMV infections.

The Development of Anti-Drug Antibodies Against a Passively Administered Triple-BnAb Combination for HIV Treatment

Presenting Author: Kenneth Vuong, B.S. (Research Tech)

Authors: Vuong Kenneth, Binuya Christian, Pahountis Ioanna, Kosman Christina, Bahadir Zeynep, Dankwa Sedem, Dennis Maria, McCarthy Janice, Ngo Julia T., Enemuoh Chiamaka A., Carnathan Diane G., Berendam Stella J., Silvestri Guido, Amara Rama, Permar Sallie, Chahrou

Department of Pediatrics

Introduction: Broadly neutralizing antibodies (bnAbs) play an important role in HIV-1 prevention and treatment strategies. While antiretroviral therapy (ART) works, it's not curative and causes metabolic complications. Given emerging resistant HIV-1 variants, previous studies suggested that passive administration of bnAb could limit virus reservoirs and prevent viral rebound. In previous studies, we observed that passive immunization of SHIV-infected infant rhesus macaques (RMs) with the triple bnAb combination selected based on its robust neutralizing and non-neutralizing functions, delayed viral rebound. However, antibody levels declined rapidly after a second bnAb administration, suggesting anti-drug antibody (ADA) development.

Objective: Assess ADA development against passively administered bnAbs in a SHIV-infected infant RMs.

Methods: At 4 weeks of age, ten infant RMs orally challenged with SHIV.C.CH505 received subcutaneous triple-bnAb (simianized 3BNC117, PGDM1400, PGT151) at ART initiation (8 weeks post-infection) and before analytical treatment interruption (ATI, 49 weeks post-infection). We measured viral loads and plasma concentration of each bnAb. To assess ADA, F(ab')₂ fragments of each bnAb were digested with IdeZ protease. The fragments were then coupled to magnetic beads. Using a mouse anti-monkey IgG secondary antibody for detection, we tested these beads in plasma samples via a binding antibody multiplex assay. The ADA responses were reported in mean fluorescent intensity (MFI).

Results: ADA responses were undetectable at 8 weeks post-infection but emerged in most animals four weeks after 1st bnAb administration. By week 24 (16 weeks post-first infusion), ADA responses were detected in all animals against PGDM1400, 3BNC117 (n=8/10), and PGT151 (n=9/10). Although ADA declined over time, 33-56% of animals still had ADA at week 49 (second bnAb administration). Four weeks after 2nd administration, ADA responses were present in nearly all animals (PGDM1400:90%, PGT151:90%, 3BNC117:100%). ADA levels 4 weeks after 2nd administration compared to 4 weeks after 1st infusion were similar for PGDM1400 (median 13541 vs 14228 MFI) but differed for 3BNC117 (16621 vs 3423 MFI) and PGT151 (2517 vs 954 MFI). PGDM1400 levels in animals declined rapidly post-second infusion, becoming undetectable in 50% of animals 2 weeks post-infusion. Virus rebound occurred 3-11 weeks post-ATI, associated with low/undetectable bnAbs levels in some animals. Most animals had detectable ADA levels at necropsy (2-14 weeks post-infusion).

Conclusion: Passive triple bnAb administration to SHIV-infected ART-treated infant RMs led to rapid ADA development, boosted after second administration. High ADA levels correlated with rapid bnAb decline and virus rebound, indicating ADA prevention is critical for successful bnAb passive immunotherapy.

The Magnitude and Breadth of SARS-CoV-2 Specific Antibody Responses in Unvaccinated Children with and Without Asthma

Presenting Author: Nicole Soo, Biological Sciences (Research Tech)

Authors: Soo Nicole, Brown Sarah, Vuong Kenneth, Permar Sallie, Nelson Ashley, Pernauld Perdita, Worgall Stefan, Goswami Ria

Department of Pediatrics

Background: 6.5% of children in the US exhibit symptoms of mild to severe asthma. While SARS-CoV-2 vaccines have significantly reduced mortality rates, 5-15% of children, including those with asthma, are still infected with multiple variants each year. While asthma exhibits an impaired respiratory epithelium and a lowered expression of surface ACE2, the key receptor for SARS-CoV-2, the immune response against this virus in asthmatic children remains partially understood.

Objectives: To determine the magnitude and breadth of SARS-CoV-2-specific antibodies in unvaccinated children with and without asthma.

Methods: Plasma was collected from WCM/NYP hospitals from asymptomatic children with (n=131) or without (n=81) asthma between 2020-2022. SARS-CoV-2-specific antibody response was measured against 14 different contemporary circulating variants of concern (VOC), using a binding antibody multiplex assay (BAMA).

Results: Both asthmatic and non-asthmatic children had antibodies against 12 SARS-CoV-2 VOCs (median). Further age-based categorization showed that children with asthma under 5, between 5–10, and over 15 years had antibodies against a median of 5, 9, and 14 VOCs, respectively, while those without asthma in the same age groups had antibodies against 5, 7, and 14 variants. The magnitude of responses was comparable between asthmatic and non-asthmatic children. Finally, 30% of children with asthma and 37% without asthma had detectable antibodies against viral nucleoprotein, indicative of a recent SARS-CoV-2 infection.

Conclusion: While our data demonstrated no differences in magnitude of antibody responses against SARS-CoV-2 VOCs between asthmatic and non-asthmatic children, the quality of immune response and their association with the severity of asthma, age, IgE levels, and other respiratory viral infections warrants further investigation.

Immunization of SHIV-Infected Infant Rhesus Macaques With Germline-Targeting Native-Like HIV-Env SOSIP Immunogens Enhanced Viral Control Post-ART Interruption

Presenting Author: Olusola Omonije, BS (Research Tech)

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Department of Pediatrics

Background: In 2024, 1.4 million children were living with HIV and relying on lifelong antiretroviral therapy (ART). Since ART cannot eliminate HIV, adjunctive therapies are needed. We recently demonstrated development of broadly neutralizing antibody precursor responses in uninfected infant rhesus macaques (RMs) upon immunization with a germline-targeting (GT) native-like HIV SOSIP trimer. The potency of this approach to achieve ART-free viral suppression in infected monkeys remains undefined.

Objective: To determine the impact of GT SOSIP trimer immunization of SHIV-infected infant RMs on viral rebound post-ART interruption (ATI).

Methods: 11 infant RMs were orally challenged with SHIV SF162P3, with ART initiation at 1-week post-infection (pi). 5 RMs were immunized with 4 doses of GT SOSIP immunogen and adjuvant 3M052-SE during ART treatment. 6 RMs remained unimmunized (controls). Treatment with ART was discontinued at week 30 for unimmunized (n=6) and week 47 for SOSIP immunized (n=5) animals. After viral rebound, the diversity of the HIV-env was assessed using single genome amplification in the 5 SOSIP immunized animals.

Results: While there was no difference in time to viral rebound, 1 immunized RM did not experience viral rebound until 18 weeks post-ATI, and 1 achieved plasma viral control 5 weeks post-rebound. Compared to controls, immunized group had a 22.9-fold lower post-rebound peak PVL ($p=0.004$) and 41.3-fold lower post-ATI PVL-AUC0-18 wk ($p=0.009$). Viral rebound was observed in the non-rebounder after anti-FcRn antibody treatment. The rebounding virus demonstrated genetic divergence from the challenge virus along with the development of mutations in the V1V2 regions of the HIV envelope.

Conclusion: Immunization with native like GT HIV envelope trimer could suppress post-ATI viral replication. Whether HIV envelope mutations contributed to viral rebound is currently under assessment.

Circulating Tumor DNA As a Marker of Minimal Residual Disease in High-Risk Neuroblastoma

Presenting Author: Rachel Hughes Rodriguez, MD (Fellow)

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Department of Pediatrics

Background: High-risk neuroblastoma, the most common extracranial solid tumor in children, has a 5-year survival of ~60%, with most relapses occurring within two years post-treatment. Current surveillance methods rely on frequent imaging (e.g., MIBG, CT, PET), which is costly, burdensome, and exposes children to radiation and anesthesia. A sensitive, non-invasive biomarker is urgently needed to detect minimal residual disease (MRD) and allow earlier relapse detection.

Objectives: We aim to validate circulating tumor DNA (ctDNA) as a biomarker of MRD in high-risk neuroblastoma and assess whether ctDNA detection during remission predicts relapse prior to radiographic evidence.

Methods: Cell-free DNA (cfDNA) samples are being prospectively collected every 6–12 months from patients in remission on a clinical trial at Memorial Sloan Kettering. Each patient's primary tumor undergoes whole genome sequencing to identify up to 96 mutations for a personalized panel. These mutations are then queried in cfDNA using SaferSeqS, a highly sensitive duplex sequencing method. Results will be compared to 2-year relapse-free and overall survival.

Results: A 10-patient pilot cohort is undergoing sequencing to validate SaferSeqS in neuroblastoma; results are expected by April 2025 and will be included in the poster presentation. Once validated, tumor and cfDNA sequencing will be completed on the remaining 100 patients. To date, tumor tissue, at least one cfDNA sample, and clinical outcomes have been collected on 110 patients; longitudinal samples are available for 77. Median time to relapse is 4.7 months (median survival not yet reached).

Conclusions: This study may establish ctDNA as a sensitive, non-invasive MRD biomarker in neuroblastoma, transforming surveillance and relapse detection.

Characterization Of HIV-1 Envelope Sequences Isolated From ART-Naïve Infants Living With HIV With Plasma Neutralization Breadth

Presenting Author: Saad Memon (Lab Assistant)

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Department of Pediatrics

Background: A HIV vaccine that induces broadly neutralizing antibodies (bnAbs) is critical for protection against most circulating virus strains. Several studies of adult cohorts have observed an association between the development of bnAbs in plasma and virological factors such as high viral load, duration of infection, and viral diversity. While children living with HIV develop plasma neutralization breadth earlier and more frequently than adults, factors associated with bnAb development in children remain unknown.

Objective: This study aims at assessing the diversity of circulating viruses in two children that developed broad plasma neutralization. We hypothesize that viral diversity contributes to neutralization breadth development in children.

Methods: We utilized archived plasma samples from two ART-naïve children living with HIV at 4 years of age. These children demonstrated broad plasma neutralization within the first 3 years of life against a global HIV-1 panel of 10 pseudo viruses. Single Genome Amplification (SGA) was conducted via nested PCR to amplify the HIV envelope(env) genome, followed by sequencing and analysis using Sequencher. Mutations within the env region were visualized using highlighter plots and phylogenetic trees were generated via the LANL HIV Database.

Results: Child 1 (PTD E0020B1) developed neutralization breadth at age 1 and maintained breadth through years 2-3 whereas Child 2 (PTD S0016B1) developed neutralization breadth at age 2 and displayed increased breadth at age 3. Highlighter plots for both children showed substantial mutations within the viral envelope genome at 4 years of age, and phylogenetic trees from both children revealed two distinct clusters of viral sequences suggesting some sequence evolution. Logo plots for both infants indicate a mix of conserved and variable sites with notable conservation around residues specific to each infant.

Conclusion: We have observed some viral diversity among circulating variants by 4 years of age in two children who developed broad plasma neutralization. Future work will incorporate longitudinal sequencing of circulating viruses to evaluate virus evolution and determine whether mutations are acquired within bnAb-targeting epitopes on the HIV envelope. Overall, the results from this study could offer key implications for the design of HIV immunogens with the goal of eliciting neutralization breadth.

BRAVE: Neutralizing antibody Response of Children and Adults Across SARS-CoV-2 Variants

Presenting Author: Sofia Zamora (Research Tech)

Authors: Zamora Sofia, Williams Caitlin A, Chen Jui Lin, Gao Lulu, Hurst Jillian, Dalapti Trisha, Ramos John, Permar Sallie, Kelly Matt, Fouda Genevieve G.

Department of Pediatrics

Background: The long-term immune responses to SARS-CoV-2 infection and their effectiveness against reinfection and new variants remain unclear. Research shows that children tend to experience less severe illness from SARS-CoV-2 than adults. There is still limited understanding of the strength, quality, longevity, and breadth of antibody responses in children with asymptomatic or mild symptoms. To close this gap in knowledge, Biospecimens from Respiratory Virus-Exposed Kids (BRAVE) were collected and enrolled in a longitudinal study where its overarching goal is to characterize immune responses induced by SARS-CoV-2 infection and vaccination across children and adults.

Objective: One of our aims is to assess whether pediatric participants can mount a robust immune response against recent SARS-CoV-2 variants akin to their adult counterparts. We want to compare antibody neutralization in convalescent or vaccinated pediatric participants and adults. We hypothesize that children generate distinct neutralizing immune responses compared to adults. These characteristics may provide insight for immunization strategies and long-term control of SARS-CoV-2.

Methods: Serum samples were collected from pediatric and adult participants at 1-month, 3-month, and 6-month post-infection or post-vaccination. These samples were screened against SARS-CoV-2 variants Omicron B.1.1.529 and D614G (n=236). We used a luciferase reporter SARS-CoV-2 Spike pseudovirion assay to compare levels of neutralization in adults and pediatric patients at the three different timepoints using inhibitory dilution (ID₅₀).

Results: Neutralization titers between children versus adult participants for Omicron B.1.1.529 and D614G variants showed no significant differences in ID₅₀ (mean, D614G Conv children: 411.0612 vs D614G Conv adults: 1869.4; D614G Vaccinated children: 1108.457 vs. D614G Vaccinated adults: 1664.6; Omicron Conv children: 370.3103 vs. Omicron Conv adults: 2769.875; Omicron vaccinated children: 2865.114 vs. Omicron vaccinated adults: 2783.692). These findings demonstrate that children develop effective neutralization responses comparable to that of adults. Vaccinated children demonstrated higher neutralization titers compared to convalescent children (meanID₅₀ D614G: 1108.5 vs 411.1, meanID₅₀ Omicron 2865.1 vs. 370.3). Testing for 3 month and 6-month post-infection or post-vaccination are currently being screened.

Conclusion: Antibody neutralization titer shows that children and adults can develop antibodies across SARS-CoV-2 variants. Children maintain neutralizing antibody levels similar to adults.

Urinary Tubular Epithelial Cells as Non-Invasive Biomarkers In Pediatric Chronic Kidney Disease: Implications For Iron-Related Nephrotoxicity And Therapy Guidance

Presenting Author: Hannah Federman, PhD (Postdoc)

Authors: Federman Hannah G, Campbell Chantalle, Munera Ana, Elsayed Heba, Lifshitz Tzeela, Freund Avery, Vinchi Francesca, Choi Mary, Akchurin Oleh
Department of Pediatrics

Background: Chronic kidney disease (CKD) affects over 200,000 U.S. children. Disease monitoring currently depends on delayed, imprecise markers like serum creatinine, as kidney biopsy is invasive. Iron supplements, though commonly used, may worsen CKD, but early detection of nephrotoxic effects remains difficult. Tubular epithelial cells (TEC), detectable in urine, offer a potential non-invasive window into kidney health. We hypothesized that systemic iron overload causes tubular injury in pediatric CKD, detectable via urinary TEC.

Objective: Define the effects of CKD and iron therapy on TEC iron status in mice and children using parallel analysis of kidney tissue and urinary TEC.

Methods: We used two mouse CKD models: adenine diet and unilateral ureteral obstruction. Kidney TECs were analyzed by flow cytometry and cell sorting. Urinary cells were collected from mice and children with or without CKD. TECs (CD45⁻AQP1⁺) were assessed for labile iron pool (LIP) using FerroOrange and classified as LIP^{high} or LIP^{low}. RNA-seq and KIM-1 staining were performed on sorted TECs.

Results: ~500,000 urinary cells per 50 mL were recovered, yielding ~1,000–10,000 viable TECs. TECs lose LIP in CKD, suggesting adaptation to chronic injury. Urinary TEC LIP and KIM-1 expression matched kidney tissue. Higher serum iron correlated with increased urinary TEC LIP, especially in advanced CKD. LIP^{high} TECs had elevated KIM-1 and expressed inflammatory, metabolic, and EMT-related transcriptional changes.

Conclusion: Urinary TEC profiling reflects iron-induced injury in CKD and offers a promising non-invasive tool for real-time kidney monitoring in children.

QUALITY IMPROVEMENT/EDUCATION/HEALTH SCIENCES

Milestones Matter: A Quality Improvement Initiative to Promote Early Intervention Completion Rate

Presenting Author: Bing Lin, MD (Resident)

Authors: Lin, Bing MD, Lee, Nancy MD, Osario, Nena S. MD

Department of Pediatrics

Background: Early identification and initiation of services through Early Intervention (EI) are critical for children with developmental delays (DD). However, many referred children are never fully evaluated. National completion rates vary from 33% to 61%, influenced by factors such as age, socio-economic status, and language.

Objective: At a resident-led primary care clinic in Manhattan, NY, we aimed to increase EI evaluation completion rates from 71% to 90% by July 1, 2025.

Methods: This ongoing QI study began in September 2022 using the Model for Improvement. Interventions were tested through four Plan-Do-Study-Act (PDSA) cycles. These included: providing EI info sheets to parents, implementing a referral process flowchart including community health worker (CHW) support, and updating the electronic medical record note template. Measures included DD screening and referral rates, EI evaluation completion, service qualification, and book distribution (balancing). Data were analyzed using SPC “P” charts to detect special cause variation.

Results: Among 1,089 patients, DD screening remained at 95%, with documentation at 96%. Detection of DD was 25%. EI evaluation completion decreased from 82% to 58%. Of those evaluated (n=142), 80% qualified for services. EI referrals for English-speaking families declined from 79% to 29%, while rates for non-English families remained low (7.5%). Book distribution stayed high at 89%.

Conclusion: Our resident-led initiative sustained high DD screening but faced declining EI referral completions. Contributing factors may include demographic shifts and systemic workflow changes. Ongoing data collection is needed to clarify these trends.

QI-01

Quality Improvement (QI) Initiative Nearly Eliminates Neonatal Hypothermia in the Delivery Room (DR) and Very Early Mortality (≤ 24 hours) In the Low-Resource Setting

Presenting Author: Chelsea Hartman, MD (Fellow)

Authors: Hartman, Chelsea, Ngowi, Ester, Shayo, Aisa, Tiwari, Priyanka, Ahn, Emily, Perlman, Jeffrey

Department of Pediatrics

Background: Neonatal hypothermia is a major global problem and has been associated with increased risk of early (≤ 7 days) and very early (≤ 24 hours) mortality, particularly in low-birth-weight infants who have disproportionately high mortality rates in low- and middle-income countries. Strategies that target prevention are critical.

Objective: To decrease the rates of a) hypothermia in the DR to 50% (aggregated (AGG) pre-QI baseline=99%) and b) very early mortality to 3% (AGG pre-QI baseline=4.2%) in infants with birthweight (BW) ≥ 2000 kilograms (Kg) by January 2025 in a large zonal referral hospital in Tanzania.

Methods: This ongoing QI initiative used baseline DR data from 2019-2022; interventions were initiated in November 2023. Interventions included a hypothermia prevention clinical guideline (Fig 1), education, utilization of occlusive wraps, and audit tool introduction. The outcome measures included DR temperature (TEMP), rates of hypothermia, and early and very early mortality. Process and balancing measures included rates of TEMP documentation and incidence of hyperthermia (> 37.5 °C), respectively. Statistical process control charts (P and X-bar/S-charts) and run charts were used to display and analyze data. Associates in Process Improvement rules for special cause were applied.

Results: The demographics of the infants in the baseline group ($n=430$) were similar to post-intervention group ($n=272$) regarding BW ($1551\text{g} \pm 304$ vs $1541\text{g} \pm 326$) and gestational age ($32\text{ weeks} \pm 2$ vs $32\text{ weeks} \pm 3$). Baseline data demonstrated a mean DR temp $35.9 \pm 0.24^\circ\text{C}$ and rate of hypothermia 99% [66% mild ($36.4\text{--}36^\circ\text{C}$), 33% moderate ($32\text{--}35.9^\circ\text{C}$)]. In the first 9 months of implementation, there were center line (CL) shifts in mean DR TEMP from 35.9°C to 36.8°C and rates of hypothermia from 99% to 5.7% (5.7% mild, 0% moderate) (Fig 2). Rates of TEMP documentation have increased from 76% to 98%. Early mortality rates have remained unchanged (CL 12.3%), but very early mortality rates had a CL shift from 5.3% to 0.5% (Fig 3). Rates of hyperthermia remained low (CL 0.6%).

Conclusion: Our QI initiative has practically eliminated hypothermia in the DR in infants $\leq 2000\text{g}$ in a low-resource setting. We hypothesize that this is due to the increased use of occlusive wraps and a significant culture change recognizing the importance of TEMP regulation in this population. The recent elimination in very early mortality (≤ 24 hours) may in part be secondary to hypothermia prevention. However, the unchanged overall early mortality (≤ 7 days) rate is supportive of a multifactorial etiology, which is the subject of ongoing research.

Resident-Led Quality Improvement Project to Enhance Postpartum Depression Screening and Care Referrals for High-Risk Mothers in an Urban Pediatric Primary Care Clinic

Presenting Author: Emily Scharf, DO (Resident)

Authors: Scharf, Emily, DO; Banks, Kelly, MD, PhD; DaVila, Julie, MD; Trimboli, Stephanie, MD; Tam, Matthew, MD; Neway, Beemnet, MD; Piccone, Sarah Allen, MD, MPH, MEd; Piszczatowski, Richard, MD, PhD; Esemenli, Alim, MD; Lee, Joanna, MD; Bruno, Samantha, MD; Lin, Bing, MD; Maniko, Jeffrey, MD; Sathanayagam, Radha, MD; Wirthschafter, Rachel, MPH, MSW; Lee, Diane, PsyD; Abramson, Erika, MD, MS; Green, Cori, MD, MSc; Osorio, S. Nena, MD, MS; Lee, Nancy, MD
Department of Pediatrics

Introduction: Postpartum depression (PPD) is a common obstetric complication, impacting approximately 12% of U.S. mothers, yet remains woefully underdiagnosed and undertreated with only half of cases identified and even fewer receiving services. In 2010, the American Academy of Pediatrics recommended leveraging the frequency of early pediatric visits to screen and intervene for PPD.

Objective: At a Medicaid-based urban pediatric primary care clinic, we performed an observational time-series study aimed at increasing PPD screening rates utilizing the Edinburgh Postpartum Depression Scale (EPDS) and referral rates of EPDS positive mothers to 90%.

Background: In 2022, HealthySteps was introduced into the Weill Cornell Pediatric Primary Care Helmsley Tower 5 (HT5) Clinic in Manhattan, New York. This Quality Improvement project aimed to utilize HS in conjunction with standardization of screening and referral of mothers who screened positive for PPD.

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Methods: Employing serial plan-do-study-act (PDSA) cycles between May 2021 and October 2024, we incorporated an integrated mental health (MH) provider, reinforced EPDS screening with the introduction of standardized documentation within Electronic Health Record (EHR) note templates for multiple visits between 2-weeks and 4-months in a child's life, and streamlined referral workflow within the clinic.

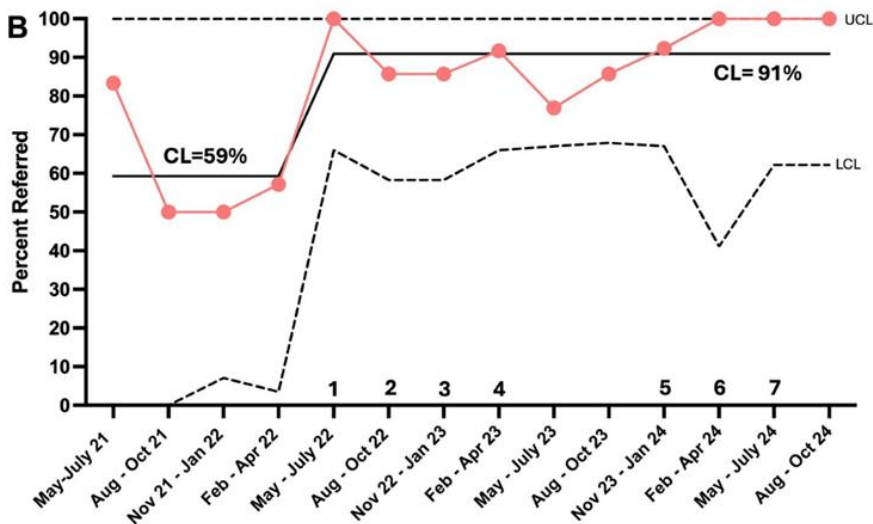
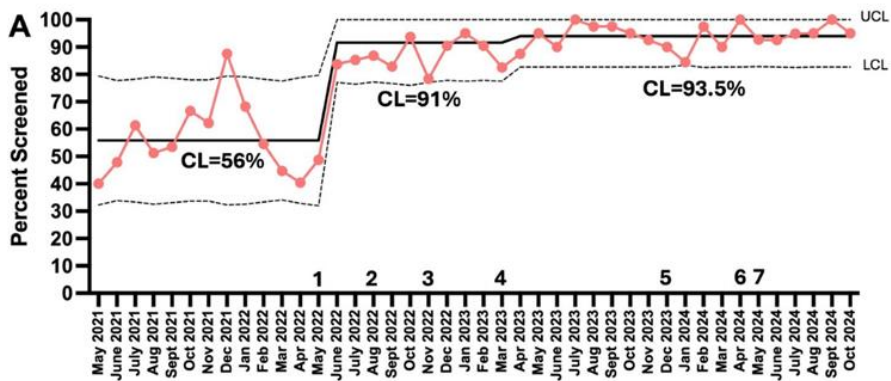
Results: Outcomes show improvement in baseline PPD screening rates from 56% to 94% and referral rates of EPDS positive mothers to care resources from 59% to 90%.

Conclusion: The most successful intervention was incorporating HealthySteps, which showed a significant and sustained increase in screening and referral rates. This emphasizes the importance of collaboration among pediatricians and mental health providers to optimize maternal-infant outcomes.

Table 1. Plan-Do-Study-Act Cycles

Plan Do Study Act Cycles		
1	May 2022	HealthySteps clinical psychologist integrated into clinic
2	Aug 2022	Folder of non-English EPDS made available
3	Nov 2022	Workflow Diagram Created
4	Mar 2023	Note templates with EPDS screening and for EPDS+ Visits
5	Dec 2023	Standardized referral process created for joint follow-up visit with integrated provider
6	Apr 2024	Workflow updated and relaunched
7	May 2024	Training of ancillary staff regarding screening

Figure 1. (A) Percentage of mothers screened for postpartum depression (PPD) via Edinburgh Postpartum Depression Scale (EPDS) at 2-week through 4-month visits, monthly Shewhart P-chart. **(B)** Percentage of Edinburgh Postpartum Depression Scale positive (EPDS+) mothers referred to an integrated mental health provider at 2-week through 4-month visits, quarterly Shewhart P-chart. Integrated mental health provider is defined as HealthySteps behavioral psychologist or social worker. Center line (CL): mean percentage. Dotted lines: Control Limits, UCL is upper control limit, LCL is lower control limit. Annotated with specific PDSA cycles and associated interventions on the X axis corresponding to Table 1.



A Quality Improvement Initiative Reduced Methicillin-Susceptible *Staphylococcus aureus* Infections in a Level IV Neonatal Intensive Care Unit

Presenting Author: Gisel Rivera, MD (Fellow)

Authors: Gisel Rivera MD, Priyanka Tiwari MD, Jean-Marie Cannon, RN BSN, , Kara Mitchell PhD, Vivien Yap MD, Rae-Jean Hemway, Katherine Lim NNP, Lars F. Westblade PhD, Karen P. Acker MD, Liana Senaldi MD

Department of Pediatrics

Background: Methicillin susceptible *Staphylococcus aureus* (MSSA) infections are a growing concern in the neonatal intensive care unit (NICU), accounting for 2.6 times more infections than methicillin resistant *Staphylococcus aureus* (MRSA). These infections are associated with substantial morbidity and mortality including longer hospital stays, neuro-developmental sequelae, and growth impairment. There is limited literature on initiatives to prevent MSSA infections in the NICU. Our NICU saw an increased number of MSSA infections, mainly skin and soft tissue infections (SSTIs), prompting the initiation of this quality improvement (QI) project.

Objective: Our SMART aim was to decrease the total MSSA infections/1000 patient days (PD) from 1/1000 PD in our level IV NICU by 20% by June 2024.

Design/Methods: Our QI team performed interventions over 18 months. Baseline data was retrospectively collected from December 2021 to October 2022. Interventions included implementation of MSSA surveillance and decolonization protocols, whole genome sequencing of MSSA isolates to aid with patient cohorting, bare below the elbows (BBE) practice, and enhanced environmental cleaning processes (Figure 1). Our outcome measure included the rate of total MSSA infections. Process measures included the rate of MSSA colonization and adherence to MSSA decolonization, BBE, and central line bundle protocols. Balancing measures included the number of late onset sepsis (LOS) evaluations and antibiotic usage rate (AUR). Statistical process control charts (U- and P-charts) and established Associates in Process Improvement rules for special cause variation were used to display and analyze data.

Results: There was a 70% reduction in the rate of total MSSA infections (from 1 to 0.3 infections per 1,000 PD) after initiation of our QI project (Figure 2), primarily driven by a reduction in MSSA SSTIs. The MSSA colonization rate remained stable over time at 19% (Figure 3A). Compliance to the MSSA decolonization protocol, BBE initiative, and central line bundle was 97%, 79% and 99%, respectively (Figure 3B-D). The rates of LOS evaluations and AUR did not increase.

Conclusion: An ongoing QI initiative aimed at infection prevention strategies led to a significant decrease in MSSA infections in our level IV NICU, specifically SSTIs. Although rates of MSSA infections decreased, overall MSSA colonization rates did not change over this period highlighting the complex dynamic between colonization and infection and emphasizing that multipronged strategies are necessary to prevent infection in a NICU.

Using QI Methodology to Implement Social Drivers of Health Screening in the Pediatric Inpatient Setting

Presenting Author: Julie Davila, MD (Residents)

Authors: Julie Davila, MD, Nicole Meyers MD, Snezana Osorio MD, MS

Department of Pediatrics

Introduction: Addressing social needs can promote health equity, improve patient care and population health, and reduce healthcare costs. Screening for social drivers of health (SDH) helps identify unmet health needs and allows families access to resources.

Objective: Increase SDH screening in the Pediatric Medical Surgical, Intermediate Care, and Pediatric Intensive Care Units to 90% by June 2025.

Methods: This is an observational time-series study starting 2/2023. Screening was performed by social workers and care coordinators. Interventions were tested via 6 PDSA cycles (Figures 1a and 1b). Screening rate (process), documentation of resources provided (outcome) and reported time needed to screen (balancing) measures were collected via EMR review and dashboard review (process and outcome) and survey (balancing). Run chart and statistical process control “P” charts were used to analyze data. Run chart and API rules were applied to detect signal of change and special cause variation.

Results: Out of 7363 patients, the SDH screening rate was 68 % (n= 4986). The percent of patients who screened positive and received an intervention improved from 73% to 97% (Figure 1a). There was also improvement in identifying patients’ needs from 2.5% to 14% (Fig1b). Most patients were positive for food insecurity (87%). There was no change in reported time needed to screen.

Conclusion: We were able to maintain screening rates and identify the need for resources. Electronic interventions such as the 4-item screening tool and ability to document intervention in EMR were the most successful interventions. Future steps include testing an electronic self-administered screen.

QI-05

Quality Improvement Initiative to Increase Resident Safety Event Reporting in The Pediatric Department

Presenting Author: Matthew Tam, MD (Resident)

Authors: Tam Matthew, Ehret, Caitlin, Abramson Erika, Osorio Nena

Department of Pediatrics

Background: The American Academy of Pediatrics (AAP) has recognized the importance of safety event reporting in minimizing adverse events, near misses, and unsafe conditions. Despite this, resident-submitted events represent a small fraction of total safety events in hospital systems. Studies have demonstrated that key barriers to resident reporting include resident perception of inadequate system change, inadequate feedback, time to submit, and failure to identify the appropriateness of events to report.

Objective: To increase the rate of resident-reported safety concerns from 1.29% to 10% by June 28th, 2025.

Design/Methods: This is an observational study with planned sequential experimentation at a tertiary academic medical center. A resident-led team, which included attending physicians and a patient safety specialist, designed the Key Driver Diagram (Figure 1). Change ideas have been implemented via 4 PDSA cycles including education, monthly meetings, a newsletter, reporting system improvement, shadowing of event reviews, incoming-PGY1 teachings, and lessons learned education (Figure 2). Data was extracted through the campus-wide self-reporting system for all pediatric care locations. The outcome measure was the rate of safety concerns submitted by pediatric residents. The process measures included timely and completed reports defined as reports submitted within 48 hours of an event, with the inclusion of setting, involved parties, and a summarized description. The balancing measure was resident self-reported time required to submit a safety concern. We used statistical process “P” charts to display and analyze data. We applied API rules to detect special cause variation.

Results: In this sample of 94 resident-reported safety concerns, the rate of reporting improved from a baseline of 1.3% to 8.0% (Figure 2). Total of 89 submitted reports were considered timely and fully completed as defined by our process measure definitions. The average self-reported time to submit a safety concern remained stable at 14 minutes (balancing measure).

Conclusion: Enhancing pediatric resident safety concern event reporting requires a multifaceted approach that addresses educational, procedural, and cultural factors. Our interventions have demonstrated special cause variation in the reporting rate of non-anonymous pediatric resident safety event reporting. Future PDSA intervention steps include sharing completed event review content with resident reporters and further enhancement of the reporting tool to facilitate resident event reporting.

Evaluation Of Nutritional Gaps in Breastmilk Delivery for Very Preterm Infants in The Neonatal Intensive Care Unit (NICU)

Presenting Author: Nicole Weitzel (Medical Student)

Authors: Weitzel Nicole C, Liu David, Senaldi Liana, Mandalaywala Divya, Liu Martha, Martin Camilia

Department of Pediatrics

Evaluation of Nutritional Gaps in Breastmilk Delivery for Very Preterm Infants in the Neonatal Intensive Care Unit (NICU)

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Introduction/Background: NICU breastmilk feeding protocols assume standard macronutrient concentrations in human milk, though actual composition varies. The MIRIS Human Milk Analyzer measures exact nutrient content but is resource intensive. Understanding variation between assumed and actual nutrient values, and impact on growth, may support identifying when individualized breastmilk fortification is needed.

Objective: To evaluate whether potential discrepancies between standard and measured nutritional content of breastmilk impact growth and inform the role of personalized milk analysis for very preterm infants.

Methods: Infants <32 weeks gestational age receiving ≥ 20 mL/kg/day of breastmilk at the NYP-ACH NICU were included. Breastmilk aliquots were collected daily, pooled weekly, and analyzed via MIRIS for protein, fat, carbohydrate and caloric content. Donor milk was also analyzed. Actual intake was calculated and compared to assumed intake. Discrepancies were examined against weekly growth velocity and z-scores.

Results: Among 35 infants, average actual energy delivery exceeded assumed values in the first 9 weeks of breastmilk feeds. However, 19-39% received fewer calories than expected in the first four weeks. Only in week 2 was energy discrepancy significantly associated with growth velocity ($p=0.014$). No other significant associations were found between weekly energy discrepancies and growth velocity or z-scores. Among infants receiving fewer calories than assumed, energy differences were not related to growth metrics in any week.

Conclusions: Despite variability in breastmilk composition, energy discrepancies generally favored higher actual intake and had minimal impact on growth. These findings suggest limited utility of routine individualized milk analysis for very preterm infants in our population.

Standardization Of Discharge Instructions for Patients at Risk of Anaphylaxis in The PED

Presenting Author: Samantha Bruno, MD (Resident)

Authors: Bruno, Samantha, Stephen, Alexander; Gerber, Nicole; Samstein, Miriam; Alfonzo, Micheal; Osorio Snezana N

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Introduction: Anaphylaxis and allergies are common in the pediatric ED. Consensus is discharge instructions should consistently include key components, but our ED relied on free-text discharge instructions from individual clinicians, leading to variability. Standardization can improve safety, preparedness, and long-term outcomes for children at risk of recurrent anaphylaxis.

Objective: This study aims to improve the rates of ‘comprehensive’ discharge instructions for anaphylaxis-risk patients from 9% to 75% by March 2025. “Comprehensive” includes an: 1) anaphylaxis action plan, 2) epinephrine prescription, and 3) allergy referral.

Methods: We conducted an observational time series with sequential planned instrumentation in a PED to improve discharge instructions for anaphylaxis. A key driver diagram informed the development of standardized instructions, including the above components. Measures included the percentage of patients discharged with ‘comprehensive’ instructions (outcome), receipt of epinephrine autoinjectors and allergy referrals (process), and 72-hour unanticipated return visits (balancing). Run charts with standard rules were used to analyze trends over time.

Results: Before implementation, 9% of 222 patients received ‘comprehensive’ discharge instructions as described above. Post-intervention, this increased to 25% among 120 patients. A non-random, sustained shift was observed in the process measure, with 8 and 7 consecutive points above the pre-intervention median, indicating improved use of action plans and epinephrine instructions. For our outcome measure, standardized instructions were used in 38% of discharges, likely contributing to this improvement.

Conclusion: A standardized protocol improved discharge instructions in the PED, allowing for more consistent anaphylaxis emergency plans, epinephrine autoinjector prescriptions, and allergy referrals. Future steps include continued staff education and periodic audits to sustain improvements.

Implementation of a Neonatal Pain Clinical Practice Guideline in a Level IV NICU: A Quality Improvement (QI) Initiative

Presenting Author: Ying Ge Wang, MD (Resident)

Authors: Ying Ge Wang, Ilaria Mignatti, Allie Weaver, Samantha Frankenburg, Sara Rostas, Yurhee Lee, Priyanka Tiwari, James Kim

Department of Pediatrics

Background: Neonates in the neonatal intensive care unit (NICU) are frequently exposed to painful stimuli, risking adverse neurodevelopmental outcomes if not adequately treated. The American Academy of Pediatrics (AAP) recommends unit-specific guidelines for assessing and managing neonatal pain. Baseline data from our unit revealed inconsistent pain assessment and management, highlighting the need for a standardized pain guideline.

Objective: We implemented a quality improvement initiative in a level IV NICU to standardize pain assessment and optimize pain management in post-operative neonates. Our SMART AIMS were to 1) improve adherence of pain assessment using Neonatal Pain, Agitation, and Sedation Scale (N-PASS) in post-operative neonates by 50% and 2) reduce the N-PASS scores in the 48 post-operative hours by 10% by the end of June 2024.

Methods: We conducted a 13-month observational, time-series study (May 2023 to June 2024), starting with a baseline period from May to August 2023. A key driver diagram was created (Figure 1) and interventions included creation of a pain management guideline, updates to N-PASS flowsheet in EMR, standardization of nursing and pharmacy education. Outcome measures included post-operative N-PASS scores, and process measures included utilization of N-PASS scale and appropriate post-op acetaminophen orders. Balancing measures included cumulative morphine equivalent dosing (MED) and timing for enteral feeds. Statistical process control charts (p and X-bar/S charts) were used to display and analyze our data. Associates for Process Improvement (API) rules for special cause variation were applied.

Results: Adherence to N-PASS scoring in the first 12 post-operative hours improved from 4% to 58% (Figure 2). Overall N-PASS scores for the first 12 hours post-operatively remained at 1.4, but a trend towards a decrease in scores was observed. In addition, for those surgeries anticipated to cause severe pain, there was a CL change in N-PASS scores from 2.5 to 1.3 (Figure 3). Post-operatively, acetaminophen orders remained at 80% with no CL change. There was no change in cumulative MED and time to enteral feeds.

Conclusion: Implementation of a neonatal pain clinical practice guideline for post-operative patients and EMR changes resulted in significant improvements in adherence of pain assessment using N-PASS scoring and a decrease in mean N-PASS pain scores for surgeries anticipated to cause severe pain. Future efforts will focus on further improving adherence to N-PASS scoring, reducing N-PASS pain scores in post-operative neonates, and implementing pain guidelines for intubated patients.

Standardizing G-Tube Teaching to Pediatric Patients and Their Caregivers

Presenting Author: Alim Esemenli, MD

Authors: Esemenli A, Peluso G, Lee J, Preston MN, McCann TA, Gasser O, Oh S, Osorio S, Rose M

Department of Pediatrics

Background: Caregiver readiness is critical for a safe transition from hospital to home after pediatric gastrostomy tube (GT) placement. Structured, hands-on education enhances caregiver confidence; however, inconsistent discharge processes can lead to variable preparedness, increasing risks of complications and readmissions.

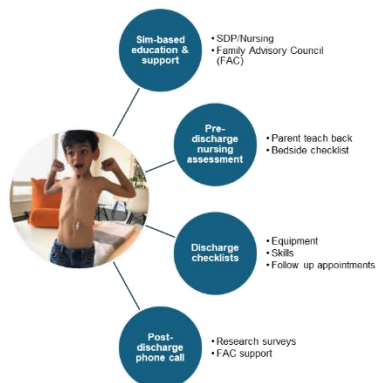
Objectives : This project aims for 80% of caregivers of pediatric patients with new GTs to achieve a perfect score (100%) on the Pediatric Transition Experience Measure (P-TEM), a validated hospital-to-home transition quality measure.

Methods: This multi-site quality improvement initiative is led by an interprofessional team utilizing a GT discharge bundle consisting of discharge checklists, simulation-based caregiver education, pre-discharge nursing skills assessments, and post-discharge follow-up calls. Metrics include P-TEM scores (primary outcome), caregiver comfort and post-discharge challenges (secondary outcomes), bundle adherence (process), and surgical site infection rates within 90 days (balancing). Data is stratified by race, ethnicity, and language for analysis using descriptive statistics and SPC chart tools.

Results: Baseline data (N=11) reveal 18% of caregivers achieved perfect P-TEM scores, with a median of 93%. Median Caregiver Comfort score was 94%. Patient ages range from 2 months to 15 years, with 73% receiving PEG tubes. Average hospitalization duration was 42 days. Among caregivers, 89% were mothers, 22% had prior GT experience, and 36% were non-English speaking. Educational attainment was distributed evenly across high school, college, and advanced degrees.

Conclusions: Standardizing the discharge process through structured education may reduce caregiver uncertainty, anxiety, and complications, fostering improved outcomes for pediatric patients and their caregivers.

Figure 1. Graphic showing the 4 elements in our proposed GT bundle.



The Effect of Simulation-based Training on Confidence and Competence in Obtaining Vital Signs in Children with Autism

Presenting Author: Arianny Martinez-Beltran, MD (Resident)

Authors: Martinez-Beltran Arianny, Lubor Brienne, Voulgaropoulos Leida, Thomas Charlene, Ching Kevin, Cross Jennifer

Department of Pediatrics

Background: Routine interventions like obtaining vital signs can be distressing for children with autism spectrum disorder (ASD), secondary to sensory sensitivities, communication difficulties, and behavioral rigidity, especially when staff lack ASD-specific training. Existing educational interventions have improved provider knowledge and attitudes but often rely on passive methods with limited impact on real-world practice. High-fidelity simulation (HFS), a hands-on training approach, has shown promise in enhancing provider performance in skill-based tasks. This study evaluates the effectiveness of a combined online module and HFS training in improving medical assistants' and nurses' confidence and competence in taking vital signs for children with ASD.

Objective: To evaluate whether an online module combined with simulation training can improve the confidence and competence of medical assistants and nurses in taking vital signs in children with ASD.

Method: This study was conducted in pediatric outpatient clinics at NewYork-Presbyterian/Weill Cornell. Participants completed a 10-minute online module on ASD-specific care strategies, followed by an HFS scenario using a mannequin representing a child with ASD and an actor portraying the parent. Surveys were administered before and after each intervention to assess knowledge, confidence, and perceived competence. Parent/guardian surveys throughout the study assessed prior experiences, satisfaction, and patient distress levels during vital sign collection.

Results: Confidence and competence scores improved significantly after the combined intervention ($p = 0.035$ – 0.036), but not after the online module alone ($p = 0.11$ – 0.12). Knowledge scores improved following the didactic module only ($p = 0.071$). Parent surveys indicated high satisfaction and low child distress.

Conclusion: Combined didactic and simulation training enhanced provider confidence and competence.

How to Prepare Medical Students for Pediatric Residency - Hindsight Advice from Pediatric Interns

Presenting author: Nicole Meyers, MD (Fellow)

Authors: Meyers Nicole, Rustici Matthew, Spector Brooke, Abramson Erika

Department of Pediatrics

Background: The undergraduate medical education (UME) to graduate medical education (GME) transition remains a challenging step along the learner continuum. Within pediatrics, the effectiveness of medical school activities designed to ease this transition remains unclear and little is known about the pediatric intern perspective.

Objectives: 1) To describe new pediatric interns' perspectives on areas they felt least and most prepared for upon starting residency
2) To elucidate the educational interventions interns found or would have found valuable in the transition to residency (TTR)

Methods: From 2/2024-4/2025, we conducted a qualitative study consisting of 1:1 semi-structured interviews with pediatric interns from an academic, tertiary-care medical center. Our interview guide was informed by self-determination theory: a leading theory on human motivation utilized within health professions education emphasizing autonomy, competence, and relatedness. We analyzed transcripts using thematic content analysis.

Results: Sixteen interviews were conducted with interns from 14 medical schools. Four themes were identified: (1) Interns felt most comfortable with medical knowledge and patient presentations, while they struggled with autonomy and counseling families in the outpatient setting; (2) UME experiences e.g., pediatric-specific sub-internships and TTR courses were most valuable; (3) Early GME programming should prioritize distinct skills in order to best prepare interns; (4) A supportive environment allows interns to grow through experiential learning. (Table 1) These themes inform a novel conceptual model (Figure 1).

Conclusions: Our model should guide UME/GME educators in facilitating a smoother transition to pediatric residency through programming in line with intern needs.

Integrating Mental Health Into Pediatric Practice for the School-Aged Child

Presenting Author: Sarah Piccone, MD, MPH, Med (Resident)

Authors: Piccone, Sarah A, Green, Cori, Huttler, A, Sassay, F

Department of Pediatrics

Background: Over 20% of children in the U.S. have a behavioral or mental health condition, yet only 20-25% receive treatment due to under-identification and limited access to services. Pediatricians are well-positioned to routinely screen and address these needs in primary care, but many report feeling inadequately trained. Currently, no standardized curriculum exists for pediatric residents on identifying and delivering brief interventions for mental and behavioral health concerns (MBHCs).

Objective: To design and implement a standardized pilot curriculum for second-year pediatric residents in New York City, focusing on brief interventions using common factors and common elements, with the goal of improving residents' confidence and competence in addressing MBHCs.

Methods: From October 2024 to March 2025, we pilot-tested a simulation-based curriculum at one pediatric residency program. Participation rates and pre- and post-intervention surveys measured feasibility, acceptability, appropriateness, and changes in residents' confidence.

Results: Four residents completed the curriculum. Following participation, residents demonstrated significant improvement in confidence when screening for risk factors using the PSC-17 ($p < 0.0001$) and applying both common factors and common elements approaches ($p < 0.0015$ for both). These findings support the potential effectiveness of targeted training in increasing pediatricians' preparedness to manage MBHCs.

Conclusion: A standardized simulation-based curriculum improved pediatric residents' confidence in addressing MBHCs. With new ACGME requirements emphasizing mental health training, this curriculum offers a promising tool for enhancing resident education and improving outcomes for children in primary care settings.

Evaluating Equitable Access and Referral Rates to Mental Health Services in Pediatric Subspecialty Clinics: A Comparative Study of Medicaid and Commercial Insurance

Presenting Author: Jimenez, Luz, MS3 (Medical Student)

Authors: Jimenez L, Green CM, Huttler A, Jagpal A, Rajan M, Catarozoli C

Weill Cornell Medical School

Introduction: Pediatric mental health disorders are rising and patients with chronic medical conditions are disproportionately at risk. Integrated mental health care improves access to care especially for historically marginalized populations. The Weill Cornell Pediatric Behavioral Health Integration and Innovation Program integrates mental health care into pediatric subspecialty practices.

Methods: This is a retrospective study using data from the Research Data Repository for Pediatric Behavioral Health of patients aged 0–21 referred by a pediatric subspecialist from October 2023 to September 2024. Patient characteristics include insurance, age, race/ethnicity, language, and sex. The outcome variable (completion of referral) was defined by at least one visit with a mental health provider within 90 days of referral. Analyses including descriptive statistics and regression models will examine associations between access to care, COI, and patient characteristics.

Results: The final cohort includes 593 patients - 405 with commercial insurance and 188 with Medicaid, reflecting the 28% baseline Medicaid rate in subspecialty care. Referral completion was higher in patients on Medicaid (65.4%) compared to those on commercial insurance (57.0%). Caucasian patients made up the majority of commercial referrals (45.7%) and Hispanic/Latino patients made up the majority of Medicaid referrals (31.9%). Access rates were lowest in African American patients in both the Medicaid and commercial insurance groups.

Conclusion: These data suggest integrated care is a promising way for marginalized patients to access to mental health care. Next steps include regression analyses, which are under way. This study may inform future policy efforts to sustain integrated models of care.

Variation in State-Mandated Insurance Coverage for Fertility Care

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Background: Fertility services, including infertility diagnosis and treatment, and fertility preservation, are often considered elective and not covered by health insurance plans. Some states have mandated health plans to provide coverage for fertility services. This project aims to describe the status of state mandates using a legal epidemiologic framework.

Methods: A 50-state survey was performed to evaluate and compare current mandates surrounding infertility diagnosis, treatment, and in-vitro fertilization, as well as fertility preservation for iatrogenic infertility or those individuals at risk of losing their fertility due to medically necessary treatments.

Results: In total, 23 states were found to have mandates related to fertility insurance coverage. Nineteen states required coverage for infertility diagnosis and treatment, while 16 required coverage for fertility preservation. Only two states, Montana and Utah, mandate that Medicaid cover fertility preservation services for patients with cancer.

Conclusion: Overall, state mandates for fertility services vary significantly regarding the types of plans covered, eligibility criteria, and minimum coverage.

